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Research paper

# Infant hedonic/anhedonic processing index (HAPI-Infant): Assessing infant anhedonia and its prospective association with adolescent depressive symptoms

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ABSTRACT

*Background:* Anhedonia, an impairment in the motivation for or experience of pleasure, is a well-established transdiagnostic harbinger and core symptom of mental illness. Given increasing recognition of early life origins of mental illness, we posit that anhedonia should, and could, be recognized earlier if appropriate tools were available. However, reliable diagnostic instruments prior to childhood do not currently exist.
*Methods:* We developed an assessment instrument for anhedonia/reward processing in infancy, the Infant Hedonic/Anhedonic Processing Index (HAPI-Infant). Exploratory factor and psychometric analyses were conducted using data from 6- and 12-month-old infants from two cohorts ($N = 188$, $N = 212$). Then, associations were assessed between infant anhedonia and adolescent self-report of depressive symptoms.
*Results:* The HAPI-Infant (47-items), exhibited excellent psychometric properties. Higher anhedonia scores at 6 ($r = 0.23$, $p < .01$) and 12 months ($r = 0.19$, $p < .05$) predicted elevated adolescent depressive symptoms, and these associations were stronger than for established infant risk indicators such as negative affectivity. Subsequent analyses supported the validity of short (27-item) and very short (12-item) versions of this measure.
*Limitations:* The primary limitations of this study are that the HAPI-Infant awaits additional tests of generalizability and of its ability to predict clinical diagnosis of depression.
*Conclusions:* The HAPI-Infant is a novel, psychometrically strong diagnostic tool suitable for recognizing anhedonia during the first year of life with strong predictive value for later depressive symptoms. In view of the emerging recognition of increasing prevalence of affective disorders in children and adolescents, the importance of the HAPI-Infant in diagnosing anhedonia is encouraging. Early recognition of anhedonia could target high-risk individuals for intervention and perhaps prevention of mental health disorders.

## 1. Introduction

Anhedonia refers to blunted sensitivity, reactivity, and approach to typically rewarding or pleasurable stimuli (Thomsen, 2015), and it arises from aberrant pleasure/reward circuit maturation and function (Birnie et al., 2020). Anhedonia and related dysfunction in pleasure/reward processing are transdiagnostic risk factors for the onset and maintenance of psychopathology (Conway et al., 2019; Nusslock and Alloy, 2017; Risbrough et al., 2018; Trøstheim et al., 2020), and are associated with poorer response to psychological and pharmacological treatments (McMakin et al., 2012). There is also elevated risk of suicidal ideation in those with anhedonia and a concurrent mood disorder (Ducasse et al., 2021).

Although considerable progress has been made in understanding

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anhedonia and reward processing in adolescents and adults, the developmental trajectory of these phenomena in human infants remains largely unexplored (Gutkovich, 2014; Luby, 2010). There is a critical gap in the literature concerning reward processing deficits in infants and their connection to subsequent psychopathology. The earliest examinations suggest that anhedonia is experienced as early as three years of age and is a specific predictor of severity of preschool depression (Luby et al., 2009; Luby et al., 2004), which is not transient but part of a chronic and persisting trajectory from preschool to adolescence (Gaffrey et al., 2018). However, investigations into infancy, potentially revealing even earlier origins of these trajectories, are conspicuously absent. Recently, Villanueva et al. (2021) emphasized the need for and importance of adopting a lifespan developmental perspective when characterizing positive emotion and reward responsivity, in order to better identify risk and resilience factors for the emergence or continuation of psychopathology from early through late life.

Considering the sensitive developmental periods for the maturation of the reward circuit (Birnie et al., 2020), early identification of disrupted reward behaviors becomes paramount as it offers the best opportunity for reversal of early symptoms and prevention of psychopathology. Pleasure/reward processing deficits detected in the preschool period, with continuity into adolescence, underscore the urgency of early intervention (Luby, 2010) in order to disrupt dysfunctional trajectories before they canalize (Barch et al., 2020). Despite the transdiagnostic significance of anhedonic phenotypes, the absence of developmentally appropriate measures for anhedonia assessment before the age of three has hindered comprehensive research.

Our study addresses this critical gap by leveraging an existing widely-used and validated measure of infant behavior to characterize anhedonia during infancy to create the first developmentally appropriate infant anhedonia assessment. First, the factor structure and psychometric properties of this novel measure of infant anhedonia were evaluated from prospective data collected in two longitudinal cohorts that began in infancy and continued into adolescence. Then, prospective associations between infant anhedonia and depressive symptoms 10 years later were assessed to verify the predictive validity of the measure. This study marks a pioneering effort to extend our understanding of anhedonia's developmental origins, contributing significantly to early identification and intervention strategies in mental health.

## 2. Methods

### 2.1. Study overview

This study consists of three primary goals. The first aim was to develop a reliable measure of infant anhedonia/reward processing and validate it using two combined longitudinal cohorts. The second aim was to evaluate whether this infant anhedonia measure demonstrates evidence of concurrent validity, through association with behavioral observation of infant pleasure (available only for Cohort 1), and discriminant validity, through a lack of association with an index of infant negative affectivity. Finally, the third aim tested its predictive validity by determining whether the infant anhedonia measure is associated with the development of depressive symptoms, as assessed via self-report in a longitudinal follow up of these infants approximately 10 years later (available only for Cohort 2). Secondary analyses evaluated the internal consistency and predictive validity of short (27 items) and very short (12 items) versions of the measure.

