Cognitive Aspects of Response to Treatment for Weight-related Health to Improve Eating and Exercise Earlier in Life

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ABSTRACT.

Executive functions (EF) are higher-order cognitive processes, such as inhibitory control and decision-making that facilitate goal-directed behavior via the regulation of behavior, emotions, and thoughts. Impairments in EF have been associated with obesity in children and adults; thus, EF has been demonstrated to play an important role in weight management. A limited number of studies have demonstrated that children with EF problems (e.g., impulsivity) have poorer weight loss treatment outcomes. Despite the significant role of parents in the "gold standard" family-based behavioral treatment for pediatric obesity, none of these studies, to our knowledge, have examined parental EF in the context of family-based treatment. Albeit, other parental factors such as weight change are salient child treatment outcome predictors. Unfortunately, body mass index (BMI) has been used as the primary indicator of weight status in most studies examining EF and obesity, as well as family-based behavioral treatment outcomes, but it has limitations for underserved groups such as racial/ethnic minorities that have the greatest need for tailored treatment. Thus, we propose to examine whether child and parental EF predict body composition treatment outcomes and adherence to a 6-month family-based behavioral treatment for pediatric obesity. We hypothesize that children with poorer EF, and those who have parents with poorer EF, will have poorer body composition and adherence outcomes. Findings will be used to submit a larger grant (e.g., R01) to examine EF as a predictive tool for family-based behavioral treatment for pediatric obesity and to develop EF-focused treatment enhancement strategies. The **specific aims and hypotheses** of the current proposal include the following: *Aim 1:* To examine the effect of child pre-treatment EF on change in body composition outcomes and adherence to treatment at 6 months (i.e., post-treatment). *Hypothesis 1*: Children with low/impaired EF will have poorer treatment outcomes than children with high/intact EF, such that they will demonstrate less decrease in body fat, fewer sessions attended, and less self-monitoring. *Aim 2:* To examine whether parental pre-treatment EF predicts change in child body composition outcomes and adherence to treatment at 6 months. *Hypothesis 2:* Parents with low/impaired EF will have children who lose less body fat and demonstrate poorer adherence to treatment compared to children of parents with high/intact EF. *Aim 3:* To examine the association between parent and child EF at pre- and post-treatment. *Hypothesis 3:* Child and parental EF will demonstrate a strong association at pre- and post-treatment. Participants will include 16 children aged 8-12 and their parents with obesity recruited from the Children's Weight Management Clinic. Child and parent EF will be assessed at pre- and post-treatment with performance-based and subjective measures including the NIH Toolbox Cognitive Battery and the Behavioral Rating Inventory of Executive Function – Adult and Parent. The primary outcome is change in body composition measured by Dual-energy X-ray Absorptiometry (DXA). Secondary outcomes will include indicators of adherence to treatment measured by number of sessions attended and number of completed days of diet and activity self-monitoring using the USDA SuperTracker software. Statistical analyses will include Wilcoxon-Mann-Whitney Tests to compare high vs. low EF group outcomes (Aims 1 and 2), as well as simple correlations to examine the association between parent and child EF (continuous EF variables) in addition to Chi-Square or Fisher's Exact Tests and kappa agreement analyses (binary EF variables) (Aim 3).

SPECIFIC AIMS.

Family-based behavioral treatment (FBT) is the leading evidenced-based intervention for children with overweight or obesity and their families.[1,2] FBT typically involves working with children and caregivers to modify diet and physical activity using behavioral strategies such as problem solving, goal setting, and self-monitoring.[2] Approximately one-third of children who complete FBT show clinically meaningful, long-term improvements in weight status;[3-5] however, two-thirds of children continue with overweight or obesity despite receipt of FBT.[5] The tremendous variability in outcomes suggests that underlying mechanisms are not well addressed in current FBT programs. **It is imperative that the factors impacting children's weight outcomes in FBT are clearly identified in order to better meet the needs of this high-risk population.**

