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Behavioral Responses to Sucrose as an Indicator of Positive Hedonic Response Across the First Six Months of Infancy

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ABSTRACT

Behavioral responses to sucrose provide an index of positive hedonic response in newborns. In 118 infants, the current study used repeated assessments to explore behavioral responses to sucrose solutions (24%/50% sucrose) compared to water across the first six months of infancy. Lip smacking and bringing fingers to mouth are more likely to occur in response to 24% sucrose relative to water. Tongue protrusions are also more likely to occur for 50% sucrose relative to water. Behavioral responses to sucrose may provide an index of positive hedonic response and could be used to investigate individual differences in the first six months of infancy.

Individual differences in positive hedonic response have important clinical implications. Heightened positive hedonic response to environmental cues has been shown to increase risk for impulsive or excessive behaviors (e.g., risky substance use, overeating; [2]), while markedly low positive hedonic response may increase risk for emotional numbing or anhedonia associated with depression [10]. In children and adults, positive hedonic response can be assessed through indices of neural functioning [4], behavioral measures, or self-report questionnaires [18]. However, assessing positive hedonic response earlier in development is difficult. Neuroimaging in young pediatric age groups is challenging, classic behavioral tasks have not yet been translated to infancy, and relying on maternal report of infant behavior introduces bias. The ability to measure positive hedonic response within the first six months of infancy is critical, as this marks a dynamic phase of postnatal brain development and growth [8]. Determining whether positive hedonic response is measurable across this age period is essential to detect whether early emerging individual differences predict later clinically relevant outcomes.

A promising method for studying positive hedonic response in infants is the examination of behavioral responses to sweet tastes (e.g., sucrose solutions; [7]). Sucrose is particularly effective at activating the endogenous opioid reward system, which underlies the experience of pleasure, from the moment of birth [11]. Newborns exhibit positive hedonic responses (listed from most to least frequent: tongue protrusion, lip smacking, bringing fingers to mouth, and smiling) to sucrose, but not aversive or neutral stimuli [16]. Existing studies investigating positive hedonic responses to sucrose in infants have been conducted within the first few hours or days after birth [1, 6, 7, 14–16]. However, it remains unknown if positive hedonic responses to sucrose continue across the first six months of infancy.

In the current study, we aimed to assess whether greater positive hedonic responses are exhibited to sucrose compared to water across the first six months of infancy via established behavioral response coding previously developed in newborns (i.e., tongue protrusion, lip smacking, bringing fingers to mouth, and smiling; [15]). In a sample of 118 infant-mother dyads followed longitudinally in the first six months of infancy, we hypothesized that infants would be more likely to display positive hedonic responses to sucrose compared to water across repeated administrations at approximately 1 month, 2 months, 4 months, and 6 months of age.

As part of a larger study on infant feeding behavior (ABC Baby), 118 infant-mother dyads were recruited from communities within a 1.5 hour radius of Ann Arbor, Michigan (see Supplemental Materials and Methods for recruitment approach and inclusion criteria). This study was conducted in accordance with the Declaration of Helsinki and was approved by the University of Michigan Institutional Review Board.

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Infant-mother dyads were recruited to begin the study when the infant was between 1-3 weeks of age. Participants were permitted to enter the study at 8 weeks of age to facilitate recruitment. All mothers in the study provided informed consent. Repeated assessments of positive hedonic response to sucrose occurred four times at approximately 1 month, 2 months, 4 months, and 6 months of age (see Supplemental **Table 1** for infant age at each assessment).