### 2.2. Participants

Participants from Cohort 1 comprised 188 infants and their mothers assessed at 6 and 12 months postpartum as part of an ongoing longitudinal study. To determine whether results would replicate, the analyses described below were repeated with the addition of participants from a second independent longitudinal cohort of mother-child pairs that had been assessed in infancy through adolescence (Cohort 2; $N = 212$). Table 1 reports descriptive information for the study samples. Although both cohorts were recruited from Southern California, they exhibit significant differences in terms of their sociodemographic characteristics. Cohort 1 is socioeconomically diverse with 51.5 % of the participants classified as low income (< 200 % of the federal poverty line) and 50.4 % relying on at least one form of government assistance. Further, mothers in Cohort 1 are more likely to be Latina, had lower household

**Table 1**
Descriptive information for study participants across cohorts.

| | Cohort 1 ($N = 188$) | Cohort 2 ($N = 212$) |
|---|---|---|
| | *M* (*SD*), Median or % | *M* (*SD*), Median or % |
| Anhedonia index, standard, 6 months | 2.4 (0.7) | 2.6 (0.7) |
| Anhedonia index, standard, 12 months | 2.4 (0.7) | 2.6 (0.7) |
| Negative affectivity, 6 months | 3.2 (0.7) | 3.0 (0.6) |
| Negative affectivity, 12 months | 3.6 (0.7) | 3.3 (0.7) |
| Depressive symptoms in adolescence | N/A | 3.9 (3.1) |
| Child characteristics | | |
| Sex at birth (% female) | 49.5 % | 47.6 % |
| Birth order (% first born) | 39.9 % | 43.4 % |
| Race/ethnicity | | |
| Hispanic or Latino/a | 48.9 %* | 27.8 %* |
| Non-Hispanic or Latino/a White | 31.4 %* | 50.5 %* |
| Asian | 9.6 % | 10.4 % |
| African American or Black | 3.2 % | 2.4 % |
| Multi-Ethnic | 6.9 % | 9.0 % |
| Maternal and familial characteristics | | |
| Married or cohabitating (% yes) | 86.7 % | 89.6 % |
| Maternal education | | |
| Less than high school | 10.1 %* | 3.7 %* |
| High school | 15.4 % | 12.2 % |
| Some college | 40.4 % | 41.5 % |
| College degree | 16.5 %* | 27.1 %* |
| Graduate degree | 17.6 % | 15.4 % |
| Income-to-needs ratio (Median) | 237.5* | 407.0* |

*Note*. Income-to-needs ratio was collected prenatally and is calculated by dividing the total annual household income by the appropriate U.S. Census Bureau poverty threshold based on family size.

* Difference between cohorts is statistically significant at the 0.05 level.

income, and were less likely to have a high school or college education than those in Cohort 2.

### 2.3. Ethical considerations

All study procedures were approved by the University of California Irvine Institutional Review Board for protection of human subjects, and mothers provided written, informed consent for themselves and their infants. In addition, the children provided assent at the 8–13 year-old visit. Both the consent and assent forms were reviewed thoroughly with the participants and they were given ample opportunities for questions and clarifications. It also was made clear that their participation was voluntary and that they could discontinue participation at any time.

### 2.4. Measures

#### 2.4.1. Infant Behavior Questionnaire-Revised (IBQ-R)

The IBQ-R (Gartstein and Rothbart, 2003) is a widely-used, caregiver-report instrument with 191 items developed to assess reactivity, regulation, and temperament in infants from 3 to 12 months of age. Items are rated on a Likert-type scale from 1 (never) to 7 (always), reflecting the frequency of objective infant behaviors in specific settings during the previous 1–2 weeks, as opposed to asking questions requiring comparative judgements or more global ratings of behaviors that have occurred over a longer period of time (Gartstein and Rothbart, 2003). The tool was designed to reduce reporter bias by asking about concrete infant behaviors rather than asking the rater to make abstract judgements (Gartstein and Rothbart, 2003). Additional concerns about reporter bias are mitigated by the fact that parental ratings correlate with observational measures of temperament in the laboratory (Goldsmith and Campos, 1990; Goldsmith and Reisner-Danner, 1986). This tool assesses three primary dimensions of temperament: Negative Affectivity, Surgency/Extraversion, and Orienting/Regulation (Gartstein and Rothbart, 2003), although the factor structure may differ across populations (Bosquet Enlow et al., 2016; Peterson et al., 2017). In addition to the standard version of the IBQ-R with 191 items, subsets of 91 and 37 items comprise the short and very short forms of the IBQ-R, respectively (Putnam et al., 2014). In both cohorts, the IBQ-R was completed by mothers when their infants were 6 and 12 months of age.

#### 2.4.2. Laboratory Temperament Assessment Battery (Lab-TAB) - Prelocomotor

To assess the validity of parent report on our anhedonia measure, an objective laboratory observational measure of pleasure was employed. In Cohort 1, at 6 months of age, the "Puppet Game" of the Lab-TAB (Goldsmith and Rothbart, 1996), which is designed to measure behavioral displays of pleasure in response to social stimulation, was administered. In this paradigm the experimenter performs a standardized interactive puppet show with the infant. For the current study, this episode was videotaped and scored by trained, reliable coders for the presence of laughter (yes/no) in the 6-month-old infants (interrater reliability was 100 %). Nine percent of the infants displayed laughter during the puppet show.

#### 2.4.3. Children's Depression Inventory, Second Edition (CDI 2): Self-Report Short Form

The CDI 2 (Kovacs, 2011) Self-Report Short Form is a 12-item self-report questionnaire that assesses the presence and severity of depressive symptoms in children 7 to 17 years of age in the two weeks prior to the assessment. Items are rated as 0 (absence of symptom), 1 (mild or probable symptom), or 2 (definite symptom). The current study used CDI 2 total scores from children and adolescents aged 8 to 13 years ($M$ = 10 years, $SD$ = 1) in Cohort 2.

