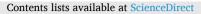
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Characterization of a Vigorous sucking style in early infancy and its predictive value for weight gain and eating behaviors at 12 months

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ABSTRACT

This study sought to identify sucking profiles among healthy, full-term infants and assess their predictive value for future weight gain and eating behaviors. Pressure waves of infant sucking were captured during a typical feeding at age 4 months and quantified via 14 metrics. Anthropometry was measured at 4 and 12 months, and eating behaviors were measured by parent report via the Children's Eating Behavior Questionnaire-Toddler (CEBQ-T) at 12 months. Sucking profiles were created using a clustering approach on the pressure wave metrics, and utility of these profiles was assessed for predicting which infants will have weight-for-age (WFA) percentile changes from ages 4–12 months that exceed thresholds of 5, 10, and 15 percentiles, and for estimating each CEBQ-T subscale score. Among 114 infants, three sucking profiles were identified: Vigorous (51%), Capable (28%), and Leisurely (21%). Sucking profiles were found to improve estimation of change in WFA from 4 to 12 months and 12-month maternal-reported eating behaviors above infant sex, race/ethnicity, birthweight, gestational age, and pre-pregnancy body mass index alone. Infants with a Vigorous sucking profile gained significantly more weight during the study period than infants with a Leisurely profile. Infant sucking characteristics may aid in predicting which infants may be at greater risk of obesity, and therefore sucking profiles deserve more investigation.

1. Introduction

Excessive weight gain in early infancy is a risk factor for cardiovascular disease and obesity across the life course (Zheng et al., 2017). Early detection and prevention of excessive weight gain has been identified as a priority (L. A. Daniels, Mallan, et al., 2015; Dattilo et al., 2012) and the American Academy of Pediatrics has called on pediatric providers to identify at-risk infants and intervene (S. R. Daniels, Mallan, et al., 2015). Although a number of interventions are known to effectively alter infant weight gain trajectory (Butler, Fangupo, Cutfield, & Taylor, 2021; Messito et al., 2020; Redsell et al., 2016; Savage, Birch, Marini, Anzman-Frasca, & Paul, 2016) the effectiveness of such programs is closely tied to the ability to identify at-risk infants early in life (Redsell et al., 2016). Previously identified risk factors for excessive weight gain in infancy include male sex (Mihrshahi, Battistutta, Magarey, & Daniels, 2011), black race or Hispanic ethnicity (Taveras, Gillman, Kleinman, Rich-Edwards, & Rifas-Shiman, 2010), and greater maternal body mass index (BMI) (Heerman, Bian, Shintani, & Barkin, 2014), but these

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Abbreviations: weight-for-age (WFA), Nfant® Feeding Solution (nFS); Children's Eating Behavior Questionnaire-Toddler (CEBQ-T), body mass index (BMI); World Health Organization (WHO), Gaussian process regression (GPR).

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factors collectively have limited predictive value. Improved sensitivity and specificity for identifying infants likely to experience excessive weight gain is therefore a public health priority.

In the search for more informative risk factors, assessment of infant eating behaviors has emerged as promising avenue of study. These behaviors are known to be identifiable in infancy and demonstrate continuity into at least early childhood (Parkinson, Drewett, Le Couteur, & Adamson, 2010; van Jaarsveld, Llewellyn, Johnson, & Wardle, 2011; Wright, Cox, & Le Couteur, 2011). Greater enjoyment of food, food responsiveness, and emotional overeating and lower satiety responsiveness have each been previously shown to predict greater weight gain (Carnell, Benson, Pryor, & Driggin, 2013). Yet, infant eating behaviors can be challenging to measure by parent report prior to age 6 months, with many studies showing poor internal consistency across multiple subscales designed to measure eating behavior constructs (Hunot-Alexander et al., 2021; Mallan, Daniels, & Susan, 2014; Plows et al., 2020). Further, parent report measures are necessarily relatively blunt instruments, asking parents to rate items such as "My baby feeds slowly", or "My baby loves milk" (C. H. Llewellyn, C. H. van Jaarsveld, L. Johnson, S. Carnell, & J. Wardle, 2011). Though parent report of infant eating behavior has value in many contexts, a more detailed and objective characterization of infant eating behavior may prove valuable-an approach possible through the direct measurement of infant nutritive sucking.

Infant nutritive sucking is one of the most neurologically complex behaviors in early infancy, representing an organized process encompassing alternating rhythms of suction via negative intraoral pressure followed by expression via positive intraoral pressure (Lau, 2015). Researchers since the 1960's have developed devices to measure infant nutritive sucking (Tamilia et al., 2014), usually generating just a few summary metrics such as mean pressure, frequency, and suck and burst duration. Using these devices, the development of nutritive sucking through infancy has been documented, demonstrating that sucking maturation is characterized by higher peak pressure (Tamilia et al., 2014), higher frequency (Lang et al., 2011; Medoff-Cooper, Bilker, & Kaplan, 2010; Sakalidis et al., 2013) and shorter inter-suck intervals (Lang et al., 2011; McGowan, Marsh, Fowler, Levy, & Stallings, 1991; Medoff-Cooper et al., 2010; Sakalidis et al., 2013). These devices have also proven useful for predicting weight gain and eating behavior. Specifically, two studies involving cohorts comprising 99 (Agras, Kraemer, Berkowitz, Korner, & Hammer, 1987) and 78 (Stunkard, Berkowitz, Schoeller, Maislin, & Stallings, 2004) infants demonstrated associations of higher mean peak amplitudes and frequency with greater BMI/weight gain (Agras et al., 1987; Agras, Kraemer, Berkowitz, & Hammer, 1990; Stunkard et al., 2004) and greater intake (Agras et al., 1987), as well as associations of fewer sucks per feeding with greater preschool-age food fussiness (Jacobi, Agras, Bryson, & Hammer, 2003).

