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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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Abstract
Objective  Emerging evidence suggests that individual appetitive traits may usefully explain patterns of weight loss 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 conducted between 2011 and 2015 evaluated children’s appetitive traits and weight loss. Children with overweight and obesity (mean age = 10.4; mean BMI z = 2.0; 67% girls; 32% Hispanic) and their parent (mean age = 42.9; mean BMI = 31.9; 87% women; 31% Hispanic) participated in weight loss programs and completed assessments at baseline, 3, 6, 12, and 24 months. Repeated assessments of child appetitive traits, including satiety responsiveness, food responsiveness and emotional eating, were used to identify parsimonious grouping of change trajectories. Linear mixed-effects models were used to identify the impact of group trajectory on child BMIz change over time.

Results  One hundred fifty children and their parent enrolled in the study. The three-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).

Conclusions  Distinct trajectories of child appetitive traits were associated with differential weight loss maintenance. Identified high-risk subgroups may suggest opportunities for targeted intervention and maintenance programs.

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 various appetite subtypes of obesity, such as low responsiveness to internal satiety signals [5], high responsiveness to external cues [6, 7], learned patterns and preference for specific foods [8], and emotional eating [9] may differentially impact overeating and weight gain [7, 10]. When examined individually, satiety responsiveness, emotional eating, and food responsiveness are known to be related to a higher body mass index among children [11–14].
Behavioral food challenge tasks of eating in the absence of hunger differentiate children and adolescents with poor satiety responsiveness [15–17]. Given such evidence, it is possible that appetitive phenotypes could differentially influence childrens’ responsiveness to behavioral weight loss programs.

The majority of research to date has evaluated behavioral phenotypes associated with obesity using cross-sectional data. Conventional univariate approaches do not take full advantage of the dynamic information available in longitudinal data as children interact with the behavioral weight loss program. Differential progression of changes in patterns of appetitive behaviors associated with these phenotypes may be useful in characterizing concurrent efforts to lose weight. An understanding of common patterns of appetitive behaviors among children with overweight and obesity could lead to the identification of high-risk subgroups, provide a dynamic method for evaluating ongoing responsiveness to these treatments and facilitate development of targeted treatments.

We used a multivariate group-based trajectory modeling (GBTM) approach to describe changes in multiple indicators of appetitive traits (satiety responsiveness, food responsiveness, and emotional eating) in school-aged children during a 6-month weight loss program and subsequent 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 be associated with differential weight changes in children enrolled in a weight loss program.

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) that 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 the PBT arm did not attend any treatment meetings. Primary analyses showed that PBT was not inferior to FBT [18] and thus, for these analyses, groups were collapsed.

Eligibility included a child between 8.0 and 12.9 years of age with a BMI between the 85th and 99.9th percentiles, a parent in the household with a BMI of at least 25 kg/m² 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.

Subjects

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), post-
treatment (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)** [21] is a 35-item parent-reported 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 the tendency to terminate eating in response to perceived satiety. The FR scale measures the tendency to eat in response to external food cues.

**Emotional Eating Scale for Children (EES-C)** [23, 24] is a 25-item child-reported 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 five-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)** [25] is a 14-item child-reported questionnaire that assesses 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.

**Demographics** Surveys included self-reported gender, ethnicity, and age.

**Statistical analysis**

A multivariate GBTM [26], a generalization of the basic univariate GBTM, and an extension of the latent-class trajectory model were used to identify subgroups of individuals exhibiting similar pattern progressions across multiple indicators of appetitive traits [26–28]. 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 [27]. 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, the average posterior probability assignment (APPA), the odds of correct classification (OCC), and the standard deviation of group membership probabilities [27, 29].

GBTM were estimated with PROC TRAJ [28], and any missing values were assumed to be missing completely at random (MCAR). This MCAR assumption was supported by Little’s MCAR significance >0.9 [30] and GBTM models were estimated using all available observations on eating behavior measures using a direct maximization with the quasi-Newton procedure [31]. Under the MCAR assumption, 150 subjects were included in the analysis as they had at least one valid observation on each examined appetitive indicator.

Linear mixed effects (LME) regression models were used to evaluate relationships between phenotype group and child BMIz score assessed at mid treatment, initial post treatment, 6-month follow-up, and 18-month follow-up. These models were evaluated with planned covariates, baseline values of BMIz and treatment group assignment using LME models of child BMIz that include a random effect to control for their associated intraclass correlation.