### 2.5. Procedure and data analysis

#### 2.5.1. Aim 1: development of Infant Hedonic/Anhedonic Processing Index (HAPI-Infant)

The steps in development of the HAPI-Infant were: First, operational definitions of infant anhedonia were derived based on theory (Donohue et al., 2019; Feldman, 2012; Luby, 2010; Luby et al., 2003, 2004, 2006, 2009; Pizzagalli, 2014; Thomsen, 2015). These definitions included descriptions of how pursuit and experience of pleasure manifest in infants at 6 and 12 months of age. Then, seven experts independently identified which IBQ-R items were consistent with the developed definitions, and the individual items chosen with at least 85 % agreement among the seven independent evaluators were retained for factor analyses. Using full-information maximum likelihood (FIML) with robust standard errors as the estimator, exploratory factor analyses (EFA) with oblique (geomin) rotation were conducted in Mplus, version 8.4 (Muthén and Muthén, 1998–2017). Cronbach's alpha was then calculated as a measure of internal consistency. As a test of replicability, EFA and reliability analyses were repeated after the addition of Cohort 2.

#### 2.5.2. Aim 2: evidence of concurrent and discriminant validity

Anhedonia scores at 6 and 12 months were derived by calculating the mean across items at each age. Pearson correlations were then used to examine evidence of concurrent validity by correlating the anhedonia scores and presence of laughter from the Lab-TAB at 6 months (as an objective measure of pleasure), and discriminant validity by correlating the anhedonia scores and the IBQ-R Negative Affectivity subscale scores at 6 and 12 months.

#### 2.5.3. Aim 3: evidence of predictive validity with adolescent depressive symptoms

Pearson correlations were used to determine the associations between anhedonia scores in infancy and CDI scores a decade later.

## 3. Results

### 3.1. 1: development of infant anhedonia measure

There were 47 items from the standard version of the IBQ-R identified as relevant to anhedonia/reward processing in infancy with at least 85 % agreement among the independent evaluators (see Table 2). These items belonged to six different subscales on the IBQ-R and so exploratory factor analyses were run for one to six factors successively.

The scree plots and associated $p$ values for the models with $K$ versus $K$-1 factors indicated that, at both 6 and 12 months in Cohort 1, a one-factor solution was the best fit to the data, and each of the 47 items loaded ($p$'s $< 0.05$) on the single factor (see Supplement Table 1 for geomin-rotated factor loadings). These results were corroborated in a parallel analysis performed in Cohort 2 at both 6 and 12 months, where a one-factor solution similarly demonstrated the best fit to the data (Supplement Table 2). In light of the similarity across the two cohorts, and ages, we pooled the two cohorts. The geomin-rotated factor loadings for the merged cohorts (see Table 2) continued to support a one-factor solution, with all items demonstrating statistically significant loadings (see Table 2). Reliability analyses across cohorts suggested excellent internal consistency, with average Cronbach's α values of 0.92 at 6 months and 0.94 at 12 months (see Supplement Table 3).

### 3.2. 2: evidence of concurrent and discriminant validity

Infants who did not exhibit laughter during the positive pleasure episode of the Lab-TAB had higher anhedonia scores than the infants who did laugh ($r = -0.20$, $p < .05$), providing evidence of concurrent validity. Discriminant validity between the anhedonia measure and the IBQ-R Negative Affectivity subscale was demonstrated by a lack of a correlation between the two measures at 6 and 12 months ($r$'s = 0.04, $p$'s

**Table 2**
Anhedonia items and associated factor loadings from exploratory factor analyses at 6 ($N = 365$) and 12 ($N = 338$) months of age.