As technology has advanced and the capacity for managing and manipulating voluminous data has evolved in recent years, researchers are now able to measure sucking in even greater detail. Whereas prior approaches captured only mean and maximum sucking pressure, sucking frequency, number of sucks and bursts, and durations of bursts and inter-suck and inter-burst intervals, newer technologies are able to capture many more sucking features. For example, it is now possible to characterize a feeding session through measures of total pressure generated across the feeding (i.e., area under the curve), the smoothness of the sucking pressure wave, time to rise from baseline to the peak amplitude of the suck (i.e., increasing phase), time to decline from the peak amplitude of the suck to baseline (i.e., decreasing phase), the location within the pressure wave where the greatest pressure is located (i.e., the spectral centroid), and the spread (i.e., standard deviation) of the pressure wave from the spectral centroid (i.e., the spectral spread). Additionally, coefficients of variation for these metrics can be calculated reflecting suck-to-suck fluctuation. Using these approaches, researchers have documented declines of coefficients of variation of sucking parameters with maturity (Tamilia et al., 2014), and associations of lower

sucking smoothness with future infant feeding difficulties (Capilouto, Cunningham, Giannone, & Grider, 2019).

The prior body of work suggesting that sucking in early infancy may be an important indicator of future weight gain and eating behavior, in combination with the emergence of more sophisticated approaches for measuring sucking, together point to several important next steps in this research area. First, the work of Agras in 1987 and Stunkard in 2004 linking features of sucking to weight gain and eating behavior needs replication. Second, the more detailed sucking metrics made possible by recent technology should be examined for their predictive value for weight gain and eating behavior. Finally, the prior sucking metrics examined by Agras and Stunkard were only included individually as independent factors in predictive models. This approach fails to incorporate our understanding of sucking as a neurologically complex coordinated process. Research is needed that captures the many metrics generated by newer technology in a comprehensive manner and examines their combined predictive value for weight gain and eating behaviors.

Therefore, the primary objective of this study was to determine if infants cluster into sucking profiles based on combinations of multiple sucking metrics. The secondary objective was to determine if these sucking profiles have predictive value for excessive weight gain and parent-reported eating behaviors. The identification of sucking profiles broadly predictive of future obesity and cardiovascular risk could aid in the targeting of early infancy interventions as well as open lines of research into understanding the mechanisms underlying vigorous eating behavior and its development.

2. Methods

2.1. Study overview and participant sample

This study used an experimental design embedded within a longitudinal observational cohort study. The overall study sought to examine development of infant eating behavior over the first year of life. Data collection included questionnaires (including measures of eating behavior and other maternal, infant, and family behaviors and psychosocial factors), feeding assessment protocols, and anthropometry. All data were collected via home visits by trained research assistants. The University of Michigan Institutional Review board approved the study (protocol #HUM00103575) and mothers provided written informed consent.

Mother-infant dyads were recruited from the community. Inclusion criteria were: gestational age at delivery 37.0–42.0 weeks; weight appropriate for gestational age; no significant perinatal or neonatal complications; biological mother was legal and custodial guardian; and infant consumed \geq 2 ounces in one feeding from an artificial nipple \geq once per week. Exclusion criteria were: mother is not fluent in English; mother <18 years old; infant has medical problems or diagnosis affecting current or future eating, growth, or development; or child protective services involvement. This report describes infants who participated in measurement of sucking metrics during a typical feeding at age 4 months. The analytic sample was further limited to participants with complete data for the study outcomes and key covariates.

2.2. Sucking measurement and generation of metrics

Mothers fed the infant with a Dr. Brown's® standard neck bottle outfitted with a Nfant® standard nipple and non-invasive Nfant® Feeding Solution (nFS, NFANT Labs, Atlanta, GA, USA) connected with a disposable coupling cufflink to measure nipple dynamics during feeding. The nFS generates the sucking parameters shown in Table 1.

2.3. Anthropometry

Trained research assistants weighed infants at ages 4 and 12 months

Table 1

Sucking metrics.

Category	Sucking Feature	Definition
Suck-Level Features	Mean Peak Amplitude	Mean amplitude of peaks for calibrated nipple movement (derived from pressure wave and normalized over a feeding session)
	Maximum Peak Amplitude	Maximum amplitude of peaks for calibrated nipple movement (derived from pressure wave and normalized over a feeding session)
	Effect	Summation integral of calibrated nipple movement (derived from pressure wave and normalized over a feeding session)
	Frequency (Hz)	Mean frequency of nipple movement during a feeding session (limited to within sucking bursts)
	Interval	Mean time between end of nipple movement event and start of next nipple movement event
Intra-Suck Measures	Smoothness	Mean number of velocity changes in the waveform of each suck during a feed
Medibareb	Increasing Phase (IP) Duration	Time to rise from baseline to peak amplitude of suck
	Decreasing Phase (DP) Duration	Time to decline to baseline from peak
Coefficient of Variability (CV)	Peak Amplitude CV	amplitude of suck Variability of peak amplitude metric across all sucks during the feeding session
	Frequency CV	Variability of Frequency metric across all sucks during the feeding session
	Smoothness CV	Variability of Smoothness metric across all sucks during the feeding session
Derived Metrics	Spectral Centroid	Spectral centroid of the calibrated nipple movement measurement over a feeding session, i.e., location within the pressure wave where the greatest
	Spectral Spread	pressure is located Spectral spread of the calibrated nipple movement measurement over a feeding session, i.e., the spread (i.e., standard deviation) of the pressure wave from the
	Entropy	spectral centroid Entropy of the calibrated nipple movement measurement over a feeding session

without clothing or a diaper on a Tanita Digital Infant Scale in duplicate and weights averaged. If the weights differed by more than 0.1 kg, a third weight was obtained. Recumbent length was also measured in duplicate to the nearest 0.1 cm using standardized approaches (Shorr, 1984) with a Pediatric Stadiometer (Ellard Instruments item# M-PED LB 35-107-X) and lengths averaged. If measurements differed by more than 0.2 cm, a third measurement was obtained. Weight-for-age (WFA) percentile was calculated based on the World Health Organization (WHO) Growth Charts. Our primary outcome was change in WFA percentile from ages 4–12 months (ΔWFA percentile), given the previously reported association of WFA percentile change in infancy with adult adiposity and obesity (Ekelund et al., 2006).

