RESEARCH ARTICLE

Lability of prenatal stress during the COVID-19 pandemic links to negative affect in infancy

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Abstract

The association between prenatal stress and children's socioemotional development is well established. The COVID-19 pandemic has been a particularly stressful period, which may impact the gestational environment. However, most studies to-date have examined prenatal stress at a single time point, potentially masking the natural variation in stress that occurs over time, especially during a time as uncertain as the pandemic. This study leveraged dense ecological momentary assessments from a prenatal randomized control trial to examine patterns of prenatal stress over a 14-week period (up to four assessments/day) in a U.S. sample of 72 mothers and infants. We first examined whether varied features of stress exposure (lability, mean, and baseline stress) differed depending on whether mothers reported on their stress before or during the pandemic. We next examined which features of stress were associated with 3-month-old infants' negative affect. We did not find differences in stress patterns before and during the pandemic. However, greater stress lability, accounting for baseline and mean stress, was associated with higher infant negative affect. These findings suggest that pathways from

prenatal stress exposure to infant socioemotional development are complex, and close attention to stress patterns over time will be important for explicating these pathways.

1 | INTRODUCTION

Emotion dysregulation, or difficulty in managing one's arousal to respond appropriately in a given emotional experience (Eisenberg & Fabes, 1992), is common in early childhood and is a transdiagnostic indicator of later-developing internalizing and externalizing psychopathology (Beauchaine & Cicchetti, 2019; Wakschlag et al., 2019). High infant temperamental negative affect, in particular, is a key indicator of emotion dysregulation and is a developmentally sensitive marker for fearful and inhibited temperament, as well as later-emerging psychopathology (Clauss & Blackford, 2012; Fox et al., 2001; Fox & Pine, 2012). Temperamental negative affect in early infancy is characterized by individual differences in fear, distress to limitations, and sadness. Because negative affect in the first few months of life is an early indicator of dysregulation (Gartstein & Rothbart, 2003), recent research has examined whether mothers' perceived stress during the prenatal period is an important predictor (Austin et al., 2005; Bhat et al., 2015; Coplan et al., 2005; Davis et al., 2007; Korja et al., 2017; Savory et al., 2020).

The COVID-19 pandemic has resulted in higher stress levels than average during pregnancy (López-Morales et al., 2021), including worries surrounding safety and support in healthcare settings, job security, and overall health. Despite increases in stress for pregnant women, the existing literature (albeit small) has not found significant associations between stress during COVID-19 and infant outcomes (Deoni et al., under review; Provenzi et al., 2021). Notably, many studies have examined prenatal stress as a static construct, often at a single time point. Although this measurement may reflect generalized stress, it does not capture the fluctuating experience of stress, particularly during the pandemic which has resulted in constant disruptions in family routines and uncertainty. The lability of stress, or the extent to which stress changes from one point in the day to the next, may add utility for prediction of adverse neurodevelopmental outcomes beyond baseline and average levels of stress, in a manner with important implications for prevention. Previous studies on the effects of mood and behavioral lability on adolescent problem behavior show promise for adopting these lability measures earlier in the developmental sequence (Fosco et al., 2019; Weinstein et al., 2008).

Ecological Momentary Assessment (EMA) allows for collecting intensive stress data via text message, enabling an unparalleled perspective on the fluctuations in stress in pregnant women's daily lives that more closely matches the gestational experience than retrospective questions about past stress or questions measured at one point in time. In the current study, we leveraged the COVID-19 pandemic as a natural experiment to examine whether stress patterns during pregnancy differed depending on whether they were measured before or during the pandemic. Our first aim was to examine whether general perceived stress at baseline, as well as average and lability levels of stress across a 14-week EMA period, were associated with the timing of the assessment relative to the onset of the pandemic (i.e., first stay-at-home order). As a secondary aim, we investigated whether these prenatal stress exposure patterns were linked to young infants' negative affect.

1.1 | Stress during pregnancy

Emerging evidence suggests that the prenatal environment programs the developing fetus during sensitive periods of brain growth, which can have lasting implications for children's development (Buss et al., 2012). The Developmental Origins of Health and Disease (DOHAD) hypothesis has laid important groundwork for better understanding how perinatal environmental exposures impact early neurodevelopment and disease risk (Bale et al., 2010). Both genetics and environment influence brain development during gestation (Tau & Peterson, 2010), and this hypothesis has emphasized the critical role pregnant women's mental health plays for healthy child development. High neuroplasticity makes the brain particularly susceptible to environmental exposure of "nonoptimal" levels of maternal distress (Monk et al., 2013). Stress during pregnancy, via altered fetus physiology, has been related to poorer infant regulation (Fuller et al., 2018; Huizink et al., 2002; Lin et al., 2014), more negative affect (Davis et al., 2004; Graham et al., 2019), and corollary neural disruptions in early life (Clark et al., 2016; Demir-Lira et al., 2016; O'Connor et al., 2014; Talge et al., 2007).

