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COGNITIVE-AFFECTIVE CORRELATES OF PEDIATRIC FOOD INTAKE: NEURAL FOOD CUE REACTIVITY AND REWARD-RELATED DECISION-MAKING

A Dissertation in

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by

Bari Allison Fuchs

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The dissertation of Bari Allison Fuchs was reviewed and approved by the following:

Kathleen L. Keller
Professor, Department of Nutritional Sciences & Department of Food Science
Dissertation Advisor
Chair of Committee

Karolina P. Skibicka
Associate Professor, Department of Nutritional Sciences

Jennifer Savage-Williams
Associate Professor, Department of Nutritional Sciences

Stephen J. Wilson
Professor, Department of Psychology

Frank G. Hillary
Professor, Department of Psychology

Meg Bruening
Professor and Department Head, Department of Nutritional Sciences

Abstract

Between 2017 and 2020, over 20% of children in the United States had obesity. As diet and behavioral interventions to treat and prevent obesity are ineffective or produce small and variable effects, a better understanding of the factors that facilitate increased energy intake is needed. Theoretical models posit that psychological, physiological, and neural responses to food cues (i.e., food cue reactivity) and reward-related decision-making (RRDM) promote overeating and susceptibility to obesity in the present-day food environment. These theories are supported by research showing behavioral and neural responses to food cues are associated with eating behaviors and weight gain, and reward learning, executive functioning, and decision-making are altered in obesity. Nevertheless, it remains unclear how food cue reactivity and RRDM relate to pediatric eating behaviors. Therefore, this dissertation examined how neural responses to food cues (chapters 2 and 3) and decision-making processes (chapter 4) relate to laboratory-assessed food intake in children.

To shed light on the mechanisms that increase intake in response to large portions of food (i.e., the portion size effect; PSE), chapter 2 examined neural responses to food and non-food (office supplies) images presented in larger and smaller (i.e., age-appropriate) amounts. On average, neural responses to amount (larger vs. smaller) were stronger but less extensive in visual processing areas for foods relative to office supplies. Neural responses to food energy density (kcal/g; higher vs. lower) differed in extent between larger and smaller amounts in regions implicated in value-based decision-making (orbitofrontal cortex, ventromedial prefrontal cortex). These results highlight potentially distinct neural pathways for encoding food energy content and quantity.

To build on chapter 2, chapter 3 examined how neural responses to food portion size cues relate to children's susceptibility to the PSE. To do so, neural responses to food amount (larger vs. smaller) were regressed on individual-level linear and quadratic relationships between intake and portion size, estimated from children's intake data at four meals that varied in portion size. Relationships were examined within the appetitive network and cerebellum to extend prior work examining these associations in reward- and control-related brain regions. Response to food amount in cerebellar lobules IV-VI was negatively associated with the quadratic portion size slope; greater activation to larger portions was associated with smaller increases or larger decreases in intake as portions got larger, while greater activation to smaller portions was associated with greater increases in intake as portions got larger. Neural responses within the appetitive network were not associated with linear or quadratic portion size slopes. These results suggest decreased cerebellar activation in response larger amounts of food may increase children's susceptibility to overeating when faced with "supersized" portions of food.

While chapters 2 and 3 shed light on the neural correlates of the PSE, they did not elucidate specific cognitive or affective processes that drive eating behaviors. Therefore, chapter 4 examined the relationships between decision-making processes and food intake in children. Decision-making was assessed with a task where children make selections with unknown reward outcomes, and decision-making processes were quantified with a reinforcement learning model. Food intake was measured with three paradigms: (1) a standard *ad libitum* meal, (2) an eating in the absence of hunger (EAH) protocol, and (3) a palatable buffet meal. Decision-making processes that influence the tendency to repeatedly make the same choice (i.e., perseverate) were associated with energy intake: (1) increases in the tendency to perseverate after a gain were positively associated with intake at all three paradigms and indirectly associated with higher

weight status through standard and buffet meal intake, and (2) increases in the tendency to perseverate after a loss were positively associated with EAH, but only in children whose tendency to perseverate persisted across trials. These results suggest that children who are more likely to repeat a behavior after a reward have a tendency to eat more at laboratory meals. If this generalizes to contexts outside the laboratory, these children may be susceptible to obesity.

Together, these chapters sheds light on how stimulus-driven (Pavlovian, operant) and goal-directed decision-making systems relate to food intake and the development of obesity: (1) chapter 2 suggests that brain regions implicated in valuation and goal-directed decision-making differentially process food cues based on energy density and portion size, (2) chapter 3 suggests that a brain region implicated in the modulation of stimulus-driven and goal-directed signals influences susceptibility to the portion size effect, and (3) chapter 4 suggests that operant conditioning increases food intake and can contribute to the development of pediatric obesity. These findings may help identify children who are at risk for overeating, but future research is needed to assess whether results generalize to more diverse samples. For insight into causal relationships between cognitive-affective processes and food intake, experimental and longitudinal studies are needed.

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List of abbreviations

Abbreviation	Definition
ACC	Anterior cingulate cortex
AFNI	Analysis of Functional Neuroimages
BMI	Body mass index
CEBQ	Children's Eating Behavior Questionnaire
dlPFC	Dorsolateral prefrontal cortex
EAH	Eating in the absence of hunger
ED	Energy density
FEIS	Fixed-effects individual slopes
fMRI	Functional magnetic resonance imaging
g	Grams
GLM	General linear model
kcal	Kilocalories
NTS	Nucleus tractus solitarius
OFC	Orbitofrontal cortex
OSF	Open Science Framework
PFC	Prefrontal cortex
PSE	Portion size effect
RRDM	Reward-related decision-making
V1	Primary visual cortex
vmPFC	Ventromedial prefrontal cortex

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Chapter 1 General Introduction

1. Pediatric obesity

Between 2017 and 2020, over 20% of children in the United States had obesity (i.e., body mass index (BMI)-for-age percentile ≥ 95th based on Center for Disease Control and Prevention growth charts) [1]. Pediatric obesity is associated with negative physical and psychosocial health outcomes [2] including cardiovascular and metabolic risk [3,4] and depression [5,6]. Relative to peers with health weight, a child with obesity is 5 times more likely to have obesity in adulthood [7] and is estimated to incur an additional $19,000 of lifetime medical costs [8]. Diet and behavioral interventions to treat and prevent obesity are ineffective or produce small and variable effects that are not sustained [9,10]. Pharmacological approaches (e.g., semaglutide) appear safe and effective for reducing BMI and cardiometabolic risk factors in adolescents with obesity [11], but they are expensive and inaccessible [12] and may not be appropriate for long-term use or tolerated (e.g., due to gastrointestinal distress) in younger children. As obesity is caused by a sustained positive energy balance (i.e., greater energy consumption than expenditure) [13], a better understanding of the factors that facilitate increased energy intake may improve and expand pediatric obesity prevention and treatment approaches.

2. Neural control of food intake

The neural system underlying feeding behavior evolved over the past 2 million years to "seek out and eat as many nutritionally high-dense foods as possible" [14]. This system integrates metabolic, sensory, hedonic, and cognitive information to drive food-related decisions (Figure 1.1). Metabolic information, such as the availability of nutrients in the gastrointestinal system, blood, and adipose tissue, is primarily processed by the hindbrain and hypothalamus [15] and is transmitted from the gut and periphery to the brain via nerve impulses and hormones. For example, vagal afferent fibers innervate the gastrointestinal tract, detect the presence of food and

gastrointestinal hormones (e.g., leptin, ghrelin), and convey this nutritional information to the nucleus tractus solitarius (NTS) in the brainstem [15,16]. The NTS relays this information to a variety of brain regions including the hypothalamus, striatum, and hippocampus [16]. The hypothalamus also directly senses nutrients and metabolic hormones in the bloodstream [17–19].

Interacting with the hindbrain and hypothalamus is the cortico-limbic system, which includes prefrontal cortex (PFC), cingulate cortex, basal ganglia, amygdala, and hippocampus (Figure 1.1A) [15]. The cortico-limbic system supports cognitive-affective processes (e.g., reward, memory, and executive control) that underlie the generation of neural food representations (Figure 1.1B) [15]. Exteroceptive (e.g., visual, olfactory) information is relayed via the thalamus and other brain regions to the orbitofrontal cortex (OFC), which forms representations of food through interactions with hippocampus, amygdala, PFC, and insula [15,17]. The hippocampus encodes episodic memories of food and associations between external food cues and post-ingestive consequences [20], while the amygdala forms conditioned responses that underlie cue-potentiated feeding through interactions with the lateral hypothalamus and medial PFC [21,22]. The insula encodes and integrates gustatory, olfactory, and interoceptive representations [23–25].

In addition to generating representations of food, the cortico-limbic system supports reward-related decision-making (RRDM; Figure 1.1B). During RRDM, stimulus-driven (Pavlovian, operant/instrumental) and goal-directed signals are integrated to influence behaviors towards rewards (e.g., food) [26,27]; during stimulus-driven processes, sensory information or environmental cues trigger associations based on past experiences, whereas during goal-directed processes, there is an evaluation of anticipated outcomes along with goals and intentions [28]. The striatum, a component of the basal ganglia innervated by the ventral tegmental area, supports

both stimulus-driven and goal-directed signals [29,30]. It has been suggested that, within the dorsal striatum, the putamen generates stimulus-response associations (operant conditioning/habits) and the caudate stores response-outcome associations integral to goal-directed behavior [29]. Within the ventral striatum, the nucleus accumbens generates stimulus-outcome associations (Pavlovian conditioning) [29], which support the attribution of incentive salience or "wanting" to predictive reward cues [31]. The PFC and anterior cingulate cortex are implicated in the goal-directed processes of generating action-value representations across different aspects of decisions (e.g., reward representations, effort, uncertainty) [32,33] and comparing action-value signals across options [34].

Metabolic information influences cognitive-affective processes either directly or indirectly via projections from the hypothalamus. For example, lateral hypothalamic signals of hunger and satiety modulate activity in meso-cortico-limbic regions (e.g., ventral striatum) that generate incentive salience, resulting in enhanced or suppressed motivation to eat based on physiological state [31].

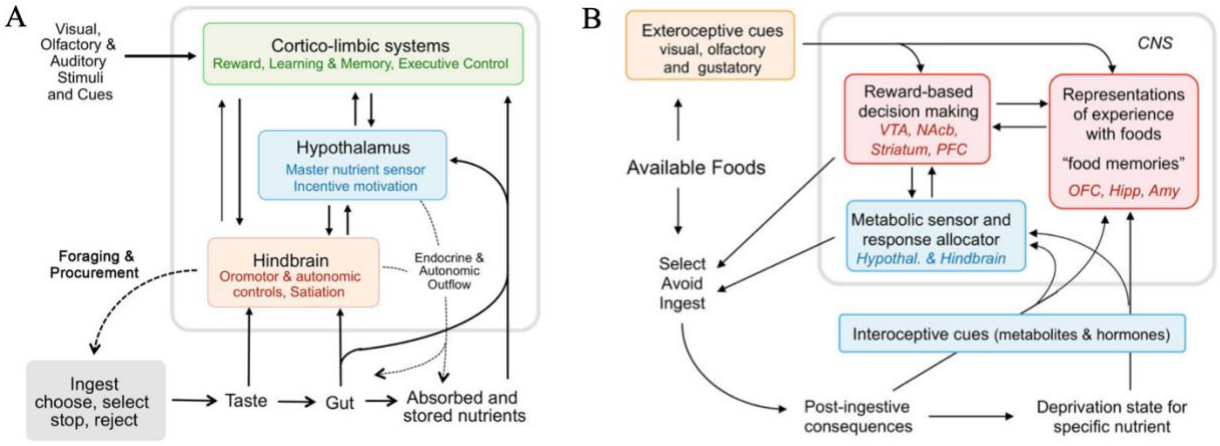

Figure 1.1 Neural control of food intake. Image have been re-used from Berthound et al., [15] with permission from Publisher. (A) Interactions between hindbrain, hypothalamus, and cortico-

limbic systems integrate metabolic information (e.g., absorbed nutrients) and exteroceptive information (e.g., visual cues) to drive the initiation and cessation of food intake. (B) Exteroceptive and interoceptive cues influence the generation of food representations and reward-based decisions by the cortico-limbic system to drive the selection and intake of food. VTA: ventral tegmental area; NAcb: nucelus accumbens; PFC: prefrontal cortex; OFC: orbitofrontal cortex; Hipp: hippocampus; Amy: amygdala

3. Susceptibility to the present-day food environment

The present-day food environment is characterized by increased access to large portions of energy-dense, palatable foods and heighted exposure to cues signaling the availability of foods (e.g., advertisements) [35,36]. These characteristics can increase energy intake [37–39], supporting the idea that the current food environment is "obesogenic" [40]. Nevertheless, ~80% of children do not have obesity [1], suggesting differences in susceptibility to the present-day food environment.

Theoretical models posit that psychological, physiological, and neural responses to food cues (i.e., food cue reactivity) and RRDM promote overeating and susceptibility to obesity in the present-day food environment. For example, the Behavioral Susceptibility Theory (BST) suggests genes that increase responsiveness to external food cues will make an individual more likely to overeat in an obesogenic environment [41]. An extension of the BST posits that food responsiveness is strengthened through Pavlovian and operant conditioning [42]. Similarly, a model of binge eating posits that conditioned responses to cues that reliably signal food intake increase the likelihood of excessive food intake [43]. Incorporating both stimulus-driven and goal-directed processes, a neuroeconomic model of decision-making posits that excess energy intake can results from Pavlovian, operant, and/or goal-directed signals [44]. For example,

heighted stimulus-driven processes that promote cue-potentiated intake alongside limited goal-directed processes that support cognitive regulation could result in overconsumption. Overall, these models suggest that food cue reactivity and RRDM contribute to the development of obesity by increasing energy intake (Figure 1.2A).

In general, the aforementioned theories are supported by empirical research showing behavioral and neural responses to food cues are associated with eating behaviors and weight gain [45], and reward learning, executive functioning, and decision-making are altered in obesity [46,47]. Nevertheless, it remains unclear how food cue reactivity and RRDM relate to pediatric eating behaviors. Therefore, this dissertation will examine how neural responses to food cues and decision-making processes relate to laboratory-assessed food intake in children.

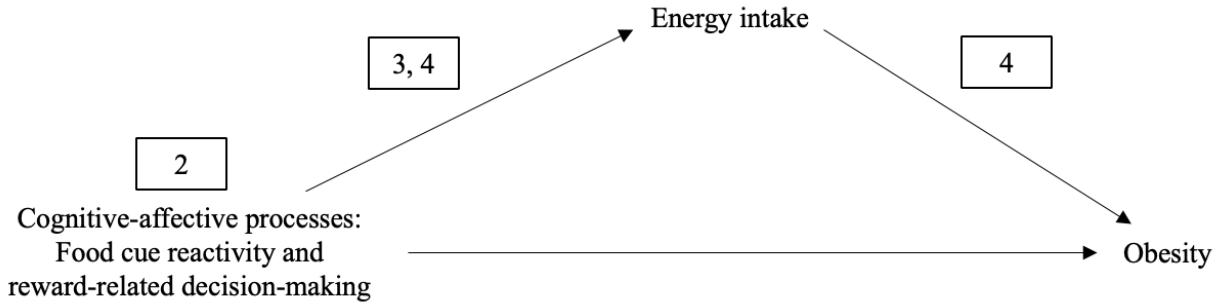

Figure 1.2 Theoretical model. Cognitive-affective processes (food cue reactivity and reward-related decision-making) contribute to the development of obesity by increasing energy intake. Numbers in squares correspond to dissertation chapters. In the domain of food cue reactivity, chapter 2 will characterize neural responses to portion size cues, and chapter 3 will examine the association between neural responses to portion size cues and patterns of intake across four meals varying in portion size. In the domain of reward-related decision-making (RRDM), chapter 4 will examine how decision-making processes during a RRDM task relate to child

weight status through intake at three eating paradigms: a standard meal, eating in the absence of hunger, and a palatable buffet.

4. Neural food cue reactivity

Food cue reactivity can be assessed through self-report, physiological recording (e.g., heart rate), and neuroimaging. However, neuroimaging can explain variance in eating behaviors above and beyond other approaches [48]. One non-invasive approach to studying neural food cue reactivity is to present food-related stimuli (e.g., images, odors) to individuals during functional magnetic resonance imaging (fMRI) and measure blood oxygen level-dependent (BOLD) signals. The fMRI BOLD signal is an indirect measure of neuronal activity, as it is a correlate of the hemodynamic response that results from neurovascular coupling, which is triggered by inhibitory and excitatory neuronal activity [49]. By contrasting BOLD signals elicited by different stimuli (e.g., food vs. non-food), fMRI can be used to identify brain regions that activate in response to food cues and food characteristics.

fMRI studies in children and adolescents show that food cues (vs. non-food cues) elicit greater activation in regions associated with reward and salience (e.g., striatum, OFC, amygdala), nutrient regulation (e.g., hypothalamus), the integration of cognitive, reward, and sensory information (e.g., insula), memory (e.g., hippocampus), response inhibition (e.g., inferior frontal gyrus) and visual processing (e.g., fusiform, occipital cortex) [50,51]. Further, neural responses to food cues are modulated by food characteristics, such as energy content and portion size. In 7-10-year-olds, foods higher (vs. lower) in energy density (ED; kcal/gram) elicited greater activation in fusiform, insula, superior temporal gyrus, caudate, parahippocampal gyrus, posterior and anterior cingulate, cerebellum, and precentral gyrus [52], while in older children and adolescents (10-17y), “unhealthy” (vs. “healthy”) food cues elicited greater activation in

temporal/occipital gyri, inferior frontal gyrus, precentral gyrus, hippocampus, middle frontal gyrus and dorsolateral PFC [53]. In children, large (vs. small) portions of food elicited greater activation in inferior frontal gyrus/OFC [52] and lingual gyrus [54]. As the neural response to portion size has only been examined in one participant sample and has implications for understanding intake in response to large portions, chapter 2 of this dissertation aims to further characterize neural portion size reactivity.

Neural responses to food cues have been associated with food intake in children and adolescents across a variety of food-cue paradigms and eating behavior measurements; see Table 1-1 for a summary of associations and proposed functions by brain region. In adolescents, neural responses to fast food commercials were related to meal intake in a simulated fast food environment [55,56]. Responses to "unhealthy" fast food commercials vs. nonfood commercials in nucleus accumbens and caudate nucleus were positively associated with total food intake, whereas responses to "healthier" fast food commercials vs. nonfood commercials in nucleus accumbens, hippocampus, and anterior cerebellum were positively associated with total food and "unhealthier" food intake, but not "healthier" food intake. Further, responses to "unhealthy" vs. "healthier" fast food commercials in precuneus was negatively associated with "healthier" food intake [55]. Additional support that neural responses to marketing-related cues relate to food intake comes from research in children showing responses to images of food brands and non-food brands vs. control images in fusiform were negatively associated with energy intake at a branded meal vs. unbranded meal [57].

Additional research in adolescents suggests neural responses to food images are related to food responsiveness and caloric compensation [58]. When adolescents were in a fasted state, responses to high- vs. low-ED food images in insula, rolandic operculum and putamen were

positively associated with parent-reported food responsiveness. In contrast, the difference between fed and fasted responses to food vs. non-food images in thalamus and supramarginal gyrus were positively associated with caloric compensation [58].

In children, neural responses to cues signaling the potential to win and the receipt of food rewards were related to standard meal intake, buffet intake, and snack intake following a standard meal (eating in the absence of hunger; EAH) [59]. Responses to cues signaling the potential to win food vs. money in medial PFC were positively associated with standard and buffet meal intake, whereas responses to receipt of food vs. money rewards in dorsolateral PFC and amygdala were positively associated with buffet meal intake and EAH, or just buffet meal intake, respectively [59]. Children's hippocampal responses to the taste of sucrose or water solution were also positively associated with EAH, as well as parent-reported child food responsiveness and enjoyment of food [60].

Further, children's neural responses to depictions of food amount (i.e., portion size) related to changes in intake across meals varying in portion size [61]. Greater responses to larger vs. smaller amounts of food (across high- and low-ED foods) in ventromedial PFC and OFC related to more negative quadratic associations between portion size and total meal intake. Similarly, greater responses to larger vs. smaller amounts of high-ED foods in caudate and OFC related to more negative quadratic associations between portion size and high-ED food intake. In contrast, reduced responses to larger vs. smaller amounts of high-ED foods in inferior frontal gyrus related to more negative quadratic associations between portion size and intake [61].

In general, these studies suggest neural food cue reactivity relates to eating behaviors or food intake in youth, although the brain regions demonstrating associations with eating behaviors

differ across methodologies. Chapter 3 of this dissertation aims to increase our understanding of how neural portion size reactivity relates to intake across meals varying in portion size.

5. Reward-related decision-making

RRDM can be probed using tasks that require an individual to make decisions for rewards in the face of uncertainty or risk (e.g., Iowa Gambling Task; IGT [62]). Decision-making behavior during these tasks can be summarized using metrics that reflect overall performance, while affective and cognitive processes that guide decisions can be estimated using computational (mathematical) models of reinforcement and cognition [63,64]. Affective and cognitive processes that guide reward-related decisions (e.g., food reinforcement) can also be assessed with more targeted approaches (e.g., reinforcing value of food task).

Performance during a RRDM task as been associated with the development of eating behaviors in elementary-school children [65]. During the task, children had to choose from options with different reward and punishment probabilities, and performance was quantified by number of "advantageous" vs. "disadvantageous" choices. In girls, fewer advantageous choices was associated with greater 1-year increases in a food approach behavior (restrained eating) and, contrary to hypotheses, two food avoidance behaviors (slowness in eating, and satiety responsiveness) [65]. In boys, fewer advantageous choices was associated with greater 1-year increases in a different food approach behavior (food responsiveness) [65].

While decision-making processes during the IGT (estimated with cognitive models) have been associated with eating disorders [66,67] and weight-management in adults [68,69], to my knowledge, their associations with non-clinical eating behaviors or food intake have not been evaluated. However, two processes underlying food-related decisions have been elucidated through measures of food reinforcement and food sensitivity. The reinforcing value of food

refers to how capable food is at eliciting a behavior and reflects how motivating food is [65]; it can be quantified by how many responses (e.g., button clicks) an individual makes to obtain food (the reinforcer) in a behavioral choice task [70] or using a questionnaire [71,72]. Reward sensitivity reflects an individual's general tendency to approach rewards and can be assessed using questionnaires (e.g., Sensitivity to Reward Scale [73], Behavioral Approach Scale [74]).

Research suggests that reinforcing values of specific foods are associated with energy intake of that food. In adults, the reinforcing value of preferred snack foods was positively associated with energy intake during *ad libitum* eating tasks where a variety of palatable snacks (including the preferred snack) were presented [75,76]. In preschool children (3-5 years), the reinforcing value of graham crackers was associated with graham cracker intake in an *ad libitum* snack task [77]. In contrast, in older children (8-10 years) the relative reinforcing value of a preferred snack vs. a preferred activity was not associated with intake at meals, which did not include the preferred snack [36]. While reward sensitivity is consistently associated with eating behaviors according to a meta-analysis [78], few studies have assessed associations with objective food intake. In adults exposed to appetitive food advertisements, reward sensitivity was indirectly associated with food consumption at a bogus taste test via urge to eat [79]. In children, reward sensitivity was positively associated with parent-reported child fast-food consumption frequency [80], particularly when children had greater access to "unhealthy, palatable snacks" at home [81].

Processes akin to reinforcement and reward sensitivity, amongst other affective and cognitive processes, can be estimated using RRDM tasks. There are several benefits to using this approach over targeted assessments. First, by incorporating risk or uncertainty into the paradigm, RRDM tasks can better reflect the complexity of decision-making in the real-world. Thus,

cognitive-affective processes engaged during RRDM tasks may be more similar to those engaged during decisions outside the laboratory. Second, RRDM tasks require the interaction between multiple affective and cognitive processes. By estimating these processes from the same behavioral dataset, it is possible to conduct a more comprehensive examination of decision-making processes and their interactions. Third, compared to questionnaires, RRDM tasks enable a more objective assessment of cognitive-affective processes. Therefore, chapter 4 of this dissertation will examine the associations between affective and cognitive processes during a RRDM task and energy intake at three laboratory eating paradigms. In addition, it will examine whether decision-making processes are indirectly associated with child weight status through energy intake.

6. Dissertation aims

This dissertation will examine how food cue reactivity (chapters 2 and 3) and RRDM (chapter 4) relate to pediatric eating behaviors. Aims of each chapter are listed below, while hypotheses are described within each chapter.

Chapter 2: Does 'portion size' matter? Neural responses to food and non-food cues presented in varying amounts

- Aim 1: Compare neural responses to amount between food and non-food images
- Aim 2: Compare neural responses to amount between images of foods higher and lower in energy density (kcal/g)
- Exploratory: Compare neural responses to energy density and food amount in children without obesity who varied by familial risk for obesity

Chapter 3: Cerebellar response to visual portion size cues is associated with the portion size effect in children

- Aim 1: Assess the associations between patterns of intake across four meals varying in portion size and neural responses to larger vs. smaller amounts of food (i.e., portion size reactivity) within midbrain, subcortical, and cortical brain regions involved in the control of food intake (i.e., 'the appetitive network')
- Aim 2: Assess the associations between patterns of intake across four meals varying in portion size and portion size reactivity in cerebellum

Chapter 4: Decision-making processes related to perseveration are indirectly associated with weight status in children through laboratory-assessed energy intake

- Aim 1: Assess the associations between decision-making processes and children's energy intake at three laboratory eating paradigms
- Aim 2: Assess the indirect associations between decision-making processes and weight status through energy intake

Table 1-1. Brain regions associated with eating behaviors in fMRI studies in youth (children, adolescents)

Table 1. Brain regions associated with eating behaviors in fMRI studies in youth (children, adolescents)

Region	Proposed Function(s)	Response to food cues	Associations with eating behaviors
Cerebellum	Modulation of motivational processes [82]; hedonic satiation [83]; motor control of eating, hunger/satiety processing, cue processing, meal anticipation [84]; optimization of goal-directed action [82] 2/21/2024 6:21:00 PM	High-ED > low-ED food images [52]	Response to "healthier" fast food commercials vs. nonfood commercials was positively associated with total food and "unhealthier" food intake [85] Fasted response to high- vs. low-ED food images was positively associated with parent-reported enjoyment of eating [58] Response to high- vs. low-ED food images was negatively associated with parent-reported food responsiveness [52]
Nucleus accumbens	Pavlovian (stimulus-outcome) conditioning, PIT [21]; generation of incentive salience or "wanting" [86]	Food > non-food images [50]	Response to "unhealthy" fast food commercials vs. nonfood was positively associated with total food intake in adolescents [85] Response to "healthier" fast food commercials vs. nonfood commercials was positively associated with total food and "unhealthier" food intake [85]
Hippocampus	Episodic meal-related memories, conditional associative learning between food cues and post-ingestive consequences [20]	Food > non-food images [50] Unhealthy > healthy food images [53]	Response to "healthier" fast food commercials vs. nonfood commercials was positively associated with total food and "unhealthier" food intake [85] Response to taste of sucrose or water solution was positively associated with EAH [60]
Putamen	Operant (stimulus-response) conditioning [29]	Food > non-food images [50]	Fasted response to high- vs. low-ED food images was positively associated with parent-reported food responsiveness [58]
Caudate	Goal-directed (response-outcome) conditioning [29]	High-ED > low-ED food images [52]	Response to "unhealthy" fast food commercials vs. nonfood was positively associated with total food intake [85] Greater response to larger vs. smaller amounts of high-ED food related to more negative quadratic associations between portion size and high-ED food intake [61]
Amygdala	Cue-potentiated feeding, PIT [21]; encoding expected reward value and establishing reward representations [87,88]	Food > non-food images [50,51]	Response to winning food vs. money was positively associated buffet meal intake [59]
Fusiform	Object recognition and representation [89]	High-ED > low-ED food images [52]	Responses to food and non-food brands vs. control images were negatively associated with energy intake at branded meal vs. unbranded meal [57]
Insula	Processing and integration of gustatory, olfactory,	Food > non-food images [50,51]	Fasted responses to high- vs. low-ED food images was positively associated with parent-reported food responsiveness [58]

	interoceptive, affective, and cognitive stimuli [24]	High-ED > low-ED food images [52]	Response to high- vs. low-ED food images was negatively associated with parent-reported enjoyment of food [52]
Rolandic operculum	Processing integrated exteroceptive–interoceptive signals, self-consciousness-related processes [90,91]		Fasted responses to high- vs. low-ED food images was positively associated with parent-reported food responsiveness [58]
Precuneus	Supporting integrated tasks including episodic memory retrieval and self-centered mental imagery [92]		Response to "unhealthy" vs. "healthier" fast food commercials was negatively associated with "healthier" food intake [85]
Ventromedial PFC	Assigning overall subjective value during decision-making; integration of value signals across food-related attributes (e.g., taste, health) [93]		Response to larger vs. smaller amounts of food was associated with more negative quadratic portion size effect [61]
Medial PFC	Mediates the capacity of context in cue-potentiated feeding [21]; modulation of reward-seeking behavior [94]2/21/2024 6:21:00 PM	Food > non-food [50]	Response to anticipating food vs. money was positively associated with standard meal and buffet meal intake [59]
Dorsolateral PFC	Value-based evidence accumulation during self-control contexts [95]; Goal-directed modulation of vmPFC value signals during decision-making [96]	Unhealthy > healthy food images [53]	Response to winning food vs. money rewards was positively associated with buffet meal intake and EAH [59]
Lateral OFC	Encodes value and information about specific food attributes during decision-making [97]	Large > small portion images [52]	Response to larger vs. smaller amounts of food was associated with more negative quadratic portion size effect [61]
Inferior frontal gyrus	Response inhibition [98]; stimulus-driven attention and detection of behaviorally relevant stimuli [98]	Large > small portion images [52] Unhealthy > healthy food images [53]	Response to larger vs. smaller amounts of food high-ED foods was associated with less negative quadratic associations between portion size and intake [61]
Thalamus	Relay of exteroceptive info to OFC [17]	Food > non-food images [50]	The difference between fed and fasted responses to food vs. non-food images was positively associated with caloric compensation [58]
Supramarginal gyrus	Somatosensory processing [99]; working memory [100]	Food > non-food images [51]	The difference between fed and fasted responses to food vs. non-food images was positively associated with caloric compensation [58]

ED: energy density (kcal/g); PIT: Pavlovian-to-instrumental transfer; PFC: prefrontal cortex; EAH: eating in the absence of hunger

7. Citations

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Chapter 2 Does 'portion size' matter? Neural responses to food and non-food cues presented in varying amounts

Fuchs BA, Pearce AL, Rolls BJ, Wilson SJ, Rose EJ, Geier CF, Keller KL.

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Abstract

Larger portions of food elicit greater intake than smaller portions of food, particularly when foods are high in energy density (kcal/g; ED). The neural mechanisms underlying this effect remain unclear. The present study used fMRI to assess brain activation to food (higher-ED, lower-ED) and non-food (office supplies) images presented in larger and smaller (i.e., age-appropriate) amounts in 61, 7-8-year-olds (29 male, 32 female) without obesity. Larger amounts of food increased activation in bilateral visual and right parahippocampal areas compared to smaller amounts; greater activation to food amount (larger>smaller) in this cluster was associated with smaller increases in food intake as portions increased. Activation to amount (larger > smaller) was stronger for food than office supplies in primary and secondary visual areas, but, for office supplies only, extended into bilateral parahippocampus, inferior parietal cortex, and additional visual areas (e.g., V7). Activation was greater for higher- vs. lower-ED food images in ventromedial prefrontal cortex for both larger and smaller amounts of food; however, this activation extended into left lateral orbital frontal cortex for smaller amounts only. Activation to food cues did not differ by familial risk for obesity. These results highlight potentially distinct neural pathways for encoding food energy content and quantity.

1. Introduction

Larger portions of food, particularly those high in energy density (ED; kcal/g), elicit greater intake than smaller portions, termed "the portion size effect" (PSE). This effect has been demonstrated across food type [1], environmental context [2,3], and developmental stage [1], and is sustained over 5 days in children [4]. Nevertheless, the mechanisms underlying this effect remain elusive [5,6]. Large portions of high-ED food may drive excess food intake by influencing reward [7], cognitive [8], and/or perceptual processes [9]. Examining brain responses to visual food cues that vary by amount (i.e., portion size) and ED can shed light on how these food characteristics interact to influence eating behaviors.

Previous studies using functional magnetic resonance imaging (fMRI) characterized brain responses to food cues in general as well as food ED, but brain responses to food amount (i.e., portion size) are less clear. Meta-analyses show that cues depicting palatable, typically higher-ED foods activate brain regions associated with reward and valuation, response inhibition, and visual processing more than non-food related cues [10,11]. Brain regions implicated in reward, cognitive, and visual processes also show greater activation to high- compared to low-energy foods [10]. While fewer studies have characterized the brain response to food images that vary in portion size, our lab previously showed children aged 7-10 years had greater activation in regions implicated in inhibitory control (inferior/orbital frontal gyri) [12] and visual processing (left lingual gyrus) [13] when viewing images of larger than smaller food portions. However, these prior studies presented only food items in varying amounts; thus, it was not possible to examine whether brain responses to amount differ between food and non-biologically relevant stimuli. While differences in image properties (e.g., object size, complexity) can influence perceptual processing (e.g., in early visual cortex) [14], food is a primary reinforcer. Therefore,

variations in the amount of food depicted may differentially engage regions sensitive to reward magnitude (e.g., medial orbitofrontal cortex, striatum) [15]. Comparing brain responses to amount (i.e., larger vs. smaller) between food and non-food items will help identify brain regions uniquely sensitive to food amount. Additionally, as higher-ED foods differentially influence brain processes [10] and increase energy intake [16] relative to lower-ED foods, brain response to food amount may also differ by ED [12]. Assessing the interaction between food amount and ED will shed light on how large portion sizes specifically impact brain responses to food items that drive overconsumption.

In addition to identifying brain regions that are responsive to visual depictions of food amount, the present study also advances the literature by examining food cue reactivity in a cohort of children without obesity who vary by familial risk for obesity. Examining food cue reactivity in children without obesity may reduce variability in brain responses due to body weight status [17,18], increasing statistical power to detect effects of food characteristics on brain activity. Second, stratifying children by familial risk for obesity can provide insight into neurobiological traits that may elevate risk for excess energy intake and weight gain. Children at higher familial risk for obesity are twice as likely to develop obesity themselves [19] and have reduced prefrontal cortical and anterior cingulate activation to food vs. non-food images [20] and high- vs. low-ED food words [21]. However, it remains unclear how familial risk impacts brain responses to images that vary in ED and portion size.

To better understand the influence of portion size on brain food cue reactivity, this study used fMRI to examine brain responses to food and non-food images presented in varying amounts. To build on prior work from our lab [12,13], analyses (1) were conducted in a sample that was larger, more homogeneous in age and weight status, and characterized by familial

obesity risk and (2) included explicit comparisons between responses to amount for food and non-food cues. We hypothesized that (1) larger amounts of food would elicit greater activation than smaller amounts of food in brain regions associated with reward, cognitive control, and visual processing and that (2) activation to food amount (larger > smaller) would be greater than activation to non-food amount (larger > smaller) in brain regions associated with reward, cognitive control, and visual processing. To gain insight into risk for childhood obesity, we compared activation to food characteristics (i.e., energy density and amount) between children at high and low familial risk for obesity. We hypothesized that, compared to children at low familial risk, children with high familial risk would show (1) greater activation to energy density (higher > lower) and food amount (larger > smaller) in brain regions associated with reward processing and (2) decreased activation to energy density (higher > lower) and food amount (larger> smaller) in brain regions associated with cognitive control.

2. Methods

2.1. Participants

Participants in this study were 88 (45 male, 43 female) 7-8-year-old children (mean [SD] age=7.8 [0.62] years) who attended the MRI session (visit 6) of a 7-visit prospective study. Children were accompanied by a parent from each family (76 mothers, 12 fathers). Children were without obesity (BMI-for-age-and-sex percentile < 90) by study design and were classified as having high (n=36; maternal BMI > 30 kg/m^2 ± 1 unit) or low (n=52; maternal BMI < 25 kg/m^2 ± 1 unit) familial risk for obesity [22]. Exclusion criteria included the biological mother not meeting BMI requirements for one of the familial risk groups and parents reporting their child was colorblind, not reading at grade level, not fluent in English, had a learning (e.g., dyslexia) or neurodevelopmental (e.g., ADHD) disability, had a diagnosed psychological

condition (e.g., anxiety), was taking medications known to influence appetite, cognition, or blood flow, or had any MRI contraindications (e.g., metal in the body, claustrophobic). 61 children were included in analyses while 27 were excluded (see 3.3.3). Children excluded from analyses did not differ demographically from those who were included (see 4.1).

2.2. Design

As part of a prospective study aiming to identify neurocognitive risk factors for pre-adolescent obesity (ClinicalTrials.gov NCT03341247), participants attended six baseline visits and one follow-up visit a year later (study protocol and materials available on Open Science Foundation (OSF) at https://osf.io/ynjqw/). Primary assessments included child body composition, actigraphy, laboratory eating behaviors, and brain food cue reactivity. Methods and results related to meal intake, cognitive and behavioral assessments, and resting-state functional connectivity have been published elsewhere [22–24]. Visits took place at the University Park campus of The Pennsylvania State University. Parental consent and child assent were obtained in accordance with the Institutional Review Board of The Pennsylvania State University. Baseline data collection occurred between 2017 and 2022 but was interrupted for ~8 months due to COVID-19.

Data for the present analyses included parent-reported demographics (visit 1; see section 2.3), child and parent anthropometrics (visit 1; see section 2.4), portion size meals (visits 2-5; see section 2.5), and brain food cue reactivity (visit 6; see sections 2.6-2.8). Children completed a mock-MRI protocol on visits 4 and 5 (see supplement). Children fasted for at least 3 hours prior to each visit and fullness was measured upon arrival using an age-appropriate visual analog scale [25].

2.3. Demographics

The accompanying parent reported child race, child ethnicity, yearly family income and parental education in a demographic questionnaire (see Table 2-1). Family income and maternal education were used as proxies for socioeconomic status [26].

2.4. Anthropometrics

Height and weight of children and their accompanying parents were measured twice by a trained researcher using a standard scale (Scale Tronix model 5002, Welch Allyn, Chicago, IL; precision to nearest 0.1 kg) and stadiometer (precision to nearest 0.1cm) with shoes and heavy clothing items removed. Height and weight for the parent who did not attend the visit were reported by the accompanying parent. Maternal BMI was calculated from average measured (86%) or parentally reported (14%) maternal height and weight. Child BMI was calculated from averaged height and weight with BMI-for-age-and-sex percentile computed using the Centers for Disease control growth charts [27]. Children also completed whole-body dual energy x-ray absorptiometry (DEXA; Hologic Inc., Waltham, MA), which was used to calculate fat mass index (fat mass (kg)/height, m^2).

2.5. Portion size meals

Details about the meals that were varied in portion size were described previously [22]. Briefly, children were served 4 meals of varying portion sizes in a counterbalanced order. All meals were served in the laboratory at the child's usual meal times. Portion size conditions included a reference amount and 133%, 166%, and 199% of the reference condition by food weight. Food items (i.e., chicken nuggets, macaroni and cheese, grapes, and steamed broccoli) were consistent across meals and access to water was provided *ad libitum*. Children were given 30 minutes to eat *ad libitum* until they reached satiation and could notify the researcher if they reached satiation before 30 minutes. Food weight was assessed before and after each meal to the

nearest 0.1 g. Prior to each meal, children reported liking in response to tasting small samples (~2-3g) of the meal foods using a five-point facial hedonic scale and reported fullness using a child-friendly visual analog scale [25].

2.6. Visit 6 procedures

To scan children in a neutral appetitive state, those who reported fullness levels <25% upon arrival received a small snack (6.75 fl oz apple juice, Quaker Chewy granola bar). Following consumption, children rated their fullness again. If fullness rating remained <25%, a second snack was offered. Children also rated their state anxiety before and after the scan using the Children's Anxiety Meter Scale (CAMS) [28]. Following the scan, children viewed and rated each image of the food-cue task for liking and anticipated fullness using a computerized visual analog scale. For each image, children were instructed to answer, "how much do you like this object/food?" (0 = not at all; 100 = like very much). For each food image, children were also instructed to answer, "how full would your stomach be if you ate this food?" (0 = not at all full; 100 = very much full). Children rated images in the same order they were presented in the scanner.

2.7. fMRI acquisition

fMRI was conducted using a Siemens MAGNETOM Trio 3 T MRI scanner with a 20-channel head coil. Padding was placed around the head to limit movement. Stimuli were projected onto an MRI-compatible screen and viewed by the child using a mirror. A T1-weighted MPRAGE was acquired using Siemens' integrated parallel acquisition technique (iPAT) generalized autocalibrating partially parallel sequences (GRAPPA, acceleration factor 2; [29]) and the following parameters: TR=1650, TE=2.03 ms, flip angle=9°, FOV=256x256 mm^2, 160 sagittal slices, voxel size 1x1x1 mm^3. Functional scans were performed to assess the blood

oxygen dependent response (BOLD), an indirect measure of neuronal activation [30]. Functional scans were collected using a T2*-weighted gradient single-shot echo planar imaging sequence (TR=2000 ms, TE=26 ms, flip angle=90°, FOV=220x220 mm^2) with a voxel size of 3×3×3 mm^3 to acquire 33 axial slices (no gap) in descending order. Functional images were aligned along the AC-PC plane and adjusted vertically to optimize signal in the temporal lobe and cerebellum based on findings in these regions from our group [12]. Six functional runs were collected including one resting-state scan [180 volumes; ,23] and five food-cue scans (80 volumes each). Two volumes were automatically discarded prior to the start of each functional run. Following the functional runs, a field map was acquired using a double-echo gradient-echo sequence (TR=400 ms, TE_1=5.12 ms, TE_2=7.65 ms, flip angle=60°, FOV=220x220 mm^2) with a voxel size of 3×3×3 mm^3 to acquire 33 axial slices (no gap) in descending order. MRI data are available on OpenNeuro [31].

2.8. fMRI food-cue task

The food-cue task was administered using E-Prime 2.0 [32]. Children viewed 120 food and 60 non-food (i.e., office supply) images from a standardized dataset [33]. Prior to the task, children were instructed to answer the question “Do you want this?” for each item by selecting either “Do not want/Frown face” or “Want/Smiley face” with their dominant hand. Office supplies were selected for the non-food condition because they are not biologically salient, but they are familiar to children and visual characteristics (e.g., size, color, contrast) could be balanced with food items. Food conditions varied by amount (larger, smaller) and ED (higher, lower), while office supply conditions varied by amount (larger, smaller) only. Higher-ED foods (e.g., bacon, brownie) had >2.0 kcal/g, while lower-ED foods (e.g., strawberries, turkey) had <1.5 kcal/g. The portions of food depicted in the smaller amount condition were based on

standard servings from the Nutrition Facts Panel and reflected the amount of food typically consumed by children [34]. The portions of food depicted in the larger amount condition were approximately double the weight of food shown in the smaller amount condition. Images were presented over five runs of six blocks each (one per condition; Figure 2.1).

2.9. Analyses

Code is available OSF (https://osf.io/x8j56/).

2.10. Descriptive statistics

We compared demographic variables between children at high and low familial risk for obesity using 2-sample t-tests for continuous variables and $\chi 2$ or Fisher's Exact Test for categorical variables. To ensure there were no meaningful differences between children included and excluded (e.g., due to motion) from analyses, we examined demographic differences by inclusion status.

We tested associations between MRI-related variables (e.g., pre-MRI fullness, average framewise displacement—FD) and familial risk for obesity, age, and sex using Pearson's correlation, 2-sample t-tests, and $\chi 2$. Pre-MRI fullness was indexed as the fullness rating that occurred closest to the scan with one value imputed due to recording error (see supplement).

2.11. fMRI preprocessing

MRI data were preprocessed using fMRIPrep 20.2.3 [35] using standard pre-processing steps (see supplement for full report). Volume-based spatial normalization used Montreal Neurological Institute's (MNI) unbiased template for pediatric cohort 3 (ages 7 – 11y) [36,37]. Functional preprocessing included susceptibility distortion correction, estimation of head-motion parameters, slice-time correction, co-registration to anatomical space, and resampling into standard space. Quality assessment reports generated by fMRIPrep were visually inspected, and

data were excluded (see 3.3.3) or re-processed as needed. Subsequent processing and individual- and group-level analyses were conducted using AFNI v21.3.04 [38,39]; this included applying a 6.0 mm FWHM BOLD Gaussian blur and scaling the time-series data so results can be represented as percent signal change.

2.12. Percent wanting

For each food-cue task block, we calculated the percent of items children reported wanting out of items responded to (%want). We used two separate linear mixed-effects models using lme4 [40] in R 4.2.2 [41] with subject as random effect to assess (1) the interaction between cue type (food, office) and amount (larger, smaller) on %want and (2) the interaction between ED (higher-ED, lower-ED) and food amount (larger, smaller) on %want, controlling for run.

