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Authors
Howland, Mariann
Davis, Elysia
Phelan, Michael
et al.

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Prenatal Maternal Mood Entropy is Associated with Child Neurodevelopment

Mariann A. Howland[1], **Curt A. Sandman**[2], **Elysia Poggi Davis**[2,3], **Hal S. Stern**[4], **Michael Phelan**[4], **Tallie Z. Baram**[5,6,7], **Laura M. Glynn**[2,8]

[1]Institute of Child Development, University of Minnesota, Minneapolis, MN, USA

[2]Department of Psychiatry & Human Behavior, University of California, Irvine, CA, USA

[3]Department of Psychology, University of Denver, Denver, CO, USA

[4]Department of Statistics, University of California, Irvine, CA, USA

[5]Department of Anatomy/Neurobiology, University of California, Irvine, CA USA

[6]Department of Pediatrics, University of California, Irvine, CA, USA

[7]Department of Neurology, University of California, Irvine, CA, USA

[8]Department of Psychology, Chapman University, Orange, CA, USA

Abstract

Emerging evidence indicates that the predictability of signals early in life may influence the developing brain. This study examines links between a novel indicator of maternal mood dysregulation, mood entropy, and child neurodevelopmental outcomes. Associations between prenatal maternal mood entropy and child neurodevelopment were assessed in two longitudinal cohorts. Maternal mood was measured several times over pregnancy beginning as early as 15 weeks' gestation. Shannon's entropy was applied distributions of mothers' responses on mood questionnaires. Child cognitive and language development were evaluated at 2 and 6–9 years of age. Higher prenatal maternal mood entropy was associated with lower cognitive development scores at 2 years of age and lower expressive language scores at 6-9 years of age. These associations persisted after adjusting for maternal pre and postnatal mood levels and for other relevant sociodemographic factors. Our findings identify maternal mood entropy as a novel predictor of child neurodevelopment. Characterizing components of maternal mood in addition to level of severity or valence may further our understanding of specific processes by which maternal mood shapes child development.

Keywords

prenatal; unpredictability; maternal; mood; child development

Correspondence: Mariann A. Howland, Institute of Child Development, University of Minnesota, 51 East River Parkway, Minneapolis, MN 55455, howla042@umn.edu.

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The effects of maternal mood and psychopathology on the developing child are well-documented (Goodman et al., 2011; Kingston, Tough, & Whitfield, 2012; Martins & Gaffan, 2000). Accumulating evidence indicates that the prenatal period in particular is a sensitive window during which maternal mood states may shape the developing fetal brain and exert persisting influences on child emotional and cognitive function (Dunkel Schetter & Tanner, 2012; O'Connor, Monk, & Fitelson, 2014; Sandman, Glynn, & Davis, 2016; Talge, Neal, & Glover, 2007). Prenatal maternal negative mood (depression, anxiety, pregnancy-specific anxiety) predicts child cognitive and language outcomes from infancy (Davis & Sandman, 2010; Huizink, Robles De Medina, Mulder, Visser, & Buitelaar, 2003; Tran et al., 2013) and toddlerhood (Brouwers, Van Baar, & Pop, 2001; Ibanez et al., 2015; Koutra et al., 2013; Lin et al., 2017; Tse, Rich-Edwards, Rifas-Shiman, Gillman, & Oken, 2010) into childhood (Buss, Davis, Hobel, & Sandman, 2011; Evans et al., 2012; Loomans et al., 2012) and adolescence (Mennes, Stiers, Lagae, & Van den Bergh, 2006; Van Den Bergh et al., 2005). Complementary to cognitive and language outcome findings are studies linking prenatal maternal negative mood states with structural alterations in brain regions governing these functions (Adamson, Letourneau, & Lebel, 2018; Buss, Davis, Muftuler, Head, & Sandman, 2010; Lebel et al., 2016; Qiu et al., 2013; Sandman, Buss, Head, & Davis, 2015). Cumulatively, these results suggest that maternal negative mood states during pregnancy have lasting implications for child neurodevelopment.

In addition to valence (e.g., positive or negative) or levels (e.g., severity) of maternal mood states, other indicators of maternal mood dysregulation may shape fetal and child neurodevelopment and predict cognitive and language outcomes. A broader literature indicates that intraindividual patterns in mood (e.g., its instability, variability) are quantifiable and meaningful components of mood (Ebner-Priemer, Eid, Kleindienst, Stabenow, & Trull, 2009; Eid & Diener, 1999; Jahng, Wood, & Trull, 2008; Thompson, Dizén, & Berenbaum, 2009), emotion regulation (Cole, Michel, & Teti, 1994; Thompson, 1994), and mental health (Broome, Saunders, Harrison, & Marwaha, 2015; Fernandez, Jazaieri, & Gross, 2016; Houben, Van Den Noortgate, & Kuppens, 2015; Koenigsberg, 2010). These aspects of mood dysregulation have been largely ignored when examining associations between maternal mood and fetal and child development.

