LiTTLe Me: Learning Together to Love Mealtime

NCT number NCT04502979
Document Date 01/01/2017

Complete Title: ***LiTTLe Me: Learning Together to Love Mealtime***
Short Title: LiTTLe Me
Drug or Device Name(s): N/A
FDA IND/IDE (if applicable): N/A
Sponsor: The University of North Carolina at Chapel Hill
Protocol Date: January 1, 2017
Amendment 1 Date:
Amendment 2 Date:
Amendment 3 Date:
Amendment 4 Date:

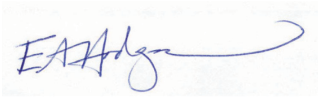
Funding Source:
NIH/NICHD
1 Center Dr.
Bethesda, MD 20892
The United States of America

Study Principal Investigator: Eric A. Hodges, PhD, FNP-BC, FAAN
5016 Carrington Hall, CB 7460
Chapel Hill, NC 27599-7460
Phone: 919-966-0534
email: eahodges@email.unc.edu

PROTOCOL TITLE: LiTTLe Me: Learning Together to Love Mealtime
Short Title: LiTTLe Me

Lead Investigator:
Eric A. Hodges, PhD, FNP-BC, FAAN
University of North Carolina at Chapel Hill
Protocol Version: 1.0
Version Date: January 1, 2017

I confirm that I have read this protocol and understand it.
Principal Investigator Name: Eric A. Hodges, PhD, FNP-BC, FAAN

Principal Investigator Signature: 

Date: January 1, 2017

TABLE OF CONTENTS

Table of Contents 1
Abbreviations and Definitions of Terms 2
Protocol Synopsis 3
1 BACKGROUND AND RATIONALE 6
2 STUDY OBJECTIVES 12
3 INVESTIGATIONAL PLAN 12
4 STUDY PROCEDURES 13
5 STUDY EVALUATIONS AND MEASUREMENTS 14
6 STATISTICAL CONSIDERATIONS 15
7 STUDY INTERVENTION (DEVICE OR OTHER INTERVENTION) 16
8 STUDY INTERVENTION ADMINISTRATION 17
9 SAFETY MANAGEMENT 17
10 DATA COLLECTION AND MANAGEMENT 17
11 RECRUITMENT STRATEGY 19
12 CONSENT PROCESS 19
13 PUBLICATION 20
14 REFERENCES 20

ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Definition
ASL	American Sign Language
RSA	Respiratory Sinus Arrhythmia
T1	Time 1
T2	Time 2
T3	Time 3
BMI	Body Mass Index
SES	Socio-economic status
RCFCS	Responsiveness to Child Feeding Cues Scale
NDS-R	Nutrition Data System for Research
CEBQ-T	Child Eating Behavior Questionnaire-Toddler
IFSQ	Infant Feeding Styles Questionnaire
IBQR	Revised Infant Behavior Questionnaire
NGSE	New Generalized Self-Efficacy Scale
IIQ	Infant Intentionality Questionnaire
PHQ-4	Patient Health Questionnaire-4
PI	Principal Investigator
Co-I	Co-Investigator
IRB	Institutional Review Board
ECG	Electrocardiogram
IBI	Interbeat Interval
REDCap	Research Electronic Data Capture
UNC	The University of North Carolina at Chapel Hill
CTSA	Clinical and Translational Science Awards Program
FTP	File Transfer Protocol
ITS	Information Technology Services
WIC	The Special Supplemental Nutrition Program for *Women, Infants, and Children*

PROTOCOL SYNOPSIS

Study Title	*Enhancing Caregiver-Infant Communication to Prevent Obesity*
Funder	Eunice Kennedy Shriver National Institute of Child Health and Human Development
Clinical Phase	Stage 1 for Behavioral Intervention Development
Study Rationale	Once obese as an infant, the relative risk of remaining obese appears to rise with increasing age. Thus, the early years of life have been posited as an important target period for obesity prevention. Widely viewed as a response to genetic, interpersonal, and environmental factors, obesity fundamentally reflects an imbalance between energy intake and expenditure. Self-regulation of energy intake aligned with physiologic need is essential to this balance. The process(es) by which infants begin to disassociate eating behavior from physiologic need is unclear, thus it is crucial to better understand predictors of individual differences in self-regulation of energy intake. A chronic mismatch between a caregiver's feeding behavior and the infant's state (feeding in the absence of hunger and/or feeding beyond fullness), is thought to contribute to obesity by undermining the infant's capacity to self-regulate intake; the current proposal will be the first to examine the effects on autonomic regulation.
Study Objective(s)	**Primary Outcome** To evaluate the initial impact of the intervention. We expect the following for the experimental group: Infants will have more optimal growth (weight-for-length Z scores closer to 50th %) than the control group by T3. **Secondary Outcome** To evaluate the initial impact of the intervention. We expect the following for the experimental group: o Infants will have enhanced self-regulation of energy intake (closer to estimated energy requirements) than the control group by T3. **Tertiary Outcomes** To evaluate the initial impact of the intervention. We expect the following for the experimental group: o A) Dyads will demonstrate (1) improvement in observed feeding responsiveness and (2) higher observed feeding responsiveness than the control group by T3 (6-months post-baseline). o B) Mothers will (1) perceive higher infant satiety responsiveness and (2) report more responsiveness

	feeding behaviors and beliefs than the control group by T3. Evaluate the feasibility and acceptability (e.g., burden) of the intervention and study methods including recruitment, enrollment, and data collection (self-report, anthropometrics, video observations, and respiratory sinus arrhythmia [RSA]) for infants and their mothers. **Exploratory Outcome** • Explore preliminary data on concordance between dyadic feeding interactions and autonomic regulation in both mothers and infants (RSA). We expect higher observed dyadic feeding responsiveness to be associated with larger change scores in RSA (enhanced self-regulation) for both mother and infant.
Test Article(s) *(If Applicable)*	N /A
Study Design	Two-group randomized repeated measures design.
Subject Population **key criteria for Inclusion and Exclusion:**	Inclusion Criteria 1. Subjects age 3 months to 50 years. 2. Mothers must be able to read, understand, and speak English or Spanish and be willing to be randomized and participate in data collection. Those who are randomized into the experimental group must also be willing to learn ASL specific to communication of hunger, thirst, and fullness. Exclusion Criteria 1. Dyads will be excluded if infants: a. were born more than 6 weeks earlier than their estimated due date, b. have any developmental delays or disabilities that make it difficult for them to eat, drink, or communicate, c. attend regular daycare, d. or will be younger than 4 months or older than 9 months at the time of the first ASL training.
Number of Subjects	160
Study Duration	Each subject's participation will last between 6-6.5 months depending on how long it takes to schedule the last dietary recalls. The entire study is expected to last 2 years.
Study Phases **Screening**	Screening: screening for eligibility and obtaining consent

Study Treatment Follow-Up	Study Treatment: study intervention/experimental treatment from baseline visit (T1) monthly until 3-months post-baseline (T2) Follow-up: 6-months post-baseline (T3)
Efficacy Evaluations	Primary efficacy evaluation measures: 1. Infants in the intervention group will have more optimal growth (weight-for-length Z scores closer to 50th %) than the control group by T3.
Pharmacokinetic Evaluations	N/A
Safety Evaluations	• Assessment of self-reported health of parent and infant prior to data collection • Monitoring of parent's and infant's responses during intervention and data collection • Reports of adverse events
Statistical And Analytic Plan	To evaluate the initial impact of the intervention longitudinally for each maternal and infant outcome listed in the primary, secondary, and first two tertiary outcomes above, we will fit separate linear mixed-effects random coefficients models. These will model the linear trajectories of the group-specific means across all available time points using the actually observed timing. The initial impact of the intervention will be formally assessed through a statistical hypothesis test of model parameter representing the difference in these slopes. More specifically, these models will include terms for the intervention group (as an indicator variable), actual time of data collection (as continuous weeks from baseline), and their interaction. Covariates identified above to correct for imbalance will be included, as well as the factors stratified in the randomization, and the models will account for the repeated measures correlation structure. Statistical contrasts will also be constructed to estimate and test the changes over time separate for each group.
DATA AND SAFETY MONITORING PLAN	Study personnel will be on-site in subjects' homes for the duration of data collection and will monitor the response of subjects during data collection. Should any concerns arise during data collection, they will be addressed immediately by study personnel and the PI and Co-I will be notified as soon as possible if they are not on site. Though unlikely, should any concerns arise after data collection, subjects will be given the PI's contact information to share their concerns and the PI will address concerns directly or through appropriate referrals. Any concerns that arise over the course of the study will be recorded and aggregated as part of the feasibility data and shared with the research team and the IRB as necessary.