Research visits took place at the infant's home. The sucrose protocol with the infant lasted approximately seven minutes. During the protocol, infants were positioned in a car seat so they could be observed and videotaped. Parents sat out of the infant's line of sight. A trained research assistant (RA) administered sterile water and sucrose solutions slowly and steadily to the central dorsal portion of the tongue via syringe. A second RA videotaped the protocol. Both RAs were blind to the content of the solutions. At the 1 and 2 month assessments, the infant was first given 0.2 mL of sterile water and videotaped for 30 seconds (timing began as soon as the syringe entered the baby's mouth). Next, the infant was given 0.2 mL of either 24% or 50% sucrose and videotaped for 60 seconds. The 24% solution strength was chosen based on established protocols of oral sucrose delivery for newborns [1, 7]. However, because no prior study has assessed positive hedonic response to sucrose in infants outside of the newborn stage, a 50% sucrose solution was also implemented based on studies that have used oral sucrose as a pain analgesic in infants up to one year of age [17]. This stronger solution also accounted for the possibility that, relative to newborns, older infants may have developed a tolerance to lower strength sucrose solutions due to repeated experiences consuming rewarding liquids (i.e., breast milk or formula; [19]). Following the administration of the first sucrose solution, an RA administered 0.4 mL of sterile water as a “wash out” and waited 3 minutes before conducting a second trial. This phase served to clear the mouth of any remaining sucrose from the previous trial and provide sufficient time for responses to sucrose to abate. Following the wash out, the protocol steps were repeated for a second sterile water administration and the remaining sucrose solution (summary of paradigm in supplemental **Figure 1**).

Order of delivery of 24% and 50% sucrose solutions was counterbalanced across participants and the initial order of administration was maintained at all future assessments for each infant. To account for infant size at 4 and 6 months assessments, the volume of liquid administered was increased to 0.3 mL for the sucrose and water solutions and 0.6 mL for the washout period. These methods are based on previously established sucrose administration paradigms [15].

Infant behaviors were reliably coded from videotape during the sucrose protocol. Behaviors of interest were defined based on established positive hedonic responses exhibited in response to sucrose [15]: (1) *Tongue Protrusion*: tongue sticking out of the mouth; (2) *Lip smacking*: compression of the lips, followed by opening of the mouth; (3) *Bringing Fingers to Mouth*: contact between the hand or finger with the mouth; (4) *Smiling*: anything from a slight upward curve of the baby's mouth to a wide open-mouth smile. Codes were not mutually exclusive. Behaviors were coded following solution delivery for water (two 30-second observation periods combined), 24% sucrose and 50% sucrose solutions (60-second observation periods each), resulting in six 10-second intervals coded for each participant for each solution. Variables were created to indicate the proportion of intervals in which each behavior occurred ranging from 0 (no behavior in any interval) to 1 (behavior occurred in every interval). See **Table 1** for descriptive statistics of positive hedonic responses.

All statistical tests were completed using SAS 9.4 Software. We investigated whether there were differences between the two water administrations in the protocol. None were detected ($p > .05$). Thus, we combined water administrations in analyses. We also investigated whether there were differences between the delivery orders for sucrose (i.e., 24% first or 50% first). None were detected ($p > .05$). Thus, order is not included as a variable in the models. Separate repeated measures linear regression models (Proc Genmod) were conducted to investigate if each positive hedonic response was more likely to occur in response to sucrose solution relative to water across the four assessments. In each model, the two doses of sucrose were separately compared to water (24% sucrose vs. water, 50% sucrose vs. water), and age was included as a covariate. We also investigated whether behavioral responses to sucrose relative to water were moderated by age, birth weight, or sex by examining whether behavioral responses to sucrose relative to water interacted with these variables.

The proportion of 10-second intervals where a hedonic behavioral response occurred ranged from 0 (no expression) to 1 (expression within every 10-second intervals) across infants for each facial expression (with the exception of smiling in response to 24% sucrose, which ranged from 0 to 0.83; see **Table 1**). Data completeness ranged from 55.1% of infants completing the protocol at the first assessment (1 month) to 82.2% of infants completing the protocol at the third assessment (4 months). Thirty-four percent of participants had complete data at all four ages and 10% of participants had data for only one age. This level of missingness is likely indicative of the difficulty in collecting repeated assessments across the first six months of infancy when families are adjusting to a major life transition. Infants who completed the protocol for at least one age were included in the analytic sample ($n = = 118$; see **Table 2** for sample demographics).