Mood dynamics have been characterized through examination of patterning across time (e.g., across days or weeks); across situations; and at a single point in time, capturing a snapshot of emotional experience (Ed & Diener, 1999; Kuppens & Verduyn, 2015; Penner, Shiffman, Paty, & Fritzsche, 1994). Recently, we identified a novel indicator of mood dysregulation using a measure of normalized entropy (Glynn, Howland, Sandman, et al., 2018). Shannon's entropy is used to measure the randomness or unpredictability of the probability distribution of a random variable (Cover & Thomas, 2006); we applied it to the distribution of item responses on maternal mood questionnaires. In two independent, prospective, longitudinal cohorts, we found that elevated prenatal maternal mood entropy was associated with higher levels of child negative affectivity across childhood and higher levels of depressive and anxiety symptoms in early adolescence. Importantly, the associations were independent of maternal mood *level*.

The current investigation expanded upon Glynn et al. (2018) to examine associations between prenatal maternal mood entropy and child neurodevelopmental outcomes at 2 and 6-9 years of age in the same independent, prospective, longitudinal cohorts of women and their children. We hypothesized that elevated prenatal maternal mood entropy would be associated with impaired cognitive and language development and that these associations would not be explained by the well-established effects of maternal mood level. We expected to replicate established effects of maternal negative mood level, hypothesizing that maternal negative mood levels would be associated with lower cognitive and language development scores.

Methods

Study Overview

Women recruited during the first trimester of pregnancy completed three to five prenatal laboratory visits and participated with their children in postnatal visits at 2 years and/or 6-9 years of age (see Figure 1 for data collection protocol). Maternal psychological distress was evaluated at each pre and postnatal assessment with reliable and valid self-report indices, from which entropy measures were computed. Child neurodevelopment was evaluated at each postnatal visit using standardized, developmentally appropriate assessments of verbal and non-verbal cognition. The study protocol was approved by the institutional IRB, and written informed consent was obtained from the mothers and assent from the children beginning at age 7.

Participants

Pregnant women were initially recruited from affiliated clinics at two large university medical centers in Southern California through separate National Institutes of Health (NIH)-funded projects. Mother-child pairs from both cohorts were then recruited together when the children were 6-9 years of age into a third NIH-funded study (see Supplemental Material for additional details). Inclusion criteria for women at recruitment were: English-speaking, adult (≥ 18 years old) women with intrauterine, singleton pregnancies. Exclusion criteria were: the presence of uterine or cervical abnormalities; conditions such as endocrine, hepatic or renal disorders or use of corticosteroid medication that could dysregulate neuroendocrine function; and abuse of tobacco, alcohol, or recreational drugs in the pregnancy. Mother-child pairs were included in the current study if child neurodevelopmental outcome data were available at 2 years and/or 6-9-years of age (total $N = 299$). Different numbers of children were assessed at each age. This was based upon the number of children in these longitudinal cohorts who had aged into the assessment window during each of the grant cycles. Demographic characteristics of the mother-child pairs are presented in Table 1. Sample sizes for the three cohorts were based on power analyses conducted for initial NIH grant applications, which were designed to address prenatal influences (including maternal mood) on child development.

Measures

Maternal mood.

Assessments.: Reliable and valid measures of maternal depressive symptoms (Beck Depression Inventory: Beck, Ward, Mendelson, Mock, & Erbaugh, 1961; Beck, Steer, & Carbin, 1988; Center for Epidemiologic Studies-Depression Scale-Short Form: Santor & Coyne, 1997), anxiety symptoms (State-Trait Personality Inventory: Spielberger, Jacobs, Crane, & Russell, 1979; Spielberger & Reheiser, 2009), pregnancy-specific anxiety (Dunkel-Schetter & Glynn, 2010; Rini, Dunkel-Schetter, Wadhwa, & Sandman, 1999), and perceived stress (Perceived Stress Scale: Cohen, Kamarck, & Mermelstein, 1983; Cohen & Williamson, 1988) were administered.

