Published in final edited form as:

Physiol Behav. 2013 September 10; 121: . doi:10.1016/j.physbeh.2013.02.015.

Appetitive traits from infancy to adolescence: Using behavioral and neural measures to investigate obesity risk

Susan Carnell¹, Leora Benson¹, Katherine Pryor², and Elissa Driggin³

¹New York Obesity Nutrition Research Center, St Luke's Hospital, Columbia University College of Physicians & Surgeons, Babcock Building, Suite 10A, 1111 Amsterdam Avenue, New York, NY 10025, USA

²Duke University School of Medicine, DUMC 3951, Durham, North Carolina, NC 27710, USA

³Cornell University Department of Nutritional Sciences, Cornell University, Ithaca, NY 14853, USA

Abstract

We come into the world with enduring predispositions towards food, which interact with environmental factors to influence our eating behaviors and weight trajectories. But our fates are not sealed – by learning more about this process we can identify ways to intervene. To advance this goal this we need to be able to assess appetitive traits such as food cue responsiveness and satiety sensitivity at different developmental stages. Assessment methods might include behavioral measures (e.g. eating behavior tests, psychometric questionnaires), but also biomarkers such as brain responses to food cues measured using fMRI. Evidence from infants, children and adolescents suggests that these indices of appetite differ not only with body weight, but also with familial obesity risk as assessed by parent weight, which reflects both genetic and environmental influences, and may provide a useful predictor of obesity development. Behavioral and neural approaches have great potential to inform each other: examining eating behavior can help us identify meaningful appetitive endophenotypes whose neural bases can be probed, while increasing knowledge of the shared neurobiology underlying appetite, obesity, and related behaviors and disorders may ultimately lead to innovative generalized interventions. Another challenge will be to combine comprehensive behavioral and neural assessments of appetitive traits with measures of relevant genetic and environmental factors within long-term prospective studies. This approach may help to identify the biobehavioral precursors of obesity, and lay the foundations for targeted neurobehavioral interventions that can interrupt the pathway to excess weight.

Keywords

External eating; maternal obesity; parental obesity; genetic obesity risk; neuroimaging; high-risk; review

© 2012 Elsevier Inc. All rights reserved

Corresponding author: Susan Carnell susan.carnell@gmail.com Phone: 212-523-2503, Fax: 212-523-4293.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

1. Introduction

We live in an obesity-promoting environment but only some of us become obese. This could be because some individuals possess an 'obesogenic' set of enduring predispositions towards food (appetitive traits), which interact with environmental factors to influence eating behaviors and, ultimately, weight trajectories. Investigating the early signs of these predispositions, and factors that underlie their development, may help us develop interventions that can either alter obesogenic traits, or ameliorate potentially detrimental effects such as excess weight gain. The purpose of the current paper is twofold: 1) to give an up-to-date taste of behavioral and neural methods that can be used to *assess* these predispositions in different age groups (along with evidence that they predict body weight), and 2) to describe research using *familial risk* and other designs to identify neurobehavioral predictors of obesity development that might form useful intermediate endophenotypes we can directly relate to relevant genetic and environmental precursors. We conclude by outlining some suggestions for how behavioral, and neural approaches can inform each other going forward, and discussing practical applications of a neurobehavioral susceptibility model of child obesity.

2. Measuring weight-related appetitive traits in childhood

2.1 Behavioral measures (laboratory studies)

2.1.1 Food cue responsiveness and other aspects of food approach—Food responsiveness may be defined as the degree to which external food cues, such as the sight or smell of food, encourage an individual to eat, potentially to excess. An explicit way to assess this is to administer a test of *eating in the absence of hunger* (EAH) in which children eat to satiety, then are offered a meal or snack which they can consume ad libitum, simultaneously with an alternative rewarding activity such as access to a selection of toys or games, for a set amount of time. The calories consumed provide an index of how much the child ignores internal satiety signals in favor of responding to the external cue of the presentation of palatable food [1], and intake in such paradigms is higher among 5–18 y olds who are overweight [2, 3], linearly associated with BMI across the distribution in 7–12 y olds [4] and positively related to weight in 13–17 y olds [5]. Another index might be intake after exposure to *different types of food cue*. In one study overweight 8 and 12 year-olds consumed more palatable high-calorie foods than lean counterparts after smelling them (food odor cues) [6], while in another overweight 4–6 y olds ate more of the same selection of foods when they were presented in branded packaging (fppd branding cues) than when they were presented in plain packaging, while lean controls ate relatively less in the branded condition [7].

Other investigators have used *implicit assessments* of food cue responsivity, designed to probe underlying attentional biases towards food. In an adapted Stroop study 9–16 y olds in a residential CBT program for severe obesity were slower than lean adolescents at identifying the color of food words (e.g. whipped cream, bread, pizza) relative to control words (e.g. siren, postman, and radiator), but not at identifying the color of negative-emotion words (e.g. angry, panic, stress), relative to control words [8]. Overweight 7–9 y olds performing an adapted stop signal task, in which responses towards pictures of foods or toys (i.e. pressing a button to indicate whether a picture was on the left or right side of the computer screen) had to be inhibited at the presentation of an auditory cue, with rewards for fast and accurate responses, were less effective in inhibiting responses towards food [9]. Another study found that overweight 12–18 y olds showed better memory for food vs. control words imbedded in a grid, although there was no evidence for attentional interference in the overweight group as measured by the number of food vs. control words initially identified [10]. A study using a self-concept Implicit Association Task, in which

participants had to categorize words or pictures as fat vs. non-fat and self vs. other, found that 9–18 y olds who were lean, but not those who were obese, were quicker to respond when 'non-fat' and 'self' categorizations required the same key press; the authors suggest this might indicate a greater self-identification with healthy than unhealthy foods among the lean children [11]. Another study found that overweight 6–11 y olds showed increased lip sucking in response to high energy food pictures and food odors, and were more likely to classify non-food odors as food odors during the pre-prandial state, suggesting a number of potential orofacial indicators of food cue responsiveness [12].

A more proactive dimension of food approach is the willingness to consciously work to obtain food, i.e. the *reinforcing value of food* [13]. This is usually operationalized by a computer task in which the child must perform some kind of work (e.g. button presses) in order to obtain a palatable foodstuff, but the demands are systematically varied, and the amount of work done for food relative to that for an alternative reward, or the time spent working for food before switching to a less demanding non-food reward, provides an index of the reinforcing value of food. Studies using this paradigm have shown that overweight (vs. lean) children (8–12 y) work harder for food than non food-related activities [14], show a slower decline in the amount of work done for food over a 20-minute period (8–10 y olds) [15], and that higher relative reinforcing value of food at baseline predicts 1-year weight gain in 7–10 y olds [16]. A related construct is *delay of gratification* (also known as *temporal discounting* or *delay discounting*), i.e. the degree to which a child is willing to wait for a food reward that is bigger in size as opposed to a smaller one available now, e.g. two marshmallows in 15 minutes vs. one marshmallow now [17]. In a classic delayed gratification study, one group demonstrated that obese children were less likely than lean children to reject a food reward today in favor of receiving a twofold reward a day later – a phenomenon that did not apply to alternative, non-food (toy) rewards [18]. A more recent version found that children who failed to delay gratification in a standard food task at 4 y were more likely to be overweight by 11 y [19] while a follow-up of Mischel's original cohort of 4 y olds found that those who struggled to delay gratification had higher BMIs in their mid thirties [20].

2.1.2 Satiety sensitivity and other aspects of food avoidance—Satiety sensitivity, or satiety responsiveness, may be defined as the degree to which children are capable of ceasing consumption in response to internal signals, which might include gut hormone release and gastric distension. One way of tapping this ability is to test how well they are able to offset calories consumed in a preload meal or snack in a subsequent ad libitum meal, often referred to as *caloric compensation*. Since Schachter et al's early observation of decreased compensation for an earlier meal of roast beef sandwiches (vs. nothing) at a subsequent ad libitum snack of crackers among obese (15% overweight or more) compared to lean male college students [21], weight-related differences have been observed in a number of samples. A study of 3–5 y olds reported poorer compensation at a standard lunch following a high vs. low orange-flavored drink among heavier girls [22], and a subsequent paper by the same group reported that compensation ability predicted 24-hour energy intake in 4–6 y old girls, which in turn predicted relative weight [3]. In a cohort of 3–5 y olds, we demonstrated a trend for poorer average compensation at a standard lunch following sensorily-matched and sensorily-distinguishable preloads with successively higher weight groups [23], and others have found weight-related differences in laboratory-tested compensation even when both the preload and the meal use the same foodstuffs [6]. Compensation may also be ascertained in a free-living environment: When adolescents were given a fast food meal in a food court and ate it in a group setting, following a standard breakfast, the overweight subjects consumed significantly more in terms of both absolute calories, and calories relative to energy requirements [24]. In another study by the same group, intake was assessed via dietary recall for two days when fast food was consumed and

two days when it was not, and overweight vs. lean adolescents were less likely to compensate for the fast food calories consumed [24]. Compensation ability may depend somewhat on the macronutrients involved: in a study measuring food intake following various preloads, obese 9–14 y old boys showed poorer compensation at a subsequent pizza meal for a whey protein preload, with no weight-related differences in compensation for a glucose preload [25]. It should also be noted that associations are not entirely robust: several studies have failed to find a relationship with child weight, suggesting that compensation measured in a single laboratory test may fail to capture adequately the repeated episodes of poor compensation across a wide variety of situations that ultimately lead to weight gain [26–28].