1 BACKGROUND AND RATIONALE

1.1 Introduction

Once obese as an infant, the relative risk of remaining obese appears to rise with increasing age.[1,2] Thus, the early years of life have been posited as an important target period for obesity prevention.[3] Widely viewed as a response to genetic, interpersonal, and environmental factors, obesity fundamentally reflects an imbalance between energy intake and expenditure.[3] Self-regulation of energy intake aligned with physiologic need is essential to this balance.[3,4] The process(es) by which infants begin to disassociate eating behavior from physiologic need is unclear, thus it is crucial to better understand predictors of individual differences in self-regulation of energy intake. It is well established that autonomic regulation may support infant behavioral regulation[5], suggesting that autonomic function may be a critical area to consider here. Moreover, self-regulation is strongly influenced by dyadic interaction quality during infancy, and findings reveal that more responsive interactions are associated with more effective autonomic regulation.[6] A chronic mismatch between a caregiver's feeding behavior and the infant's state (feeding in the absence of hunger and/or feeding beyond fullness), is thought to contribute to obesity by undermining the infant's capacity to self-regulate intake[7–9]; the current proposal will be the first to examine the effects on autonomic regulation.

We propose an intervention to enrich the capacity of mother-infant dyads to perform their respective interactive tasks. We plan to teach mothers American Sign Language (ASL) signs indicative of hunger, thirst, and satiety, which they will in turn teach their preverbal infant. This training in ASL will be augmented with targeted information for mothers about infants' capacities to self-regulate energy intake in response to hunger and satiety and communicate those states with intention. Mothers also will be taught about expected development of infants' eating behaviors and nutritional requirements to support healthy growth.

Using a two-group randomized repeated measures design, this study aims to 1) evaluate the feasibility and acceptability of the intervention and study methods, including recruitment, enrollment, and data collection (self-report, anthropometrics, video observations, and respiratory sinus arrhythmia [RSA]) for infants and their mothers; 2) evaluate the initial impact of the intervention on infant growth and nutritional intake, observed feeding interactions, and reported infant feeding behaviors and maternal feeding behaviors/beliefs; and, 3) explore preliminary data on concordance between dyadic feeding interactions and autonomic regulation in both mothers and infants (RSA). In addition to a variety of self-report and anthropometric measures, this study will use integrated behavioral (video) and physiologic (RSA) measures to better understand feeding dynamics and their relationship with obesity risk. Understanding these processes is essential for developing appropriate preventions, or interventions, that will help reduce the prevalence of early childhood obesity and its extension into later childhood and beyond.

The study's interventions and data collection will take place in participants' homes.

1.2 Name and Description of Investigational Product or Intervention

We propose an intervention to enrich the capacity of mother-infant dyads to perform their respective interactive tasks. We plan to teach mothers American Sign Language (ASL) signs indicative of hunger, thirst, and satiety, which they will in turn teach their preverbal infant. This training in ASL will be augmented with targeted information for mothers about infants' capacities to self-regulate energy intake in response to hunger and satiety and communicate those states with intention. Mothers also will be taught about expected development of infants' eating behaviors and nutritional requirements to support healthy growth.

1.3 Non-Clinical and Clinical Study Findings

Nearly 10% of U.S. infants were obese in 2009-2010. [10] Given increased relative risk of remaining obese later in life[1,2] and poor health consequences of childhood obesity during childhood[11] and adulthood,[12]

obesity prevention during infancy has become a priority for research.[13,14] Research in this area is relatively new and results have been mixed regarding measures of obesity.[15–25] Obesity intervention components have included: teaching caregivers strategies for improving infant sleep quality/duration[19,20], increasing infant physical activity[21–23], providing nutritional education to support breastfeeding[20–22,24], increasing food variety[16–19,21–23], appropriate timing of complementary food introduction[16–23], and increased responsiveness to infant hunger and satiety cues.[16–20,23,25] These studies report improvements in several factors that have been associated with obesity risk, including: improved infant sleep,[19,20] less TV exposure[20,22,23], decreased sweet/juice intake[18,23], delayed introduction of solids[19–21], increased breastfeeding duration[20] and/or rates[24], and increased parental responsiveness (self-reported) to infant hunger and satiety cues.[16,17] Most studies have failed to impact significantly body mass index (BMI) or Weight/Length.[17,18,20,23] Two have found a decrease in either weight for length %[19] or BMI[22] while two other studies have noted an increase in weight and length[25] or BMI.[24] While impact on BMI or Weight/Length appears equivocal, it is quite possible that effects on obesity status and growth will become evident later in development; most of the studies reported outcomes < 6 months after delivery of the last intervention component. Of importance regarding safety, none of the intervention studies demonstrated concerning weight loss or growth delay.

While the etiology of obesity is considered multifactorial, it arises fundamentally through an imbalance in energy intake and output. The aforementioned studies used multi-focal intervention components, yet there was little focus on the assessment of support for energy intake self-regulation and no focus on evidence of self-regulation (eating behavior responsive to physiologic state [i.e., hungry or satiated]). Several studies included efforts to increase caregiver responsiveness to infant hunger and satiety cues[14–18,21,23], which is thought to support self-regulation[7–9], yet only one investigative team has reported improvement in parental responsiveness (self-reported).[16,17] In short-term protocols (meal to meal), infants have demonstrated the ability to self-regulate energy intake over days[26] and weeks[27], through compensation or adjustment for variations in the energy content of food. This self-regulatory capacity appears to increasingly diminish in the years following toddlerhood, at least in short-term protocols.[28–31] Thus, it has been suggested that the first 2 years of life may be a critical period for the development of self-regulation of intake.[30]

There is strong evidence in the extant literature that social, emotional, and cognitive self-regulation[6] can be nurtured or derailed within the caregiver-infant relationship; evidence among older children suggests that self-regulation of energy intake may be influenced by the caregiving environment, too.[28,31–33] This is an integral component of our theoretical orientation, which is guided by a model linking feeding responsiveness to obesity (Figure 1). For our study, this model is situated within the larger relational developmental systems paradigm[34], in which the biological, psychological, and sociocultural systems interpenetrate and mutually influence one another over the course of development. This paradigm requires us to acknowledge that energy intake self-regulation is modifiable by relational developmental processes. Thus, we examine this phenomenon across multiple levels in order to understand its development and consider how interventions may affect it.

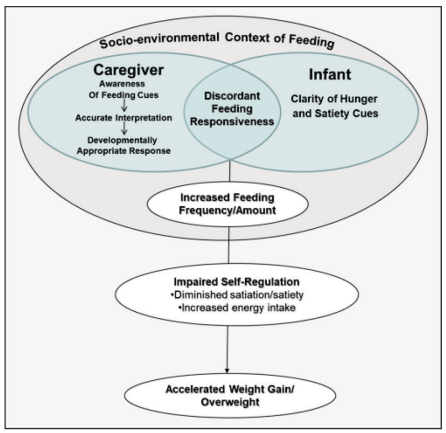


Figure 1. Feeding Responsiveness & Obesity

Although self-regulation is most easily assessed by observable behavioral patterns, it is critical to understand the psychobiological processes that support these behaviors. One of the most studied correlates of behavioral self-regulation is within the autonomic nervous system, more specifically vagal tone, which is often assessed through respiratory sinus arrhythmia (RSA).[35] Baseline cardiac patterns are considered to be a neurophysiological mechanism underlying autonomic and behavioral reactivity. Although RSA is relatively stable during a calm and restful state, it is sensitive to environmental demands and thus extant research also measures change in RSA from baseline to an external challenge.[35]

The ability to effectively reduce RSA during challenge, followed by a return to baseline levels, may be an adaptive process allowing participation in demanding tasks by shifting attention from internal homeostatic demands to external ones to support the use of coping strategies to control affective or behavioral arousal. Withdrawal of RSA (larger RSA change scores) during a challenging situation has been related to better emotion regulation in infants[5,36,37] and caregivers.[38]

Thus far, most studies of infant and toddler self-regulation of eating have focused on the contributions of temperament (e g., attention spans, soothability, negative reaction to food). Findings have revealed an association between these characteristics at 1 year of age and larger weight increases over time and obesity at 6 years of age.[39] To our knowledge, only one study has looked at the autonomic correlates of these behaviors, and found that older children (5.5 years old) who demonstrated lower levels of RSA withdrawal (a purported indicator of less regulation) during lab stressors were significantly more likely to be overweight five years later, but this was only true among African-American children.[40] This finding was unclear, but the authors suggested, "future research should examine whether individual differences in cardiac regulation relate to observable differences in children's eating behavior"(p. 1824).

In adults, obesity has been related to low baseline RSA[41–43] and smaller RSA change during a stressor.[44] Increased vagal control in adult dieters could be a physiological endophenotype of successful eating self-regulation.[45] Findings revealed that dieting success (i.e., self-control of food intake) was associated with increased parasympathetic control, even after controlling for BMI, smoking, alcohol, and exercise. We propose an innovative assessment of the development of parasympathetic function during feeding interactions earlier in life to better understand the direction of this effect. We are particularly interested in exploring patterns of infant and maternal RSA change in relation to infant and maternal behaviors during feeding, as an index of engagement and early regulation of food intake. This is particularly relevant in light of global[46] and particularly energy intake[30] development of self-regulation in infancy and toddlerhood.