2.4. Eating behavior

At infant age 4 months, mothers completed the concurrent version of the Baby Eating Behavior Questionnaire (BEBQ) (C. H. Llewellyn, C. H. M. van Jaarsveld, L. Johnson, S. Carnell, & J. Wardle, 2011), an 18-item parent-report measure of infant eating behaviors that asked respondents to rate their baby's eating style at a typical daytime breastmilk or formula feeding. All items are rated on a 5-point Likert scale (never = 1; rarely = 2; sometimes = 3; often = 4; always = 5), and mean scores for each of 4 subscales are calculated with reverse scoring as appropriate. Subscales include Enjoyment of Food (4 items, Cronbach's $\alpha = 0.70$); Food Responsiveness (6 items, Cronbach's $\alpha = 0.78$); Satiety

Responsiveness (3 items, Cronbach's $\alpha = 0.44$); Slowness in Eating (4 items, Cronbach's $\alpha = 0.57$); and General Appetite (1 item). Given the suboptimal internal reliability of the Satiety Responsiveness and Slowness in Eating subscales, analyses included only Enjoyment of Food, Food Responsiveness, and General Appetite subscales.

At infant age 12 months, mothers completed the Children's Eating Behavior Questionnaire-Toddler (CEBQ-T), which is a 26-item measure adapted from the Children's Eating Behavior Questionnaire (Carnell & Wardle, 2007; Wardle, Guthrie, Sanderson, & Rapoport, 2001) developed for children between ages 6 and 18 months which has shown good reliability and validity in several studies with young children (Kininmonth, Smith, Llewellyn, & Fildes, 2020; Lumeng, Miller, Appugliese, Rosenblum, & Kaciroti, 2018; Miller et al., 2019). Mothers respond on a scale of 1 = never to 5 = always. Items are reverse scored as appropriate and responses are averaged to calculate subscale scores. The CEBQ-T generates the following subscales, each of which had acceptable internal consistency in this cohort: Enjoyment of Food (4 items, Cronbach's α = 0.85), Emotional Overeating (3 items, α = 0.89), Food Fussiness (6 items, $\alpha = 0.84$), Food Responsiveness (4 items, $\alpha = 0.83$), Slowness in Eating (4 items, $\alpha = 0.72$), and Satiety Responsiveness (5 items, $\alpha =$ 0.71).

2.5. Infant and maternal characteristics

Mothers reported infant sex, race/ethnicity, birthweight, and due date and birth date (from which gestational age was calculated); as well as their pre-pregnancy weight and height, from which BMI was calculated.

2.6. Analysis

All analyses were completed using Python v3.8.8, SAS 9.4, Scikitlearn v0.24.1 (Pedregosa et al., 2011), Pandas v1.2.4 (McKinney, 2010), NumPy v1.20.1 (Harris et al., 2020).

2.6.1. Development of sucking profiles

Given the inter-related nature of the nFS sucking metrics, sucking profiles were developed using a clustering approach. With known associations between time since last feeding and energy intake (Birch, Johnson, Andresen, Peters, & Schulte, 1991; Fox, Devaney, Reidy, Razafindrakoto, & Ziegler, 2006; McConahy, Smiciklas-Wright, Birch, Mitchell, & Picciano, 2002; Shea, Stein, Basch, Contento, & Zybert, 1992; Syrad, Johnson, Wardle, & Llewellyn, 2016), we attempted to mitigate bias within the sucking metrics attributed to recency of infants' last feeding. To do so, the time elapsed since the last feeding for each infant was regressed against each nFS feature independently and the residual values for each infant's data were used in place of the raw sucking metric. Data were also standardized given differing scales across sucking metrics.

A k-means clustering (k-means++, with 20 restarts for stability) was performed to identify profiles. For all analyses the number of clusters (k) was set to 3. In contrast to a single metric to determine optimal cluster count (e.g., gap statistic), k was selected utilizing a cluster stability approach (Hennig, 2007). A full explanation of this method, and stability scores for several alternative values of k can be found in Supplementary Material. A post-hoc exploration of profile clusters was performed, characterizing profiles by the patterns of nFS data used to construct them, and with respect to external factors including demographics and pre-/peri-natal characteristics.

2.6.2. Predictive value of sucking profiles for change in WFA from 4 to 12 months

To estimate the potential of these models to screen for at-risk infants, the analysis was framed as a classification exercise and repeated three times; discretizing the cohort of infants into those with a "high-degree" of weight change – defined as those whose WFA increased at least (\geq) 5,

10, and 15 percentiles between ages 4 and 12 months. These cut-points were selected to act as a sensitivity analysis of results across varying degrees of class imbalance, spanning the proportion of positive cases (number of infants who reach the threshold), where a majority of infants (58%) reach a change of at least 5 percentiles, while only a minority (38%) of infants achieve a threshold of at least 15%. In turn allowing for a more generalizable assessment for the profile's predictive value. In addition, future obesity is the result of very small calorie imbalances and slow weight gain (Hall et al., 2011), and interventions to prevent rapid infant weight gain have been considered successful and subsequently been disseminated based on a change of 5–10 percentiles over the 12 months of infancy (Savage et al., 2016).