Mood entropy.: Shannon's entropy was computed for each mother's responses on each of the four questionnaires at each assessment. For a single questionnaire at a single point in time the entropy score quantifies the unpredictability or inconsistency of responses across the items on that questionnaire. The responses are tabulated over items into a probability distribution that records the relative frequency of each response choice. The formula for Shannon's entropy is: $\Sigma i\ Pi \log 2\ Pi$, where Pi is the proportion of items for which the i-th response choice was made, log2 indicates the logarithm to the base two, and Σ indicates that the sum is to be taken over all possible response choices. For example, a mother who reports never worried and always relaxed on the state anxiety scale would have a low entropy score, whereas a mother with entirely random responses on the anxiety scale would have a very high entropy score. To apply this approach across the different mood questionnaires, entropy scores were normalized by expressing each as a percentage of its maximum value, with entropy scores ranging from 0 (perfectly consistent or predictable) to 100 (random and unpredictable). Mood entropy scores were calculated using an R (R Core Team, 2019) function which is available at: https://contecenter.uci.edu/measuring-maternal-mood/. Each questionnaire also was scored conventionally as an index of mood level.

Test of discriminant validity.: To address the alternate explanation that our entropy measure reflects a general tendency to report or respond to questionnaire items in an unpredictable or inconsistent manner, rather than a profile that is specific to mood or affect, we calculated entropy in responses on a questionnaire unrelated to mood (parallel to our test of discriminant validity in Glynn et al., 2018). Entropy was computed from a Likert-type scale measuring physical activity during the prenatal period, and its associations with mood entropy and with child neurodevelopmental outcomes were examined.

Characterization of mood entropy: Links to indicators of emotion dysregulation.: We have previously reported that mood entropy is positively associated with an established, momentary measure of mood variability across hours and days assessed with ecological momentary assessment (affective instability using the standard root mean square successive difference; see Glynn, Howland, Sandman, et al., 2018). In the current study, we further examined correlates of our mood entropy measure by assessing its associations with widely-used, validated self-report measures of affective instability, emotional awareness, and emotional clarity. In a third prospective longitudinal study of pregnant women, mood entropy scores were derived exactly as described above from the same four mood

questionnaires collected at a laboratory visit at approximately 35 weeks' gestation. At this same visit, women completed three self-report measures of emotional experience. The 18-item version of the Affective Lability Scale (Look, Flory, Harvey, & Siever, 2010) assesses the degree to which individuals report that they tend to shift from normal mood states to states of anger, depression, elation, and anxiety, as well as their tendency to oscillate between different mood states. To assess emotional awareness and emotional clarity, we administered the 20-item Toronto Alexithymia Scale (Bagby, Parker, & Taylor, 1994) as well as and the 36-item Difficulties in Emotion Regulation Scale (Gratz & Roemer, 2004), which includes lack of emotional awareness (6 items) and lack emotional clarity (5 items) subscales.

Child neurodevelopmental outcomes.

Assessment at 2 years of age.: At 2 years of age, the Bayley Scales of Infant Development, Second Edition (BSID-II; Bayley, 1993) was administered. The composite Mental Development Index (MDI) assesses a combination of early cognitive (sensory perception, knowledge, memory, problem solving) and receptive and expressive language abilities. The BSID is one of the most widely used measures of infant development, both for research and clinical applications (Strauss, Sherman, & Spreen, 2006). Examiners in the current study were trained by a clinician with more than 15 years of experience with BSID administration and were directly supervised by a clinical psychologist. An independent observer reviewed 20% of videotaped assessments, with an interrater reliability of 93%.

We acknowledge that the BSID has demonstrated limited predictive validity for later child cognitive outcomes, specifically among high-risk infants (Hack et al., 2005). However, in our sample, BSID-II MDI scores were associated with 6-9-year non-verbal cognitive ability (Perceptual Reasoning Index of the Wechsler Intelligence Scale for Children, Fourth Edition; $r(70) = .24$, $p = .04$) and expressive language (Expressive Vocabulary Test, Second Edition; $r(70) = .50$, $p < .001$) scores.

Assessment at 6-9 years of age.: At the 6-9-year assessment, children were administered the Perceptual Reasoning Index (PRI) of the Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV; Wechsler, 2003). The PRI measures perceptual and fluid reasoning, visual-motor and visual-spatial skills and comprises three subtests (Block Design, Picture Concepts, and Matrix Reasoning). The PRI is relatively language free, and two of the subscales (Block Design and Matrix Reasoning) have been designated as good indicators of general intelligence (Groth-Marnat, 2009).