Less clear, however, is the amount or pattern of stress that defines these nonoptimal stress levels. Stress is a normative part of everyday life, and experiencing some stress is important for attuning to threats in the environment to remain safe and healthy. Stress is also common in pregnancy, a time period marked by myriad transitions and concerns surrounding one's own health and the health of the fetus. Most pregnant women (78%) report experiencing some-to-moderate levels of stress (Ibrahim & Lobel, 2020). Because stress experienced during pregnancy may have critical downstream consequences for maternal mental health and children's adaptive socioemotional development, better characterizing patterns of stress may be key for understanding how to "move the dial" on stress processes that influence maternal and child health (Wakschlag et al., 2021). Elucidating intraindividual variation in perceived stress, and the contexts under which this variation occurs, may help pinpoint nonoptimal patterns of stress and therefore aid in the translation from research to prevention of poor child outcomes. Such prevention/intervention efforts in pregnancy may be particularly advantageous because the majority of US women receive regular prenatal care (Brown et al., 2021).

1.2 | Stress during COVID-19

During the pandemic, existing stressors have been exacerbated, and individuals have been met with new challenges and disruptions to daily life. Concerns surrounding physical and mental health were and continue to be prevalent during the pandemic. Individuals have had to navigate unstable or risky care situations for their children or family members with chronic conditions. Financial concerns, such as job insecurity or loss, also emerged as widespread fears. In the general population, there have been increases in mental health problems and lower levels of well-being (Rajkumar, 2020; Torales et al., 2020). Pandemic-related stress has been linked to greater mental health and adjustment problems in both adults and children (Cohodes et al., 2021; Rajkumar, 2020).

For pregnant women in particular, the pandemic has been characterized by a great deal of fears and uncertainty regarding their own health and the health of others, viral infection affecting pregnancy and fetus, hospital visits and delivery without support systems, being unprepared for delivery or changes to birth plans, decreased access to health care and social services, and safety in healthcare settings (Corbett et al., 2020; Lebel et al., 2020; Preis et al., 2020; Yassa et al., 2020). In a study examining specific pandemic-related stressors in pregnant women during the pandemic, the authors found that close to 30% of pregnant women felt unprepared for birth and were concerned about risk of infection to themselves or the fetus (Preis et al., 2020). Overall, during the pandemic, pregnant women in the

general population have reported high levels of pregnancy-related stress, COVID-related stress, anxiety, and depression (Lebel et al., 2020; Pope et al., 2021; Saccone et al., 2020; Salehi et al., 2020; Taubman-Ben-Ari et al., 2020). A short-term study of pregnant and non-pregnant women assessed three times over 50 days in quarantine during COVID-19 demonstrated pregnant women showed a sharper increase in mental health indicators compared to non-pregnant women (López-Morales et al., 2021).

Despite the clear uptick in stress for pregnant women during the pandemic, the few findings that have emerged have not found significant associations between prenatal stress during COVID-19 specifically and infant outcomes. For instance, in a community sample, general perceived stress measured at one time point in pregnancy during the pandemic was not linked to infant cognitive functioning (Deoni et al., under review). A study examining prenatal pandemic-related stress during the third trimester in a community sample found that prenatal stress did not predict 3-month-old infants' temperamental regulatory capacity (Provenzi et al., 2021). It is important to note that this literature base is in its infancy, given the recency of the pandemic and the longitudinal nature of predicting from pregnancy to infant outcomes. Still, existing research both during the pandemic and irrespective of the pandemic has typically measured stress at one point in time during pregnancy, which may not capture the ebbs and flows of stress, particularly during the period of uncertainty that has defined the COVID-19 pandemic.