Two distinct classification models were used to help ensure results were not an artifact of a singular fitting method. First a K-nearest neighbors (KNN) model, which employs a majority vote between outcome of the K-closest infants (set to 3) as defined by cosine-distance. Votes were weighted by distance to help reduce bias on highly distinct infants. Second, a l2-regularized (ridge) logistic regression to ensure models that required learning distributions of feature weights and associated error produced comparable results. Both models were adjusted for factors known to be associated with infant WFA, including infant sex (Male/Female), race/ethnicity (represented as a binary variable [non-Hispanic white vs. Hispanic or not white] due to sample size), birthweight, gestational age, and WFA at age 4 months as well as maternal self-reported pre-pregnancy BMI.

Performance in identifying high-growth infants was quantified using measures of sensitivity, specificity, positive and negative predictive value. To robustly evaluate model performance, a repeated stratified kfold analysis was performed (stratified by the proportion of high-change infants at a respective threshold). In this paradigm, a k-fold validation is performed, and performance across each test-set fold is averaged together. Then utilizing a new random seed, another k-fold validation is performed using different test/train splits. Performance across k-fold iterations is ultimately reported, having been shown to provide more stable generalization estimates (Vanwinckelen & Blockeel, 2015). The proportion of outcome classes in the training data of a given fold were balanced using SMOTE-ENC (Mukherjee & Khushi, 2021), an extension of the Synthetic Minority Oversampling Technique (SMOTE) algorithm (Chawla, Bowyer, Hall, & Kegelmeyer, 2002) that generates synthetic data, deigned to handle both nominal and continuous features. Finally, it is understood the selection of k can impact model performance [as k increases size of training data increases resulting in decrease in test set size thus producing higher variability across the performance metrics, and inversely, smaller values of k produce more stable results but may negatively impact performance with smaller training datasets]. For completeness, we evaluated k = 3, 5, and 10 independently.

To prevent data leakage, sucking profiles were recomputed using training data at each fold. Profiles for test data were assigned based on kmeans predictions (distance to nearest cluster). Cluster profiles were hot encoded into binary features and added to the set of demographic and baseline data for each infant.

In an effort to isolate how profiles drive predictive performance, several baseline versions of each model were fit. These included: 1) an absolute baseline, which included all control variables but excluded the profile indicator; 2) a series of baseline models including all control variables as well as common sucking metrics (mean amplitude, max amplitude, interval and frequency – each modeled independently and adjusted for time since last feeding as detailed previously); and 3) a series of baseline models including all control variables as well as the respective subscales of subjective eating behaviors from the parent reported BEBQ (modeled independently) obtained at the same age that sucking was measured (4 m).

2.6.3. Post-hoc exploration of sucking profiles with change in WFA from 4 to 12 months

robust assessment of generalized performance for the profile generating *process* relative to baseline characteristics (i.e., does creating sucking profiles reliably predict weight gain?). Yet potentially differing clusters resulting from thousands of permutations of included infant training data at each fold precludes a direct assessment of how any specific profile relates to a given outcome. To address this, we conducted a posthoc analysis of the WFA percentile changes with respect to the overall profiles identified on the overall data to provide insight into how specific profiles may be related to infant weight gain. To do so, we fit a robust linear regression (M-estimator) adjusting for baseline factors (sex, race/ethnicity, birthweight, gestational age, maternal pre-pregnancy BMI, and 4-month WFA percentile) to examine the association of sucking profile membership with change in WFA percentile from 4 to 12 months.

2.6.4. Predictive value of sucking profiles for eating behaviors at 12 months

Our second analysis focused on association of sucking profiles with infant eating behaviors at age 12 months, as indicated by each of the six CEBQ-T subscales. As the subscales do not provide a minimum clinically important difference, measures were treated as continuous outcomes. Thus, rather than repeated K-fold, we performed a 1000-iteration bootstrap evaluation. In this way, the original data were sampled with replacement until the size of the original data was reached to form the training data. Given the replacement of data, it has been shown that on average 36.8% of data is left out of each sample. These data, known as out-of-bag samples, are then used as an ad-hoc test set. As before, sucking profiles were regenerated for each bootstrap iteration using only training data and assigned to the out-of-bag test infants based on distance to the learned clusters.

To estimate the expected subscale score, we utilized a Gaussian process regression (GPR) model. In contrast to traditional (linear) regression models that attempt to fit a best singular line through data based on specified functional form, GPR models are non-parametric models that operate under a Bayesian framework, utilizing observed prior distribution from data to improve inference. Through use of kernel functions, GPR allow for modeling of non-linear functions and are well suited for prediction of potentially noisy data. As in the first analysis, the model was adjusted for baseline demographics and maternal information and used five restarts to aid in optimization convergence. A baseline GPR model with all factors except for the profile indicator was fit on the data at each iteration and used for comparison. Predictive performance was measured using root-mean-squared-error (RMSE).

3. Results

Participant flow to define the cohorts for each analysis is shown in Fig. 1. The nFS was added to the protocol after the study had been underway and is therefore available for only a subset of the cohort (n = 147), of which 119 participated at 4 months and 114 had complete data for all covariates. The sample included for analysis (n = 114) did not differ from the sample not included (n = 170) with regard to infant sex, race/ethnicity, birthweight, or gestational age. Demographic and pre-/ peri-natal characteristics of the cohort included in each model are described in Table 2. Briefly, the sample from which sucking profiles were generated (n = 114) was 46% male, 63% non-Hispanic white, and had an average birthweight of 3.5 kg and gestational age of 39.5 weeks. The subsample with complete growth data from 4 to 12 months (n = 71), had a mean WFA percentile of 46 at 4 months and 55 at 12 months. More than half (58%) of the sample increased their WFA by > 5 percentile points from 4 to 12 months, 46% increased by \geq 10 percentile points, and 38% by \geq 15 percentile points. Broadly, the subsample with complete CEBQ-T data at 12 months (n = 56), was found to have *Enjoyment* of Food scores towards the upper bound of the scale, Emotional Overeating scores on the lower end of the scale, with the remaining scales providing scores distributed across the range of possible values.