Our proposed linkage of dyadic feeding responsiveness and autonomic regulation (RSA) with indicators of enhanced energy intake self-regulation, optimal growth, and adiposity addresses the call for obesity prevention efforts focused on the bidirectional, mutually responsive orientation between parent and child.[47] The study will be the first systematic assessment of a well-established communication system (ASL) to enhance dyadic communication between infants and their caregivers specific to feeding. The study acknowledges the caregiver and infant as each having a responsibility during feeding and moves beyond a focus on the caregiver to both partners, equipping them with new ways of communicating and perceiving one another during feeding. We propose to use ASL as it has been shown to facilitate communication, parental perception of infants' capacity to communicate with intent, and caregiver responsiveness with hearing infants.[48–51] Our focus on hunger, thirst, and satiety signs should not overwhelm the dyad. The public health impact could be profound if the intervention is found to be promising.

While this is an exploratory/developmental study, we do acknowledge the existing literature on additional characteristics that may affect mutual responsiveness between infant and caregiver. These include infant characteristics (temperament) and caregiver characteristics (education, socio-economic status (SES), prior parenting experience, depression and anxiety, perception of infant intention, and parenting self-efficacy).[51–54] Therefore, we plan to assess the feasibility of measuring these characteristics as part of planning for our larger future study of biopsychosocial systems and their role in obesity risk in infancy and early childhood.

1.4 Relevant Literature and Data

1. Baird J, Fisher D, Lucas P, Kleijnen J, Roberts H, Law C. Being big or growing fast: systematic review of

size and growth in infancy and later obesity. *BMJ*. 2005;331(7522):929. doi:10.1136/bmj.38586.411273.E0
2. Mei Z, Grummer-Strawn LM, Scanlon KS. Does overweight in infancy persist through the preschool years? An analysis of CDC Pediatric Nutrition Surveillance System data. *Sozial-und Präventivmedizin/Social and Preventive Medicine*. 2003;48(3):161-167.
3. Birch LL, Parker L, Burns A, eds. *Early Childhood Obesity Prevention Policies*. Washington, D.C.: National Academies Press; 2011. doi:10.17226/13124
4. Herman CP, Polivy J. The self-regulation of eating: Theoretical and practical problems. In: Vohs KD, F. BR, eds. 2nd ed. Handbook of self-regulation: Research, theory, and applications. New York: The Guilford Press; 2011:522-536.
5. Calkins SD. Cardiac vagal tone indices of temperamental reactivity and behavioral regulation in young children. *Developmental psychobiology*. 1997;31(2):125-135.
6. Propper CB, Holochwost SJ. The influence of proximal risk on the early development of the autonomic nervous system. *Developmental Review*. 2013;33(3):151-167. doi:10.1016/j.dr.2013.05.001
7. Bruch H. *Eating Disorders. Obesity, Anorexia Nervosa, and the Person Within*. Routledge & Kegan Paul.; 1974.
8. Costanzo PR, Woody EZ. Domain-specific parenting styles and their impact on the child's development of particular deviance: the example of obesity proneness. *J Soc Clin Psychol*. 1985;3(4):425-445.
9. DiSantis KI, Hodges EA, Johnson SL, Fisher JO. The role of responsive feeding in overweight during infancy and toddlerhood: a systematic review. *Int J Obes*. 2011;35(4):480-492. doi:10.1038/ijo.2011.3
10. Ogden CCL. Prevalence of Obesity and Trends in Body Mass Index Among US Children and Adolescents, 1999-2010. *JAMA : the journal of the American Medical Association*. 2012;307(5):483.
11. Pulgarón ER. Childhood obesity: a review of increased risk for physical and psychological comorbidities. *Clin Ther*. 2013;35(1):A18-32. doi:10.1016/j.clinthera.2012.12.014
12. Reilly JJ, Kelly J. Long-term impact of overweight and obesity in childhood and adolescence on morbidity and premature mortality in adulthood: systematic review. *Int J Obes*. 2011;35(7):891-898. doi:10.1038/ijo.2010.222
13. Birch LL, Anzman-Frasca S, Paul IM. Starting Early: Obesity Prevention during Infancy. 2012.
14. Dattilo AM, Birch L, Krebs NF, Lake A, Taveras EM, Saavedra JM. Need for early interventions in the prevention of pediatric overweight: a review and upcoming directions. *J Obes*. 2012;2012:1-18.
15. Barlow J, Whitlock S, Hanson S, et al. Preventing obesity at weaning: parental views about the EMPOWER programme. *Child Care Health Dev*. 2010;36(6):843-849. doi:10.1111/j.1365-2214.2010.01107.x
16. Daniels LA, Mallan KM, Battistutta D, Nicholson JM, Parey R, Magarey A. Evaluation of an intervention to promote protective infant feeding practices to prevent childhood obesity: outcomes of the NOURISH RCT at 14 months of age and 6 months post the first of two intervention modules. *International journal of obesity (2005)*. 2012;36(10):1292-1298.
17. Daniels LA, Mallan KM, Nicholson JM, Battistutta D, Magarey A. Outcomes of an early feeding practices intervention to prevent childhood obesity. *Pediatrics*. 2013;132(1):e109-18. doi:10.1542/peds.2012-2882
18. French GM, Nicholson L, Skybo T, et al. An evaluation of mother-centered anticipatory guidance to reduce obesogenic infant feeding behaviors. *Pediatrics*. 2012;130(3):e507-17. doi:10.1542/peds.2011-3027
19. Paul IM, Savage JS, Anzman SL, et al. Preventing obesity during infancy: a pilot study. *Obesity (Silver Spring)*. 2011;19(2):353-361. doi:10.1038/oby.2010.182
20. Taveras EM, Blackburn K, Gillman MW, et al. First steps for mommy and me: a pilot intervention to improve nutrition and physical activity behaviors of postpartum mothers and their infants. *Matern Child Health J*. 2011;15(8):1217-1227. doi:10.1007/s10995-010-0696-2
21. Wen LM, Baur LA, Simpson JM, Rissel C, Flood VM. Effectiveness of an early intervention on infant