Children also completed the Expressive Vocabulary Test, Second Edition (EVT-2; Williams, 2007), which assesses expressive vocabulary and word retrieval of the spoken word in standard American English. Parts of speech assessed include nouns, verbs, and attributes. The measure has demonstrated good validity, internal consistency, and stability in children ages 6 – 10 years of age (Williams, 2007).

Maternal cognitive ability.: At the child's 6-9-year assessment, mothers were administered the Perceptual Organization Index (POI) of the Wechsler Adult Intelligence Scale, Third Edition (WAIS-III; Wechsler, 1997). The three subtests comprising the POI are parallel to

the WISC-IV PRI subscales administered to children. This index is similarly considered to be language and culture free and a valid indicator of general intelligence (Groth-Marnat, 2009).

Statistical Analyses

At 2 years, 112 children provided BSID-II MDI scores. At 6-9 years, 259 children had neurodevelopmental outcome data; WISC-IV PRI scores were missing for 2 children, and 1 child was missing an EVT-2 score. All mothers had mood entropy scores, and no data were missing for covariates considered in final analyses.

Mood entropy scores were relatively stable across gestation (*r*s = .32 - .61; see Supplemental Table 1 and Supplemental Figure 1), so entropy scores were averaged within each assessment across gestation (e.g., CESD entropy scores from each of the 5 timepoints were averaged to create a prenatal CESD entropy score). The four prenatal mood entropy measures were moderately associated (see Supplemental Table 2), and there were no reliable differences in their patterns of associations with child neurodevelopmental outcomes (see Supplemental Table 3). Also, gestational timing did not moderate associations between maternal mood entropy and child outcomes (see Supplemental Table 4). Therefore, the four scores were averaged to create a single prenatal mood entropy index. Similar composite variables also were created for prenatal maternal mood level and for maternal mood entropy and mood level at the time of the child assessments.

Bivariate correlations were performed to assess relations between prenatal mood entropy and child neurodevelopment. Child neurodevelopmental outcomes that were associated with prenatal mood entropy were then treated as dependent variables in multiple regression models to assess whether associations held when adjusting for other potential confounds. Covariates were selected based on the literature and included: gestational age at birth, child sex, birth order, maternal age, socioeconomic status (composite of standardized prenatal annual household income and maternal years of education), maternal self-identified race/ethnicity, cohabitation with the child's father during pregnancy, maternal cognitive ability and study cohort. Only variables associated with both the predictor and the outcome at $p < .10$ were included as covariates in the multiple regression models because these are the variables most likely to impact associations between mood entropy and the outcomes (see Supplemental Table 5 for zero-order correlations between these study variables). Those that met criteria for inclusion were: maternal age, socioeconomic status, cohabitation with the child's father, and maternal cognitive ability. Because prenatal maternal mood entropy scores were correlated with prenatal maternal mood levels (see Supplemental Table 2), and because pre and postnatal maternal mood levels are established predictors of child neurodevelopment, both prenatal and concurrent postnatal maternal mood levels were included in the models. Additionally, to test if maternal mood entropy effects are specific to the prenatal period, we included mood entropy assessed concurrently at the time of child assessment in each model. Finally, because sex differences have been reported for fetal exposures to stress and adversity (Sandman, Glynn, & Davis, 2013; Sutherland & Brunwasser, 2018), exploratory analyses tested the addition of child sex and its interaction

with prenatal maternal mood entropy in the models. All analyses were conducted using SPSS (v. 24.0).

Results

Maternal Mood Entropy

Paired samples *t*-tests indicated that maternal mood entropy scores were higher during the prenatal period ($M = 55.97$, $SD = 12.32$) compared with values at 2 years ($M = 48.65$, $SD = 18.29$) and 6-9 years ($M = 47.88$, $SD = 16.09$) postnatally, $t(112) = 2.83$, $p = .01$ and t (260) = 8.92, $p < .001$, respectively. Prenatal maternal mood entropy was associated with mood entropy at both postnatal time points, $r(110) = .54$ and $r(259) = .42$, ps < .001.

Prenatal Maternal Mood Level and Child Neurodevelopment

Consistent with previous findings in the literature, higher levels of prenatal maternal negative mood were associated with lower cognitive development (BSID-II MDI) scores at 2 years of age, $r(110) = -.31$, $p = .001$, and lower expressive language (EVT- 2) scores at 6-9 years of age, $r(256) = -.15$, $p = .02$. Prenatal maternal mood level was not associated with children's non-verbal cognitive development (WISC-IV PRI) scores at 6-9 years of age, $r(255) = -.04$, $p = .52$.

