Title

Role of appetitive phenotype trajectory groups on child body weight during a family-based treatment for children with overweight or obesity

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Title of the paper

Role of appetitive phenotype trajectory groups on child body weight during a family-based treatment for children with overweight or obesity

Running title

The appetitive phenotype trajectory groups

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Abstract

Objective: Children with obesity are heterogenous, and emerging evidence suggests that appetitive traits are important constructs in behavioral weight loss treatments for children. The objective of this study was to identify trajectories of child appetitive traits and the impact on child weight changes over time.

Methods: Secondary data analyses of a randomized noninferiority trial which evaluated two child weight loss programs with 12-months of follow-up conducted between 2011-2015. One hundred and fifty children with overweight and obesity and their parent participated in a weight loss program and completed assessments at baseline, 3-,6-,12- and 24 months. Group trajectories were developed using child appetitive traits measured over time, including satiety responsiveness, food responsiveness and emotional eating. Linear mixed-effects models were used to identify the impact of group trajectory on child BMIz change over time. Parent feeding behaviors were evaluated as moderators of the appetitive trajectories on child BMIz.

Results: One hundred fifty children (mean age=10.4; mean BMIz=2.0; 67% girls; 32% Hispanic) and their parent (mean age=42.9; mean BMI=31.9; 87% women; 31% Hispanic) enrolled in the study. The 3-group trajectory model was the most parsimonious and included a high satiety responsive group (HighSR; 47.4%), a high food responsive group (HighFR; 34.6%), and a high emotional eating group (HighEE; 18.0%). Children in all trajectories lost weight at approximately the same rate during treatment, however, only the HighSR group maintained their weight loss during follow-ups while the HighFR and HighEE groups regained weight (adjusted p-value <0.05).

Parent concern over child’s weight moderated weight loss in children in the HighFR group, but no other parent feeding behaviors were moderators.

Conclusions: These child appetitive trajectory groups were associated with differential weight loss maintenance and can be used to identify high-risk subgroups and facilitate development of targeted intervention and maintenance programs.

Trial Registration Clinicaltrials.gov Identifier: NCT01197443

Introduction

Obesity is a major public health problem, and approximately one-third of children in the US have overweight or obesity.[1] Children with obesity are likely to remain obese into adulthood as weight trajectories track across the lifespan.[2] Therefore, while prevention is necessary, effective weight loss treatments are required to help children who have overweight or obesity.[3, 4] Unfortunately, only one-third of children who participate in weight loss programs are no longer overweight in adulthood, suggesting that individual level factors may contribute to responsiveness to weight loss interventions.

Emerging investigations suggest that individuals with overweight and obesity are a heterogeneous group and that various appetite and eating behaviors may differentially impact overeating and weight gain.[5, 6] Previously identified appetitive subtypes of obesity include low responsiveness to internal satiety signals,[7] high responsiveness to external cues,[6, 8] learned patterns and preference for specific foods,[9] and emotional eating.[10] Satiety responsiveness and emotional eating can differentiate children of different weight status.[11, 12] Behavioral food challenge tasks of eating in the absence of hunger have identified poor satiety responsiveness among both heavier children and adolescents.[13-15] Similarly, lower satiety responsivenss, higher food responsiveness, and higher enjoyment of food among school age children has been related to higher body mass index for age.[16, 17] Given such evidence, it is possible that appetitive phenotypes could differentially influence childrens' responsiveness to state of the art weight loss programs.

The majority of research to date has evaluated behavioral phenotypes associated with obesity using cross-sectional data and cannot evaluate any changes in behaviors related to proposed phenotypes during efforts to lose weight. Conventional univariate statistical analysis fall short of taking full advantage of the information available in multivariate longitudinal data, which can be used to evaluate the differential progression of changes in patterns of appetitive behaviors associated with these phenotypes and concurrent efforts to lose weight. An understanding of the complex heterogeneity among children with overweight and obesity could lead to the identification of high-risk subgroups, facilitate development of targeted treatments, and serve as an index to evaluate responsiveness to these treatments.