feeding practices and "tummy time": a randomized controlled trial. *Arch Pediatr Adolesc Med*. 2011;165(8):701-707. doi:10.1001/archpediatrics.2011.115
22. Wen LM, Baur LA, Simpson JM, Rissel C, Wardle K, Flood VM. Effectiveness of home based early intervention on children's BMI at age 2: randomised controlled trial. *BMJ: British Medical Journal*. 2012;344.
23. Campbell KJ, Lioret S, McNaughton SA, et al. A parent-focused intervention to reduce infant obesity risk behaviors: a randomized trial. *Pediatrics*. 2013;131(4):652-660. doi:10.1542/peds.2012-2576
24. Karanja N, Lutz T, Ritenbaugh C, et al. The TOTS community intervention to prevent overweight in American Indian toddlers beginning at birth: a feasibility and efficacy study. *Journal of community health*. 2010;35(6):667-675.
25. Kavanagh KF, Cohen RJ, Heinig MJ, Dewey KG. Educational intervention to modify bottle-feeding behaviors among formula-feeding mothers in the WIC program: impact on infant formula intake and weight gain. *J Nutr Educ Behav*. 2008;40(4):244-250. doi:10.1016/j.jneb.2007.01.002
26. Pearcey SM, De Castro JM. Food intake and meal patterns of one year old infants. *Appetite*. 1997;29(2):201-212. doi:10.1006/appe.1997.0099
27. Fomon SJ, Filmer IJ, Thomas LN, Anderson TA, Nelson SE. Influence of formula concentration on caloric intake and growth of normal infants. *Acta Paediatr*. 1975;64(2):172-181. doi:10.1111/j.1651-2227.1975.tb03818.x
28. Cecil JE, Palmer CNA, Wrieden W, et al. Energy intakes of children after preloads: adjustment, not compensation. *Am J Clin Nutr*. 2005;82(2):302-308. doi:10.1093/ajcn.82.2.302
29. Fox MK, Devaney B, Reidy K, Razafindrakoto C, Ziegler P. Relationship between portion size and energy intake among infants and toddlers: evidence of self-regulation. *J Am Diet Assoc*. 2006;106(1 Suppl 1):S77-83. doi:10.1016/j.jada.2005.09.039
30. Kral TVE, 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*. 2007;86(1):41-47. doi:10.1093/ajcn/86.1.41
31. Johnson SL, Taylor-Holloway LA. Non-Hispanic white and Hispanic elementary school children's self-regulation of energy intake. *Am J Clin Nutr*. 2006;83(6):1276-1282. doi:10.1093/ajcn/83.6.1276
32. Birch LL, McPheee L, Shoba BC, Steinberg L, Krehbiel R. "Clean up your plate": Effects of child feeding practices on the conditioning of meal size. *Learn Motiv*. 1987;18(3):301-317. doi:10.1016/0023-9690(87)90017-8
33. Faith MS, Scanlon KS, Birch LL, Francis LA, Sherry B. Parent-child feeding strategies and their relationships to child eating and weight status. *Obes Res*. 2004;12(11):1711-1722. doi:10.1038/oby.2004.212
34. Overton WF. Relationism and relational developmental systems: a paradigm for developmental science in the post-Cartesian era. *Advances in Child Development and Behavior*. 2012;44:21-64.
35. Porges S. Vagal tone: An autonomic mediator of affect. In: Garber J, Dodge KA, eds. *The Development of Emotion Regulation and Dysregulation*. Cambridge: Cambridge University Press; 1991:111-128. doi:10.1017/CBO9780511663963.007
36. Porges SW, Doussard-Roosevelt JA, Portales AL, Greenspan SI. Infant regulation of the vagal "brake" predicts child behavior problems: a psychobiological model of social behavior. *Dev Psychobiol*. 1996;29(8):697-712. doi:10.1002/(SICI)1098-2302(199612)29:8<697::AID-DEV5>3.0.CO;2-O
37. Santucci AK, Silk JS, Shaw DS, Gentzler A, Fox NA, Kovacs M. Vagal tone and temperament as predictors of emotion regulation strategies in young children. *Developmental psychobiology*. 2008;50(3):205-216.
38. Moore GA, Hill-Soderlund AL, Propper CB, Calkins SD, Mills-Koonce WR, Cox MJ. Mother–Infant Vagal Regulation in the Face-To-Face Still-Face Paradigm Is Moderated by Maternal Sensitivity. *Child development*. 2009;80(1):209-223.
39. 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*. 2010;34(10):1515-1523. doi:10.1038/ijo.2010.156
40. Graziano PA, Calkins SD, Keane SP, O'Brien M. Cardiovascular regulation profile predicts developmental trajectory of BMI and pediatric obesity. *Obesity (Silver Spring)*. 2011;19(9):1818-1825. doi:10.1038/oby.2011.98
41. Coles J, Vögele C, Hilbert A, Tuschen-Caffier B. Fasten und (Über)-essen. *Zeitschrift für Klinische Psychologie und Psychotherapie*. 2005;34(2):95-103.
42. Karason K, Mølgaard H, Wikstrand J, Sjöström L. Heart rate variability in obesity and the effect of weight loss. *Am J Cardiol*. 1999;83(8):1242-1247. doi:10.1016/s0002-9149(99)00066-1
43. Latchman PL, Mathur M, Bartels MN, Axtell RS, De Meersman RE. Impaired autonomic function in normotensive obese children. *Clin Auton Res*. 2011;21(5):319-323. doi:10.1007/s10286-011-0116-8
44. Friederich HC, Schild S, Schellberg D, et al. Cardiac parasympathetic regulation in obese women with binge eating disorder. *Int J Obes*. 2006;30(3):534-542. doi:10.1038/sj.ijo.0803181
45. Meule A, Lutz A, Vögele C, Kübler A. Food cravings discriminate differentially between successful and unsuccessful dieters and non-dieters. Validation of the Food Cravings Questionnaires in German. *Appetite*. 2012;58(1):88-97. doi:10.1016/j.appet.2011.09.010
46. Calkins SD. The emergence of self-regulation: Biological and behavioral control mechanisms supporting toddler competencies.
47. Skouteris H, McCabe M, Ricciardelli LA, et al. Parent-child interactions and obesity prevention: a systematic review of the literature. *Early Child Dev Care*. 2012;182(2):153-174.
48. Thompson RRH. Enhancing Early Communication through Infant Sign Training. *J Appl Behav Anal*. 2007;40(1):15-23.
49. Vallotton CD. Infant signs as intervention? Promoting symbolic gestures for preverbal children in low-income families supports responsive parent–child relationships. *Early Child Res Q*. 2012;27(3):401-415. doi:10.1016/j.ecresq.2012.01.003
50. Góngora X, Farkas C. Infant sign language program effects on synchronic mother-infant interactions. *Infant Behav Dev*. 2009;32(2):216-225. doi:10.1016/j.infbeh.2008.12.011
51. Kirk E, Howlett N, Pine KJ, Fletcher BC. To sign or not to sign? The impact of encouraging infants to gesture on infant language and maternal mind-mindedness. *Child Dev*. 2013;84(2):574-590. doi:10.1111/j.1467-8624.2012.01874.x
52. Kochanska G, Aksan N. Development of mutual responsiveness between parents and their young children. *Child development*. 2004;75(6):1657-1676.
53. Murray L, Fiori-Cowley A, Hooper R, Cooper P. {The impact of postnatal depression and associated adversity on early mother-infant interactions and later infant outcome}. *Child development*. 1996;67(5):2512-2526.
54. Skuban EM, Shaw DS, Gardner F, Supplee LH, Nichols SR. The correlates of dyadic synchrony in high-risk, low-income toddler boys. *Infant Behavior and Development*. 2006;29(3):423-434.
55. Birch LL, Fisher JO. Development of eating behaviors among children and adolescents. *Pediatrics*. 1998;101(3 Pt 2):539-549.
56. Hodges EA, Johnson SL, Hughes SO, Hopkinson JM, Butte NF, Fisher JO. Development of the responsiveness to child feeding cues scale. *Appetite*. 2013;65:210-219. doi:10.1016/j.appet.2013.02.010
57. van Jaarsveld CHM, Llewellyn CH, Johnson L, Wardle J. Prospective associations between appetitive traits and weight gain in infancy. *Am J Clin Nutr*. 2011;94(6):1562-1567. doi:10.3945/ajcn.111.015818
58. Thompson AL, Mendez MA, Borja JB, Adair LS, Zimmer CR, Bentley ME. Development and validation of the Infant Feeding Style Questionnaire. *Appetite*. 2009;53(2):210-221. doi:10.1016/j.appet.2009.06.010
59. Gartstein MA, Rothbart MK. Studying infant temperament via the Revised Infant Behavior Questionnaire. *Infant Behavior and Development*. 2003;26(1):64-86. doi:10.1016/S0163-6383(02)00169-8
60. Chen G, Gully SM, Eden D. Validation of a New General Self-Efficacy Scale. *Organizational Research Methods*. 2001;4(1):62-83. doi:10.1177/109442810141004
61. Reznick JS, Feldman R. {Infant Intentionality Questionnaire—Version 4.2. Psychology Department,

University of North Carolina at Chapel Hill, CB{\#} 3270, Chapel Hill, NC 27599-3270}.
62. Löwe B, Wahl I, Rose M, et al. A 4-item measure of depression and anxiety: validation and standardization of the Patient Health Questionnaire-4 (PHQ-4) in the general population. *J Affect Disord*. 2010;122(1-2):86-95. doi:10.1016/j.jad.2009.06.019
63. Butte NF. Energy requirements of infants. *Public Health Nutr*. 2005;8(7A):953-967. doi:10.1079/PHN2005790
64. Brage S, Brage N, Franks PW, Ekelund U, Wareham NJ. Reliability and validity of the combined heart rate and movement sensor Actiheart. *European journal of clinical nutrition*. 2005;59(4):561-570.
65. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381. doi:10.1016/j.jbi.2008.08.010
66. Willett W. *Nutritional Epidemiology*. 2nd ed. New York: Oxford University Press; 1998.

2 STUDY OBJECTIVE

2.1 Primary Objective

To evaluate the initial impact of the intervention. We expect the following for the experimental group:

- Infants will have more optimal growth (weight-for-length Z scores closer to 50th %) than the control group by T3.

2.2 Secondary Objective

To evaluate the initial impact of the intervention. We expect the following for the experimental group:

- Infants will have enhanced self-regulation of energy intake (closer to estimated energy requirements) than the control group by T3.

3 INVESTIGATIONAL PLAN

3.1 Study Design

Two-group randomized repeated measures design with an intervention group and a control group of mother-infant dyads. For the intervention, we plan to teach mothers American Sign Language (ASL) signs indicative of hunger, thirst, and satiety, which they will in turn teach their preverbal infant. This training in ASL will be augmented with targeted information for mothers about infants' capacities to self-regulate energy intake in response to hunger and satiety and communicate those states with intention. Mothers also will be taught about expected development of infants' eating behaviors and nutritional requirements to support healthy growth. For the control group, dyads will participate in the same data collection as the intervention group and engage in their usual care provided by their health care provider, but they will not receive intervention content unless they elect to receive written lesson content once the study's data collection has ended and they have been debriefed.