Prenatal Maternal Mood Entropy and Child Neurodevelopment

Higher prenatal maternal mood entropy was associated with lower cognitive development (BSID-II MDI) scores at 2 years of age, $r(110) = -.37$, $p < .001$, and lower expressive language (EVT-2) scores at 6-9 years of age, $r(256) = -.21$, $p = .001$ (Figure 2). Prenatal maternal mood entropy was not associated with non-verbal cognitive (WISC-IV PRI) scores at 6-9 years of age, $r(255) = -.07$, $p = .26$.

In multiple regression models, prenatal maternal mood entropy was associated with children's cognitive development scores at 2 years of age, $B = -0.34$, $\beta = -.27$, $p = .03$, and children's expressive language scores at 6-9 years of age, $B = -0.18$, $\beta = -.16$, $p = .04$, after adjusting for relevant sociodemographic variables (maternal age, socioeconomic status, cohabitation with child's father during pregnancy), maternal cognitive ability, pre and postnatal maternal mood levels, and concurrent postnatal maternal mood entropy (see Table 2).

When child sex (1 = female) and its interaction with prenatal maternal mood entropy were included in the models, the results provided some evidence that the slope relating maternal mood entropy to children's cognitive development scores at 2 years of age differed by child sex, $B = -0.37$, $\beta = .24$, $p = .08$. Simple slope analyses indicated that higher prenatal maternal mood entropy was associated with lower child cognitive development scores at 2 years in girls, slope = −0.47, $t = -2.80$, $p = .01$, but not in boys, slope = −0.10, $t = -0.54$, $p = .59$. There was no evidence for a difference in slope for children's expressive language scores at 6-9 years of age, $B = -0.03$, $\beta = -.02$, $p = .83$ for the interaction term.

Test of Discriminant Validity

Prenatal maternal mood entropy was not associated with entropy in maternal responses to the prenatal physical activity questionnaire, $r = .05$, $p = .38$. Further, when entropy in responses on the physical activity questionnaire replaced prenatal maternal mood entropy in the same regression models described above, it was not predictive of child cognitive development at 2 years of age or expressive language development at 6-9 years of age, ps > .30.

Characterization of Mood Entropy: Links to Indicators of Mood Dysregulation

Mood entropy scores were positively associated with self-reported levels of affective lability (r = .49, p < .001), alexithymia (r = .44, p = .001), lack of emotional awareness (r = .38, p = .004), and lack of emotional clarity (r = .33, p = .01). See Supplemental Table 6 and Figure 2 for further details.

Discussion

Maternal mood entropy was identified as a novel predictor of child neurodevelopmental outcomes at 2 and 6-9 years of age. Importantly, prenatal maternal mood entropy was negatively associated with child neurodevelopmental outcomes after accounting for the well-established effects of pre and postnatal mood levels. In concert with our previous work (Glynn, Howland, Sandman, et al., 2018; Sandman, Davis, & Glynn, 2012), these results support the premise that entropy in maternal mood may have persisting effects on offspring development that are independent of other established influences. Furthermore, results indicate that considering components of maternal mood dysregulation such as mood entropy can enhance our understanding of the specific processes by which maternal signals influence child development.

Fetal exposure to maternal mood entropy was associated with lower scores on assessments of cognitive development at 2 years of age and of expressive language at 6-9 years of age. The EVT-2 assesses of expressive language, and many of the BSID-II MDI items rely heavily upon verbal ability (Bayley, 1993). In contrast, subtests of the WISC-IV PRI assess primarily nonverbal abilities. In our sample, 2-year BSID-II MDI scores were more strongly associated with 6-9-year EVT-2 scores than WISC-IV PRI scores. Maternal mood entropy may have greater effects on verbal cognitive ability compared to non-verbal cognitive ability. However, this possibility requires replication and further exploration in the future.

The potential for child sex to determine these associations also requires additional investigation. That our exploratory analyses provide some evidence that the association between prenatal mood entropy and 2-year child cognitive development scores appears to be present among girls, but not boys is consistent with findings from previous studies documenting sex differences in fetal programming (Sandman et al., 2013; Sutherland & Brunwasser, 2018). However, we did not find a sex difference in the association between maternal mood entropy and 6-9-year child expressive language scores.