To address these gaps in the literature, we employed a multivariate group-based trajectory modeling (GBTM) to describe trajectories of multiple indicators of appetitive traits (satiety responsiveness, food responsiveness, and emotional eating) in school-aged children during a 6-month weight loss program with 18-month follow-up (total 24 months).[18, 19] The two main objectives of these secondary analyses are: 1) to identify appetitive phenotypes among children with overweight or obesity and 2) to determine whether appetitive phenotypes may explain differential weight changes in children enrolled in an effective weight loss program. As an exploratory aim, we evaluated whether parent feeding behaviors at baseline were related to observed phenotypes or impacted any association between phenotypes and weight changes.

Materials and Methods

Study design

The Family, Responsibility, Education, Support and Health (FRESH) study was a randomized clinical non-inferiority trial which was conducted between July 2011 and July 2015 in San Diego, California (Clinical Trial: NCT01197443). A detailed explanation of the design, methods and primary results are reported elsewhere.[18, 19] In brief, parent/child dyads were randomized to either family-based treatment (parent+child treatment; FBT) or parent-based treatment (parent-only treatment; PBT) which included nutrition and physical activity recommendations, parenting skills, and behavioral modification strategies. Both the FBT and PBT treatment programs included 20 visits over 6 months. In FBT, parents and children attended simultaneous but separate groups. In PBT, only the parents attended groups. Children in PBT did not attend any treatment meetings. Measures were collected at baseline, midtreatment (month 3;weight only), initial posttreatment (month 6), 6-month follow-up (month 12) and 18-month follow-up (month 24). Primary analyses showed that PBT was not inferior to FBT [18] and thus, for this analyses, groups were collapsed.

Eligibility included a child between 8.0 and 12.9 years of age with a BMI between the 85^{th} and 99.9^{th} percentiles, a parent in the household with a BMI of at least 25 kg/m^2 who could read English at a minimum of a fifth-grade level, and availability to participate in the study on designated evenings. Exclusion criteria included a major child or parent psychiatric disorder, child diagnosis of a serious current physical disease, child with physical limitations, or a family with food restrictions.

The Institutional Review Boards of the University of California San Diego and Rady Children’s Hospital, San Diego, California approved the study. Written consent and assent were obtained from parents and children, respectively.

<u>Subjects</u>

In total, 150 children who met the inclusion criteria and their parents were recruited through local advertisements, school listservs, and local pediatric clinics. Participant demographics are included in Table 1.

Assessment and outcome measures

Assessments with child-parent dyads were conducted at baseline, midtreatment (month 3;weight only), initial posttreatment (month 6), 6-month follow-up (month 12) and 18-month follow-up (month 24).

Anthropometrics. Parent and child's height and weight measurements were obtained by a trained staff member at all the assessment timepoints. BMI was calculated as weight in kilograms divided by height in meters squared. BMIz scores were estimated from age and gender specific Center of Disease Control and Prevention (CDC) growth reference values.[20]

Child Eating Behavior Questionnaire (CEBQ; parent report) [21] is a 35-item questionnaire that assesses appetitive traits in children.[22] Two subscales were included in the analyses; satiety responsiveness (SR; Cronbach's α= 0.70) and food responsiveness (FR; α= 0.85). *The SR scale measures differences in the tendency to terminate eating or cease to initiate eating in response to perceived satiety. The FR scale measures individual differences in the tendency to eat in response to external cues.*

Emotional Eating Scale for Children (EES-C; child report) [23, 24] is a 25-item questionnaire that assesses eating in response to a variety of emotional cues among children.[23] *The questionnaire asks participants to rate how much they have a desire to* *eat on a 5-point Likert scale ("I have no desire to eat" to "I have a very strong desire to eat").* The total score (α =0.77) was used in analyses.

Eating in the Absence of Hunger for Children (EAH-C; child report) [25] is a 14-item survey that assess how often child eats when not hungry.[25] Two subscales were utilized in the analyses; Negative affect eating (NAE; α=0.94) and the external eating scale (α=0.80). The NAE subscale measures eating in the absence of hunger in response to negative emotions and the external eating scale measures eating in the absence of hunger in response to external food cues. The NAE subscale was used in the primary analyses, the external eating scale was used in post-hoc evaluation.