1.3 | Leveraging ecological momentary assessment to examine fluctuations in prenatal stress

Although average levels of stress during the pandemic vary between individuals (e.g., Cohodes et al., 2021; Webb Hooper et al., 2020), far less is known about how stress varies within an individual during the pandemic and especially during pregnancy. Despite the wealth of literature characterizing pregnancy as a period of mood instability and vulnerability to stress (Li et al., 2021), there are hardly any studies examining fluctuations in women's affective states across pregnancy in relation to child outcomes. A couple studies have examined entropy (i.e., unpredictability) in mood across five time points during pregnancy in relation to infant and child outcomes. Glynn et al. (2018) found that greater entropy was associated with higher levels of infant negative affect at 6 and 12 months. Howland et al. (2021) demonstrated that higher entropy was associated with worse cognitive performance at 2 years of age. These studies provide some support for mood instability as a key marker of maternal dysregulation that can impact child developmental functioning. In the current study, we leveraged the COVID-19 pandemic as a natural experiment for examining fluctuations in one's stress levels multiple times per day during the already-challenging period of pregnancy.

Specifically, we distinguish between three indicators of stress: (1) *baseline*, or stress measured at one point in time in early-mid pregnancy, (2) *average* levels of stress measured over a period of time during pregnancy, and (3) *lability* in stress, or the extent to which stress levels fluctuate over a period of time during pregnancy. For instance, two people may demonstrate the same average stress level during pregnancy, but one may show a consistent level over time while the other moves between extremes. Stress lability may contribute to infant developmental outcomes beyond global levels of stress (Ram & Gerstorf, 2009).

EMAs may be an ideal method for measuring heterogeneity in stress during pregnancy. EMAs are repeated survey assessments in real-time, often assessed via a mobile phone. Participants are instructed to respond at particular intervals or when they feel a given way, typically receiving text message prompts or reminders to complete the survey. Clear advantages of EMAs are that they assess

experiences proximal to events happening on a frequent (e.g., hourly, daily) basis, and they minimize error that can occur when recalling information over long periods of time. Participants can also complete these assessments in their own space, which both minimizes participant burden and enhances ecological validity (Almeida, 2005; Shiffman et al., 2008). Importantly, they capture both between- and within-person variation in the construct of interest (Bolger & Laurenceau, 2013). EMAs allow researchers to collect a large amount of data, thus increasing the chances of capturing typical patterns of feelings, thoughts, and behaviors, as well as those experiences that might occur less often but have important consequences for child development (Bolger & Laurenceau, 2013; de Barbaro, 2019). Further, in addition to these rare occurrences, EMAs can capture the more minor stressors that characterize and disrupt everyday life and well-being (Almeida, 2005). The current study used EMAs to measure mothers' perceived stress up to four times a day for 14 consecutive weeks during pregnancy to capture variations in stress during the prenatal period and determine whether these variations were related to infants' socioemotional development.

1.4 | The current study

Existing studies on prenatal stress have measured stress retrospectively or have related prenatal stress to distal developmental outcomes. To improve our understanding of prenatal programming, or the concept that exposures during pregnancy have a causal impact on the health of the developing fetus, research should optimally measure child outcomes proximal to stress exposure (Wakschlag et al., 2021). Although the pandemic's effects on stress are rapidly unfolding in developmental research, this research has yet to examine whether different stress patterns across the prenatal period vary as a function of the pandemic. Additionally, these stress patterns have yet to be examined in relation to infant outcomes. To our knowledge, the current study is the first to investigate prenatal baseline, mean, and lability of stress in the context of a pandemic, as well as whether they relate to 3-month-old infants' negative affect.

Our first and primary research questions aimed to better understand whether the COVID-19 pandemic was linked to prenatal perceived stress patterns. In this study, we conceptualized the pandemic as any time after the first stay-at-home order in Chicago, IL. Because participant enrollment spanned before and during the pandemic, this was a unique opportunity to study these associations at the crossroads to elucidate the underpinnings of prenatal stress related to the pandemic. Aim 1A of the study was to examine whether baseline stress levels measured at approximately 9–22 weeks gestation differed depending on whether mothers completed the baseline assessment before or during the pandemic. We hypothesized that pregnant women whose baseline stress measurements were taken during the pandemic would have higher baseline stress levels. Aim 1B was to examine whether average stress levels and stress lability across the 14-week period were related to the timing of the EMA data collection period relative to the onset of the pandemic, or the proportion of EMAs pregnant women completed during the pandemic. We hypothesized that the proportion of EMAs completed during the pandemic (i.e., more EMAs completed by mothers after the stay-at-home order) would be positively correlated with mean stress levels and stress lability.

As a secondary, more exploratory aim, we examined whether these stress patterns were associated with infants' negative affect at 3 months of age. We hypothesized that higher stress lability (i.e., more within-person variation in stress), accounting for baseline stress and mean stress over the 14-week period, would be associated with greater levels of infant negative affect.