Another putative measure of satiety sensitivity is the pattern of eating rate over a meal, since, if someone is sensitive to internal satiety signals accumulating during the consumption period, we would expect their rate of eating to slow down throughout the meal episode. Since the early publication of observational results showing that obese children ate at a faster rate, took more bites, and chewed each bite fewer times at cafeteria meals [29], studies have variously found that obese 11 y olds eat faster and do not show any deceleration of eating rate towards the end of the meal [30], that obese 5–18 year olds and those with Prader-Willi syndrome also show a lack of deceleration [31], and that heavier 10–12 y olds have faster eating rates (but no deceleration differences) throughout the BMI distribution [32]. Other research has demonstrated prospective relationships. One group found that number of mouthfuls of food per minute in 4 y olds predicted changes in BMI, skinfolds and total fat from 4 to 6 y [33]. Others have observed similar relationships even earlier in life, with one study finding that a vigorous sucking rate during feeding at 2 and 4 wks of age predicted greater skinfolds and BMI at 1 and 2 y, and high pressure sucking predicted adiposity at 3 y [34], and another that sucking behavior at 3 mo predicted weight gain at 2 y [35].

It should of course be noted that although we have organized tests into two broad categories, which roughly map onto the concepts of hedonic vs. homeostatic eating, there is significant conceptual and behavioral overlap, which is probably reflected by overlap in the underlying neurobiology. For example, eating in the absence of hunger is by definition a function of the degree to which internal satiety cues are overwhelmed by the presentation of palatable foods, while the mechanism for fast eating and failure to compensate could be heightened responsivity to the external cues provided by the presence of the remaining palatable food on the plate. The term 'satiety sensitivity' is also somewhat ambiguous, as apparently low levels could result not just from a failure to act according to internal cues, but also from a normative response to genuinely dysregulated internal cues, e.g. relatively lesser release of satiety hormones such as PYY and GLP-1 in response to intake.

2.2 Behavioral measures (questionnaire studies)

Perhaps the best known questionnaire measure of eating-related traits is the Dutch Eating Behavior Questionnaire (DEBQ, [36]), which is available in both a child-report form, initially validated in 7–12 y olds (DEBQ-C [37]) and a parent-report form (DEBQ-P [38]). The DEBQ contains scales measuring external eating (i.e. eating in response to food stimuli without regard to internal hunger or satiety), emotional eating (i.e. excessive eating in response to states such as anger, fear or anxiety), and cognitive restraint (i.e. the tendency to consciously restrict food intake to control body weight). A first set of results using the DEBQ-C in a clinical sample of obese 9–12 y olds suggested higher emotional eating in obese 9–12 y olds [8], but studies often report lower, rather than higher, scores on both external [39] [40] and emotional [39] eating, and levels of restrained eating are typically higher among overweight children [37] [39] [40] [8] – a pattern of results which likely reflects cognitive efforts to control eating and socially-desirable responding more than

underlying appetitive dispositions. Likewise, initial results using the DEBQ-P revealed higher emotional, external and restrained eating among obese 9–12 y olds [38], but a more recent study replicated only the association with restrained eating [41].

An alternative parent-report instrument for assessing children's appetitive traits is the Child Eating Behaviour Questionnaire (CEBQ, [42]), which was designed to capture normative eating behavior rather than the disordered behaviors and attitudes addressed by the DEBQ. The CEBQ includes a number of scales assessing food approach, e.g. food responsiveness (FR; e.g. My child is always asking for food), enjoyment of food (EF; e.g. My child is interested in food), desire to drink (DD; e.g. My child is always asking for a drink) and emotional overeating (EOE; e.g. My child eats more when anxious), and others assessing food avoidance, e.g. satiety responsiveness (SR; e.g. My child gets full before his/her meal is finished), slowness in eating (e.g. My child eats slowly), emotional undereating (EUE; e.g. My child eats less when he/she is upset), and food fussiness (FF; e.g. My child is difficult to please with meals). A study using both the CEBQ and a selection of behavioral measures designed to tap the same constructs (intake without hunger, caloric compensation, eating rate) found that the combined tests explained 56% of the variance in SR, 33% variance in FR and 40% of the variance in EF [43], providing good evidence for cross-validation between behavioral and psychometric measures. In a longitudinal study, food approach scores increased and food avoidance scores decreased from 4 y to 11 y, but scores at both time-points were also positively correlated, indicating continuity over time [44]. Significant negative correlations between adiposity and scores on traits measuring food avoidance, and positive correlations between adiposity and scores on traits measuring food approach scales, have now been reported in a number of samples [45–50].

Parent-report measures may also be used to assess appetitive traits in infancy. Several studies have measured appetite with simple questions such as “How is your baby's appetite?” or “Is your baby feeding enough?” [51], and have revealed associations between derived eating avidity scores in infancy, and higher food approach and lower food avoidance scores on the CEBQ (but not weight) when assessed at 6–8 y [51] [52]). More general aspects of temperament may also predict weight: a prospective study found that parents' reports of more negative reactions towards food and greater general soothability were associated with greater weight gain from 1 to 6y, and a higher likelihood of obesity at 6y among girls, while lower parent-reported attention span was associated with greater weight gain and a greater likelihood of obesity among boys [53]. Others have used comprehensive infant appetite measures assessing different aspects of appetite. For example, the Baby Eating Behaviour Questionnaire (BEBQ [54]) was designed for completion by mothers of 0–3 mo old infants either during the milk/bottle-feeding stage (i.e. before the introduction of solid foods), or retrospectively, a few months after the introduction of solids. The items are closely based on CEBQ items, with scales measuring enjoyment of food (e.g. My baby loved milk), food responsiveness (e.g. My baby was always demanding a feed), slowness in eating (e.g. My baby fed slowly) and satiety responsiveness (e.g. My baby got full up easily). Prospective evidence suggests that all four scales, assessed retrospectively at the age of 3 mo, predicts weight at 9 mo and trajectories up to the age of 15 mo. Further, the path from appetitive trait to weight is larger than that from weight to appetite, suggesting that appetitive traits predict weight rather than vice versa [55].

2.3 Neural measures

A problem with using laboratory and questionnaire methods to measure appetitive traits is that they are vulnerable to social desirability bias, and may only give a partial picture of an individual's food response. In contrast, biological (e.g. neurological) markers of appetite have the potential to capture the various components of an individual's response more completely. For example, brain activation triggered by a food cue could represent both

reward anticipation responses, and cognitive attempts to inhibit those responses, while behavioral data might only reflect the already-inhibited response. Recent studies examining neural responses to food pictures in children could therefore be thought of as neural measures of the many different aspects of food cue responsiveness. Studies of healthy-weight samples have variously revealed greater activation in the amygdala, medial frontal/orbitofrontal cortex (OFC) and insula to food vs. non-food cues among 10–17 y olds [56]; in the OFC, hippocampus, cerebellum, putamen, anterior cingulate cortex (ACC), middle and inferior temporal gyri and fusiform gyrus to high-calorie vs. non-food cues, and ACC, cerebellum and middle temporal gyrus to high-calorie vs. low-calorie cues among 9–15 y old girls [57]; and in the OFC and inferior frontal gyrus (IFG) in response to food logos (another potent external food cue) vs. baseline, and the posterior cingulate cortex (PCC) in response to food vs. non-food logos, among 10–14 y olds [58]. The variability of the results likely reflects phenotypic variability among samples as well as differences in analysis – issues that will need to be resolved by larger studies, meta-analyses of multiple studies, and more careful consideration of subject characteristics – but together they suggest that activity in a number of brain structures within key reward and motivation circuits may be important for the phenomenon of food cue responsiveness.

Consistent with this possibility, neural food cue responses appear to differ by body weight, which is associated with behavioral measures of food cue responsiveness. For example, one study found that obese vs. lean 10–17 y olds showed greater pre-meal (post 4h fast) activation in the prefrontal cortex (PFC), greater post-meal activation in the OFC, and relatively smaller post-meal (vs. pre-meal) decreases in nucleus accumbens (NAc), limbic, and PFC activation in response to food pictures [59]. Another found that higher BMI was associated with greater OFC, frontal operculum and putamen responses to appetizing food pictures among adolescent girls following a 4–6 h fast [60], with another finding that obese vs. lean adolescent girls showed greater activation in the anterior and middle insula and somatosensory area in response to conditioned cues associated with milkshake delivery [61]. However, results are not entirely consistent across protocols. In a study with no experimental control of prior nutritional state, overweight/obese 9–16 y olds showed increased dLPFC responses but *lesser* caudate and hippocampus responses to food pictures [62]. Following a 4h fast, obese 9–16 y olds showed greater activation of midbrain and postcentral gyrus together with *lesser* activation in middle frontal gyrus and middle temporal gyrus in response to food logos compared to blurred baseline images, and *lesser* activation than lean children in a range of frontal, temporal and limbic areas, as well as the insula, in response to food vs. non-food logos [63]. There is also some evidence for lower OFC volume among obese than lean 14–21 y olds, with lower OFC volume associated with higher scores on dietary disinhibition – a measure of how likely one is to be triggered to eat after a period of restraint, after being exposed to environmental food cues – although only among the lean group [64]. Again, the diverse results may be attributable to between and within-sample variability in appetitive phenotypes and the character of the subjective response to food cues, supporting endophenotype-based sample selection, increased specificity of functional tasks (see section 4.1.1), and meta-analysis of large data-sets to extract the most robust results (e.g. [65]).