Birch Child Feeding Questionnaire (parent-report) [26, 27] is a 21-item survey that assesses parental beliefs, attitudes and practices regarding child feeding. Four scales were included; concern about child weight (α=0.62), restriction (α=0.70), pressure to eat (α=0.63), and monitoring of eating (α=0.93). The concern about child weight scale measures parental perception and concerns regarding child risk for obesity; the restriction subscale, the pressure to eat scale, and the monitoring subscale measures parents' use of controlling feeding practices. *Items are scored on a 5-point Likert scale ranging from 1 (low) to 5 (high).* Each scale was dichotomized using the median score for exploratory moderator analyses.

Demographics. Surveys included self-reported gender, enthnicity, and age.

Statistical analysis

A multivariate GBTM,[28] a generalization of the basic univariate GBTM, and an extension of the latent-class trajectory model were used to identify subgroups of individuals exhibiting a similar progression across multiple indicators of appetitive traits.[28-30] The GBTM uses iterative procedures to simultaneously obtain parameter estimates of changes in appetitive trait indicators and posterior estimates of the probability of individual's membership in each of the possible groups.[29] The GBTM does not presume a certain number of a priori defined groups and selection of a parsimonious number of groups is based on the fit of each model. The censored normal distribution was used to allow modeling of responses that may be clustered at the minimum or maximum of the subscales. Selection of the number of groups and model fit were evaluated using multiple fit-indices, including the information-based Bayesian information criterion (BIC), the Akaike information criterion (AIC), the average posterior probability assignment (APPA), the odds of correct classification (OCC), and the standard deviation of group membership probabilities.[29, 31]

GBTM were estimated with PROC TRAJ,[30] and any missing values were assumed to be missing completely at random (MCAR). This MCAR assumption was supported by Little's MCAR sigfniciance greater than 0.9 [32] and GBTM models were estimated using all available observations on eating behavior measures. Subjects were included in the analysis if they had at least one valid observation on each examined appetitive indicator.

We also conducted an exploratory moderator analyses evaluating the impact of parent feeding behaviors on child BMIz changes or differential effect on BMIz changes within identified appetite groups (parenting * group). Linear mixed effects regression models were used to evaluate relationship with child BMIz score assessed at midtreatment (month 3;weight only), initial posttreatment (month 6), 6-month follow-up (month 12) and 18-month follow-up (month 24). Main effects of appetitive group membership on child BMIz score change over time were plotted as a function after adjusting for planned covariates. The interactions of dummy-coded indices for identified appetitive groups and parenting style measures were evaluated with planned covariates and treatment group assignment using linear mixed effect models of child BMIz that include a random effect to control for their associated intraclass correlation. Weight changes within appetitive groups were plotted as a function of parenting factors to explore potential moderation of effects of appetitive group membership on weight changes. Benjamini-Hochberg corrections were used for multiple comparisons.[33] All statistical analyses were done in R (version 3.4) [34-36] and SAS (version 9.4, North Carolina).

Results

Identification of Appetitive Groups: The GBTM modeled repeated assessment of the four appetitive trait measures (SR, FR, EES, NAE) assessed at baseline, initial posttreatment (month 6), 6-month follow-up (month 12) and 18-month follow-up (month 24). Successive GBTM that allowed increasing numbers of groups (one to 10 groups) were compared on the basis of multiple fit indices. The Bayesian Information Criterion (BIC) suggested similar minimum scores in models with three and five groups. The APPA, OCC, and standard deviation of group membership probabilities (SD-GMP) limits (APPA>0.70; OCC>5.0; lowest SD-GMP) favored models with three groups over other models. The three-group model was the most parsimonious and interpretable in its distinctiveness of temporal patterns of appetitive indicators. Using the maximum probability rule, 47.4%, 34.6%, and 18.0% children were assigned to trajectory groups 1, 2, and 3, respectively.