Mood entropy was relatively stable over gestation and across measures, consistent with findings demonstrating that related metrics (mood variability and affective instability)

may be stable traits (Eid & Diener, 1999; Penner et al., 1994). The current investigation supports our earlier finding of discriminant validity of the mood entropy measure as a predictor of child outcomes (Glynn, Howland, Sandman, et al., 2018) by demonstrating that entropy scores from a scale unrelated to mood did not predict child neurodevelopmental outcomes. This indicates that the associations between maternal mood entropy and child outcomes are not simply reflective of maternal reporting or response style, but instead are specific to mood. We documented previously that mood entropy is positively associated with variability in mood across hours and days collected via ecological momentary assessment (Glynn et al., 2018). In the current study, we also demonstrate that mood entropy scores are associated with higher levels of affective instability and lower levels of emotional awareness and emotional clarity as measured by validated self-report questionnaires. These findings provide further support for mood entropy as an indicator of multiple aspects of mood dysregulation, specifically that women who exhibit higher mood entropy may experience more variation in their emotional experiences (e.g., affective instability) or difficulties identifying or differentiating between emotions (e.g., alexithymia, emotional awareness, emotional clarity). In addition to the possibility that mood entropy indexes several components of mood dysregulation, another strength is that it relies on item response patterns rather than direct self-report of mood dysregulation.

Our findings complement evidence from cross-species research indicating that exposure to unpredictable maternal signals has consequences for neurodevelopmental outcomes, particularly hippocampal-dependent memory tasks and their underlying neural circuitry (Baram et al., 2012; Davis et al., 2017, 2019; Ivy et al., 2010; Molet et al., 2016). Throughout gestation, the fetal brain is rapidly developing, and its primary structures and neural pathways are formed and refined (Fox, Levitt, & Nelson, 2010; Lebel et al., 2016; Stiles, Brown, Haist, & Jernigan, 2015; Tau & Peterson, 2010). It is plausible that predictable patterns of maternal signals have organizing effects, whereas unpredictable patterns have disorganizing effects, on the developing fetal brain. Rodent models demonstrate that patterns of stimulation during early life influence synaptic development and function (Baram et al., 2012; Gunn et al., 2013; Singh-Taylor et al., 2018). For example, exposure to predictable and recurrent patterns of maternal signals results in a reduction of excitatory synapses onto stress-sensitive hypothalamic neurons (Singh-Taylor et al., 2018), but exposure to unpredictable signals results in enhanced excitatory synaptic transmission in these same neurons (Gunn et al., 2013). In humans, exposure to greater entropy of maternal sensory signals during the first year of life is associated with lower child cognitive development at age 2 and with poorer performance on a delayed-recall memory task at age 6 (Davis et al., 2017). Notably, the quantity or quality of the maternal signals do not account for these associations, underscoring the importance of predictability of inputs to the developing brain (Baram et al., 2012; Davis et al., 2017; Molet et al., 2016).

The mechanisms underlying associations between unpredictability of maternal signals and child development in humans are currently unknown. Studies examining possible mechanisms linking prenatal maternal mood *levels* with fetal and child outcomes have considered neural, endocrine, immune and cardiovascular pathways (Christian, 2012; Coussons-Read, Okun, & Nettles, 2007; Dipietro, 2010; Giesbrecht, Campbell, Letourneau, Kooistra, & Kaplan, 2012; Kane, Dunkel Schetter, Glynn, Hobel, & Sandman, 2014;

Teixeira, Fisk, & Glover, 1999), which also may be relevant for mood entropy. One possibility is that maternal mood entropy is associated with vagally mediated heart rate variability (HRV), a physiological marker of emotion regulation (Appelhans & Luecken 2006). Lower HRV is associated with indicators of emotional dysregulation such as higher affectivity instability (Koval et al., 2013) and alexithymia (Lischke et al., 2018; Panayiotou & Constantinou, 2017) in non-pregnant individuals. While these associations have not been assessed in the context of pregnancy, one study has demonstrated that experimentally-induced reductions in HRV modulate maternal-fetal heart rate synchrony (Van Leeuwen et al., 2009). Fetal heart rate is an established indicator of fetal neurodevelopment and central nervous system integrity, and fetal heart rate variability predicts cognitive functioning into postnatal life (DiPietro, Bornstein, Hahn, Costigan, & Achy-Brou, 2007). These studies highlight the potential for prenatal maternal mood entropy-induced changes in HRV to alter fetal neurodevelopment.