Main effects of age were detected for smiling and tongue protrusion. Regardless of solution (i.e., sucrose or water), infants exhibited more smiling ($p = .03$) and less tongue protrusion ($p < .001$) at older ages. No main effects of age were revealed for lip smacking or bringing fingers to mouth ($p > .05$; see **Table 3**).

In response to 24% sucrose solution versus water, infants demonstrated more lip smacking ($p = .02$) and bringing fingers to mouth ($p = .004$), but not more tongue protrusion or smiling ($p > .05$; see **Table 3**). In response to 50% sucrose solution versus water, infants demonstrated more tongue protrusion ($p = .001$), lip smacking ($p < .001$), and bringing fingers to mouth ($p = .004$), but not more smiling ($p > .05$; see **Table 3**). No interaction terms for sex, birth weight, or age were significant (all $p > .05$). Results are reported in Table 3 and visualized in Figure 1.

Two of the four established behavioral responses that indicate liking in newborn infants (i.e., lip smacking, and bringing fingers to mouth; [16]) were exhibited more frequently in response to 24% sucrose solution compared to water across the first six months of infancy. When increased to 50% sucrose, lip smacking and bringing fingers to mouth continued to be more likely to occur for sucrose relative to water, and tongue protrusion was also more likely to occur. Smiling did not differ between water and sucrose. Sex, birth weight, and age did not moderate the findings. Thus, lip smacking, bringing fingers to mouth, and tongue protrusion continue to indicate sucrose liking across the first six months of infancy and may provide an index of positive hedonic response for this age range.

This index may be predictive of important biological and phenotypic markers later in development, particularly continued trajectories of positive hedonic response. Individual differences in response to sucrose were apparent with all behavioral responses (except smiling) ranging from no expression to expression in every interval. This indicates that even within the first six months, infants already exhibit individual differences in positive hedonic responses to sucrose. Future research should determine how infant positive hedonic response to sucrose may be associated with ongoing development of hedonic systems, overall growth, and related health risks (e.g., addiction, obesity).

While tongue protrusion was the most prevalent positive hedonic response to either solution (e.g., water, sucrose) among the infants, there was no difference in tongue protrusion for 24% sucrose solution compared to water. At 50% sucrose, infants did demonstrate more tongue protrusion compared to water, suggestingthere may be a dose-response relationship between intensity of sucrose concentration and tongue protrusion. There is likely a threshold at which the concentration of sucrose is optimal [13]. Children prefer stronger levels of

Table 1
Descriptives of each behavioral response to water, 24% and 50% sucrose solutions collapsed across ages

Solution Type	Rank order	Outcome variable	Mean interval proportion	SD	Minimum	Maximum
Water	1	Tongue protrusion	0.44	0.27	0.00	1.00
	2	Lip smacking	0.40	0.23	0.00	1.00
	3	Bringing fingers to mouth	0.13	0.20	0.00	1.00
	4	Smiling	0.06	0.11	0.00	0.75
24% sucrose	1	Tongue protrusion	0.46	0.32	0.00	1.00
	2	Lip smacking	0.42	0.28	0.00	1.00
	3	Bringing fingers to mouth	0.16	0.27	0.00	1.00
	4	Smile	0.05	0.12	0.00	0.83
50% sucrose	1	Tongue protrusion	0.48	0.32	0.00	1.00
	2	Lip smacking	0.45	0.29	0.00	1.00
	3	Bringing fingers to mouth	0.15	0.27	0.00	1.00
	4	Smiling	0.05	0.14	0.00	1.00

Table 2
Sample Demographics (n = 118)