Notably, functional MRI methods might also be used to illuminate the neural correlates of satiety sensitivity, and its interactions with food cue responsiveness. For example, studies contrasting neural food cue responses in fed or fasted conditions could be thought of as a neural measure of how much desire to eat changes depending on internal satiety cues (e.g. [59]). In contrast, activation changes resulting from the intake of varying amounts of food may constitute a direct index of how the brain changes in response to accumulating internal satiety signals. One study of adolescent girls showed that obese participants showed lower caudate responsivity to delivery of a small taste of milkshake [61]; however, we are not

aware of any imaging studies that have systematically tested the relative effects of different degrees of intake in either healthy-weight or obese children. Resting state studies, which identify regions that interact when subjects are not performing a task, might also give some indication of basal levels of satiety. Although there have not yet been any resting state studies relating to eating or weight in children, there is some evidence to suggest obese adults may show altered patterns of resting activity in two networks containing areas implicated in appetite and obesity: the default mode network which includes the precuneus, PCC, medial PFC, and inferior parietal cortex, and the temporal mode network, which includes the primary and secondary auditory cortices and the insula, which forms part of the primary gustatory cortex [66]. Together these findings suggest that, as the corpus of research grows and refines – and reliability studies testing the consistency of neural responses across multiple occasions are conducted, it may be possible to identify distinct sets of neural correlates corresponding with distinct appetitive traits in children.

3. Identifying neurobehavioral predictors of obesity development: the familial risk approach

The presence of weight-related neurobehavioral differences in young cohorts is consistent with the possibility that the activation differences represent neural indicators of risk that may go on to predict weight trajectories later in life. However, since selection is based on current obesity and much of the data is cross-sectional, it is not always clear whether we are seeing meaningful risk factors or merely correlates of current weight, metabolic status and intake patterns. One way of identifying biobehavioral risk markers is to investigate those we already know to be at higher risk for becoming obese based on familial (e.g. parental) overweight or obesity. Estimates and analysis techniques vary between samples (e.g. [67] [68, 69], but a representative study using 2001 and 2006 data from a large sample of 2–15 y olds recently reported that having normal-weight parents was associated with a 2.3% rate of childhood obesity, overweight parents with a 4.9% rate (OR [Odds Ratio] 2.2), obese parents with 21.7% (OR 12.0), and severely obese parents (BMI ≥ 35) with 35.3% (OR 22.3), with a stronger association between child and parent BMI evident for 6–15 y olds than for 2–5 y olds. A similar pattern was evident when using maternal weight categories only (i.e. 3.0% rate for a normal-weight mother, 5.8% (OR 1.8) for overweight mother, 14.3% (OR 4.4) for obese mother, 18.0% (OR 5.1) for severely obese mother), and the pattern was similar, but weaker, for paternal weight [70]. Studies have also demonstrated significant prospective relationships, with analyses of cohorts from the UK, US and elsewhere demonstrating that parental overweight and obesity increase the likelihood of the offspring developing overweight and obesity later in childhood [71] [72], and also in adulthood [73] [74].

3.1 Relationships with behavioral measures of appetite

A number of studies have reported differences in behavioral measures of appetite according to familial risk for obesity. In a study of 5 y old boys born to heavier or leaner mothers based on pre-pregnancy weight percentile (greater than 66th vs. less than 33rd), intake in the absence of hunger was higher among those with the heavier mothers (mean intake 326 vs. 151 kJ), and this result was unchanged when controlling for child BMI z score [75]. In a study using an alternative indicator of familial risk, overweight/obese 5–12 y olds showed higher EAH compared to their normal-weight siblings [76]. As far as we are aware, no studies have reported relationships between parent weight and caloric compensation in children as tested in the laboratory, but one study using 3-day food records reported that from age 3 y to 6 y, the likelihood of over-consuming by failing to compensate for an increased energy-density diet increased in children with heavier mothers (maternal pre-pregnancy BMI $> 66^{\text{th}}$ percentile) increased, but decreased in children with leaner mothers

(maternal pre-pregnancy BMI < 33rd percentile). In this sample there was no significant difference in BMI z scores between risk groups and the results remained significant when child BMI z-score was added as a covariate [77].

Other studies using questionnaire measures have also revealed differences according to familial risk. In a large study of 4–5 y olds children with obese or overweight parents (based on self-report height and weight, but with maternal weight confirmed by measurement) scored higher than those with normal-weight parents on the CEBQ sub-scale Desire for Drinks, and also showed a trend towards higher scores on CEBQ Food Responsiveness and Emotional Eating. Current child weight was not controlled for in this study so the difference may have been related to current weight as well as to familial risk, but percentage body fat did not differ between groups, and very few children were overweight [78]. Familial risk differences may also be evident in infancy: a study of 1–3 day old infants found that those with overweight parents sucked relatively more in response to a higher glucose solution compared to infants with normal weight parents [79] and a study assessing infant feeding using a nutritive sucking apparatus found higher intake, total number of sucks and sucking rates in 3 mo old infants with obese mothers [35, 80]. However, not all studies have produced positive findings: one study failed to show a relationship between maternal BMI and eating rate in 4 y olds as measured at a standardized, parent-supervised multi-item meal, or child weight change from 4 to 6 y [33]. The presence of these negative findings likely reflects the challenges of obtaining a reliable behavioral measure of dispositional appetite and the fact that the relationship between parent weight and child eating behaviors is complex and under the influence of many other family-specific factors.

With the exception of [77], the above studies focused on differences between high and low risk groups in terms of appetite characteristics that are conceived as relatively independent of what is eaten, or at least measured without taking food types into account. There are perhaps a larger number of studies describing differences between high and low risk groups in preferences for specific types of food, or the macronutrient composition of intake. In the study of 4–5 y olds cited above [78], children with obese/overweight parents showed a higher preference for fatty foods in a taste test and a lower liking for vegetables, as well as having slightly higher BMIs (although not percentage body fat). Another study of preschoolers found that children with two overweight parents consumed a higher percentage of total intake from fat than those with no overweight parents, despite having a similar body weight [81], while another observed a higher absolute (but not relative to total energy intake) fat intake in obese 5–8 y olds when compared to lean controls with 2 lean parents, but no differences from lean children with at least one obese parent [82]. There may also be differences in beverage consumption: in a longitudinal study using 3-day weighed food records, children of mothers who were obese pre-pregnancy consumed a greater percentage of daily calories from beverages at 3 y, more fruit juice at 3 and 4 y, more soft drinks at 3–5 y, and more soda at 6 y than children of mothers with a normal pre-pregnancy weight, independent of child BMI z score [83]. Together the results suggest that parent obesity may indeed be associated 'obesogenic' eating behavior among children. However, since there is not a one-to-one relationship between parent and child obesity, prospective studies will be essential to determine whether the observed behaviors translate into weight gain later in life.

3.2 Relationships with neural measures of appetite

As far as we are aware, only one group has reported differences in functional brain activation relating to familial risk for obesity [84]. This study found that adolescents with 2 obese or overweight (vs. 2 lean) parents showed greater caudate, frontal operculum and parietal operculum responses to milkshake tastes, consistent with greater engagement of circuitry relating to taste reward during consumption. However, contrary to the authors' predictions, there were no group differences in response to a cue indicating imminent

administration of a milkshake taste (i.e. anticipated food reward). A number of interpretations for the enhanced neural responses are possible. First, they could indicate a hyper-responsivity to food tastes, which could lead to later obesity. However, since the authors have tended to observe *blunted* taste responses in the same areas among currently obese individuals – a phenomenon that they have attributed to excessive experience with consuming high-calorie foods – it is also possible that the enhanced responses could indicate a relative *resilience* to obesity which might explain their current leanness despite increased familial risk for obesity.

In addition, a number of studies have operationalized obesity risk using alternative methods. One group, for example, found that 2 days of overfeeding produced an attenuation of insula, hypothalamus and visual cortex responses to food pictures in thin adults, but not in those who had recently been obese and were therefore at risk of a further episode of excessive weight gain in the future [85]. A subsequent study demonstrated lower gray matter volume in the insula, medial OFC and cerebellum in individuals who were obese prone vs. obese resistant (based on self-identification, current BMI and personal/family weight history), independent of body fat mass [86]. In contrast, a study of formerly-obese individuals who had maintained significant weight loss for a minimum of 3 years – possibly indicating a relatively low risk of weight regain – found that this group showed greater responses to food pictures in the superior frontal and middle temporal cortices than obese and normal-weight controls [87].

Another approach is to investigate individuals at high genetic risk for obesity. In a study of adolescents with congenital leptin deficiency, there were increased ventral striatal responses to food vs. non-food images in both fed and fasted states – a response which was reduced following 7-day leptin treatment [88]. In addition, individuals with Prader-Willi syndrome, a genetic disorder characterized by heightened appetite and high ghrelin levels, showed increased OFC, insula, hippocampus, parahippocampal gyrus and medial PFC responses to food vs. non-food pictures when compared with healthy controls [89]. Few studies have examined associations between imaging outcomes and commonly occurring obesity- and appetite- associated genetic variants (e.g. FTO). One structural MRI study reported reduced volume in the frontal and occipital lobes among those carrying at least one FTO risk allele, but BMI was not controlled, making it difficult to tell whether the effect is mostly driven by current weight [90].