Study Phases:

Screening: screening for eligibility and obtaining consent

Study Treatment: study intervention/experimental treatment from baseline visit (T1: age 4-9-months) monthly until 3-months post-baseline (T2: age 7-12-months)

Follow-up: 6-months post-baseline (T3: age 10-15-months)

3.2 Allocation to Treatment Groups and Blinding

Randomization will be stratified by age group (for developmental differences; 4-5-months-old, 6-7-months-old, and 8-9-months old). Computerized randomization lists will be generated by study

statistician and will be administered by the project manager. Study personnel who code videos of feeding interactions will be blind to group status.

3.3 Study Duration, Enrollment and Number of Subjects

We plan for 80 parent-infant dyads (160 subjects) randomized to invention (40 dyads) or control (usual care; 40 dyads). Length of participation will be 6-6.5 months and planned study duration is 2 years.

3.4 Study Population

Inclusion Criteria

1. Subjects age 3 months to 50 years.
2. Mothers must be able to read, understand, and speak English or Spanish and be willing to be randomized and participate in data collection. Those who are randomized into the experimental group must also be willing to learn ASL specific to communication of hunger, thirst, and fullness.

Exclusion Criteria

1. Dyads will be excluded if infants:
    a. were born more than 6 weeks earlier than their estimated due date,
    b. have any developmental delays or disabilities that make it difficult for them to eat, drink, or communicate,
    c. attend regular daycare,
    d. or will be younger than 4 months or older than 9 months at the time of the first ASL training.

4 STUDY PROCEDURES

4.1 Screening/Baseline Visit procedures: Families will be recruited from a community sample through a variety of means, including email listservs, in-person interactions with study personnel, social media posting to local parenting groups, and publicly posted flyers. Those wishing to learn more about the study will contact our project manager, who will conduct screening and enrollment for those wishing to participate in the study.

4.2 Intervention/Treatment procedures (by visits): Intervention families will receive approximately 4 hours of ASL and development specific content related to language and feeding during home visits and phone calls. The initial in-home session with families will focus on teaching ASL signs indicative of hunger, thirst, and satiety. A video and placemat of mealtime signs will be left with families at the completion of the first visit. The remaining sessions, in-home over the next 3 months and by phone monthly thereafter for 6 months total, will focus on reinforcing ASL signing in addition to focused education on particular aspects of language development (receptive language preceding expressive language and increasing intentional communication), feeding development (such as hunger and fullness cues, fear of new foods, the importance of repeated food exposures, variations in intake from meal-to-meal, and the propensity to reject bitter tastes [many vegetables][55]], and appropriate portion sizes and variety for healthy growth.

In person visit lesson schedule (monthly from baseline at 4-9 months of age):
Visit 1 (baseline: T1): Signing with infants
Visit 2: Infant communication and responsive feeding
Visit 3: Nutrition, portion sizes, and neophobia
Visit 4 (T2): Infant intentionality

All families will be offered $25, $30, and $35 at T1, T2, and T3 data collections, respectively. At the end of the study, control families will have the opportunity at the end of the 6-month study period to learn about what educational content was offered to the Experimental Group and study personnel will provide a booklet of this content to them and an ASL Signs of Feeding placemat if they wish.
If subjects withdraw or are withdrawn from the study prior to arrival of the study personnel at their home for data collection, then no monetary incentive will be offered. If participating parent or infant withdraws or is withdrawn from the study once data collection has been initiated in their home, they will be offered one half of the possible monetary incentive amount for that visit for their attempt to participate. All subjects will be thanked for their interest and participation regardless of whether they complete all data collections.

See section 5 below for data collected at each visit.

4.3 Follow- up procedures (by visits): Within a week of T1, T2, and T3 (6-months post-baseline), two 24-hour dietary recalls (to account for day-to-day variation) will be collected using NDS-R software by telephone five to 10 days apart. Intervention participants will also be contacted by the project manager with 48-hours of in-home study visits (1-4 above) to assess whether relevant intervention content was delivered.

4.4 Unscheduled visits: N/A

4.5 Concomitant Medication documentation: N/A

4.6 Rescue medication administration (if applicable): N/A

4.7 Subject Completion/ Withdrawal procedures: Subjects will complete the study at the completion of data collection associated with T3. At the end of the in-home data-collection visit at T3, all participants will be asked to provide feedback on their experiences with recruitment, interactions with study personnel, data collection, and anything else they would like to share about the study. If a participating dyad chooses to withdraw from the study or we are unable to reach them after three attempts for scheduling of visits or data collection, they will be withdrawn from the study, but their data will be kept for analysis. All subjects will be thanked for their interest and participation regardless of whether they complete all data collections.

4.8 Screen failure procedures: If the subject and/or child do not meet inclusion criteria, then inform them that they do not meet inclusion criteria for this particular study, ask if they would be interested in being contacted about future studies, and thank them for their time.

5 STUDY EVALUATIONS AND MEASUREMENTS

Variables and Their Measurement	**Measure**	**Data Source**	**T1**	**T2**	**T3**	**Alpha**
Aims 1: Feasibility & Acceptability	Screening and Enrollment logs	Project Manager	X			
	Field Notes	RA's	X	X	X	
	Exit Interview	Mothers			X	
Aims 2 & 3						
Dyadic Feeding Responsiveness						
Mutual Responsiveness during	Responsiveness to Child Feeding Cues Scale (RCFCS) [56]	Infants & Mothers	X	X	X	0.85-0.94

Feeding						
Infant Eating Behavior						
Dietary Intake	Nutrition Data System for Research (NDS-R)	Mothers	X	X	X	
Eating Behavior	Child Eating Behavior Questionnaire-Toddler (CEBQ-T) [57]	Mothers	X	X	X	0.65-0.87
Infant Anthropometry						
Growth	Weight-for-length% & Z score	Infants	X	X	X	
Maternal Feeding Behavior/Beliefs	Infant Feeding Styles Questionnaire (IFSQ) [58]	Mothers	X	X	X	0.75-0.94[b]
Autonomic Regulation	Respiratory Sinus Arrythmia (RSA)	Infants & Mothers	X	X	X	
Additional Characteristics						
Infant						
Temperament	Revised Infant Behavior Questionnaire (IBQR) [59]	Mothers	X	X	X	0.91-0.92
Sex, Birthweight, & Gestational Age	Demographics	Mothers	X			
Maternal						
Parental Self-Efficacy	New Generalized Self-Efficacy Scale (NGSE) [60]	Mothers	X	X	X	0.85-0.88
Perception of Infant Intentionality	Infant Intentionality Questionnaire (IIQ) [61]	Mothers	*X*	*X*	*X*	0.77-0.87
Depression & Anxiety	Patient Health Questionnaire-4 (PHQ-4) [62]	Mothers	X	X	X	0.82
Demographic Characteristics	Demographics & Pregnancy History	Mothers	X			

5.1 Efficacy Evaluation: N/A

5.2 Pharmacokinetic Evaluation (if applicable): N/A

5.3 Safety Evaluations: Study visit confirmation will occur prior to study visits and assessment of self-reported health of parent and infant will be conducted prior to data collection. Study personnel will be on-site in subjects' homes for the duration of data collection and will monitor the response of subjects during data collection. Should any concerns arise during data collection, they will be addressed immediately by study personnel and the PI and Co-I will be notified as soon as possible if they are not on site. Though unlikely, should any concerns arise after data collection, subjects will be given the PI's contact information to share their concerns and the PI will address concerns directly or through appropriate referrals. Any concerns that arise over the course of the study will be recorded and aggregated as part of the feasibility data and shared with the research team and the IRB as necessary.

6 STATISTICAL CONSIDERATION

6.1 Primary Endpoint

T3 (6-months post-baseline) will serve as the primary endpoint for the study.

6.2 Secondary Endpoint

There are no plans for a secondary endpoint, though safety will be monitored as discussed above in 5.3.

6.3 Statistical Methods

Descriptive statistics will be calculated for each measure (see Aims 2 & 3 in Table of Measures, Section 5) at each time point by group. All analyses will be conducted using an intention-to-treat approach.

Preliminary analyses will be conducted to determine whether, despite randomization, the intervention and control groups exhibit a random imbalance at baseline on any measured variable. If important imbalances are found, the corresponding variable will be considered as a covariate in subsequent models to statistically correct for the imbalance. To evaluate the initial impact of the intervention longitudinally for each maternal and infant outcome listed above as primary, secondary, and the first two tertiary outcomes (i.e., more optimal growth, indicators of enhanced self-regulation of energy intake [NDS-R data compared to age- and sex-specific estimated energy requirements[63]], reported infant feeding behavior and maternal feeding behaviors/beliefs , and observed dyadic feeding responsiveness), we will fit separate linear mixed-effects models. These could include a random coefficients model to examine the linear trajectories of the group-specific means across all available time points using the actually observed timing. The initial impact of the intervention will be formally assessed through a statistical hypothesis test of model parameter representing the difference in these slopes. More specifically, these models will include terms for the intervention group (as an indicator variable), actual time of data collection (as continuous weeks from baseline), and their interaction. An alternative modeling strategy would be to utilize mixed-effects model in a repeated measures context to examine the trajectories of the group-specific means across all available time points using the visit timepoint; these models will include terms for the intervention group (as an indicator variable), visit timepoint (as one or more indicators to reflect this categorical variable), and their interaction term(s). In this scenario, the initial impact of the intervention will be formally assessed through a statistical hypothesis test of linear contrasts of model parameters representing the between-group difference at each timepoint. Covariates identified above to correct for imbalance will be considered for inclusion in these models, as well as the factors stratified in the randomization, and the models will account for the repeated measures correlation structure. Statistical contrasts will also be constructed to estimate and test the changes over time separately for each intervention group. As useful information for planning subsequent studies, effect sizes for each measure will be calculated for each follow-up time point as the ratio of the mean difference between the intervention and the control groups to its standard deviation, as well as the producing the estimated correlation matrices across the repeated measures.