Children with poorer weight loss outcomes in weight loss interventions often exhibit characteristics (e.g., impulsivity;[6] eating disorder symptomology)[7] which suggest that there are underlying problems with executive function (EF). EF is an umbrella term for higher-order cognitive processes that facilitate goal-directed behavior, much like a "control center" in the brain. Youth with obesity demonstrate poorer EF in several domains including inhibitory control, cognitive flexibility, and attention.[8] Thus, these youth tend to have selective attention toward energy-dense foods,[9] greater perseverative thinking about these foods,[10] and more difficulty resisting them.[11,12] In our research in children with obesity, almost 1 in 3 exhibited *clinically significant* levels of executive dysfunction.[13] Similarly, we recently collected EF data demonstrating that up to 1 in 5 adults with obesity enrolled in a randomized controlled trial for weight management reported clinically significant EF impairment. The frequent co-occurrence of EF problems and obesity is problematic,[8,14-16] as FBT relies heavily on EF skills such as self-monitoring, problem solving, and cognitive flexibility to make successful lifestyle changes. Moreover, the majority of parents participating in FBT also have overweight/obesity, which suggests that **EF may be impaired in both the parent and child participating in FBT for weight management.**

Yet, despite the significant role of parents in the "gold standard" family-based behavioral treatment for pediatric obesity, **no study, to our knowledge, has examined parental EF in the context of FBT outcomes**. Thus, we propose to examine whether child and parental EF predict body composition outcomes and adherence in the context of a 6-month FBT protocol for pediatric obesity. Unfortunately, body mass index (BMI) has been used as the primary indicator of weight status in most studies examining EF and obesity, as well as FBT outcomes, but it has limitations for certain groups. However, BMI may not be as sensitive an indicator of cardiometabolic health for racial/ethnic minorities.[17] Yet, racial/ethnic disparities in FBT have been understudied including a dearth of literature on the role of EF in obesity among different racial/ethnic groups. To address these gaps in the literature, our overarching aims are to: (1) examine the effects of parent and child EF on treatment outcomes and adherence in a 6-month FBT program for obesity in a diverse group of children aged 8-12 (N=16 child-parent dyads), and (2) examine the association between parent and child EF.

Specific Aim 1: To examine the effect of pre-treatment (0 months) child EF on child body composition outcomes and adherence to treatment at post-treatment (6 months).
***Hypothesis 1*:** Children with low EF will have poorer treatment outcomes than children with high EF, such that children with low EF will demonstrate less decrease in body fat, fewer sessions attended, and less self-monitoring.

Specific Aim 2: To examine the effect of pre-treatment (0 months) parental EF on child body composition outcomes and adherence to treatment at post-treatment (6 months).
Hypothesis 2: Parents with low EF will have children who demonstrate less decrease in body fat, fewer sessions attended, and less self-monitoring than children of parents with high EF.

Specific Aim 3: To examine the association between parent and child EF at pre- and post-treatment.
Hypothesis 3: Child and parent EF will demonstrate a strong association at pre- and post-treatment.

This predictive approach targets a cognitive factor potentially associated with high variability in weight-related outcomes and adherence to standard FBT for pediatric obesity.[18] The findings from this project will be used to submit a larger grant (R01) to examine EF as a predictive tool for outcomes in FBT for pediatric obesity and to develop EF-focused treatment enhancement strategies. Findings may also inform future research examining EF as a factor involved in the intergenerational transmission of obesity.

SIGNIFICANCE. There is remarkable variability in outcomes for evidence-based behavioral treatment for pediatric obesity.[1,5] Family-based behavioral treatment (FBT) is the leading evidence-based intervention for pediatric obesity.[2] Yet, two-thirds of children who complete FBT fail to achieve a healthy weight in adulthood.[5] As self-management behaviors are key for successful FBT outcomes, FBT is designed to help families develop self-management skills, including goal-setting, self-monitoring, problem-solving, and action-planning.[2] However, EF may impact self-management behaviors and treatment outcomes. Self-regulation theory posits that EF underlies self-regulation[19,20] and likens self-regulation to a muscle that fatigues with demand (e.g., resisting temptation). As such, EF has been associated with various weight-related behaviors, weight status, and obesity in observational, non-intervention studies the lifespan.[21-23] Furthermore, EF has been associated with bariatric surgery outcomes such that pre-surgical EF levels predicted weight loss and adherence outcomes (higher baseline EF, greater weight loss and better adherence).[24-27] However, few studies have investigated the role of EF in predicting pediatric outcomes in FBT,[28] and no studies to our knowledge have examined the effect of parental EF on child outcomes despite their involved role in FBT.

INNOVATION. The current study proposes to utilize baseline levels of EF from children and their parents to predict treatment outcomes in FBT, which has not been done before to our knowledge. This will provide a better understanding of parental cognitive factors that may influence child outcomes in treatment to serve as a stepping stone to treatment tailoring. Furthermore, the study utilizes children's body fat mass which may be a more sensitive estimate of cardiometabolic health as the primary outcome, but is less frequently studied in association with EF, particularly in the context of FBT including racial/ethnic minorities. This may improve the bio-behavioral understanding of the effect of EF on body composition in treatment among various racial/ethnic groups.