2.13. Image ratings

Similar to analyses of %want, we calculated children's average liking and anticipated fullness ratings for each food-cue task block. Two separate linear mixed-effects models with subject as random effect were used to assess the interactions between (1) cue type (food, office) and amount (larger, smaller) and (2) ED (higher-ED, lower-ED) and food amount (larger, smaller) on liking, controlling for run. In addition, a linear mixed-effects model with subject as random effect was used to assess the interaction between ED (higher-ED, lower-ED) and food amount (larger, smaller) on anticipated fullness, controlling for run.

2.14. fMRI Analyses

2.14.1. Individual-level

Using AFNI's 3dDeconvolve, we conducted individual-level general linear models (GLMs) that included 14 nuisance regressors computed by fMRIPrep (6 rigid-body motion

parameters and their derivatives, average signal within the cerebrospinal fluid and white matter masks). Each image condition (i.e., larger amount higher-ED foods, larger amount lower-ED foods, larger amount office supplies, smaller amount higher-ED foods, smaller amount lower-ED foods, smaller amount office supplies) was modeled by convolving block onsets and durations to the hemodynamic response (AFNI's 'BLOCK' function). From these GLMs, we generated a total of 8 first-level contrasts: (1) food > office, (2) higher-ED foods (larger + smaller amounts) > lower-ED foods (larger + smaller amounts), (3) larger amount higher-ED foods > larger amount lower-ED foods, (4) smaller amount higher-ED foods > smaller amount lower-ED foods, (5) larger food amounts (higher-ED + lower-ED) > smaller food amounts (higher-ED + lower-ED), (6) larger amount higher-ED foods > smaller amount higher-ED foods, (7) larger amount lower-ED foods > smaller amount lower-ED foods, and (8) larger amount office supplies > smaller amount office supplies. We also conducted separate GLMs to assess the parametric modulation of BOLD responses to office supplies, higher-ED foods, lower-ED foods, larger food amounts, and smaller food amounts by %want.

To remove signal outliers and high-motion timepoints from analyses, volumes were censored by 3dDeconvolve if they (1) were identified as steady state outliers by fMRIPrep or (2) had a FD>0.9mm [42], respectively. The FD threshold selected matches that used by the Adolescent Brain Cognitive Development (ABCD ®) Study [43]. Runs were excluded from first-level analyses if >20% of volumes across food- and office supply blocks were censored.

2.14.2. fMRI exclusion criteria

We excluded children from fMRI analyses if they declined to scan (n=4), completed <3 runs of the food-cue task (n=4), had <3 runs of the food-cue task included in first-level analyses after censoring (see 3.2.2; n=17), or had poor-quality functional data (e.g., extreme loss of field

of view due to motion) detected via visual inspection (n=2). Children were also excluded from parametric analyses if they had 1 or more food-cue blocks with no response data (n=4 excluded from all models) or no variability in %want for 1 or more of the conditions included in the model (n excluded: office supply=8; ED=3; food amount=2).

2.14.3. Group-level

Group-level analyses were conducted using 3dttest++. Z-statistic maps were thresholded at voxel-wise $p<0.001$ (two-tailed) and cluster-corrected to $p<0.05$ except for exploratory analyses with familial risk status and fat mass index, which were cluster-corrected to $p<0.1$. 3dClustStim was used to determine cluster extents (Cox *et al.*, 2017; Table S2). Unthresholded maps are available on Neurovault.org [1] (https://identifiers.org/neurovault.collection:14535). Models included average FD, sex, pre-MRI fullness, and pre-MRI CAMS as covariates and were restricted to voxels scanned in at least 80% of subjects included in the given analysis (see supplement; Figure S1). We conducted sensitivity analyses by testing models with snack intake (yes/no) as an additional covariate; results were similar with the addition of this covariate (Tables S5-S10), so results from models without the snack intake as a covariate are reported in the main text.

2.14.3.1. BOLD responses to image condition

To assess the main effects of cue type (food vs. office), ED (higher vs. lower), and food amount (larger vs. smaller) on BOLD responses, we conducted three 1-sample t-tests on the following first-level contrasts: (1) food > office, (2) higher-ED foods (larger + smaller amounts) > lower-ED foods (larger + smaller amounts), and (3) larger food amounts (higher-ED + lower-ED) > smaller food amounts (higher-ED + lower-ED).

To visualize similarities (i.e., conjunction) and differences (i.e., disjunction) in the extent of BOLD responses to ED for larger and smaller amounts of food, we conducted and overlayed binarized results of two 1-sample t-tests on the following first-level contrasts: (1) larger amount higher-ED foods > larger amount lower-ED foods and (2) smaller amount higher-ED foods > smaller amount lower-ED foods.

Similarly, to visualize similarities and differences in the extent of BOLD responses to amount for higher-ED foods, lower-ED foods, and office-supplies, we conducted and overlayed binarized results of three 1-sample t-tests on the following first-level contrasts: (1) larger amount higher-ED foods > smaller amount higher-ED foods, (2) larger amount lower-ED foods > smaller amount lower-ED foods, and (3) larger amount office supplies > smaller amount office supplies.

To formally test whether BOLD responses to amount differed by cue type or ED, we conducted two paired t-tests on first-level amount (larger > smaller) contrasts.

2.14.3.2. Associations with %want

To assess how in-scanner wanting related to BOLD responses, we conducted five 1-sample t-tests on the parametric modulation of BOLD responses by %want for (1) office supply, (2) higher-ED food, (3) lower-ED food, (4) larger food amount, and (5) smaller food amount conditions. We conducted two paired t-tests to assess whether the parametric modulation of BOLD responses by %want differed by (1) ED (higher vs. lower) or (2) food amount (larger vs. smaller).

2.14.3.3. Associations with obesity risk and fat mass index

To explore whether familial risk for obesity or fat mass index were associated with BOLD responses, we conducted six regressions with risk status (high vs. low) and fat mass index as separate predictors of the following first-level contrasts: (1) food > office, (2) higher-ED foods

(larger + smaller amounts) > lower-ED foods (larger + smaller amounts), and (3) larger food amounts (higher-ED + lower-ED) > smaller food amounts (higher-ED + lower-ED). Associations with risk status were assessed explored using the whole analysis sample as well as only in children with measured maternal height and weight (N = 52).

2.14.3.4. Post-hoc associations with the PSE

To assess whether BOLD responses in clusters responsive to image conditions were associated with eating behaviors, we extracted first-level average contrast values from clusters exhibiting significant effects of cue type, ED (across amount), food amount (across ED), and office supply amount, as well as differential responses to amount by cue type (analyses described in section 2.14.3.1). The contrast values extracted corresponded to the contrast that the cluster was significantly responsive to (i.e., for a cluster responsive to cue type, we extracted the average BOLD response to cue type across all voxels in that cluster). Using extracted contrast values, we conducted 2 linear mixed-effects models for each cluster using lme4 [40] in R 4.2.2 [41]. Models included subject as a random effect and predicted either the weight (grams) or energy (kcal) of food consumed from (1) the extracted BOLD response, (2) the proportion increase in meal size from the reference portion (i.e., meal size condition, [0.00, 0.33, 0.66, 0.99]) and (3) the interaction between the extracted BOLD response and meal size condition, controlling for pre-meal fullness, average food liking, meal order, sex and BMI.

3. Results

3.1. Participant characteristics (Table 1)

Most parents reported their children were White, non-Hispanic/Latinx, the child's mother had a bachelor's degree or higher, and the yearly family income was greater than $51,000. Children at low familial risk for obesity were more likely to have mothers who completed a

bachelor's degree (Fisher's exact $p<0.001$) and had lower fat mass indices ($p<0.01$) than those at high familial risk. Age, sex, BMI percentile, and income did not differ by familial risk for obesity (ps>0.05). Children included in analyses did not differ from those excluded by age, sex, BMI percentile, fat mass index, income, maternal education, or familial risk for obesity (ps>0.43; Table S1).

On average, children included in analyses had acceptable data for 4.48 out of 5 possible runs and 332 out of 398 possible time points. Children at low familial risk for obesity had acceptable data for more runs and timepoints (ps<0.05) and lower average FD ($p=0.05$) than children at high familial risk for obesity. Pre-MRI anxiety, fullness, and snack consumption did not differ by risk (ps>0.17). MRI-related variables were not associated with age or sex (p>0.08) except for snack consumption, which was more frequent in girls (80%) than boys (50%) ($\chi 2(1)=5.55$, $p=0.02$).

3.2. Percent wanting

%want was higher for foods (estimated marginal mean (EMM)=67.5%, SE=2.4%) compared to office supplies (EMM=41.8%, SE=2.5%; $p<0.001$, Figure 2.2A). There was no main effect of amount or interaction between cue type and amount on %want (ps>0.42). Similarly, %want was greater for higher-ED foods (EMM=78.2%, SE=2.4%) than lower-ED foods (EMM=57.0%, SE=2.4%; ps<0.001; Figure 2.2B). There was no main effect of food amount or interaction between ED and food amount on %want (ps>0.31).

3.3. Image liking and anticipated fullness ratings

Liking was higher for foods (EMM=58.9, SE=2.1) compared to office supplies (EMM=47.8, SE=2.2; $p<0.001$, Figure 2.3A). There was no main effect of amount or interaction between cue type and amount on liking (ps>0.49). Similarly, liking was greater for higher-ED

foods (EMM=67.9, SE=2.1) compared to lower-ED foods (EMM=49.9, SE=2.1; p<0.001; Figure 6B). There was no main effect of food amount or interaction between ED and food amount on liking (ps>0.23).

Anticipated fullness was greater for larger amounts of food (EMM=51.4, SE=2.1) compared to smaller amounts of food (EMM=41.3, SE=2.1; ps<0.001; Figure 3C) and greater for higher-ED foods (EMM=49.6, SE=2.1) compared to lower-ED foods (EMM=43.1, SE=2.1; ps<0.001; Figure 2.3C). There was no interaction between ED and food amount on anticipated fullness (ps>0.23).

3.4. BOLD response to cue type

There was greater activation to food than office supplies in a cluster extending bilaterally through anterior cingulate cortex (ACC), medial prefrontal/orbitofrontal cortex (mOFC), frontopolar cortex and caudate, into left lateral OFC and left pallidum (Figure 2.4; Table 2-2). In addition, there was greater activation to food than office supplies in bilateral primary visual cortex (V1) and posterior insula extending into middle insula. There was lower activation to food than office supplies in bilateral clusters extending through inferior parietal cortex, visual cortices (V4, V7), ventromedial visual areas, fusiform face area, parahippocampal areas, and lateral occipital and posterior temporal cortices, as well as bilateral clusters extending from inferior frontal cortex to dorsolateral prefrontal cortex (dlPFC).

3.5. BOLD response to ED

When larger and smaller food amounts were combined, there was greater activation to higher- than lower-ED foods in bilateral ACC/mOFC extending into bilateral dorsomedial prefrontal cortex and left ventromedial prefrontal cortex (vmPFC)/mOFC, frontopolar cortex, and lateral OFC (lOFC; Figure 2.5A; Table 2-3).

When analyzed individually by food amount, both smaller and larger food amount conditions showed greater activation for higher-ED relative to lower-ED foods in primarily distinct regions of bilateral ACC/mOFC, which overlapped in left ACC/mOFC (Figure 2.3B; Table 2-5). For smaller amounts only, activation extended laterally into left frontopolar and lOFC. Additionally, for smaller amounts only, there was less activation to images of higher- than lower-ED foods in fusiform face area, posterior inferotemporal complex, and lateral occipital cortex.

3.6. BOLD response to amount

When higher-ED and lower-ED foods were combined, there was greater activation to larger than smaller food amounts in bilateral visual areas (V1-V4, V8, ventromedial visual area), and right parahippocampal area (Figure 2.6A; Table 2-4). There was less activation to larger than smaller food amounts in right angular gyrus.

When analyzed individually by image type, higher-ED food, lower-ED food, and office supply conditions all showed greater activation for larger relative to smaller amounts in V1-V4 and V8 (Figure 2.6B; Table 2-4). For higher-ED food and office supply conditions only, activation extended into additional bilateral ventromedial visual areas, right visual area V3B and right posterior parahippocampal area. For the office supply condition only, activation extended even further into right fusiform face area, bilateral posterior inferotemporal complex, bilateral parahippocampal areas, bilateral visual areas V7 and V3A, and bilateral inferior parietal cortex.

The BOLD response to amount (larger>smaller) was greater for food cues than office supplies in bilateral V1 and V2 (Figure 2.6C; Table 2-5) but did not differ by ED.

3.7. Associations between BOLD responses and percent wanting (%want)

BOLD responses to higher-ED foods, lower-ED foods, larger food amounts, smaller food amounts, and office supplies did not show significant covariation with %want parametric regressors, indicating that, within children, the intensity of the BOLD responses to each image condition was not significantly associated with the % of images that children reported wanting. However, the association between BOLD response and %want was weaker for higher-ED foods compared to lower-ED foods in right early visual cortex (V4; Table S3). The association between BOLD response and %want did not differ between food amount conditions.

3.8. Associations between BOLD responses, familial risk status and fat mass index

BOLD responses to cue type, ED, and amount were not significantly associated with familial risk status or fat mass index. Exploratory assessment of subthreshold results revealed higher fat mass index was associated with greater BOLD responses to higher- than lower-ED food cues in left dlPFC ($p<0.06$) and left V1 ($p<0.09$; Table S4).

3.9. Associations between BOLD responses and the PSE

In the cluster responsive to food amount that extended through visual and parahippocampal areas (peak coordinates = -20, -88, -16; Table 4), BOLD response to larger > smaller food amounts was negatively associated with the PSE for the weight of food consumed (stats; Table S11); the greater the BOLD response to larger > smaller food amounts, the smaller the increase in intake as portion sizes increased (Figure 2.7). This association was not observed for the PSE for energy consumption (Table S12). Food intake was not associated with BOLD responses in clusters responsive to cue type, ED, office supply amount, or the interaction between cue type and amount (Tables S13-S20).

4. Discussion

Consistent with prior work showing independent effects of energy density and food amount (i.e., portion size [12,13]), the present study found higher-ED food images elicited greater activation than lower-ED food images in regions associated with reward-related decision making and valuation while larger amounts of food elicited greater activation than smaller amounts in regions associated with visual processing. Extending prior work, we observed greater activation for higher- than lower-ED food cues in distinct regions of the OFC depending on whether foods were presented in larger or smaller (i.e., age-appropriate for children) amounts and identified different patterns of activation to amount in visual processing areas for foods and office supplies. These findings suggest brain responses to food ED vary depending on the amount of food presented, highlighting potential mechanistic avenues whereby the brain makes distinctions between food energy content and quantity.

Overall, there was greater activation for higher- than lower-ED foods across ACC, medial PFC, and OFC. However, BOLD responses to ED diverged for foods depending on whether they were presented in larger or smaller portion sizes. For both larger and smaller portions, BOLD responses to ED were found in the vmPFC (e.g., mOFC, ACC), whereas for smaller amounts *only*, the BOLD response to ED extended into lOFC. While both vmPFC and lOFC are implicated in food-related decision making [46–48] and food valuation [49], functional differences have been reported between these regions. vmPFC is thought to encode overall value signals for food by integrating signals for multiple food attributes (e.g., taste, health) while lOFC encodes information about specific food attributes [49], such as taste pleasantness [50], sensory characteristics [51], and specific nutrients [52]. In particular, a subregion of lOFC shown to encode perceptions of fat quantity in a food [52] overlaps with the subregion we showed was responsive to ED for smaller portions. While children may value higher-ED foods more than

lower-ED foods regardless of portion, they may only incorporate perceptions of energy content or associated nutrients (e.g., fat) into valuations when portions are more age-appropriate (i.e., the smaller amount). Additionally, it is possible when less food is available for consumption, the brain prioritizes calculations of energy content to ensure biological adequacy of the meal. Future research should assess how perceptions about different food attributes (e.g., macronutrients, taste, health) are incorporated into value-based decisions for varying portions.

The BOLD response to ED also differed by food amount in regions implicated in object recognition and representation [53,54]; greater activation to lower- than higher-ED foods was observed in fusiform face and posterior inferotemporal areas for smaller but not larger portions of food. Fusiform has been shown to be more responsive to food and faces than other objects [55,56], to food in a fasted than fed state [57–59], and to higher- than lower-energy foods [13,60], suggesting motivational relevance (i.e., value) drives activation in this region [55]. While we observed greater activation to lower- than higher-energy dense foods in this region, our finding aligns with previous work showing food attributes impact fusiform responses, particularly for smaller, age-appropriate portion sizes.

For food and office supply conditions, larger amounts were associated with greater activation in visual processing regions than smaller amounts. However, in primary and early visual cortices, the response to amount was stronger for food than office supplies, which may be due to differences in low-level visual characteristics (e.g., size, color, complexity) between these image conditions [33]. Alternatively, this pattern could indicate children had greater value-based modulation of early visual cortex [61] for larger vs. smaller amounts of food compared to larger vs. smaller amounts of office supplies. Further, the BOLD response to amount was more widespread for office supplies than food items, extending bilaterally to regions associated with

object recognition (e.g., fusiform [53]) and associative processing and episodic memory (e.g., parahippocampal regions [62]). Given common school items were depicted, this response may reflect associative processes or memories related to experiences with larger amounts of office supplies in this context. Future research using other non-food categories can shed light on whether these distinct responses to amount for food vs. office supplies reflect differences in biological relevance or are due to previous experiences with the stimuli.

In contrast to our hypotheses, larger amounts of food did not elicit greater engagement in regions associated with reward or cognitive control compared to smaller amounts of food. This differs from a previous study in which we observed greater inferior frontal gyrus/OFC activation to larger vs. smaller portion sizes in children 7-10 years old [12]. The younger age range and restricted weight status of the current sample may contribute to differences in findings. Further, as children's susceptibility to the 'portion size effect' has been associated with food cue reactivity [13,63], weight status and appetitive traits (i.e., food and satiety responsiveness [4]) and executive functions [22], it is possible large portion size cues may only influence reward and cognitive processes, but only among some children [63]. Alternativity, large portion size cues may modulate eating behaviors predominantly through perceptual processes rather than primary reward or cognitive mechanisms. In support of this, post-hoc analyses revealed that the average BOLD response to food amount (larger > smaller) in regions implicated in visual processing was negatively associated with the PSE measured across four laboratory meals. As the BOLD response to office supply amount (larger > smaller) in a similar, overlapping region was not associated with the PSE, results suggest a food-specific association where children who are *more* sensitive to visual portion size cues in brain regions associated with visual and associative processes are *less* susceptible to eating more as portion sizes increase. One possibility is that the

inability to perceptually distinguish larger from smaller portions, whether implicit or explicit in nature, may make children more susceptible to the PSE because they are less aware that portions are increasing. Whether overtly telling children about the portion size manipulations would help to mitigate the effects of portion size on intake remains to be tested.

Also in contrast to our hypotheses, we found no differences in children's BOLD responses to food cues by familial risk for obesity, defined using maternal BMI. This differs from prior studies in youth [20,21] that observed associations between maternal BMI and food cue reactivity in regions associated with self-regulation, perceptual processes, and memory. Based on a comparison of methods and sample characteristics to studies by Carnell et al., [21] and Luo et al., [20], the lack of differences by familial risk status in the current study could be due to variations in physiological state, developmental stage, and/or demographic characteristics. Alternatively, loss of data due to motion may have left us underpowered to robustly test differences in food cue reactivity by familial risk and child adiposity; therefore, more work is needed to address these questions.

The present study has several strengths. First, we used a publicly-available, standardized set of images [33], which facilitates interpretation of results and replication in future studies. Second, children completed a two-session mock-MRI protocol prior to scanning, allowing them to become familiar with the MRI environment. Third, by using conjunction and interaction analyses, we were able to build on prior research examining BOLD responses to food ED and portion size [12] to provide insight into how foods at varying levels of energy density are distinctly processed when portions are smaller (age-appropriate) and larger. Fourth, by sharing raw data and unthresholded statistical maps, this study has the potential to contribute to future meta- and mega-analyses on food cue reactivity in children.

In addition to strengths, the present study has several limitations. First, our sample lacked racial and ethnic diversity. Future research is needed to assess whether results generalize to more diverse populations. Second, while office supplies were selected as the non-food condition because they are familiar to children and can be presented in varying colors/quantities, comparisons between food and office supplies may not generalize to comparisons between food and other non-food objects. For example, while prior studies have shown greater responses to food than non-food items (e.g., scenery, animals) in higher-order visual processing regions (see [10] for meta-analysis), we observed the opposite pattern in comparisons between food and office supplies. Office supplies may be similar to tools in their ability to elicit greater activation in dorsal and ventral visual streams compared to other non-food categories (e.g., animals [64]). Future analyses comparing brain responses to amount between food and other non-food categories are needed in order to determine if there is a "food-specific" response to amount. Third, the binary wanting responses provided by children in the scanner may have limited our ability to detect whether BOLD responses are modulated by wanting. To better examine these associations, future studies could use a wanting scale that allows for more granularity in responses (e.g., a multi-point scale). Fourth, while we assessed in-scanner wanting and post-scan ratings of anticipated fullness and liking, it remains unclear how children perceived and interpreted the food cues during the scan. Future research could qualitatively investigate how children perceive images of large food portions or provide more explicit prompts to induce specific mental states (e.g., imagine you have to eat the full portion). Finally, some children categorized as having high familial risk for obesity in the present study may develop obesity and some may be resilient to obesity. Such heterogeneity could preclude the detection of brain phenotypes that promote adiposity gain in children. To better understand neurobiological traits

that pre-dispose children to obesity, future analyses could stratify initial "at-risk" groups based on future weight gain and subsequently compare baseline food cue reactivity.

In conclusion, we showed that ED influenced BOLD responses in vmPFC for larger and smaller (i.e., age-appropriate) amounts of food, but influenced BOLD responses in lOFC and fusiform for smaller amounts only. Further, the response to amount was stronger and more localized in early visual processing areas for food images than non-food images, and that BOLD responses to food amount across visual and parahippocampal areas was associated with the effect of portion size on measured intake. These results suggest portion size impacts valuation processes related to food energy content and influences perceptual processes differently than non-food amount. These findings improve our understanding of how portion size impacts brain food cue reactivity in children and elucidate potential neurobiological mechanisms underlying the "portion size effect."

Table 2-1. Descriptive statistics for demographic and MRI-related variables by familial risk for obesity

Table 1. Descriptive statistics for demographic and MRI-related variables by familial risk for obesity

	Low Risk (N=36)	High Risk (N=25)	Overall (N=61)
Age, yrs			
Mean (SD)	7.9 (0.63)	7.7 (0.55)	7.8 (0.60)
Min, Max	7.02, 8.99	7.00, 8.84	7.00, 8.99
BMI percentile			
Mean (SD)	41.5 (25.7)	52.8 (23.6)	46.2 (25.3)
Min, Max	3.91, 86.8	9.38, 89.0	3.91, 89.0
Fat mass index			
Mean (SD)	4.10 (0.80)	4.81 (0.86)	4.39 (0.89)
Min, Max	3.18, 6.44	3.57, 7.42	3.18, 7.42
Sex; n (%)			
Male	18 (50.0%)	11 (44.0%)	29 (47.5%)
Female	18 (50.0%)	14 (56.0%)	32 (52.5%)
Race; n (%)			
White	34 (94.4%)	25 (100%)	59 (96.7%)
American Indian/Alaskan Native	0 (0%)	0 (0%)	0 (0%)
Asian	2 (5.6%)	0 (0%)	2 (3.3%)
Black/African American	0 (0%)	0 (0%)	0 (0%)
Hawaiian/Pacific Islander	0 (0%)	0 (0%)	0 (0%)
Ethnicity; n (%)			
Not Hispanic or Latino	36 (100%)	25 (100%)	61 (100%)
Hispanic or Latino	0 (0%)	0 (0%)	0 (0%)
Family Income; n (%)			
< $51,000K	4 (11.1%)	5 (20.0%)	9 (14.8%)
51-100K	13 (36.1%)	14 (56.0%)	27 (44.3%)
> $100K	18 (50.0%)	5 (20.0%)	23 (37.7%)
Missing	1 (2.8%)	1 (4.0%)	2 (3.3%)
Maternal Education; n (%)			
< BA	3 (8.3%)	10 (40.0%)	13 (21.3%)
BA	16 (44.4%)	13 (52.0%)	29 (47.5%)
> BA	16 (44.4%)	2 (8.0%)	18 (29.5%)
Missing	1 (2.8%)	0 (0%)	1 (1.6%)
Analyzed runs, n; Mean (SD)	4.7 (0.58)	4.2 (0.99)	4.5 (0.81)
Analyzed timepoints, n; Mean (SD)	350 (52)	310 (82)	330 (69)
Average framewise displacement; Mean (SD)	0.32 (0.19)	0.45 (0.29)	0.37 (0.24)
Pre-MRI fullness; Mean (SD)	73 (30)	67 (28)[a]	71 (29)[1]
Pre-MRI anxiety; Mean (SD)	1.8 (1.6)	2.7 (3.1)	2.2 (2.3)
Consumed snack; n (%)			
no	13 (36.1%)	8 (32.0%)	21 (34.4%)
yes	23 (63.9%)	16 (64.0%)	39 (63.9%)
Missing	0 (0%)	1 (4.0%)	1 (1.6%)

Note: table reflects data for children included in analyses; BA: bachelor's degree

[a] 1 value missing. Value was imputed for neuroimaging analyses but not included in descriptive statistics.

Table 2-2. Regions showing BOLD response to cue type (food vs. office supplies)

Table 2. Regions showing BOLD response to cue type (food vs. office supplies)

Effect	Region	H	k^a	Z^b	*x*	*y*	*z*
Food > Office Supplies	Anterior cingulate cortex (ACC)	L	25,375	6.28	-5	41	3
	V1 / Inferior occipital gyrus	L	6,210	7.42	-17	-98	-10
	V1 / Lingual gyrus	R	5,328	7.84	19	-95	-9
	Posterior insula	L	3,664	7.97	-37	3	-10
	Posterior insula	R	2,877	7.31	37	5	-10
Food < Office Supplies	Inferior parietal cortex / middle occipital gyrus	L	52,337	-7.94	-27	-67	29
	Parahippocampal area	R	47,831	-7.76	30	-47	-8
	Inferior frontal sulcus / Prefrontal gyrus	L	16,484	-6.42	-47	0	32
	dlPFC / Inferior frontal gyrus	R	13,874	-5.93	45	25	22

Results from 1-sample t-test on cue type contrast (food - office supplies) controlling for average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety (CAMS); Cluster p-values were cluster-corrected to $p < 0.05$

[a] cluster-extent in 1x1x1 mm^3; [b] peak cluster z-value derived from the general linear model

x, y, z: MNI coordinates of cluster peak; H: hemisphere; V1: primary visual cortex

Table 2-3. Regions showing BOLD response to energy density (higher vs. lower)

Table 3. Regions showing BOLD response to energy density (higher vs. lower)

Effect	Region	H	k^a	Z^b	x	y	z
BOLD response to ED across larger and smaller food amounts							
Higher > Lower	ACC / medial OFC	L	13,492	5.49	-3	48	-7
BOLD response to ED for larger food amounts							
High > Low	ACC / medial OFC	L	2,673	4.43	-3	48	-8
BOLD response to ED for smaller food amounts							
High > Low	Lateral OFC	L	3,287	4.64	-24	59	-16
High < Low	Ventral visual complex / fusiform gyrus	L	2,091	-4.44	-36	-71	-16

Results from 1-sample t-tests on energy density (ED) contrast (higher - lower) controlling for average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety (CAMS); Cluster p-values were cluster-corrected to $p < 0.05$
[a] cluster-extent in 1x1x1 mm^3; [b] peak cluster z-value derived from the general linear model
x, y, z: MNI coordinates of cluster peak; H: hemisphere

Table 2-4. Regions showing BOLD response to amount (larger vs. smaller)

Table 4. Regions showing BOLD response to amount (larger vs. smaller)

Effect	Region	H	k^a	Z^b	*x*	*y*	*z*
BOLD response to food amount across higher- and lower-ED foods							
Larger > Smaller	V3 / Lingual gyrus	L	53,596	13	-20	-88	-16
Larger < Smaller	Angular gyrus	R	2,416	-4.73	47	-56	31
BOLD response to food amount for higher-ED foods							
Larger > Smaller	V2 / Inferior occipital gyrus	L	44,433	13	-16	-92	-9
BOLD response to amount **for** lower-ED foods							
Larger > Smaller	V2 / Lingual gyrus	R	13,776	13	15	-91	-8
Larger > Smaller	V2/3 / Lingual gyrus	L	12,648	7.78	-16	-88	-11
BOLD response to amount **for** office supplies							
Larger > Smaller	V3 / Lingual gyrus	L	73,549	13	-20	-88	-17

Results from 1-sample t-tests on amount contrasts (larger - smaller) controlling for average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety (CAMS); Cluster p-values cluster-corrected to $p < 0.05$

[a] cluster-extent in 1x1x1 mm^3; [b] peak cluster z-value derived from the general linear model (maximum value output by AFNI is 13)

x, y, z: MNI coordinates of cluster peak; H: hemisphere; V1: primary visual cortex, V2: secondary visual cortex, V3: third visual cortex

Table 2-5. Regions showing differential BOLD responses to amount by cue type and energy density (ED)

Table 5. Regions showing differential BOLD responses to amount by cue type and energy density (ED)

Effect	Region	H	k^a	Z^b	*x*	*y*	*z*
BOLD response to amount (larger - smaller) by cue type (food vs. office)							
Food > Office Supplies	V2 / Calcarine gyrus	L	4,838	7.24	-15	-94	-7
	V1 / Calcarine gyrus	R	4,078	6.83	18	-91	0
BOLD response to food amount (larger - smaller) by ED (higher vs. lower)							
n.s							

Results from paired t-tests using first-level amount contrasts (larger - smaller) controlling for average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety (CAMS); Cluster p-values were cluster-corrected to $p < 0.05$

[a] cluster-extent in 1x1x1 mm^3; [b] peak cluster z-value derived from the general linear model

x, y, z: MNI coordinates of cluster peak; H: hemisphere; V1: primary visual cortex, V2: secondary visual cortex; n.s: no clusters surviving cluster-correction

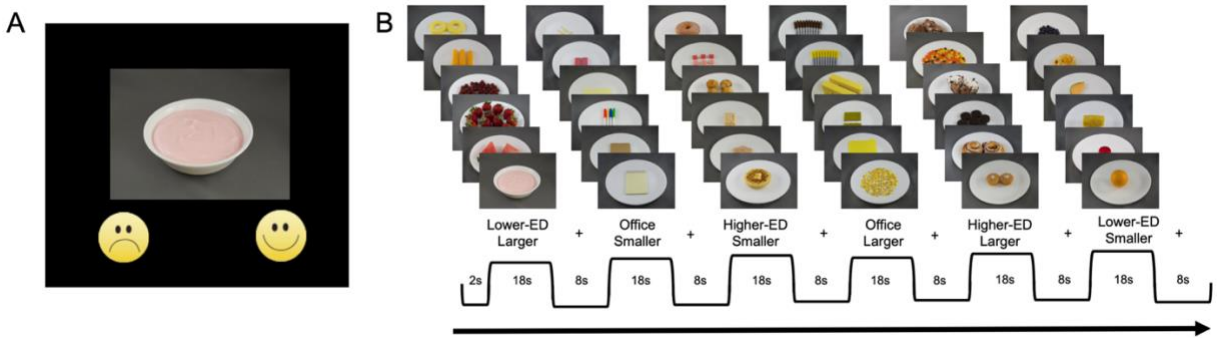

Figure 2.1 Food-cue task. Children viewed 120 food and 60 non-food (i.e., office supply) images from a standardized dataset [30]. Food conditions varied by amount (larger, smaller) and energy density (ED; higher, lower), while office supply conditions varied by amount (larger, smaller) only. For each image, children indicated whether they wanted the item by pressing one of two buttons (thumb for "yes", index finger for "no") on a response grip with their dominant hand. (A) Image presentation: Images were presented on a black screen above a smiley face and a frowny face, which were included to remind children to make a response. (B) Example run: Images were presented over five runs. Each run contained six blocks (one per image condition) with six images per block. Images were presented for 2.0 s with a 0.5 s inter-trial fixation cross. Each block was followed by an 8.0 s white fixation cross presented on a black screen. Two versions of the task with pseudorandomized block orders were counterbalanced across participants.

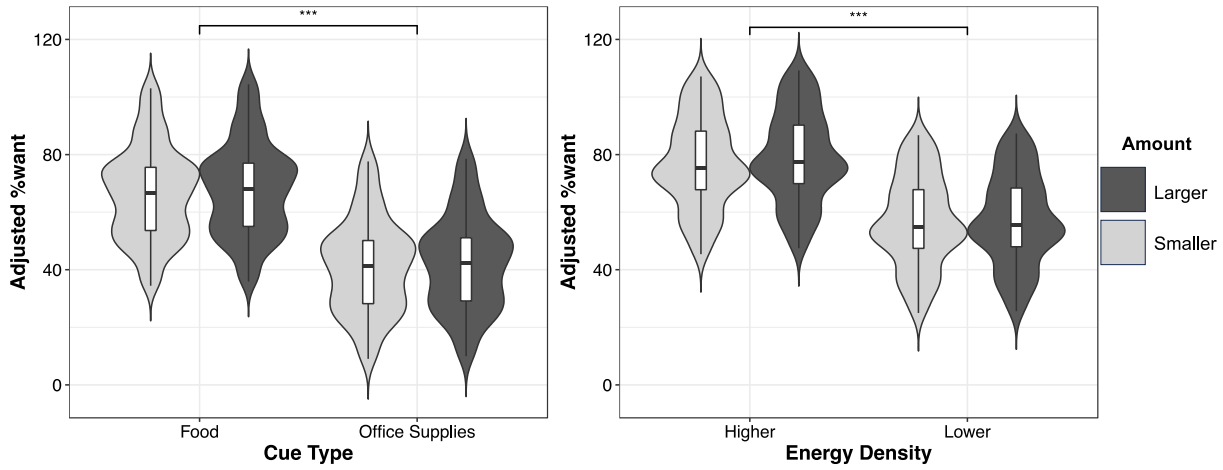

Figure 2.2 Adjusted percent wanting (%want) of items by cue type (left; food vs. office supplies) and energy density (right; higher vs. lower) presented in larger (dark grey) and smaller (light grey) amounts. Percent wanting was adjusted based on linear mixed effects models with subject as random effect, controlling for run. Significance code: ***, $p < 0.001$.

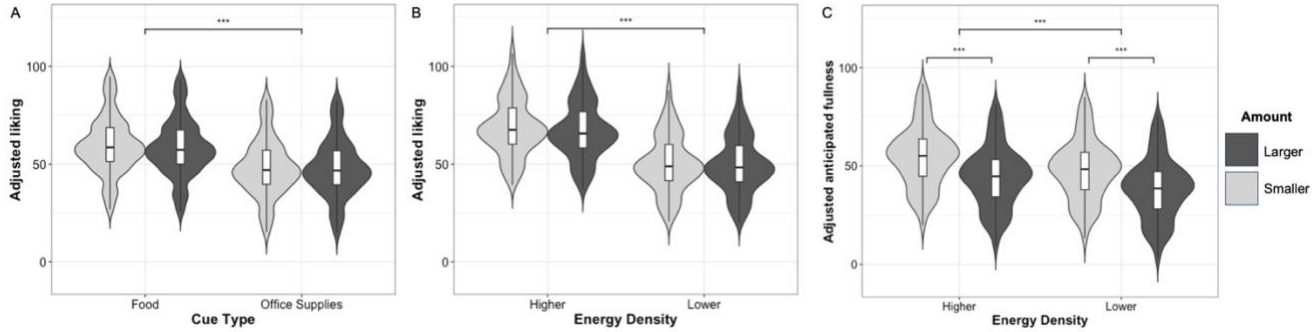

Figure 2.3 Image ratings by condition. Ratings were adjusted based on linear mixed effects models with subject as random effect, controlling for run. (A) Adjusted liking of items by cue type (food vs. office supplies) presented in larger (dark grey) and smaller (light grey) amounts. (B) Adjusted liking of items by energy density (ED; higher-ED vs. lower-ED) presented in larger (dark grey) and smaller (light grey) amounts. (C) Adjusted anticipated fullness by ED (higher-ED vs. lower-ED) presented in larger (dark grey) and smaller (light grey) amounts. Significance code: ***, $p < 0.001$.

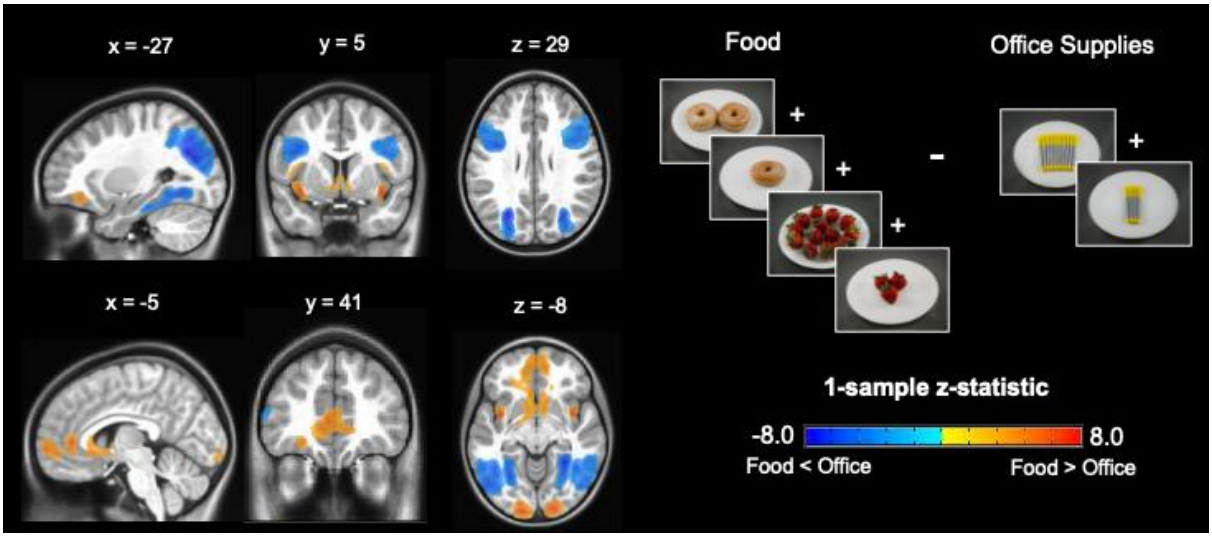

Figure 2.4 Neural response to cue type. Coordinates are in MNI space. Thresholded z-statistic map (voxel-wise $p < 0.001$, cluster-corrected to $p < 0.05$) of 1-sample t-test on cue type contrast (food - office supplies). Orange clusters show regions with greater responses to food cues than office supplies. Blue clusters show regions with greater responses to office supplies than food cues. Food and office supply images are examples of photographs presented to children during fMRI.

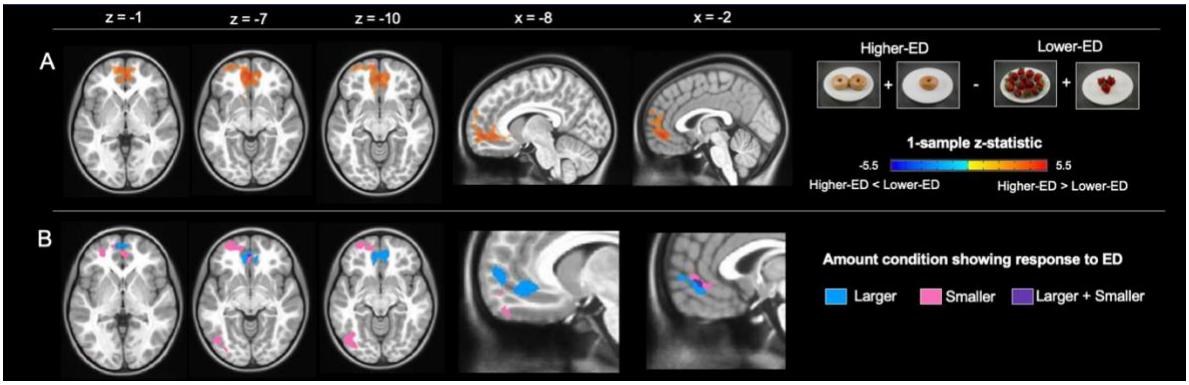

Figure 2.5 Neural responses to energy density (ED). Coordinates are in MNI space. Z-statistic maps were thresholded at voxel-wise $p < 0.001$ and cluster-corrected to $p < 0.05$. (A) Neural response to ED: thresholded z-statistic map for 1-sample t-test on energy density contrast (higher - lower) across larger and smaller amount conditions. Orange clusters show regions with greater responses to higher-ED than lower-ED foods. No regions showed greater responses to lower-ED than higher-ED foods. Higher-ED and lower-ED food images are examples of photographs presented to children during fMRI. (B) ED combination map: z-statistic maps from separate 1-sample t-tests on ED contrasts for larger and smaller amount conditions were thresholded and binarized and then combined to show conjunction and disjunction in the extent of responses to ED. Colors reflect whether voxels exhibited responses to ED (higher vs. lower) for larger amounts (blue), smaller amounts (pink), or both smaller and larger amounts (purple).

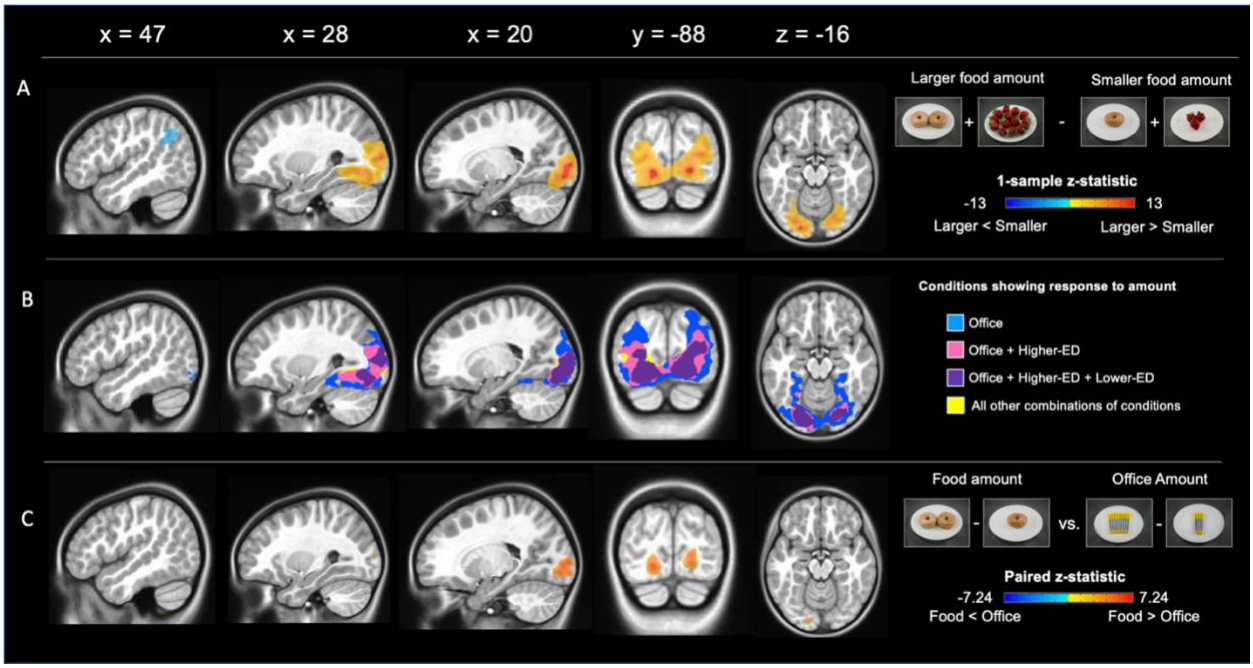

Figure 2.6 BOLD responses to amount. Coordinates are in MNI space. Z-statistic maps were thresholded at voxel-wise $p < 0.001$ and cluster-corrected to $p < 0.05$. (A) BOLD response to food amount: thresholded z-statistic map for 1-sample t-test on food amount contrast across higher- and lower-ED food conditions (i.e., larger food amounts (higher-ED + lower-ED) > smaller food amounts (higher-ED + lower-ED)). Orange clusters show regions with greater responses to larger food amounts than smaller food amounts. Blue clusters show regions with greater responses to smaller food amounts than larger food amounts. Larger and smaller amount food images are examples of photographs presented to children during fMRI. (B) Amount combination map: z-statistics maps from separate 1-sample t-tests on amount contrasts (larger > smaller) for higher-ED, lower-ED, and office supply conditions were thresholded and binarized and then combined to show conjunction and disjunction in the extent of responses to amount. Colors reflect whether voxels exhibited responses to amount (larger vs. smaller) for office supplies (blue), office supplies and higher-ED foods (pink), or all conditions (purple), or other combinations of conditions (e.g., higher-ED foods, higher-ED + lower-ED foods; yellow). (C) BOLD response to amount by cue type: thresholded z-statistic map for paired t-test comparing BOLD responses to amount (larger > smaller) between food and office supply conditions. Orange clusters show regions with greater responses to food amount than office supply amount. No regions showed greater responses to office supply amount than food amount. Food and office supply images are examples of photographs presented to children during fMRI.