Pregnancy is a period of heightened vulnerability for some mood disturbances in the female lifespan, with documented consequences for both mother and developing child (Glynn, Howland, & Fox, 2018; Sandman, Davis, Buss, & Glynn, 2012). To date, interventions focused on preventing or reducing prenatal maternal psychological distress have met with limited success (Fontein-Kuipers, Nieuwenhuijze, Ausems, Budé, & De Vries, 2014). In the current study, we observed that fetal exposure to maternal mood entropy was associated with less optimal child neurodevelopmental outcomes, even after adjusting for maternal mood level. These findings, along with evidence indicating the maladaptive effects of mood instability on mental health outside of the prenatal period (Houben et al., 2015), suggest that maternal mood patterns may be a new target for prenatal intervention. In non-pregnant samples, increased self-reported mindfulness is associated with lower levels of mood variability and instability (Hill & Updegraff, 2012; Keng & Tong, 2016), and meditation has been shown to increase HF-HRV, a potential physiological signature of mood variability or instability (Libby, Worhunsky, Pilver, & Brewer, 2012; Tang et al., 2009). Other interventions may include those aimed at reducing affective instability and lability in mood, such as dialectal behavioral therapy (Stepp, Epler, Jahng, & Trull, 2008). If mood entropy is demonstrated as a modifiable target, it may inform new avenues of prenatal intervention to support mothers and their developing children.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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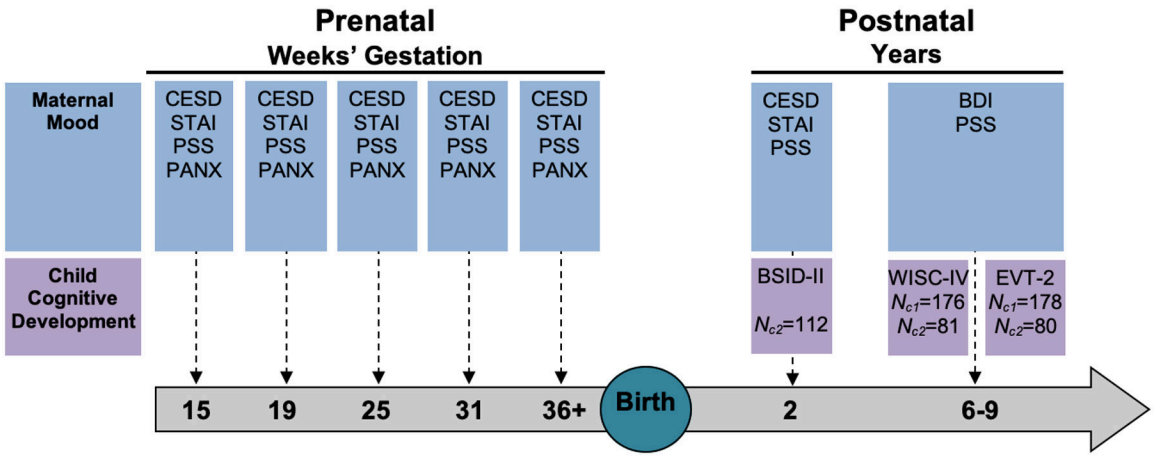

Figure 1.

Description of study protocol for the two cohorts (total N = 299). CESD = Center for Epidemiologic Studies Depression Scale– Short Form. STAI = State Trait Anxiety Inventory. PSS = Perceived Stress Scale. PANX = Pregnancy Specific Anxiety Scale. BDI = Beck Depression Inventory. BSID-II = Bayley Scales of Infant Development, Second Edition. WISC-IV = Wechsler Intelligence Scale for Children, Fourth Edition. EVT-2 = Expressive Vocabulary Test, Second Edition. The PSS was not administered at 25 weeks' gestation in Cohort 2.