APPROACH.

Participants and Setting. While adolescent obesity levels continue to rise, those in children (aged 6-11) appear to have leveled off despite remaining high.[29] Thus, the pre-adolescent years may be an ideal window for identifying individual and familial characteristics affecting outcomes in FBT. We will recruit a total of 16 children aged 8-12 and their parents from the Children's of Alabama Weight Management Clinic. Almost half (48%) of the children from the Weight Management clinic are in our target age range. The majority (64%) are female with a diverse racial/ethnic breakdown: African American (51%), non-Hispanic White (41%), Hispanic (6%), and Other (1%). Thus, we expect to recruit a diverse sample. All research visits will take place at the main campus of the Children's of Alabama Hospital, where the PI has reserved space. Children will be escorted to the UAB Webb Building for the DXA scan which is a short walk from the Children's Hospital.

Recruitment and Screening. The PI is a provider in the Children's of Alabama Weight Management Clinic which will serve as a recruitment base, averaging ~220 new patient referrals each year (5 new patients per week). Interested parents will contact study personnel in clinic or by phone to receive information about the study and undergo a screening to assess inclusion/exclusion criteria. *Inclusion criteria.* Children who: (1) have a BMI ≥ 85th percentile; (2) are ≥8 and ≤12 years old at the beginning of treatment; (3) can read, write, and speak English, along with their parent; (4) plan to stay living within the local area during the study period; (5) have a consenting parent who can commit to all study procedures and provide reliable travel. Siblings will be eligible for study inclusion if they meet the above criteria and will be allowed to use the same participating parent (sibling effects would then be addressed in statistical analyses). *Exclusion criteria.* Children who: (1) have been diagnosed with a medical condition and/or are taking medication known to affect appetite/weight; (2) are currently participating in a formal weight management program beyond their usual medical care or have a parent participating in a formal weight management program; (3) have been diagnosed with an intellectual disability or traumatic brain injury; (4) have medical contraindications to physical activity.

Procedures. Children and caregivers who meet preliminary eligibility will be scheduled for a baseline visit within one month of the first treatment session during which eligibility will be confirmed including BMI assessment and informed consent/assent procedures will be conducted. Dyads providing informed consent/assent will complete the assessment items outlined below in the Measures section. Pre- and post-evaluations are estimated to take 90 minutes. There will be 2 groups of FBT on after-school evenings including 8 dyads in each group (a total of 16 child-caregiver dyads) based on previous experience and feasibility. A total of 18 treatment sessions will be held over 6 months: 12 weekly sessions during the first 3 months and 6 bi-weekly sessions over the last 3 months. FBT is a manualized, group intervention for children with obesity and their caregivers that incorporates dietary modification, physical activity prescription, a variety of session topics on nutrition, physical activity, and behavioral support for reaching goals. The intervention will be coordinated and

supervised by the PI, a Ph.D. level clinical psychologist. Each group will be co-led by the PI and a graduate research assistants: one leader for the child group and one leader for the caregiver group. Lifestyle intervention programs for pediatric obesity, demonstrate 6-12 month retention rates >70%. Given our 6-month protocol, we have estimated a 75% retention rate for the 6-month assessment. We will employ a variety of retention strategies including: (1) FBT at no-cost; (2) escalating monetary incentives for completion of assessments - $40 (baseline) and $75 (month 6); and (3) reimbursement of on-site parking for all study-related visits. To assure assessment and treatment fidelity, EF testing will be conducted using validated, computerized instruments and standardized scripts and administration protocols. The PI will provide training and regular supervision with all individuals participating in treatment delivery and cognitive assessments. Assessment and treatment sessions will be audio recorded and evaluated by the PI and any adherence issues will be immediately addressed, including re-training.

Measures. Child and parent demographic data and medical history will be assessed at baseline via parent questionnaire. The remaining measures will be administered at pre- (baseline, 0 months) and post-treatment (6-months). Child and parent height and weight will be measured in light clothing and no shoes. Height will be measured to the nearest 0.1 cm with a Seca 213 portable stadiometer. Weight will be measured to the nearest 0.1 kg with a Tanita SC-240 bio-electrical impedance (BIA) analyzer and standard scale. Child height/weight measurements will be converted to zBMI using CDC age and sex specific scales. Child and parent performance-based EF will be tested using the NIH Toolbox Cognitive Battery. Subjective EF will be measured using the Behavioral Rating Inventory of Executive Function – Adult and Parent. Primary outcome will be body fat mass using Dual-energy X-ray Absorptiometry (DXA). Secondary outcome will include adherence to treatment measured by number of sessions attended and number of completed days of diet and activity self-monitoring using the USDA SuperTracker software, defined by ≥2 meals and exercise minutes recorded daily.