Description of Appetitive Groups: *Reactions During Treatment:* Figure 1 presents the identified trait trajectories of appetitive groups. Appetitive group 1 (HighSR; 47.4% of the children) showed an increasing pattern in SR, a decreasing pattern in FR, and a low stable pattern in the EES and NAE. Appetitive group 2 (HighFR; 34.6% of the children) showed a low stable pattern in SR, high stable pattern in FR, and a decreasing pattern in EES and NAE. Appetitive group 3 (HighEE; 18.0% of the children) included an increasing pattern in SR and moderately decreasing pattern in FR. However, EES and NAE were consistently high over time in this group. While the HighSR group stayed within the low range on EES and NAE over time, the HighEE group stayed within the high range for EES and showed a reverse-U shaped pattern for NAE over time.

Weight Changes Among Appetitive Groups: Figure 2 presents estimated marginal means of BMIz score over time of the 3 trajectory groups after adjusting for covariates (age, sex, treatment allocatoin, ethnicity, and baseline BMIz). The weight trajectories of all groups decreased at approximately the same level from baseline to post-treatment (6-mo); however, only the HighSR group was able to maintain weight loss throughout the follow-up assessments (12- and 24-months). Both HighFR and HighEE groups had significant increase in their weight after the post-treatment assessment. The magnitude of change in child BMIz for both HighFR and HighEE groups compared to the HighSR group was statistically significant at 12-months and 24-months (supplement table 1). Of note, moderation effect of the two treatments (trajectories*times*random) was tested and found no effect of the treatment on child weight loss with all p-values greater than 0.2.

Parenting Behaviors and Weight Changes: The influence of parent feeding behaviors on weight changes were evaluated as potential moderators of the differences in weight changes observed in the three appetitive groups. Children in HighFR group with parents who had high compared to parents with low concerns about their child's weight showed significantly lower BMIz at the follow-up assessments (adjusted p-values 0.05 and 0.06; see Figure 3 and supplement Table 2). None of the other feeding behaviors moderated child weight loss in these analyses.

Discussion

This study identified three trajectories of appetitive phenotypes in children with overweight and obesity enrolled in a 6-month family-based weight loss treatment program with their parents. The appetitive groups that emerged - High Satiety Responsiveness (HighSR), High Food Responsiveness (HighFR) and High Emotional Eating (HighEE) - showed differential responsiveness to the weight loss program. While, on average, all children lost weight at the same rate from baseline to post-treatment, only children in the HighSR trajectory maintained their weight loss while children in the HighFR and the HighEE trajectories gained weight post-treatment. With regards to parent feeding behaviors, parent concern about child weight at baseline was a moderator of child weight in the HighFR trajectory, but did not influence weight loss in the HighSR and HighEE trajectories. Although all the children in the program had overweight or obesity, these appetitive groups differentiated weight loss over time in this study, supporting the importance of evaluating behavioral phenotypes and ultimately developing targeted treatments.

This study is consistent with our previous cross-sectional study[16] which evaluated latent classes of appetitive phenotypes among 117 children with overweight and obesity using multiple indicators of appetite, eating behaviors, and nutrition. The final three latent classes were driven mainly by food responsiveness and satiety responsiveness (High Food Responsiveness, High Satiety Responsiveness and moderate Food Responsiveness/Satiety Responsiveness) and results showed that the High Food Responsive group was heavier than the other two groups, even though all the children were above the 85%BMI. The current study supports this initial cross-sectional evaluation and is the first to demonstrate that appetitive phenotypes are associated with differential child weight loss trajectories in a family-based treatment program.

The importance of satiety responsiveness and food responsiveness as traits that contribute to obesity was originally described by Stanley Schachter.[37, 38] There is increasing evidence supporting the influence of appetitive traits such as reward sensitivity, hunger and satiety mechanisms, and food cue responsiveness on obesity risk.[12, 39-41] These appetitive traits along with an abundance of food (such as in the current food environment) may contribute to overeating and weight gain in vulnerable children. Importantly, this study demonstrates that these appetitive traits were associated with how well children maintained their weight loss. While children in the HighSR group lost weight and kept the weight off, children in the HighFR group regained weight post-treatment. These differentiations among subgroups are consistent with data suggesting that overweight children are hypersensitive to food cues and tastes in neuroimaging studies.[42, 43] Being high on food responsiveness may be a risk factor in today's environment where food cues are ubiquitous.