Others have examined associations with genes related to reward and drug addiction. For example, the Taq1A A1 allele – a genetic marker of altered dopamine function – may exaggerate the association between blunted neural responses to tastes of a milkshake and obesity [91] and interact with neural responsivity to food cues to predict weight increases [60] in adolescence, and predict relatively lesser (or absent) OFC, midbrain and thalamus responses to milkshake tastes in adults [92]. A recent study using a multilocus composite score made up of several genotypes putatively associated with low dopamine signaling capacity (i.e. Taq1A A1 allele, DRD2-141C Ins/Ins genotype, DRD4 7-repeat or longer allele, DAT1 10-repeat allele, and the Met/Met COMT genotype) found that higher risk scores were associated with greater activation in the pallidum, IFG, precuneus, and inferior parietal lobule in response to a milkshake taste, but unassociated with responses to anticipatory food cues in adolescents. Those with a greater number of these genotypes also showed greater activation in the precuneus, and less activation in the putamen, caudate, and insula in response to monetary reward [93]. Large, long-term prospective studies that are capable of systematically comparing and contrasting paradigms and risk levels, and monitoring dynamic changes over time, will be necessary to fully understand familial risk for obesity and its neural basis.

4. Next steps – integrating behavioral and neural approaches

4.1 Neuroimaging studies of appetitive endophenotypes

The above discussion focuses primarily on imaging studies that examine the relationship between body weight and neural activation assessed while viewing food pictures, as well as a number of studies from the same research group testing neural responses to the delivery of very small tastes of milkshake and cues signalling the delivery of those tastes. However, there is scope to significantly advance our understanding of the food cue response by refining and expanding cue-based paradigms based on our knowledge of different aspects of the obese behavioral phenotype. For example, obese individuals may experience heightened subjective appetitive responses not only when exposed to visual food cues, but also when exposed to other types of cues (e.g. odors [94] and other tastes [95] [96]). In addition, overconsumption requires habitual repetition of a series of food-directed actions, which could include allocating heightened attention to highly palatable, high-calorie food cues in the environment, tending to prioritize the more immediate benefit of taste over the longer-term benefit of health when making food decisions, and failure of attempts at deliberate self-regulation. An obvious first step is to test which of the observed neural responses in established food cue paradigms are associated with appetitive responses measured via other methods, e.g. by testing correlations with subsequent food intake, or with subjective appetite ratings (e.g. [97] [98]). This approach also has the potential to shed light upon commonalities and differences in the neurobiology underlying dimensions of appetite that are generally treated as conceptually distinct (e.g. satiety sensitivity vs. food responsiveness, wanting vs. liking, hedonic vs. homeostatic eating).

Additionally, by either inducing or manipulating different aspects of appetite – and measuring the associated pattern of neural activity – we can effectively decompose cognitive and affective elements of the neural food cue response and examine how these relate to body weight and obesity risk. A number of studies from the literature on goal-directed decision-making, for example, have examined neural correlates of the process of *food choice*, i.e. making a choice whether or not to eat a certain food, or between two different foods, and have produced a nuanced picture of the roles of structures within the PFC, OFC and striatum. In one such study [99], subjects were serially presented with food pictures and asked to decide whether or not they wanted to eat each item at the end of the experiment – a decision with consequence since they would genuinely have to eat one of the selected foods. Decision-making triggered activation in both the vmPFC and dlPFC, with a longer decision time corresponding to a longer duration of activation, and dlPFC activations correlated with but lagging behind vmPFC activations. Interestingly, vmPFC and dlPFC activation was unrelated to how closely the decisions made corresponded to liking ratings made earlier, or to whether participants made their decisions based on health or taste, suggesting that activity within and interaction between the vmPFC and dlPFC may be important for decision-making, whatever decision is made. Indeed, the vmPFC signal may be involved in integrating subjectively different aspects of value. In a study by the same group, when subjects were asked to choose between particular foods and neutral items, those who made decisions based on both health and taste, and those who made decisions based on taste alone, all showed value-correlated activation in the vmPFC [100]. Regions involved in computing goal values may be activated regardless of whether the evaluated objects have positive or negative taste value: when subjects had to bid on their right to eat or avoid certain liked or disliked foods activation in the medial OFC and the dlPFC was observed when making both appetitive and aversive evaluations [101]. Signals are also modulated by attention: when subjects were instructed to fixate on only one of a pair of food pictures before choosing between them, value-related activation in both the vmPFC and the ventral striatum was relative to the level of visual attention, supporting a role for both structures in conscious, value-based decision-making [102].

Other studies have used *cognitive manipulations* to temporarily change the evaluative lens through which the food stimuli are viewed. For example, when viewing high-calorie foods while imagining taste and evaluating palatability – but not when viewing them passively – overweight/obese (vs. healthy-weight) subjects showed greater activation in a large number of brain regions including key reward areas, limbic structures, and frontal regions [103]. Another study observed greater lateral OFC activation and OFC connectivity with primary taste areas while evaluating the presence, pleasantness and identity of a selection of tastes, but greater connectivity between the primary taste cortex (anterior dorsal insula/frontal operculum) and amygdala during passive viewing; this result is consistent with a role for the OFC in conscious food-related decision-making, as suggested by the studies above [104]. Another used a cognitive manipulation directly within a decision-making paradigm: when healthy non-dieters made decisions on whether they wanted to eat certain foods during a health-focused (vs. taste-focused or natural) condition, in which the healthiness of each food was considered, healthier food decisions were made, and associated health value-related signals were observed in the vmPFC, with the effect being modulated by activity in the dlPFC [105].

Since obese individuals often attempt, but fail, to restrict their intake, another approach is to operationalize a form of *dietary self-restraint* and observe associated neural activations. For example, in a study using a food-specific 'go-no go' task which required button responses to vegetables (go trials), but inhibition of button responses to desserts (no go trials), higher BMI was associated with reduced activation during 'no go' trials in a variety of inhibition-associated regions including the superior frontal gyrus, middle frontal gyrus, ventrolateral PFC, medial PFC and OFC, as well as increased activation in reward areas such as the temporal operculum/insula, in response to food images [106], giving clues about a possible neural circuit for food restriction. At present, few of the other paradigms described above have been conducted within studies designed to contrast obese and lean individuals, or those at high or low risk for obesity. However it is plausible that activation patterns, behavior, or the relationship between activation patterns and behavior in these paradigms could differ in relation to appetite and weight. One study, for example, recently reported lesser responses to food pictures in gustatory cortex, somatosensory cortex, and IFG among obese vs. lean women when the pictures were accompanied by a low-fat vs. regular label, suggesting potential differences in reward anticipation and neural response patterns according to weight [107].

4.2 Neuroimaging studies of appetite-related behaviors

One of the most striking observations to emerge from neuroimaging literature on of appetite and obesity is that the neural systems implicated overlap heavily with those known to be involved in drug-related behaviors, such as smoking [108], and more general cognitive, affective and behavioral phenomena such as reward and self-regulation. This is somewhat consistent with the small body of evidence for comorbidity between overweight status and substance use [109], but perhaps more consistent with the persuasive evidence for *lower* lifetime rates of substance use among the obese [110], which suggests that either food *or* drugs are selected as the preferred stimulus for the same circuitry. Indeed, recent reports of increased frequency of alcohol consumption [111] and substance use (drug use, alcohol use, and smoking combined) [112] 24 mo after bariatric surgery (either Roux-en-Y Gastric Bypass (RYGB) or gastric banding), as well as of increased frequency of alcohol use [112] and symptoms of alcohol use disorder 24 mo after RYGB [111], could be explained not only by RYGB-induced changes in alcohol pharmacokinetics but also by the occurrence of substance substitution – although the lack of correlation between alcohol or substance use and post-surgical weight loss argues against this interpretation to some degree. A shared neurobiological model for eating and non-eating-related behaviors has exciting implications

for prevention and treatment, because it suggests that early interventions targeted at general behaviors could potentially reduce risk for both obesity and other disorders by 'retraining' the underlying neural circuits. Likewise, interventions targeted at eating behaviors could have spillover effects on more general behaviors. Is there any evidence to support such a model?

Certainly there is some evidence that obesogenic eating behavior in childhood may be related to differential behavior in other, non eating-related domains. In one study a clinical sample of obese children kept gambling longer than lean children in a computer task in which they could open doors to either obtain or lose monetary rewards, with the chance of winning gradually decreasing throughout the task, suggesting increased sensitivity to reward in general. The obese children also showed poorer inhibitory control on a stop signal task, in which a learned button press response to a stimulus must occasionally be inhibited at the sound of a tone, with the gap between the stimulus and the tone increasing to enhance difficulty if the subject inhibits successfully [113]. In another, overweight children demonstrated less effective response inhibition (stop signal task) than normal-weight children. In this study, there were no weight-related differences in reward sensitivity (door opening task), but greater reward sensitivity was correlated with greater ad libitum food intake across the whole sample [114]. In the adapted stop signal study described earlier, percentage overweight predicted a lower ability to inhibit responses in general (i.e. across both food-specific and control stimuli) [9]. Others have suggested the ability to delay gratification in obese children may be a generalized phenomenon, with one recent paper reporting that obese 8–12 y olds in treatment were less likely than lean and overweight children to save points for a large toy prize at the end of the 12-week program, preferring instead to use them to buy small toy prizes each week [115]. Additionally, others have shown that obese adolescents have reduced levels of inhibition when required to count the number of digits contained in a box of cards (rather than merely naming the digit within, without counting), reduced flexibility when required to switch between counting and naming in the aforementioned experiment or change trail-making strategies in another, and more disadvantageous decisions in a card gambling task, when compared to lean adolescents [116].