6.4 Sample Size and Power: Dyads will be randomized to either the intervention (n = 40) or the control (n = 40) group. Conservatively, a 20% attrition rate will be assumed, though less attrition will result in greater statistical power. Hence, we assume two-group, longitudinal comparisons of complete data on 32 dyads per group, as well as incomplete data (at some, but not all, time points), for analyses of each measure. Power calculations are performed with the POWERLIB20 SAS/IML module, which incorporates methods to calculate power for the general linear multivariate model, which is closely related to the general linear mixed model, assuming a first-order autoregressive correlation structure across the repeated measures with parameter p=0.9. We intend to estimate the power for the initial impact of the intervention through a test of mean linear change between the two groups across the three timepoints for each maternal and infant outcome in Aim 2 in separate multivariate models. The study will be well-powered to detect moderate changes in slope across the group trajectories over time. A linear difference of .4 SD by T3 with 32 dyads per group will provide statistical power exceeding .86 at the one-sided .05 significance level.

6.5 Interim Analysis: N/A

7 STUDY INTERVENTION

Intervention families will receive approximately 4 hours of ASL and development specific content related to language and feeding during home visits and phone calls. The initial in-home session with families will focus on teaching ASL signs indicative of hunger, thirst, and satiety. A video and placemat of mealtime signs will be left with families at the completion of the first visit. The remaining sessions, in-

home over the next 3 months and by phone monthly thereafter for 6 months total, will focus on reinforcing ASL signing in addition to focused education on particular aspects of language development (receptive language preceding expressive language and increasing intentional communication), feeding development (such as hunger and fullness cues, fear of new foods, the importance of repeated food exposures, variations in intake from meal-to-meal, and the propensity to reject bitter tastes [many vegetables][55]], and appropriate portion sizes and variety for healthy growth.

In person visit lesson schedule (monthly from baseline at 4-9 months of age):
Visit 1 (baseline: T1): Signing with infants
Visit 2: Infant communication and responsive feeding
Visit 3: Nutrition, portion sizes, and neophobia
Visit 4 (T2): Infant intentionality

Intervention participants will be contacted by the project manager with 48-hours of in-home study visits (1-4 above) to assess and record whether relevant intervention content was delivered.

8 STUDY INTERVENTION ADMINISTRATION

Randomization will be stratified by age group (for developmental differences; 4-5-months-old, 6-7-months-old, and 8-9-months old). Computerized randomization lists will be generated by study statistician and will be administered by the project manager. Study personnel who code videos of feeding interactions will be blind to group status.

9 SAFETY MANAGEMENT

Study visit confirmation will occur prior to study visits and assessment of self-reported health of parent and infant will be conducted prior to data collection. Study personnel will be on-site in subjects' homes for the duration of data collection and will monitor the response of subjects during data collection. Should any concerns arise during data collection, they will be addressed immediately by study personnel and the PI and Co-I will be notified as soon as possible if they are not on site. Though unlikely, should any concerns arise after data collection, subjects will be given the PI's contact information to share their concerns and the PI will address concerns directly or through appropriate referrals. Any concerns that arise over the course of the study will be recorded and aggregated as part of the feasibility data and shared with the research team and the IRB as necessary.

We do not anticipate that any questions, anthropometric measurements, observations, or collection of cardiac data will cause discomfort or embarrassment, but mothers may stop interviews at any time, tell us that they do not wish to answer a question, refuse to allow infant measurement, stop an observation, or refuse collection of cardiac data at any time. We will respect their wishes. We will also let parents/primary caregivers know the following: "In addition, there may be uncommon or previously unknown risks that might occur. You should report any problems to the researchers. We are mandated to report any instances of child abuse."

Thus, individual subjects may electively withdraw from the study or the PI may withdraw an individual subject, or in this case mother-infant dyad, if they fail or are unable to comply with study procedures.

10 DATA COLLECTION AND MANAGMENT

Home visits will be scheduled to start about 45 minutes before a normal feeding time. Mothers will provide all food and will be encouraged to feed their children a typical meal. Upon arrival, four tripod-mounted digital video cameras will be set up; two in the typical place the baby is fed and two in the room

where the rest of data collection will take place to minimize participant reactivity. After ASL and knowledge content delivery by the parent educator (experimental group only), participants will then prepare for cardiac data monitoring and video-recording. The initial period of training by the parent educator should allow some time for mother and child to adjust to the presence of study staff in their home and recover from any physiological arousal or reactivity in response to them. Then, an ambulatory electrocardiogram (ECG) monitor will be placed on mother's and infant's chests in order to record RSA patterns throughout the observation. This single channel ECG waveform recorder (Actiwave Cardio; Camntech) will be connected to two disposable ECG electrodes (ConMed Neonatal/Pediatric Huggables) placed below the sternum and on the left side of the body (connected to each other by a short lead). The Actiwave Cardio monitors are flat, lightweight (<8 g), and comfortable with high levels of intra- and inter-instrument reliability as well as good validity of measures.[64] Interbeat interval (IBI) data will be monitored and recorded for R-wave detection (providing an estimate of the degree of vagal influence on heart rate). RA's will instruct mothers on how to place 2 electrodes onto her chest and her infant's chest. After a brief test of the signal strength, the infant's length and weight (in clean dry diaper only) will be measured in triplicate, using a calibrated length board and digital scale. Given the much shorter duration of our proposed monitoring (~1 hour), we feel confident in our ability to capture RSA data in both mother and infant. Then, mothers and infants will be given a 5-minute break to relax in order to give them time for de-escalation after physical measurements. Next, infants will listen to soothing music while seated in a baby seat (or other arrangement recommended by mother; for example, if infant is more comfortable and less likely to become distressed on a blanket or in a crib, we will do this instead) and mothers will read a neutral magazine (gardening) for a 4-min baseline measurement. Monitors will be worn for the entirety of the visit and feeding events will be marked within the time-stamped data. Video-recording will begin after intervention (or usual care) delivery, with mothers asked to wait at least 10 minutes after the video-recording begins before feeding their child. They can then feed their child whenever they feel it is appropriate. One camera will focus on the mother's facial expressions and movements and the second camera will focus on the infant's facial expressions and movements. As long as the infant is stationary during feeding (in mother's lap, a highchair, or booster seat), the infant's videographer will focus the camera at the beginning of the recording and then step away from the camera to minimize intrusiveness. Both videographers will swivel the camera and use the digital zoom to follow mother or child throughout the observation. From this position, the videographers can use the digital viewfinder and be out of view from the feeding room if possible. Video-recording will last until 2 minutes after the child's last bite of food. We are currently testing and refining these data collection protocols. All other self-report data from questionnaires other than NDSR will be entered in the field using Research Electronic Data Capture (REDCap)[65] through UNC-Chapel Hill CTSA. Within a week of T1, T2, and T3, two 24-hour recalls (to account for day-to-day variation) will be collected using NDS-R software by telephone five to 10 days apart. Twenty-four-hour recalls provide intake during a specified period, are open-ended, can accommodate various foods or food combinations, do not require literacy and have a relatively low respondent burden. [66]

In order to protect against breach of confidentiality, access to relevant data will be restricted to research team members for the proposed study. All data other than the videos will be accessible only through a password-protected database (REDCap). Video and cardiac data will be downloaded from their respective collection devices and transmitted via secure authentication through the UNC ITS Research Computing Secure FTP Server. Video and cardiac data will then be downloaded onto encrypted and password protected external hard drives that will be housed in one locked room within the Observational Suite of the Biobehavioral Laboratory in the UNC School of Nursing. Research assistants involved in data collection will notify the PI and Co-I when new data is available for review in the Biobehavioral Laboratory. Dr. Hodges will supervise access to the videos by the two research assistants involved in video coding.