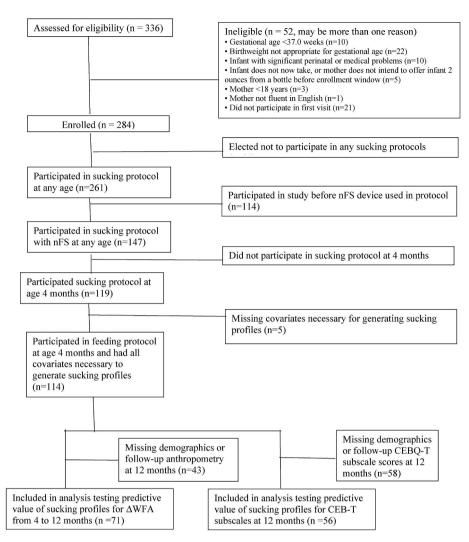


Fig. 1. Participant flow diagram.

3.1. Sucking profiles

Fig. 2 shows the distributions of sucking metrics comprising each of the three profiles and Table 3 describes each profile in detail. We refer to Profile A as Vigorous, Profile B as Capable, and Profile C as Leisurely.

Infants in the Vigorous profile comprised 51% of the sample, and were differentiated from the other two profiles by sucking that is higher in mean peak and maximum peak amplitude and effect (i.e., cumulative amplitude over the feed); shorter time to increase to peak amplitude; lower peak amplitude and smoothness coefficients of variation; lower spectral spread and higher entropy. Infants in the Vigorous profile also showed greater sucking frequency within a burst, shorter inter-suck interval, fewer velocity changes in the waveform within a suck (i.e., more smoothness), lower frequency coefficient of variation, and higher spectral centroid compared to infants in the Leisurely profile. Infants in the Vigorous profile also showed longer time to decrease from peak amplitude compared to infants in the Capable profile.

Infants in the Capable profile comprised 28% of the sample and were differentiated from the other two profiles by being intermediate between them for effect (i.e., cumulative pressure over the feed), time to increase to peak amplitude and peak amplitude coefficient of variation. Infants in the Capable profile showed lower mean and maximum peak amplitudes, greater smoothness coefficient of variation, greater spectral spread, and lower entropy compared to infants in the Vigorous profile but did not differ in these metrics from infants in the Leisurely profile. Infants in the Capable profile also showed greater suck frequency, shorter inter-suck interval, fewer velocity changes in the waveform within a suck (i.e., greater smoothness), lower frequency coefficient of variation, and greater spectral centroid as compared to infants in the Leisurely profile but did not differ in these metrics from infants in the Vigorous profile. Infants in the Capable profile also showed shorter time to decrease from peak amplitude than the other two profiles.

Infants in the Leisurely profile comprised 21% of the sample and were differentiated from the other two profiles by sucking that is lower in effect (i.e., cumulative pressure over the feed), lower frequency, longer inter-suck intervals, more velocity changes in the waveform within a suck (i.e., less smoothness), longer time to increase to peak amplitude, higher peak amplitude and frequency coefficients of variation, and lower spectral centroid. Infants in the Leisurely Profile showed lower mean and maximum peak amplitudes, higher spectral spread, lower smoothness coefficient of variation, and lower entropy compared to infants in the Vigorous profile but did not differ in these metrics from infants in the Capable profile. Finally, infants in the Leisurely profile showed greater time to decrease from peak amplitude compared to infants in the Capable profile but did not differ in this metric from infants in the Vigorous profile but did not differ in this metric from infants in the Vigorous profile.

As shown in Table 3, the sucking profiles did not differ with regard to infant sex, race/ethnicity, birthweight, gestational age, or maternal prepregnancy BMI.

Table 2

Characteristics of the analytic samples.

Model	Sucking profiles	Predictive value of sucking profiles for Δ WFA percentiles from 4 to 12 m	Predictive value of sucking profiles for CEBQ-T subscale scores at 12 m N = 56 M (SD) or n (%)		
Sample size	N = 114	N = 71			
Characteristic	M (SD) or n (%)	M (SD) or n (%)			
Infant Sex, n (%)					
Male	53 (46%)	33 (46%)	22 (39%)		
Female	61 (54%)	38 (54%)	34 (61%)		
Infant race/ethnicity,					
Non-Hispanic white	71 (63%)	44 (62%)	33 (59%)		
Non-Hispanic black	18 (16%)	9 (13%)	8 (14%)		
Hispanic any race	6 (5%)	4 (6%)	4 (7%)		
Other or more than one race	18 (16%)	14 (20%)	11 (20%)		
Birthweight (kg), mean (SD)	3.5 (0.4)	3.5 (0.4)	3.4 (0.4)		
Gestational age (wks.), mean (SD)	39.5 (1.1)	39.6 (1.0)	39.6 (1.1)		
Maternal pre- pregnancy BMI, mean (SD)	27.7 (7.1)	27.1 (7.1)	26.9 (7.1)		
Time since last feeding (hours), mean (SD)	2.4 (1.0)	2.5 (0.9)	2.5 (0.9)		
Infant WFA percentile	e (n = 71)				
4 m, mean (SD)		46 (27)			
12 m, mean (SD)		55 (28)			
Δ from 4 to 12 m, mean (SD)		9 (20)			
Δ from 4 to 12 m \geq 5%, n (%)		41/71 (58%)			
Δ from 4 to 12 m \geq 10%, n (%)		33/71 (46%)			
Δ from 4 to 12 m > 15%, n (%)		27/71 (38%)			
	Questionnair	e-Toddler Subscales at a	ge 12 m, mean (SD)		
Enjoyment of Food			4.3 (0.6)		
Emotional			1.9 (0.7)		
Overeating					
Food Fussiness			2.2 (0.6)		
Food			2.6 (0.8)		
Responsiveness Slowness in			2.9 (0.7)		
Eating Satiety			2.8 (0.6)		
Responsiveness					

3.2. Predictive value of sucking profiles for change in WFA from 4 to 12 months

Fig. 3 presents the predictive performance, for both models (KNN, Ridge regression) with and without sucking profiles included. Distributions for each metric are computed across the 500-repeated 5-fold cross-validation splits are provided at each threshold of high-change (5,10,15) WFA percentiles. Performance metrics using k-fold values of 3 and 10 can be found in supplementary material. As shown, using both modeling approaches, the addition of 4 month sucking profile significantly increases the Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value for WFA percentile gain above infant sex, race/ethnicity, birthweight, gestational age, WFA at 4 months and maternal pre-pregnancy BMI alone.