There is also some evidence for weight-related differences in patterns of neural activation associated with non food-related tasks. One recent study used a standard, non food-related stop signal task, which measured cognitive control by assessing the degree to which a subject is able to repress prepotent motor responses when given a 'stop' signal in the midst of a preponderance of 'go' signals. Obese vs. lean women demonstrated no differences in accuracy and response time for 'stop' trials, but showed diminished activations in the insula, inferior parietal cortex, cuneus and supplementary motor area, which the authors suggest could indicate diminished processing of saliency [117]. Similarly, a study of obese women found no cross-sectional relationship between BMI and delay discounting, but greater activation of the inferior, middle, and superior frontal gyri on difficult vs. easy trials (i.e. those where the participant's preferences between immediate and delayed choices were closer together) accurately predicted greater weight gain over the next 1–3 years [118]. The executive functioning deficits that have been associated with higher BMIs may also have neural correlates. In a study of older women, higher BMI was associated with gray matter reductions and white matter increases in a range of brain areas, and lower gray matter volume in the left OFC was associated with poorer executive functioning [119]. There may be weight-related differences in the neural circuitry underlying other characteristics which could relate to eating behavior, such as stress-reactivity: overweight/obese vs. normal-weight individuals showed greater self-reported anxiety and VS activation during imagination of a personalized stressor, and similar results even when imagining a relaxing, neutral situation [120]. Task-related neural correlates could also differ according to familial

risk for obesity – in [84] the adolescents with heavier parents also showed greater caudate, putamen, insula, thalamus, and OFC responses to monetary reward (although no differences in relation to anticipated monetary reward), which is consistent with a generalized striatal hyper-responsivity in this group.

5. Conclusions

There is now a good deal of behavioral evidence to suggest that individuals differ in specific appetitive traits, i.e. enduring dispositions towards food, and that these trait differences are associated with differences in body weight. There is also evidence to suggest that these traits are likely to be associated with certain patterns of neural responses, which can be detected via neuroimaging and may function as biological indicators of trait appetite. Studies using familial risk and other (e.g. prospective) designs suggest that these behavioral and neural indicators of appetite may be useful markers of future obesity risk, and findings from eating behavior studies and non-food-related studies suggest that there may be shared neurobehavioral factors underlying the risk for both obesity and other disorders.

There is considerable scope to improve our scientific understanding of neurobehavioral appetitive traits. For example, refining our behavioral paradigms both inside and outside the scanner may help to isolate individual aspects of appetite that could be differentially affected in obesity sub-types. Given a satisfactory set of measures, there is also scope to integrate neural and behavioral measures to shed light on the etiology of obesity risk, for example to investigate the neural mechanisms underlying the process by which how specific genetic factors (e.g. FTO) and environmental factors (e.g. parent feeding behaviors) interact to influence appetitive behavior and weight ([121]).

Adopting an expansive neurobehavioral susceptibility model could also have important practical implications. The costs of imaging are currently prohibitive and the additional predictive value of imaging data over more easily-measured characteristics for other disorders is debatable [122] – but it may soon be plausible to use neuroimaging as well as behavioral assays as clinical tools to understand more about an individual's particular sub-type of obesity, then use the information gained to guide treatment choices and help predict prognosis and treatment response. The benefits (and potential disadvantages) of giving individuals personalized feedback about their biobehavioral appetitive traits, and issuing trait-tailored behavioral advice, should be explored. It could also be feasible to use behavioral techniques and environmental interventions to change appetitive traits or ameliorate their effects on body weight.

In the future there may also be potential to develop neuroimaging-assisted interventions to help 'reprogram' appetitive traits. For example, one study of predominantly lean and overweight (BMI 20.2–31.2) women recently reported changes in activation within brain areas involved in reward and self-regulation while subjects deliberately down-regulated their desire to eat triggered by food cues by thinking about negative long-term consequences of consuming those foods [123]. It is currently unclear whether such an activity would be helpful for long-term appetite regulation and weight control (particularly among obese individuals with high food cue responsiveness), and whether repetition of the activity could engender a repatterning of habitual neural and behavioral responses over time. However, the fact that it produces measurable, regionally-specific differences in brain activation – in combination with what we know about cognitive training and activity-dependent neuroplasticity – suggests that repeated training could ultimately lead to systematic alterations in the automatic neural response. In addition, we now know not only that eating and non-eating related behaviors seem to share common neurobiological underpinnings, but that interventions designed to improve self-regulation in one dimension can improve self-

regulation in other domains [124]. It is therefore possible that simple self-control tasks could also have the benefit of decreasing the risk of overeating, and might therefore be usefully incorporated as part of a more comprehensive obesity intervention.

Acknowledgments

This article is based on a presentation by Susan Carnell during the 2012 Annual Meeting of the Society for the Study of Ingestive Behavior, Zurich, Switzerland, July 10–14, 2012, made possible in part by generous donations from Research Diets, Inc., Sanofi, Inc., and TSE, Inc. This work was partly supported by K99DK088360 [PI: SC], and a research grant from the St. Luke's-Roosevelt Hospital Associate Trustees [PI: SC].

References

- [1]. Birch LL, Fisher JO, Davison KK. Learning to overeat: maternal use of restrictive feeding practices promotes girls' eating in the absence of hunger. *Am J Clin Nutr.* Aug; 2003 78(2):215–20. [PubMed: 12885700]
- [2]. Fisher JO, Cai G, Jaramillo SJ, Cole SA, Comuzzie AG, Butte NF. Heritability of hyperphagic eating behavior and appetite-related hormones among Hispanic children. *Obesity (Silver Spring).* Jun; 2007 15(6):1484–95. [PubMed: 17557986]
- [3]. Birch LL, Fisher JO. Mothers' child-feeding practices influence daughters' eating and weight. *Am J Clin Nutr.* May; 2000 71(5):1054–61. [PubMed: 10799366]
- [4]. Hill C, Llewellyn CH, Saxton J, Webber L, Semmler C, Carnell S, et al. Adiposity and 'eating in the absence of hunger' in children. *Int J Obes (Lond).* Oct; 2008 32(10):1499–505. [PubMed: 18645573]
- [5]. Shomaker LB, Tanofsky-Kraff M, Zocca JM, Courville A, Kozlosky M, Columbo KM, et al. Eating in the absence of hunger in adolescents: intake after a large-array meal compared with that after a standardized meal. *Am J Clin Nutr.* Oct; 2010 92(4):697–703. [PubMed: 20720255]
- [6]. Jansen A, Theunissen N, Slechten K, Nederkoorn C, Boon B, Mulkens S, et al. Overweight children overeat after exposure to food cues. *Eat Behav.* Aug; 2003 4(2):197–209. [PubMed: 15000982]
- [7]. Forman J, Halford JC, Summe H, MacDougall M, Keller KL. Food branding influences ad libitum intake differently in children depending on weight status. Results of a pilot study. *Appetite.* Aug; 2009 53(1):76–83. [PubMed: 19481125]
- [8]. Braet C, Crombez G. Cognitive interference due to food cues in childhood obesity. *J Clin Child Adolesc Psychol.* Mar; 2003 32(1):32–9. [PubMed: 12573930]
- [9]. Nederkoorn C, Coelho JS, Guerrieri R, Houben K, Jansen A. Specificity of the failure to inhibit responses in overweight children. *Appetite.* Oct; 2012 59(2):409–13. [PubMed: 22664299]
- [10]. Soetens B, Braet C. Information processing of food cues in overweight and normal weight adolescents. *Br J Health Psychol.* May; 2007 12(Pt 2):285–304. [PubMed: 17456287]
- [11]. Craeynest M, Crombez G, De Houwer J, Deforche B, De Bourdeaudhuij I. Do children with obesity implicitly identify with sedentariness and fat food? *J Behav Ther Exp Psychiatry.* Dec; 2006 37(4):347–57. [PubMed: 16701077]
- [12]. Soussignan R, Schaal B, Boulanger V, Gaillet M, Jiang T. Orofacial reactivity to the sight and smell of food stimuli. Evidence for anticipatory liking related to food reward cues in overweight children. *Appetite.* Apr; 2012 58(2):508–16. [PubMed: 22245131]
- [13]. Epstein LH, Leddy JJ, Temple JL, Faith MS. Food reinforcement and eating: a multilevel analysis. *Psychol Bull.* Sep; 2007 133(5):884–906. [PubMed: 17723034]
- [14]. Temple JL, Legierski CM, Giacomelli AM, Salvy SJ, Epstein LH. Overweight children find food more reinforcing and consume more energy than do nonoverweight children. *Am J Clin Nutr.* May; 2008 87(5):1121–7. [PubMed: 18469229]
- [15]. Temple JL, Giacomelli AM, Roemmich JN, Epstein LH. Overweight children habituate slower than non-overweight children to food. *Physiol Behav.* Jun 8; 2007 91(2–3):250–4. [PubMed: 17459429]