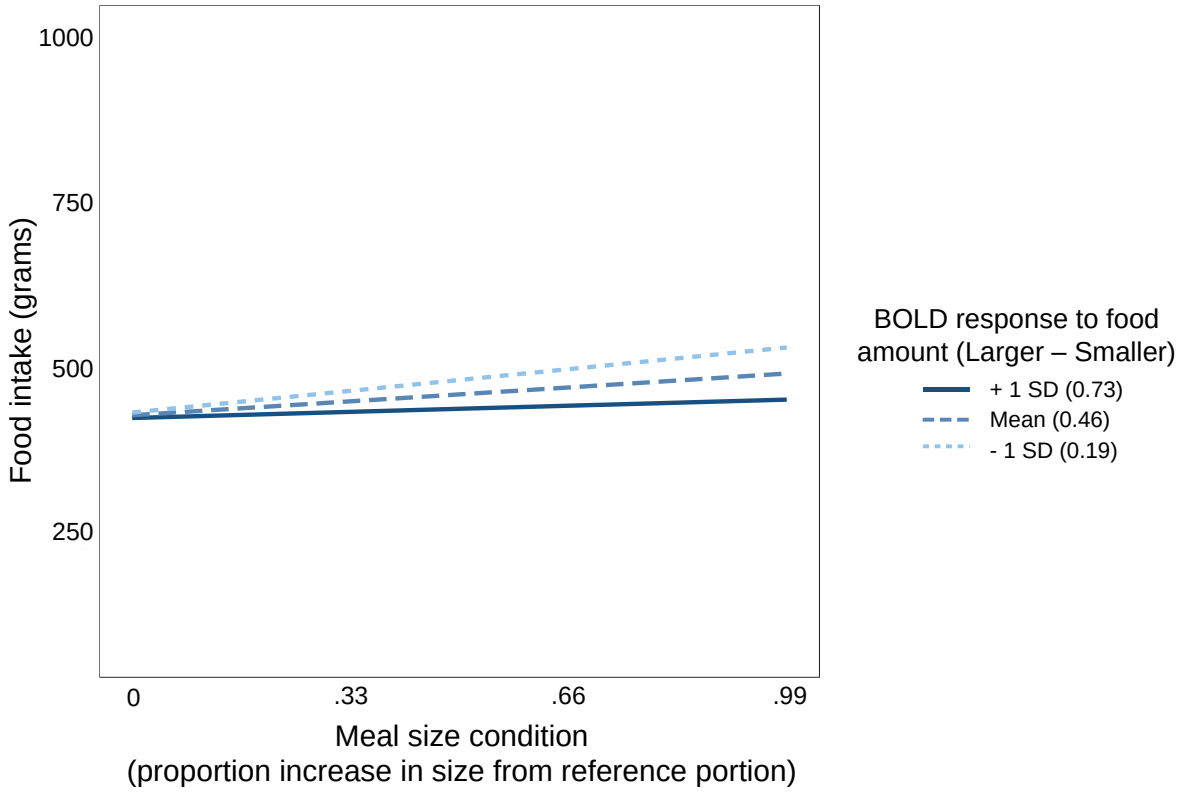

Figure 2.7 Interaction between BOLD responses to food amount (larger > smaller) and laboratory meal size condition on food intake. BOLD responses were extracted from a cluster extending through visual and parahippocampal areas that showed greater responses to larger > smaller food amounts in a 1-sample t-test (peak = -20, -88, -16). Regression lines for the association between meal size condition (i.e., proportion increase in size from reference portion; x-axis) and food intake in grams (y-axis) are plotted for three values of BOLD response to food amount: 1 SD below the mean (dotted line), the mean (dashed line), and 1 SD above the mean (solid line).

5. Supplement

5.1. Methods

Mock-MRI protocol

On visits 4 and 5, children received training for the MRI across two sessions in a mock MRI environment. Using a protocol developed in our lab [65] children were familiarized with the scanning environment in two stages: 1) seeing the mock scanner and asking questions (visit 4) and 2) completing a mock scanning session in which they viewed non-food items (stuffed animals) and experienced simulated MRI sounds (visit 5). During the mock scanning session, children practiced using button boxes to indicate their wanting of the items they saw. Similar to the food-cue task, children were instructed to answer the question "Do you want this?" for each item by selecting either "Do not want/Frown face" or "Want/Smiley face" with their dominant hand.

fMRI pre-processing

Results included in this manuscript come from preprocessing performed using fMRIPrep 20.2.3 (Esteban, Markiewicz, et al. (2018); Esteban, Blair, et al. (2018); RRID:SCR_016216), which is based on Nipype 1.6.1 (Gorgolewski et al. (2011); Gorgolewski et al. (2018); RRID:SCR_002502).

Anatomical data preprocessing. A total of 1 T1-weighted (T1w) images were found within the input BIDS dataset.The T1-weighted (T1w) image was corrected for intensity non-uniformity (INU) with N4BiasFieldCorrection (Tustison et al. 2010), distributed with ANTs 2.3.3 (Avants et al. 2008, RRID:SCR_004757), and used as T1w-reference throughout the workflow. The T1w-reference was then skull-stripped with a Nipype implementation of the antsBrainExtraction.sh workflow (from ANTs), using OASIS30ANTs as target template. Brain

tissue segmentation of cerebrospinal fluid (CSF), white-matter (WM) and gray-matter (GM) was performed on the brain-extracted T1w using fast (FSL 5.0.9, RRID:SCR_002823, Zhang, Brady, and Smith 2001). Brain surfaces were reconstructed using recon-all (FreeSurfer 6.0.1, RRID:SCR_001847, Dale, Fischl, and Sereno 1999), and the brain mask estimated previously was refined with a custom variation of the method to reconcile ANTs-derived and FreeSurfer-derived segmentations of the cortical gray-matter of Mindboggle (RRID:SCR_002438, Klein et al. 2017). Volume-based spatial normalization to three standard spaces (MNIPediatricAsym:cohort-3, MNI152NLin2009cAsym, MNI152NLin6Asym) was performed through nonlinear registration with antsRegistration (ANTs 2.3.3), using brain-extracted versions of both T1w reference and the T1w template. The following templates were selected for spatial normalization: MNI's unbiased standard MRI template for pediatric data from the 4.5 to 18.5y age range [(???), RRID:SCR_008796; TemplateFlow ID: MNIPediatricAsym:cohort-3], ICBM 152 Nonlinear Asymmetrical template version 2009c [Fonov et al. (2009), RRID:SCR_008796; TemplateFlow ID: MNI152NLin2009cAsym], FSL's MNI ICBM 152 non-linear 6th Generation Asymmetric Average Brain Stereotaxic Registration Model [Evans et al. (2012), RRID:SCR_002823; TemplateFlow ID: MNI152NLin6Asym],

Functional data preprocessing. For each of the 6 BOLD runs found per subject (across all tasks and sessions), the following preprocessing was performed. First, a reference volume and its skull-stripped version were generated using a custom methodology of fMRIPrep. A B0-nonuniformity map (or fieldmap) was estimated based on a phase-difference map calculated with a dual-echo GRE (gradient-recall echo) sequence, processed with a custom workflow of SDCFlows inspired by the epidewarp.fsl script and further improvements in HCP Pipelines (Glasser et al. 2013). The fieldmap was then co-registered to the target EPI (echo-planar

imaging) reference run and converted to a displacements field map (amenable to registration tools such as ANTs) with FSL's fugue and other SDCflows tools[1]. Based on the estimated susceptibility distortion, a corrected EPI (echo-planar imaging) reference was calculated for a more accurate co-registration with the anatomical reference. The BOLD reference was then co-registered to the T1w reference using bbregister (FreeSurfer) which implements boundary-based registration (Greve and Fischl 2009). Co-registration was configured with six degrees of freedom. Head-motion parameters with respect to the BOLD reference (transformation matrices, and six corresponding rotation and translation parameters) are estimated before any spatiotemporal filtering using mcflirt (FSL 5.0.9, Jenkinson et al. 2002). BOLD runs were slice-time corrected using 3dTshift from AFNI 20210206 (Cox and Hyde 1997, RRID:SCR_005927). The BOLD time-series were resampled onto the following surfaces (FreeSurfer reconstruction nomenclature): fsaverage5. The BOLD time-series (including slice-timing correction when applied) were resampled onto their original, native space by applying a single, composite transform to correct for head-motion and susceptibility distortions. These resampled BOLD time-series will be referred to as preprocessed BOLD in original space, or just preprocessed BOLD. The BOLD time-series were resampled into several standard spaces, correspondingly generating the following spatially-normalized, preprocessed BOLD runs: MNIPediatricAsym:cohort-3, MNI152NLin2009cAsym. First, a reference volume and its skull-stripped version were generated using a custom methodology of fMRIPrep. Automatic removal of motion artifacts

[1] Fieldmap-based susceptibility distortion correction (SDC) was used for all but one subject (N = 60). For one subject, *fieldmap-less* SDC was used due to a low-quality fieldmap (i.e., motion) and improved fMRIPrep output using the fieldmap-less approach. For this approach, a deformation field to correct for susceptibility distortions was estimated based on *fMRIPrep*'s *fieldmap-less* approach. The deformation field is that resulting from co-registering the BOLD reference to the same-subject T1w-reference with its intensity inverted (Wang et al. 2017; Huntenburg 2014). Registration is performed with antsRegistration (ANTs 2.3.3), and the process regularized by constraining deformation to be nonzero only along the phase-encoding direction, and modulated with an average fieldmap template (Treiber et al. 2016).

using independent component analysis (ICA-AROMA, Pruim et al. 2015) was performed on the preprocessed BOLD on MNI space time-series after removal of non-steady state volumes and spatial smoothing with an isotropic, Gaussian kernel of 6mm FWHM (full-width half-maximum). Corresponding "non-aggresively" denoised runs were produced after such smoothing. Additionally, the "aggressive" noise-regressors were collected and placed in the corresponding confounds file. Several confounding time-series were calculated based on the preprocessed BOLD: framewise displacement (FD), DVARS and three region-wise global signals. FD was computed using two formulations following Power (absolute sum of relative motions, Power et al. (2014)) and Jenkinson (relative root mean square displacement between affines, Jenkinson et al. (2002)). FD and DVARS are calculated for each functional run, both using their implementations in Nipype (following the definitions by Power et al. 2014). The three global signals are extracted within the CSF, the WM, and the whole-brain masks. Additionally, a set of physiological regressors were extracted to allow for component-based noise correction (CompCor, Behzadi et al. 2007). Principal components are estimated after high-pass filtering the preprocessed BOLD time-series (using a discrete cosine filter with 128s cut-off) for the two CompCor variants: temporal (tCompCor) and anatomical (aCompCor). tCompCor components are then calculated from the top 2% variable voxels within the brain mask. For aCompCor, three probabilistic masks (CSF, WM and combined CSF+WM) are generated in anatomical space. The implementation differs from that of Behzadi et al. in that instead of eroding the masks by 2 pixels on BOLD space, the aCompCor masks are subtracted a mask of pixels that likely contain a volume fraction of GM. This mask is obtained by dilating a GM mask extracted from the FreeSurfer's aseg segmentation, and it ensures components are not extracted from voxels containing a minimal fraction of GM. Finally, these masks are resampled into BOLD space and

binarized by thresholding at 0.99 (as in the original implementation). Components are also calculated separately within the WM and CSF masks. For each CompCor decomposition, the k components with the largest singular values are retained, such that the retained components' time series are sufficient to explain 50 percent of variance across the nuisance mask (CSF, WM, combined, or temporal). The remaining components are dropped from consideration. The head-motion estimates calculated in the correction step were also placed within the corresponding confounds file. The confound time series derived from head motion estimates and global signals were expanded with the inclusion of temporal derivatives and quadratic terms for each (Satterthwaite et al. 2013). Frames that exceeded a threshold of 0.5 mm FD or 1.5 standardised DVARS were annotated as motion outliers. All resamplings can be performed with a single interpolation step by composing all the pertinent transformations (i.e. head-motion transform matrices, susceptibility distortion correction when available, and co-registrations to anatomical and output spaces). Gridded (volumetric) resamplings were performed using antsApplyTransforms (ANTs), configured with Lanczos interpolation to minimize the smoothing effects of other kernels (Lanczos 1964). Non-gridded (surface) resamplings were performed using mri_vol2surf (FreeSurfer).

Many internal operations of fMRIPrep use Nilearn 0.6.2 (Abraham et al. 2014, RRID:SCR_001362), mostly within the functional processing workflow. For more details of the pipeline, see the section corresponding to workflows in fMRIPrep's documentation.

Analyses

Imputation of missing pre-MRI fullness value. For the subject with missing pre-MRI fullness data, **t**hree pre-MRI fullness values were imputed from sex, age, and BMI percentile using multivariate imputation by chained equations in R [64] with 5 iterations per imputation. To

assess the impact of the imputed value on results, fMRI analyses were conducted with each of the three imputed values. Clusters were consistent (i.e., same peak voxels, minor differences in cluster size) across analyses with the 3 imputed values, so results using the median value are reported.

fMRI processing and individual-level analyses. For each individual, a "food-cue mask" was generated by taking the union of BOLD masks generated by fMRIprep for each Food-Cue run. Individual-level analyses were restricted to voxels included in an individual's food-cue mask. As fMRIprep registers to the middle slice during slice time correction, onset times used to model image conditions in GLMs were shifted by subtracting half a TR (i.e., 1 second) to align event onsets with fMRIprep output. To reduce the effects of MRI signal instability, the first two volumes of each run were censored from first-level analyses (following the automatically discarded volumes).

Group-level fMRI analyses. Group-level analyses were restricted to voxels scanned during the food-cue task in at least 80% of subjects included in the given analysis (i.e., voxels included in at least 80% of subject's individual-level food-cue masks); Figure S1.

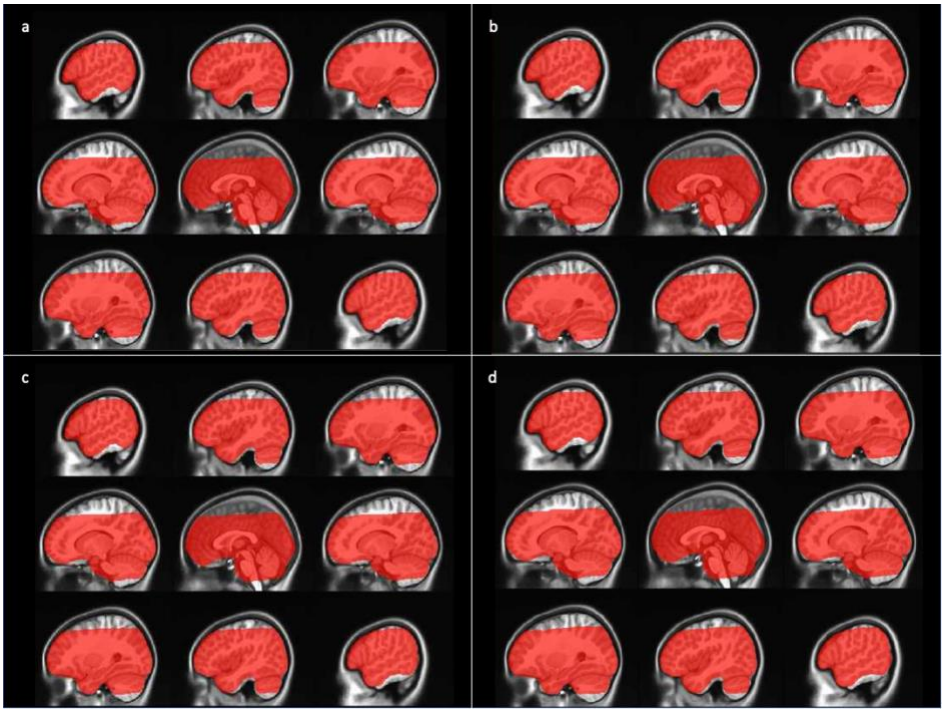

Figure S1. Masks (red) used for group-level analyses. Masks contain voxels scanned during the Food-Cue task for at least 80% of children included in (a) non-parametric analyses (n = 61), (b) parametric analyses of neural responses to energy density (n = 54), (c) parametric analyses of neural responses to food amount (n = 55), and (d) parametric analyses of neural responses to office supplies (n = 49). Masks are overlayed on Montreal Neurological Institute (MNI)'s unbiased standard MRI template for pediatric data cohort 3 (ages 7 – 11y). Masks extended from approximately Z = -52 to Z = 55.

Table S1. Descriptive statistics for demographic variables by inclusion status and overall

	Excluded (N=27)	Included (N=61)	Overall (N=88)
Sex			
Male	16 (59.3%)	29 (47.5%)	45 (51.1%)
Female	11 (40.7%)	32 (52.5%)	43 (48.9%)
Age, yrs			
Mean (SD)	7.79 (0.57)	7.82 (0.60)	7.79 (0.618)
Min, Max	7.03, 8.81	7.00, 8.99	7.00, 8.99
Race			
White	26 (96.3%)	59 (96.7%)	85 (96.6%)
American Indian/Alaskan Native	0 (0%)	0 (0%)	0 (0%)
Asian	1 (3.7%)	2 (3.3%)	3 (3.4%)
Black/African American	0 (0%)	0 (0%)	0 (0%)
Hawaiian/Pacific Islander	0 (0%)	0 (0%)	0 (0%)
Family Income			
< $51,000K	2 (7.4%)	9 (14.8%)	11 (12.5%)
51-100K	15 (55.6%)	27 (44.3%)	42 (47.7%)
> $100K	9 (33.3%)	23 (37.7%)	32 (36.4%)
Missing	1 (3.7%)	2 (3.3%)	3 (3.4%)
Maternal Education			
< BA	5 (18.5%)	13 (21.3%)	18 (20.5%)
BA	12 (44.4%)	29 (47.5%)	41 (46.6%)
> BA	10 (37.0%)	18 (29.5%)	28 (31.8%)
Missing	0 (0%)	1 (1.6%)	1 (1.1%)
Familial risk status			
Low	16 (59.3%)	36 (59.0%)	52 (59.1%)
High	11 (40.7%)	25 (41.0%)	36 (40.9%)
BMI percentile			
Mean (SD)	50.7 (24.5)	46.3 (25.4)	47.7 (25.0)
Min, Max	6.69, 89.5	3.91, 89.0	3.91, 89.5
Fat mass index			
Mean (SD)	4.63 (1.05)	4.39 (0.89)	4.46 (0.94)
Min, Max	3.02, 7.04	3.18, 7.42	3.02, 7.42

Table S2. Cluster size thresholds

	Cluster size threshold (1x1x1 mm^3)			
	Initial Models [a]		Sensitivity analyses [b]	
	for $p < 0.05$	for $p < 0.1$ [c]	for $p < 0.05$	for $p < 0.1$ [c]
1-sample t-tests				
Cue type contrast (food - office)	1,475	-	1,472	-
ED contrast (higher - lower), across amount	1,519	-	1,461	-
ED contrast (higher - lower), large amount	1,438	-	1,436	-
ED contrast (higher - lower), small amount	1,541	-	1,398	-
Amount contrast (larger – smaller), across foods	1,498		1,535	
Amount contrast (larger – smaller), High-ED foods	1,585	-	1,515	-
Amount contrast (larger – smaller), Low-ED foods	1,361	-	1,431	-
Amount contrast (larger – smaller), Office Supplies	1,521	-	1,647	-
Paired t-tests				
ED contrast (higher - lower) by amount (larger vs. smaller)	1,457	-	1,545	-
Cue type contrast (food - office) by amount (larger vs. smaller)	1,544	-	1,523	-
Parametric analyses (BOLD vs. percent wanting)				
Office supplies (1-sample t-test)	895	-	918	-
Larger food amounts (1-sample t-test)	1,205	-	1,266	-
Smaller food amounts (1-sample t-test)	1,118	-	1,160	-
Higher-ED foods (1-sample t-test)	1,486	-	1,372	-
Lower-ED foods (1-sample t-test)	1,323	-	1,293	-
By ED (higher vs. lower; paired t-test)	1,546	-	1,588	-
By food amount (larger vs. smaller; paired t-test)	1,243	-	1,265	-
2-sample t-tests – full analysis sample				
Cue type contrast by familial risk for obesity (high vs. low)	1,859	1,152	1,744	1,104
ED contrast by familial risk for obesity (high vs. low)	1,715	1,078	1,916	1,144
Food amount contrast by familial risk for obesity (high vs. low)	2,155	1,317	2,264	1,404
2-sample t-tests – measured maternal anthropometrics sample [d]				
Cue type contrast by familial risk for obesity (high vs. low)	1,743	1,112	-	-
ED contrast by familial risk for obesity (high vs. low)	1,630	999	-	-
Food amount contrast by familial risk for obesity (high vs. low)	2,125	1,244	-	-
Associations with FMI				
Cue type contrast (food - office)	1,437	897	1,447	909
ED contrast (higher – lower, across amount)	1,539	921	1,628	943
Food amount contrast (larger – smaller, across ED)	1,503	930	1,495	897

Note: Results from AFNI's 3dClustSim used with 3dttest++, using voxel-wise intensity $p < 0.001$ (cluster method: NN2, 2-sided test)

[a] Initial models included average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety (CAMS) as covariates

[b] Sensitivity analyses were the same as Initial models with the addition of a snack intake (yes/no) as a covariate

[c] Exploratory analyses with familial risk for obesity and fat mass index thresholded at $p < 0.1$

[d] Initial Models comparing BOLD responses between children and high and low familial risk for obesity (2-sample t-tests) were repeated in a reduced sample (N = 52) that only included children with measured maternal height and weight

Table S3. Regions showing parametric modulation of BOLD responses by percent wanting

Region	H	*k* [a]	Z [b]	*x*	*y*	*z*
BOLD response to higher-ED foods [1]						

n.s							
BOLD response to lower-ED foods [1]							
n.s							
BOLD response to larger food amounts [1]							
n.s							
BOLD response to smaller food amounts [1]							
n.s							
BOLD response to office supplies [1]							
n.s							
BOLD response to higher vs. lower ED [2]							
V4 / Fusiform gyrus	R	1,958	-4.48	28	-81	-8	
BOLD response to larger vs. smaller food amount [2]							
n.s							

[1] Results from 1-sample t-tests controlling for average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety (CAMS)
[2] Results from paired t-tests controlling for average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety (CAMS)
Cluster p-values were cluster-corrected to $p < 0.05$
[a] cluster-extent in 1x1x1 $mm^{3;}$ [b] peak cluster z-value derived from the general linear model
x, y, z: MNI coordinates of cluster peak; H: hemisphere; V4: fourth visual cortex; n.s: no clusters surviving cluster-correction

Table S4. Regions showing associations between BOLD responses and fat mass index

Region	H	*k* [a]	Z [b]	*x*	*y*	*z*	*p-value*
Response to cue type (food – office) vs. FMI							
n.s							
Response to ED (higher – lower) vs. FMI							
Dorsolateral PFC	L	1,262	4.54	-44	46	12	< 0.07
Response to food amount (larger – smaller) vs. FMI							
n.s							

Results from regressions with fat mass index (FMI) covariate, controlling for average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety (CAMS); Cluster p-values were cluster-corrected to $p < 0.1$
[a] cluster-extent in 1x1x1 $mm^{3;}$ [b] peak cluster z-value derived from the general linear model
x, y, z: MNI coordinates of cluster peak; H: hemisphere ; V1: primary visual cortex; n.s: no clusters surviving cluster-correction

Table S5. Regions showing BOLD response to cue type – sensitivity analyses with snack intake covariate

Effect	Region	H	*k* [a]	Z [b]	*x*	*y*	*z*
Food > Office Supplies	OFC	L	26451	6.37	-24	36	-14
	V1 / Inferior occipital gyrus	L	6421	7.51	-17	-98	-10
	V2 / Lingual gyrus	R	5360	7.84	19	-95	-9
	Posterior insula	L	3712	7.96	-37	3	-10
	Posterior insula	R	2844	7.31	37	5	-10
Food < Office Supplies	Inferior parietal cortex / middle occipital gyrus	L	50489	-7.84	-26	-67	29
	Parahippocampal area	R	46725	-7.61	30	-47	-8
	Inferior frontal sulcus / Prefrontal gyrus	L	16244	-6.35	-47	0	32
	dlPFC / Inferior frontal gyrus	R	13472	-5.83	45	25	22

Results from 1-sample t-test on cue type contrast (food - office supplies) controlling for average framewise displacement, sex, pre-MRI fullness, pre-MRI anxiety (CAMS), and pre-MRI snack intake (yes/no); Cluster p-values were cluster-corrected to $p < 0.05$

[a] cluster-extent in 1x1x1 $mm^{3;}$ [b] peak cluster z-value derived from the general linear model

x, y, z: MNI coordinates of cluster peak; H: hemisphere; V1: primary visual cortex; V2: secondary visual cortex

Table S6. Regions showing BOLD response to energy density – sensitivity analyses with snack intake covariate

Effect	Region	H	*k* [a]	Z [b]	*x*	*y*	*z*
BOLD response to ED across larger and smaller food amounts							
Higher > Lower	ACC / medial OFC	L	13531	5.40	-3	47	-8
BOLD response to ED for larger food amounts							
Higher > Lower	ACC / medial OFC	L	1788	4.37	-3	49	-8
BOLD response to ED for smaller food amounts							
Higher > Lower	Lateral OFC	L	2525	4.60	-24	59	-16
Higher < Lower	Ventral visual complex / fusiform gyrus	L	1565	-4.47	-35	-71	-16

Results from 1-sample t-tests on energy density (ED) contrast (higher - lower) controlling for average framewise displacement, sex, pre-MRI fullness, pre-MRI anxiety (CAMS), and pre-MRI snack intake (yes/no); Cluster p-values were cluster-corrected to $p < 0.05$

[a] cluster-extent in 1x1x1 $mm^{3;}$ [b] peak cluster z-value derived from the general linear model

x, y, z: MNI coordinates of cluster peak; H: hemisphere

Table S7. Regions showing BOLD response to amount – sensitivity analyses with snack intake covariate

Effect	Region	H	*k* [a]	Z [b]	*x*	*y*	*z*
BOLD response to food amount across higher- and lower-ED foods							
Larger > Smaller	V3 / Lingual gyrus	L	52423	13	-20	-87	-15
Larger < Smaller	Angular gyrus	R	2175	-4.66	47	-56	31
BOLD response to food amount for higher-ED foods							
Larger > Smaller	V2 / Middle occipital gyrus	L	42781	13	-15	-96	-3
BOLD response to amount for lower-ED foods							
Larger > Smaller	V1 / Calcarine gyrus	R	13528	13	15	-91	-8
Larger > Smaller	V3 / Lingual gyrus	L	12465	7.65	-16	-88	-12
BOLD response to amount for office supplies							
Larger > Smaller	V3 / Lingual gyrus	L	71340	13	-20	-88	-17

Results from 1-sample t-tests on amount contrasts (larger - smaller) controlling for average framewise displacement, sex, pre-MRI fullness, pre-MRI anxiety (CAMS), and pre-MRI snack intake (yes/no); Cluster p-values cluster-corrected to $p < 0.05$

[a] cluster-extent in 1x1x1 $mm^{3;}$ [b] peak cluster z-value derived from the general linear model (maximum value output by AFNI is 13)

x, y, z: MNI coordinates of cluster peak; H: hemisphere; V1: primary visual cortex, V2: secondary visual cortex, V3: third visual cortex

Table S8. Regions showing differential BOLD responses to amount by cue type and energy density (ED) – sensitivity analyses with snack intake covariate

Effect	Region	H	*k* [a]	Z [b]	*x*	*y*	*z*
BOLD response to amount (larger - smaller) by cue type (food vs. office)							
Food > Office Supplies	V2 / Calcarine Gyrus	L	4724	7.10	-15	-94	-7
	V1 / Calcarine Gyrus	R	3905	6.65	18	-91	0
BOLD response to food amount (larger - smaller) by ED (higher vs. lower)							
n.s							

Results from paired t-tests using first-level amount contrasts (larger - smaller) controlling for average framewise displacement, sex, pre-MRI fullness, pre-MRI anxiety (CAMS), and pre-MRI snack intake (yes/no); Cluster p-values were cluster-corrected to $p < 0.05$

[a] cluster-extent in 1x1x1 $mm^{3;}$ [b] peak cluster z-value derived from the general linear model

x, y, z: MNI coordinates of cluster peak; H: hemisphere; V1: primary visual cortex, V2: secondary visual cortex; n.s: no clusters surviving cluster-correction

Table S9. Regions showing parametric modulation of BOLD responses by percent wanting – sensitivity analyses

Region	H	*k* [a]	Z [b]	*x*	*y*	*z*
BOLD response to higher-ED foods [1]						
n.s						
BOLD response to lower-ED foods [1]						
n.s						
BOLD response to larger food amounts [1]						
n.s						
BOLD response to smaller food amounts [1]						
n.s						
BOLD response to office supplies [1]						
n.s						
BOLD response to higher vs. lower ED [2]						
V4 / Fusiform gyrus	R	1,641	-4.33	28	-81	-8
BOLD response to larger vs. smaller food amount [2]						
n.s						

[1] Results from 1-sample t-tests controlling for average framewise displacement, sex, pre-MRI fullness, pre-MRI anxiety (CAMS), and pre-MRI snack intake (yes/no)
[2] Results from paired t-tests controlling for average framewise displacement, sex, pre-MRI fullness, pre-MRI anxiety (CAMS), and pre-MRI snack intake (yes/no)
Cluster p-values were cluster-corrected to $p < 0.05$
[a] cluster-extent in 1x1x1 $mm^{3;}$ [b] peak cluster z-value derived from the general linear model
x, y, z: MNI coordinates of cluster peak; H: hemisphere; V4: fourth visual cortex; n.s: no clusters surviving cluster-correction

Table S10. Regions showing associations between BOLD responses and fat mass index – sensitivity analyses

Region	H	*k* [a]	Z [b]	*x*	*y*	*z*	*p*
Response to cue type (food – office) vs. FMI							
n.s							
Response to ED (higher – lower) vs. FMI							
Dorsolateral PFC	L	1395	4.52	-44	45	12	P < 0.06
V1 / superior occipital gyrus	L	1052	4.33	-9	-98	3	P < 0.09
Response to food amount (larger – smaller) vs. FMI							
n.s							

Results from regressions with fat mass index (FMI) covariate, controlling for average framewise displacement, sex, pre-MRI fullness, pre-MRI anxiety (CAMS), and pre-MRI snack intake (yes/no); Cluster p-values were cluster-corrected to $p < 0.1$
[a] cluster-extent in 1x1x1 $mm^{3;}$ [b] peak cluster z-value derived from the general linear model
x, y, z: MNI coordinates of cluster peak; H: hemisphere; V1: primary visual cortex; n.s: no clusters surviving cluster-correction

Table S11. Estimates for mixed-effects models predicting food intake in grams from BOLD responses to food amount (larger > smaller)

	L V3 / Lingual gyrus	R Angular gyrus
Predictors	B (se)	B (se)
(Intercept)	-90.83 (244.35)	-109.18 (241.12)
Pre-meal fullness	-0.52 (0.27)	-0.56 * (0.27)
Average meal food liking	9.75 (19.32)	10.61 (19.63)
Meal order	-5.17 (4.76)	-4.43 (4.83)
Sex [Female]	-20.20 (38.65)	-24.80 (38.81)
BMI	33.90 * (14.65)	35.04 * (14.78)
Meal portion size	121.54 *** (28.46)	53.81 ** (17.89)
BOLD (larger food amounts > smaller food amounts)	-14.95 (76.76)	44.18 (84.13)
Meal portion size × BOLD	-128.93 * (53.41)	-48.85 (59.64)
Marginal R^2 / Conditional R^2	0.139 / 0.785	0.117 / 0.777

** p<0.05 ** p<0.01 *** p<0.001;* BOLD responses were extracted from clusters identified in a 1-sample t-test on BOLD responses to food amount (larger – smaller) controlling for average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety (CAMS)

Table S12. Estimates for mixed-effects models predicting food intake in kcal from BOLD responses to food amount (larger > smaller)

	L V3 / Lingual gyrus	R Angular gyrus
Predictors	B (se)	B (se)
(Intercept)	-462.64 (304.06)	-399.92 (293.39)
Pre-meal fullness	-0.89 * (0.38)	-0.93 * (0.38)
Average meal food liking	38.71 (27.45)	34.97 (27.36)
Meal order	5.52 (7.15)	5.83 (7.14)
Sex [Female]	-66.76 (47.73)	-53.76 (46.89)
BMI	52.80 ** (18.08)	53.57 ** (17.85)
Meal portion size	157.44 *** (42.70)	141.09 *** (26.45)
BOLD (larger food amounts > smaller food amounts)	104.83 (97.51)	107.14 (104.73)
Meal portion size × BOLD	-61.64 (80.18)	69.19 (88.15)
Marginal R^2 / Conditional R^2	0.191 / 0.724	0.204 / 0.724

** p<0.05 ** p<0.01 *** p<0.001;* BOLD responses were extracted from clusters identified in a 1-sample t-test on BOLD responses to food amount (larger – smaller) controlling for average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety (CAMS)

Table S13. Estimates for mixed-effects models predicting food intake in grams from BOLD responses to cue type (food > office supplies)

	L Inferior parietal cortex	R Parahippoca-mpal area	L Anterior cingulate cortex	L Inferior frontal sulcus	R Dorsolateral PFC	L V1	R V1	L Posterior insula	R Posterior insula
Predictors	B (se)	B (se)	B (se)	B (se)	B (se)	B (se)	B (se)	B (se)	B (se)
(Intercept)	-127.90 (241.26)	-120.19 (241.24)	-153.23 (239.79)	-101.88 (240.78)	-98.96 (243.45)	-70.86 (245.44)	-75.36 (246.36)	-112.12 (241.62)	-90.23 (245.55)
Pre-meal fullness	-0.56 * (0.27)	-0.56 * (0.27)	-0.56 * (0.27)	-0.55 * (0.27)	-0.55 * (0.27)	-0.54 * (0.27)	-0.56 * (0.27)	-0.56 * (0.27)	-0.55 * (0.27)
Average meal food liking	8.76 (19.53)	9.06 (19.53)	7.41 (19.45)	7.82 (19.52)	8.04 (19.58)	8.80 (19.52)	10.37 (19.50)	8.54 (19.54)	8.49 (19.68)
Meal order	-4.46 (4.84)	-4.46 (4.83)	-4.59 (4.83)	-4.50 (4.83)	-4.50 (4.84)	-4.45 (4.83)	-4.17 (4.81)	-4.49 (4.87)	-4.47 (4.84)
Sex [Female]	-21.30 (38.66)	-23.41 (38.68)	-23.33 (38.11)	-26.63 (38.57)	-25.86 (38.72)	-32.55 (39.67)	-30.18 (39.26)	-25.66 (38.66)	-24.66 (38.72)
BMI	37.40 * (14.90)	36.26 * (14.87)	36.22 * (14.58)	34.14 * (14.77)	34.32 * (15.02)	33.81 * (14.80)	33.83 * (14.84)	34.81 * (14.78)	34.39 * (14.85)
Meal portion size	58.25 ** (21.17)	67.35 ** (21.30)	71.36 *** (20.29)	57.88 ** (19.82)	60.93 ** (19.59)	57.50 ** (20.07)	43.66 * (19.73)	62.94 ** (22.07)	60.70 ** (21.10)
BOLD (food > office supplies)	88.87 (93.57)	47.95 (99.33)	133.00 (87.11)	-47.25 (82.68)	-16.16 (77.41)	-46.68 (57.72)	-54.64 (54.06)	35.98 (111.78)	-43.59 (110.23)
Portion size × BOLD	-17.30 (65.91)	22.91 (70.10)	-40.80 (62.85)	-19.50 (58.69)	-5.63 (54.38)	14.01 (40.03)	52.64 (37.72)	-3.16 (81.84)	8.31 (81.05)
Marginal R^2 / Conditional R^2	0.125 / 0.776	0.121 / 0.777	0.137 / 0.777	0.124 / 0.777	0.118 / 0.777	0.125 / 0.777	0.123 / 0.779	0.117 / 0.776	0.042 / 0.770

** $p<0.05$ ** $p<0.01$ *** $p<0.001$;* BOLD responses were extracted from clusters identified in a 1-sample t-test on BOLD responses to cue type (food – office supplies) controlling for average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety (CAMS)

Table S14. Estimates for mixed-effects models predicting food intake in kcal from BOLD responses to cue type (food > office supplies)

	L Inferior parietal cortex	R Parahippoca-mpal area	L Anterior cingulate cortex	L Inferior frontal sulcus	R Dorsolateral PFC	L V1	R V1	L Posterior insula	R Posterior insula
Predictors	B (se)	B (se)	B (se)	B (se)	B (se)	B (se)	B (se)	B (se)	B (se)
(Intercept)	-375.87 (301.32)	-377.19 (299.78)	-438.88 (298.75)	-383.73 (297.51)	-379.82 (301.61)	-344.50 (303.59)	-380.55 (306.24)	-397.35 (299.50)	-350.42 (303.22)
Pre-meal fullness	-0.85 * (0.38)	-0.87 * (0.38)	-0.87 * (0.38)	-0.86 * (0.38)	-0.86 * (0.38)	-0.85 * (0.38)	-0.87 * (0.38)	-0.87 * (0.38)	-0.84 * (0.38)
Average meal food liking	32.50 (27.38)	33.72 (27.38)	33.43 (27.31)	33.77 (27.33)	34.15 (27.46)	33.84 (27.35)	35.79 (27.46)	35.16 (27.41)	31.45 (27.52)
Meal order	6.02 (7.12)	5.74 (7.14)	5.65 (7.14)	5.78 (7.14)	5.75 (7.15)	5.72 (7.14)	5.95 (7.15)	5.81 (7.20)	5.47 (7.14)
Sex [Female]	-60.52 (47.97)	-62.18 (47.75)	-58.80 (47.20)	-62.75 (47.33)	-61.46 (47.64)	-70.73 (48.76)	-62.87 (48.47)	-61.09 (47.61)	-57.90 (47.51)
BMI	52.31 ** (18.49)	51.30 ** (18.35)	53.35 ** (18.05)	50.79 ** (18.12)	51.16 ** (18.47)	50.52 ** (18.19)	51.65 ** (18.32)	51.98 ** (18.20)	50.78 ** (18.22)
Meal portion size	102.27 ** (31.16)	113.40 *** (31.44)	142.23 *** (29.99)	120.37 *** (29.28)	124.97 *** (28.94)	138.37 *** (29.66)	120.64 *** (29.31)	129.34 *** (32.63)	147.08 *** (31.13)
BOLD (food > office supplies)	55.25 (118.77	-7.67 (125.62)	138.11 (110.61)	-70.66 (104.16)	-18.70 (97.68)	-44.02 (72.72)	-23.54 (68.41)	24.61 (141.22)	-53.64 (138.75)
Portion size × BOLD	-115.58 (97.03)	-71.11 (103.51)	-59.03 (92.93)	-38.72 (86.75)	-17.29 (80.39)	-26.74 (59.15)	23.91 (56.02)	-1.07 (120.96)	-95.97 (119.45)
Marginal R^2 / Conditional R^2	0.187 / 0.728	0.188 / 0.726	0.198 / 0.726	0.198 / 0.727	0.188 / 0.726	0.196 / 0.727	0.188 / 0.726	0.187 / 0.725	0.195 / 0.727

** p<0.05 ** p<0.01 *** p<0.001;* BOLD responses were extracted from clusters identified in a 1-sample t-test on BOLD responses to cue type (food – office supplies) controlling for average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety (CAMS)

Table S15. Estimates for mixed-effects models predicting food intake in grams from BOLD responses to ED (higher > lower) across food amount

	L ACC / medial OFC
Predictors	B (se)
(Intercept)	-102.79 (241.65)
Pre-meal fullness	-0.57 * (0.27)
Average meal food liking	8.83 (19.48)
Meal order	-4.29 (4.84)
sex [Female]	-22.52 (39.05)
BMI	33.79 * (14.93)
Meal portion size	69.30 *** (18.83)
BOLD (higher-ED foods > lower-ED foods)	34.43 (51.71)
Meal portion size × BOLD	-21.33 (35.97)
Marginal R^2 / Conditional R^2	0.119 / 0.777

** p<0.05 ** p<0.01 *** p<0.001;* BOLD responses were extracted from the cluster identified in a 1-sample t-test on BOLD responses to energy density (higher – lower) across food amount, controlling for average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety (CAMS)

Table S16. Estimates for mixed-effects models predicting food intake in kcal from BOLD responses to ED (higher > lower) across food amount

	L ACC / medial OFC
Predictors	B (se)
(Intercept)	-394.54 (299.98)
Pre-meal fullness	-0.85 * (0.38)
Average meal food liking	34.46 (27.33)
Meal order	5.45 (7.15)
sex [Female]	-63.37 (48.15)
BMI	53.20 ** (18.42)
Meal portion size	116.17 *** (27.82)
BOLD (higher-ED foods > lower-ED foods)	-39.62 (65.34)
Meal portion size × BOLD	39.27 (53.14)
Marginal R^2 / Conditional R^2	0.188 / 0.726

** p<0.05 ** p<0.01 *** p<0.001;* BOLD responses were extracted from the cluster identified in a 1-sample t-test on BOLD responses to energy density (higher – lower) across food amount, controlling for average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety (CAMS)

Table S17. Estimates for mixed-effects models predicting food intake in grams from BOLD responses to office supply amount (larger > smaller)

	L V3 / Lingual gyrus
Predictors	B (se)
(Intercept)	-129.15 (241.20)
Pre-meal fullness	-0.57 * (0.27)
Average meal food liking	6.38 (19.67)
Meal order	-4.48 (4.84)
Sex [Female]	-25.28 (38.45)
BMI	35.42 * (14.70)
Meal portion size	65.79 **(23.28)
BOLD (larger amount office supplies > smaller amount office supplies)	79.41 (87.92)
Meal portion size × BOLD	-12.39 (62.64)
Marginal R^2 / Conditional R^2	0.125 / 0.777

** p<0.05 ** p<0.01 *** p<0.001;* BOLD responses were extracted from clusters identified in a 1-sample t-test on BOLD responses to office supply amount (larger > smaller) controlling for average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety (CAMS)

Table S18. Estimates for mixed-effects models predicting food intake in kcal from BOLD responses to office supply amount (larger > smaller)

	L V3 / Lingual gyrus
Predictors	B (se)
(Intercept)	-397.01 (300.21)
Pre-meal fullness	-0.88 * (0.38)
Average meal food liking	35.32 (27.65)
Meal order	5.92 (7.15)
Sex [Female]	-61.05 (47.59)
BMI	52.17 ** (18.20)
Meal portion size	119.64 *** (34.42)
BOLD (larger amount office supplies > smaller amount office supplies)	3.75 (111.72)
Meal portion size × BOLD	32.6 (92.59)
Marginal R^2 / Conditional R^2	0.188 / 0.726

** p<0.05 ** p<0.01 *** p<0.001;* BOLD responses were extracted from clusters identified in a 1-sample t-test on BOLD responses to office supply amount (larger > smaller) controlling for average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety (CAMS)

Table S19. Estimates for mixed-effects models predicting food intake in grams from BOLD responses to amount (larger > smaller) for food and office supplies

	L V2		R V1	
Predictors	B (se)	B (se)	B (se)	B (se)
(Intercept)	-115.67 (240.41)	-139.71 (243.90)	-109.10 (250.70)	-48.53 (242.25)
Pre-meal fullness	-0.57 * (0.27)	-0.57 * (0.27)	-0.53 (0.27)	-0.56 * (0.27)
Average meal food liking	5.79 (19.70)	6.58 (19.73)	8.58 (19.43)	7.43 (19.44)
Meal order	-4.48 (4.83)	-4.47 (4.84)	-4.73 (4.81)	-4.60 (4.85)
Sex [Female]	-29.30 (38.76)	-29.03 (38.82)	-24.34 (38.80)	-14.00 (38.85)
BMI	34.52 * (14.72)	35.89 * (14.76)	34.61 * (14.82)	34.76 * (14.53)
Meal portion size	70.52 ** (25.96)	66.45 * (28.98)	110.45 ** (38.46)	72.80 * (35.56)
BOLD, office supply amount (larger > smaller)	82.28 (88.10)		68.60 (88.55)	
Meal portion size × BOLD (office supply amount)	-24.20 (62.05)		-10.58 (62.46)	
BOLD, food amount (larger – smaller)		8.81 (74.81)		-74.18 (59.94)
Meal portion size × BOLD (food amount)		-71.18 (52.62)		-13.83 (42.39)
Marginal R^2 / Conditional R^2	0.123 / 0.777	0.119 / 0.779	0.122 / 0.777	0.141 / 0.777

** p<0.05 ** p<0.01 *** p<0.001;* BOLD responses were extracted from clusters identified in a paired t-test comparing the response to amount (larger > smaller) between food and office supply conditions controlling for average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety (CAMS)

Table S20. Estimates for mixed-effects models predicting food intake in kcal from BOLD responses to amount (larger > smaller) for food and office supplies

	L V2		R V1	
Predictors	B (se)	B (se)	B (se)	B (se)
(Intercept)	-395.23 (299.34)	-477.54 (308.74)	-388.98 (303.03)	-407.14 (305.15)
Pre-meal fullness	-0.87 * (0.39)	-0.88 * (0.38)	-0.87 * (0.38)	-0.87 * (0.38)
Average meal food liking	34.86 (27.73)	35.86 (27.29)	35.19 (27.73)	35.48 (27.39)
Meal order	5.79 (7.15)	5.73 (7.15)	5.78 (7.15)	5.99 (7.17)
Sex [Female]	-60.72 (47.94)	-64.72 (47.42)	-60.12 (47.96)	-64.44 (48.61)
BMI	52.18 ** (18.21)	53.43 ** (18.11)	51.97 ** (18.25)	52.19 ** (18.17)
Meal portion size	132.56 *** (38.41)	146.66 * (57.14)	132.37 ** (42.85)	114.18 * (52.59)
BOLD, office supply amount (larger > smaller)	2.02 (111.96)		-9.35 (112.35)	
Meal portion size × BOLD (office supply amount)	-9.95 (91.77)		-8.09 (92.33)	
BOLD, food amount (larger – smaller)		92.07 (93.89)		15.07 (76.72)
Meal portion size × BOLD (food amount)		-26.01 (78.20)		19.55 (62.69)
Marginal R^2 / Conditional R^2	0.186 / 0.725	0.194 / 0.725	0.187 / 0.725	0.188 / 0.725

** p<0.05 ** p<0.01 *** p<0.001;* BOLD responses were extracted from clusters identified in a paired t-test comparing the response to amount (larger > smaller) between food and office supply conditions controlling for average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety (CAMS)

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Chapter 3 Cerebellar response to visual portion size cues is associated with the portion size effect in children

Fuchs BA, Pearce AL, Rolls BJ, Wilson SJ, Rose EJ, Geier CF, Garavan H, Keller KL.