Results comparing the sucking profiles to the univariate metrics and parent-reported eating behaviors at 4 m (BEBQ) can be found in the supplementary material and highlight similar results, with improved predictive performance when multivariate profiles are considered.

Values for all indicators generally range between 0.4 and 0.6, and

overall sensitivity and positive predictive value tended to be greatest for predicting a 5% increase (vs. not) in WFA between 4 and 12 months. It is not unexpected that performance is highest at this threshold, as a majority of children experience a change of at least 5 percentiles from 4 to 12 m, making the prediction easier even for a random baseline. Notably, we observe a widening gap in performance between the profiles and baseline models as the prediction task becomes more challenging (fewer children meeting the definition of "sufficient change" at 10 and 15 percentiles) further supporting the utility of these profiles in identifying high-risk infants.

3.3. Post-hoc exploration of sucking profiles with change in WFA from 4 to 12 months

In post-hoc analyses, Profile A (Vigorous) had a mean increase in WFA of 13.74 percentiles (SD 19.04), Profile B (Capable) had a mean increase of 5.75 (SD 23.31), and Profile C (Leisurely) had a mean increase of 1.63 (SD 18.00). Profile A (Vigorous) WFA percentile change from 4 to 12 months was significantly greater than that of Profile C (Leisurely) (coefficient 14.83, p = .013). There was no significant difference in WFA percentile change in Profile B (Capable) compared to Profile A (Vigorous) (coefficient -6.43, p = .237), or in Profile C (Leisurely) compared to Profile B (Capable) (coefficient -8.4, p = .204).

3.4. Predictive value of sucking profiles for eating behaviors at 12 months

With respect to estimation of eating behaviors, Fig. 4 shows the distribution of RMSE for each CEBQ-T subscale across a 1000-iteration bootstrap. Performance is again compared between models with and without the sucking profiles included. Lower RMSE represents a more accurate prediction. As shown, the addition of sucking profile at age 4 months increases the predictive value for all parent-reported CEBQ-T subscale scores at 12 months, above infant sex, race/ethnicity, birthweight, gestational age, WFA percentile at 4 months and maternal pre-pregnancy BMI alone.

4. Discussion

This study had two main findings. First, among healthy, full-term infants, three profiles of infant nutritive sucking were identifiable at age 4 months, characterized as Vigorous, Capable, and Leisurely. The profiles exhibited significantly different values across several metrics characterizing the sucking behavior during a typical 4-month feeding and were not associated with demographic or pre-/peri-natal characteristics. Second, the sucking profiles offered predictive value for both the identification of infants with a high-degree of future weight gain from ages 4–12 months and for increasing precision of the estimate for parent-reported infant Enjoyment of Food, Emotional Overeating, Food Fussiness, Food Responsiveness, Slowness in Eating, and Satiety Responsiveness at age 12 months above and beyond infant sex, race/ ethnicity, birthweight, gestational age, WFA percentile at 4 months and maternal pre-pregnancy BMI alone.

Our findings expand on prior work in several important ways. First, whereas prior studies reported univariate correlations among up to five sucking metrics and chose just a single metric to predict future weight gain (Agras et al., 1987, 1990; Stunkard et al., 2004), our study included a more robust set of 14 sucking metrics and identified novel sucking profiles using a clustering approach jointly considering the values *across* multiple metrics. In one cohort of infants from the late 1980's, higher mean sucking pressure was associated with greater caloric intake and higher BMI to age 3 years (Agras et al., 1987, 1990). Likewise, in a second cohort from the 1990's, greater sucking frequency predicted greater future weight gain in infancy (Stunkard et al., 2004). Our findings align with this limited prior literature and extend this work by demonstrating that sucking profiles hold predictive value for weight gain. Yet, the sucking style associated with greater weight gain is

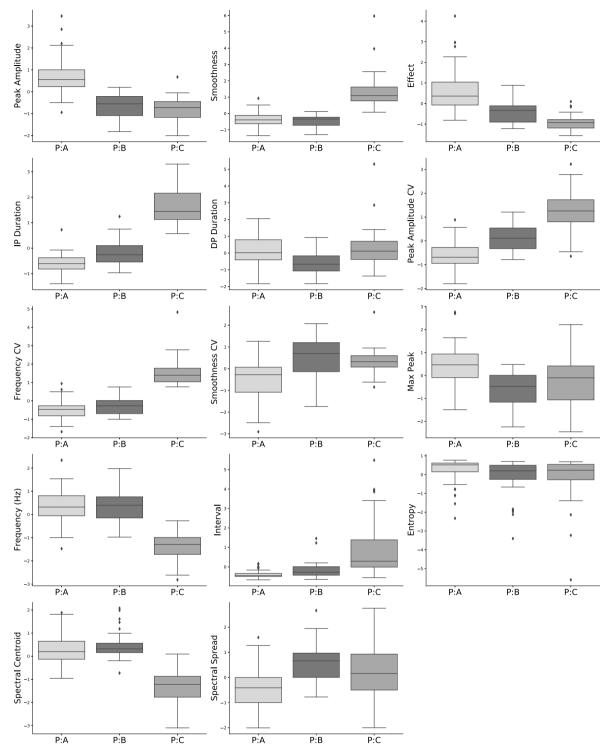


Fig. 2. Sucking Profiles. To aid in visualization and comparison between measures, each metric has been min-max scaled. N = 114. Sucking metrics used are adjusted for time elapsed since last feeding. Profile A (Vigorous), Profile B (Capable), Profile C (Leisurely).

characterized by more than just higher mean sucking pressure and greater sucking frequency, but also by greater cumulative pressure generation over a feed (both due to higher peak amplitude and higher sustained amplitude) and smoother and more consistent sucking. Our study also focused on the predictive value of sucking metrics above and beyond more traditional predictors of future infant weight gain. However, it is important to note this work did not aim to create an optimal predictor of weight change. To do so would require a wider set of variables. Rather it aimed to highlight the potential use of quantitative measures of infant nutritive sucking as they relate to the development of multivariate profiles, and relationships of these profiles with future weight change and behaviors as compared to baseline and univariate data alone.