Data Management and Statistical Analyses. SPSS Version 24 will be used for all statistical analyses. Statistical analyses will include Wilcoxon-Mann-Whitney Tests to compare high vs. low EF group treatment outcomes (Aims 1 and 2), as well as simple correlations to examine the association between parent and child EF (continuous EF variables) in addition to Fisher's Exact Tests and kappa agreement analyses (binary EF variables) (Aim 3). A composite score of EF will be created and used for NIH Toolbox. Published age-adjusted norms are available for the NIH Toolbox. Individuals at or above the mean level normed scores will be considered "high EF" and those below the corresponding mean level score will be considered "low EF". Clinical cutoffs are published for the BRIEF/BRIEF-A. A T-score ≥60 (i.e., subclinical to clinical) in any domain will be considered "low" whereas a score <60 will be considered "high".

Potential Challenges and Alternative Approaches. Several potential confounders of EF effects on treatment outcomes have been identified (e.g., binge eating, ADHD). We expect a low endorsement rate of these in our study sample but will assess at baseline for future research purposes, although given our sample size we will not be able to adjust for these factors in data analyses. In addition, there is potential for reverse causality. We hypothesize that EF will affect treatment outcomes based on theory and previous research, but we acknowledge that the alternative direction of weight/body fat loss impacting EF is also important and possible. Our data will allow for exploratory examination of alternative directions between these constructs since EF and body fat will be measured pre- and post-treatment.

PLANS FOR FUTURE FUNDING. Findings will be used in an extramural grant proposal (R01) to conduct a larger scale study that builds upon this proposal to increase the understanding of the bio-behavioral relationships between EF and metabolic factors and outcomes (e.g., glucose, inflammation) in a large, RCT comparing FBT to a treatment that targets EF for pediatric obesity. In addition, these data could be used to develop a grant related to family-based treatment planning and tailoring (e.g., SMART design) for underserved groups. Several current R01 program announcements would fit well with these goals: NIDDK's *PAR-16-304* Ancillary Studies to Identify Behavioral and/or Psychological Phenotypes Contributing to Obesity and NINR's *PA-17-115* Chronic Condition Self-Management in Children and Adolescents, *PA-17-118* Reducing Health Disparities Among Minority and Underserved Children, and *PA-14-112* A Family-Centered Self-Management of Chronic Conditions.

NORC CORE USE. The NORC Metabolism and Biostatistics Cores are essential to the successful implementation and completion of the proposed study. The Metabolism Core will be used to conduct DXA scans on participating children pre- and post-intervention to assess body fat mass. The Biostatistics Core will be utilized for data analysis consultation and support.