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Abstract

Susceptibility to eating more in response to large portions (i.e., the portion size effect; PSE) has been associated with neural responses to food portion size cues, but prior analyses only examined associations in a limited number of brain regions implicated in reward and cognitive control. Thus, the present study examined how neural responses to portion size within the appetitive network and cerebellum relate to changes in food intake as portions increase. Children without obesity (N=63; 55% female) viewed images of larger and smaller portions of food during fMRI and ate four meals that varied in portion size. Individual-level linear and quadratic relationships between intake and portion size were estimated. Response to portion size (larger vs. smaller) in cerebellar lobules IV-VI was negatively associated with the quadratic portion size slope; greater activation to larger portions was associated with smaller increases in intake as portions got larger, while greater activation to smaller portions was associated with greater increases in intake as portions got larger. Within the appetitive network, neural responses were not associated with linear or quadratic portion size slopes. Decreased cerebellar activation in response larger amounts of food may increase children's susceptibility to overeating when faced with "supersized" portions of food.

1. Introduction

Serving larger portions of food increases intake across a variety of food types [1] and environmental settings [2,3]. The tendency to consume more food in terms of weight and energy when exposed to larger portions (i.e., "the portion size effect"—PSE) emerges as early as infancy [4] and is evident across the lifespan [1]. The PSE is persistent up to five days with no compensation evident in children, leading to sustained increases in energy intake [5]. As excess energy intake is associated with the development of obesity and long-term health risks [6,7], it is important to understand the neurobiological mechanisms that underly this behavior.

The control of eating behavior involves a network of cortical (e.g., prefrontal cortex, insula) and subcortical (e.g., basal ganglia, amygdala, hippocampus, hypothalamus) regions that integrate exteroceptive signals (e.g., visual portion size cues) with interoceptive signals from the gut and periphery [8]. This network contributes to a range of processes relevant for appetitive behavior, including energy homeostasis, perception, reward responsiveness, learning, memory, cognitive regulation, and interoception [9–11]. Presentation of visual food cues (e.g., images) elicits patterns of neural engagement across the appetitive network [12] that are associated with eating behaviors in both children [13–15] and adults [16]. For example, prior analyses from our group [15] found that greater activation to images of larger (vs. smaller) portions of food in orbitofrontal cortex (OFC) and ventromedial prefrontal cortex (vmPFC) was positively associated with children's food intake in response to larger food portions, whereas the opposite relationship was observed in inferior frontal gyrus (IFG). These data suggest that susceptibility to the PSE is associated with neural responses to food portion size cues in brain regions implicated in valuation (e.g., OFC, vmPFC) and cognitive control (e.g., IFG). Nevertheless, these analyses only examined neural responses in a limited number (n = 9) of regions using a region-of-interest based approach; thus, a

more comprehensive voxel-wise examination of the appetitive network is needed to identify regions sensitive to the PSE.

Although the cerebellum is typically excluded or minimally integrated into models of eating behavior [8–11], it is involved in many processes that may contribute to food intake including sensorimotor [17], reward [18,19], affective [20], and cognitive [21] processing. Growing evidence suggests the cerebellum contributes to hunger and satiety processing [22,23], meal anticipation [24,25], food cue processing [26,27], and satiation/meal cessation [28] through connections with cortical and subcortical regions [23,28]. For example, cerebellar neurons respond to food cues and nutrients, and their activation can suppress food intake via signals to subcortical reward pathways [29]. In humans, there is evidence that cerebellar responses to food cues (e.g., images, commercials) differ by adolescent weight status [27], child-reported loss of control eating [30], and parent-reported child food responsiveness [26], suggesting cerebellar processing of visual food cues may contribute to pediatric eating behaviors. Therefore, it is important to characterize how cerebellar processing of food cues relates to objectively measured intake in youth.

Our group's prior examination of associations between neural food cue reactivity and the PSE tested a cohort that was heterogeneous in body weight [15]. However, since weight status is associated with both neural responses to food cues [31] and the PSE [5], including children with and without obesity may confound results. Taking this into account, the present study aimed to examine how neural responses to food images varying in portion size relate to the PSE in children without obesity. To do so, children who had BMI-for-age-and-sex percentiles < 90 viewed images of larger and smaller portions of food during functional magnetic resonance imaging (fMRI), and individual-level PSEs were estimated from intake at four laboratory meals that varied in portion

size. We hypothesized that children's patterns of intake across the four portion size meals would relate to their neural responses to portion size within an a priori defined appetitive network and cerebellum. More specifically, we anticipated that increased susceptibility to the PSE would be associated with greater activation to larger vs. smaller portion size cues in regions implicated in reward and value processing (e.g., OFC, vmPFC) and less engagement in regions implicated in cognitive control (e.g., dorsolateral PFC, IFG), interoception (e.g., insula), and satiation (e.g., cerebellum).

2. Materials and Methods

2.1. Participants

As part of a 7-visit, prospective study aiming to identify risk factors for pre-adolescent obesity (ClinicalTrials.gov NCT03341247), 88 (45 male, 43 female) children (mean [SD] age = 7.8 [0.62] years) attended 6 baseline visits. Children were accompanied by the parent primarily responsible for feeding decisions and were required to be 7-8 years old and have a BMI-for-age-and-sex percentile < 90 (i.e., not have obesity). Children were ineligible if they were colorblind, not reading at grade level, not fluent in English, had a learning (e.g., dyslexia) or neurodevelopmental disorder (e.g., ADHD), had a diagnosed psychological condition (e.g., anxiety), were taking medications known to influence appetite, cognition, or blood flow, or had any MRI contraindications (e.g., metal in the body, claustrophobic). Consent and assent were obtained in accordance with the Institutional Review Board of The Pennsylvania State University.

Neural responses to food and non-food cues in this cohort will be examined in a separate paper, and the PSE has been examined in a larger behavioral sample [32]. Additional analyses from this cohort have examined meal eating behaviors [33], executive functioning [32,34], sleep [35], and

resting state functional connectivity [36]. The associations between food cue reactivity and the PSE in the present publication have not been reported elsewhere.

2.2. Data collection

Data for the present analyses were collected across six baseline visits between 2017 and 2022, with an ~8-month interruption due to the COVID-19 pandemic (study protocol and materials are available on Open Science Foundation at https://osf.io/ynjqw/). Procedures pertinent to the present analyses include: collection of demographics (see 2.2.1) and anthropometrics (see 2.2.2), assessment of parent-reported child appetitive traits (see 2.2.3), laboratory meals to assess the PSE (see 2.2.4), a mock-MRI protocol (see 2.2.5), and a food-cue task during fMRI (see 2.2.6-2.2.8; Figure 3.1). Parents were instructed to have their child fast for at least 3 hours prior to each visit to create a physiological state similar to what would be experienced prior to a meal.

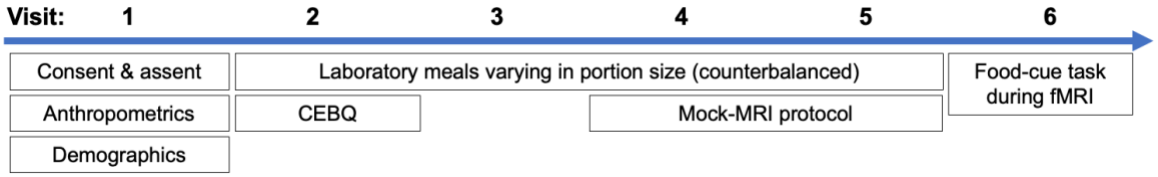

Figure 3.1 Timeline of procedures related to the present analyses. During visit 1, parental consent and child assent were obtained in accordance with the Institutional Review Board of The Pennsylvania State University, anthropometrics were assessed, and parents reported demographic information. During visits 2-5, children were served four meals that varied in portion size. During visits 4 and 5, children completed a 2-session mock-MRI protocol to familiarize them with the scanning environment. During visit 6, children completed a food-cue task during functional magnetic resonance imaging (fMRI).

2.2.1. Demographics

Parents completed a questionnaire assessing child race and ethnicity, yearly family income and parental education (see Table 3-2). Family income and maternal education were included as socioeconomic status indicators [37].

2.2.2. Anthropometrics

Children's height and weight were measured twice by a trained researcher using a standard scale (Scale Tronix model 5002, Welch Allyn, Chicago, IL; precision to nearest 0.1 kg) and stadiometer (precision to nearest 0.1cm), respectively. Children removed shoes and heavy clothing items prior to measurement. BMI-for-age percentile was computed using averaged height and weight measurements based on growth charts from the Centers for Disease Control and Prevention [38].

2.2.3. Laboratory portion size meals

Across four visits, children were served four laboratory meals that varied in the amount of food served [32]. Meals contained varied amounts of macaroni and cheese, chicken nuggets, broccoli with margarine, and grapes, as well as fixed amounts of ketchup, and ad libitum access to water. The smallest portion size condition was the reference amount, and subsequent conditions increased all food weights by 33%, 66%, and 99% relative to the reference amount (Table S1). Reference amounts were based on the Continuing Survey of Food Intake by Individuals [39] and previous laboratory meal paradigms [15,40]. The order of portion sizes was randomly assigned and counterbalanced across the four meals. Foods were weighed before and after meals to the nearest 0.1 g, and nutrition facts labels or reliable online databases (https://fdc.nal.usda.gov/) were used to convert the weight consumed to kcal.

Prior to each meal, children reported liking in response to tasting small samples (~2-3g) of the meal foods using a five-point facial hedonic scale. They also reported fullness using a child-

friendly visual analogue scale before and after each meal [42]. Children were told they had 30 min to eat ad libitum until they reached satiation. If they reached satiation before 30 minutes, they could notify the researcher. Children were notified during the meal when 15 minutes had passed and when they had a few minutes remaining. Meals were served in an observation room that had a table and chairs, a rug with child-friendly images (e.g., trains), and non-food pictures (e.g., animals) on the wall. To serve as a neutral distraction during meals, children were read an age-appropriate, non-food related book by either a trained researcher or computer (i.e., audio book); methodologies were consistent within a child but switched during the COVID-19 pandemic to comply with social distancing restrictions. Mealtimes (i.e., lunch or dinner) varied across children based on participant availability but were consistent within a child.

2.2.4. Mock-MRI protocol

Children completed a two-session mock-MRI protocol [41] to familiarize them with the scanning environment. During the first session, children visited the mock scanning room and had an opportunity to ask questions. During the second session, children completed a mock scanning protocol where they entered a mock MRI bore, viewed non-food images, experienced simulated MRI sounds, and practiced using the response grip to making ratings.

2.2.5. fMRI visit protocol

Children arrived for the fMRI visit following at least a 3 hour fast. As individuals with and without overweight show increased food cue response during fasted conditions [42], we scanned children in neutral appetitive state. To achieve this, children who reported fullness levels below 25% using a child-friendly visual analogue scale [43] upon arrival were given a snack (6.75 fl oz apple juice, Quaker Chewy granola bar) and then re-rated their fullness after consumption. This process was repeated a second time if a child continued to report fullness below 25%. The fullness

rating collected closest to the scan was used as index of pre-MRI fullness (imputed for one participant due to recording error; see supplement). Before and after the scan, children rated their state anxiety using the Children's Anxiety Meter Scale [44].

2.2.6. MRI data acquisition

A 3 Tesla MRI scanner (Siemens, Magnetom Trio) and 20-channel head coil were used to collect imaging data. A T1-weighted MPRAGE (160 sagittal slices; TR = 1650; TE = 2.03 ms; flip angle = 9°; FOV = 256x256 mm^2; voxel size = 1x1x1 mm^3) was acquired using generalized autocalibrating partially parallel acquisition (GRAPPA; acceleration factor 2) [46]. During each run of the food-cue task (~2.7 minutes), 80 T2*-weighted images were acquired using echo planar imaging (EPI; slice thickness = 3mm (no gap); 33 descending slices; TR = 2000 ms; TE = 26 ms; flip angle = 90°; FOV = 220x220 mm^2; voxel size 3x3x3 mm^3). To optimize temporal lobe and cerebellar signal based on prior findings relevant to our aims [26], EPI scans were aligned parallel to the AC-PC line and adjusted vertically. Each EPI scan was preceded by two unsaved "dummy scans" to establish a stable magnetization state prior to data collection. Lastly, a field map was acquired using a double-echo gradient-echo sequence (slice thickness = 3mm (no gap); 33 descending slices, TR = 400 ms, TE 1 = 5.12 ms, TE 2, 7.65 ms, flip angle = 60°, FOV = 220x220 mm^2, voxel size = 3x3x3 mm^3).

2.2.7. Food-cue task

During the food-cue task, children viewed images of 120 food items and 60 non-food items (i.e., office supplies) presented one at a time (Figure 3.2). Images were sourced from a standardized dataset [45] and presented above smiley and frowny faces on a black screen (Figure 3.2a). To encourage engagement and attention during the task, children were instructed to indicate whether they wanted each item by pressing one of two buttons with their dominant hand (index finger for

"no"/frowny face and thumb for "yes"/smiley face). Food images were categorized based on amount (i.e., portion size; larger, smaller) and energy density (ED; higher: <1.5 kcal/g, lower: <1.5 kcal/g) creating four conditions with 30 images each: (1) larger amount of higher-ED food, (2) larger amount of lower-ED food, (3) smaller amount of higher-ED food, and (4) smaller amount of lower-ED food. Food items depicted included those served during the meals (macaroni and cheese, chicken nuggets, broccoli, and grapes) as well as other foods commonly consumed by children (e.g. strawberries, cake, deli meat, pizza). Portions depicted in the smaller amount condition were based on servings from Nutrition Facts labels and reflected amounts consumed per eating occasion by children in the 1990s [39]. Office supplies were also categorized based on amount (larger, smaller) creating two conditions. Images were presented in a block design over five runs; each run began with a 4.0 s fixation and contained one block (n = 6 images) per cue condition (i.e., 6 blocks per run; Figure 3.2b). Each image was presented for 2.0 s followed by a 0.5 s fixation. Each block was followed by an 8.0 s fixation. Children viewed blocks in one of two pseudorandomized and counterbalanced orders.

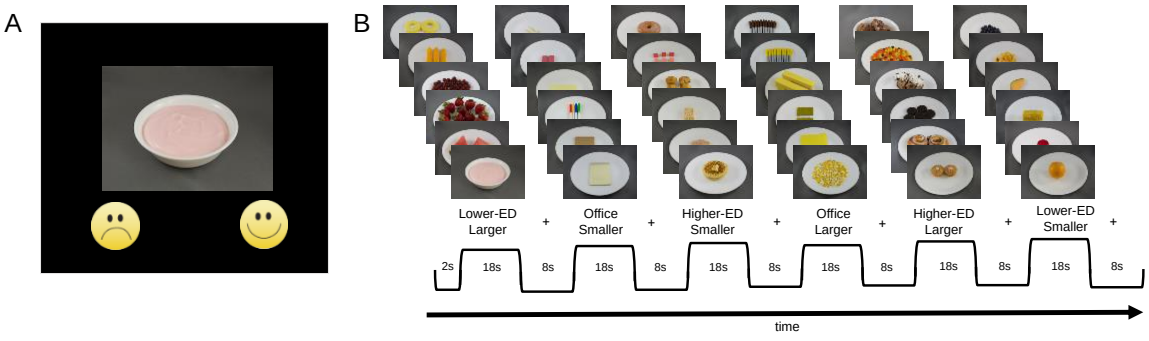

Figure 3.2 Food-cue task. Children viewed images of food and non-food (i.e., office supply) items from a standardized dataset [45] in a block design. Images were categorized into six conditions with 30 images each: (1) larger amount of higher-energy dense (ED) food, (2) larger amount of lower-ED food, (3) smaller amount of higher-ED food, and (4) smaller amount of lower-ED food, (5) larger amount of office supplies, and (6) smaller amount of office supplies. Images were presented over five ~2.7minute runs. (A) Image presentation: Images were presented on a black screen above a smiley face and a frowny face. For each image, children

answered the question “do you want this?” by pressing one of two buttons with their dominant hand (index finger for “no”/frowny face and thumb for “yes”/smiley face). (B) Example run: Each run contained one block per image condition. Block orders were pseudorandomized across runs. Each block contained six images. Each image was presented for 2.0 s followed by a 0.5 s fixation cross on a black screen. Each block was followed by an 8.0 s fixation cross on a black screen.

2.3. fMRI data processing

Standard preprocessing steps were implemented using fMRIPrep 20.2.3 [46] (see supplement for full report). MNI’s unbiased template for pediatric cohort 3 (MNIped; ages 7-11y) [47,48] was used for volume-based spatial normalization. Brain masks from BOLD signal (i.e., BOLD brain masks) and head-motion parameters were estimated from functional scans. Susceptibility distortion correction was applied to functional scans using a fieldmap-based approach (n = 62) or fieldmap-less approach (n = 1) if fieldmap quality was poor. Functional scans were also slice-time corrected (i.e., realigned) to the middle of each TR, co-registered to anatomical space, and resampled into MNIped space. Preprocessed data were visually inspected using summary reports generated by fMRIPrep. If quality of preprocessed data was poor, scans were excluded (see 2.4.1) or re-processed. Data were subsequently blurred with a 6 mm FWHM Gaussian kernel, scaled so results could be represented as percent signal change, and analyzed (see 2.11.2, 2.12.5) using AFNI v21.3.04 [49,50].

Individual-level general linear models (GLMs) included 1 parameter per food cue condition and were modeled by convolving block onset times and durations with the canonical hemodynamic response function. Onset times were shifted by subtracting half a TR (i.e., 1 second) to account for fMRIPrep’s default slice time realignment to the middle of each TR. In addition, GLMs included 14 nuisance regressors computed by fMRIPrep (6 rigid-body motion parameters and their derivatives, average signal within CSF and white matter masks). To ensure analyzed data were acquired during a stable magnetization state, the first two volumes of each run and any additional

steady-state outliers identified by fMRIPrep were censored. To reduce the effects of motion, volumes with a framewise displacement [51] >0.9mm were censored, matching the motion threshold used by the Adolescent Brain Cognitive Development (ABCD ®) Study [52]. Runs with >20% of volumes censored across task blocks were excluded from GLMs. A first-level portion size contrast (larger – smaller food amounts, across ED) was generated from each GLM.

2.3.1. Masks

Separate appetitive network and cerebellum masks were generated using the Wake Forest University (WFU) PickAtlas toolbox for Statistical Parametric Mapping 12 (SPM12 [53]). Masks were dilated by 4mm to avoid small, isolated regions and irregular boundaries and restricted to voxels scanned in at least 80% of children (e.g., to only include voxels inside the brain). Regions in the appetitive network mask (Table 1) were selected based on previous reviews [10,54,55]; cortical regions were defined using Brodmann areas and subcortical regions were defined based on anatomical boundaries (Figure 3.3). The cerebellum was anatomically defined (Figure S1).

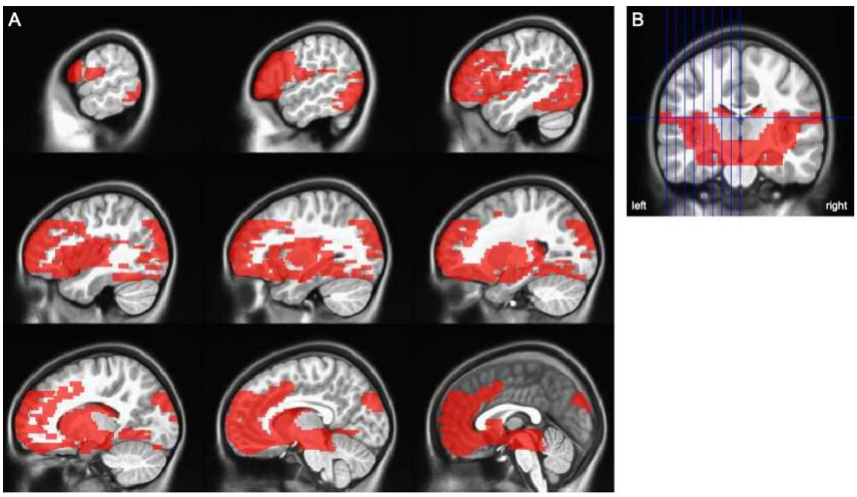

Figure 3.3 Appetitive network mask: (a) Sagittal slices with appetitive network mask (red) overlayed on MNI's unbiased template for pediatric cohort 3. Regions included in mask are listed in Table 3-1; (b) Coronal slice with appetitive network mask (red) overlayed on MNI's unbiased template for pediatric cohort 3. Blue vertical lines indicate location of sagittal slices depicted in (a).

Table 3-1. Regions in appetitive network mask

Table 3-1. Regions in appetitive network mas

Region	Brodmann area(s)
Dorsolateral PFC	9, 46
Anterior PFC	10
Orbitofrontal cortex	11, 12
Insula	13, 14, 16
Associative visual cortex	19
Subgenual area	25
Dorsal anterior cingulate cortex	32
Fusiform	37
Primary gustatory cortex	43
Inferior frontal gyrus	44, 45, 47
Hippocampus	-
Hypothalamus	-
Globus Pallidus (lateral, medial)	-
Caudate (body, tail, head)	-
Putamen	-
Substania Nigra	-
Subthalamic nucleus	-
Amygdala	-
Midbrain	-

PFC: prefrontal cortex

2.4. Group-level analyses

2.4.1. Analysis sample.

Children were excluded from analyses if they declined to enter the MRI (n = 4), did not complete at least 3 runs of the food-cue task (n = 4), or had fewer than 3 runs included in first-level analyses (see 2.11.2; n = 17). Children were also excluded from some analyses of eating behavior if they had data for < 4 meals (due to measurement error) and thus could not be included in quadratic fixed-effects individual slopes models (n = 3; see 2.12.2). In addition, children were excluded from analyses within the appetitive mask if they had reduced cortical field of view identified via visual inspection (n = 2). In sum, sample sizes for analyses ranged from N= 58 to 63.

2.4.2. Estimation of individual-level portion size slopes

The PSE (i.e., relationship between portion size and intake) was estimated for both weight (g) and energy (kcal) of food consumed. As large portions of food have been shown to increase intake in a curvilinear manner [56–58], we tested both linear and quadratic PSE models: 1) intake (g or kcal) ~ intercept + linear portion size; and 2) intake (g or kcal) ~ intercept + linear portion size + quadratic portion size. In subsequent sections, we refer to the linear slope of the linear model as the "linear portion size slope" and the quadratic slope of the quadratic model as the "quadratic portion size slope". Meal portion size was modeled using the proportion increase from the reference portion (i.e., 0, 0.33, 0.66, 0.99) so that a 1-unit increase in portion size reflects the estimated change in intake between the reference portion and approximately the largest portion (100% increase). Fixed-effects individual slopes (FEIS) models were used to extract child-specific slope estimates for the linear and quadratic PSE models (feisr [59] in R 4.2.2 [60]). Both models adjusted for meal-related influences on intake (i.e., pre-meal fullness, average pre-meal liking of foods at the meal, and meal order).

2.4.3. Descriptive statistics

Histograms and Kolmogorov-Smirnov tests were used to assess the normality of linear and quadratic portion size slopes and imaging covariates (i.e., pre-MRI fullness, pre-MRI anxiety, framewise displacement). Mean and standard deviation are reported for normally distributed quantitative variables while quartiles (25% (Q1), 50%, 75% (Q3)) are reported for non-normally distributed variables. Pearson correlations were used to assess associations between linear and quadratic portion size slopes estimated for weight and energy consumed (Table S2). Associations between portion size slopes and child characteristics (age, BMI percentile, sex) were assessed using Pearson correlations for age and BMI percentile and 2-sample t-tests for sex (Table S3). Demographic variables and imaging covariates were compared between children included and

excluded from analyses using 2-sample t-tests and $\chi 2$ or Fisher's Exact Test for continuous and categorical variables, respectively.

2.4.4. Wanting responses during the food-cue task

Using lme4 [61] in R 4.2.2 [60], a mixed-effects linear model with subject as random effect was used to compare the percent of items children reported wanting per block (%want) during the food-cue task between larger and smaller portion size conditions; models predicted %want from portion size (larger, smaller), controlling for run. The estimated marginal means (EMM) and corresponding 95% confidence intervals from this model are reported for larger and smaller portion size conditions.

To explore whether wanting responses might mediate the observed association between neural responses and the PSE, a post-hoc correlation was conducted between the average difference in %want between larger and smaller portion size conditions and the neural response to portion size (larger – smaller) extracted from the cerebellar cluster associated with the quadratic portion size slope identified in fMRI analyses (see 2.4.5).

2.4.5. Neural responses to portion size and the PSE

Within each mask (see 2.3.1), four regression analyses (3dttest++) were used to test associations between the neural response to portion size (larger - smaller) and child-specific portion size slopes; models included parameter estimates from a) linear or b) quadratic PSE models (see 2.4.2) estimated from a) weight (g) or b) energy (kcal) of food consumed. The predictors of interest include the linear and quadratic portion size slopes. Since individual slope estimates (e.g., linear slope) cannot be interpreted outside the context of the overall curve for each child (e.g., linear slopes depend on intercepts), all child-specific FEIS model coefficients were included in regression models (i.e., linear model: intercept + linear slope; quadratic model: intercept + linear

slope + quadratic slope). Models were adjusted for average framewise displacement, sex, pre-MRI fullness, and pre-MRI anxiety to control for their potential effects on the BOLD response. Within each mask, cluster thresholds derived from 3dClustStim [62] were used to adjust for multiple comparisons (voxel-wise threshold $p<0.001$, cluster-corrected to $p<0.05$). To examine whether significant results were confounded by weight status, sensitivity analyses were conducted by including BMI percentile as a covariate.

3. Results

3.1. Participant characteristics

The analyzed sample was predominantly White (n=61; 97%) and non-Hispanic/Latinx (n=63; 100%), had family incomes >$50,000 and had mothers with a bachelor's degree or higher (Table 3-2). Children included and excluded from analyses did not differ in demographics (ps > 0.59), pre-MRI anxiety ($p > 0.05$) or pre-MRI fullness ($p > 0.88$) As expected, children included in analyses exhibited less motion (i.e., average framewise displacement) during the food-cue task than those excluded ($t(19) = -4.6$, $p < 0.001$).

Table 3-2. Participant characteristics by analysis inclusion status

Table 2. Participant characteristics by analysis inclusion status

		Included (N=63)	Excluded (N=25)
Sex			
	Male	30 (47.6%)	15 (60.0%)
	Female	33 (52.4%)	10 (40.0%)
Age, yrs			
	Mean (SD)	7.82 (0.587)	7.79 (0.595)
	Min, Max	7.00, 8.99	7.03, 8.81
Race			
	Asian	2 (3.2%)	1 (4.0%)
	White/Caucasian	61 (96.8%)	24 (96.0%)
Ethnicity			
	Not Hispanic/Latinx	63 (100%)	25 (100%)
Family Income			
	< $51,000	9 (14.3%)	2 (8.0%)
	$51,000 - $100,000	28 (44.4%)	14 (56.0%)
	>$100,000	24 (38.1%)	8 (32.0%)
	Missing	2 (3.2%)	1 (4.0%)
Maternal Education			
	< Bachelor Degree	13 (20.6%)	5 (20.0%)
	Bachelor Degree	30 (47.6%)	11 (44.0%)
	> Bachelor Degree	19 (30.2%)	9 (36.0%)
	Missing	1 (1.6%)	0 (0%)
BMI percentile			
	Mean (SD)	47.0 (25.5)	49.0 (24.2)
	Min, Max	3.91, 89.3	6.69, 89.5
Pre-MRI fullness			
	Mean (SD)	71.3 (30.1)	70.2 (33.2)
	Min, max	4.00, 150	3.00, 139
	Missing	1 (1.6%)	0 (0%)
Pre-MRI anxiety			
	Median [Q1, Q3]	2.0 [0.0, 3.0]	3.0 [0.75, 6.0]
	Min, Max	0, 10	0, 10
	Missing	0 (0%)	1 (4.0%)
Average framewise displacement			
	Median [Q1, Q3]	0.30 [0.19, 0.38]	1.52 [0.89, 1.67]
	Min, Max	0.0800, 1.29	0.500, 4.79
	Missing	0 (0%)	6 (24.0%)

3.2. Child-specific portion size curves

Child-specific linear portion size slopes (adjusted for meal order, average liking, and fullness) ranged from a decrease of 194 g or 205 kcal to an increase of 370 g or 647 kcal between the reference and largest portion sizes (Table 3-3). Despite the large range, 76% and 73% of children had positive linear portion size slope estimates for weight and energy consumed, respectively, indicating most children increased intake with increasing portions as expected. Adjusting for meal

order, average liking, and fullness, 38% (n = 23) of children had positive quadratic portion size slopes estimated from weight consumed, while 50% (n = 37) had positive quadratic portion size slopes estimated from energy consumed. Example quadratic portion size curves can be found in Figure S2.

Table 3-3 Descriptive statistics for portion size slopes estimated from weight (g) and energy (kcal) consumed

Portion size slope	**N**	**Mean (SD)**	**Min, Max**
Linear portion size slope, g [a]	63	58.0 (113)	-194, 370
Linear portion size slope, kcal [b]	63	124 (175)	-205, 647
Quadratic portion size slope, g [c]	60	-66.8 (419)	-953, 1090
Quadratic portion size slope, kcal [d]	60	-26.8 (628)	-1500, 1470

[a] Slope extracted from linear fixed-effects individual slope (FEIS) model predicting weight consumed (g)
[b] Slope extracted from linear FEIS model predicting energy consumed (kcal)
[c] Slope extracted from quadratic FEIS model predicting weight consumed (g)
[d] Slope extracted from quadratic FEIS model predicting energy consumed (kcal)

3.3. Behavioral responses during the food-cue task

The median response rate during the food-cue task was 97.5% (Q1 = 95.8%, Q3 = 99.2%). The percent of items wanted per block (%want) did not significantly differ between larger (EMM = 66.9; 95% CI: 62.1-71.6) and smaller (EMM = 68.3; 95% CI: 63.6-73.1) portion size conditions (F(1, 1141.2 = 1.02, p = 0.31). The average difference in %want between larger and smaller portion size conditions was not significantly correlated with the neural response to portion size (larger – smaller) in the cerebellar cluster associated with the quadratic portion size slope (see 3.4.2; r(56); = -0.50, p=0.62).

3.4. Association between neural responses to portion size and the PSE

3.4.1. Appetitive network mask

In models adjusted for framewise displacement, sex, pre-MRI fullness, pre-MRI anxiety, and FEIS model coefficients, there was no association between the linear or quadratic portion size slopes (weight or energy) and neural response to portion size (larger vs. smaller) within the appetitive network ($p > 0.05$).

3.4.2. Cerebellum mask

Adjusting for the same variables listed above (3.4.1), the quadratic portion size slope estimated from gram intake was negatively associated with neural response to portion size (larger – smaller) in cerebellar lobules IV-VI (MNI peak: 7, -62, -13; cluster size = 1,853 1x1x1mm^3 voxels; peak z-statistic = -4.83; Figure 4; Figure S3). More positive quadratic portion size slopes were associated with lower activation to images depicting larger than smaller food portions while more negative quadratic portion size slopes were associated with greater activation to images depicting larger than smaller food portions. Therefore, children who showed steeper increases in weight consumed with increasing portion sizes had lower cerebellar activation to images depicting larger than smaller food portions. In contrast, children who showed plateaus or steeper declines weight consumed with increasing portion sizes had greater cerebellar activation to images depicting larger than smaller food portions (see Figure 3.4. Results were similar after additionally adjusting for BMI percentile (MNI peak: 7, -61, -13; cluster size = 1,935 1x1x1mm^3 voxels; peak z-statistic = -4.94). Cerebellar responses to portion size were not associated with linear portion size slopes (g or kcal) or the quadratic portion size slope estimated from kcal.

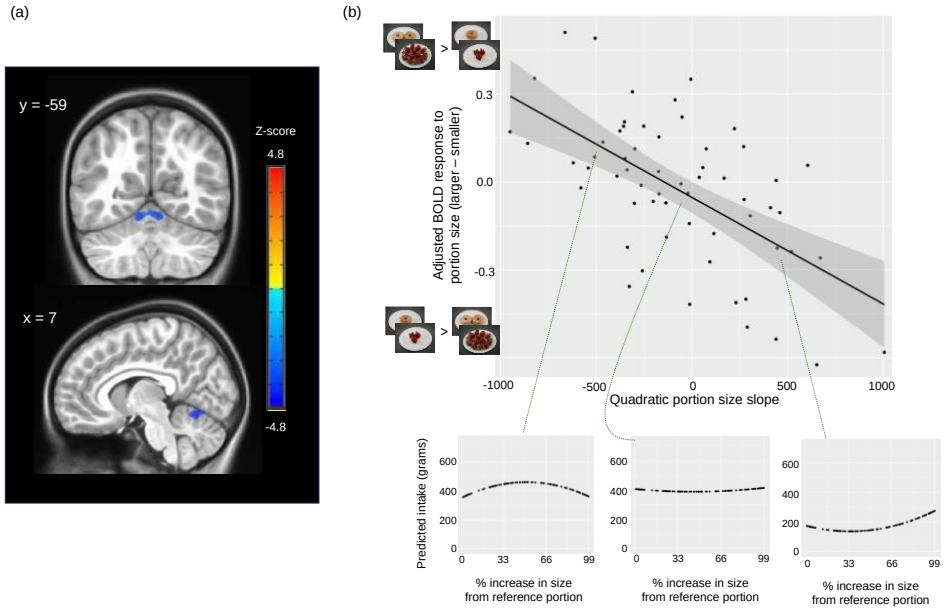

Figure 3.4 Association between cerebellar response to portion size (larger – smaller) and quadratic portion size slope estimated from gram intake (N = 58): (a) Z-statistic map for prediction of BOLD response to portion size (larger – smaller) by quadratic portion size slope controlling for sex, average framewise displacement, pre-MRI fullness, pre-MRI anxiety and intercept and linear slope from quadratic FEIS model. Analyses were conducted within cerebellum mask. Quadratic portion size slope was negatively associated with activation in cluster (blue) spanning cerebellum lobules IV-VI (peak: 7, -62, -13; k = 1,853 1x1x1 mm^3 voxels; peak z-statistic = -4.83); (b) Scatterplot of adjusted BOLD response to portion size (larger – smaller; y-axis) vs. quadratic portion size slope (x-axis). BOLD responses to portion sizes were extracted from cluster depicted in (a) and adjusted for covariates included in imaging analyses. Using individual-level intercepts and slopes estimated from quadratic FEIS models, portion size curves (i.e., predicted gram intake vs. percent increase in portion size from reference portion) were plotted for three subjects (circled in green) to exemplify patterns of intake for children with negative (left), approximately zero (middle) and positive (right) quadratic slopes.

4. Discussion

The present study examined how neural responses to food portion size relate to the PSE in children without obesity. Results revealed an association between food-cue activation in cerebellum (culmen, declive) and amount (weight) of food consumed across meals varying in portion size. As cerebellar activation to larger (relative to smaller) portion sizes increased, children exhibited plateaus or steeper declines in intake with increasing portion sizes. Conversely, as

cerebellar activation to larger (relative to smaller) portion sizes decreased, children exhibited steeper increases in intake with increasing portion sizes. These findings suggest that decreased cerebellar activation in response larger amounts of food may increase children's susceptibility to overeating when faced with "supersized" portions of food.

Cerebellum lobules IV-VI (culmen, declive) are implicated in multiple processes relevant to feeding behavior [29], including leptin sensitivity [22], chewing [63], food cue reactivity [26,27], reward anticipation and expectation [18], and emotional conditioning [64]. For example, in adults with leptin deficiency, a greater number of days receiving of leptin replacement was associated with greater lobule VI activation to high-energy food vs. non-food images [22], suggesting hormones that influence satiety alter food-cue responding in the cerebellum. The function and structure of lobules IV-VI have also been associated with self-reported eating behavior (e.g., disinhibition [65], loss of control [30,66]) and weight status [22,67–69]. These findings, along with our observation that activation in lobules IV-VI relates to objectively measured food intake in children, indicate that cerebellar processes contribute to susceptibility to overconsumption.

With the addition of the present findings, there is growing evidence that intact cerebellar function supports the development of satiation [23,70] and meal cessation [28]. For example, in mice, activation of anterior deep cerebellar nuclei reduced meal size and feeding duration leading to reductions in food intake [28]. This change was mediated by blunted phasic dopamine responses to food consumption, suggesting cerebellar induction of satiation via reward-related pathways (i.e., hedonic satiation [29]). Low and colleagues [28] proposed that the cerebellum fine-tunes predictive reward signals by integrating information about the expected nutrient value from food (or food cues) with physiological nutrient status. Over the course of a meal, cerebellar neurons sense nutrient status and induce dopamine efflux, leading to an eventual blunting of food-

dependent phasic dopamine responses that is necessary to reduce the value of further consumption and bring about meal cessation [28]. Thus, children who have reduced cerebellar activation to larger portions of food may not be adequately fine-tuning predictive reward signals based on nutrient status during a meal, enabling sustained motivation to eat and delayed meal cessation when they are presented with excessively large portions. This postulation aligns with behavioral research demonstrating that increased susceptibility to the PSE in children is associated with decreased sensitivity to internal fullness signals (i.e., satiety responsiveness) and increased sensitivity to external food cues (i.e., food responsiveness) [5]. Alternatively, in line with behavioral research showing associations between the PSE and executive functions [32], the cerebellum may influence satiation via modulation of cognitive processes [71,72]. PFC-cerebellar interactions are thought to enable optimization of behaviors according to context [73], and modulation of PFC-cerebellar interactions has been shown to modulate food-induced appetite and hunger in individuals with obesity [23]. As the cerebellum is implicated in a variety of additional processes that could underlie its association with child appetitive behavior (e.g., oral behaviors [74,75], ocular control to visualize objects of interest [76], affect [77]), our interpretations are speculative, and additional research is needed to delineate the role of the cerebellum in meal cessation and the PSE.

In contrast to our hypotheses, we did not observe associations between portion size slopes estimated from weight or energy consumed and neural responses within the appetitive network (i.e., a mask of cortical and subcortical regions implicated in the control of food intake). This is in contrast to a previous study in 7-10-year-old children [15] where linear and quadratic relationships between portion size and intake were modulated by neural responses to portion size cues in OFC, vmPFC, IFG, and caudate. Differences in results may be due to demographic differences between

the samples: the present sample was younger (7-8 years) than the sample in [15] and did not include children with obesity. As puberty influences the development brain regions implicated in reward and cognitive control [78], associations observed in older children may not generalize to younger children. Further, neural responses to portion size in brain regions associated with valuation and cognitive control may not influence food intake prior to the development of excess adipose tissue. In addition, differences in results may be due to methodology: the present study examined susceptibility to the PSE with fixed-effect individual slopes models rather than mixed-effects models and examined voxel-wise associations within a masked area rather than using a region-of-interest based approach. The two studies also used different data processing methodology (e.g., choice of structural atlas, use of spatial smoothing) and software, which could impact results. To better understand how neural responses within the appetitive network relate the PSE, future research should test the moderating effects of puberty and weight status and compare analytic methods.

This study has several strengths. First, we objectively measured food intake to quantify intake rather than using self-reported measures of dietary behavior, which are subject to misreporting [79]. Second, intake was assessed at four laboratory meals, allowing us to capture both linear and quadratic relationships between intake and portion size. Third, using a voxel-wise analytic approach within masks allowed us to explore associations between individual-level portion size slopes and neural responses within a larger brain area than previous region-of-interest based analyses [15]. Despite these strengths, the sample size of the present study was smaller than proposed (https://www.clinicaltrials.gov/study/NCT03341247) due to data loss (e.g., from motion) and difficulty recruiting during the COVID-19 pandemic. Small sample sizes can increase the risk of both false negatives and false positives [80], thus, results will need to be replicated in

other samples. In addition, the sample was predominately White and not Hispanic, so results may not generalize to more diverse populations. Further, while objective assessment of food intake mitigates error compared to self-report methods, eating behaviors observed in the laboratory may not generalize outside the laboratory environment. Lastly, the identified association between cerebellar function and intake was observational and does not indicate causality. The causal relationship between cerebellar function and the portion size effect could be tested empirically by modulating cerebellar activation (e.g., with transcranial direct current stimulation, as done in [23]) prior to assessments of food intake.

This is the first study to examine how neural responses to portion size cues across the appetitive network and cerebellum relate to changes in objectively measured intake as portion sizes increase. The present results suggest that decreased cerebellar activation to large portion size cues in children without obesity may be a risk factor for overeating in response to large portions. Based on prior studies [23,28,70], reduced activation may influence the PSE by increasing hunger or reducing satiation via reward or cognitive mechanisms; nevertheless, additional research is needed to test this. If future research supports a causal mechanism between cerebellar function and the PSE, interventions that modulate cerebellum activity (e.g., non-invasive stimulation [81], mindfulness training [82], cognitive training [83], cognitive behavioral therapy [84]) may mitigate increased intake in response to large portions.

5. Supplement

5.1 Methods

fMRI pre-processing

Results included in this manuscript come from preprocessing performed using fMRIPrep 20.2.3 (Esteban, Markiewicz, et al. (2018); Esteban, Blair, et al. (2018); RRID:SCR_016216), which is based on Nipype 1.6.1 (Gorgolewski et al. (2011); Gorgolewski et al. (2018); RRID:SCR_002502).

Anatomical scans were not de-identified prior to preprocessing, but were de-identified (i.e., de-faced) using the PyDeface software package (Gulban et al., 2022) prior to sharing data on OpenNeuro (https://openneuro.org/datasets/ds004697/versions/1.0.2).