| Item # | Item text | Factor loadings | |
|---|---|---|---|
| | | 6 months | 12 months |
| 5 | In the last week, while being fed in your lap, how often did the baby seem to enjoy the closeness? | 0.37* | 0.41* |
| 6 | In the last week, while being fed in your lap, how often did the baby snuggle even after she was done? | 0.36* | 0.32* |
| 46 | How often during the last week did the baby look at pictures in books and/or magazines for 2–5 minutes at a time? | 0.32* | 0.33* |
| 47 | How often during the last week did the baby look at pictures in books and/or magazines for 5 minutes or longer at a time? (S, VS) | 0.32* | 0.33* |
| 49 | How often during the last week did the baby play with one toy or object for 5–10 minutes? (S, VS) | 0.42* | 0.35* |
| 50 | How often during the last week did the baby play with one toy or object for 10 minutes or longer? (S) | 0.39* | 0.28* |
| 53 | How often during the last week did the baby laugh aloud in play? (S) | 0.48* | 0.60* |
| 56 | How often during the last week did the baby smile or laugh after accomplishing something (e.g., stacking blocks, etc.)? (S) | 0.54* | 0.46* |
| 57 | How often during the last week did the baby smile or laugh when given a toy? (S, VS) | 0.60* | 0.63* |
| 58 | How often during the last week did the baby smile or laugh when tickled? | 0.45* | 0.64* |
| 59 | How often during the last week did the baby enjoy being sung to? | 0.55* | 0.55* |
| 60 | How often during the last week did the baby enjoy being read to? (S, VS) | 0.59* | 0.50* |
| 61 | How often during the last week did the baby enjoy hearing the sound of words, as in nursery rhymes? (S, VS) | 0.59* | 0.61* |
| 62 | How often during the last week did the baby enjoy looking at picture books? | 0.65* | 0.54* |
| 63 | How often during the last week did the baby enjoy gentle rhythmic activities, such as rocking or swaying? (S, VS) | 0.50* | 0.54* |
| 64 | How often during the last week did the baby enjoy lying quietly and examining his/her fingers or toes? | 0.53* | 0.39* |
| 65 | How often during the last week did the baby enjoy being tickled by you or someone else in your family? (S) | 0.50* | 0.55* |
| 66 | How often during the last week did the baby enjoy being involved in rambunctious play? | 0.47* | 0.48* |
| 67 | How often during the last week did the baby enjoy watching while you, or another adult, playfully made faces? | 0.60* | 0.63* |
| 68 | How often during the last week did the baby enjoy touching or lying next to stuffed animals? | 0.62* | 0.47* |
| 69 | How often during the last week did the baby enjoy the feel of soft blankets? (S) | 0.55* | 0.45* |
| 70 | How often during the last week did the baby enjoy being rolled up in a warm blanket? (S) | 0.21* | 0.37* |
| 71 | How often during the last week did the baby enjoy listening to a musical toy in a crib? (S) | 0.50* | 0.43* |
| 72 | When playing quietly with one of her/his favorite toys, how often did your baby show pleasure? | 0.66* | 0.63* |
| 73 | When playing quietly with one of her/his favorite toys, how often did your baby enjoy lying in the crib for more than 5 min? (S) | 0.45* | 0.23* |
| 74 | When playing quietly with one of her/his favorite toys, how often did your baby enjoy lying in the crib for more than 10 min? | 0.43* | 0.22* |
| 77 | When tossed around playfully how often did the baby smile? (S) | 0.50* | 0.71* |
| 78 | When tossed around playfully how often did the baby laugh? (S, VS) | 0.46* | 0.66* |
| 79 | During a peekaboo game, how often did the baby smile? (S) | 0.40* | 0.65* |
| 80 | During a peekaboo game, how often did the baby laugh? (S, VS) | 0.41* | 0.60* |
| 81 | How often did your baby enjoy bouncing up and down while on your lap? (S) | 0.48* | 0.59* |
| 82 | How often did your baby enjoy bouncing up and down on an object, such as a bed, bouncer chair, or toy? (S) | 0.54* | 0.48* |
| 85 | When your baby saw a toy s/he wanted, how often did s/he get very excited about getting it? (S) | 0.60* | 0.68* |
| 86 | When your baby saw a toy s/he wanted, how often did s/he immediately go after it? | 0.58* | 0.63* |
| 87 | When given a new toy, how often did your baby get very excited about getting it? | 0.64* | 0.65* |
| 88 | When given a new toy, how often did your baby immediately go after it? (S) | 0.55* | 0.62* |
| 89 | When given a new toy, how often did your baby seem not to get very excited about it? | −0.23* | −0.22* |
| 97 | How often during the last week did the baby move quickly toward new objects? (S, VS) | 0.51* | 0.53* |
| 98 | How often during the last week did the baby show a strong desire for something s/he wanted? (S) | 0.55* | 0.57* |
| 106 | When being held, how often did the baby seem to enjoy him/herself? (S, VS) | 0.43* | 0.48* |
| 107 | When being held, how often did the baby mold to your body? | 0.51* | 0.36* |
| 123 | When rocked or hugged, in the last week, how often did your baby seem to enjoy her/himself? (S, VS) | 0.57* | 0.49* |
| 126 | When reuniting after having been away during the last week how often did the baby seem to enjoy being held? | 0.52* | 0.51* |
| 129 | When being carried, in the last week, how often did your baby seem to enjoy him/herself? | 0.52* | 0.49* |
| 131 | While sitting in your lap how often did your baby seem to enjoy her/himself? | 0.54* | 0.46* |
| 149 | When you returned from having been away and the baby was awake, how often did s/he smile or laugh? | 0.41* | 0.59* |
| 159 | When visiting a new place, how often did the baby get excited about exploring new surroundings? (S, VS) | 0.38* | 0.45* |

*Note*. S = Included in short form of anhedonia measure. VS = Included in very short form of anhedonia measure. Geomin-rotated factor loadings from the one-factor model are presented. Each item is reverse-scored when calculating the anhedonia score, except for item 89.
* $p < .05$.

$> 0.05$).

### 3.3. 3: evidence of predictive validity with adolescent depressive symptoms

Infant anhedonia at 6 months ($r = 0.23$, $p < .01$) and 12 months ($r = 0.19$, $p < .05$) was associated with adolescent self-report of depressive symptoms (Table 3). The potential significance of examining anhedonia in infancy is supported by the finding that the IBQ-R Negative Affectivity subscale scores at 6 and 12 months were much more weakly (and not statistically significantly) associated with adolescent depressive symptoms ($r = 0.08$, $p = .35$, and $r = 0.07$, $p = .43$, respectively; Table 3).

### 3.4. Development of short and very short versions

Because administration of 47 items may be burdensome in some settings and studies, and to enhance the probability of its use as a screening tool, we next evaluated the anhedonia items from the short and very short forms of the IBQ-R (See Supplement Table 4 for descriptives). Of the 47 total anhedonia items, 27 were on the short form and 12 on the very short form of the IBQ-R. Both the short (27-item) and very short (12-item) forms showed strong internal consistency across ages, versions and cohorts (average Cronbach's alpha = 0.86; see Supplement Table 3). Further, the associations with adolescent depressive symptoms were similar in magnitude and level of statistical significance to the full 47-item version (see Supplement Table 5), demonstrating the theoretical agreement of the short and very short forms of the anhedonia measure with the standard form.