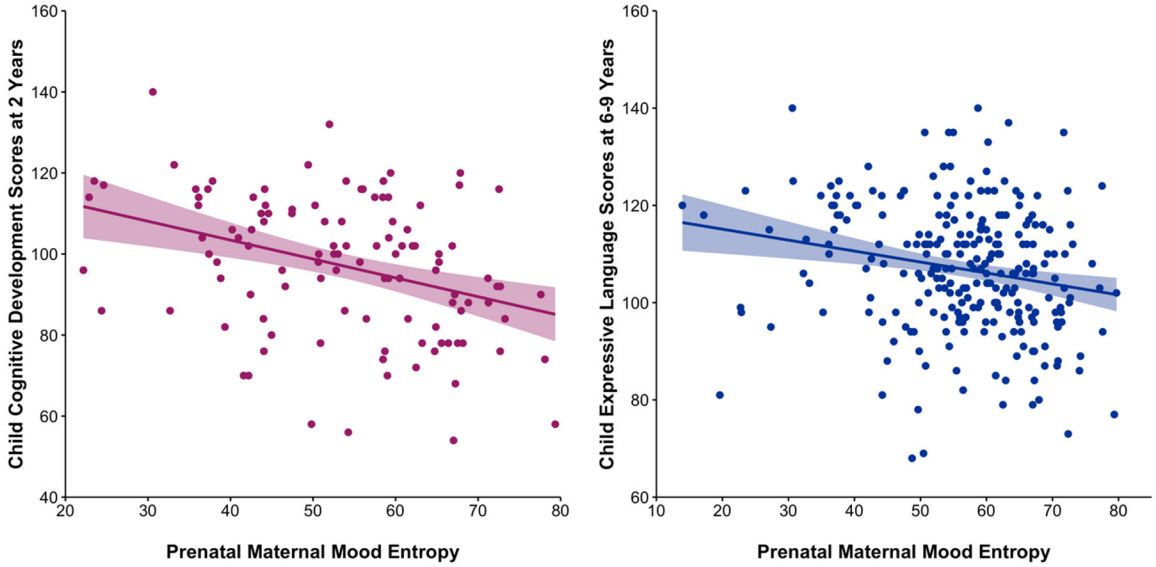

Figure 2.

Associations between prenatal maternal mood entropy and child neurodevelopmental outcomes at 2 and 6-9 years of age.

Table 1.

Participant characteristics for two cohorts (overall N = 299).

	Cohort 1 ***n*** **= 178**	**Cohort 2** ***n*** **= 121**
Maternal age at delivery (mean years)	30.8	29.7
Maternal race (%)		
Caucasian, non-Hispanic	49.4	47.9
Latina	21.3	33.9
Asian	11.8	6.6
Black	10.7	3.3
Multi-ethnic	6.7	8.3
Maternal education (%)		
High school or less	16.9	13.3
Associates or vocational degree	30.9	38.8
4-year college degree	30.3	29.8
Graduate degree	19.7	18.2
Annual household income (mean USD)	77,669	70,103
Cohabitation with child's father (% yes)	87.1	88.4
Child sex (% female)	53.9	47.1
Child birth order (% first born)	57.9	53.7
Length of gestation (mean weeks)	39.0	39.3
Child BSID-II MDI scores	-	97.4
Child WISC-IV PRI scores	108.3	108.1
Child EVT-2 scores	106.8	107.3

Note. Sociodemographic information was collected during the prenatal period. BSID-II = Bayley Scales of Infant Development, Second Edition. WISC-IV = Wechsler Intelligence Scale for Children, Fourth Edition. EVT-2 = Expressive Vocabulary Test, Second Edition.

Table 2.

Multiple regression models predicting child neurodevelopmental outcomes.

Predictors	**DV: Child cognitive development at 2 years of age (*N* = 112)**			**DV: Child expressive language at 6-9 years of age (*N* = 258)**		
	B (SE)	**95% CI**	***β***	***B (SE)***	**95% CI**	***β***
Maternal age	−0.42 (0.34)	[−1.10, 0.25]	−.13	0.05 (0.14)	[−0.23, 0.33]	.02
SES	5.78 * (2.54)	[0.75, 10.81]	.29	5.50 *** (1.09)	[3.35, 7.65]	.36
Cohabitation with child's father	2.01 (4.90)	[−7.71, 11.73]	.04	0.15 (2.23)	[−4.25, 4.54]	.00
Maternal cognitive ability	0.30 ** (0.10)	[0.10, 0.49]	.31	0.19 *** (0.05)	[0.10, 0.28]	.24
Prenatal maternal mood level	2.12 (3.46)	[−4.75, 8.98]	.09	2.16 (1.39)	[−0.57, 4.90]	.13
Concurrent maternal mood level	0.40 (3.17)	[−5.88, 6.68]	.02	−1.06 (1.13)	[−3.29, 1.18]	−.07
Concurrent maternal mood entropy	0.02 (0.13)	[−0.24, 0.28]	.02	0.02 (0.06)	[−0.10, 0.15]	.03
Prenatal maternal mood entropy	**−0.34 * (0.15)**	**[−0.64, −0.03]**	**−.27**	**−0.18 * (0.08)**	**[−0.34, −0.01]**	**−.16**
Total R^2			.33 ***			.31 ***

* p < .05

** p < .01

*** p < .001