- [16]. Hill C, Saxton J, Webber L, Blundell J, Wardle J. The relative reinforcing value of food predicts weight gain in a longitudinal study of 7--10-y-old children. *Am J Clin Nutr.* Aug; 2009 90(2): 276–81. [PubMed: 19535428]
- [17]. Mischel W, Ebbesen EB, Zeiss AR. Cognitive and attentional mechanisms in delay of gratification. *J Pers Soc Psychol.* Feb; 1972 21(2):204–18. [PubMed: 5010404]
- [18]. Johnson WG, Parry W, Drabman RS. The performance of obese and normal size children on a delay of gratification task. *Addict Behav.* 1978; 3(3–4):205–8. [PubMed: 735906]
- [19]. Seeyave DM, Coleman S, Appugliese D, Corwyn RF, Bradley RH, Davidson NS, et al. Ability to delay gratification at age 4 years and risk of overweight at age 11 years. *Arch Pediatr Adolesc Med.* Apr; 2009 163(4):303–8. [PubMed: 19349558]
- [20]. Schlam TR, Wilson NL, Shoda Y, Mischel W, Ayduk O. Preschoolers' Delay of Gratification Predicts their Body Mass 30 Years Later. *J Pediatr.* Jan; 2013 162(1):90–3. [PubMed: 22906511]
- [21]. Schachter S, Goldman R, Gordon A. Effects of fear, food deprivation, and obesity on eating. *J Pers Soc Psychol.* Oct; 1968 10(2):91–7. [PubMed: 5725907]
- [22]. Johnson SL, Birch LL. Parents' and children's adiposity and eating style. *Pediatrics.* Nov; 1994 94(5):653–61. [PubMed: 7936891]
- [23]. Carnell, S.; Gibson, EL.; Wardle, J., editors. Benjamin Franklin Lafayette Symposium. 2009. Caloric compensation in 3–5 y olds (invited talk).
- [24]. Ebbeling CB, Sinclair KB, Pereira MA, Garcia-Lago E, Feldman HA, Ludwig DS. Compensation for energy intake from fast food among overweight and lean adolescents. *JAMA.* Jun 16; 2004 291(23):2828–33. [PubMed: 15199032]
- [25]. Bellissimo N, Desantadina MV, Pencharz PB, Berall GB, Thomas SG, Anderson GH. A comparison of short-term appetite and energy intakes in normal weight and obese boys following glucose and whey-protein drinks. *Int J Obes (Lond).* Feb; 2008 32(2):362–71. [PubMed: 17700578]
- [26]. Faith MS, Keller KL, Johnson SL, Pietrobelli A, Matz PE, Must S, et al. Familial aggregation of energy intake in children. *Am J Clin Nutr.* May; 2004 79(5):844–50. [PubMed: 15113724]
- [27]. Cecil JE, Palmer CN, Wrieden W, Murrie I, Bolton-Smith C, Watt P, et al. Energy intakes of children after preloads: adjustment, not compensation. *Am J Clin Nutr.* Aug; 2005 82(2):302–8. [PubMed: 16087972]
- [28]. Johnson SL, Taylor-Holloway LA. Non-Hispanic white and Hispanic elementary school children's self-regulation of energy intake. *Am J Clin Nutr.* Jun; 2006 83(6):1276–82. [PubMed: 16762937]
- [29]. Drabman RS, Cordua GD, Hammer D, Jarvie GJ, Horton W. Developmental trends in eating rates of normal and overweight preschool children. *Child Dev.* Mar; 1979 50(1):211–6. [PubMed: 446206]
- [30]. Barkeling B, Ekman S, Rossner S. Eating behaviour in obese and normal weight 11-year-old children. *Int J Obes Relat Metab Disord.* May; 1992 16(5):355–60. [PubMed: 1319970]
- [31]. Lindgren AC, Barkeling B, Hagg A, Ritzen EM, Marcus C, Rossner S. Eating behavior in Prader-Willi syndrome, normal weight, and obese control groups. *J Pediatr.* Jul; 2000 137(1):50–5. [PubMed: 10891821]
- [32]. Llewellyn CH, van Jaarsveld CH, Boniface D, Carnell S, Wardle J. Eating rate is a heritable phenotype related to weight in children. *Am J Clin Nutr.* Dec; 2008 88(6):1560–6. [PubMed: 19064516]
- [33]. Berkowitz RI, Moore RH, Faith MS, Stallings VA, Kral TV, Stunkard AJ. Identification of an obese eating style in 4-year-old children born at high and low risk for obesity. *Obesity (Silver Spring).* Mar; 2010 18(3):505–12. [PubMed: 19779474]
- [34]. Agras WS, Kraemer HC, Berkowitz RI, Hammer LD. Influence of early feeding style on adiposity at 6 years of age. *J Pediatr.* May; 1990 116(5):805–9. [PubMed: 2329430]
- [35]. Stunkard AJ, Berkowitz RI, Schoeller D, Maislin G, Stallings VA. Predictors of body size in the first 2 y of life: a high-risk study of human obesity. *Int J Obes Relat Metab Disord.* Apr; 2004 28(4):503–13. [PubMed: 14758342]

- [36]. van Strien T, Frijters JER, Bergers GPA, Defares PB. The Dutch Eating Behavior Questionnaire (DEBQ) for assessment of restrained, emotional, emotional, and external eating behavior. *Int J Eat Disord.* 1986; 5(2):295–315.
- [37]. van Strien T, Oosterveld P. The children's DEBQ for assessment of restrained, emotional, and external eating in 7- to 12-year-old children. *Int J Eat Disord.* Jan; 2008 41(1):72–81. [PubMed: 17634965]
- [38]. Braet C, Van Strien T. Assessment of emotional, externally induced and restrained eating behaviour in nine to twelve-year-old obese and non-obese children. *Behav Res Ther.* Sep; 1997 35(9):863–73. [PubMed: 9299807]
- [39]. Ledoux T, Watson K, Baranowski J, Tepper BJ, Baranowski T. Overeating styles and adiposity among multiethnic youth. *Appetite.* Feb; 2011 56(1):71–7. [PubMed: 21115080]
- [40]. Banos RM, Cebolla A, Etchemendy E, Felipe S, Rasal P, Botella C. Validation of the Dutch Eating Behavior Questionnaire for Children (DEBQ-C) for use with Spanish children. *Nutr Hosp.* Jul-Aug; 2011 26(4):890–8. [PubMed: 22470039]
- [41]. Caccialanza R, Nicholls D, Cena H, Maccarini L, Rezzani C, Antonioli L, et al. Validation of the Dutch Eating Behaviour Questionnaire parent version (DEBQ-P) in the Italian population: a screening tool to detect differences in eating behaviour among obese, overweight and normal-weight preadolescents. *Eur J Clin Nutr.* Sep; 2004 58(9):1217–22. [PubMed: 15054434]
- [42]. Wardle J, Guthrie CA, Sanderson S, Rapoport L. Development of the Children's Eating Behaviour Questionnaire. *J Child Psychol Psychiatry.* Oct; 2001 42(7):963–70. [PubMed: 11693591]
- [43]. Carnell S, Wardle J. Measuring behavioural susceptibility to obesity: validation of the child eating behaviour questionnaire. *Appetite.* Jan; 2007 48(1):104–13. [PubMed: 16962207]
- [44]. Ashcroft J, Semmler C, Carnell S, van Jaarsveld CH, Wardle J. Continuity and stability of eating behaviour traits in children. *Eur J Clin Nutr.* Aug; 2008 62(8):985–90. [PubMed: 17684526]
- [45]. Carnell S, Wardle J. Appetite and adiposity in children: evidence for a behavioral susceptibility theory of obesity. *Am J Clin Nutr.* Jul; 2008 88(1):22–9. [PubMed: 18614720]
- [46]. Viana V, Sinde S, Saxton JC. Children's Eating Behaviour Questionnaire: associations with BMI in Portuguese children. *Br J Nutr.* Aug; 2008 100(2):445–50. [PubMed: 18275626]
- [47]. Webber L, Hill C, Saxton J, Van Jaarsveld CH, Wardle J. Eating behaviour and weight in children. *Int J Obes (Lond).* Jan; 2009 33(1):21–8. [PubMed: 19002146]
- [48]. Spence JC, Carson V, Casey L, Boule N. Examining behavioural susceptibility to obesity among Canadian pre-school children: the role of eating behaviours. *Int J Pediatr Obes.* Jun; 2011 6(2-2):e501–7. [PubMed: 20831463]
- [49]. Jansen PW, Roza SJ, Jaddoe VW, Mackenbach JD, Raat H, Hofman A, et al. Children's eating behavior, feeding practices of parents and weight problems in early childhood: results from the population-based Generation R Study. *Int J Behav Nutr Phys Act.* Oct 30; 2012 9(1):130. [PubMed: 23110748]
- [50]. Santos JL, Ho-Urriola JA, Gonzalez A, Smalley SV, Dominguez-Vasquez P, Cataldo R, et al. Association between eating behavior scores and obesity in Chilean children. *Nutr J.* 2011; 10:108. [PubMed: 21985269]
- [51]. Wright CM, Cox KM, Le Couteur A. How does infant behaviour relate to weight gain and adiposity? *Proc Nutr Soc.* Nov; 2011 70(4):485–93. [PubMed: 21861948]
- [52]. Parkinson KN, Drewett RF, Le Couteur AS, Adamson AJ. Do maternal ratings of appetite in infants predict later Child Eating Behaviour Questionnaire scores and body mass index? *Appetite.* Feb; 2010 54(1):186–90. [PubMed: 19887093]
- [53]. Faith MS, Hittner JB. Infant temperament and eating style predict change in standardized weight status and obesity risk at 6 years of age. *Int J Obes (Lond).* Oct; 2010 34(10):1515–23. [PubMed: 20805827]
- [54]. Llewellyn CH, van Jaarsveld CH, Johnson L, Carnell S, Wardle J. Development and factor structure of the Baby Eating Behaviour Questionnaire in the Gemini birth cohort. *Appetite.* Oct; 2011 57(2):388–96. [PubMed: 21672566]