### 3.5. Stability across development

In further support of the robustness of our anhedonia scale, we observed significant and consistent correlations between 6 and 12 months for the standard, short, and very short versions (r's = 0.67, 0.65 and 0.58 respectively; Supplement Table 5). These observations further underscore the reliability of our measure across different versions and

**Table 3**
Bivariate correlations among the study variables (pooled across cohorts when possible).

| | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| 1. Anhedonia index | 1 | | | | | |
| 6 months | $N = 365$ | | | | | |
| 2. Anhedonia index | 0.67*** | 1 | | | | |
| | [0.60, 0.73] | | | | | |
| 12 months | $N = 303$ | $N = 338$ | | | | |
| 3. Presence of laughter | −0.20* | −0.12 | 1 | | | |
| | [−0.35, −0.04] | [−0.28, 0.05] | | | | |
| 6 months† | $N = 145$ | $N = 137$ | $N = 157$ | | | |
| 4. Negative affectivity | 0.04 | 0.04 | 0.06 | 1 | | |
| | [−0.06, 0.14] | [−0.08, 0.15] | [−0.11, 0.22] | | | |
| 6 months | $N = 365$ | $N = 303$ | $N = 145$ | $N = 365$ | | |
| 5. Negative affectivity | −0.05 | 0.04 | −0.02 | 0.64*** | 1 | |
| | [−0.17, 0.06] | [−0.07, 0.15] | [−0.19, 0.15] | [0.57, 0.70] | | |
| 12 months | $N = 303$ | $N = 338$ | $N = 137$ | $N = 303$ | $N = 338$ | |
| 6. Depressive symptoms | 0.23** | 0.19* | | 0.08 | 0.07 | 1 |
| | [0.06, 0.39] | [0.01, 0.36] | | [−0.09, 0.25] | [−0.11, 0.25] | |
| In adolescence‡ | $N = 130$ | $N = 118$ | $N = 0$ | $N = 130$ | $N = 118$ | $N = 138$ |

*Notes:* Values in square brackets indicate the lower and upper limits of the 95 % confidence interval for each correlation. Adjustment for age at time of assessment of depressive symptoms did not alter the associations between these symptoms and infant anhedonia at either six (partial r = 0.23, $p = .009$) or 12 months (partial r = 0.19, $p = .04$) of age.

* $p < .05$.

** $p < .01$.

*** $p < .001$.

† Only available for Cohort 1.

‡ Only available for Cohort 2.

time points, reinforcing its stability and validity in capturing infant anhedonia.

## 4. Discussion

Here we present a measure of infant anhedonia, the HAPI-Infant, for assessment of anhedonia as early as 6 months of age. The HAPI-Infant demonstrates robust psychometric properties, including excellent face validity, internal consistency, stability across infancy, concurrent validity with observational assessment of pleasure behavior, and discriminant validity from infant negative affectivity. These properties, observed across the full, short, and very short versions of the measure in two independent cohorts, support its feasibility and developmental appropriateness as a screener in clinical and research settings. The current study also suggests that the meaningful individual variation in pleasure/reward processing in infancy predicts subsequent development of depressive symptoms 10 years later in early adolescence. These observations collectively provide initial support for a window of opportunity for intervention specific to pleasure/reward processing that is much earlier than previously documented (Luby et al., 2004). The identification of anhedonia during infancy holds significant theoretical and clinical implications for understanding the developmental origins of neuropsychiatric disorders. The well-established and broad transdiagnostic significance of anhedonic and reward processing profiles underscores the critical importance of assessments that facilitate early characterization of these phenotypes. Further, the brain's adaptive ability to modify and rewire its billions of neural pathways is especially pronounced in the first years of life, contributing to the unique effectiveness of interventions during this stage (Inguaggiato et al., 2017).

Anhedonia has been identified as the most specific symptom of preschool depression (Luby et al., 2003), when compared to other common symptoms including: depressed, sad, or irritable mood; negative affect; psychomotor agitation; sleep disturbance; weight or appetite changes; fatigue; guilt; and cognitive impairment (Donohue et al., 2019; Luby et al., 2009). The extension of these observations from preschool depression studies to demonstrate that anhedonia in infancy is a more robust predictor of adolescent depressive symptoms than infant negative affectivity signifies a critical advancement in understanding of developmental origins of mental health. More broadly, these findings add to the literature identifying anhedonia as a risk factor for mood disorders (De Fruyt et al., 2020) that may be apparent beginning very early in life.

Presentation of anhedonia symptoms in early life that predict later risk for depressive symptoms underscores the need to better understand the developmental origins of neuropsychiatric disorders. The results of the current study align with ontogenetic studies emphasizing the impact of pre- and post-natal influences on physical and psychological health across the lifespan. These studies of health and disease have purported that exposure to a variety of organizing and disorganizing influences in pre- and post-natal life shape physical and psychological health across the lifespan (Barker et al., 2002; Felitti et al., 2019; McLaughlin et al., 2019). Growing evidence from preclinical models implicates exposure to early life adversity as a determinant of anhedonic phenotypes and underlying reward circuitry (Birnie et al., 2020; Bolton et al., 2018a, 2018b; Kangas et al., 2022; Pryce et al., 2004; Wendel et al., 2021). These findings are complemented by human studies documenting links between exposures to adversity in early life to altered structure and function of the reward system as well as anhedonic symptoms (Glynn et al., 2019; Goff and Tottenham, 2015; Pechtel and Pizzagalli, 2011). Thus, the evidence from both preclinical and clinical studies of developmental origins of anhedonia, combined with its transdiagnostic significance across the lifespan, emphasize the importance of the HAPI-Infant to further elucidate the developmental cascade toward neuropsychiatric disorders.