Anatomical data preprocessing. A total of 1 T1-weighted (T1w) images were found within the input BIDS dataset.The T1-weighted (T1w) image was corrected for intensity non-uniformity (INU) with N4BiasFieldCorrection (Tustison et al. 2010), distributed with ANTs 2.3.3 (Avants et al. 2008, RRID:SCR_004757), and used as T1w-reference throughout the workflow. The T1w-reference was then skull-stripped with a Nipype implementation of the antsBrainExtraction.sh workflow (from ANTs), using OASIS30ANTs as target template. Brain tissue segmentation of cerebrospinal fluid (CSF), white-matter (WM) and gray-matter (GM) was performed on the brain-extracted T1w using fast (FSL 5.0.9, RRID:SCR_002823, Zhang, Brady, and Smith 2001). Brain surfaces were reconstructed using recon-all (FreeSurfer 6.0.1, RRID:SCR_001847, Dale, Fischl, and Sereno 1999), and the brain mask estimated previously was refined with a custom variation of the method to reconcile ANTs-derived and FreeSurfer-derived segmentations of the cortical gray-matter of Mindboggle (RRID:SCR_002438, Klein et

al. 2017). Volume-based spatial normalization to three standard spaces (MNIPediatricAsym:cohort-3, MNI152NLin2009cAsym, MNI152NLin6Asym) was performed through nonlinear registration with antsRegistration (ANTs 2.3.3), using brain-extracted versions of both T1w reference and the T1w template. The following templates were selected for spatial normalization: MNI's unbiased standard MRI template for pediatric data from the 4.5 to 18.5y age range [(???), RRID:SCR_008796; TemplateFlow ID: MNIPediatricAsym:cohort-3], ICBM 152 Nonlinear Asymmetrical template version 2009c [Fonov et al. (2009), RRID:SCR_008796; TemplateFlow ID: MNI152NLin2009cAsym], FSL's MNI ICBM 152 non-linear 6th Generation Asymmetric Average Brain Stereotaxic Registration Model [Evans et al. (2012), RRID:SCR_002823; TemplateFlow ID: MNI152NLin6Asym],

Functional data preprocessing. For each of the 6 BOLD runs found per subject (across all tasks and sessions), the following preprocessing was performed. First, a reference volume and its skull-stripped version were generated using a custom methodology of fMRIPrep. A B0-nonuniformity map (or fieldmap) was estimated based on a phase-difference map calculated with a dual-echo GRE (gradient-recall echo) sequence, processed with a custom workflow of SDCFlows inspired by the epidewarp.fsl script and further improvements in HCP Pipelines (Glasser et al. 2013). The fieldmap was then co-registered to the target EPI (echo-planar imaging) reference run and converted to a displacements field map (amenable to registration tools such as ANTs) with FSL's fugue and other SDCflows tools[2]. Based on the estimated

[2] Fieldmap-based susceptibility distortion correction (SDC) was used for all but one subject (N = 60). For one subject, *fieldmap-less* SDC was used due to a low-quality fieldmap (i.e., motion) and improved fMRIPrep output using the fieldmap-less approach. For this approach, a deformation field to correct for susceptibility distortions was estimated based on *fMRIPrep*'s *fieldmap-less* approach. The deformation field is that resulting from co-registering the BOLD reference to the same-subject T1w-reference with its intensity inverted (Wang et al. 2017; Huntenburg 2014). Registration is performed with antsRegistration (ANTs 2.3.3), and the process regularized by constraining deformation to be nonzero only along the phase-encoding direction, and modulated with an average fieldmap template (Treiber et al. 2016).

susceptibility distortion, a corrected EPI (echo-planar imaging) reference was calculated for a more accurate co-registration with the anatomical reference. The BOLD reference was then co-registered to the T1w reference using bbregister (FreeSurfer) which implements boundary-based registration (Greve and Fischl 2009). Co-registration was configured with six degrees of freedom. Head-motion parameters with respect to the BOLD reference (transformation matrices, and six corresponding rotation and translation parameters) are estimated before any spatiotemporal filtering using mcflirt (FSL 5.0.9, Jenkinson et al. 2002). BOLD runs were slice-time corrected using 3dTshift from AFNI 20210206 (Cox and Hyde 1997, RRID:SCR_005927). The BOLD time-series were resampled onto the following surfaces (FreeSurfer reconstruction nomenclature): fsaverage5. The BOLD time-series (including slice-timing correction when applied) were resampled onto their original, native space by applying a single, composite transform to correct for head-motion and susceptibility distortions. These resampled BOLD time-series will be referred to as preprocessed BOLD in original space, or just preprocessed BOLD. The BOLD time-series were resampled into several standard spaces, correspondingly generating the following spatially-normalized, preprocessed BOLD runs: MNIPediatricAsym:cohort-3, MNI152NLin2009cAsym. First, a reference volume and its skull-stripped version were generated using a custom methodology of fMRIPrep. Automatic removal of motion artifacts using independent component analysis (ICA-AROMA, Pruim et al. 2015) was performed on the preprocessed BOLD on MNI space time-series after removal of non-steady state volumes and spatial smoothing with an isotropic, Gaussian kernel of 6mm FWHM (full-width half-maximum). Corresponding “non-aggresively” denoised runs were produced after such smoothing. Additionally, the “aggressive” noise-regressors were collected and placed in the corresponding confounds file. Several confounding time-series were calculated based on the

preprocessed BOLD: framewise displacement (FD), DVARS and three region-wise global signals. FD was computed using two formulations following Power (absolute sum of relative motions, Power et al. (2014)) and Jenkinson (relative root mean square displacement between affines, Jenkinson et al. (2002)). FD and DVARS are calculated for each functional run, both using their implementations in Nipype (following the definitions by Power et al. 2014). The three global signals are extracted within the CSF, the WM, and the whole-brain masks. Additionally, a set of physiological regressors were extracted to allow for component-based noise correction (CompCor, Behzadi et al. 2007). Principal components are estimated after high-pass filtering the preprocessed BOLD time-series (using a discrete cosine filter with 128s cut-off) for the two CompCor variants: temporal (tCompCor) and anatomical (aCompCor). tCompCor components are then calculated from the top 2% variable voxels within the brain mask. For aCompCor, three probabilistic masks (CSF, WM and combined CSF+WM) are generated in anatomical space. The implementation differs from that of Behzadi et al. in that instead of eroding the masks by 2 pixels on BOLD space, the aCompCor masks are subtracted a mask of pixels that likely contain a volume fraction of GM. This mask is obtained by dilating a GM mask extracted from the FreeSurfer's aseg segmentation, and it ensures components are not extracted from voxels containing a minimal fraction of GM. Finally, these masks are resampled into BOLD space and binarized by thresholding at 0.99 (as in the original implementation). Components are also calculated separately within the WM and CSF masks. For each CompCor decomposition, the k components with the largest singular values are retained, such that the retained components' time series are sufficient to explain 50 percent of variance across the nuisance mask (CSF, WM, combined, or temporal). The remaining components are dropped from consideration. The head-motion estimates calculated in the correction step were also placed within the corresponding

confounds file. The confound time series derived from head motion estimates and global signals were expanded with the inclusion of temporal derivatives and quadratic terms for each (Satterthwaite et al. 2013). Frames that exceeded a threshold of 0.5 mm FD or 1.5 standardised DVARS were annotated as motion outliers. All resamplings can be performed with a single interpolation step by composing all the pertinent transformations (i.e. head-motion transform matrices, susceptibility distortion correction when available, and co-registrations to anatomical and output spaces). Gridded (volumetric) resamplings were performed using antsApplyTransforms (ANTs), configured with Lanczos interpolation to minimize the smoothing effects of other kernels (Lanczos 1964). Non-gridded (surface) resamplings were performed using mri_vol2surf (FreeSurfer).

Many internal operations of fMRIPrep use Nilearn 0.6.2 (Abraham et al. 2014, RRID:SCR_001362), mostly within the functional processing workflow. For more details of the pipeline, see the section corresponding to workflows in fMRIPrep's documentation.

Laboratory portion size meals

Table S1. Amount of food served by portion size condition

	Reference portion	33% increase from reference portion	66% increase from reference portion	99% increase from reference portion
Total amount served, grams	769	1011.4	1255.8	1492.2
Total amount served, kcal	1048	1376.8	1706.6	2030.4

Table S1. Amount of food served by portion size condition

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Total amount served, grams	769	1011.4	1255.8	1492.2
Total amount served, kcal	1048	1376.8	1706.6	2030.4

Analyses

Imputation of missing pre-MRI fullness value. For one subject with missing data, three pre-MRI fullness values were imputed from sex, age, and BMI percentile using multivariate imputation by chained equations in R [87] with 5 iterations per imputation. As group-level responses to portion size were not impacted by the imputed values [33], the median value was used in the present analyses.

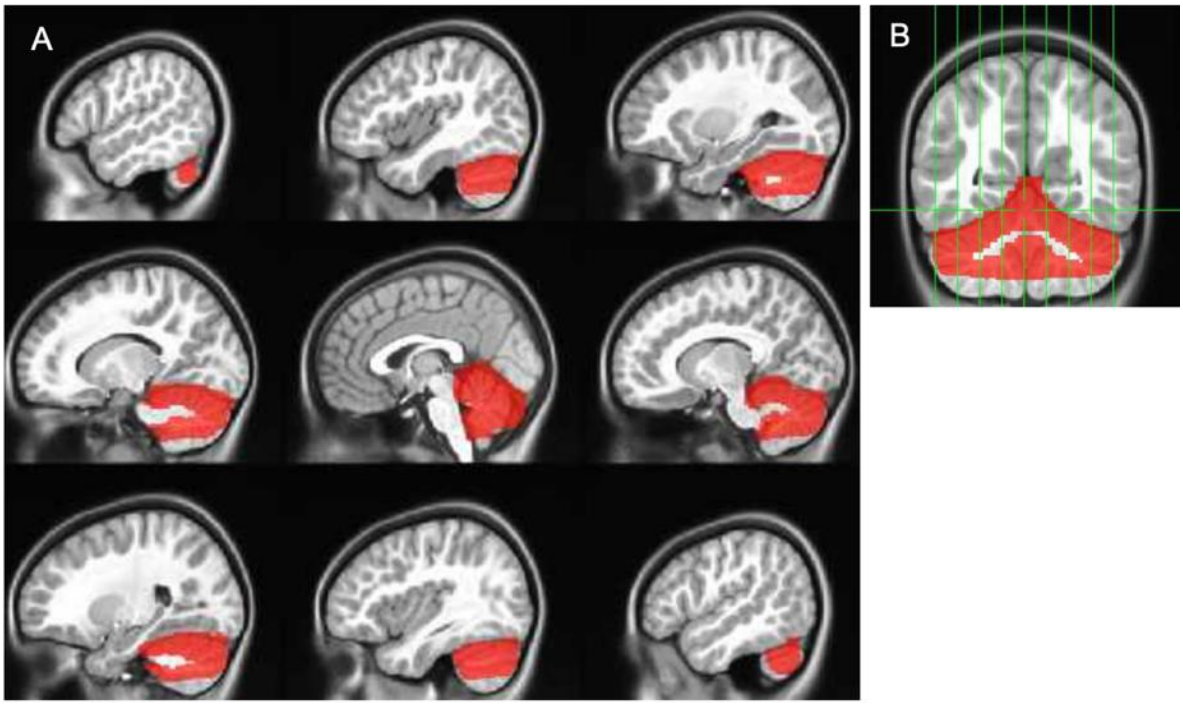

Figure S1. Cerebellum mask: (a) Sagittal slices with cerebellum mask (red) overlayed on MNI's unbiased template for pediatric cohort 3. (b) Coronal slice with cerebellum mask (red) overlayed on MNI's unbiased template for pediatric cohort 3. Green vertical lines indicate location of sagittal slices depicted in (a)

5.2 Results

Descriptive statistics

Table S2. Pearson correlation coefficients between individual-level portion size slopes

	1	*2*	*3*	*4*
Linear portion size slope, estimated from g	-			
Linear portion size slope, estimated from kcal	0.76***	-		
Quadratic portion size slope, estimated from g	0.01	-0.2	-	
Quadratic portion size slope, estimated from kcal	-0.02	-0.22	0.79***	-

** FDR-adjusted p < 0.05, **FDR- adjusted p < 0.01, *** FDR-adjusted p < 0.001.*

Table S3. Associations between portion size slopes and child characteristics

	Linear slope, g (n = 61)	Linear slope, kcal (n = 61)	Quadratic slope, g (n = 58)	Quadratic slope, kcal (n = 58)
Age, r [a]	0.07	0.02	0.21	-0.07
BMI percentile, r [a]	-0.12	0.02	-0.15	-0.17
Sex, t-stat (df) [b]	-0.92 (60.7)	0.32 (60.7)	-1.00 (55.9)	0.60 (58.0)

All p-values were > 0.1 (unadjusted)

[a] Associations assessed with Pearson correlations

[b] Associations assessed with 2-sample t-tests (equal variance between groups not assumed); male participants were treated as the reference group

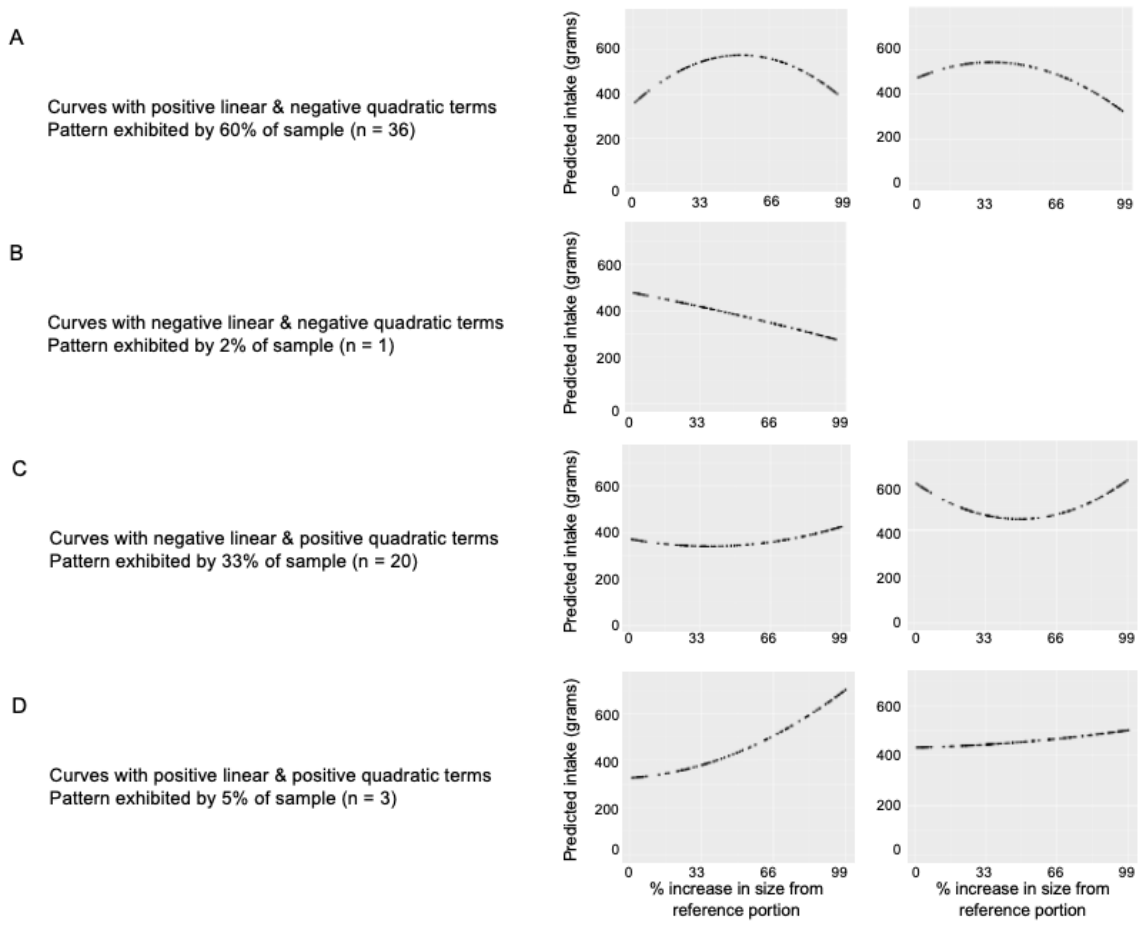

Figure S2. Example portion size curves for gram intake. Graphs show predicted intake in grams (y-axis) by % increase in portion size relative to the study's reference condition (x-axis). Data for each curve was simulated using individual-level intercepts and slopes derived from fixed-effects individual slopes (FEIS) models predicting intake (grams) from the linear increase in portion size from the reference portion [0, 33%, 66%, 99%] and the quadratic (i.e., linear * linear) increase in portion size from the reference portion, controlling for pre-meal fullness, average liking of foods at the meal, and meal order. Graphs show examples of curves characterized by (A) positive linear and negative quadratic terms, (B) negative linear and negative quadratic terms, (C) negative linear and positive quadratic terms, and (D) positive linear and positive quadratic terms.

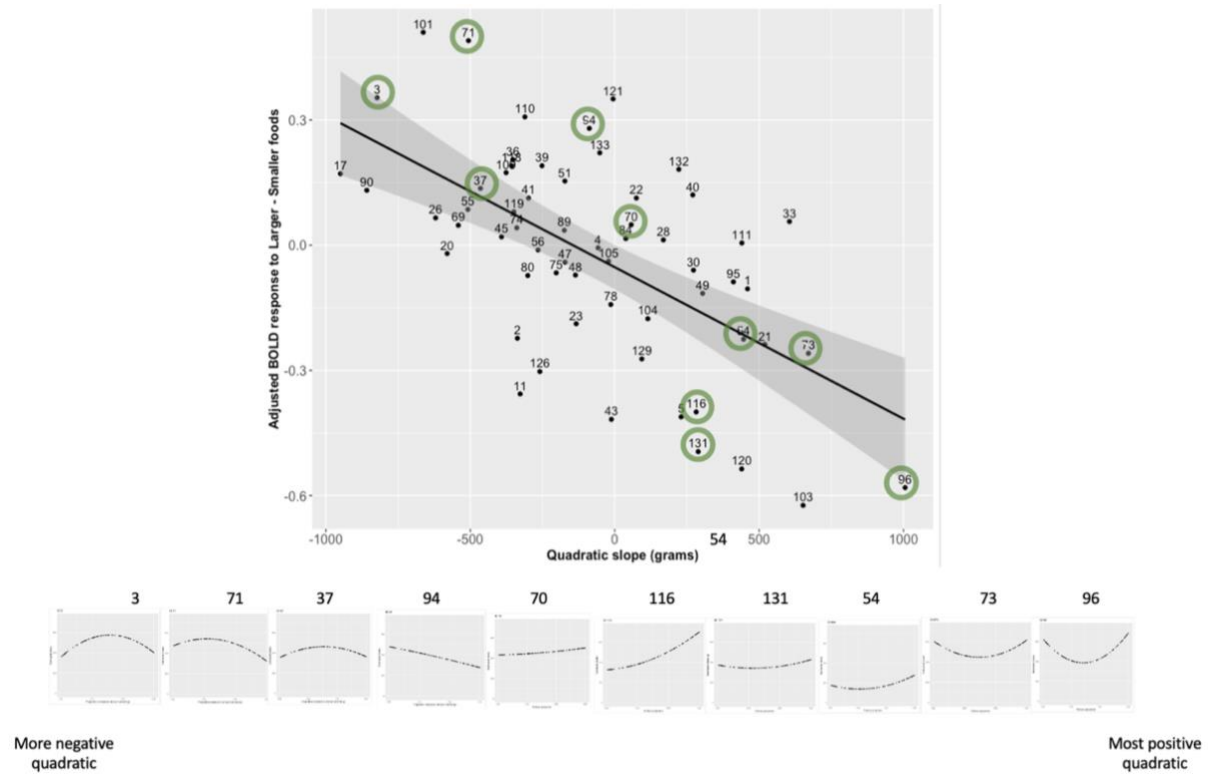

Figure S3. Association between cerebellar response to portion size (larger – smaller) and quadratic portion size slope (N = 58). This is the same association shown in Figure 2 (main text), but with portion size curves (bottom) shown for 10 children (circled in green). Subject IDs above each point on the graph correspond to the ID above the portion size curves

6. Citations

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Chapter 4 Decision-making processes related to perseveration are indirectly associated with weight status in children through laboratory-assessed energy intake

Fuchs BA, Roberts NJ, Adise S, Pearce AL, Geier CF, White C, Oravecz Z, Keller KL

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Abstract

Decision-making contributes to what and how much we consume, and deficits in decision-making have been associated with increased weight status in children. Nevertheless, the relationships between cognitive and affective processes underlying decision-making (i.e., decision-making processes) and laboratory food intake are unclear. We used data from a four-session, within-subjects laboratory study to investigate the relationships between decision-making processes, food intake, and weight status in 70 children 7-to-11-years-old. Decision-making was assessed with the Hungry Donkey Task (HDT), a child-friendly task where children make selections with unknown reward outcomes. Food intake was measured with three paradigms: (1) a standard *ad libitum* meal, (2) an eating in the absence of hunger (EAH) protocol, and (3) a palatable buffet meal. Individual differences related to decision-making processes during the HDT were quantified with a multilevel reinforcement learning model. Path analyses were used to test whether decision-making processes that contribute to children's (a) expected value of a choice and (b) tendency to perseverate (i.e., repeatedly make the same choice) were indirectly associated with weight status through their effects on intake (kcal). Results revealed that increases in the tendency to perseverate after a gain outcome were positively associated with intake at all three paradigms and indirectly associated with higher weight status through intake at both the standard and buffet meals. Increases in the tendency to perseverate after a loss outcome were positively associated with EAH, but only in children whose tendency to perseverate persisted across trials. Results suggest that decision-making processes that shape children's tendencies to repeat a behavior (i.e., perseverate) are related to laboratory energy intake across multiple eating paradigms. Children who are more likely to repeat a choice after a positive outcome have a tendency to eat more at laboratory meals. If this

generalizes to contexts outside the laboratory, these children may be susceptible to obesity. By using a reinforcement learning model not previously applied to the study of eating behaviors, this study elucidated potential determinants of excess energy intake in children, which may be useful for the development of childhood obesity interventions.

1. Introduction

Approximately 18% of children in the United States have obesity, and an additional 16% meet the criteria for overweight [1]. These statistics are concerning given the associations between childhood obesity and adverse physical and psychosocial health outcomes [2]. Behavioral interventions to reduce energy intake can produce beneficial weight-loss results [3,4], however, they are not effective for all children and lack long-term efficacy [5]. One reason for this may be a lack of understanding of food-related decision-making in middle childhood (i.e., 6-to-12 years-old), a period where children gain autonomy over food-related decisions [6]. In particular, while research has examined the decision-making mechanisms underlying *what* foods children select [6–10], the mechanisms underlying *how much* children consume are unclear. To close this gap, this study aims to identify decision-making processes that are associated with increased energy intake and weight status in middle childhood.

Decision-making is a multi-stage process that involves the assessment of options, the selection of an action, and the evaluation of an outcome [11]. This is applicable to food-related decisions that impact overall energy intake [12]. For example, when food is available, a decision to eat may occur when the estimated value of eating is greater than the estimated value of not eating [13]. Following a decision to eat, the consequences of taking a bite (e.g., taste, physiological changes) are evaluated and can influence subsequent value assessments. In general, decision-making is supported by affective and cognitive processes [11] referred to as decision-making processes; however, the decision-making processes that underlie food-related decision-making in middle childhood are unknown. The protracted development of prefrontal cortex in childhood and adolescence [14] supports improvements in executive functioning [e.g., inhibitory control, working memory, and cognitive flexibility; ,15–17], which may improve

future-oriented decision-making [18]; however, children in this stage make less future-oriented decisions compared to both adolescents and adults [19]. Given the unique stage of cognitive development and increasing autonomy over food-related decisions, identifying the decision-making processes that relate to energy intake in middle childhood is warranted.

One approach to studying decision-making is to have children complete tasks that assess choice behaviors in response to uncertain outcomes. One such task is the Hungry Donkey Task (HDT) [19], the child-friendly version of the Iowa Gambling task (IGT) [20] where children are instructed to accumulate as many rewards as possible ("apples" for the hungry donkey) by choosing from options with different reward and punishment probabilities. Cross-sectional analyses indicate that performance on these tasks (i.e., the proportion of advantageous versus disadvantageous choices) is negatively associated with weight status in children [21–24], although performance has not been related to self-reported measures of overeating [25] or food approach behavior [26]. Examining the decision-making processes that underlie HDT performance may provide a more nuanced understanding of the mechanisms that underlie energy intake and weight status in children.

To isolate decision-making processes, computational models can be applied to behavioral data from decision-making tasks [e.g., 27,28]. Using this approach on the present data, Roberts et al. [29] revealed that children's decisions on the HDT were best characterized by the Value-Plus-Perseveration (VPP) reinforcement learning model [28]. The VPP model allows for the examination of individual-level decision-making processes that impact children's (a) estimated expected value of a decision and (b) their tendency to perseverate (repeat) a decision [28]. In the context of food-related decision-making, the concepts of expected value and perseveration are theoretically relevant. For example, a child might take a bite of ice cream because the expected

value of taking a bite is greater than the expected value of an alternative option (e.g., not taking a bite) and/or because they previously took a bite and have a tendency to repeat selections associated with positive outcomes (e.g., the ice cream tasted good). Thus, we hypothesized that decision-making processes (i.e., VPP model parameters) related to expected value and perseveration would be directly associated with children's laboratory energy intake and indirectly associated with children's weight status through energy intake.

As decision-making and eating behaviors may differ across contexts, we captured food-related decisions by measuring energy intake during three different paradigms: (1) a standard meal, designed to examine intake at a typical meal, (2) an eating in the absence of hunger (EAH) protocol designed to elicit disinhibited intake of snack foods when children are not hungry [30], and (3) a buffet meal designed to elicit overeating in a meal context. Using separate path models for each eating context, we assessed: 1) the associations between decision-making processes and children's energy intake; and 2) the indirect associations between decision-making processes and child weight status through energy intake. Hypotheses for these analyses are detailed in the methods (see section 2.4.2). These analyses have the potential to elucidate the decision-making processes underlying children's food-intake decisions and childhood obesity.

2. Materials and Methods

Data for these analyses were drawn from a larger, cross-sectional study on the associations between decision-making, eating behavior, and weight status in children (NCT02855398). Data were collected between April 2015 and September 2016 in State College, Pennsylvania. The study was approved by the Pennsylvania State University Institutional Review Board (IRB approval number: 674).

2.1. Participants

Seventy children participated in the primary study. Data for the HDT, standard meal, and EAH protocol were available for all 70 children, however only 69 children completed the buffet meal because one child was lost to follow-up. Participants were recruited through flyers and postings on popular websites. Children were eligible for the study if they were 7-to-11-years-old and did not have underweight (i.e., BMI-for-age < 5%), pre-existing food allergies and/or dietary restrictions, learning disabilities, psychiatric/neurological conditions, a family history of psychiatric conditions, and were not currently using medications known to affect neural function or appetite. Due to the use of functional magnetic resonance imaging (MRI) in the primary study, children were also excluded if they were left-handed, had impaired or uncorrected vision, or had common MRI contraindications (e.g., metal in body and/or mouth). Lastly, adopted children were not included due to potentially unknown familial medical history. The sample was balanced by sex (n=34 male; n=36 female) and weight status (n=35 healthy weight: <85th %tile BMI-for-age; n=35 overweight/obesity: ≥ 85th% BMI-for-age; (Cole et al., 2000). Children exhibited a wide range of BMI-z values (-1.25 to 2.57) and were predominately white (91%) and non-Hispanic (94%; Table 4-1). Parents provided written consent to allow their child to participate and children provided verbal and written assent on the first visit.

2.2. Experimental design and procedures

As part of the larger study, child-parent dyads attended four laboratory sessions conducted over either lunch (11:00 AM-1:00 PM) or dinner time (4:00–6:30 PM), scheduled approximately one week apart. Session times (i.e., lunch or dinner) were consistent within families and, to the extent possible, counterbalanced across families. The order of the first three sessions (A, B, C)

was randomly assigned and counterbalanced across families while the fourth session always included the fMRI scan [see 32,33]. Session A included a computerized food-choice task [see 9] and a delay discounting questionnaire. Session B included the Hungry Donkey Task (HDT) followed by the standard meal and EAH protocol; Session C include an inhibitory control task [see 34] followed by the buffet meal. The current study included data from the HDT and the three eating paradigms (i.e., the standard meal, EAH protocol, and the buffet meal). Children were asked to fast for at least three hours prior to each visit so that the standard and buffet meals occurred during a state when children would typically be hungry. No additional instructions were provided to control what children ate prior to the requested fasting period. Children were allowed to consume *ad libitum* during all eating paradigms and were not required to consume any of the foods.

2.3. Measures

2.3.1. Anthropometric Measurements

On the first visit to the laboratory, children's height (to the nearest 0.1cm) and weight (to the nearest 0.1kg) were measured twice by a trained researcher using a standard scale (Detecto model 437, Webb City, MO) and stadiometer (Seca model 202, Chino, CA) while children were in stocking feet and light clothing. Children's average height and weight across the two measurements, along with sex and age, were used to calculate BMI (kg/m^2) *z*-score (BMI-z) based on the Centers for Disease Control and Prevention growth curves [31].

2.3.2. Laboratory eating paradigms

Before and after each eating paradigm, children rated their fullness level using a validated, age-appropriate, 150 mm visual analog scale [35]. A rating of 0 mm indicated their stomach felt empty, whereas a rating of 150 mm indicated they felt so full they could not eat any

more. After rating pre-meal/EAH fullness and before the start of each eating paradigm, children rated their liking of small samples (< 5 grams) of each meal component using a 5-point facial hedonic scale (1=most negative, 5=most positive). For the EAH protocol, children also indicated their rank-order preference (Birch 1979) for the food items. Food and drink items were individually weighed to the nearest 0.1g on a scale (Ohaus, Parsippany, NJ) before and after each eating paradigm to compute grams consumed (i.e., difference in pre- and post-meal weight). Grams consumed for each item were used to calculate the energy (kcal) consumed during each paradigm based on information from the nutritional facts panel and/or from standard nutrition databases (http://www.ars.usda.gov/ba/bhnrc/ndl).

2.3.2.1. Standard Meal

To examine intake at a typical meal, children were presented with a multi-item meal of common, age-appropriate food items. Food items were selected based on those commonly eaten by children this age from the Continuing Survey of Food Intakes of Individuals [36] and included macaroni and cheese, garlic bread, broccoli, tomatoes, grapes, and water (Table 4-2). Foods were presented on trays with no packaging (Figure 4.2A). Children were told that they had 30 minutes to eat as much as they wanted and they could ask for extra helpings at any point. A researcher sat with the child during the meal and read a nonfood-related book to serve as a neutral distraction and to avoid the child engaging in conversations about food and/or the meal. Similar methods have been used in other studies with this age group [37,38].

2.3.2.2. Eating in the Absence of Hunger (EAH)

To assess children's disinhibited eating of palatable snacks when not hungry, children were presented with a variety of sweet and savory snacks (Table 4-3) 15 minutes following the standard meal [30]. Snack items were presented on trays in separate containers with no

packaging (Figure 4.2B). In addition to snack items, children were provided with toys (e.g., coloring, playing cards) and books. Children were left alone in the room for 15 minutes and told they could play with any of the toys or eat any of the foods while the researcher worked in an adjacent room.

2.3.2.3. Buffet meal

To assess children's tendency to overeat from a variety of highly palatable foods approached in a fasted state, children were presented with a palatable buffet meal consisting of savory-fat (e.g., cheese bagel bites), sweet-fat (e.g., chocolate chip cookies) and sweet (e.g., red licorice) food and drink items (Table 4-4). Food items were presented on trays in separate containers with no packaging (Figure 4.2C). Children were told that they had 30 minutes to eat as much or as little as they want and that they could ask for extra helpings. Similar to the standard meal, a researcher sat with the child during the meal and read a nonfood-related book to serve as a neutral distraction.

2.3.3. Decision-making measurements

2.3.3.1. The Hungry Donkey Task (HDT)

Decision-making was assessed using the HDT [19]. In the HDT, children select from four doors (A, B, C, D) with different gain and loss probabilities in order to win "apples" for a hungry donkey. Children are not informed of the gain and loss probabilities, but they can be inferred throughout the task through feedback received after each selection [19]. Doors A and B are associated with a higher gain magnitude (4 apples gained on 100% of trials) and higher loss magnitude (Door A: 0, 8, 10, or 12 apples lost per trial; Door B: 0 or 50 apples lost per trial), whereas doors C and D are associated with a lower gain magnitude (2 apples gained on 100% of trials) and lower loss magnitude (Door C: 0, 1, 2, or 3 apples lost per trial; Door D: 0 or 10

apples lost per trial). Consistently choosing doors A or B would ultimately result in a negative net yield while consistently choosing doors C or D would result in a positive net yield. Thus, doors A and B are considered "disadvantageous" choices, and doors C and D are considered "advantageous" choices [19,20].

The task was presented electronically using E-Prime 2.0 software (Psychology Software Tools, Inc., Pittsburgh, PA, USA). Prior to the task, children were (a) instructed to select doors to win as many apples as possible for the hungry donkey, (b) told that choosing a door would result in one of two outcomes: (1) winning apples, or (2) winning some apples and losing some apples, and (c) told they would play the game several times and could pick different doors any time they wished. Following the instructions, children completed 200 trials of the task. At the start of each trial, children were presented with a selection screen (Figure 4.1A) which displayed: (1) four doors (A, B, C, D) presented horizontally in the center of the screen, (2) an image of a donkey below the doors, and (3) the instructions "Choose the most favourable door!" above the doors. Children chose a door by using one of four keyboard keys (C, V, B, N) that corresponded to each door from left to right. Children had unlimited time to select a door. After each selection, an outcome screen (Figure 4.1B) displayed the numbers of apples gained and lost in the current trial pictorially as green and red apples, respectively, in place of the chosen door and numerically on the right side of the screen. Further, the net total (gained-lost) number of apples won in the task so far was presented numerically in the lower half of the screen, in place of the donkey. To reduce working memory demands of the task, a vertical bar on the right side of the screen displayed the proportion of apples gained (in green) and lost (in red) in the task so far, averaged across all doors. The outcome screen was displayed for 2 seconds and then the next selection screen appeared.

2.3.3.2. Value-Plus-Perseveration (VPP) Model

To assess decision-making processes, the VPP model [28] was fit to decision-making data from the HDT. The VPP model assumes that the probability of selecting a door during an HDT trial is based on the overall value of that door relative to other doors. In the VPP model, the overall value of a door is the weighted average of two mathematical terms: (1) an Expected Value (EV) term and (2) a Perseveration term, summarized below. The relative weight given to each term is determined by the expectancy weighting parameter w ($0 < w < 1$), with values greater than 0.5 ($w > 0.5$) indicating greater weight given to the EV term and values less than 0.5 ($w < 0.5$) indicating greater weight given to the Perseveration term. The likelihood that the door with the highest overall value will be selected is influenced by the response consistency parameter c ($0 < c < 5$), which reflects the tendency to make decisions that align with value computations. Higher values of c indicate a tendency to make selections consistent with computed values, whereas lower values of c indicate more exploratory and random behavior. For a more detailed mathematical explanation of the VPP model, see Worthy, Pang, et al. [28].

The EV term quantifies the expected value of a chosen door after feedback is presented on a given trial by (1) determining the value derived from that trial's outcome (i.e., a trial's utility) and (2) integrating the trial's utility with the previous expected value of the chosen door. A trial's utility is influenced by a feedback sensitivity parameter and a loss aversion parameter. The feedback sensitivity parameter α ($0 < \alpha < 1$) indicates how sensitive a child is to the size of gains and losses; higher values reflect greater sensitivity to outcome magnitude. The loss aversion parameter λ ($0 < \lambda < 5$) indicates sensitivity to losses relative to gains; values greater than 1 ($\lambda > 1$) indicate greater sensitivity to losses relative to gains, values less than 1 ($\lambda < 1$) indicate greater sensitivity to gains relative to losses, and the value 1 ($\lambda=1$) indicates equal

sensitivity to gains and losses. The impact of a trial's utility on the expected value of the chosen door is determined by an updating parameter ø ($0 < ø < 1$), which reflects the influence of the given trial's evaluation relative to the previous expected value of the chosen door. A value of zero ($ø = 0$) indicates no updating of expected value based on the given trial's utility (i.e., expected value of given trial equals the expected value from the previous trial), whereas a value of one ($ø = 1$) indicates complete updating (i.e., expected value of the given trial equals the trial's utility). Thus, higher values reflect more weight given to the most recent evaluation (i.e., more updating).

The Perseveration term quantifies a door's tendency to elicit a perseverative response (i.e., perseveration strength) after feedback is presented on a given trial. This term builds on a 'win-stay-lose-shift' heuristic which proposes an individual will repeat an option following a gain, or select a different option following a loss [39,40]. Gain and loss outcomes impact the perseveration strength of the chosen door according to the impact of gain ($-1< \varepsilon_{pos} <1$) and loss ($-1< \varepsilon_{neg} <1$) on perseveration strength parameters, respectively. Specifically, the perseveration strength for the chosen door will be incrementally increased or decreased by ε_{pos} after a gain (net outcome $\geq$ zero) or by ε_{neg} after a loss (net outcome < zero). A positive ε_{pos} value indicates a tendency to perseverate (i.e., select the same door) after a gain, whereas a negative value indicates a tendency to switch to a different door after a gain. Similarly, a positive ε_{neg} value indicates a tendency to perseverate after a loss, whereas a negative value indicates a tendency to switch to a different door after a loss. The perseveration strength for all doors decays each trial according to the perseveration decay parameter k ($0 < k < 1$). Higher values of k indicate less decay in perseveration strength on each subsequent trial (k of 1 = no decay, k of 0 = complete decay).

2.3.3.3. Behavioral Metrics

Because there is limited work using the VPP model in children, we also wanted to examine how VPP model parameters related to previously-used behavioral metrics of IGT/HDT performance. Therefore, three behavioral metrics were computed: 1) 'Netscore' was calculated by subtracting the number of times doors A and B (i.e., disadvantageous choices) were chosen from the number of times doors C and D (i.e., advantageous choices) were chosen [Net score = (C + D) – (A + B)]; 2) 'win-stay' was calculated as the proportion of trials where the door chosen on the current trial, t, was the same as the door chosen on the previous trial, t-1, given a "win" (net outcome ≥ zero) on the previous trial (WS = $p(stay_t|win_{t-1})$; and 3) 'lose-shift' was calculated as the proportion of trials where the door chosen on the current trial differed from the door chosen on the previous trial, given a "loss" (net outcome < 0) on the previous trial (LS = $p(shift_t|loss_{t-1})$. Although a "win" has also been defined as the absence of points lost regardless of net outcome [41], the definitions of "win" and "loss" used here align with the definitions of "gain" and "loss" in the VPP model (see section 2.3.2.2). These definitions are consistent with those previously used to assess win-stay and lose-shift strategies in children [42].

2.4. Statistical analyses

Statistical analyses were conducted in R ≥ 3.4 [43] and the VPP model was fit using a Bayesian framework[3] with the hBayesDM package [44]. Child-specific VPP model parameter point estimates were used for all analyses. Path analyses were conducted using the Lavaan package 0.6-8 [45]. The significance threshold was set to 0.05. Analysis code is available through the Open Science Framework (osf.io/mwqz9/).

2.4.1. Descriptive Statistics

[3] Two chains with 5000 iterations each (including a 1000 warmup phase that was discarded) were used

Mean and standard deviation were calculated for pre-meal fullness ratings and intake, which exhibited approximately normal distributions (assessed via skewness and kurtosis). Due to non-normal distributions of several decision-making variables, median and percentile measures (25^{th}, 75^{th}) were calculated for VPP model parameters and behavioral metrics. For normally distributed outcomes (e.g., intake and pre-meal fullness), Pearson correlations and two-sample t-tests were used to test associations with child age and sex, respectively. Spearman rank order correlations were used to test associations amongst decision-making variables, and between decision-making variables and continuous characteristics (i.e., BMI-z, age, and pre-meal fullness). Mann-Whitney-Wilcoxon and Kruskal-Wallis tests were used to test associations between decision-making variables and categorical child characteristics (i.e., sex, maternal education, and household income). The Benjamini-Hochberg procedure was used to adjust for multiple comparisons [46] such that adjustment was applied for: 1) all pair-wise associations between the eight VPP model parameters (28 tests); 2) associations between VPP model parameters and each behavioral metrics (8 tests per behavioral metric); and 3) associations between participant characteristics and each VPP model parameter (6 tests per VPP model parameter).

2.4.2. Path analyses

We used path analyses to test our hypotheses that decision-making processes related to expected value and perseveration would be associated with weight status through their effects on energy intake. Hypotheses were developed based on theoretical relationships between VPP model parameters and intake-related processes (Table 4-5). Because expected value and perseveration are two conceptually different aspects of decision-making, separate path models were used to test hypotheses related to each, referred to as the "expected value (EV)" and

"perseveration" models, respectively. Further, separate path models were used to test hypotheses related each eating paradigms, resulting in a total of six models.

For the EV models, we hypothesized that two parameters would relate to intake at all three eating paradigms, while one parameter would only relate to EAH and buffet meal intake, as these two paradigms contain a variety of highly palatable foods and are designed to elicit overeating. For all three eating paradigms, we hypothesized that children who update expected value less (i.e., lower ø) would eat more because they may modify the perceived value of eating in response to within-meal decreases in pleasantness [47] or increases in satiation [48] to a smaller degree. Further, we hypothesized that children who are less sensitive to the amount gained or lost (i.e., lower α) would eat more because they may be less sensitive to within-meal decreases in food pleasantness. Lastly, for EAH and the buffet meal only, we hypothesized that children who are less loss averse (i.e., lower λ) would eat more because they may be less impacted by negative consequences from overeating (e.g., physical discomfort [49]).

For the perseveration models, we once again hypothesized that two parameters would relate to intake at all three eating paradigms, while one parameter would only relate to EAH and buffet meal intake. We hypothesized that children whose tendency to perseverate decays more slowly (i.e., greater *k*) would eat more because their motivation to eat may be sustained longer throughout the meal. Further, we hypothesized that children with greater increases in perseveration strength following gains (i.e., greater ε_{pos}) would eat more because they may be more reinforced by rewarding experiences with food [50,51]. Lastly, for the EAH and buffet paradigms, we hypothesized that children with greater increases in perseveration strength following losses (i.e., greater ε_{neg}) would eat more because they may overeat despite negative consequences [52].

For EV and perseveration models, we tested whether updating and perseveration decay, respectively, moderated the associations between other hypothesized parameters and intake. This is because in the VPP model, updating modifies the effects of other parameters related to expected value, and perseveration decay modifies the effects of other parameters related to perseveration strength. If the moderation was not significant, it was not included in the final path model. Additionally, for each eating paradigm, we hypothesized that intake would be positively associated with BMI-z and that VPP model parameters would be indirectly associated with BMI-z through intake. Specifically, we hypothesized that expected value parameters (i.e., updating (α), loss aversion (λ), and feedback sensitivity (ø)) would be negatively associated with BMI-z through reduced intake, while perseveration parameters (i.e., the impact of gain (ε_{pos}) and loss (ε_{neg}) on perseveration strength, and perseveration decay (k)) would be positively associated with BMI-z through increased intake.

Variables with skewness > |2| and kurtosis > |7| were considered to have distributions exceeding acceptable non-normality for path analyses with this sample size [53]. Therefore, the loss aversion parameter (skew = 2.88, kurtosis = 11.36) was log transformed for path analyses (log transformed skew = 0.23, kurtosis = 2.20). To facilitate the interpretation of relationships across VPP parameters, all parameters were normalized (mean = 0, SD = 1). Meal intake (kcal) was scaled by a factor of 100 to make the scale more closely match the scale of the other parameters. Models were estimated using maximum likelihood estimation and robust standard errors. Initial and final models met the recommended sample size to number of free parameters ratio of >10:1 by Bentler & Chou [54], ranging from 11.5:1 to 35:1. Models had good fit (Table S1) according to the following measures and recommendations by Hooper et al. [55]: Satorra-Bentler (SB) scaled $\chi 2$ test statistic $p > 0.05$ [56,57], robust root mean square error of

approximation (RMSEA) < 0.07 [58], robust comparative fit index (CFI) > 0.95 [59], and the standardized root mean square residual (SRMR) < 0.08 [60]. Robust standard errors, SB scaled test statistic, and robust RMSEA/CFI were used to reduce bias resulting from non-normal distributions of decision-making parameters.

Given that meal intake was associated with age and pre-meal fullness, we conducted sensitivity analyses by including age and pre-meal fullness as covariates in each model. In addition, we tested each final model with a reduced sample (n = 64 for standard meal/EAH models, n = 63 for buffet meal models) that excluded three children who did not fully comply with the protocol (e.g., did not fast) and three children who exhibited attentional issues during the HDT (e.g., talked throughout the task). Lastly, because the EAH protocol is designed to assess eating when not hungry, final EAH models were also tested with a reduced sample (n = 57) that excluded thirteen children who rated their pre-EAH fullness as < 75% on the visual analog scale, replicating the threshold used in the primary study [32].

3. Results

3.1. Descriptive Statistics

Descriptive statistics for decision-making variables, food intake, and pre-meal fullness ratings are presented in Table 4-6. Age was positively associated with buffet meal intake (r(67) = 0.30, $p = 0.01$), but not standard meal intake ($r(68) = 0.22$, $p = 0.07$) or EAH ($r(68) = 0.03$, $p = 0.81$). Intake for the three eating paradigms did not vary by sex (*p's* > 0.06). Pre-standard meal fullness was negatively associated with standard meal intake ($r(68) = -0.24$, $p < 0.05$), however, pre-EAH and pre-buffet meal fullness were not associated with EAH ($r(68) = 0.06$, $p = 0.62$) or buffet meal intake ($r(67) = -0.02$, $p = 0.86$), respectively. Foods in all three paradigms were generally well-liked (Tables 4-2 to 4-4).

Correlation analyses were conducted to examine how decision-making variables related to each other (Table 4-7). All VPP model parameters were associated with at least one other VPP model parameter (-0.56 to 0.39, adjusted *p*'s < 0.05), with the exception of perseveration decay. While loss aversion was negatively associated with other EV parameters (i.e., updating and feedback sensitivity), EV parameters were not associated with perseveration parameters, expectancy weighting, or consistency. In contrast, the impact of gain and loss on perseveration strength were positively correlated with each other and expectancy weighting, but were negatively associated with consistency.

All VPP model parameters were associated with at least one of three behavioral metrics (-0.90 to 0.93, adjusted *p*'s < 0.05), with the exception of perseveration decay (Table 4-7). Conversely, each behavioral metric was associated with at least four of eight VPP model parameters. EV parameters related to processing gain and loss outcomes (i.e., feedback sensitivity, loss aversion) were positively associated with netscore, while perseveration parameters related to processing gain and loss outcomes (i.e., the impact of gain and loss on perseveration strength) were negatively associated with netscore. In line with the 'win-stay-lose-shift' heuristic, the impact of gain on perseveration strength was strongly related to win-stay ($r_s(68) = 0.93$, adjusted $p < 0.001$), while the impact of loss on perseveration strength was strongly related to lose-shift ($r_s(68) = -0.90$, adjusted $p < 0.001$).