11 RECRUITMENT STRATEGY

Families will be recruited from a community sample through a variety of means, including email listservs, in-person interactions with study personnel, social media posting to local parenting groups, publicly posted flyers, posting on Craigslist, and contact through local church leaders. Those wishing to learn more about the study will contact our project manager, who will conduct screening and initial enrollment for those wishing to participate in the study. In the case of social media (a local parenting group on Facebook in this case), our rationale is accessing a local community of parents as potential participants in the study. Dr. Hodges has permission from the moderator of this local parenting group to post information about the study to their group. The information would match what we have submitted to the IRB for consideration as the email to go out across the UNC listserv. We will designate that the posting is only to let families know about the study and that any questions should not be asked on the Facebook site, but instead directed to our project manager at her email or phone. No data will be collected through social media; it is purely informational to facilitate recruitment contact through email or phone directly to project manager. As Dr. Hodges will be the one posting the announcement about the study within the group, he can respond to anyone who does pose questions on Facebook and direct them to contact our project manager rather than use Facebook. If possible, Dr. Hodges will turn off the comment feature on the post to prevent disclosure of the identities of people interested in the study. In-person recruitment strategies include approaching caregivers with infants in waiting rooms of WIC clinics to ask if they are interested in learning about the study. Any conversation regarding the specifics of the study should be conducted in a private location. The onsite recruiter will notify subjects that their decision to participate in the study will not affect the care they receive at the clinic. To protect the privacy of potential subjects during recruitment, eligible and interested subjects will be screened in a private room. If a private room is unavailable, subjects will be screened and initially enrolled in the study via phone at a later date. Identification through local church leaders will be through church leaders' willingness to share information from our study flyer with their congregation.

Those wishing to learn more about the study will contact our project manager, who will conduct screening and initial enrollment for those wishing to participate in the study. Screening and initial enrollment occurs by telephone. Any contact information for individuals who decline to participate or are not eligible is immediately deleted from the contact database.

Potential subjects will be contacted through their preferred method, telephone or email. An initial email from the project manager, research assistant, or PI will include a question about whether our research team can leave a voicemail with a request for call back. If potential subjects choose to call rather than email and they are put through to voicemail, the voicemail will instruct them to answer the question about whether our research team can leave a voicemail with a request for call back. Contact information will be entered into a password protected contact database.

12 CONSENT PROCESS

Subjects will be contacted by telephone prior to the home visit for data collection. During the telephone conversation, the study will be described and telephone consent to participate will be obtained. Once in the family home, the study will be described once more and written consent will be obtained.

We have put together a combined Adult Consent and Parental Permission form. Parents will be given the form for review on-site and study staff will go through the permission form verbally with the parent(s)

and offer to answer any questions prior to parental signature. If mothers of infants are adolescents, we will obtain their permission for their infant to participate, their assent to participate, and their parent or legal guardian's permission for them (the adolescent parent) to participate. We will have Spanish language versions of the Combined Adult Consent and Parental Permission forms for review in Spanish-speaking participants' homes. A bilingual research staff member on site will provide oral interpretation as needed.

13 PLANS FOR PUBLICATION

We plan to disseminate findings from primary, secondary, and tertiary outcomes through top-tier pediatric and nutrition journals.

14 REFERENCES: See Bibliography below.

Bibliography

1. Baird J, Fisher D, Lucas P, Kleijnen J, Roberts H, Law C. Being big or growing fast: systematic review of size and growth in infancy and later obesity. *BMJ*. 2005;331(7522):929. doi:10.1136/bmj.38586.411273.E0
2. Mei Z, Grummer-Strawn LM, Scanlon KS. Does overweight in infancy persist through the preschool years? An analysis of CDC Pediatric Nutrition Surveillance System data. *Sozial-und Präventivmedizin/Social and Preventive Medicine*. 2003;48(3):161-167.
3. Birch LL, Parker L, Burns A, eds. *Early Childhood Obesity Prevention Policies*. Washington, D.C.: National Academies Press; 2011. doi:10.17226/13124
4. Herman CP, Polivy J. The self-regulation of eating: Theoretical and practical problems. In: Vohs KD, F. BR, eds. 2nd ed. Handbook of self-regulation: Research, theory, and applications. New York: The Guilford Press; 2011:522-536.
5. Calkins SD. Cardiac vagal tone indices of temperamental reactivity and behavioral regulation in young children. *Developmental psychobiology*. 1997;31(2):125-135.
6. Propper CB, Holochwost SJ. The influence of proximal risk on the early development of the autonomic nervous system. *Developmental Review*. 2013;33(3):151-167. doi:10.1016/j.dr.2013.05.001
7. Bruch H. *Eating Disorders. Obesity, Anorexia Nervosa, and the Person Within*. Routledge & Kegan Paul.; 1974.
8. Costanzo PR, Woody EZ. Domain-specific parenting styles and their impact on the child's development of particular deviance: the example of obesity proneness. *J Soc Clin Psychol*. 1985;3(4):425-445.
9. DiSantis KI, Hodges EA, Johnson SL, Fisher JO. The role of responsive feeding in overweight during infancy and toddlerhood: a systematic review. *Int J Obes*. 2011;35(4):480-492. doi:10.1038/ijo.2011.3
10. Ogden CCL. Prevalence of Obesity and Trends in Body Mass Index Among US Children and Adolescents, 1999-2010. *JAMA : the journal of the American Medical Association*. 2012;307(5):483.
11. Pulgarón ER. Childhood obesity: a review of increased risk for physical and psychological comorbidities. *Clin Ther*. 2013;35(1):A18-32. doi:10.1016/j.clinthera.2012.12.014
12. Reilly JJ, Kelly J. Long-term impact of overweight and obesity in childhood and adolescence on morbidity and premature mortality in adulthood: systematic review. *Int J Obes*. 2011;35(7):891-898. doi:10.1038/ijo.2010.222
13. Birch LL, Anzman-Frasca S, Paul IM. Starting Early: Obesity Prevention during Infancy. 2012.
14. Dattilo AM, Birch L, Krebs NF, Lake A, Taveras EM, Saavedra JM. Need for early interventions in the prevention of pediatric overweight: a review and upcoming directions. *J Obes*. 2012;2012:1-18.
15. Barlow J, Whitlock S, Hanson S, et al. Preventing obesity at weaning: parental views about the

EMPOWER programme. *Child Care Health Dev*. 2010;36(6):843-849. doi:10.1111/j.1365-2214.2010.01107.x
16. Daniels LA, Mallan KM, Battistutta D, Nicholson JM, Parey R, Magarey A. Evaluation of an intervention to promote protective infant feeding practices to prevent childhood obesity: outcomes of the NOURISH RCT at 14 months of age and 6 months post the first of two intervention modules. *International journal of obesity (2005)*. 2012;36(10):1292-1298.
17. Daniels LA, Mallan KM, Nicholson JM, Battistutta D, Magarey A. Outcomes of an early feeding practices intervention to prevent childhood obesity. *Pediatrics*. 2013;132(1):e109-18. doi:10.1542/peds.2012-2882
18. French GM, Nicholson L, Skybo T, et al. An evaluation of mother-centered anticipatory guidance to reduce obesogenic infant feeding behaviors. *Pediatrics*. 2012;130(3):e507-17. doi:10.1542/peds.2011-3027
19. Paul IM, Savage JS, Anzman SL, et al. Preventing obesity during infancy: a pilot study. *Obesity (Silver Spring)*. 2011;19(2):353-361. doi:10.1038/oby.2010.182
20. Taveras EM, Blackburn K, Gillman MW, et al. First steps for mommy and me: a pilot intervention to improve nutrition and physical activity behaviors of postpartum mothers and their infants. *Matern Child Health J*. 2011;15(8):1217-1227. doi:10.1007/s10995-010-0696-2
21. Wen LM, Baur LA, Simpson JM, Rissel C, Flood VM. Effectiveness of an early intervention on infant feeding practices and "tummy time": a randomized controlled trial. *Arch Pediatr Adolesc Med*. 2011;165(8):701-707. doi:10.1001/archpediatrics.2011.115
22. Wen LM, Baur LA, Simpson JM, Rissel C, Wardle K, Flood VM. Effectiveness of home based early intervention on children's BMI at age 2: randomised controlled trial. *BMJ: British Medical Journal*. 2012;344.
23. Campbell KJ, Lioret S, McNaughton SA, et al. A parent-focused intervention to reduce infant obesity risk behaviors: a randomized trial. *Pediatrics*. 2013;131(4):652-660. doi:10.1542/peds.2012-2576
24. Karanja N, Lutz T, Ritenbaugh C, et al. The TOTS community intervention to prevent overweight in American Indian toddlers beginning at birth: a feasibility and efficacy study. *Journal of community health*. 2010;35(6):667-675.
25. Kavanagh KF, Cohen RJ, Heinig MJ, Dewey KG. Educational intervention to modify bottle-feeding behaviors among formula-feeding mothers in the WIC program: impact on infant formula intake and weight gain. *J Nutr Educ Behav*. 2008;40(4):244-250. doi:10.1016/j.jneb.2007.01.002
26. Pearcey SM, De Castro JM. Food intake and meal patterns of one year old infants. *Appetite*. 1997;29(2):201-212. doi:10.1006/appe.1997.0099
27. Fomon SJ, Filmer IJ, Thomas LN, Anderson TA, Nelson SE. Influence of formula concentration on caloric intake and growth of normal infants. *Acta Paediatr*. 1975;64(2):172-181. doi:10.1111/j.1651-2227.1975.tb03818.x
28. Cecil JE, Palmer CNA, Wrieden W, et al. Energy intakes of children after preloads: adjustment, not compensation. *Am J Clin Nutr*. 2005;82(2):302-308. doi:10.1093/ajcn.82.2.302
29. Fox MK, Devaney B, Reidy K, Razafindrakoto C, Ziegler P. Relationship between portion size and energy intake among infants and toddlers: evidence of self-regulation. *J Am Diet Assoc*. 2006;106(1 Suppl 1):S77-83. doi:10.1016/j.jada.2005.09.039
30. Kral TVE, 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*. 2007;86(1):41-47. doi:10.1093/ajcn/86.1.41
31. Johnson SL, Taylor-Holloway LA. Non-Hispanic white and Hispanic elementary school children's self-regulation of energy intake. *Am J Clin Nutr*. 2006;83(6):1276-1282. doi:10.1093/ajcn/83.6.1276
32. Birch LL, McPheee L, Shoba BC, Steinberg L, Krehbiel R. "Clean up your plate": Effects of child feeding practices on the conditioning of meal size. *Learn Motiv*. 1987;18(3):301-317. doi:10.1016/0023-9690(87)90017-8