Variable	Infants (n)	%
Infant Sex		
Male	58	49.15
Female	60	50.85
Infant Race/Ethnicity		
Black, non-Hispanic	10	8.47
Hispanic, any race	11	9.32
White	79	66.95
Other, non-Hispanic	18	15.25
Maternal Race/Ethnicity		
Black, non-Hispanic	11	9.48
Hispanic, any race	8	6.90
White, non-Hispanic	86	73.50
Other, non-Hispanic	11	9.48
Maternal Education		
High School Diploma or Less	11	9.32
Some College Credit	21	17.08
College Degree	46	38.98
Post-graduate Degree	40	33.90
Variable	Mean	SD
Maternal Age (years)	31.37	4.82
Infant Gestational Age (weeks)	39.64	1.06
Infant Birth Weight (g)	3453.37	411.82
Birth Weight for Gestational Age and Sex (z-score)	-0.05	0.88

Note: SD = standard deviation; Missingness for Maternal Race/Ethnicity (n = =2)

sweetness (18.48% to 19.17%) than adults do (14.38%%15.06%; [12]). This is thought to be an evolutionary advantage, as sweet flavors signal high-calorie content which supports the substantial energy demands of rapid growth during childhood [3]. Infants may like even higher levels of sweetness to support a period of extraordinary growth (i.e., doubling of body weight in the first 3-5 months after birth; Grummer-Strawn, Reinold, Krebs, & Centers for Disease Control and Prevention [[9], 2010].

Infant smiling [15, 16] did not occur significantly more in response to sucrose compared to water in our sample. One explanation for this is that alternative behavioral responses (i.e., tongue protrusion and lip smacking) compete with infant smiling. Higher occurrence of these behavioral responses may have reduced the likelihood of infant smiling. Although infants smiled more as they aged, smiling was not exhibited differentially to the solution type delivered. Because smiling occurs more rarely than other behavioral responses to sucrose and exhibits developmental changes as the infant ages, smiling may be a less useful index of positive hedonic response to sucrose [7].

There are limitations to consider. There was likely variability in infant hunger levels. Infant hunger is difficult to standardize, particularly at earlier ages [5]. It will also be important to investigate whether these findings generalize to more diverse and less well-resourced samples. Aversion responses to sucrose were not coded in the current study, due to limited evidence that they reliably occur in infants [7]. However, investigating the role of aversion to sucrose across development is an important future direction.

This was the first study to investigate positive hedonic responses to sucrose in infants beyond the newborn period using a repeated measures design in a relatively large sample of 118 infants. Positive hedonic behavioral responses were more likely to occur in response to sucrose than water across the first six months of infancy, thereby providing an index of positive hedonic response during this period. Tongue protrusion, lip smacking, and bringing fingers to mouth appear to be the most robust indicators, while smiling may be less useful. Positive hedonic responses to sucrose represent an avenue for assessing individual differences in infancy.

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Declaration of Competing Interest

The authors have no potential conflicts of interest.

Supplementary materials

Supplementary material associated with this article can be found, in

Table 3
Repeated measures linear regression for behavioral response of 24% and 50% sucrose solutions compared to water and main effect of age

Variable	Tongue Protrusion b (SE)	Lip Smacking b (SE)	Bringing Fingers to Mouth, b (SE)	Smiling b (SE)
24% vs. water	.02 (.012)	.03 (.010)*	.03 (.011)**	-.01(.006)
50% vs. water	.04(.013)**	.05 (.012)***	.02(.009)**	.00(.006)
Age	-.05(.007)***	-0.01(.007)	.00(.007)	.01(.002)*

Note: SE = standard error; *p < .05, **p < .01, ***p < .001.; *b* refers to the magnitude of the difference between solution types (i.e. 24% vs. water; 50% vs. water) across age