2 | METHOD

2.1 | Sample

Data from this study come from the Promoting Healthy Brains Project, a randomized controlled trial (RCT) of prenatal stress reduction with an enrollment of 100 pregnant women. Women were recruited from prenatal clinics affiliated with a large, urban U.S. Midwestern university-based hospital where they planned to deliver. Women were recruited at approximately 9–20 weeks gestation and are being followed through their child's second birthday. Criteria for enrollment included ability to provide consent (e.g., 18 years of age or older), as well as access to a smartphone and WiFi Internet. Women were ineligible if their infant had a known medical complication or were at risk for neurological, chromosomal, or congenital disorders.

We restricted analyses to women with at least two responses to EMA messages during the 14-week period and whose children had 3-month outcome data at the time of this analysis. Therefore, 72 women had available prenatal data and infant outcome data for analyses. Of the 28 remaining participants, one participant withdrew and requested removal of her data from the study. Therefore, we had incomplete data on the remaining 27 participants (excluded sample) for the following reasons: active dropout out after intervention randomization and therefore did not have EMA or infant data (12), passive dropout after randomization and therefore did not have EMA or infant data (2), no EMA data provided but continued in the study (1), no 3-month infant negative affect data provided (12). The 72 participants in the analytic sample enrolled between August 2019 and May 2021, spanning before and during the pandemic. The current analytic sample was a largely middle-to upper-class sample that was racially and ethnically diverse (72.22% White, 9.72% Asian, 9.72% Black or African American, 6.94% more than one race/other, 1.39% unknown race; 12.50% Hispanic or Latina), the majority were highly educated (94.44% had a college degree or higher level of education), and the average maternal age at baseline was 33.10 years (SD = 4.60). Their household income ranged from $20,001/year to >$300,000/year with 73.6% reporting income >$100,000/year. The sample was relatively healthy, with 1.39% of mothers having a State-Trait Anxiety scale (Spielberger, 1983) score greater than the clinically meaningful threshold of 40 on the Trait subscale (Grant et al., 2008), and 4.16% having a PROMIS Depression T Score (Pilkonis et al., 2011) greater than 60 (+1 SD). Although not the focus of the current study, 36 participants in the current reduced sample had been randomized into an intervention group that received a 12-session Wellness-4-2 stress management intervention starting in the second trimester of pregnancy, and the other 36 were in the no-intervention control group.

There were 39 female and 33 male infants in the current sample, and their average age at the outcome was 3.45 months (SD = 0.63, Range = 2.20–6.80). The infant sample was 52.78% White, 4.17% Asian, 6.94% Black or African American, 12.50% more than one race, 23.61% unknown race, and 9.72% Hispanic or Latino. The present study was conducted according to guidelines laid down in the Declaration of Helsinki, with written informed parental consent obtained before any data were collected. All procedures in this study were approved by the Institutional Review Board at Ann and Robert H. Lurie Children's Hospital at Chicago (approval #2019–2639).

2.2 | Procedure

Participants completed an online baseline survey assessment, via REDCap, at approximately 9–22 weeks gestation. Following the baseline assessment, real-time stress monitoring was conducted over a 14-week period via self-reported data administered by text message to the participants' phones.

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These EMA text messages were delivered 4 times per day, between participant-specified wake and bed times, during that period. Each text message prompt, delivered to participants through Twilio, a cloud-based communications platform that automates SMS message delivery (www.twilio.com), contained a link to a brief REDCap survey. Participants also received a weekly message that showed their percentage of adherence to EMA response as a form of encouragement to continue responding to the EMAs. Infant data were collected through a survey time point completed by the mother, administered via REDCap, when the infant was approximately 3 months of age.

2.3 | Measures

Prenatal Baseline Stress. Mothers completed the 10-item version of the Perceived Stress Scale (PSS-10; Cohen & Williamson, 1988) at the baseline assessment to assess their perceived stress over the last month. The PSS measures the degree to which an individual perceives their life in general (rather than event-specific) to be overwhelming, uncontrollable, and unpredictable, and has shown strong reliability and validity (Cohen & Williamson, 1988). All items were rated on a 5-point scale, from 0 ("Never") to 4 ("Very Often"). In this analysis, we derived a baseline stress sum score via four items from the PSS to be consistent with the four items used in the EMAs (see below). Higher scores indicate more stress ($M = 4.61$, SD $= 3.08$). The 4-item scale had good internal consistency ($\alpha = 0.81$) and was relatively normally distributed (skewness $= 0.25$; kurtosis $= -0.82$).