33. Faith MS, Scanlon KS, Birch LL, Francis LA, Sherry B. Parent-child feeding strategies and their relationships to child eating and weight status. *Obes Res*. 2004;12(11):1711-1722. doi:10.1038/oby.2004.212
34. Overton WF. Relationism and relational developmental systems: a paradigm for developmental science in the post-Cartesian era. *Advances in Child Development and Behavior*. 2012;44:21-64.
35. Porges S. Vagal tone: An autonomic mediator of affect. In: Garber J, Dodge KA, eds. *The Development of Emotion Regulation and Dysregulation*. Cambridge: Cambridge University Press; 1991:111-128. doi:10.1017/CBO9780511663963.007
36. Porges SW, Doussard-Roosevelt JA, Portales AL, Greenspan SI. Infant regulation of the vagal "brake" predicts child behavior problems: a psychobiological model of social behavior. *Dev Psychobiol*. 1996;29(8):697-712. doi:10.1002/(SICI)1098-2302(199612)29:8<697::AID-DEV5>3.0.CO;2-O
37. Santucci AK, Silk JS, Shaw DS, Gentzler A, Fox NA, Kovacs M. Vagal tone and temperament as predictors of emotion regulation strategies in young children. *Developmental psychobiology*. 2008;50(3):205-216.
38. Moore GA, Hill-Soderlund AL, Propper CB, Calkins SD, Mills-Koonce WR, Cox MJ. Mother–Infant Vagal Regulation in the Face-To-Face Still-Face Paradigm Is Moderated by Maternal Sensitivity. *Child development*. 2009;80(1):209-223.
39. 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*. 2010;34(10):1515-1523. doi:10.1038/ijo.2010.156
40. Graziano PA, Calkins SD, Keane SP, O'Brien M. Cardiovascular regulation profile predicts developmental trajectory of BMI and pediatric obesity. *Obesity (Silver Spring)*. 2011;19(9):1818-1825. doi:10.1038/oby.2011.98
41. Coles J, Vögele C, Hilbert A, Tuschen-Caffier B. Fasten und (Über)-essen. *Zeitschrift für Klinische Psychologie und Psychotherapie*. 2005;34(2):95-103.
42. Karason K, Mølgaard H, Wikstrand J, Sjöström L. Heart rate variability in obesity and the effect of weight loss. *Am J Cardiol*. 1999;83(8):1242-1247. doi:10.1016/s0002-9149(99)00066-1
43. Latchman PL, Mathur M, Bartels MN, Axtell RS, De Meersman RE. Impaired autonomic function in normotensive obese children. *Clin Auton Res*. 2011;21(5):319-323. doi:10.1007/s10286-011-0116-8
44. Friederich HC, Schild S, Schellberg D, et al. Cardiac parasympathetic regulation in obese women with binge eating disorder. *Int J Obes*. 2006;30(3):534-542. doi:10.1038/sj.ijo.0803181
45. Meule A, Lutz A, Vögele C, Kübler A. Food cravings discriminate differentially between successful and unsuccessful dieters and non-dieters. Validation of the Food Cravings Questionnaires in German. *Appetite*. 2012;58(1):88-97. doi:10.1016/j.appet.2011.09.010
46. Calkins SD. The emergence of self-regulation: Biological and behavioral control mechanisms supporting toddler competencies.
47. Skouteris H, McCabe M, Ricciardelli LA, et al. Parent-child interactions and obesity prevention: a systematic review of the literature. *Early Child Dev Care*. 2012;182(2):153-174.
48. Thompson RRH. Enhancing Early Communication through Infant Sign Training. *J Appl Behav Anal*. 2007;40(1):15-23.
49. Vallotton CD. Infant signs as intervention? Promoting symbolic gestures for preverbal children in low-income families supports responsive parent–child relationships. *Early Child Res Q*. 2012;27(3):401-415. doi:10.1016/j.ecresq.2012.01.003
50. Góngora X, Farkas C. Infant sign language program effects on synchronic mother-infant interactions. *Infant Behav Dev*. 2009;32(2):216-225. doi:10.1016/j.infbeh.2008.12.011
51. Kirk E, Howlett N, Pine KJ, Fletcher BC. To sign or not to sign? The impact of encouraging infants to gesture on infant language and maternal mind-mindedness. *Child Dev*. 2013;84(2):574-590. doi:10.1111/j.1467-8624.2012.01874.x
52. Kochanska G, Aksan N. Development of mutual responsiveness between parents and their young children. *Child development*. 2004;75(6):1657-1676.

53. Murray L, Fiori-Cowley A, Hooper R, Cooper P. {The impact of postnatal depression and associated adversity on early mother-infant interactions and later infant outcome}. *Child development*. 1996;67(5):2512-2526.
54. Skuban EM, Shaw DS, Gardner F, Supplee LH, Nichols SR. The correlates of dyadic synchrony in high-risk, low-income toddler boys. *Infant Behavior and Development*. 2006;29(3):423-434.
55. Birch LL, Fisher JO. Development of eating behaviors among children and adolescents. *Pediatrics*. 1998;101(3 Pt 2):539-549.
56. Hodges EA, Johnson SL, Hughes SO, Hopkinson JM, Butte NF, Fisher JO. Development of the responsiveness to child feeding cues scale. *Appetite*. 2013;65:210-219. doi:10.1016/j.appet.2013.02.010
57. van Jaarsveld CHM, Llewellyn CH, Johnson L, Wardle J. Prospective associations between appetitive traits and weight gain in infancy. *Am J Clin Nutr*. 2011;94(6):1562-1567. doi:10.3945/ajcn.111.015818
58. Thompson AL, Mendez MA, Borja JB, Adair LS, Zimmer CR, Bentley ME. Development and validation of the Infant Feeding Style Questionnaire. *Appetite*. 2009;53(2):210-221. doi:10.1016/j.appet.2009.06.010
59. Gartstein MA, Rothbart MK. Studying infant temperament via the Revised Infant Behavior Questionnaire. *Infant Behavior and Development*. 2003;26(1):64-86. doi:10.1016/S0163-6383(02)00169-8
60. Chen G, Gully SM, Eden D. Validation of a New General Self-Efficacy Scale. *Organizational Research Methods*. 2001;4(1):62-83. doi:10.1177/109442810141004
61. Reznick JS, Feldman R. {Infant Intentionality Questionnaire—Version 4.2. Psychology Department, University of North Carolina at Chapel Hill, CB{\#} 3270, Chapel Hill, NC 27599-3270}.
62. Löwe B, Wahl I, Rose M, et al. A 4-item measure of depression and anxiety: validation and standardization of the Patient Health Questionnaire-4 (PHQ-4) in the general population. *J Affect Disord*. 2010;122(1-2):86-95. doi:10.1016/j.jad.2009.06.019
63. Butte NF. Energy requirements of infants. *Public Health Nutr*. 2005;8(7A):953-967. doi:10.1079/PHN2005790
64. Brage S, Brage N, Franks PW, Ekelund U, Wareham NJ. Reliability and validity of the combined heart rate and movement sensor Actiheart. *European journal of clinical nutrition*. 2005;59(4):561-570.
65. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381. doi:10.1016/j.jbi.2008.08.010
66. Willett W. *Nutritional Epidemiology*. 2nd ed. New York: Oxford University Press; 1998.