Interestingly, the HighEE group also had increasing satiety responsiveness over time, similar to the HighSR group, however, they had the highest scores on negative affect eating and emotional eating. This HighEE group was also the least stable compared to the other two groups, mainly due to the low sample size, so interpretations regarding this phenotype should be considered tentative. Since the HighSR and HighEE groups were similar on satiety responsiveness but differed on scores on the emotional eating scales, emotional eating is possibly a risk factor among children with overweight and obesity and should be considered a mechanism to target to improve treatment programs. While few children demonstrated this trait at this age, emotional eating may become more salient as children age into adulthood, suggesting that targeting this mechanism in childhood could prevent future emotional eating and weight gain.

This study also showed that HighFR children whose parents were low on concern over child's weight at baseline did not lose as much weight and regained weight faster than children whose parents were high on concern over child's weight. Parents who are low on concern about their child's weight may in fact be less likely to implement parenting skills and monitor their child, which could lead to the child overeating, especially if the child is highly food responsive. The parent concern over child's weight scale includes three questions, one which queries about the parent's concern over the "child eating too much when parents were not around." To explore this hypothesis, we evaluated the correlations between the parent's responses on the question regarding concern over the child eating too much when parents were not around, food responsiveness, and the external eating scale on the children's eating in the absence of hunger questionnaire.[25] We found that there were significant positive correlations between the parent's concern over the child eating too much when the parents were not around and both the probability of being in the HighFR trajectory (r=0.317, p=0.001) and score on the EAH external eating scale (r=0.351, p=0.001). We also found that the probability of being in HighFR trajectory was significantly associated with the EAH external eating scale (r=0.342, p=0.001), suggesting that these scales may be measuring similar constructs. Although these results are not conclusive, they suggest that parent monitoring behavior may impact children in the HighFR trajectory potentially due to the child's eating in the absence of hunger behavior. This preliminary hypothesis deserves further investigation in future studies.

Strengths of the study include the multiple measurements of appetitive traits and child weight over time within the context of a 6-month family-based weight control treatment program and the state of the art analyses evaluating trajectories of child weight changes. However, study participants were limited to treatment-seeking 8- to 12-year-old children and their parents, and these results may not generalize to non-treatment seeking samples. As the GBTM is a model-based for approximating the unknown group distribution of trajectories, the latent trajectory groups should not be thought of as literally distinct groups but rather as clusters of individuals following approximately the same trajectory. Additionally, this study utilized self-report measures with parents and children and these trajectory groupings may be subject to self-report biases.

Conclusion

This is the first study to evaluate trajectories of appetitive phenotypes in children with overweight and obesity during a weight loss program. Appetitive phenotypes were associated with differential outcomes, attesting to the importance of understanding the underlying mechanisms in obesity treatment. The identification of these mechanism-based phenotypes could identify high-risk subgroups and guide the development of intervention programs targeting these appetite pathways. Ultimately, this approach could improve outcomes for a larger proportion of children with overweight and obesity.

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Conflict of interest. The authors declare that they have no conflict of interest.

Supplementary information is available at IJO's website

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Figure Titles & Legends

Figure 1. Multi-trajectory groups of appetitive traits in children with overweight and obesity over time [a]

[a] Mean and 90th confidence intervals are shown

Figure 2. Changes in child BMIz over time by trajectory group [b]

[b] Means are reported after adjusting for age, sex, randomization, ethnicity, baseline BMIz

* $p<0.05$ (p-value adjusted using the Benajamini-Hochberg correction; ref: HighSR group)

Figure 3. Baseline parent concern about child's weight as a moderator of child BMIz change by trajectory group over time [b]

Blue = low on concern about child's weight; Orange = high on concern about child's weight

[b] Means are reported after adjusting for age, sex, randomization, ethnicity, baseline BMIz

* $p<0.05$; $^{+}$ $p<0.10$