### 4.1. Strengths and limitations

The strengths of the current study include (1) identification of a reliable method for recognizing anhedonia during infancy (2) the establishment of the strong psychometric properties in two large independent cohorts (3) the validation of parent report of anhedonic symptoms with concurrent behavioral observations of positive affect in infants and (4) the prospective longitudinal assessments, which allowed a robust test of predictive validity linking infant anhedonic profiles to adolescent depressive symptoms. Further, we discovered that infant anhedonia accounted for more variance in adolescent depressive symptoms than negative affectivity, a previously established risk indicator. The primary limitation is the reliance on a single parent report, which is subject to reporter bias.

### 4.2. Directions for future research

Our study has laid a crucial foundation for understanding the predictive role of infant anhedonia in adolescent depressive symptoms. To further enhance the clinical applicability of the HAPI-Infant, investigations should extend to determine its ability to predict clinical diagnoses of depression, moving beyond dimensional self-reports. The transdiagnostic relevance of infant anhedonia also warrants exploration beyond its association with depression. Future research should examine its links with a broader spectrum of mental health outcomes, contributing to a comprehensive understanding of its developmental implications as a potential general vulnerability factor for various psychopathologies. Additionally, exploring the long-term trajectory of infant anhedonia is essential. Investigating whether the associations observed in adolescence persist into adulthood will deepen our understanding of the enduring impact of early anhedonia on mental health outcomes, informing interventions across the lifespan. To strengthen the generalizability and robustness of our findings, further confirmatory studies in diverse samples with additional reporters are recommended. Exploring how cultural, socioeconomic, and contextual factors may influence the expression and consequences of infant anhedonia will enrich the validity of the measure across different populations. Addressing these research directions will advance our knowledge, refine predictive validity, and contribute to the identification of early risk factors with broader transdiagnostic relevance.

### 4.3. Conclusions

The HAPI-Infant emerges as a pivotal tool addressing two key unmet needs: (1) enabling the identification of anhedonia during infancy using a brief, clinically useful measure, and (2) identifying a new predictive marker for subsequent mental health disorders. Its focus on aberrant reward processing in infancy offers the possibility to enhance our ability to recognize and address cognitive, emotional, and behavioral patterns in early life that may confer risk for broad neuropsychiatric outcomes.

In summary, our study contributes to a nuanced understanding of the developmental trajectory of anhedonia, emphasizing its early emergence, transdiagnostic relevance, and predictive power for later mental health outcomes. The HAPI-Infant stands as a valuable tool for advancing research and clinical efforts aimed at identifying and addressing neuropsychiatric risk factors in early life.

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## CRediT authorship contribution statement

**Jessica L. Irwin:** Conceptualization, Data curation, Formal analysis, Methodology, Writing – original draft, Writing – review & editing. **Elysia Poggi Davis:** Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Writing – review & editing. **Curt A. Sandman:** Conceptualization, Funding acquisition, Project administration, Writing – review & editing. **Tallie Z. Baram:** Conceptualization, Funding acquisition, Writing – review & editing. **Hal S. Stern:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Methodology, Writing – review & editing. **Laura M. Glynn:** Conceptualization, Funding acquisition, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing.

## Declaration of competing interest

The authors have nothing to disclose.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2024.01.225.

## References

Barch, D.M., Whalen, D., Gilbert, K., Kelly, D., Kappenman, E.S., Hajcak, G., Luby, J.L., 2020. Neural indicators of anhedonia: predictors and mechanisms of treatment change in a randomized clinical trial in early childhood depression. Biol. Psychiatry 88, 879–887. https://doi.org/10.1016/j.biopsych.2020.06.032.

Barker, D.J.P., Eriksson, J.G., Forsén, T., Osmond, C., 2002. Fetal origins of adult disease: strength of effects and biological basis. Int. J. Epidemiol. 31, 1235–1239. https://doi.org/10.1093/ije/31.6.1235.

Birnie, M.T., Kooiker, C.L., Short, A.K., Bolton, J.L., Chen, Y., Baram, T.Z., 2020. Plasticity of the reward circuitry after early-life adversity: mechanisms and significance. Biol. Psychiatry 87, 875–884. https://doi.org/10.1016/j.biopsych.2019.12.018.

Bolton, J.L., Molet, J., Regev, L., Chen, Y., Rismanchi, N., Haddad, E., Yang, D.Z., Obenaus, A., Baram, T.Z., 2018a. Anhedonia following early-life adversity involves aberrant interaction of reward and anxiety circuits and is reversed by partial silencing of amygdala corticotropin-releasing hormone gene. Biol. Psychiatry 83, 137–147. https://doi.org/10.1016/j.biopsych. 2017.08.023.

Bolton, J.L., Ruiz, C.M., Rismanchi, N., Sanchez, G.A., Castillo, E., Huang, J., Cross, C., Baram, T.Z., Mahler, S.V., 2018b. Early-life adversity facilitates acquisition of cocaine self-administration and induces persistent anhedonia. Neurobiol. Stress 8, 57–67. https://doi.org/10.1016/j. ynstr.2018.01.002.

Bosquet Enlow, M., White, M.T., Hails, K., Cabrera, I., Wright, R.J., 2016. The Infant Behavior Questionnaire-Revised: factor structure in a culturally and sociodemographically diverse sample in the United States. Infant Behav. Dev. 43, 24–35. https://doi.org/10.1016/J.INFBEH.2016. 04.001.

Conway, C.C., Li, Y.I., Starr, L.R., 2019. Trait anhedonia is a transdiagnostic correlate of internalizing problems during adolescence. J. Res. Pers. 81, 56–63. https://doi.org/10.1016/j.jrp.2019.05.004.