- [55]. van Jaarsveld CH, Llewellyn CH, Johnson L, Wardle J. Prospective associations between appetitive traits and weight gain in infancy. *Am J Clin Nutr.* Dec; 2011 94(6):1562–7. [PubMed: 22071702]
- [56]. Holsen LM, Zarcone JR, Thompson TI, Brooks WM, Anderson MF, Ahluwalia JS, et al. Neural mechanisms underlying food motivation in children and adolescents. *Neuroimage.* Sep; 2005 27(3):669–76. [PubMed: 15993629]
- [57]. Killgore WD, Yurgelun-Todd DA. Developmental changes in the functional brain responses of adolescents to images of high and low-calorie foods. *Dev Psychobiol.* Dec; 2005 47(4):377–97. [PubMed: 16284969]
- [58]. Bruce AS, Bruce JM, Black WR, Lepping RJ, Henry JM, Cherry JB, et al. Branding and a child's brain: an fMRI study of neural responses to logos. *Soc Cogn Affect Neurosci.* Sep 20.2012
- [59]. Bruce AS, Holsen LM, Chambers RJ, Martin LE, Brooks WM, Zarcone JR, et al. Obese children show hyperactivation to food pictures in brain networks linked to motivation, reward and cognitive control. *Int J Obes (Lond).* Oct; 2010 34(10):1494–500. [PubMed: 20440296]
- [60]. Stice E, Yokum S, Bohon C, Marti N, Smolen A. Reward circuitry responsivity to food predicts future increases in body mass: moderating effects of DRD2 and DRD4. *Neuroimage.* May 1; 2010 50(4):1618–25. [PubMed: 20116437]
- [61]. Stice E, Spoor S, Bohon C, Veldhuizen MG, Small DM. Relation of reward from food intake and anticipated food intake to obesity: a functional magnetic resonance imaging study. *J Abnorm Psychol.* Nov; 2008 117(4):924–35. [PubMed: 19025237]
- [62]. Davids S, Lauffer H, Thoms K, Jagdhuhn M, Hirschfeld H, Domin M, et al. Increased dorsolateral prefrontal cortex activation in obese children during observation of food stimuli. *Int J Obes (Lond).* Jan; 2010 34(1):94–104. [PubMed: 19806158]
- [63]. Bruce AS, Black WR, Lepping RJ, Bruce JM, Henry JM, Cherry JBC, et al. Brain responses to food logos in obese and healthy weight children. *Journal of Pediatrics.* in press.
- [64]. Maayan L, Hoogendoorn C, Sweat V, Convit A. Disinhibited eating in obese adolescents is associated with orbitofrontal volume reductions and executive dysfunction. *Obesity (Silver Spring).* Jul; 2011 19(7):1382–7. [PubMed: 21350433]
- [65]. van der Laan LN, de Ridder DT, Viergever MA, Smeets PA. The first taste is always with the eyes: a meta-analysis on the neural correlates of processing visual food cues. *Neuroimage.* Mar 1; 2011 55(1):296–303. [PubMed: 21111829]
- [66]. Kullmann S, Heni M, Veit R, Ketterer C, Schick F, Haring HU, et al. The obese brain: Association of body mass index and insulin sensitivity with resting state network functional connectivity. *Hum Brain Mapp.* Apr 21.2011
- [67]. Berkowitz RI, Stallings VA, Maislin G, Stunkard AJ. Growth of children at high risk of obesity during the first 6 y of life: implications for prevention. *Am J Clin Nutr.* Jan; 2005 81(1):140–6. [PubMed: 15640473]
- [68]. Danielzik S, Langnase K, Mast M, Spethmann C, Muller MJ. Impact of parental BMI on the manifestation of overweight 5–7 year old children. *Eur J Nutr.* Jun; 2002 41(3):132–8. [PubMed: 12111051]
- [69]. Sekine M, Yamagami T, Hamanishi S, Handa K, Saito T, Nanri S, et al. Parental obesity, lifestyle factors and obesity in preschool children: results of the Toyama Birth Cohort study. *J Epidemiol.* Jan; 2002 12(1):33–9. [PubMed: 11848182]
- [70]. Whitaker KL, Jarvis MJ, Beeken RJ, Boniface D, Wardle J. Comparing maternal and paternal intergenerational transmission of obesity risk in a large population-based sample. *Am J Clin Nutr.* Jun; 2010 91(6):1560–7. [PubMed: 20375189]
- [71]. Semmler C, Ashcroft J, van Jaarsveld CH, Carnell S, Wardle J. Development of overweight in children in relation to parental weight and socioeconomic status. *Obesity (Silver Spring).* Apr; 2009 17(4):814–20. [PubMed: 19165162]
- [72]. Burke V, Beilin LJ, Dunbar D. Family lifestyle and parental body mass index as predictors of body mass index in Australian children: a longitudinal study. *Int J Obes Relat Metab Disord.* Feb; 2001 25(2):147–57. [PubMed: 11410813]

- [73]. Whitaker RC, Wright JA, Pepe MS, Seidel KD, Dietz WH. Predicting obesity in young adulthood from childhood and parental obesity. *N Engl J Med.* Sep 25; 1997 337(13):869–73. [PubMed: 9302300]
- [74]. Lake JK, Power C, Cole TJ. Child to adult body mass index in the 1958 British birth cohort: associations with parental obesity. *Arch Dis Child.* Nov; 1997 77(5):376–81. [PubMed: 9487953]
- [75]. Faith MS, Berkowitz RI, Stallings VA, Kerns J, Storey M, Stunkard AJ. Eating in the absence of hunger: a genetic marker for childhood obesity in prepubertal boys? *Obesity (Silver Spring).* Jan; 2006 14(1):131–8. [PubMed: 16493131]
- [76]. Kral TV, Allison DB, Birch LL, Stallings VA, Moore RH, Faith MS. Caloric compensation and eating in the absence of hunger in 5- to 12-y-old weight-discordant siblings. *Am J Clin Nutr.* Sep; 2012 96(3):574–83. [PubMed: 22854400]
- [77]. Kral TV, Stunkard AJ, Berkowitz RI, Stallings VA, Brown DD, Faith MS. Daily food intake in relation to dietary energy density in the free-living environment: a prospective analysis of children born at different risk of obesity. *Am J Clin Nutr.* Jul; 2007 86(1):41–7. [PubMed: 17616761]
- [78]. Wardle J, Guthrie C, Sanderson S, Birch L, Plomin R. Food and activity preferences in children of lean and obese parents. *Int J Obes Relat Metab Disord.* Jul; 2001 25(7):971–7. [PubMed: 11443494]
- [79]. Milstein RM. Responsiveness in Newborn-Infants of Overweight and Normal Weight Parents. *Appetite.* 1980; 1(1):65–74.
- [80]. Stunkard AJ, Berkowitz RI, Stallings VA, Schoeller DA. Energy intake, not energy output, is a determinant of body size in infants. *Am J Clin Nutr.* Mar; 1999 69(3):524–30. [PubMed: 10075340]
- [81]. Eck LH, Klesges RC, Hanson CL, Slawson D. Children at familial risk for obesity: an examination of dietary intake, physical activity and weight status. *Int J Obes Relat Metab Disord.* Feb; 1992 16(2):71–8. [PubMed: 1316329]
- [82]. McGloin AF, Livingstone MB, Greene LC, Webb SE, Gibson JM, Jebb SA, et al. Energy and fat intake in obese and lean children at varying risk of obesity. *Int J Obes Relat Metab Disord.* Feb; 2002 26(2):200–7. [PubMed: 11850751]
- [83]. Kral TV, Stunkard AJ, Berkowitz RI, Stallings VA, Moore RH, Faith MS. Beverage consumption patterns of children born at different risk of obesity. *Obesity (Silver Spring).* Aug; 2008 16(8):1802–8. [PubMed: 18535546]
- [84]. Stice E, Yokum S, Burger KS, Epstein LH, Small DM. Youth at risk for obesity show greater activation of striatal and somatosensory regions to food. *J Neurosci.* Mar 23; 2011 31(12):4360–6. [PubMed: 21430137]
- [85]. Cornier MA, Salzberg AK, Endly DC, Bessesen DH, Rojas DC, Tregellas JR. The effects of overfeeding on the neuronal response to visual food cues in thin and reduced-obese individuals. *PLoS One.* 2009; 4(7):e6310. [PubMed: 19636426]
- [86]. Smucny J, Cornier MA, Eichman LC, Thomas EA, Bechtell JL, Tregellas JR. Brain structure predicts risk for obesity. *Appetite.* Dec; 2012 59(3):859–65. [PubMed: 22963736]
- [87]. McCaffery JM, Haley AP, Sweet LH, Phelan S, Raynor HA, Del Parigi A, et al. Differential functional magnetic resonance imaging response to food pictures in successful weight-loss maintainers relative to normal-weight and obese controls. *Am J Clin Nutr.* Oct; 2009 90(4):928–34. [PubMed: 19675107]
- [88]. Farooqi IS, Bullmore E, Keogh J, Gillard J, O'Rahilly S, Fletcher PC. Leptin regulates striatal regions and human eating behavior. *Science.* Sep 7. 2007 317(5843):1355. [PubMed: 17690262]
- [89]. Holsen LM, Zarcone JR, Brooks WM, Butler MG, Thompson TI, Ahluwalia JS, et al. Neural mechanisms underlying hyperphagia in Prader-Willi syndrome. *Obesity (Silver Spring).* Jun; 2006 14(6):1028–37. [PubMed: 16861608]
- [90]. Ho AJ, Stein JL, Hua X, Lee S, Hibar DP, Leow AD, et al. A commonly carried allele of the obesity-related FTO gene is associated with reduced brain volume in the healthy elderly. *Proc Natl Acad Sci U S A.* May 4; 2010 107(18):8404–9. [PubMed: 20404173]