We also examined the effect of baseline scores and change scores reflecting the effectiveness of weight loss treatment by evaluating relationships between simple differences between baseline and post treatment of each questionnaire and levels of child’s BMIz scores at 6- and 18-month assessments. Main effects of follow-up BMIz score were evaluated using linear regression models with spline functions, and included planned covariates, baseline BMIz and treatment group assignment. Benjamini–Hochberg p-value corrections were used for multiple comparisons among trajectory groups [32]. Statistical analyses were conducted using R (version 3.4) [33–35] 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, and NAE) assessed at baseline, post-treatment (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 ten groups) were compared on the basis of multiple fit indices. The 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 (High Satiety Responsiveness (HighSR); 47.4% of the children; 36.6% boys; 38.0% Hispanic; mean baseline BMI = 26.24 (3.42); mean baseline BMIz = 1.97 (0.34); mean age in years = 10.59 (1.32)) 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; 30.8% boys; 28.6% Hispanic; mean baseline BMI = 27.14 (3.93); mean baseline BMIz = 2.09 (0.34); mean age in years = 10.37 (1.18)) showed a low stable pattern in SR, high stable pattern in FR, and a decreasing pattern in EES and NAE. Appetitive group 3 (high emotional eating (HighEE); 18.0% of the children; 29.6% boys; 22.2% Hispanic; mean baseline BMI = 25.13 (3.22); mean baseline BMIz = 1.93 (0.33); mean age in years = 10.03 (1.25)) included an increasing pattern in SR and moderately decreasing pattern in FR. However, EES and NAE were consistently high over time in this group. Thus, HighSR and HighEE group differed in that the HighSR group stayed within the low range on EES and NAE over time, whereas 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 three trajectory groups after adjusting for covariates (age, sex, treatment allocation, ethnicity, and...
baseline BMIz). The weight trajectories of all groups decreased at approximately the same level from baseline to post treatment (6 months). While the HighSR group was able to maintain weight loss throughout the follow-up assessments (6- and 18-month follow-up), both the HighFR and HighEE groups had statistically significant increases in their weight after the post-treatment assessment (adjusted parameters at 6-month follow-up: HighFR = 0.11, HighEE = 0.11; at 18-month follow-up: HighFR = 0.14, HighEE = 0.13; all adjusted p-values < 0.05). Of note, the moderating effect of the treatments (trajectories × times × random) was tested and found to be non-significant (all p-values > 0.2).

**Baseline and change scores as predictors of subsequent weight outcomes**

The influence of baseline-only and change scores between baseline and post treatment were evaluated as potential predictors of the follow-up weight status at 6- and 18-month assessments. None of the measures were significant in predicting subsequent weight outcomes in these analyses (all adjusted p-values >0.05).

**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 treatment 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. 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 more targeted treatments.

This study is consistent with our previous cross-sectional study [13], 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 (HighFR, HighSR, and moderate FR/SR) and results showed that the HighFR group entered treatment at a heavier weight than the other two groups, even though all the children were above the 85% BMI.

The importance of satiety responsiveness and food responsiveness as traits that contribute to obesity was originally described by Schachter [36, 37]. Only relatively recently has increasing evidence re-emerged supporting the influence of appetitive traits such as reward sensitivity, hunger, and satiety mechanisms, and food cue responsiveness on obesity risk [12, 38–40]. 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 from neuroimaging studies suggesting that overweight children are hypersensitive to food cues and tastes [41, 42]. Being highly food responsive may be a risk factor in today’s environment where food cues are ubiquitous. Thus, in addition to the current obesogenic food environment, these appetitive traits may contribute to overeating and weight gain in vulnerable children [16].

Interestingly, the HighEE group had increasing satiety responsiveness over time, similar to the HighSR group, however, this was coupled with elevated reporting of emotional eating. This HighEE group was also the least stable compared with the other two groups, mainly due to the low sample size, so interpretations regarding this phenotype should be considered tentative. Nonetheless, as the HighSR and HighEE groups were similar on satiety responsiveness but differed in their scores on the emotional...
eating scales, emotional eating is possibly another risk factor among children with overweight and obesity and should be considered a mechanism to address in future treatment programs. While few children endorsed this trait, emotional eating may become more salient as children transition into adolescence and adulthood, suggesting that targeting this mechanism in childhood could prevent future emotional eating and weight gain.

This study provides a starting point for understanding clinical patterns of treatment response by representing reliable interrelationship of multiple clinically relevant indicators and the relationship to differential patterns of weight loss. Describing particular types of change patterns could help clinicians understand the heterogeneity in how children with overweight and obesity respond to common weight-loss treatments and could suggest early identification of high-risk subgroups. Our longitudinal approach of clustering the pattern of changes looked for a minimum number of parsimonious subgroups with distinct patterns of weight changes. For example, our approach suggested that characteristics of weight change for those with HighEE were similar to patterns observed among those with the HighFR despite theoretically distinct motivational influences that underly these risk factors. These findings suggest both the limitation of static predictors and promise of a more dynamic identification of at-risk participants, perhaps using updated information over time, for prognostic modeling or to develop new intervention approaches [43]. Using information about the changing internal context of individuals may help to identify the type or dose of intervention [44].

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. In addition, it is the first to demonstrate that appetitive phenotypes are associated with differential child weight loss trajectories in a family-based treatment program. However, as study participants were treatment-seeking 8- to 12-year-old children and their parents, generalizability of these results to non-treatment seeking samples should be further explored. Moreover, 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. Lastly, this study utilized self-report measures with parents and children and these trajectory groupings may be subject to self-report biases. Future studies should explore the correspondence between such self-report and more objective measures of these phenotypes.

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, highlighting 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 appetitive pathways. Ultimately, this approach could improve outcomes for a larger proportion of children with overweight and obesity.

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Compliance with ethical standards

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

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