Additional analyses conducted to examine how decision-making variables related to participant characteristics revealed that updating, the impact of gain on perseveration strength and win-stay were positively associated with child age (0.35 to 0.49, adjusted *p*'s < 0.05), while loss aversion was negatively associated with age ($r_s(68) = -0.40$, *adjusted* $p < 0.01$). Netscore was higher in girls (*median* = 0.00) compared to boys (*median* = -13.00 ; $U = 379$, *adjusted* $p = 0.04$).

Decision-making variables were not related to BMI-z, maternal education, family income, or pre-standard meal fullness, (adjusted *p*'s > 0.05; Tables S2-3).

3.2. Path Analyses

Results for the final path models (i.e., models with non-significant moderations excluded for parsimony, see section 2.4.2) are summarized below. Results for initial models, which contain all tested moderations, are reported in Table S4. Direct and indirect paths are described using unstandardized coefficients (B) and the standard errors (SE) for these estimates. Because path models include multiple predictors of intake, coefficients for paths directed at intake reflect partial regressions (i.e., associations are controlled for other predictors of intake). In contrast, coefficients for paths directed at BMI-z from intake reflect simple regressions [61].

3.2.1. Expected Value Models

3.2.1.1. Standard Meal

The EV model for the standard meal tested our hypotheses that feedback sensitivity (α) and updating (ø) would be negatively associated with intake at the standard meal and BMI-z through intake. In contrast to hypotheses, neither parameter was associated with intake (*p*'s > 0.12; Table 4-8). Our hypotheses about BMI-z were partially supported in that intake was positively associated with BMI-z, such that a 100 kcal increase in intake was associated with a 0.15 increase in BMI-z (B = 0.15, SE = 0.04, $p < 0.001$). However, there were no indirect associations between EV parameters and BMI-z through standard meal intake (*p*'s > 0.16). The pattern of results was maintained after adjusting for age (Table S5) and excluding children who were non-compliant (n = 6; Table S7). However, after adjusting for pre-meal fullness, updating was positively associated with intake (B = 0.55, SE = 0.25, $p = 0.03$) such that intake increased by 55 kcal for every 1 SD increase in updating (Table S6; Figure 4.3).

3.2.1.2. EAH

The EV model for the EAH protocol tested our hypotheses that feedback sensitivity (α), updating (ø) and loss aversion (λ) would be negatively associated with EAH and BMI-z through EAH. In contrast to hypotheses, none of the parameters were associated with EAH (p's > 0.50; Table 4-8). Similarly, there was no association between EAH and BMI-z (p = 0.23) or indirect associations between EV parameters and BMI-z through EAH (p's > 0.50). The pattern of results was maintained when adjusting for age and pre-EAH fullness and when excluding children who were non-compliant (n = 6) or who indicated they were not completely full after the test meal (n = 13; Tables S5-8).

3.2.1.3. Buffet Meal

The EV model for the buffet meal tested our hypotheses that feedback sensitivity (α), updating (ø) and loss aversion (λ) would be negatively associated with buffet meal intake and BMI-z through buffet meal intake. In contrast to hypotheses, none of the parameters were associated with buffet intake (p's > 0.36; Table 4-8). As with the standard meal, our hypotheses related to BMI-z were partially supported in that buffet meal intake was positively associated with BMI-z, such that a 100 kcal increase in intake was associated with a 0.07 increase in BMI-z (B = 0.07, SE = 0.03, p = 0.007. However, there were no indirect associations between EV parameters and BMI-z through buffet meal intake (p's > 0.40). The pattern of results was maintained when adjusting for age and pre- buffet meal fullness and when excluding children who were non-compliant (n = 6; Table S5-7).

3.2.2. Perseveration Models

3.2.2.1. Standard Meal

The perseveration model for the standard meal tested our hypotheses that the impact of gain on perseveration strength (ε_{pos}) and perseveration decay (k) would be positively associated with standard meal intake and BMI-z through standard meal intake (Figure 4.4A). As hypothesized, the impact of gain on perseveration strength was positively associated with standard meal intake (B = 0.88, SE = 0.20, $p < 0.001$; Table 8) such that a 1 SD increase in ε_{pos} was associated with an 88 kcal increase in standard meal intake (Figure 4.5A). However, perseveration decay was not associated with standard meal intake ($p = 0.58$). As in the EV model, standard meal intake was positively associated with BMI-z such that a 100 kcal increase in intake was associated with 0.15 increase in BMI-z (B = 0.15, SE = 0.04, $p < 0.001$). Further, ε_{pos} was indirectly associated with BMI-z through standard meal intake such that a 1 SD increase in ε_{pos} was associated with a 0.13 increase in BMI-z (B = 0.13, SE = 0.05, $p = 0.005$). Perseveration decay was not indirectly associated with BMI-z through intake ($p = 0.59$). The pattern of results was maintained when adjusting for age and pre-standard meal fullness and when excluding children who were non-complaint (n = 6 Table S5-7).

3.2.2.2. EAH

The perseveration model for the EAH protocol tested our hypotheses that the impact of gain (ε_{pos}) and loss (ε_{neg}) on perseveration strength and perseveration decay (k) would be positively associated with EAH and BMI-z through EAH (Figure 4.4B). Further, based on the initial model, the interaction between k and ε_{neg} was include as a predictor of intake. As hypothesized, the impact of gain on perseveration strength was positively associated with EAH (B = 0.40, SE = 0.17, $p = 0.02$; Table 8) such that a 1SD increase in ε_{pos} was associated with a 40 kcal increase in EAH (Figure 4.5B). While we hypothesized independent associations with the impact of loss on perseveration strength and perseveration decay, there was a significant

interaction between these parameters indicating that the association between ε_{neg} and EAH was more positive when decay was slower (i.e., at higher values of *k*; B = 0.89, SE = 0.27, *p* = 0.001). In children with the fastest perseveration decay (normalized *k* (i.e., SD) -2.15 to 0.03), greater increases in perseveration strength after a loss (ε_{neg}) were associated with lower EAH, while in children with the slowest perseveration decay (normalized *k* (i.e., SD) 0.08 to 2.39), greater increases in perseveration strength after a loss (ε_{neg}) were associated with greater EAH (Figure 4.6). As in the EV model, EAH was not associated with BMI-z (*p* = 0.23; Table 8) and there were no indirect effects of perseveration parameters on BMI-z through EAH (*p's* > 0.21). The pattern of results was maintained when adjusting for age and pre-EAH fullness and when excluding children who were non-complaint (n = 6; Table S5-7). When excluding children with pre-EAH fullness ratings < 75% (n = 13), the pattern of results were similar, however, reduced power caused the association between ε_{pos} and intake to lose significance (*p* = 0.07).

3.2.2.3. Buffet Meal

The perseveration model for the buffet meal tested our hypotheses that the impact of gain (ε_{pos}) and loss (ε_{neg}) on perseveration strength and perseveration decay (*k*) would be positively associated buffet meal intake and BMI-z through buffet meal intake (Figure 4.4C). As hypothesized, the impact of gain on perseveration strength (ε_{pos}) was associated with intake (B = 1.36, SE = 0.38, *p* < 0.001; Table 8) such that a 1 SD increase in ε_{pos} was associated with a 136 kcal increase in buffet meal intake (Figure 4.5C). In contrast to hypotheses, neither perseveration decay nor ε_{neg} were associated with buffet intake (*p's* > 0.76). Our hypotheses about BMI-z were partially supported. As in the EV model, buffet intake was positively associated with BMI-z (B = 0.07, SE = 0.03, *p* = 0.007). Further, ε_{pos} was indirectly associated with BMI-z through buffet meal intake, such that a 1 SD increase in $\varepsilon_{pos,}$ was indirectly associated with a 0.10 increase in

BMI-z (B = 0.10, SE = 0.05, p = 0.03). However, neither the impact of loss on perseveration strength nor perseveration decay were indirectly associated with BMI-z (p's > 0.75). The pattern of results was maintained when adjusting for age and pre-standard meal fullness and when excluding children who were non-complaint (n = 6; Table S5-7).

4. Discussion

The current study examined the relationships between decision-making processes, laboratory food intake, and BMI-z in a sample of 7-to-11-year-old children. By using a reinforcement learning model (the VPP model) to quantify decision-making processes during the HDT, we demonstrated that processes related to the tendency to repeatedly choose the same option (i.e., perseverate) were associated with intake across multiple eating paradigms. Children who exhibited greater increases in the tendency to repeat a choice after a gain consumed more from a standard meal, a palatable buffet, and from a selection of snacks provided following the standard meal (i.e., an EAH protocol). Moreover, increases in the tendency to repeat a choice after a gain were indirectly associated with greater child weight status through intake at the standard and buffet meals, but not EAH. This study advances the field by demonstrating that decision-making process related to perseveration may be associated with increased weight status in children because they facilitate excess consumption in multiple eating contexts.

4.1. Decision-making processes and behavioral metrics

Given that there has been limited research applying the VPP model to children's decision-making, we assessed the associations between decision-making processes (i.e., VPP model parameters) and three previously-used metrics of HDT behavior: netscore, win-stay, and lose-shift. Results revealed that each behavioral metric was significantly associated with at least four of eight VPP model parameters. For example, better performance on the HDT (i.e., higher

netscore) was associated with greater feedback sensitivity and updating, and smaller increases in perseveration strength following gain and loss outcomes. These results suggest that VPP model parameters reflect nuanced decision-making processes that underlie traditional behavioral metrics. This demonstrates the utility in applying computational models to understand the decision-making mechanisms that contribute to energy intake and the development of overweight and obesity.

4.2. Decision-making processes related to expected value, intake, and weight status

Updating of expected value was positively associated with intake during the standard meal when controlling for fullness. This contradicts our hypothesis and suggests that children whose estimation of value was more heavily influenced by recent outcomes (i.e., updated faster) tended to eat more during the standard meal. Potentially, children who rely more on time-distant information (i.e., update slower) during decision-making better incorporate experiences from prior meals (e.g., how satiating foods were) into their meal choices, and this contributes to reduced intake. However, updating was not related to buffet meal intake or EAH. This suggests that, independent of pre-meal fullness levels, relying more on time-distant information may help children moderate energy intake during moderately palatable meals but not eating contexts with increased variety and palatability. Alternatively, children may have had more experience with the foods in the standard meal than the buffet meal or EAH protocol, and therefore had more relevant prior information to incorporate into decisions made during the standard meal. Although we observed an association between updating and intake at a single meal, there were no indirect effects on weight status; however, this does not rule out the possibility that updating may be associated with long-term energy balance. Support for this comes from work demonstrating that adults who successfully lost weight in a weight-loss intervention relied more on time-distant

information during decision-making than adults who were unsuccessful [62]. Thus, relying more on time-distant information during decision-making may contribute to reduced energy intake and have long-term benefits for maintenance of a healthy weight.

4.3. Decision-making processes related to perseveration, intake, and weight status

As hypothesized, the impact of gain on perseveration strength was positively associated with intake at all three eating paradigms and was indirectly associated with BMI-z through standard and buffet meal intakes. These results indicate that children who had greater increases in the tendency to repeat a choice after a gain consumed more energy. Further, indirect associations suggest that greater increases in the tendency to repeat a choice after a gain may contribute to increased weight status by facilitating excess consumption at meals, but not necessarily from snack foods consumed after a meal. Previous research has demonstrated that behavioral responses to rewards correlate with intake and weight status in youth. For example, greater motivation to work for food, as assessed with the reinforcing value of food task, has been positively associated with children's energy intake [50,51] and weight gain [63]. In addition, children with higher drive scores on the Behavioral Approach Scale, indicative of greater reward sensitivity [64], show increased frequency of fast food and sweet drink consumption [65]. Thus, our results are consistent with previous research suggesting that altered behavioral responses to rewards may contribute to excess energy intake and obesity. These results provide insight into a cognitive process that may underlie these associations; children who are more likely to repeat behaviors following rewards may be prone to overeating and weight gain.

In addition to the observed associations with the impact of gain on perseveration strength, we observed that the interaction between the impact of loss on perseveration strength and perseveration decay was related to EAH. Children who had greater increases in the tendency to

perseverate after a loss ate less during the EAH protocol if their tendency to perseverate decayed quickly but ate more if their tendency to perseverate decayed slowly. This interaction suggests the tendency to eat in the absence of hunger following a negative experience (e.g., physical discomfort) may depend on the persistence of this tendency over time. Further, given that the impact of loss on perseveration strength reflects a process similar to positive punishment (i.e., a decrease in behavior following an aversive outcome) [66], the moderation by perseveration decay may explain why prior studies have shown inconsistent relationships between sensitivity to punishment and weight status [67–69]. Interestingly, neither the impact of loss on perseveration strength or perseveration decay were related to buffet meal intake, suggesting the influence of these decision-making processes on overeating may depend on factors such as physiological status at the start of the meal, types of food served, or the availability of alternative activities (i.e., toys during EAH or books during the standard meal). Future studies should examine the long-term implications of these decision-making processes on weight status and test why they may be associated with the tendency to overeat snack foods after a meal but not the tendency to overeat palatable foods within a meal.

Overall, our results suggest that decision-making processes related to perseveration contribute to energy intake and weight status in children. Similarly, previous research has demonstrated positive associations between perseverative behaviors during the Wisconsin Card Sorting Task (WCST) or Door Opening Task and both cross-sectional weight status in children and adolescents [70–72] and weight re-gain in children following a weight-loss program [73]. Further, making more perseverative errors during the WCST has been shown to moderate the relationship between cognitive restraint and *ad libitum* energy intake in adults, such that those with high perseverative errors and low restraint ate the most [74]. In sum, prior research suggests

that having a greater tendency to perseverate may contribute to increased energy intake and weight status. Our study builds on this by identifying specific decision-making processes related to perseveration that may underlie these associations.

4.4. Limitations and future research

There are several limitations to this study that should be highlighted. First, the study was cross-sectional, and although we used path analyses to test directed relationships, these analyses do not allow for assessment of cause and effect [75]. To understand whether decision-making processes impact future weight gain through their effects on intake, longitudinal research is necessary. Second, in our theoretical models, we proposed directed relationships from intake to BMI-z, given that excess energy intake can increase weight status. However, increased weight status also increases energy requirements [76], so the relationship between intake and weight status may be bidirectional. Further, adiposity can influence cognitive processes [77], so BMI-z may also impact decision-making processes. Thus, additional research examining the relationships between these variables is warranted to characterize the causal pathway.

Additional limitations pertain to our sample which was relatively homogeneous, with the majority of children being white and non-Hispanic. To improve the generalizability of these results, similar analyses should be conducted in more diverse cohorts. In addition, the age range of children tested was broad, spanning a period of neurocognitive development that can impact decision-making [15,78]. While our sample size was too small to test interactions with age, future studies with larger sample sizes should examine whether age in middle childhood moderates the relationship between decision-making processes and food intake, as this will have implications for the development of targeted approaches to reduce excess energy intake.

Lastly, there are several variables that were not assessed in this study that are relevant for future research. First, future research should include an external indicator of neuropsychological maturation, such as parental assessment of child executive functioning. Second, given that affective processes, such as anxiety, relate to both decision-making [79] and eating behaviors [80], future research should include assessments of state and trait affect and test whether these processes mediate or moderate the relationships between decision-making processes and food intake. Third, future research should examine how decision-making processes relate to food choices or within-meal eating behaviors (e.g., bite rate) which may mediate the observed relationships with energy intake.

4.5. Implications

Despite these limitations, the current study makes contributions to the field. We demonstrated that a reinforcement learning model can be used to estimate decision-making processes that overlap with, but are more nuanced than, traditional decision-making outcomes in children. Further, we demonstrated the feasibility and advantage of using a reinforcement learning model to understand mechanisms underlying children's food intake. By using path models to examine the relationships between VPP model parameters, objectively assessed intake, and BMI-z, we informed the underlying mechanisms linking decision-making processes to child weight status. In addition, by measuring intake during three different eating paradigms, we demonstrated that some decision-making processes (e.g., the impact of gain on perseveration strength) may contribute to children's intake across various eating contexts, whereas other decision-making processes (e.g., the impact of loss on perseveration strength, perseveration decay) may be context specific. This highlights the need for future studies to identify the

contexts most likely to promote overeating among children who vary in decision-making capabilities.

Finally, while additional research is needed to understand the long-term and causal relationships between decision-making processes and child weight status, we speculate on two practical implications related to the finding that increases in the tendency to repeat a choice after a gain were indirectly associated with greater weight status through standard and buffet meal intake. First, children who are more likely to repeat a behavior after a reward may be at higher risk for future weight gain and, therefore, may benefit from early interventions to reduce energy intake. Identifying children who exhibit this decision-making characteristic would be feasible through the administration of the Hungry Donkey Task. Second, intervention approaches to reduce the reinforcing effects of reward outcomes may be beneficial for reducing energy intake across multiple contexts.

4.6. Conclusion

This study showed that decision-making processes related to perseveration were associated with energy intake in children across a variety of eating contexts. Children who exhibited greater increases in the tendency to repeat a choice after a gain had a tendency to eat more across multiple eating contexts in the laboratory. Further, greater impact of gain on perseveration strength was indirectly associated with increased weight status through its association with greater intake at both the standard and buffet meals. These results suggest that this decision-making process may contribute to increased weight status by increasing intake at both moderately palatable (e.g., standard meal) and highly palatable (e.g., buffet meal) eating occasions. Future studies are needed to examine how decision-making processes impact future

weight status and whether interventions that target decision-making processes related to perseveration can mitigate excess energy intake.

Table 4-1. Demographic characteristics

Age in years, Mean (SD); range	9.47 (1.38); 7.04-11.97
Sex, N	34 Male /36 Female
BMI-z, Mean (SD); range	0.92 (0.92); -1.25-2.57
Ethnicity, N	
Not Hispanic	66
Hispanic	4
Race, N	
White	64
Black	3
Asian	2
Other	1
Household income[%], N	
<$50,000	17
$50-100,000	32
>$100,000	20
Maternal Education	
<Bachelor's Degree	23
Bachelor's Degree	28
>Bachelor's Degree	19

Table 4-2. Food items in Standard Meal

Food	Company, Brand	ED (kcal/g)	Serving size	kcal per serving	Liking Mean (sd)^
Macaroni and Cheese Dinner, Original	Kraft Foods, Inc.	1.05	400g	420	4.14 (0.84)
Garlic Bread	Pepperidge Farm, Inc	3.44	100g	344	4.36 (0.83)
Broccoli with:	Bird's Eye	0.31	180g	56	3.36 (1.24)
Sweet cream butter	Land O'Lakes Inc				
Butter Flavoring	Molly McButter, B&G Foods Inc.				
Cherry tomatoes	Wegmans	0.21	100g	21	2.61 (1.65)
Red Seedless grapes	Wegmans	0.77	200g	154	4.46 (0.79)
Angel Food Bundt Cake	Sara Lee Desserts, Hillshire Brands Co.	2.31	80g	185	4.40 (0.77)
Water	Tap, State College	0	1000g	0	4.34 (0.83)
Total food		1.35	1060g	1180	3.89 (0.53)
Total food & water		1.15	2060g	1180	3.95 (0.50)

Note: Table has been adapted from Adise et al. [32]

^ Liking ratings were collected prior to the meal using 5-point smiley face scale (1=most negative, 5=most positive)

Table 4-3. Food items in EAH protocol

Food	Brand, Company	ED (kcal/gram)	Serving size	kcal per serving	Liking Mean (sd)^
Potato Chips	Lay's, FritoLay	5.64	58g	327	4.27 (0.74)
Buttered Popcorn	Herr's	5.28	15g	79	4.10 (0.76)
Tiny Twists Pretzels	Rold Gold, FritoLay	5.89	39g	230	3.91 (0.83)
Cheese cracker	Ritz	5.37	6 crackers (~44g)	236	3.36 (1.22)
Fudge brownies	Little Bites, Entenmann's	4.36	4 brownies (~51g)	222	4.63 (0.73)
Chocolate Chip Cookies	Chips A'Hoy!, Mondelez Int'l	4.97	6 cookies (~66g)	327	4.49 (0.79)
Fruit-flavored candies	Starbursts.	4.08	66g	269	4.63 (0.66)
Chocolate candies	M&Ms, Mars Inc	4.86	66g	321	4.49 (0.79)
Tortilla Chips, Nacho Cheese Flavored	Doritos, FritoLay	5.14	58g	298	4.37 (0.94)
Chocolate kisses	The Hershey Company	5.37	66g	354	4.46 (0.85)
Total food		4.89	529g	2663	4.27 (0.46)

Note: Table has been adapted from Adise et al. [32]
^ Liking ratings were collected prior to the paradigm using a 5-point smiley face scale (1=most negative, 5=most positive)

Table 4-4. Food items in Buffet Meal

Food	Brand, company	ED (kcal/g)	Serving size	kcal per serving	Liking Mean (sd)^
Cheese bagel bites, three cheese	H.J. Heinz Company	2.28	8 pieces (~145g)	331	3.65 (1.04)
Cheese pizza rolls	Totino's, General Mills	2.51	7 pieces (~85g)	213	4.17 (1.00)
Chicken nuggets	Tyson Foods Inc	2.99	7 nuggets (~105g)	314	4.41 (0.69)
Mozzarella Sticks	Friday's	3.03	4 sticks (~125g)	379	4.09 (1.01)
Potato Chips	Lay's, Frito Lay	5.64	28g	158	4.22 (0.78)
Fudge brownies	Little Bites, Entenmann's	4.36	4 brownies (60g)	262	4.52 (0.80)
Chocolate cupcakes	Hostess	4.71	1 cupcake (50g)	236	4.25 (0.99)
Donut Holes, Vanilla Glazed	Entenmann's	5.07	4 donuts (58g)	295	4.49 (0.76)
Whole-fat chocolate milk	Schneider Valley Farms	0.83	1 cup (~245g)	203	4.01 (1.06)
Chocolate Chip Cookies	Chips A'Hoy!, Mondelez Int'l	4.98	4 cookies (44g)	219	4.4 (0.76)
Strawberry licorice twists	Twizzlers, The Hershey Company	3.39	50g	170	3.65 (1.16)
Strawberry Fruit Leather	Fruit Roll-up, Betty Crocker, General Mills	4.07	2 pieces (30g)	122	4.54 (0.70)
Gummy Candy	Goldbears, Haribo	3.49	105g	366	4.36 (0.79)
Fruit-flavored candies	Skittles, Mars Inc.	4.04	86g	357	4.38 (0.93)
Tropical Punch	Kool Aid Bursts, Kraft Foods Inc.	0.09	1 cup (~235g)	21	4.03 (0.91)
Total food		3.89	971g	3412	4.24 (0.42)
Total food & drink		3.43	1451g	3636	4.21 (0.44)

Note: Table has been adapted from Adise et al. [32]

^ Liking ratings were collected prior to the meal using a 5-point smiley face scale (1=most negative, 5=most positive)

Table 4-5. Summary of hypotheses between VPP model parameters and intake

VPP model parameters	Potential processes influencing intake	Intake hypotheses[#]:
Expected value parameters		
Updating (ø)	Degree to which information about hedonics and fullness are updated	Standard meal (-) EAH protocol (-) Buffet meal (-)
Feedback sensitivity (α)	Sensitivity to changes in hedonics	Standard meal (-) EAH protocol (-) Buffet meal (-)
Loss aversion (λ)	Relative impact of negative (e.g., physical discomfort) versus positive (e.g., food) experiences	EAH protocol (-) Buffet meal (-)
Perseveration Strength parameters		
Perseveration decay (k)	Influence of early-meal motivation to eat on behavior later in the meal	Standard meal (+) EAH protocol (+) Buffet meal (+)
The impact of gain on perseveration strength (ε_{pos})	Impact of food reward on the tendency to take another bite	Standard meal (+) EAH protocol (+) Buffet meal (+)
The impact of loss on perseveration strength (ε_{neg})	Impact of negative experience on the tendency take another bite	Buffet meal (+) EAH protocol (+)

[#] (+) denotes hypothesized positive association between VPP model parameter and intake; (-) denotes hypothesized negative association between VPP model parameter and intake

Table 4-6. Descriptive statistics

VPP Model Parameters[#]	**25th percentile**	**Median**	**75th percentile**
Updating, ø	0.05	0.11	0.35
Feedback sensitivity, α	0.30	0.52	0.74
Loss Aversion, λ	0.03	0.10	0.39
Impact of gain on Pers., ε_{pos}	-3.97	-0.42	2.60
Impact of loss on Pers., ε_{neg}	-8.18	-6.48	-4.34
Perseveration decay, *k*	0.34	0.46	0.57
Expectancy weighting, *w*	0.78	0.81	0.85
Consistency, *c*	0.93	1.04	1.17
Behavioral Metrics	**25th percentile**	**Median**	**75th percentile**
Win-stay	0.12	0.30	0.50
Lose-shift	0.84	0.93	0.97
Netscore	-26.50	-6.00	5.50
Laboratory Eating Paradigm	**Mean**	**SD**	**Min - Max**
Standard meal (N=70)			
Pre-standard meal fullness (mm)	38.4	30.8	0 – 100
Intake (kcal)	643.9	212.3	202.5 - 1130.2
EAH (N=70)			
Pre-EAH fullness (mm)	125.8	24.7	31 – 150
Intake (kcal)	379.9	205.4	0.8 - 1046.1
Buffet meal (N=69)			
Pre-buffet meal fullness (mm)	35.5	29.1	0 – 110
Intake (kcal)	1271.3	367.6	474.8 - 2025.4

[#] Quartile values for VPP model parameters were determined using the distribution of person-specific point estimates (i.e., the average estimate across simulations) for each parameter

Table 4-7. Spearman rank correlation coefficients between decision-making variables

	1	*2*	*3*	*4*	*5*	*6*	*7*	*8*
1. Updating, ø	-							
2. Feedback sensitivity, α	-0.07	-						
3. Loss Aversion, λ	-0.42**	-0.56***	-					
4. Impact of gain on Per., ε_{pos}	**0.29**	0.07	-0.24	-				
5. Impact of loss on Per., ε_{neg}	-0.07	0.17	-0.09	0.39**	-			
6. Perseveration decay, *k*	-0.10	-0.17	0.24	-0.04	-0.14	-		
7. Expectancy weighting, *w*	0.03	-0.11	-0.18	0.31*	0.36*	-0.13	-	
8. Consistency, *c*	-0.14	-0.09	-0.17	-0.34*	-0.35*	-0.04	0.00	-
Netscore	-0.05	-0.69***	0.72***	-0.27*	-0.42***	0.16	-0.23	-0.09
Win-Stay	0.44***	0.00	-0.33*	0.93***	0.30*	-0.02	0.31*	-0.20
Lose-Shift	0.05	-0.19	0.04	-0.45***	-0.90***	-0.01	-0.30*	0.48***

Bolded value indicates statistical significance ($p < 0.05$) before, but not after, adjustment for multiple comparisons.

** adjusted $p < 0.05$, ** adjusted $p < 0.01$, *** adjusted $p < 0.001$.*

Table 4-8. Summary of path analyses for final models predicting BMI-z from intake, and intake from VPP model parameters

			Perseveration Models[%]						Expected Value Models[^]			
			B	se	p	r^2			B	se	p	r^2
Standard Meal	Intake	ε_{pos}	0.88	0.20	<0.001	0.17	Intake	ø	0.44	0.29	0.12	0.06
		k	-0.12	0.22	0.58			α	0.30	0.24	0.21	
	BMI-z	Intake	0.15	0.04	<0.001	0.11	BMI-z	Intake	0.15	0.04	<0.001	0.11
EAH	Intake	ε_{pos}	0.40	0.17	0.02	0.25	Intake	ø	0.26	0.37	0.50	0.04
		k	-0.55	0.22	0.01			α	-0.08	0.31	0.80	
		ε_{neg}	-0.45	0.23	0.06			λ (log)	-0.24	0.36	0.51	
		k:ε_{neg}	0.89	0.27	0.001							
	BMI-z	Intake	0.08	0.06	0.23	0.03	BMI-z	Intake	0.08	0.06	0.23	0.03
Buffet Meal	Intake	ε_{pos}	1.36	0.38	<0.001	0.14	Intake	ø	0.47	0.53	0.37	0.06
		k	0.12	0.38	0.76			α	0.18	0.59	0.76	
		ε_{neg}	-0.07	0.47	0.89			λ (log)	-0.52	0.57	0.36	
	BMI-z	Intake	0.07	0.03	0.01	0.09	BMI-z	Intake	0.07	0.03	< 0.01	0.09

[%] Perseveration models contain VPP parameters involved in computing Perseveration Strength (i.e., ε_{pos}, *k*, ε_{neg})

[^]Expected value models contain VPP parameters involved in computing Expected Value (i.e., ø, α, λ)

Note: VPP model parameters were normalized and intake (kcal) was scaled by a factor of 100

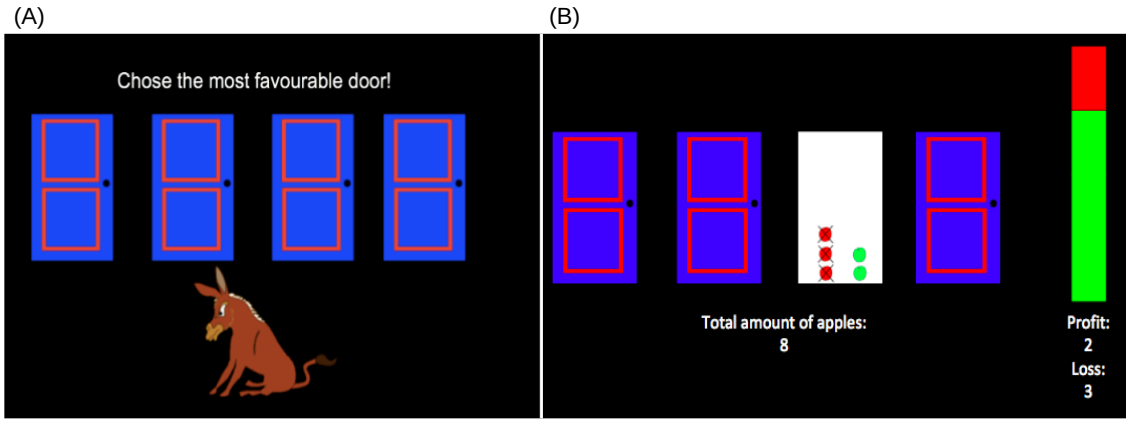

Figure 4.1 Hungry Donkey Task. During each trial of the task, children were presented with a Selection screen (A). During the selection screen, children selected one door by using one of four keyboard keys (C, V, B, N) that corresponded to each door from left to right. Following a selection, children were presented with an outcome screen (B). The number of apples won and lost during that trial were displayed in the frame of the selected door as green and red apples, respectively, and numerically as "profit" and "loss" values under the vertical bar. The vertical bar provided global feedback about the ratio of apples won (green) and lost (red) in the game so far, and the net total amount of apples won in the game so far was indicated under the doors.

Figure 4.2. Trays of food and drinks presented during the three eating paradigms. (A) Standard Meal: (left tray) water, angel food cake, grapes, (right tray) broccoli, garlic bread, cherry tomatoes, macaroni and cheese; (B) Eating in the Absence of Hunger protocol: (left tray) chocolate kisses, buttered popcorn, nacho-flavored tortilla chips, fruit-flavored candies, chocolate chip cookies, (right tray) pretzels, fudge brownies, potato chips, chocolate candies, cheese crackers; (C) Buffet meal: (left tray) fruit-flavored candies, potato chips, donut holes, chocolate chip cookies, cheese bagel bites, strawberry licorice twists, (middle tray) fruit punch, chocolate cupcake, chocolate milk, cheese pizza rolls, strawberry fruit leather, (right tray) mozzarella sticks, gummy candy, fudge brownies, chicken nuggets.

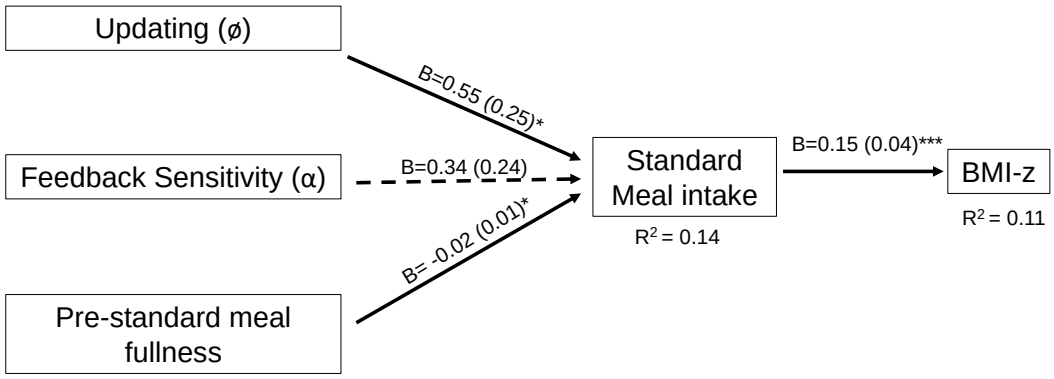

Figure 4.3 Final expected value model for the standard meal with pre-standard meal fullness covariate. Expected value models include VPP model parameters involved in computing expected value. For path analyses, VPP model parameters were normalized and intake (kcal) was scaled by a factor of 100. Pre-standard meal fullness was rated on a 150mm visual analog scale prior to the eating paradigm. Arrows indicate paths tested in the final model and are labeled with the unstandardized parameter estimate (B) and standard error for that path. Dotted lines indicate paths did not reach statistical significance ($p > 0.05$). Solid lines indicate statistically significant paths (*$p<0.05$, **$p <0.01$, ***$p <0.001$). Explained variance (R^2) is reported for endogenous variables.

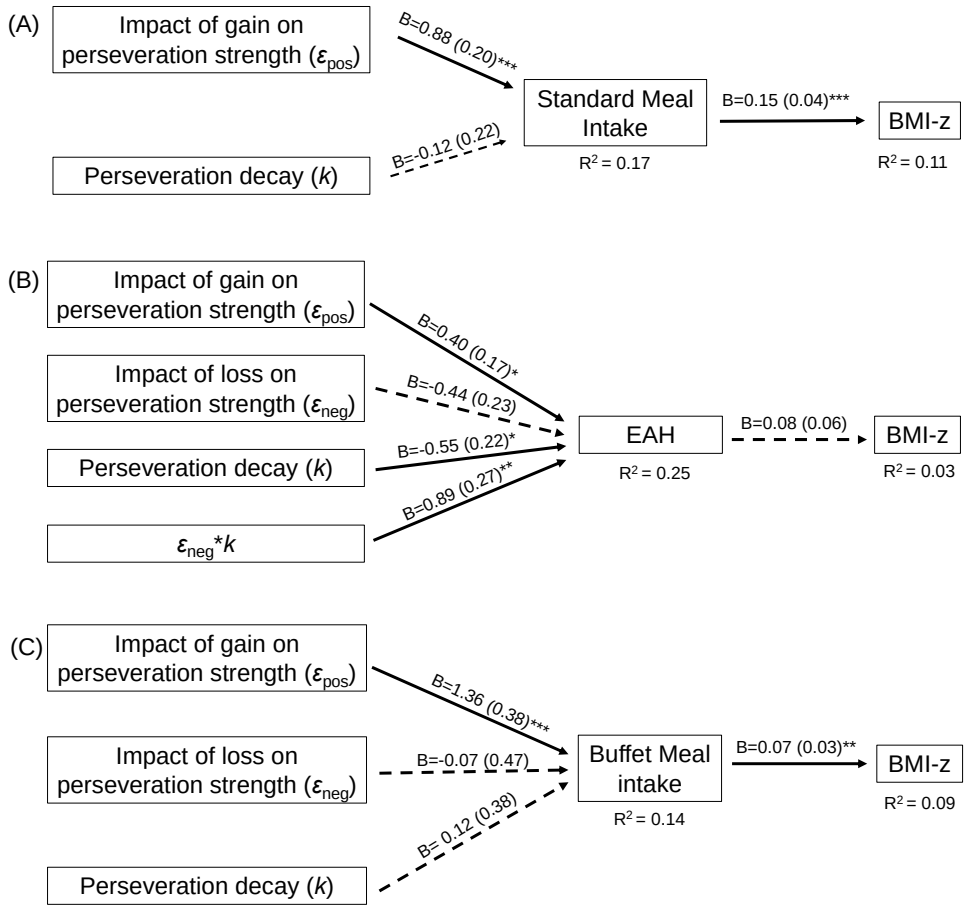

Figure 4.4 Final perseveration model for the (A) Standard Meal, (B) Eating in the Absence of Hunger (EAH) protocol and (C) Buffet meal. Perseveration models contain VPP model parameters involved in computing perseveration strength. For path analyses, VPP model parameters were normalized and intake (kcal) was scaled by a factor of 100. Arrows indicate paths tested in the final model and are labeled with the unstandardized parameter estimate (B) and standard error for that path. Dotted lines indicate paths did not reach statistical significance ($p > 0.05$). Solid lines indicate statistically significant paths (*$p<0.05$, **$p <0.01$, ***$p <0.001$). Explained variance (R^2) is reported for endogenous variables.

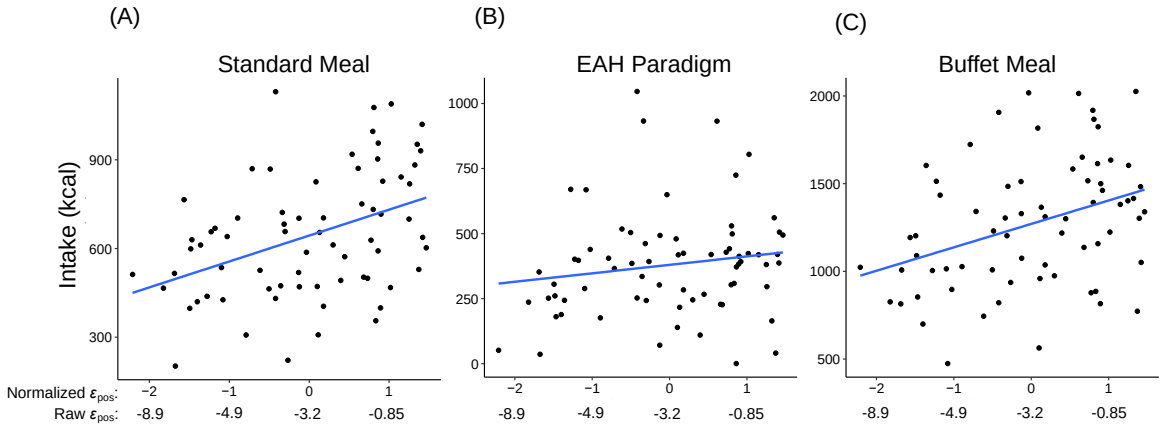

Figure 4.5 Relationship between the impact of gain on perseveration strength (i.e., ε_{pos}; x-axis) and intake (kcal; y-axis) during the (A) Standard meal, (B) Eating in the Absence of Hunger (EAH) protocol, and (C) Buffet meal. Blue lines reflect the best fit for the linear model between ε_{pos} and intake. Shaded grey regions reflects 95% confidence interval for the line of best fit.

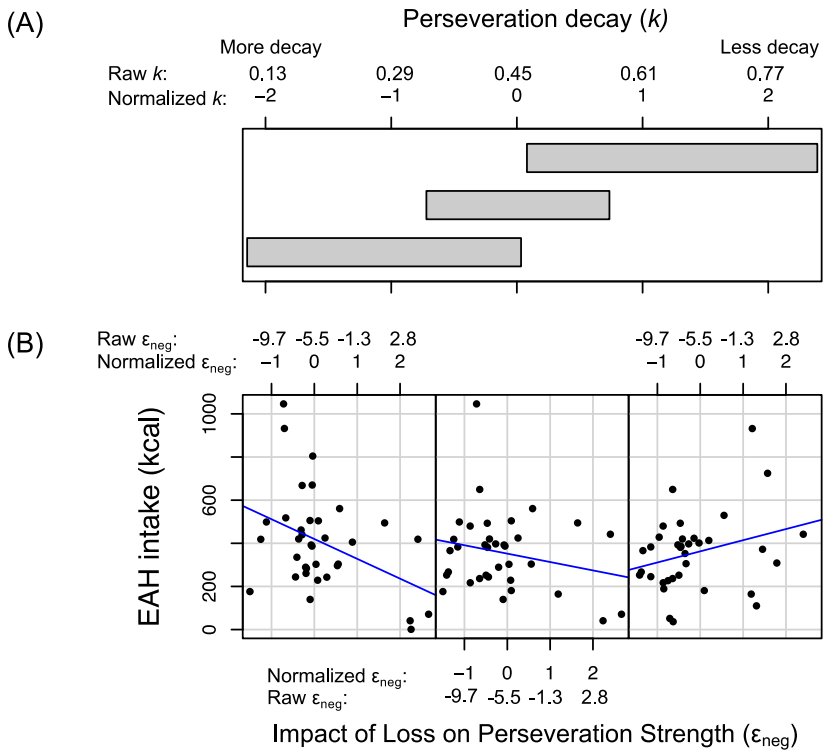

Figure 4.6 Relationship between the impact of loss on perseveration strength (i.e., ε_{neg}) and intake (kcal) during the Eating in the Absence of Hunger (EAH) protocol at three levels of perseveration decay (i.e., *k*). (A) Three overlapping intervals of *k* that correspond to the three scatterplots in panel (B). (B) Scatterplots between ε_{neg} (x-axis) and EAH (y-axis). Normalized and raw values of ε_{neg} and *k* are presented. Left scatter plot: at the lower interval of *k* (normalized values: -2.15 to 0.03), the association between ε_{neg} and intake is negative. Middle scatter plot: at the middle interval of *k* (normalized values: -0.72 to 0.74), the association between ε_{neg} and intake is negative, less negative than the lower interval. Right scatter plot: at the higher interval of *k* (normalized values: 0.08 to 2.39), the association between ε_{neg} and intake is positive.

5. Supplement

Supplemental Table 1. Goodness of fit measures for path models

Model[#]		Meal	Satorra-Bentler (SB) scaled test statistic	CFI robust	SRMR	RMSEA robust
Initial model	Perseveration	Standard	$\chi^2_{SB}(3, n=70) = 1.79, p = 0.62$	1.00	0.04	0.00
		EAH	$\chi^2_{SB}(5, n=70) = 4.30, p = 0.51$	1.00	0.04	0.00
		Buffet	$\chi^2_{SB}(5, n=69) = 2.95, p = 0.71$	1.00	0.03	0.00
	Expected value	Standard	$\chi^2_{SB}(3, n=70) = 1.75, p = 0.63$	1.00	0.03	0.00
		EAH	$\chi^2_{SB}(5, n=70) = 1.05, p = 0.96$	1.00	0.02	0.00
		Buffet	$\chi^2_{SB}(5, n=69) = 2.12, p = 0.83$	1.00	0.04	0.00
Final model	Perseveration	Standard	$\chi^2_{SB}(2, n=70) = 0.76, p = 0.69$	1.00	0.03	0.00
		EAH	$\chi^2_{SB}(4, n=70) = 1.94, p = 0.75$	1.00	0.03	0.00
		Buffet	$\chi^2_{SB}(3, n=69) = 0.92, p = 0.82$	1.00	0.03	0.00
	Expected value	Standard	$\chi^2_{SB}(2, n=70) = 1.62, p = 0.45$	1.00	0.04	0.00
		EAH	$\chi^2_{SB}(3, n=70) = 0.75, p = 0.86$	1.00	0.03	0.00
		Buffet	$\chi^2_{SB}(3, n=69) = 1.34, p = 0.72$	1.00	0.04	0.00
Final model with age covariate	Perseveration	Standard	$\chi^2_{SB}(3, n=70) = 0.82, p = 0.84$	1.00	0.03	0.00
		EAH	$\chi^2_{SB}(5, n=70) = 2.00, p = 0.85$	1.00	0.03	0.00
		Buffet	$\chi^2_{SB}(4, n=69) = 1.08, p = 0.9$	1.00	0.02	0.00
	Expected value	Standard	$\chi^2_{SB}(3, n=70) = 1.68, p = 0.64$	1.00	0.03	0.00
		EAH	$\chi^2_{SB}(4, n=70) = 1.26, p = 0.87$	1.00	0.03	0.00
		Buffet	$\chi^2_{SB}(4, n=69) = 1.43, p = 0.84$	1.00	0.03	0.00
Final model with fullness covariate	Perseveration	Standard	$\chi^2_{SB}(3, n=70) = 0.81, p = 0.85$	1.00	0.03	0.00
		EAH	$\chi^2_{SB}(5, n=70) = 2.13, p = 0.83$	1.00	0.03	0.00
		Buffet	$\chi^2_{SB}(4, n=69) = 1.07, p = 0.9$	1.00	0.02	0.00
	Expected value	Standard	$\chi^2_{SB}(3, n=70) = 1.65, p = 0.65$	1.00	0.03	0.00
		EAH	$\chi^2_{SB}(4, n=70) = 0.81, p = 0.94$	1.00	0.02	0.00
		Buffet	$\chi^2_{SB}(4, n=69) = 1.58, p = 0.81$	1.00	0.03	0.00

[#] Initial models contain all tested moderations; final models exclude non-significant moderations; perseveration models contain VPP parameters involved in computing perseveration strength (i.e., $\varepsilon_{pos}, k, \varepsilon_{neg}$); expected value models contain VPP parameters involved in computing expected value (i.e., $\text{ø}, \alpha, \lambda$). CFI robust = robust comparative fit index; SRMR = standardized root mean square residual; RMSEA robust = robust root mean square error of approximation.