- [91]. Stice E, Spoor S, Bohon C, Small DM. Relation between obesity and blunted striatal response to food is moderated by TaqIA A1 allele. *Science*. Oct 17; 2008 322(5900):449–52. [PubMed: 18927395]
- [92]. Felsted JA, Ren X, Chouinard-Decorte F, Small DM. Genetically determined differences in brain response to a primary food reward. *J Neurosci*. Feb 17; 2010 30(7):2428–32. [PubMed: 20164326]
- [93]. Stice E, Yokum S, Burger K, Epstein L, Smolen A. Multilocus genetic composite reflecting dopamine signaling capacity predicts reward circuitry responsivity. *J Neurosci*. Jul 18; 2012 32(29):10093–100. [PubMed: 22815523]
- [94]. Bragulat V, Dzemidzic M, Bruno C, Cox CA, Talavage T, Considine RV, et al. Food-related odor probes of brain reward circuits during hunger: a pilot fMRI study. *Obesity (Silver Spring)*. Aug; 2010 18(8):1566–71. [PubMed: 20339365]
- [95]. Carnell S, Gibson C, Benson L, Ochner CN, Geliebter A. Neuroimaging and obesity: current knowledge and future directions. *Obes Rev*. Jan; 2012 13(1):43–56. [PubMed: 21902800]
- [96]. Eldeghaidy S, Marciani L, McGlone F, Hollowood T, Hort J, Head K, et al. The cortical response to the oral perception of fat emulsions and the effect of taster status. *J Neurophysiol*. May; 2011 105(5):2572–81. [PubMed: 21389303]
- [97]. Mehta S, Melhorn SJ, Smeraglio A, Tyagi V, Grabowski T, Schwartz MW, et al. Regional brain response to visual food cues is a marker of satiety that predicts food choice. *Am J Clin Nutr*. Nov; 2012 96(5):989–99. [PubMed: 22990034]
- [98]. Nolan-Poupert S, Veldhuizen MG, Geha P, Small DM. Midbrain response to milkshake correlates with ad libitum milkshake intake in the absence of hunger. *Appetite*. Oct 12; 2012
- [99]. Sokol-Hessner P, Hutcherson C, Hare T, Rangel A. Decision value computation in DLPFC and VMPFC adjusts to the available decision time. *Eur J Neurosci*. Apr; 2012 35(7):1065–74. [PubMed: 22487036]
- [100]. Hare TA, Camerer CF, Rangel A. Self-control in decision-making involves modulation of the vmPFC valuation system. *Science*. May 1; 2009 324(5927):646–8. [PubMed: 19407204]
- [101]. Plassmann H, O'Doherty JP, Rangel A. Appetitive and aversive goal values are encoded in the medial orbitofrontal cortex at the time of decision making. *J Neurosci*. Aug 11; 2010 30(32):10799–808. [PubMed: 20702709]
- [102]. Lim SL, O'Doherty JP, Rangel A. The decision value computations in the vmPFC and striatum use a relative value code that is guided by visual attention. *J Neurosci*. Sep 14; 2011 31(37):13214–23. [PubMed: 21917804]
- [103]. Frankort A, Roefs A, Siep N, Roebroek A, Havermans R, Jansen A. Reward activity in satiated overweight women is decreased during unbiased viewing but increased when imagining taste: an event-related fMRI study. *Int J Obes (Lond)*. Nov 8; 2011
- [104]. Bender G, Veldhuizen MG, Meltzer JA, Gitelman DR, Small DM. Neural correlates of evaluative compared with passive tasting. *Eur J Neurosci*. Jul; 2009 30(2):327–38. [PubMed: 19614981]
- [105]. Hare TA, Malmaud J, Rangel A. Focusing attention on the health aspects of foods changes value signals in vmPFC and improves dietary choice. *J Neurosci*. Jul 27; 2011 31(30):11077–87. [PubMed: 21795556]
- [106]. Batterink L, Yokum S, Stice E. Body mass correlates inversely with inhibitory control in response to food among adolescent girls: an fMRI study. *Neuroimage*. Oct 1; 2010 52(4):1696–703. [PubMed: 20510377]
- [107]. Ng J, Stice E, Yokum S, Bohon C. An fMRI study of obesity, food reward, and perceived caloric density. Does a low-fat label make food less appealing? *Appetite*. Aug; 2011 57(1):65–72. [PubMed: 21497628]
- [108]. Tang DW, Fellows LK, Small DM, Dagher A. Food and drug cues activate similar brain regions: a meta-analysis of functional MRI studies. *Physiol Behav*. Jun 6; 2012 106(3):317–24. [PubMed: 22450260]
- [109]. Petry NM, Barry D, Pietrzak RH, Wagner JA. Overweight and obesity are associated with psychiatric disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychosom Med*. Apr; 2008 70(3):288–97. [PubMed: 18378873]

- [110]. Simon GE, Von Korff M, Saunders K, Miglioretti DL, Crane PK, van Belle G, et al. Association between obesity and psychiatric disorders in the US adult population. *Arch Gen Psychiatry*. Jul; 2006 63(7):824–30. [PubMed: 16818872]
- [111]. King WC, Chen JY, Mitchell JE, Kalarchian MA, Steffen KJ, Engel SG, et al. Prevalence of alcohol use disorders before and after bariatric surgery. *JAMA*. Jun 20; 2012 307(23):2516–25. [PubMed: 22710289]
- [112]. Conason A, Teixeira J, Hsu CH, Puma L, Knafo D, Geliebter A. Substance Use Following Bariatric Weight Loss Surgery. *Arch Surg*. Oct 15.2012 :1–6.
- [113]. Nederkoorn C, Braet C, Van Eijs Y, Tanghe A, Jansen A. Why obese children cannot resist food: the role of impulsivity. *Eat Behav*. Nov; 2006 7(4):315–22. [PubMed: 17056407]
- [114]. Guerrieri R, Nederkoorn C, Jansen A. The interaction between impulsivity and a varied food environment: its influence on food intake and overweight. *Int J Obes (Lond)*. Apr; 2008 32(4): 708–14. [PubMed: 18059403]
- [115]. Bruce AS, Black WR, Bruce JM, Daldalian M, Martin LE, Davis AM. Ability to delay gratification and BMI in preadolescence. *Obesity (Silver Spring)*. May; 2011 19(5):1101–2. [PubMed: 21151018]
- [116]. Verdejo-Garcia A, Perez-Exposito M, Schmidt-Rio-Valle J, Fernandez-Serrano MJ, Cruz F, Perez-Garcia M, et al. Selective alterations within executive functions in adolescents with excess weight. *Obesity (Silver Spring)*. Aug; 2010 18(8):1572–8. [PubMed: 20057376]
- [117]. Hendrick OM, Luo X, Zhang S, Li CS. Saliency Processing and Obesity: A Preliminary Imaging Study of the Stop Signal Task. *Obesity (Silver Spring)*. Jun 30.2011
- [118]. Kishinevsky FI, Cox JE, Murdaugh DL, Stoeckel LE, Cook EW 3rd, Weller RE. fMRI reactivity on a delay discounting task predicts weight gain in obese women. *Appetite*. Apr; 2012 58(2):582–92. [PubMed: 22166676]
- [119]. Walther K, Birdsill AC, Glisky EL, Ryan L. Structural brain differences and cognitive functioning related to body mass index in older females. *Hum Brain Mapp*. Jul; 2010 31(7): 1052–64. [PubMed: 19998366]
- [120]. Jastreboff AM, Potenza MN, Lacadie C, Hong KA, Sherwin RS, Sinha R. Body mass index, metabolic factors, and striatal activation during stressful and neutral-relaxing states: an FMRI study. *Neuropsychopharmacology*. Feb; 2011 36(3):627–37. [PubMed: 21048702]
- [121]. Carnell S, Kim Y, Pryor K. Fat brains, greedy genes, and parent power: a biobehavioural risk model of child and adult obesity. *Int Rev Psychiatry*. Jun; 2012 24(3):189–99. [PubMed: 22724640]
- [122]. The ADHD-200 Sample. International Neuroimaging Data-sharing Initiative. Jan 1. 2012 Available from: http://fcon_1000.projects.nitrc.org/indi/adhd200/results.html
- [123]. Hollmann M, Hellrung L, Pleger B, Schlogl H, Kabisch S, Stumvoll M, et al. Neural correlates of the volitional regulation of the desire for food. *Int J Obes (Lond)*. Jun 28.2011
- [124]. Baumeister RF, Gailliot M, DeWall CN, Oaten M. Self-regulation and personality: how interventions increase regulatory success, and how depletion moderates the effects of traits on behavior. *J Pers*. Dec; 2006 74(6):1773–801. [PubMed: 17083666]

Highlights

- We come into the world endowed with appetitive traits that affect our eating behavior and weight.
- We can assess these traits using behavioral measures, and potentially using biomarkers such as neural responses to food cues.
- Evidence from infants, children and adolescents suggests that appetite differs not only with body weight, but also with familial obesity risk.
- Behavioral and neural approaches have potential to inform each other and enhance our understanding of obesity risk.
- Large prospective studies will help us identify genetic, environmental and neurobehavioral predictors of weight and suggest novel intervention approaches.