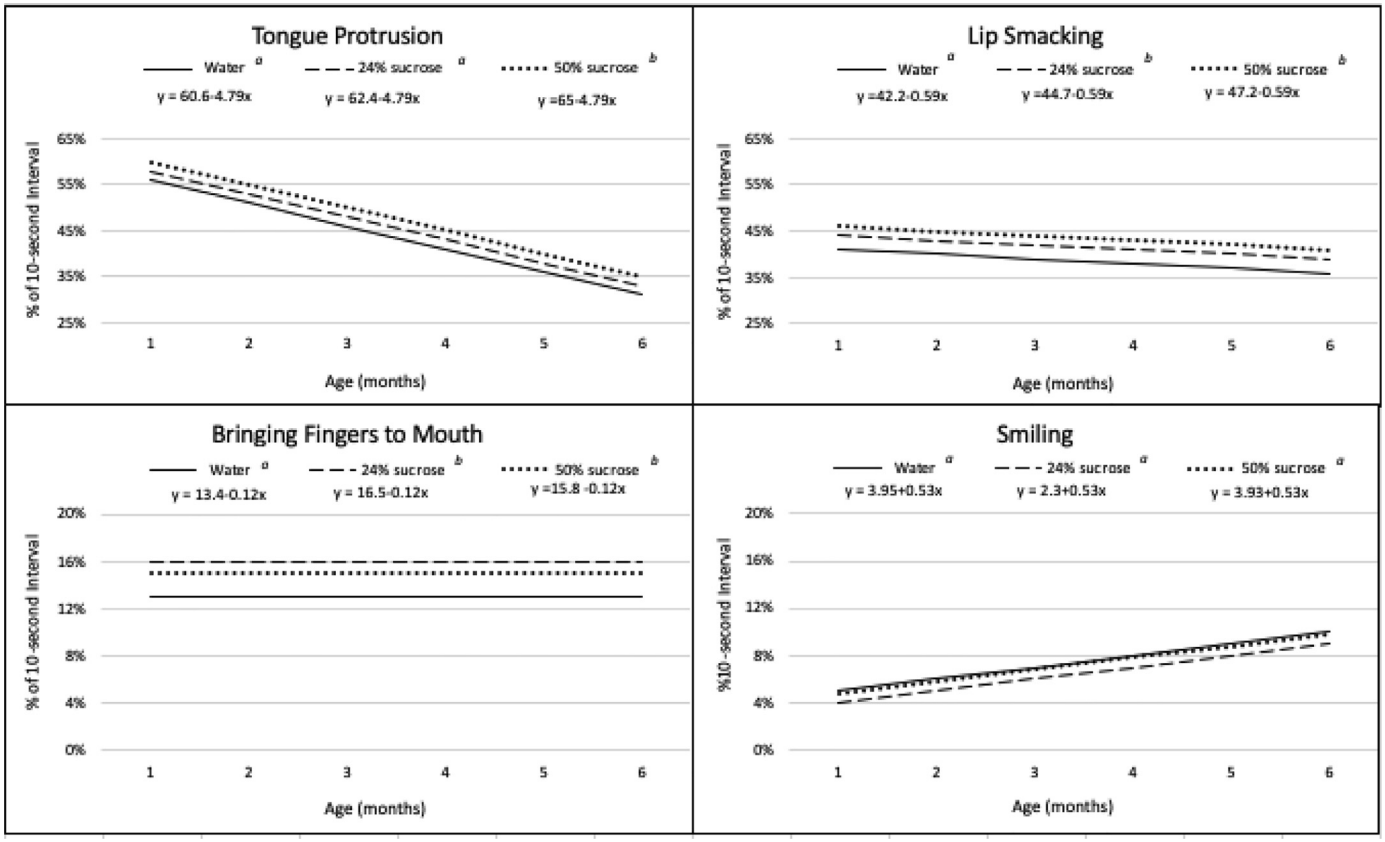

Figure 1. Proportion of Behavioral Responses to Sucrose by Solution Across Time

Note: The presence of different letters (*a* or *b)* next to solution types denote those that are significantly different at $p < 0.05$; statistical significance refers to the comparison of solution types and water (i.e. 24% vs. water; 50% vs. water) across age. Magnitude of behavioral response to sucrose is measured as the percentage of intervals (10 seconds) the behavior was expressed during the post-delivery observation period (60 seconds). The equations for generating the slopes are included under each solution type for each behavioral response. Main effects for age were detected for decreased tongue protruding ($p < .001$) and increased smiling over time ($p < .05$; see Table 3).

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