Supplemental Table 2. Median and interquartile range (IQR) for decision-making variables by categorical participant characteristics

		ø	α	λ	ε_{pos}	ε_{neg}	*k*	*w*	*c*	Netscore	Win-Stay	Lose-Shift
Sex	Male	0.12 (0.19)	0.58 (0.48)	0.09 (0.19)	-0.26 (5.30)	**-5.26 (5.02)**	0.42 (0.26)	**0.84 (0.07)**	1.03 (0.24)	*-13.00 (47.50)*	0.28 (0.21)	**0.88 (0.19)**
	Female	0.10 (0.36)	0.48 (0.32)	0.15 (0.78)	-0.47 (7.87)	**-7.28 (2.54)**	0.47 (0.20)	**0.80 (0.05)**	1.04 (0.22)	*0.00 (32.00)*	0.31 (0.45)	**0.95 (0.06)**
Maternal Education	<bachelor's	0.07 (0.15)	0.59 (0.43)	**0.10 (0.39)**	-2.55 (7.97)	-6.34 (2.65)	0.39 (0.24)	0.80 (0.04)	1.06 (0.32)	**0.00 (24.00)**	0.20 (0.36)	0.94 (0.09)
	bachelor's degree	0.10 (0.32)	0.44 (0.41)	**0.32 (0.87)**	0.85 (5.05)	-6.83 (5.74)	0.50 (0.19)	0.81 (0.06)	1.04 (0.19)	**-4.00 (21.50)**	0.36 (0.36)	0.94 (0.19)
	>bachelor's degree	0.17 (0.31)	0.56 (0.43)	**0.05 (0.09)**	-0.12 (4.96)	-5.65 (5.32)	0.44 (0.22)	0.83 (0.08)	1.04 (0.09)	**-20.00 (61.00)**	0.29 (0.27)	0.90 (0.16)
Income	<$50,000	0.09 (0.09)	0.47 (0.45)	0.11 (0.40)	-2.55 (6.37)	-6.31 (3.29)	0.39 (0.24)	0.80 (0.05)	1.10 (0.25)	-6.00 (38.00)	0.19 (0.26)	0.93 (0.18)
	$50,000-$100,000	0.18 (0.40)	0.55 (0.36)	0.10 (0.30)	0.42 (6.20)	-5.95 (5.42)	0.44 (0.23)	0.81 (0.06)	1.03 (0.17)	-7.00 (23.00)	0.36 (0.33)	0.92 (0.18)
	>$100,000	0.10 (0.15)	0.52 (0.53)	0.10 (0.47)	-0.04 (4.95)	-7.28 (1.89)	0.47 (0.13)	0.82 (0.07)	1.03 (0.12)	-2.00 (38.00)	0.32 (0.34)	0.94 (0.10)

Bolded cells indicate a main effect of condition with $p < 0.05$ before, but not after, adjustment for multiple comparisons
Italicized cells indicate a main effect of condition with $p < 0.05$ after adjustment for multiple comparisons

Supplemental Table 3. Spearman's rank correlation coefficient between decision-making variables and continuous participant characteristics

	ø	α	λ	ε_{pos}	ε_{neg}	*k*	*w*	*c*	Netscore	Win-Stay	Lose-Shift
BMI-z	0.01	0.05	0.01	0.13	0.08	0.05	0.04	**-0.29**	0.05	0.08	-0.13
Age	0.35*	**0.29**	-0.40*	0.49***	0.00	-0.23	0.12	-0.02	-0.22	0.47***	0.02
Pre-standard meal Fullness	0.23	0.08	-0.09	0.03	0.09	-0.01	0.11	-0.08	-0.11	0.02	-0.10

Bolded values indicate statistical significance of $p < 0.05$ before, but not after, adjustment for multiple comparisons
** adjusted p < 0.05, ** adjusted p < 0.01, *** adjusted p < 0.001.*

Supplemental Table 4. Summary of path analyses for initial models predicting BMI-z from intake, and intake from VPP model parameters

			Perseveration Models						Expected Value Models			
			B	se	p	r^2			B	se	p	r^2
Standard Meal (n = 70)	Intake	ε_{pos}	0.90	0.20	<0.001	0.18	Intake	ø	0.41	0.29	0.16	0.07
		k	-0.13	0.23	0.57			α	0.29	0.24	0.24	
		ε_{pos}:*k*	-0.16	0.22	0.46			ø*α	-0.20	0.34	0.55	
	BMI-z	Intake	0.15	0.04	<0.001	0.11	BMI-z	Intake	0.15	0.04	<0.001	0.11
EAH (n = 70)	Intake	ε_{pos}	0.39	0.18	0.03	0.25	Intake	ø	0.30	0.47	0.52	0.04
		k	-0.53	0.23	0.02			α	-0.08	0.30	0.80	
		ε_{pos}:*k*	-0.45	0.24	0.06			λ (log)	-0.19	0.39	0.62	
		ε_{neg}	0.12	0.21	0.57			ø*α	-0.10	0.22	0.66	
		ε_{neg}:*k*	0.83	0.29	<0.01			ø* λ(log)	0.11	0.35	0.76	
	BMI-z	Intake	0.08	0.06	0.23	0.03	BMI-z	Intake	0.08	0.06	0.23	0.03
Buffet Meal (n = 69)	Intake	ε_{pos}	1.35	0.39	0.001	0.14	Intake	ø	0.17	0.59	0.77	0.08
		k	0.08	0.34	0.82			α	0.27	0.58	0.65	
		ε_{pos}:*k*	0.03	0.36	0.93			λ (log)	-0.55	0.56	0.33	
		ε_{neg}	-0.09	0.46	0.85			ø*α	-0.32	0.52	0.54	
		ε_{neg}:*k*	0.17	0.49	0.74			ø* λ(log)	-0.61	0.42	0.15	
	BMI-z	Intake	0.07	0.03	<0.01	0.09	BMI-z	Intake	0.07	0.03	<0.01	0.09

Note: Given the role of parameters *k* (perseverance decay) and ø (updating) in the VPP model, initial models tested if *k* and ø moderated the impact of other Perseveration Strength and Expected Value parameters, respectively, on intake.

Supplemental Table 5. Sensitivity analyses for final models with age covariate. Summary of path analyses for models predicting BMI-z from intake, and intake from VPP model parameters and age covariate

			Perseveration Models						Expected Value Models			
			B	se	p	r^2			B	se	p	r^2
Standard Meal (n = 70)	Intake	ε_{pos}	0.87	0.25	0.001	0.17	Intake	ø	0.35	0.30	0.24	0.08
		K	-0.12	0.22	0.59			α	0.21	0.25	0.38	
		age	0.01	0.19	0.95			age	0.22	0.17	0.20	
	BMI-z	Intake	0.15	0.04	<0.001	0.11	BMI-z	Intake	0.15	0.04	<0.001	0.11
EAH (n = 70)	Intake	ε_{pos}	0.49	0.20	0.02	0.25	Intake	ø	0.27	0.39	0.48	0.04
		K	-0.57	0.24	0.02			α	-0.06	0.32	0.84	
		ε_{neg}	-0.48	0.25	0.05			λ (log)	-0.26	0.35	0.45	
		K:ε_{neg}	0.86	0.27	0.001			age	-0.07	0.18	0.68	
		age	-0.11	0.18	0.56							
	BMI-z	Intake	0.08	0.06	0.22	0.03	BMI-z	Intake	0.08	0.06	0.23	0.03
Buffet Meal (n = 69)	Intake	ε_{pos}	0.97	0.45	0.03	0.16	Intake	ø	0.31	0.54	0.57	0.11
		K	0.25	0.37	0.50			α	0.03	0.58	0.96	
		ε_{neg}	0.11	0.49	0.82			λ (log)	-0.34	0.58	0.56	
		age	0.49	0.35	0.17			age	0.63	0.32	0.05	
	BMI-z	Intake	0.07	0.03	<0.01	0.09	BMI-z	Intake	0.07	0.03	<0.01	0.09

Supplemental Table 6. Sensitivity analyses for final models with pre-meal fullness covariate. Summary of path analyses for models predicting BMI-z from intake, and intake from VPP model parameters and corresponding pre-meal fullness covariate

			Perseveration Models						**Expected Value Models**			
			B	se	p	r^2			B	se	p	r^2
Standard Meal (n = 70)	Intake	ε_{pos}	0.89	0.21	< 0.001	0.24	Intake	ø	0.55	0.25	0.03	0.14
		k	-0.14	0.21	0.50			α	0.34	0.24	0.15	
		fullness	-0.02	0.01	0.02			fullness	-0.02	0.01	0.02	
	BMI-z	Intake	0.15	0.04	< 0.001	0.11	BMI-z	Intake	0.15	0.04	< 0.001	0.11
EAH (n = 70)	Intake	ε_{pos}	0.40	0.17	0.02	0.25	Intake	ø	0.23	0.37	0.54	0.04
		k	-0.55	0.23	0.02			α	-0.11	0.32	0.74	
		ε_{neg}	-0.45	0.23	0.05			λ (log)	-0.28	0.37	0.46	
		K:ε_{neg}	0.89	0.27	0.001			fullness	0.01	0.01	0.55	
		fullness	0.00	0.01	0.92							
	BMI-z	Intake	0.08	0.06	0.23	0.03	BMI-z	Intake	0.08	0.06	0.23	0.03
Buffet Meal (n = 69)	Intake	ε_{pos}	1.44	0.38	< 0.001	0.15	Intake	ø	0.53	0.53	0.32	0.07
		k	0.09	0.38	0.81			α	0.22	0.59	0.71	
		ε_{neg}	-0.04	0.46	0.93			λ (log)	-0.49	0.56	0.37	
		fullness	-0.01	0.02	0.42			fullness	-0.01	0.02	0.64	
	BMI-z	Intake	0.07	0.03	<0.01	0.09	BMI-z	Intake	0.07	0.03	<0.01	0.09

Supplemental Table 7. Sensitivity analyses for final models excluding children with compliance or behavioral issues. Summary of path analyses for models predicting BMI-z from intake, and intake from VPP model parameters

			Perseveration Models						Expected Value Models			
			B	se	p	r^2			B	se	p	r^2
Standard Meal (n = 64)	Intake	ε_{pos}	0.96	0.22	< 0.001	0.19	Intake	ø	0.46	0.30	0.12	0.06
		k	-0.15	0.24	0.53			α	0.30	0.26	0.24	
	BMI-z	Intake	0.16	0.04	< 0.001	0.14	BMI-z	Intake	0.16	0.04	< 0.001	0.14
EAH (n = 64)	Intake	ε_{pos}	0.43	0.17	0.01	0.23	Intake	ø	0.38	0.37	0.30	0.05
		K	-0.46	0.24	0.05			α	0.01	0.32	0.97	
		ε_{neg}	-0.30	0.27	0.27			λ (log)	-0.08	0.36	0.82	
		K:ε_{neg}	0.85	0.30	< 0.005							
	BMI-z	Intake	0.10	0.07	0.14	0.05	BMI-z	Intake	0.10	0.07	0.15	0.05
Buffet Meal (n = 63)	Intake	ε_{pos}	1.32	0.38	0.001	0.19	Intake	ø	0.69	0.46	0.14	0.07
		k	0.04	0.38	0.92			α	0.45	0.59	0.44	
		ε_{neg}	0.44	0.47	0.35			λ (log)	-0.19	0.53	0.72	
	BMI-z	Intake	0.10	0.03	0.001	0.13	BMI-z	Intake	0.10	0.03	0.001	0.13

Note: Three children were excluded from these analyses for not fully complying with protocols (e.g., not fasting), and three children were excluded for exhibiting attentional issues during the Hungry Donkey Task (e.g., talking throughout task)

Supplemental Table 8. Final models for the EAH paradigm with reduced sample based on pre-EAH fullness. Summary of path analyses for models predicting BMI-z from intake, and intake from VPP model parameters

			Perseveration Models						Expected Value Model			
			B	se	p	r^2			B	se	p	r^2
EAH (n = 57)	Intake	ε_{pos}	0.37	0.20	0.07	0.26	Intake	ø	0.29	0.41	0.48	0.04
		k	-0.60	0.24	0.01			α	0.01	0.35	0.97	
		ε_{neg}	-0.39	0.28	0.17			λ (log)	-0.25	0.38	0.51	
		k:ε_{neg}	0.97	0.30	< 0.001							
	BMI-z	Intake	0.07	0.07	0.31	0.03	BMI-z	Intake	0.07	0.07	0.31	0.03

Note: Because the EAH paradigm is designed to assess eating snack foods when not hungry, thirteen children were excluded in these sensitivity analyses because they rated their pre-EAH fullness as < 75% of the fullness visual analog scale.

6. Citations

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Chapter 5 General Discussion

1. Summary and discussion by domain

The overarching aim of this dissertation was to identify cognitive-affective correlates of food intake in children that may contribute to the development of obesity. Processes in two cognitive-affective domains—neural food cue reactivity and reward-related decision-making (RRDM)—and their relationships with laboratory food intake were assessed. The first part of this discussion will summarize and contextualize findings by domain.

Neural food cue reactivity (chapters 2 and 3)

To shed light on the neural mechanisms that increase intake in response to large portions of food (i.e., the portion size effect; PSE), this dissertation characterized neural portion size reactivity (chapter 2) and assessed how individual differences in neural portion size reactivity relate to the PSE (chapter 3). These chapters used baseline data from a larger longitudinal study during which children viewed images of larger and smaller amounts food and non-food items (office supplies) during fMRI and ate four meals that varied in portion size. On average, neural responses to amount (larger vs. smaller) were stronger but less extensive in visual processing areas for foods relative to office supplies. Neural responses to energy density (higher vs. lower) differed in extent between larger and smaller amounts of food in ventromedial prefrontal (vmPFC) and orbitofrontal (OFC) cortices, regions implicated in value-based decision-making [1]. Cerebellar responses to food amount were associated with quadratic relationships between gram intake and portion size; lower activation to larger portion size cues was associated with increased intake at the largest portion size conditions.

These chapters build on prior literature in youth demonstrating that food characteristics influence neural responses [2,3] and that neural responses to food cues predict eating behaviors [2,4–8]. Further, they emphasize that brain regions sensitive to food characteristics across

children (e.g., visual cortex to portion size) may not be the brain regions that relate to intake in response to those food characteristics (e.g., cerebellum response to portion size relates to PSE). This pattern, wherein distinct brain regions exhibit responses to food characteristics across a sample, while other brain regions demonstrate correlations between these responses and eating behaviors or weight status, has been demonstrated in prior work. For example, in adolescents, fasted responses to energy density in amygdala, hippocampus, parahippocampus, and visual cortex were observed across participants but not related to appetitive traits [5]. Conversely, fasted responses to energy density in insula, cerebellum, putamen, and rolandic operculum were associated with appetitive traits, but not observed across participants [5]. These results suggest that some responses to food cues may be more universal, whereas others relate to individual differences in behaviors. Relatedly, neural activation in some regions may underly the presence of an effect seen across individuals (e.g., PSE), whereas neural activation in other regions may underly person-specific effect magnitudes. As analyses in this dissertation only examined the latter, additional research is needed to understand how neural portion size reactivity relates to the PSE.

Reward-related decision-making (chapter 4)

While chapters 2 and 3 shed light on the neural correlates of the PSE, they did not elucidate specific cognitive or affective processes that drive eating behaviors. Therefore, chapter 4 examined the relationships between decision-making processes during a RRDM task and food intake in children. Decision-making processes were estimated using a reinforcement learning model [9] and intake was assessed at (1) a standard meal, (2) an eating in the absence of hunger (EAH) protocol, and (3) a palatable buffet meal. Decision-making processes that influence the tendency to repeatedly make the same choice (i.e., perseverate) were associated with energy

intake: (1) the impact of gain on perseveration strength (ε_{pos}) was positively associated with energy intake at all three eating paradigms, and (2) the impact of loss on perseveration strength (εneg) interacted with perseveration decay (k) to predict EAH. Further, ε_{pos} was positively associated with BMI-z through standard and buffet meal intake. In sum, decision-making processes that contribute to perseveration were related to meal and snack intake, and indirectly associated with weight status through meal intake.

According to the reinforcement learning model used in chapter 4, perseveration strength reflects a tendency to repeat a behavior, not because the expected value of that behavior is high, but because there is a tendency to stick with previous behaviors [9]. Therefore, a child with high perseverative tendencies may continue to eat in the presence of foods, not because the expected value of another bite is high, but because they had previously initiated eating. While chapter 4 did not assess overall perseverative tendencies, prior work has shown that response perseveration is positively associated with weight status in youth [10–13]. This dissertation extends that work by demonstrating that a decision-making process that influences perseveration (Figure 5.1) is associated with food intake and weight status; children who had the greatest increases in perseveration strength following rewards (i.e., "gains") ate more at meal and snack paradigms. Further, as ε_{pos} is conceptually similar to positive reinforcement (an increase in behavior following a stimulus [14]), results align with research showing that food reinforcement, assessed with the reinforcing value of food task, is positively associated with food intake [15,16], weight status [16–18], and weight gain [18,19] in children. Whereas the reinforcing value of food typically reflects the ability of a specific food to motivate behavior [20], ε_{pos} reflects the ability of rewards in general to motivate behavior. Thus, ε_{pos} may underlie food-specific responses observed during reinforcing value of food tasks (Figure 5.1).

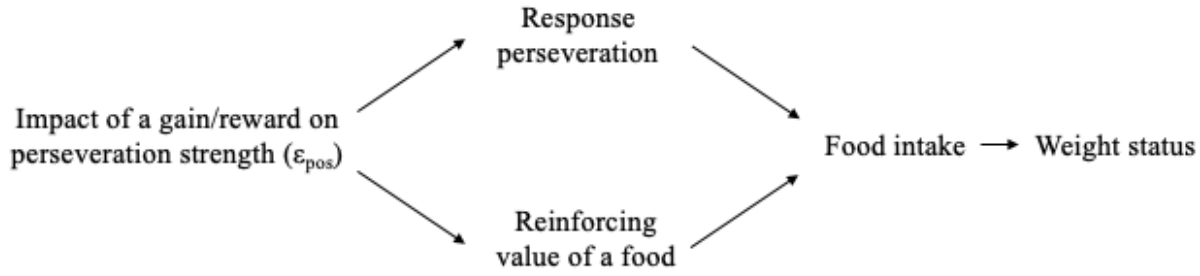

Figure 5.1 Theoretical model of how the reward-related decision-making process ε_{pos}, underlies associations between two behavioral responses to reward—response perseveration and reinforcing value of food—and food intake and weight status. ε_{pos} reflects the ability of rewards to increase perseveration, a process akin to positive reinforcement.

2. An integrated model: neural responses, decision-making processes, and food intake

As discussed in the general introduction (chapter 1), food-related decisions involve the integration Pavlovian, operant, and goal-directed signals [21]. As these signals are reflected in neural responses to food cues and decision-making behavior, this dissertation sheds light on how stimulus-driven and goal-directed systems relate to food intake and the development of obesity. In chapter 2, visual food cues varying in energy density and portion size differentially elicited neural responses in OFC and vmPFC. As these regions are implicated in generating food representations [22,23], encoding attribute value [1], and integrating value signals [1,24], these results suggest that food characteristics influence goal-directed decision-making processes in children. In chapter 3, less cerebellar activation to larger portion size cues was associated with increased intake at the largest portion size conditions. The cerebellum is engaged during reward-based decision-making [25], functionally connected with brain regions involved in reward/salience and executive function [26–28], and suggested to influence motivation by modulating affective and cognitive processes [29]. Thus, cerebellar responses to portion size

cues may influence intake by modulating both stimulus-driven and goal-directed signals. Finally, chapter 4 revealed that a decision-making process similar to positive reinforcement was positively associated weight status through meal intake. This suggests that operant conditioning increases food intake and can contribute to the development of pediatric obesity. Together, results suggest that food cues elicit stimulus-driven and goal-directed signals that, through reward-related decision-making, increase food intake and the development of obesity (Figure 5.2).

Importantly, while cue-elicited signals can influence intake, food experiences and obesity can influence cue-elicited signals. For example, daily consumption of a given beverage has been shown to modulate striatal and prefrontal responses to the receipt and anticipation of that beverage, respectively [30], and obesity-induced neuroinflammation can influence cognitive and affective processes [31]. Thus, the associations between the observed cognitive-affective processes and intake/weight status are likely bidirectional [32] or cyclical [33,34] (Figure 5.2). For example, while cerebellar responses to large portion size cues may influence intake from large portions, these responses may also be a result of experiences with large portions outside of the laboratory. Further, while path analyses assessed the indirect association between decision-making processes and weight status through intake, weight status may influence food intake through decision-making processes. Overall, additional research is needed to understand the causal relationships between the examined cognitive-affective processes, food intake, and weight status in children.

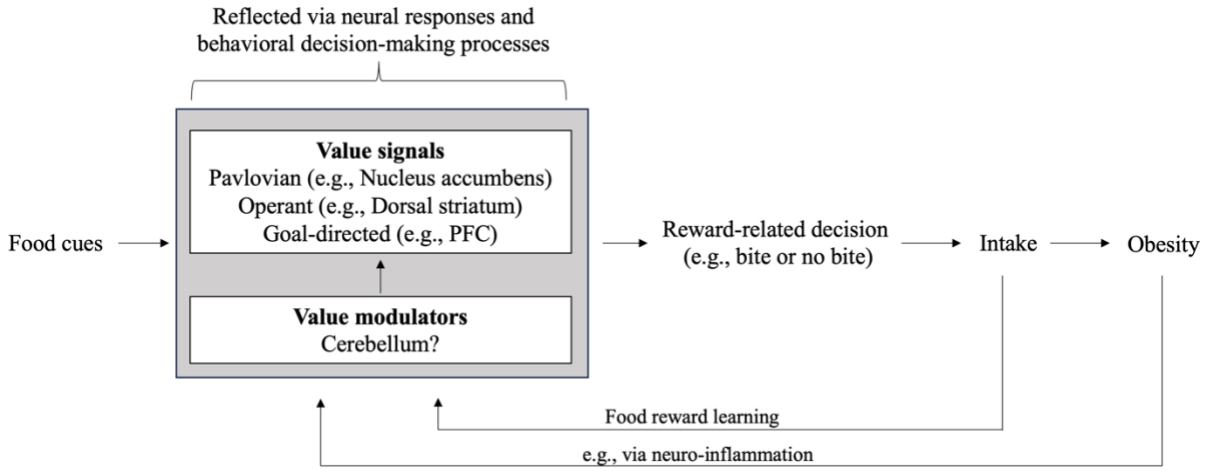

Figure 5.2 An integrated model of how neural responses and decision-making processes relate to food intake. Food cues elicit stimulus-driven (Pavlovian, operant) and goal-directed signals in subcortical and cortical regions and influence cerebellar functioning, which may modulate stimulus-driven and goal-directed signals. These signals are reflected via blood flow detected with functional magnetic resonance imaging as well as behavioral responses during decision-making tasks, and they drive reward-related decisions that increase intake and the development of obesity. Food-related experiences and obesity influence cue-elicited signals via reward learning and neuroinflammation, respectively.

3. Limitations and future directions

Several limitations are shared by all chapters in this dissertation. First, all studies involved samples which were predominantly White and non-Hispanic. Such homogeneity limits the generalizability of the findings to other populations. Therefore, research examining associations between cognitive-affective processes and food intake in more diverse populations is needed. Further, as ethnic-racial identity and racial discrimination are associated with eating

behaviors [35–37], future research should examine whether race, ethnicity, or race-related stress moderate the associations between cognitive-affective processes and food intake.

The second limitation is that analyses were cross-sectional and/or observational. This limits our understanding of temporal and causal relationships. Thus, it remains unclear (1) how/whether neural responses to portion size cues change over time, (2) how cognitive-affective processes relate to changes in eating behaviors and weight status over time, and (3) whether modulating the observed cognitive-affective processes would lead to changes in eating behavior or weight status. Understanding these relationships is critical to developing effective interventions for overeating and obesity. For example, while a decision-making process was indirectly associated with weight status, that decision-making process cannot be used to identify children at risk for obesity until we know its association with future weight gain. In addition, while an association between cerebellar function and the PSE was observed, it remains unclear whether modulating cerebellar processes would reduce intake in response to large portions. To close these gaps, studies involving longitudinal designs and experimental manipulation of cognitive-affective processes (e.g., using non-invasive brain stimulation) are needed.

The third limitation is that this dissertation did not combine neuroimaging and decision-making methodologies in the same sample. As neural activation can be suggestive of many cognitive-affective processes, neural responses alone are not enough to indicate the presence of valuation, reinforcement learning, or other mechanisms. Therefore, behavioral tasks that assess decision-making are needed in combination with neuroimaging to understand how prefrontal and cerebellar responses to food characteristics mechanistically influence food-related decisions. In addition, to elucidate how the decision-making processes examined in chapter 4 are neurally implemented, future research can correlate decision-making processes derived from cognitive

models against fMRI data. This approach is referred to as model-based fMRI [38,39]. Uncovering the neural correlates of decision-making processes that drive food intake will provide insight into how these processes could be intervened upon to reduce overeating.

4. Strengths and implications

Despite the limitations, by assessing both neural food cue reactivity and reward-related decision-making, this dissertation sheds light on multiple cognitive-affective processes that are associated with food intake in children. Even without a full understanding of causality, these results may help identify children who are at risk for overeating. In particular, (1) children with decreased cerebellar responses to large portion size cues may be at risk for overeating with large portions are served, and (2) children more likely to repeat behaviors following rewards may be at risk for overeating at both meal and snacks.

By summarizing findings using a decision-making framework (Figure 5.2), this dissertation suggests that behavioral interventions that target stimulus-driven and goal-directed systems could be used to reduce food intake in children. In particular, interventions that target habits (i.e., operant/instrumental associations) might be the effective for reducing intake across multiple contexts. Approaches to disrupt habitual behaviors include cue disruption (e.g., reducing the salience of cues that stimulate overeating) [40] and vigilant monitoring [41]. Further, mindfulness-based interventions which target both Pavlovian and operant learning may be effective [42]. While additional research is need to understand the mechanisms through which cerebellar function influences the portion size effect, if the mechanism is cravings through striatal functioning [28], cue exposure interventions aimed at reducing cravings via extinction of Pavlovian associations (e.g., Intervention for Regulation of Cues [43]) may be effective. Alternatively, if the mechanism is altered goal-directed processes, approaches that modulate food

value (e.g., go/no-go training [44]) may be effective. As intake result from the integration of stimulus-driven and goal-directed signals, combining approaches may be the most effective.

5. Conclusions

The research described in this dissertation suggests that neural portion size reactivity and reward-related decision-making processes are associated with food intake in children. Novel findings include (1) neural responses to energy density that varied by portion size in brain regions implicated in value-based decision-making (e.g., vmPFC, OFC), (2) an association between cerebellar responses to food portion size cues and laboratory intake in response to being served greater amounts of food, and (3) associations between decision-making processes related to perseveration and food intake at multiple eating contexts. These findings may help identify children who are at risk for overeating, but future research is needed to assess whether results generalize to more diverse samples. For insight into causal relationships between cognitive-affective processes and food intake, experimental and longitudinal studies are needed.

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Appendix A Consent form (chapters 2, 3)

STUDY00005357
Approval: 2/21/2023
Approval End Date: 2/20/2024

CONSENT FOR RESEARCH
The Pennsylvania State University

Title of Project: Brain Mechanisms of Overeating in Children

Principal Investigator: Kathleen Keller

Address: *321 Chandlee Lab, University Park, PA 16802*

Telephone Number: *814-863-2915*

We are asking you to be in a research study. This form gives you information about the research.

Whether or not you take part is up to you. You can choose not to take part. You can agree to take part and later change your mind. Your decision will not be held against you.

Please ask questions about anything that is unclear to you and take your time to make your choice.

Some of the people who are eligible to take part in this research study may not be able to give consent because they are less than 18 years of age (a minor). Instead we will ask their parent(s)/guardian(s) to give permission for their participation in the study. Throughout the consent form, "you" always refers to the person who takes part in the research study.

1. Why is this research study being done?

We are asking you to be in this study because you can help us learn more about how the brain works to control what we eat. This knowledge may help us understand how to help children eat a more nutritious diet.

Our study is being done to find the answer to this question: "How do children react to viewing images of different foods?" We know that some children are more likely to eat more or less of certain foods. We do not know why, but we are studying pictures of children's brains when they see foods to find out.

A total of approximately 135 children and their parents will take part in this research study at the University Park, PA Penn State Campus.

2. What will happen in this research study?

a. Consent for an initial screening

We have a large research study starting soon that includes seven visits to our lab. Before we begin this study, we must find the correct parents and children to participate. In order for you and your child to participate in the initial screening, we must receive an informed consent from you.

In this initial screening, we must ask a series of screening questions. This screening will help us

to find out more about you in order to determine if you are right for our study. After you have given consent to participate, you will be asked a series of questions to determine if you are eligible for the study. After the screening, if you are eligible to continue in the research, we will make an appointment for your first visit. We will then send you more information about the study, including parking information and a reminder of the date and time of your appointment.

b. Consent for fasting for three hours prior to visits

You and your child will attend seven visits at lunch or dinner time. We ask your child not to eat meals or snacks for three hours prior to your arrival for the first six visits. Your child may have a sip of plain water if they are thirsty.

During your first visit, you will receive more information about the study and will have a chance to ask questions and give an informed consent for the remainder of the study.

3. What are the risks and possible discomforts from being in this research study?

Loss of confidentiality: With all research studies, there is a small chance that the family's confidentiality will be breeched, even though we take precautions to maintain confidentiality. There is a risk of loss of confidentiality if your information or your identity is obtained by someone other than the investigators, but precautions will be taken to prevent this from happening. The confidentiality of your electronic data created by you or by the researchers will be maintained to the degree permitted by the technology used. Absolute confidentiality cannot be guaranteed.

4. What are the possible benefits from being in this research study?
4a. What are the possible benefits to you?

You or your child may enjoy the activities during the study, or feel it is good to contribute to a scientific study.

4b. What are the possible benefits to others?

Furthermore, this study may also benefit the community. That is because we know very little about how a child's brain processes pictures of different foods. Now that we can take pictures of the brain, there is much we can learn from taking images while children look at pictures of food, and comparing it to the foods they eat. What we learn in this study will help future studies of children and help us come up with ways to help children to eat well.

5. What other options are available instead of being in this research study?
You may decide not to participate in this research.

6. How long will you take part in this research study?

If you agree to take part in this initial screening for the study, it will take about 5 minutes to read you the consent form and answer your questions. It will then take about 5 minutes to ask the screening questions, for a total of about 10 minutes.

7. How will your privacy and confidentiality be protected if you decide to take part in this research study?

Efforts will be made to limit the use and sharing of your personal research information to people who have a need to review this information. To protect against the potential of loss of confidentiality, each participant's data records are coded with a unique ID number and no names are used.

A list that matches your name with your participant code number will be kept in a password-protected digital record. Records containing names or other identifying information are kept under lock at the PI's research office. Your research records will be labeled only with your code number, and will be kept in a locked lab. The resulting database will be retained indefinitely.

In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

We will do our best to keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people may find out about your participation in this research study. For example the following/people/groups may check and copy records about this research:

- The Office for Human Research Protections in the U. S. Department of Health and Human Services
- The Institutional Review Board (a committee that reviews and approves research studies)
- The Office for Research Protections
- The National Institutes of Health.

Some of these records could contain information that personally identifies you. Reasonable efforts will be made to keep the personal information in your research record private. However, absolute confidentiality cannot be guaranteed.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed

for auditing or program evaluation by NIH which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of mandated reporting issues regarding child abuse and neglect, harm to self or others, etc. The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document."

8. What are the costs of taking part in this research study?

8a. What happens if you are injured as a result of taking part in this research study?

We expect no risk of injury.

9. Will you be paid or receive credit to take part in this research study?

You will not be paid for the initial consent and screening process. If you are eligible for the study, families will receive $50 cash compensation per visit that will be split between parent ($30) and child ($20), for a total of $350 for the 7 visit study. Participants who live more than 20 miles from University Park, PA will be offered $20 per visit to help with travel expenses.

10. Who is paying for this research study?

This project is funded by a NIH grant.

11. What are your rights if you take part in this research study?

Taking part in this research study is voluntary.

- You do not have to be in this research.
- If you choose to be in this research, you have the right to stop at any time.
- If you decide not to be in this research or if you decide to stop at a later date, there will be no penalty or loss of benefits to which you are entitled.

12. If you have questions or concerns about this research study, whom should you call?

Please call the head of the research study (principal investigator), *Kathleen Keller* at *814-863-2915* if you:

- Have questions, complaints or concerns about the research.
- Believe you may have been harmed by being in the research study.

You may also contact the Office for Research Protections at (814) 865-1775, ORProtections@psu.edu if you:

- Have questions regarding your rights as a person in a research study.
- Have concerns or general questions about the research.

- You may also call this number if you cannot reach the research team or wish to offer input or to talk to someone else about any concerns related to the research.

INFORMED CONSENT TO TAKE PART IN RESEARCH

*Tell the researcher your decision regarding whether or not to participate in the research **OR** Your participation implies your voluntary consent to participate in the research. Please keep or print a copy of this form for your records.*

Appendix B Assent script (chapters 2, 3)

Intro:
I'm going to tell you about our project so you can decide if you want to help. We want to know what happens in kids' brains when they look at pictures of food. If you decide to help out, you'll visit us 7 times.

Visit 1:
If you help us out today, you'll have a body scan, which takes a picture of your body to see how much muscle and fat you have. Then, we'll give you yummy foods to eat. You can eat as much or as little as you like, and you don't have to eat anything you don't like.

Visits 2-3: I'll also give you a special watch for your wrist to keep track of how you move during the day on either Visit 1 or 2. You should wear it every day for a week and bring it back to us.

Visits 2-5: After Visit 1, for the next 4 times you visit, we'll also make you yummy food to eat. You can eat as much or as little as you like, and you don't have to eat anything you don't like.

Visits 1-6: For most of our visits (Visits 1-6) we will be playing games, and asking you questions. You can skip any questions that you don't want to answer. Game examples are a food waiting game, and another is trying to count your own heart beats.

Visits 4 and 5: You will be having a picture of your brain taken on Visit 6 with a special camera called an MRI, so we will need to practice using this camera. The MRI camera is a big tube that looks like a spaceship. You'll lie on a comfy bed inside the spaceship and look at pictures on a screen. You'll need to lie down really still so the pictures we take won't be fuzzy. Since the spaceship makes loud noises, you'll wear special headphones.
We'll also give you a special ball to squeeze. If you want to get out of the spaceship, you can tell us or squeeze the ball. If you really don't like being inside the practice spaceship, you can tell us and we won't go inside the real spaceship.

Visit 6: On your 6th visit, we'll use a special camera called an MRI to take pictures of your brain. It's really safe and doctors use it all the time. The MRI is a big tube that looks like a spaceship. You'll lie on a comfy bed inside the spaceship and look at pictures on a screen. You'll need to lie really still so the pictures we take won't be fuzzy. Since the spaceship makes loud noises, you'll wear special headphones. We'll also give you a special ball to squeeze. If you want to get out of the spaceship, you can tell us or squeeze the ball. We'll have you go inside the practice spaceship on visits 4 and 5 to try it out. If you really don't like being inside the practice spaceship, you can tell us and we won't go inside the real spaceship. If you ever have questions about the spaceship or our project, just ask us!

Visit 7:

A year from now, we want you and your (mom/dad) to come back for the 7th visit. We'll take your weight and height again and do another body scan to take a picture of your body. Then, we'll give you yummy foods to eat. You can eat as much or as little as you like, and you don't have to eat anything you don't like. We will play some fun computer games too. We will also ask you questions about how you eat.

Questions:
It's up to you to decide if you want to be in our project. You can change your mind anytime you want, and that's ok. Do you have any questions?
Answer child's questions
Ask follow-up assent questions to confirm understanding
"Ok, now I just need to ask you 3 questions to make sure you understand our project. Do you know what you'll be doing for our science project?"
Researcher: Explain again if they don't, or if they miss a major part of the study. Example: "I'll eat some food". Mention body scan, spaceship, and special watch.
"Are you allowed to stop being in the project whenever you want?"
Researcher: If they say no/don't know, explain again.
"Do you want to be in our project?"
Researcher: If yes, continue. Otherwise, go to parent.

Appendix C MRI screening form (chapters 2, 3)

PennState

SOCIAL, LIFE, & ENGINEERING SCIENCES IMAGING CENTER (SLEIC)
3T MRI SAFETY SCREENING FORM *version 04/13/22*

This information is strictly confidential. Please print legibly.
It is important that you complete this form carefully and completely. Please consult the MRI Technologist if you have any question or concern BEFORE you enter the MR system room.

Today's Date _____/_____/_____(mm/dd/yyyy) Name_____ ☐ Male ☐ Female

Age _____Height _____Weight _____ Body Part to be scanned_____

Date of Birth _____/_____/_____(mm/dd/yyyy)

Address _____ Telephone (home) (_____) _____-_____

City_____State_____ Zip Code _____ Telephone (cell) (_____) _____-_____

1. Have you had prior surgery or an operation (e.g., arthroscopy, endoscopy, etc.) of any kind? ☐ Yes ☐ No
   If yes, please indicate the date and type of surgery:
   Date (mm/yyyy) _/_Type of surgery _____
   Date (mm/yyyy) _/_Type of surgery _____
   Date (mm/yyyy) _____/_____Type of surgery _____

2. Do you have an implanted device(s)? ☐ Yes ☐ No
   If yes, please describe: _____

3. Have you had a prior imaging scan or examination (MRI, CT/CAT)? ☐ Yes ☐ No

If yes, please list:	Body part	Approximate Date (mm/yyyy)	Facility
MRI	_____	_____/_____	_____
CT/CAT Scan	_____	_____/_____	_____

4. Have you experienced any problem related to a previous MRI examination or MR procedure? ☐ Yes ☐ No
   If yes, please describe: _____

5. Have you ever worked with metal (grinding, fabricating, etc) as your job/employment or as a hobby/home maintenance – this includes sharpening of metal lawnmower blades, filing, etc.? ☐ Yes ☐ No

   5. a. If yes, have you ALWAYS worn eye protection/goggles while doing so? ☐ Yes ☐ No

6. Have you ever had an injury to the eye involving a metallic object or foreign body (e.g., metallic slivers, shavings, foreign body, etc.)? ☐ Yes ☐ No
   If yes, please describe: _____

7. Have you ever been injured by a metallic object or foreign body (e.g., BB, bullet, shrapnel, etc.)? ☐ Yes ☐ No
   If yes, please describe: _____

For Females:

8. Are you pregnant or experiencing a late menstrual period? ☐ Yes ☐ No

IMPORTANT INSTRUCTIONS:
Before entering the MR environment or MR system room, you must remove <u>all</u> metallic objects including hearing aids, dentures, partial plates, keys, beeper, cell phone, eyeglasses, hair pins, barrettes, jewelry, body piercing jewelry, watch, safety pins, paperclips, money clip, credit cards, bank cards, magnetic strip cards, coins, pens, pocket knife, nail clippers, tools, clothing with metal fasteners, & clothing with metallic threads.

NOTE:
You will be required to wear earplugs or other hearing protection during the MR procedure to prevent possible problems or hazards related to acoustic noise.

WARNING: Certain implants, devices, or objects may be hazardous to you and/or may interfere with the MR procedure (i.e., MRI, MR angiography, functional MRI, MR spectroscopy). DO NOT ENTER the MR system room or MR environment if you have any question or concern regarding an implant, device, or object. Consult the MRI Technologist BEFORE entering the MR system room. The MR system magnet is ALWAYS on.

Please indicate if you have any of the following:

☐ Yes	☐ No	Cardiac pacemaker	☐ Yes	☐ No	Prosthesis (eye/orbital, penile, etc.)
☐ Yes	☐ No	Implanted cardioverter defibrillator (ICD)	☐ Yes	☐ No	Artificial or prosthetic limb or joint
☐ Yes	☐ No	Aneurysm clip(s) or brain clip	☐ Yes	☐ No	IUD or diaphragm
☐ Yes	☐ No	Carotid artery vascular clamp	☐ Yes	☐ No	Pessary or bladder ring
☐ Yes	☐ No	Neurostimulation system	☐ Yes	☐ No	Other implants in body or head
☐ Yes	☐ No	Insulin or other infusion pump	☐ Yes	☐ No	Heart valve prosthesis
☐ Yes	☐ No	Implanted drug infusion device	☐ Yes	☐ No	Body piercing(s) (including ear piercing)
☐ Yes	☐ No	Spinal fusion stimulator	☐ Yes	☐ No	Intravascular stents, filters, or coils
☐ Yes	☐ No	Cochlear, otologic, or ear implant	☐ Yes	☐ No	Shunt (spinal or intraventricular)
☐ Yes	☐ No	Acupuncture needles	☐ Yes	☐ No	Vascular access port and/or catheter
☐ Yes	☐ No	Implant held in place by a magnet	☐ Yes	☐ No	Wire sutures or surgical staples
☐ Yes	☐ No	Electrodes (on body, head or brain)	☐ Yes	☐ No	Metal rods in bones; joint replacement
☐ Yes	☐ No	Claustrophobia	☐ Yes	☐ No	Bone/joint pin, screw, nail, wire plate
☐ Yes	☐ No	Magnetic Eyelashes	☐ Yes	☐ No	Wig, toupee, or hair implants
☐ Yes	☐ No	Metal fragments (eye, head, ear, skin)	☐ Yes	☐ No	Dentures or Dental retainer or expander
☐ Yes	☐ No	Internal pacing wires	☐ Yes	☐ No	Asthma or breathing disorders
☐ Yes	☐ No	Aortic clips	☐ Yes	☐ No	Seizures or motion disorders
☐ Yes	☐ No	Venous umbrella	☐ Yes	☐ No	Copper infused clothing
☐ Yes	☐ No	Metal or wire mesh implants	☐ Yes	☐ No	Odor absorbing clothing
☐ Yes	☐ No	Harrington rods (spine)	☐ Yes	☐ No	Transdermal medication patch(es) (Remove before scan)
☐ Yes	☐ No	Tattoos, Tattooed eyeliner/eyebrows, or Microblading	☐ Yes	☐ No	Hearing aid (Remove before scan)

If you checked YES to any implant or metal inside or on your body, where is the item located?
Location of any implant/metal: _____

I confirm that the above information is correct to the best of my knowledge. I read and understood the contents of this form and had the opportunity to ask questions regarding the information on this form and regarding the MR procedure that I am about to undergo.

Signature of Person Completing Form: _____ Date ____/____/____

Printed Name: _____ Form Completed By: ☐ Participant ☐ Parent/Guardian/POA

SLEIC INTERNAL USE ONLY

The MRI Technologist has reviewed this form and followed up with the participant regarding any questions where indicated. The information is deemed current at the time of the scan.

☐ Yes ☐ No Participant indicated information that led to checking the status on MRIsafety.com. MRI Safety Officer contacted if necessary.