Second, prior studies have described a "vigorous" sucking style as being characterized by higher suck frequency, higher mean pressure, longer suck and burst duration, and shorter inter-burst interval in one cohort (Agras et al., 1987), and by higher suck frequency across the feeding and within a burst and higher maximum pressure in another

Table 3

Characteristics of sucking profiles.

Characteristic	$\frac{\text{Profile A (Vigorous)}}{N = 58 (51\%)}$	Profile B (Capable) N = 32 (28%) Mean (SD) or n (%)	Profile C (Leisurely) N = 24 (21%)	p-value	Post-hoc comparisons
	Sucking metrics, mean (SD), $(n = 114)$				
Mean Peak Amplitude	28.2 (5.9)	18.1 (4.2)	16.7 (4.9)	<.0001	A > B, C
Maximum Peak Amplitude	49.9 (10.1)	37.0 (8.6)	41.3 (11.7)	<.0001	A > B, C
Effect	8155.5 (4556.2)	3836.4 (2489.7)	1574.8 (1573.5)	<.0001	A > B > C
Frequency (Hz)	1.7 (0.2)	1.7 (0.2)	1.3 (0.2)	<.0001	A, $B > C$
Interval	0.2 (0.1)	0.4 (0.4)	1.4 (1.4)	<.0001	A, B < C
Smoothness (intra-suck velocity changes)	2.2 (0.3)	2.1 (0.2)	3.4 (0.8)	<.0001	A, B < C
IP Duration	0.27 (0.04)	0.31 (0.05)	0.50 (0.07)	<.0001	A < B < C
DP Duration	0.36 (0.04)	0.32 (0.03)	0.37 (0.07)	<.0001	A, $C > B$
Peak Amplitude CV	0.32 (0.07)	0.41 (0.07)	0.56 (0.12)	<.0001	A < B < C
Frequency CV	0.31 (0.04)	0.33 (0.03)	0.48 (0.07)	<.0001	A, $B < C$
Smoothness CV	0.66 (0.08)	0.74 (0.08)	0.73 (0.06)	<.0001	A < B, C
Spectral Centroid	0.23 (0.02)	0.23 (0.01)	0.19 (0.02)	<.0001	A, $B > C$
Spectral Spread	0.21 (0.01)	0.23 (0.01)	0.22 (0.01)	<.0001	A < B, C
Entropy	0.95 (0.07)	0.91 (0.11)	0.90 (0.15)	.04	A > B, C
Infant Sex, n (%)				.32	
Male	30 (52%)	15 (47%)	8 (33%)		
Female	28 (48%)	17 (53%)	16 (67%)		
Infant race/ethnicity, n (%)				.44	
Non-Hispanic white	37 (64%)	22 (69%)	12 (52%)		
Hispanic or not white	21 (36%)	10 (31%)	11 (48%)		
Birthweight (kg), mean (SD)	3.5 (0.4)	3.4 (0.4)	3.5 (0.3)	.70	
Gestational age (wks.), mean (SD)	39.5 (1.2)	39.3 (0.9)	39.7 (1.2)	.44	
Maternal pre-pregnancy BMI, mean (SD)	29.0 (7.5)	27.3 (7.0)	25.4 (5.8)	.12	
Time since last feeding (hours), mean (SD)	2.4 (1.0)	2.6 (1.1)	2.4 (0.8)	.47	

cohort (Stunkard et al., 2004). Our Vigorous profile was, similar to the findings of others, characterized by higher suck frequency within a burst (Agras et al., 1987; Stunkard et al., 2004) and greater mean (Agras et al., 1987) and maximum (Stunkard et al., 2004) amplitudes. However, we characterized our Vigorous profile in more detail than prior studies by showing that this group generated greater cumulative pressure over the feeding (as reflected in the effect metric), and had sucking that was smoother and less variable, and rose more quickly to a higher peak per suck. This might be best understood by drawing a comparison to a weightlifter. A weightlifter akin to the Vigorous profile is able to lift a heavier maximum weight, can sustain lifting heavier weights longer, and can lift the weights up faster, more smoothly, and more consistently. In contrast, a weightlifter akin to the Leisurely profile is able to lift less maximum weight, can sustain lifting heavy weights for a shorter time period, and lifts the weights more slowly and more shakily. In addition, there is greater inconsistency in how high they can lift the weight each time, the speed with which they can do a series of lifts, and the shakiness of the lift. The weightlifter akin to the Capable profile has capabilities generally between these two groups.

Finally, we believe our study is the first to test whether sucking metrics have predictive value for a range of parent-reported eating behaviors at age 12 months. We have been able to identify only one other study which has examined this question, finding that fewer sucks per feeding in infancy predicted more food fussiness at preschool age (Jacobi et al., 2003). Our study extended this work by showing that sucking metrics have predictive value for parent-reported eating behaviors at age 12 months, including food fussiness as well as enjoyment of food, emotional overeating, food responsiveness, slowness in eating, and satiety responsiveness.