De Fruyt, J., Sabbe, B., Demyttenaere, K., 2020. Anhedonia in depressive disorder: a narrative review. Psychopathology 53, 274–281. https://doi.org/10.1159/000508773.

Donohue, M.R., Whalen, D.J., Gilbert, K.E., Hennefield, L., Barch, D.M., Luby, J., 2019. Preschool depression: a diagnostic reality. Curr. Psychiatry Rep. 21, 1–8. https://doi.org/10.1007/s 11920-019-1102-4.

Ducasse, D., Dubois, J., Jaussent, I., Azorin, J.M., Etain, B., Gard, S., Henry, C., Bougerol, T., Kahn, J.P., Aubin, V., Bellivier, F., Belzeaux, R., Dubertret, C., Dubreucq, J., Llorca, P.M., Loftus, J., Passerieux, C., Polosan, M., Samalin, L., Leboyer, M., Yrondi, A., Bennabi, D., Haffen, E., Maruani, J., Allauze, E., Camus, V., D'Amato, T., Doumy, O., Holtzmann, J., Lançon, C., Moliere, F., Moirand, R., Richieri, R.M., Horn, M., Schmitt, L., Stephan, F., Genty, J.B., Vaiva, G., Walter, M., El-Hage, W., Aouizerate, B., Olié, E., Courtet, P., 2021. Association between anhedonia and suicidal events in patients with mood disorders: a 3-year prospective study. Depress. Anxiety 38, 17–27. https://doi.org/10.1002/DA.23072.

Feldman, R., 2012. Parenting behavior as the environment where children grow. In: Mayes, L.C., Lewis, M. (Eds.), The Cambridge Handbook of Environment in Human Development. Cambridge University Press, pp. 535–567. https://doi.org/10.1017/cbo9781139016827.031.

Felitti, V.J., Anda, R.F., Nordenberg, D., Williamson, D.F., Spitz, A.M., Edwards, V., Koss, M.P., Marks, J.S., 2019. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: the Adverse Childhood Experiences (ACE) study. Am. J. Prev. Med. 56, 774–786. https://doi.org/10.1016/j.amepre.2019.04.001.

Gaffrey, M.S., Tillman, R., Barch, D.M., Luby, J.L., 2018. Continuity and stability of preschool depression from childhood through adolescence and following the onset of puberty. Compr. Psychiatry 86, 39–46. https://doi.org/10.1016/j.comppsych.2018.07.010.

Gartstein, M.A., Rothbart, M.K., 2003. Studying infant temperament via the Revised Infant Behavior Questionnaire. Infant Behav. Dev. 26, 64–86. https://doi.org/10.1016/S0163-6383(02)00169-8.

Glynn, L.M., Stern, H.S., Howland, M.A., Risbrough, V.B., Baker, D.G., Nievergelt, C.M., Baram, T.Z., Davis, E.P., 2019. Measuring novel antecedents of mental illness: the Questionnaire of Unpredictability in Childhood. Neuropsychopharmacology 44, 876. https://doi.org/10.1038/S41386-018-0280-9.

Goff, B., Tottenham, N., 2015. Early-life adversity and adolescent depression: mechanisms involving the ventral striatum. CNS Spectr. 20, 337–345. https://doi.org/10.1017/S1092852914000674.

Goldsmith, H.H., Campos, J.J., 1990. The structure of temperamental fear and pleasure in infants: a psychometric perspective. Child Dev. 61 (6), 1944–1964. https://psycnet.apa.org/doi/10.2307/1130849.

Goldsmith, H.H., Reisner-Danner, L.A., 1986. Variation among temperament theories and validation studies of temperament assessment. In: Kohnstamm, G.A. (Ed.), Temperament Discussed: Temperament and Development in Infancy and Childhood. Swets Zeitlinger, Lisse, the Netherlands.

Goldsmith, H.H., Rothbart, M.K., 1996. Prelocomotor and Locomotor Laboratory Temperament Assessment Battery, Lab-TAB; Version 3.0. Technical manual. Department of Psychology,. University of Wisconsin, Madison, WI.

Gutkovich, Z., 2014. Anhedonia in children and adolescents. In: Ritsner, M.S. (Ed.), Anhedonia: A Comprehensive Handbook Volume I: Conceptual Issues and Neurobiological Advances. Springer, Netherlands, pp. 65–80. https://doi.org/10.1007/978-94-017-8591-4_4.

Inguaggiato, E., Sgandurra, G., Cioni, G., 2017. Brain plasticity and early development: implications for early intervention in neurodevelopmental disorders. Neuropsychiatr. Enfance Adolesc. 65, 299–306.

Kangas, B.D., Short, A.K., Luc, O.T., Stern, H.S., Baram, T.Z., Pizzagalli, D.A., 2022. A cross-species assay demonstrates that reward responsiveness is enduringly impacted by adverse, unpredictable early-life experiences. Neuropsychopharmacology 47, 767–775. https://doi.org/10.1038/s41386-021-01250-9.

Kovacs, M., 2011. Children's Depression Inventory 2nd Edition (CDI 2): Technical Manual. Multi-Health Systems, Inc., North Tonawanda, NY.

Luby, J.L., 2010. Preschool depression: the importance of identification of depression early in development. Curr. Dir. Psychol. Sci. 19, 91–95. https://doi.org/10.1177/0963721410364493.

Luby, J.L., Heffelfinger, A.K., Mrakotsky, C., Brown, K.M., Hessler, M.J., Wallis, J.M., Spitznagel, E.L., 2003. The clinical picture of depression in preschool children. J. Am. Acad. Child Adolesc. Psychiatry 42, 340–348. https://doi.org/10.1097/00004583-200303000-00015.