☐ Yes ☐ No It is considered safe for this individual to (Check purpose for screening)
- ☐ enter the MR system room
- ☐ enter the MRI scanner

Comments:

MRI Technologist Signature: _____ Printed Name: _____ Date ____/____/____

SLEIC Project ID (e.g., ase1_pilt):_____ 12-digit DICOM ID (e.g., 201207250900):_____

Hours Type: _____ ☐ Billable_____hr_____min ☐ In-Kind_____hr_____min

Appendix D Anthropometric Measures Questionnaire (chapters 2 and 3)

Anthropometric Measures

Child:

Height 1 (cm): _____ Height 2 (cm):_____

Weight 1 (kg):_____ Weight 2 (kg): _____

Parent: ☐ Mother ☐ Father

Height 1 (cm): _____ Height 2 (cm):_____

Weight 1 (kg):_____ Weight 2 (kg): _____

Appendix E Demographics questionnaire (chapters 2 and 3)

ID _____ Date _____

Parent V1 – Household Demographics

Please answer the following questions about <u>your child:</u>

1. Date of birth (MM/DD/YYYY): _____
2. Birth weight: _____
3. Birth length: _____
4. Was <u>your child</u> born premature? YES NO
    a. If yes, by how many weeks? _____
5. Was your child primarily breast-fed or primarily formula-fed?
    a. Breast-fed
    b. Formula-fed
6. If your child was breast-fed, for how many months was he/she exclusively (only) fed breast milk? _____
7. What is the birth order of your child? For example, if you have 2 children and this child was born second, he/she was the 2nd of 2. _____
8. What ethnicity is <u>your child</u> (please check only one)?
    a. Hispanic or Latino
    b. Not Hispanic or Latino
9. What ethnicity is <u>your child</u> (please check only one)?
    a. American Indian/Alaskan Native
    b. Asian
    c. Black or African American
    d. White
    e. Hawaiian/Pacific Islander

Please answer the following questions about <u>yourself</u> and <u>your family</u>:

1. What is your relationship to the child?
    a. Mother
    b. Father
    c. Other (please specify): _____
2. What is <u>your</u> date of birth (MM/DD/YYYY)? _____
3. What is <u>your</u> ethnicity (please check only one)?
    a. Hispanic or Latino
    b. Not Hispanic or Latino
4. What is <u>your</u> ethnicity (please check only one)?
    a. American Indian/Alaskan Native
    b. Asian
    c. Black or African American
    d. White

e. Hawaiian/Pacific Islander

5. Please indicate how many people, INCLUDING YOURSELF, currently live in your child's primary household (the one he or she spends the most time in).
    a. Mother _____
    b. Father _____
    c. Sibling _____
    d. Uncle _____
    e. Aunt _____
    f. Grandmother _____
    g. Grandfather _____
    h. Cousin _____
    i. Others, describe _____
6. How many parental/parental figure separations your child has experienced? _____
7. How many foster care placements your child has experienced, prior to his/her current living arrangement? _____
8. Does your spouse, partner, or significant other currently reside in your child's primary household?
9. What is your marital status?
    a. Married
    b. Single (never married)
    c. Widowed
    d. Divorced
    e. Separated
    f. Remarried
    g. Living together (not married)
10. Including ALL sources (such as social security income, child support payments, government assistance, dividends from investments, etc.) what was your household's combined yearly income last year BEFORE taxes?
    a. Less than $20,000
    b. $21,000 - $35,000
    c. $36,000 - $50,000
    d. $51,000 - $75,000
    e. $76,000 - $100,000
    f. $100,000 +
11. What is <u>your</u> highest level of formal education?
    a. High school (12 years)
    b. Associates (14 years)
    c. Technical/Vocational School (14 years)
    d. Bachelor's Degree (16 years)
    e. Master's Degree (16 years)

f. PhD (20 years)
g. MD (20 years)
h. JD (20 years)
i. Other, describe _____

12. If applicable, what is your partner's highest level of formal education?
    a. High school (12 years)
    b. Associates (14 years)
    c. Technical/Vocational School (14 years)
    d. Bachelor's Degree (16 years)
    e. Master's Degree (16 years)
    f. PhD (20 years)
    g. MD (20 years)
    h. JD (20 years)
    i. Other, describe _____
13. Are you currently employed? YES NO
14. Are you currently retired? YES NO
15. How many hours per week are you at work (not traveling to & from)? _____
16. Is your partner currently employed? YES NO
17. Is your partner currently retired? YES NO
18. How many hours per week is your partner at work (not traveling to & from)?
    _____
19. Has your child's biological mother lost or gained 10 or more pounds in the past month?
    YES NO
20. Who is primarily responsible for feeding your child?
    a. You
    b. Your partner
    c. Both
    d. School
    e. Other, please specify: _____
21. Who is primarily responsible for buying food in your household?
    a. You
    b. Your partner
    c. Both
    d. Other, please specify: _____
22. On average, how frequently does your family eat out or get delivery/take-out for dinner?
    a. Once a month or less
    b. Twice a month
    c. Once a week
    d. Two times a week
    e. Three times a week

f. Four or more times a week

23. On average, how many nights a week does your family eat dinner together as a group (with most family members present)?
24. On average, how many times per week does your child eat lunch that he/she brings from home?
25. Does anyone in your household have a condition that affects the food they eat?
26. Have you or anyone in your household used any of the following programs in the past 12 months?
    a. SNAP (food stamps)
    b. WIC
    c. TNAF (cash assistance)
    d. Medicaid (Medical assistance)
    e. LIHEAP (Home energy assistance)
    f. Partial Free/Reduced School Meal Program (only some meals)
    g. Full Free/Reduced School Meal Program (all meals)
    h. Other assistance programs
27. Have you ever received food from a food pantry or soup kitchen?
28. If applicable, how many times have you received food from a food pantry or soup kitchen in the past 12 months?

29. In a typical month, how much money do you spend on food for your household, including food you buy at any stores **and** restaurants?
    a. Less than $100 a month
    b. $100-$200 a month
    c. $200-$300 a month
    d. $300-$400 a month
    e. $400-$500 a month
    f. More than $500 a month
30. Which grocery store do you use **most often** when going on a **typical food shopping trip**?
    a. Giant
    b. Sam's Club
    c. Target
    d. Trader Joe's
    e. Walmart
    f. Wegmans
    g. Weis
    h. A specialty or international food store, such as International Market
31. Imagine that you are on a **typical food shopping trip at (insert choice from #30 here)**. Listed below are the different items that you can choose from. Please rank each item based on how important it is for you to buy during your **typical grocery trip**. The most

important items should be foods that you won't leave store without, or always make it into your food budget. Items in the middle should be ones you would like to have, but are willing to cut from your budget if needed. Finally, the least important items should be foods that you don't buy on a typical trip or don't fit into your typical budget. Please

click on each item with the left mouse button and drag it up or down the list in order to rank the items.

a. Pre-packaged bread items, such as sandwich bread, hamburger buns, hotdog rolls, muffins, or bagels
b. Bakery breads or other freshly made goods, such as cake, cookies, or doughnuts
c. Salty snacks, such as chips, crackers, popcorn, or jerky
d. Sweet snacks, such as cookies or cakes
e. Cheese
f. Milk
g. Yogurt
h. Butter, margarine, or other butter substitutes
i. Eggs
j. Other dairy products, such as sour cream
k. Coffee or tea
l. Soda or other carbonated beverages
m. Fruit juices or beverages, such as orange juice or apple cider
n. Sports drinks, such as Gatorade or Powerade
o. Alcoholic beverages, such as beer or wine
p. Red meat, such as beef, pork, or lamb
q. Poultry, such as chicken or turkey
r. Seafood, such as shrimp, salmon, tilapia, tuna, crab, or lobster
s. Pasta, noodles, or rice, such as fettuccine, lasagna, white rice, or brown rice
t. Soup, such as chicken noodle or tomato
u. Nuts and seeds, such as peanuts, almonds, walnuts, or sunflower seeds
v. Nut butters, jelly and honey, such as peanut or almond butter; or strawberry or grape jelly
w. Breakfast cereals, such as oatmeal or cornflakes
x. Breakfast, meal replacement, or protein bars, such as Luna, Cliff, Quest, Quaker, or Nature Valley bars
y. Meal replacement shakes or protein powder, such as Glucerna shakes or Muscle Milk
z. Fresh prepared foods, such as pizza or salad bar entrees
aa. Fresh vegetables, such as spinach, carrots, or broccoli
bb. Fresh fruits, such as strawberries, apples, or oranges
cc. Canned vegetables
dd. Canned fruits
ee. Frozen vegetables
ff. Frozen fruits
gg. Frozen dinner items, such as pizza, macaroni and cheese, or French fries
hh. Frozen breakfast items, such as waffles

ii. Frozen desserts, such as cakes or pies
jj. Candy or gum, such as chocolate, caramel, or toffee
kk. Baking supplies, such as flour, sugar, or baking soda
ll. Condiments or sauces, such as ketchup, mustard, mayonnaise, tomato sauce, barbeque sauce, or hot sauce
mm. Dips or spreads, such as hummus, French onion dip, or ranch dip
nn. Salad dressings or toppings, such as oil and vinegar, ranch, honey mustard, or croutons
oo. Spices and seasonings, such as salt, pepper, cinnamon, basil, or oregano
pp. Oil, cooking spray, or shortening, such as olive oil or coconut oil

32. Do you grow or produce any of these food items for your household (for example, in your own garden or farm)?
    a. Fruits
    b. Vegetables
    c. Jelly, jam, or any other spreads/dips made from your fruits or vegetables
    d. Nuts or seeds
    e. Milk
    f. Cheese
    g. Butter
    h. Eggs
    i. Red Meat
    j. Poultry Meat
33. Does your child get money as an allowance? (if yes, ask #34)
34. About how much money per week do you give your child for their allowance?
    a. Less than $1 a week
    b. $1-$5 a week
    c. More than $5 a week

Appendix F Freddy Fullness scale and script (chapters 2, 3, 4)

<u>Introduction:</u> "I have a doll here whose name is Freddy. You can use Freddy to tell how full your stomach feels after eating food or a meal, like breakfast, lunch, or dinner. For example, if you hadn't eaten anything and your stomach felt empty, you'd put the slider at the very bottom. If you ate so much and were so full that you felt like you could burst and you couldn't possibly eat anymore, you'd put the slider at the top. Why don't you try to move the slider to get a feel for it? "
(Allow child to demonstrate how the slider can move up and down Freddy's tummy.)

"Now, I have a few questions for you, and I want you to move the slider up and down Freddy's tummy to tell me how full you think you would be. Okay?"

"Imagine if you ate just a little bit, like one cookie, how full do you think your stomach would feel?"
(If child moves the slider more than 25%, ask whether he/she is sure that's really a little bit. – Moving the slider too far for a little may indicate the child doesn't understand).

"Now, imagine that you ate a few more cookies, how full do you think your stomach would feel?"
(Any response between the last one and the top is acceptable.)

"Now imagine that you ate so many cookies that you didn't want any more, but you could still eat something else, how full do you think your stomach would feel?"
(Child should put the slider between 60 and 80% of the distance.)

"Now, if you ate so much that you couldn't possibly eat anymore of ANY food, how full do you think your stomach would feel?"
(Child should use the maximum.)

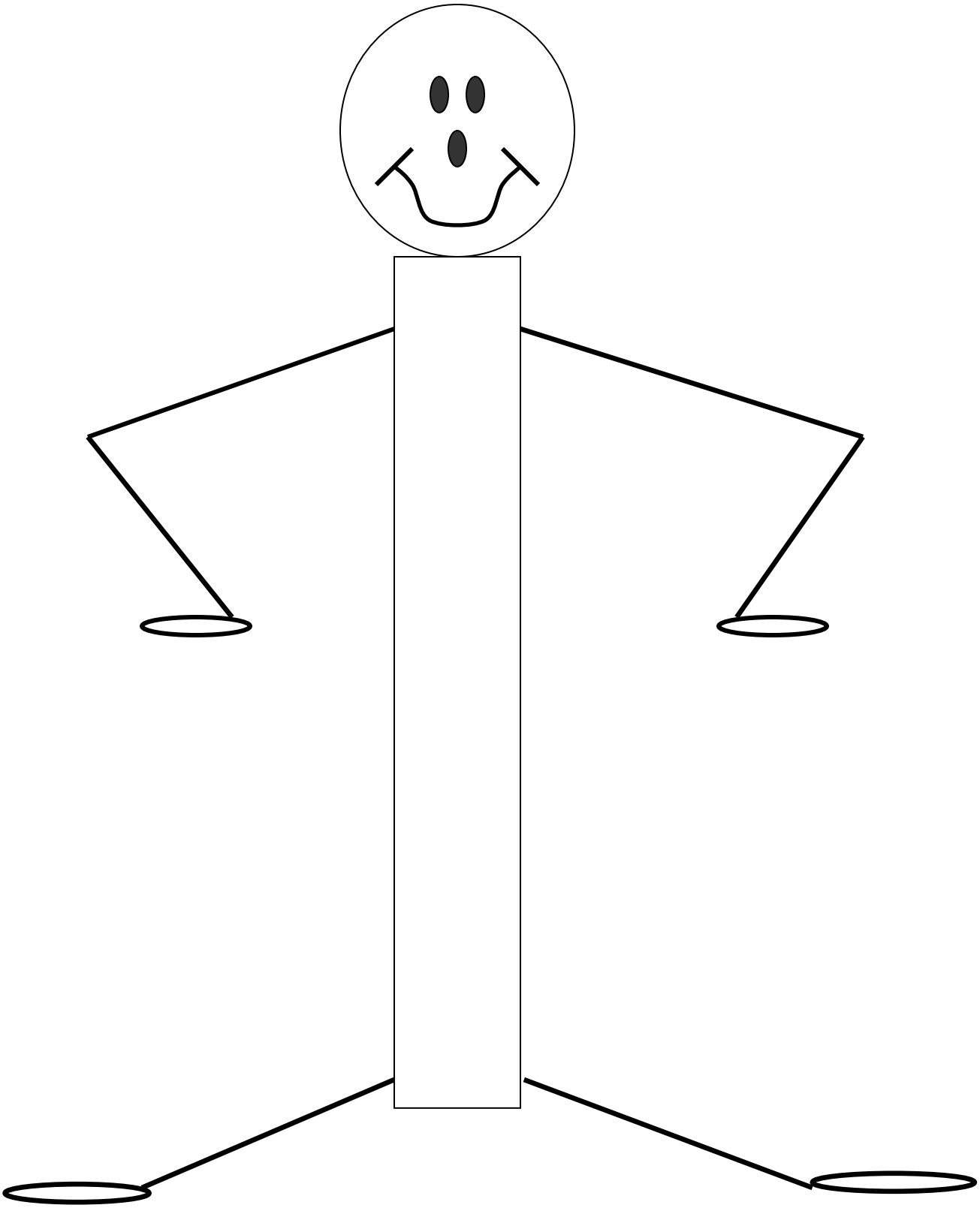
"Do you understand how Freddy works?"
(Allow child to respond. If child is still unclear, go through explanation again.)

<u>Fullness Determination and Study Meal</u>

"Can you use Freddy to show me how full your stomach feels right now? Remember, if your stomach feels empty, you push the rectangle to the bottom of the page like this."
(Push the slider to the bottom of the page).

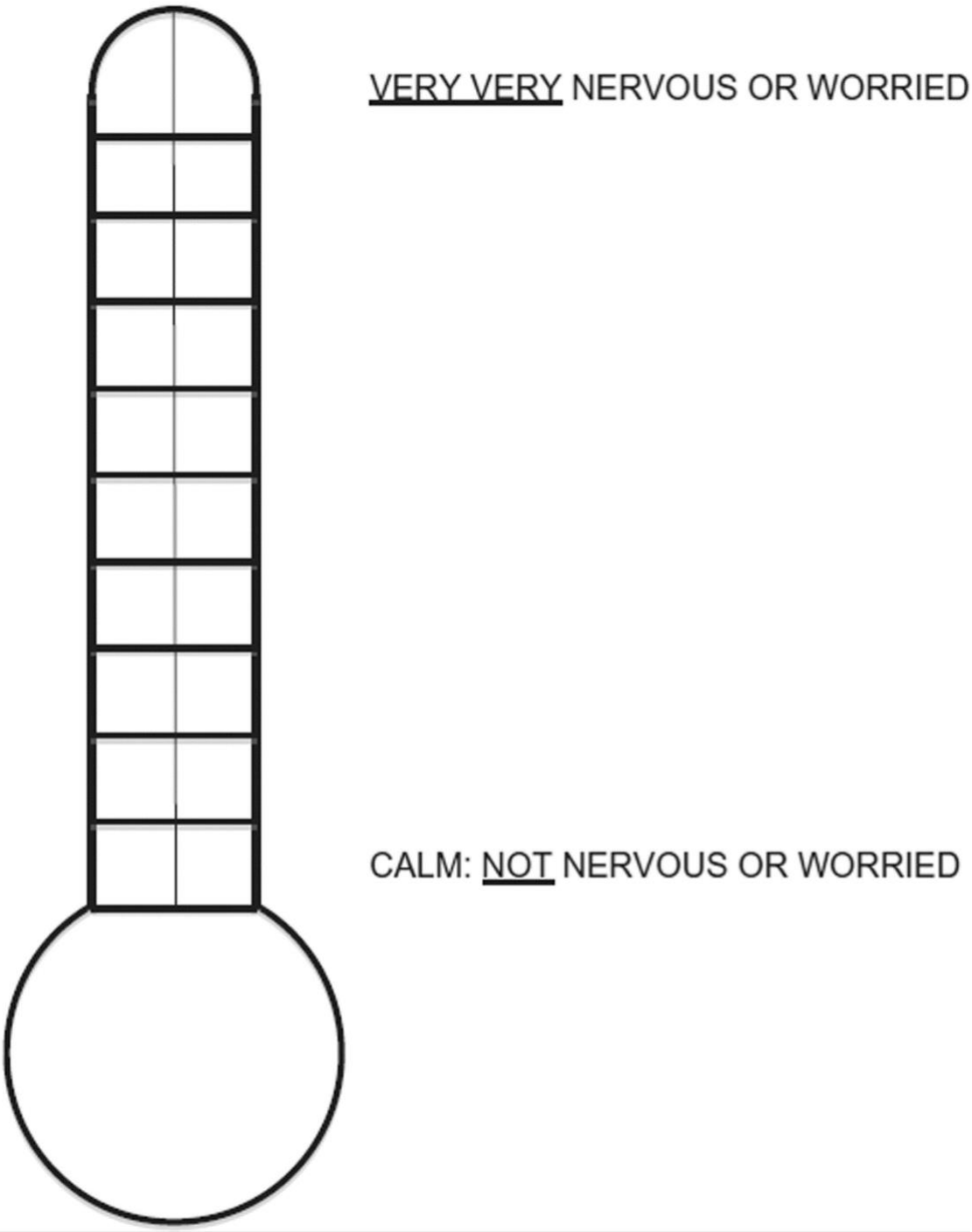
"If you have eaten a lot and you can't possibly eat anymore, you push the rectangle all the way to the top like this."
(*Push the slider to the top of the page*).

"Do you understand? Great! Move the rectangle to show me how you feel right now."
(Let child use Freddy to rate how full he/she feels. Mark it on the Pre-Meal Freddy sheet.)



Appendix G CAMS anxiety measure (chapters 2 and 3)

Pretend that all of your worried or nervous feelings are in the very bottom down here (point to scale). If you are a little bit worried or nervous, the feelings might come up just a little bit (move finger up). If you are very, very worried or nervous, the feelings might go all the way to the top (move finger up to top). Put a line showing how much worry or nervousness you feel.



Appendix H Children's Eating Behavior Questionnaire (chapter 3)

ID:

Child Eating Behaviour Questionnaire (CEBQ)

Please read the following statements and tick the boxes most appropriate to your child's eating behaviour.

	Never	Rarely	Some-times	Often	Always
My child loves food	☐	☐	☐	☐	☐
My child eats more when worried	☐	☐	☐	☐	☐
My child has a big appetite	☐	☐	☐	☐	☐
My child finishes his/her meal quickly	☐	☐	☐	☐	☐
My child is interested in food	☐	☐	☐	☐	☐
My child is always asking for a drink	☐	☐	☐	☐	☐
My child refuses new foods at first	☐	☐	☐	☐	☐
My child eats slowly	☐	☐	☐	☐	☐
My child eats less when angry	☐	☐	☐	☐	☐
My child enjoys tasting new foods	☐	☐	☐	☐	☐
My child eats less when s/he is tired	☐	☐	☐	☐	☐
My child is always asking for food	☐	☐	☐	☐	☐
My child eats more when annoyed	☐	☐	☐	☐	☐
If allowed to, my child would eat too much	☐	☐	☐	☐	☐
My child eats more when anxious	☐	☐	☐	☐	☐
My child enjoys a wide variety of foods	☐	☐	☐	☐	☐

My child leaves food on his/her plate at the end of a meal	☐	☐	☐	☐	☐
My child takes more than 30 minutes to finish a meal	☐	☐	☐	☐	☐

	Never	Rarely	Some-times	Often	Always
Given the choice, my child would eat most of the time	☐	☐	☐	☐	☐
My child looks forward to mealtimes	☐	☐	☐	☐	☐
My child gets full before his/her meal is finished	☐	☐	☐	☐	☐
My child enjoys eating	☐	☐	☐	☐	☐
My child eats more when he/she is happy	☐	☐	☐	☐	☐
My child is difficult to please with meals	☐	☐	☐	☐	☐
My child eats less when upset	☐	☐	☐	☐	☐
My child gets full up easily	☐	☐	☐	☐	☐
My child eats more when s/he has nothing else to do	☐	☐	☐	☐	☐
Even if my child is full up s/he finds room to eat his/her favourite food	☐	☐	☐	☐	☐
If given the chance, my child would drink continuously throughout the day	☐	☐	☐	☐	☐
My child cannot eat a meal if s/he has had a snack just before	☐	☐	☐	☐	☐
If given the chance, my child would always be having a drink	☐	☐	☐	☐	☐
My child is interested in tasting food s/he hasn't tasted before	☐	☐	☐	☐	☐

My child decides that s/he doesn't like a food, even without tasting it	☐	☐	☐	☐	☐
If given the chance, my child would always have food in his/her mouth	☐	☐	☐	☐	☐
My child eats more and more slowly during the course of a meal	☐	☐	☐	☐	☐

Appendix I Consent form (chapters 4)

CONSENT FOR RESEARCH
The Pennsylvania State University

Title of Project: Understanding Decision-Making and Reward for Food Choice in Children

Principal Investigator: Shana Adise

Ph.D. Candidate

Department of Nutritional Sciences

110 Chandlee Laboratory

University Park, PA 16802

814-865-4404

Advisor: Kathleen Keller, Ph.D., Assistant Professor

Department of Nutritional Sciences and

Department of Food Sciences

(814) 863 – 2915

Other Investigators:

Charles Geier, Ph.D., Assistant Professor of Human Development and Family Studies

Nicole J. Roberts, MS

Print your name here: _____. This form may contain words that you do not understand. Please ask the study personnel to explain any words or information you do not clearly understand.

We are asking you to be in a research study.

Whether or not you take part is up to you. You can choose not to take part. You can agree to take part and later change your mind. Your decision will not be held against you.

This form gives you information about the research. Please ask questions about anything that is unclear to you and take your time to make your choice.

Some of the people who are eligible to take part in this research study may not be able to give consent because they are less than 18 years of age (a minor). Instead we will ask their parent(s)/guardian(s) to give permission for their participation in the study, and we may ask them to agree (give assent) to take part. Throughout the consent form, "you" always refers to the person who takes part in the research study.
Please read every page carefully and initial the bottom of each page when you have had all of your questions answered to your satisfaction.

Purpose of study:

Our study asks how decision-making and reward influence eating behaviors. We want to know why some children are more likely to overeat than others. We are studying how children make decisions about food, particularly for foods that they find rewarding. We will try to understand how these factors relate with the types of foods your child likes and eats the most. This study will help us learn more about how children make food-based decisions, and this may help us teach children to eat more nutritious diets. We will also use magnetic resonance imaging to understand what areas of the brain are important for decision-making and rewarding value of food.

This study will use questionnaires, eating behavior tests and performance-based computer game tasks, as well as a brain imaging session. For the brain imaging, we use Magnetic Resonance Imaging (MRI). It is a tool that lets us look at your child's brain activity. In the MRI scanner your child will complete a game.

The MRI scans will assist us in understanding the structure and function of different parts of the body. In this research study, MRI scans of your child will be taken. There are two types of scans that may be done. Anatomy scans are used to image the structure of the body. Scans of function are used to image areas of activity when your child is resting or performing different tasks. I this study, we will only be scanning the brain. NONE of the scans done during this study are designed

to detect or evaluate any medical condition your child may have. They are intended solely for research purposes.

Approximately 40 children and their parents will take part in this research study at The Pennsylvania State University.

Procedures to be followed:

Visits 1-4: You and your child will attend four visits at Chandlee Laboratory. We ask that your child fast for at least three hours prior to your arrival for each visit. Visits 1-3 will take place in the Children's Eating Behavior Laboratory and the Decision-Making Laboratory, both in Chandlee. The fourth visit will be conducted at the Penn State's Imaging Center in Chandlee Laboratory.

You will fill out various computer-based questionnaires that relate to your child's eating habits, methods used for food preparation, and household characteristics. You will also fill out a survey about how much your child eats of different foods and beverages. In addition, you and your child will be shown line drawings of same-sex genitalia and asked to circle the one that looks most like them and will also be asked about the development of secondary sex characteristics such as breast development and pubic hair. This is being done to assess your child's pubertal development.

On the first visit only, you will complete the consent form, and both you and your child will complete some computer-based questionnaires. We will also take height and weight measurements for you and your child. Your child will also play video-game-like computer tasks.

On visits two and three, your child will eat a meal of common foods that we make in our kitchen. The meal will last for 30 minutes and your child can eat as much or as little as they want. We would like to video record your child as they participate in this activity. In addition, your child will also answer computer-based questionnaires and play video-game-like tasks to assess decision-making.

On the fourth visit, we will ask your child to fast for at least three hours prior to your arrival. This visit will take place at the Penn State's Imaging Center in Chandlee Laboratory. In order to help your child better understand the MRI, we will tell them that they will be helping us explore "Nittany Lion Inner Space". Inner space is the space inside of your child's head. Inner space scientists use a special machine – a scanner- to take pictures of the brain's inner space. We will provide a snack for your child to eat.

The MRI facility at Penn State has a mock scanner, which is like the real MRI Scanner, only without the magnet. Before going into the MRI room, we will ask your child to lie in the mock scanner in order to see if he or she is comfortable and able to be still. It is very important that your child does not move when we are scanning so that we can get the best pictures of your child's brain. In the mock scanner we will also show your child how they will look at the pictures they will see in the real scanner and introduce your child to the sounds that he or she will hear in the scanner. Through all these procedures, our goal is to make your child feel very comfortable while in the MRI scanner.

To date, 150 million MRI studies have been performed around the world. We will be following

standard MRI procedures and safety guidelines. MRI has been shown to be extremely safe as long as proper safety precautions are taken. MRI uses strong magnetic fields and radio waves to make pictures of the body. There is no exposure to x-rays or radioactivity during an MRI scan. Levels of energy used are within safety limits established by the U.S. Food & Drug Administration (FDA). This study will use a 3.0 Tesla MRI scanner.

You and your child will be asked to leave metal objects and personal belongings in lockers provided in the prep room of the MRI center. Articles of clothing with metal inserts or clasps must be removed before entering the MRI room. Please ask us if you are unsure about any items.

Next, we will ask your child to complete a set of simple vision screening tests in order to fit your child with special glasses that are safe to use in the scanner. The glasses will partially correct your child's vision so that he/she can see things we will display in the scanner. If your child wears contacts or has normal vision the special glasses will not be needed.

Your child will be asked to lie on a bed that slides into the long tube of the scanner. Your child will be given earphones and/or earplugs for hearing protection since the MRI scanner makes loud noises during normal operation. Your child will be asked to remain very still at these times. For scans of the head, we may put cushions around your child's head and we may lightly tape the head to help keep it from moving. Your child will be able to talk to the MRI technologist by an intercom, and you and the technologist will be able to see and hear your child at all times. Your child will also be given a squeeze-ball signaling device. If at any time your child would like to discontinue the study, he/she can tell the investigators over the intercom or press the squeeze-ball signaling device to be removed immediately from the scanner. You or your child can choose to discontinue the study at any time without penalty.

Discomforts and risks:

We will be providing foods for your child to eat. The foods used in the meals are all common foods made with ingredients that you would find at the supermarket. It is possible that your child may not like the taste of these foods and this would result in some psychological distress.

The foods used in this study will be made fresh each day using safe food preparation protocols. However, there is always a chance of food borne illness or uncovering an allergy in your child due to food exposure causing a physical risk.

We will be asking your child some sensitive questions about eating behaviors such as laxative use, vomiting, and other behaviors that are sometimes related to eating problems. These questions may make your child feel uneasy. He/she does not have to answer them. If we are concerned about your child's responses, we may speak with you and provide a name of a specialist who deals with these issues. We may also ask your child to talk to you about this or speak with a trusted health professional (e.g. school nurse, teacher).

Your child will fill out a pubertal assessment questionnaire. Your child may feel uncomfortable answering some of the questions that are sensitive in nature. In order to minimize the risk, your

child will be told that he/she does not have to complete any questions that make him/her uncomfortable.

Risk of injury is very low during an MRI scan. However, MRI is not safe for everyone. It may not be safe for your child to have an MRI scan if there is any metal containing iron in or on your child's body. This is because metal containing iron can pose a safety risk when in the presence of strong magnetic fields. Radio waves may also heat the body and metallic objects within or on the body, possibly resulting in burns. Before you or your child is allowed in the scanner room, you will be asked a set of questions to determine if it is safe for your child to have an MRI scan at this time. You will also be asked to answer the questions to determine if it is safe for you to enter the scanner room with your child. For you and your child's safety, it is very important that you answer all questions truthfully.

It is possible that your child may feel uncomfortable or confined once inside the scanner. This feeling usually passes within a few minutes after the study begins. It is possible that your child might experience dizziness, mild nausea, or see tiny flashing lights. These sensations are mostly due to movement while inside the magnet and can be minimized by holding still. All of these sensations should stop shortly after your child leaves the magnet.
As with any study that collects personal data, there is a risk of loss of confidentiality. We have set in place many guidelines to avoid this, as outlined below.

There are no other foreseeable discomforts and risks, other than what is listed above.

Benefits:

You will not benefit from this research study. However, you or your child may enjoy the activities during the study, or feel it is good to contribute to scientific study. Furthermore, this study may also benefit the community. That is because we know very little about how children respond to different foods. Now we can learn from how children make decisions to what foods they actually consume. What we learn in this study will help us come up with ways to help children eat better diets.

Voluntary participation:

Participation in this research study is voluntary. Therefore, you may choose to not be in this study. In addition, you or your child can choose to stop at any time. You do not have to answer any questions that you do not want to answer. Refusal to take part in or withdrawing from this study will involve no penalty or loss of benefits you would otherwise receive.

Duration/ time of the procedures and study:

If you agree to take part in this study, it involves four total visits, in which you and your child will return to The Children's Metabolic Kitchen and Eating Behavior Laboratory or the Smoking Laboratory at Penn State. Typically, these visits will be scheduled 1 week apart but all 4 visits can be completed between 3-6 weeks. All visits will last no longer than 2 hours.

Statement of confidentiality:

Your child's participation in this research is confidential. All possible steps have been taken to assure your child's privacy. Efforts will be made to limit the use and sharing of your personal research information to people who have a need to review this information. Your child will be assigned a code number that will be used throughout the study. Only this code (and never your child's name) will be used when analyzing or reporting the data. Any identifying information will be kept in a locked location and password protected electronic files.

This consent and any other identifying information will be kept in a locked file in Dr. Kathleen Keller's (co-investigator) locked office. All questionnaires that you and your child complete will be identified only by your child's code and stored separate from any identifying information. Only the PI (Shana Adise) and study coordinators will have access to your identifying information. All other project staff who are approved by the Penn State IRB will only have access to data files without your name.

Penn State's Office for Research Protections, the Institutional Review Board, and the Office for Human Research Protections may review records related to this research study.

In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared. The results of the research, including but not limited to your child's results, may be published and presented at lectures and professional meetings, but your child will not be identified in any such publication or presentation.

We will do our best to keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people may find out about your participation in this research study. For example the following/people/groups may check and copy records about this research.

- The Office for Human Research Protections in the U. S. Department of Health and Human Services
- The Institutional Review Board (a committee that reviews and approves research studies) and
- The Office for Research Protections.

Some of these records could contain information that personally identifies you. Reasonable efforts will be made to keep the personal information in your research record private. However, absolute confidentiality cannot be guaranteed.

We would like to video record your child as they participate in one of our tasks. However, children will be unaware that they are being recorded during the task. The video recordings will be stored on secure, networked servers in the College of Health and Human Development until three years after the study's completion, when they will be destroyed. Only research staff on this study will have access to the recordings. With permission from you and your child, we may share segments of audio, video, or photographs with students or other scientists. Once segments have been chosen, the remainder of the recordings will be destroyed three years after the study is complete.

Right to ask questions:

Please contact Shana Adise at (814) 865-4404 with any question, concern or comment about the research. Dr. Kathleen Keller, who can be reached via phone at (814) 863-2915, is supervising this study. You can also call these numbers if you feel this study has harmed you or your child in any way. If you have any questions, concerns, or comments about you or your child's rights as research participants or would like to offer input, please contact Penn State University's Office for Research Protections (ORP) at (814) 865-1775. The ORP cannot answer questions about research procedures. All questions about research procedures can be answered by Shana Adise and the research team.

Injury Clause:

In the unlikely event that you or your child is injured as a result of your participation in this study, medical care is available. It is the policy of this institution to provide neither financial compensation nor free medical treatment for research-related injury. By signing this document, you are not waiving any rights that you have against The Pennsylvania State University from negligence of the University or its investigators.

Incidental findings:

The investigators for this project are not trained to perform medical diagnosis, and the scans to be performed in the study are not optimized to find abnormalities. On occasion, a member of the research team may notice a finding on a scan that seems abnormal. When a finding is noticed, the investigator or designate may consult a physician specialist, such as a radiologist or neurologist, as to whether the finding merits further investigation. If the specialist recommends further follow-up, the investigator or another designate will contact you within **48 hours** of the recommendation and suggest that you contact your private medical provider for follow-up. To facilitate follow-up care, you may be given a copy of your child's images upon request. Being told about a finding may cause anxiety as well as suggest the need for additional tests and financial costs. Medical insurance may be affected whether or not the finding is ultimately proved to be of clinical significance. Costs for clinical follow-up are not covered in the cost of research. The decision as to whether to proceed with further examination or treatment lies with you.

Abnormal test results:

Please provide contact information so that you can be reached in the event of an incidental finding and/or abnormal test results. You will be notified within 48 hours of an incidental or abnormal finding that is determined to need further investigation. This includes the MRI scan and the language test.

Address_____

Phone_____

Payment for participation:

The total compensation possible for this study is $160. For visit 1, you will receive $30 ($20 for you and $10 for your child) reimbursement for your time. For visit 2 and 3, you will receive $40 ($25 for you and up to $15 for your child) reimbursement for your time. For visit 4, you will receive $50 ($30 for you and up to $20 for your child) reimbursement for your time. We use the wording 'up to' because in some of our tasks your child has the chance to earn additional money based on performance. If you leave before completing the study, compensation will be provided on a pro-rated basis at the rate of $10 per hour completed.

Consent:

By consenting to participate, you agree to:

- Answer questionnaires we provide for you that relate to your household, parenting styles, and methods you use, or have used in the past, to feed your child. If you feel uncomfortable with any item on a questionnaire, you may leave it unanswered.
- Answer the SLEIC 3T MRI Participant Safety & Screening questions accurately for both yourself and your child,
- Tell the investigators about all metallic devices in/on you and your child's body, and
- Not bring any metal devices (e.g., pens, coins, keys, credit cards) into the scanning room without staff approval.
- Participate in weekly sessions and try your best to follow the researcher's requests.
- Talk to the researchers if there is a problem with the study.

If you agree to take part in this research study and the information outlined above, please sign your name and indicate the date below.

You will be given a copy of this signed and dated consent form for your records.

May the researchers video record your child while he or she is participating in the research?

☐ Yes, researchers may record my child while he/she is participating in the research.

☐ No, researchers may NOT record my child while he/she is participating in the research.

Sharing Video or Photographs With Scientists or Students: We will be recording one of the procedures using video, audio recording, and photographs, which will help us more accurately analyze data. Other scientists or students learning about science may find the video, audio recordings, and photographs useful, too. So we have some questions about whether it's ok for us to share segments of the video, audio, or photographs.

Please select one of the following options:

_____ Recordings of my child's participation in this research may be shown in scientific

presentations

_____ I do not want recordings of my child's participation in this research shown in scientific presentations.

Please select one of the following options:

_____ Recordings of my child's participation in this research may be shown in scientific publications.

_____ I do not want recordings of my child's participation in this research shown in scientific publications.

Please select one of the following options:

_____ Recordings of my child's participation in this research may be used for education and training of students.

_____ I do not want recordings of my child's participation in this research used for education and training of students.

I consent to participate in this study and to have my child participate in this research study.

_____	_____	_____
Printed Name of Child	Date of Birth	Date
_____	_____	_____
Parent's Printed Name	Parent's Signature	Date
_____	_____	_____
Printed Name of Person Obtaining Consent	Signature of Person Obtaining Consent	Date

Appendix J Liking Visual Analogue Scale – Buffet meal (chapter 4)

Explanation of Five-point Scale

I am going to give you some fun foods to taste and I want you to taste each one and use these smiley faces to tell me how they taste, okay?

Hate It Dislike It It's Okay Like It Love it

1. How much do you like these cheese bagel bites?

Hate It Dislike It It's Okay Like It Love it

2. How much do you like these cheese pizza rolls?

Hate It Dislike It It's Okay Like It Love it

3. How much do you like these chicken nuggets?

Hate It Dislike It It's Okay Like It Love it

4. How much do you like these mozzarella sticks?

Hate It Dislike It It's Okay Like It Love it

5. How much do you like these potato chips?

Hate It Dislike It It's Okay Like It Love it

6. How much do you like these mini-brownies?

Hate It Dislike It It's Okay Like It Love it

7. How much do you like these chocolate cupcakes?

Hate It Dislike It It's Okay Like It Love it

8. How much do you like these donut holes?

Hate It Dislike It It's Okay Like It Love it

9. How much do you like this chocolate milk?

Hate It Dislike It It's Okay Like It Love it

10. How much do you like this red licorice?

Hate It Dislike It It's Okay Like It Love it

11. How much do you like this fruit leather?

Hate It Dislike It It's Okay Like It Love it

12. How much do you like this fruit candy?

Hate It Dislike It It's Okay Like It Love it

13. How much do you like this fruit punch?

Hate It Dislike It It's Okay Like It Love it

14. How much do you like this chocolate chip cookie?


Hate It


Dislike It


It's Okay


Like It


Love it

15. How much do you like this gummy candy?


Hate It


Dislike It


It's Okay


Like It


Love it

Appendix K Liking Visual Analogue Scale – Standard meal (chapter 4)

Explanation of Five-point Scale

I am going to give you some fun foods to taste and I want you to taste each one and use these smiley faces to tell me how they taste, okay?

Hate It Dislike It It's Okay Like It Love it

1. How much do you like this macaroni and cheese?

Hate It Dislike It It's Okay Like It Love it

2. How much do you like this garlic bread?

Hate It Dislike It It's Okay Like It Love it

3. How much do you like this broccoli?

Hate It Dislike It It's Okay Like It Love it

4. How much do you like these cherry tomatoes?


Hate It


Dislike It


It's Okay


Like It


Love it

5. How much do you like these red grapes?


Hate It


Dislike It


It's Okay


Like It


Love it

6. How much do you like this angel food cake?


Hate It


Dislike It


It's Okay


Like It


Love it

Appendix L Liking Visual Analogue Scale – EAH paradigm (chapter 4)

Explanation of Five-point Scale

I am going to give you some fun foods to taste and I want you to taste each one and use these smiley faces to tell me how they taste, okay?

Hate It Dislike It It's Okay Like It Love it

1. How much do you like this popcorn?

Hate It Dislike It It's Okay Like It Love it

2. How much do you like this potato chip?

Hate It Dislike It It's Okay Like It Love it

3. How much do you like this pretzel?

Hate It Dislike It It's Okay Like It Love it

4. How much do you like this ritz bitz?

Hate It Dislike It It's Okay Like It Love it

5. How much do you like this brownie?

Hate It Dislike It It's Okay Like It Love it

6. How much do you like these chocolate chip cookies?

Hate It Dislike It It's Okay Like It Love it

7. How much do you like this starburst?

Hate It Dislike It It's Okay Like It Love it

8. How much do you like this m & m?

Hate It Dislike It It's Okay Like It Love it

9. How much do you like this dorito?


Hate It


Dislike It


It's Okay


Like It


Love it

10. How much do you like these chocolate kisses?


Hate It


Dislike It


It's Okay


Like It


Love it

Appendix M Intake sheet – EAH paradigm (chapter 4)

Serving #:_____

Check 1: _____ Time: _____

Check 2: _____ Visit #: _____

Lunch Food	Pre-Weight		Post-Weight	Amount Consumed
Popcorn (15g)	(w/o plate)	(w/plate)		
Potato chips (58g)	(w/o plate)	(w/plate)		
Pretzels (39g)	(w/o bowl)	(w/bowl)		
Ritz Bitz (44g)	(w/o plate)	(w/plate)		
Brownies (51g)	(w/o bowl)	(w/bowl)		
Chocolate chip cookies (66g)	(w/o plate)	(w/plate)		
Starbursts (66g)	(w/o plate)	(w/plate)		
M & M's (66g)	(w/o plate)	(w/plate)		
Doritos (58g)	(w/o plate)	(w/plate)		
Hershey's Chocolate Kisses (66g)	(w/o plate)	(w/plate)		

Freddy Fullness pre-meal: _____

Freddy Fullness post-meal: _____

Appendix N Intake sheet – Standard meal (chapter 4)

Serving #:_____

Check 1: _____ Time: _____

Check 2: _____ Visit #: _____

Lunch Food	Pre-Weight		Post-Weight	Amount Consumed
Macaroni & Cheese (600g)	(w/o plate)	(w/plate)		
Garlic bread (4” piece)	(w/o plate)	(w/plate)		
Broccoli (180g)	(w/o bowl)	(w/bowl)		
Cherry Tomatoes (100g)	(w/o plate)	(w/plate)		
Red grapes (200g)	(w/o bowl)	(w/bowl)		
Angel Food Cake (80g)	(w/o plate)	(w/plate)		
Water (1L)				

Freddy Fullness pre-meal: _____

Freddy Fullness post-meal: _____

Appendix O Intake sheet – Buffet meal (chapter 4)

Serving #: _____

Check 1: _____ Time: _____

Check 2: _____ Visit #: _____

Lunch Food	Pre-Weight		Post-Weight	Amount Consumed
Cheese bagel bites (~145g; 4 pieces)	(w/o plate)	(w/plate)		
Cheese pizza rolls (~80 g; 4 pieces)	(w/o plate)	(w/plate)		
Chicken nuggets (~105g; 5 nuggets)	(w/o bowl)	(w/bowl)		
Mozzarella sticks (~100g; 4 sticks)	(w/o plate)	(w/plate)		
Potato Chips (28 g)	(w/o bowl)	(w/bowl)		
Chocolate chip cookies (~35 g; 3 cookies)	(w/o plate)	(w/plate)		
Mini-brownies (~60g; 4 mini-brownies)	(w/o plate)	(w/plate)		
Chocolate cupcakes (~50g; 2 mini-cupcakes)	(w/o plate)	(w/plate)		
Donut holes (~50g; 4 holes)	(w/o plate)	(w/plate)		
Whole-fat chocolate milk (245g; 1 cup)	(w/o plate)	(w/plate)		
Red licorice (~50g; 4 pieces)	(w/o plate)	(w/plate)		
Fruit leather (~20g; 1 package)	(w/o plate)	(w/plate)		
Gummy candies (42g)	(w/o plate)	(w/plate)		
Fruit candies (42g)	(w/o plate)	(w/plate)		
Fruit punch (235g; 1 cup)	(w/o plate)	(w/plate)		

Freddy Fullness pre-meal: _____
Freddy Fullness post-meal: _____

BARI A. FUCHS **CURRICULUM VITAE**

EDUCATION

The Pennsylvania State University University Park, PA
Ph.D. Candidate, Department of Nutritional Sciences Aug 2017 – Current
Advisor: Dr. Kathleen Keller

Emory University, College of Arts and Sciences Atlanta, GA
Bachelor of Science (B.S.), Neuroscience and Behavioral Biology May 2015

RESEARCH EXPERIENCE

Graduate Research Fellow Aug 2017 - Current
The Pennsylvania State University **University Park, PA**
The Metabolic Kitchen and Children's Eating Behavior Laboratory
Dr. Kathleen Keller

SELECTED FELLOWSHIPS, HONORS & AWARDS

Gerard P. Smith Award, Society for the Study of Ingestive Behavior (2023)
NRSA Fellow (2022 – present)
Ruth L. Pike Fellow (2019-2021)
John A. Milner Endowment Award (2017)
University Graduate Fellowship, College of Health and Human Development (2017-2018)
NIMH Intramural Research Program Trainee Travel Award (2016)
NIMH Intramural Research Training Award (IRTA) Fellowship (2015-2016)

SELECTED PUBLICATIONS

Fuchs, B., Pearce, AL., Rolls, B., Wilson, S., Rose, E., Geier, C., Keller, KL, Cerebellar response to visual portion size cues is associated with the portion size effect in children. *Nutrients*, under review

Fuchs, B., Pearce, AL., Rolls, B., Wilson, S., Rose, E., Geier, C., Keller, KL, Does 'portion size' matter? Neural responses to food and non-food cues presented in varying amounts. *Appetite*, under review

Pearce, A., **Fuchs, B**., Adise, S., Masterson, T., Fearnbach, N., English, L., Keller, K., Loss of Control Eating in Children is Associated with Altered Cortical and Subcortical Brain Structure. *Frontiers in Psychology*, 2024; 14

Keller, KL, Pearce, AL., **Fuchs, B.,** Hallisky, K., Rolls, B., Wilson, S., Geier, C., Rose, E., Children with lower ratings of executive functions have a greater response to the portion size effect. *Appetite*, 2023; 186

Pearce, AL., **Fuchs, B**., Keller, KL., The role of reinforcement learning and value-based decision-making frameworks in understanding food choice and eating behaviors, *Frontiers in Nutrition*, 2022; 9

Fuchs, B., Roberts, NJ., Adise, S., Pearce, AL., Geier, C.F., White, C., Oravecz, Z., & Keller, KL. Decision-making processes related to perseveration are indirectly associated with weight status in children through laboratory-assessed energy intake. *Frontiers in Psychology*, 2021; 12: 3399