There are several limitations to consider. The findings may not be generalizable to infants dissimilar to this cohort, which was primarily white and well-resourced. The protocol required that infants be fed from a bottle, which limits generalizability to infants who are exclusively fed from the breast (who represent a small minority of infants (Centers for Disease Control Division of Nutrition & Obesity, 2013; Labiner-Wolfe, Fein, Shealy, & Wang, 2008)). There was attrition between ages 4 and 12 months, limiting the power of analyses. The sucking profiles were

derived from a single feeding at 4 months. While we adjusted for time since last feeding, the time-of-day feeding occurred, alertness of infant, or general variability of feeding characteristics across multiple feeds may have introduced latent bias into the results. The reliability of the sucking profiles may be improved by combining data across multiple feeds in a single timeframe. Finally, as this work centered on identifying the potential utility of the sucking profiles as compared to baselines, profiles were built using only directly measured sucking features. However, future efforts to improve performance in specific prediction tasks would benefit from inclusion of additional feeding information. Additionally, patterns of change in sucking metrics with maturation and across time in a feeding (e.g., decrement in frequency) may provide additional valuable information. In addition, future work should examine sucking during breastfeeding.

Overall, this study takes an important step forward in the examination of infant sucking as an objective, quantitatively definable predictor of growth and eating behavior. Sucking profiles generated from the integration of 14 different sucking metrics obtained at age 4 months show significant and unique predictive value for excess weight gain from ages 4–12 months as well as parent-reported eating behaviors at 12 months. These results suggest measurement of sucking in early infancy could serve as a valuable indicator of future obesity risk. Future work should seek to replicate these findings in a larger sample, across multiple feedings, and with a longer follow up period. Further, additional work should seek to understand the biological or environmental predictors of these sucking profiles to determine the timeline on which they develop, if they are modifiable, or if they serve as markers for underlying genetic predisposition to obesity.

Author contributions

All authors have approved the final manuscript as submitted.

Dr. Feldman conceptualized hypotheses for this report, drafted the initial manuscript, cleaned and analyzed data, and approved the final manuscript as submitted.

Dr. Asta drafted the initial manuscript and approved the final manuscript as submitted.

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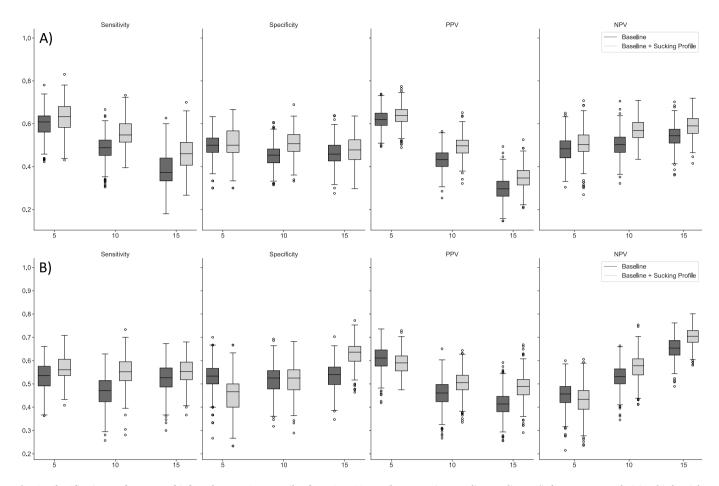


Fig. 3. Classification performance of infants by Δ WFA percentiles from 4 to 12 months comparing Baseline predictors (infant sex, race/ethnicity, birthweight, gestational age, WFA percentile at 4 months and maternal pre-pregnancy BMI alone) vs. Baseline + Sucking (infant sex, race/ethnicity, birthweight, gestational age, WFA percentile at 4 months and maternal pre-pregnancy BMI alone and sucking profile) predictors. Varying thresholds for high change are found on the X-axis. Each frame of the figure represents a performance metric (Sensitivity/Specificity/Positive Predictive Value [PPV]/Negative Predictive Value [PPV]). Panels A/B represent KNN and Ridge Classifiers respectively. Models adjusted for infant sex, race/ethnicity, birthweight, gestational age, WFA at age 4 months and maternal pre-pregnancy BMI.

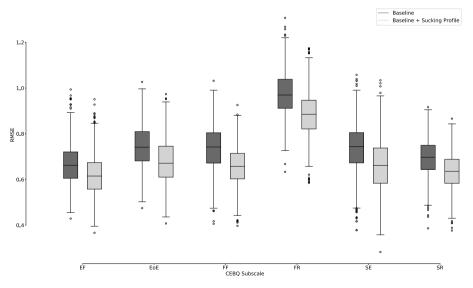


Fig. 4. Predictive performance of sucking profiles for each CEBQ-T subscale score at age 12 months (Baseline predictors vs. Baseline + Sucking profile predictors). CEBQ-T Subscale names EF: Enjoyment of Food, EoE: Emotional Overeating, FF: Food Fussiness, FR: Food Responsiveness, SE: Slowness in Eating, SR: Satiety Responsiveness.

Dr. Gearhardt conceptualized and designed the parent study, provided critical review of the manuscript, and approved the final manuscript as submitted.

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Dr. Miller conceptualized and designed the parent study, provided critical review of the manuscript, and approved the final manuscript as submitted.

Dr. Rosenblum conceptualized and designed the parent study, provided critical review of the manuscript, and approved the final manuscript as submitted.

Dr. Kong conceptualized hypotheses for this report, provided critical review of the manuscript, and approved the final manuscript as submitted.

Dr. Crandall conceptualized hypotheses for this report, provided critical review of the manuscript, and approved the final manuscript as submitted.

Dr. Lumeng conceptualized and designed the parent study and the hypotheses for this report, drafted the initial manuscript, provided critical review of the manuscript, and approved the final manuscript as submitted.

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Ethics statement

The University of Michigan Institutional Review board approved the study (protocol #HUM00103575) and mothers provided written informed consent.

Declaration of competing interest

The authors have no financial relationships or conflicts of interest to disclose.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.appet.2023.106525.

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