Luby, J.L., Mrakotsky, C., Heffelfinger, A., Brown, K., Spitznagel, E., 2004. Characteristics of depressed preschoolers with and without anhedonia: evidence for a melancholic depressive subtype in young children. Am. J. Psychiatry 161 (1998–2004). https://doi.org/10.1176/appi.ajp.161.11.1998.

Luby, J.L., Sullivan, J., Belden, A., Stalets, M., Blankenship, S., Spitznagel, E., 2006. An observational analysis of behavior in depressed preschoolers: further validation of early-onset depression. J. Am. Acad. Child Adolesc. Psychiatry 45, 203–212. https://doi.org/10.1097/01.chi.0000188894.54713.ee.

Luby, J.L., Belden, A.C., Pautsch, J., Si, X., Spitznagel, E., 2009. The clinical significance of preschool depression: impairment in functioning and clinical markers of the disorder. J. Affect. Disord. 112, 111–119. https://doi.org/10.1016/j.jad.2008.03.026.

McLaughlin, K.A., Weissman, D., Bitrán, D., 2019. Childhood adversity and neural development: a systematic review. Annu. Rev. Dev. Psychol. 1, 277–312. https://doi.org/10.1146/annurev-devpsych-121318-084950.

McMakin, D.L., Olino, T.M., Porta, G., Dietz, L.J., Emslie, G., Clarke, G., Wagner, K.D., Asarnow, J.R., Ryan, N.D., Birmaher, B., Shamseddeen, W., Mayes, T., Kennard, B., Spirito, A., Keller, M., Lynch, F.L., Dickerson, J.F., Brent, D.A., 2012. Anhedonia predicts poorer recovery among youth with selective serotonin reuptake inhibitor treatmentresistant depression. J. Am. Acad. Child Adolesc. Psychiatry 51, 404–411. https://doi.org/10.1016/j.jaac.2012.01.011.

Muthén, L.K., Muthén, B.O., 1998–2017. Mplus User's Guide, Eigth Edition. Muthén & Muthén, Los Angeles, CA.

Nusslock, R., Alloy, L.B., 2017. Reward processing and mood-related symptoms: an RDoC and translational neuroscience perspective. J. Affect. Disord. 216, 3–16. https://doi.org/10.1016/j.jad.2017.02.001.

Pechtel, P., Pizzagalli, D.A., 2011. Effects of early life stress on cognitive and affective function: an integrated review of human literature. Psychopharmacology 214, 55–70. https://doi.org/10.1007/s00213-010-2009-2.

Peterson, E.R., Waldie, K.E., Mohal, J., Reese, E., Atatoa Carr, P.E., Grant, C.C., Morton, S.M.B., 2017. Infant Behavior Questionnaire–Revised Very Short Form: A New Factor Structure's Associations With Parenting Perceptions and Child Language Outcomes, 99, pp. 561–573. https://doi.org/10.1080/00223891.2017.1287709.

Pizzagalli, D.A., 2014. Depression, stress, and anhedonia: toward a synthesis and integrated model. Annu. Rev. Clin. Psychol. 10, 393–423. https://doi.org/10.1146/annurev-clinpsy-050212-185606.

Pryce, C.R., Dettling, A.C., Spengler, M., Schnell, C.R., Feldon, J., 2004. Deprivation of parenting disrupts development of homeostatic and reward systems in marmoset monkey offspring. Biol. Psychiatry 56, 72–79. https://doi.org/10.1016/j.biopsych.2004.05.002.

Putnam, S.P., Helbig, A.L., Gartstein, M.A., Rothbart, M.K., Leerkes, E., 2014. Development and assessment of short and very short forms of the Infant Behavior Questionnaire-Revised. J. Pers. Assess. 96, 445–458. https://doi.org/10.1080/00223891.2013.841171.

Risbrough, V.B., Glynn, L.M., Davis, E.P., Sandman, C.A., Obenaus, A., Stern, H.S., Keator, D.B., Yassa, M.A., Baram, T.Z., Baker, D.G., 2018. Does anhedonia presage increased risk of posttraumatic stress disorder?: adolescent anhedonia and posttraumatic disorders. Curr. Top. Behav. Neurosci. 38, 249–266. https://doi.org/10.1007/7854_2018_51.

Thomsen, K.R., 2015. Measuring anhedonia: impaired ability to pursue, experience, and learn about reward. Front. Psychol. 6, 1–11. https://doi.org/10.3389/fpsyg.2015.01409.

Trøstheim, M., Eikemo, M., Meir, R., Hansen, I., Paul, E., Kroll, S.L., Garland, E.L., Leknes, S., 2020. Assessment of anhedonia in adults with and without mental illness: a systematic review and meta-analysis. JAMA Netw. Open 3, e2013233. https://doi.org/10.1001/jamanetworkopen.2020.13233.

Villanueva, C.M., Silton, R.L., Heller, W., Barch, D.M., Gruber, J., 2021. Change is on the horizon: call to action for the study of positive emotion and reward in psychopathology. Curr. Opin. Behav. Sci. 39, 34–40. https://doi.org/10.1016/j.cobeha.2020.11.008.

Wendel, K.M., Short, A.K., Noarbe, B.P., Haddad, E., Palma, A.M., Yassa, M.A., Baram, T.Z., Obenaus, A., 2021. Early life adversity in male mice sculpts reward circuits. Neurobiol. Stress 15, 100409. https://doi.org/10.1016/j.ynstr.2021.100409.