REFERENCES

1. Epstein LH, Paluch RA, Roemmich JN, Beecher MD. Family-based obesity treatment, then and now: twenty-five years of pediatric obesity treatment. *Health psychology : official journal of the Division of Health Psychology, American Psychological Association.* 2007;26(4):381-391.
2. Janicke DM, Steele RG, Gayes LA, et al. Systematic Review and Meta-Analysis of Comprehensive Behavioral Family Lifestyle Interventions Addressing Pediatric Obesity. *Journal of Pediatric Psychology.* 2014;39(8):809-825.
3. Ford AL, Hunt LP, Cooper A, Shield JPH. What reduction in BMI SDS is required in obese adolescents to improve body composition and cardiometabolic health? *Archives of Disease in Childhood.* 2010;95(4):256-261.
4. Reinehr T, Lass N, Toschke C, Rothermel J, Lanzinger S, Holl RW. Which amount of BMI-SDS reduction is necessary to improve cardiovascular risk factors in overweight children? *The Journal of clinical endocrinology and metabolism.* 2016:jc20161885.
5. Epstein LH, Valoski A, Wing RR, McCurley J. Ten-year follow-up of behavioral, family-based treatment for obese children. *Jama.* 1990;264(19):2519-2523.
6. Nederkoorn C, Jansen E, Mulkens S, Jansen A. Impulsivity predicts treatment outcome in obese children. *Behaviour Research and Therapy.* 2007;45(5):1071-1075.
7. Wildes JE, Marcus MD, Kalarchian MA, Levine MD, Houck PR, Cheng Y. Self-reported binge eating in severe pediatric obesity: impact on weight change in a randomized controlled trial of family-based treatment. *International journal of obesity (2005).* 2010;34(7):1143-1148.
8. Reinert KR, Po'e EK, Barkin SL. The relationship between executive function and obesity in children and adolescents: a systematic literature review. *Journal of obesity.* 2013;2013:820956.
9. Braet C, Crombez G. Cognitive interference due to food cues in childhood obesity. *Journal of Clinical Child and Adolescent Psychology.* 2003;32(1):32-39.
10. Cserjési R, Molnár D, Luminet O, Lénárd L. Is there any relationship between obesity and mental flexibility in children? *Appetite.* 2007;49(3):675-678.
11. Fisher JO, Birch LL. Eating in the absence of hunger and overweight in girls from 5 to 7 y of age. *The American Journal of Clinical Nutrition.* 2002;76(1):226-231.
12. Nederkoorn C, Braet C, Van Eijs Y, Tanghe A, Jansen A. Why obese children cannot resist food: the role of impulsivity. *Eating behaviors.* 2006;7(4):315-322.
13. Gowey MA, Lim CS, McNamara J, et al. Associations between executive functioning and overeating in youth who are overweight and obese. Society of Pediatric Psychology Annual Conference; April 16-18, 2015, 2015; San Diego, CA.
14. Liang J, Matheson BE, Kaye WH, Boutelle KN. Neurocognitive correlates of obesity and obesity-related behaviors in children and adolescents. *Int J Obes.* 2014;38(4):494-506.
15. Miller AL, Lee HJ, Lumeng JC. Obesity-associated biomarkers and executive function in children. *Pediatr Res.* 2015;77(1-2):143-147.
16. Stanek KM, Strain G, Devlin M, et al. Body mass index and neurocognitive functioning across the adult lifespan. *Neuropsychology.* 2013;27(2):141-151.
17. Gujral UP, Vittinghoff E, Mongraw-Chaffin M, et al. Cardiometabolic abnormalities among normal-weight persons from five racial/ethnic groups in the united states: A cross-sectional analysis of two cohort studies. *Annals of Internal Medicine.* 2017;166(9):628-636.
18. Whitaker RC, Wright JA, Pepe MS, Seidel KD, Dietz WH. Predicting obesity in young adulthood from childhood and parental obesity. *The New England journal of medicine.* 1997;337(13):869-873.
19. Hofmann W, Schmeichel BJ, Baddeley AD. Executive functions and self-regulation. *Trends in Cognitive Sciences.* 2012;16(3):174-180.
20. Vohs KD, Baumeister RF. *Handbook of self-regulation: Research, theory, and applications.* Guilford Publications; 2016.
21. Graziano PA, Calkins SD, Keane SP. Toddler self-regulation skills predict risk for pediatric obesity. *International Journal of Obesity.* 2010;34(4):633-641.
22. Smith E, Hay P, Campbell L, Trollor JN. A review of the association between obesity and cognitive function across the lifespan: implications for novel approaches to prevention and treatment. *Obes Rev.* 2011;12(9):740-755.

23. Goldschmidt AB, Hipwell AE, Stepp SD, McTigue KM, Keenan K. Weight Gain, Executive Functioning, and Eating Behaviors Among Girls. *Pediatrics.* 2015;136(4):e856-e863.
24. Spitznagel MB, Alosco M, Strain G, et al. Cognitive function predicts 24-month weight loss success after bariatric surgery. *Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery.* 2013;9(5):765-770.
25. Spitznagel MB, Galioto R, Limbach K, Gunstad J, Heinberg L. Cognitive function is linked to adherence to bariatric postoperative guidelines. *Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery.* 2013;9(4):580-585.
26. Spitznagel MB, Garcia S, Miller LA, et al. Cognitive function predicts weight loss after bariatric surgery. *Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery.* 2013;9(3):453-459.
27. Spitznagel MB, Hawkins M, Alosco M, et al. Neurocognitive Effects of Obesity and Bariatric Surgery. *European Eating Disorders Review.* 2015;23(6):488-495.
28. Huang T, Larsen KT, Jepsen JR, et al. Effects of an obesity intervention program on cognitive function in children: A randomized controlled trial. *Obesity (Silver Spring, Md.).* 2015;23(10):2101-2108.
29. Ogden CL, Carroll MD, Lawman HG, et al. Trends in Obesity Prevalence Among Children and Adolescents in the United States, 1988-1994 Through 2013-2014. *Jama.* 2016;315(21):2292-2299.