    Prenatal Repeated Measures of Stress. Prenatal stress was measured up to 4 times per day with the same four items of the PSS (PSS-4; Warttig et al., 2013). Participants were asked to rate their perceived stress over the past hour on a 5-point scale, from 0 ("Not at All") to 4 ("Very Much"). An example item includes, "Over the past hour, did you feel you could not control important things?" The approach of using a few questions to measure perceived stress provides a quick, concise, and practical outlook on stress that is low burden for participants (Eckenrode & Bolger, 1997). Using at least three questions in the EMA to assess the construct of interest is recommended for testing within-person variation over time (Bolger & Laurenceau, 2013). For the PSS-4, responses on the four questions were summed to create a stress score, such that higher scores indicate more perceived stress. An individual's mean score across EMA time points was then derived ($M = 3.75$, SD $= 2.30$). Mean stress was relatively normally distributed (skewness $= 0.34$; kurtosis $= -0.64$).

    Infant Temperamental Negative Affect. Mothers completed the Infant Behavior Questionnaire—Revised—Very Short Form (IBQ-R-VSF; Putnam et al., 2014) at the 3-month assessment. The IBQ-R-VSF is a frequently used, validated measure of infant temperament. Mothers reported on the frequency that their 3-month-old infants engaged in specific behaviors over the past week using a 7-point scale ranging from 1 ("Never") to 7 ("Always"). Here, we focused on the Negative Affect dimension, consisting of 12 items from three subscales: Sadness (4 items; e.g., "When tired, how often did your baby show distress?"), Distress to Limitations (4 items; e.g., "How often did the baby seem angry (crying and fussing) when you left her/him in the crib?"), and Fear (4 items; e.g., "When introduced to an unfamiliar adult, how often did the baby cling to a parent?"). Individual item response scores were summed. No numerical score was awarded for any omitted items or for items that did not apply, and the mean of valid items was calculated. Higher scores indicate more negative affect ($M = 3.52$, SD $= 0.83$). This scale had good internal consistency ($\alpha = 0.73$) and was relatively normally distributed (skewness $= 0.15$; kurtosis $= -0.39$).

2.4 | Analysis plan

To address the first aim, two approaches were used. First, for Aim 1A, a binary variable was created to group mothers by whether their timing of enrollment, or when they completed the baseline stress survey, happened before or on/after the date of the COVID-19 shutdown, March 20, 2020, in Chicago, IL (1 = study enrollment on/after March 20, 2020; 0 = before March 20, 2020). A *t*-test was used to determine whether baseline stress levels differed by the timing of study enrollment relative to the onset of pandemic (i.e., stay-at-home order).

Second, for Aim 1B, we defined timing of the EMA data collection period relative to the onset of COVID-19 as the proportion of EMAs pregnant women completed on/after the date of COVID-19 shutdown (hereafter referred to as EMA timing). In the current study, 38.89% of mothers' EMAs were completed before March 20, 2020 and 61.11% of mothers' EMAs were completed on/after March 20, 2020. Correlations between EMA timing and stress levels during the 14-week EMA period (i.e., mean and lability) were examined.

To calculate stress lability scores, we followed recommendations by Fosco and colleagues (Fosco et al., 2019). Specifically, missing EMA data points were removed and mean squared successive differences (MSSD) (Jahng et al., 2008) were computed, using the following equation:

$$\text{MSSD} = \frac{\sum_{i=1}^{n-1}(X_{i+1} - X_i)^2}{n-1}$$

The MSSD calculates the sum of the squared differences between the current stress score (X_i) and the following stress score (X_{i+1}), from the first score ($i = 1$) to the second to last stress score ($n-1$), divided by the total count of squared differences ($n-1$). Stress lability was somewhat positively skewed (skewness = 1.64; kurtosis = 3.02).

To address Aim 2, a multiple regression was used. Infant negative affect at 3 months was regressed on stress patterns (lability, mean, and baseline stress), controlling for variables with significant correlations to the outcome via Pearson correlations, in addition to the intervention group. Prior research has demonstrated effects of infant age and sex on infant temperament (Bornstein et al., 2015; Else-Quest et al., 2006); therefore, these demographic variables were included in the correlation analyses. We also included correlations with several maternal characteristics that may be tied to the outcome. Because research has found that stress levels are lower mid-pregnancy (Rallis et al., 2014) and participants were enrolled across a wide window across the pandemic, we examined the correlation with gestational age at baseline. Younger mothers have reported more child behavior problems (Fox et al., 1995), thus we considered maternal age. Although we did not aim to test a longitudinal stress model, we thought it was important to examine whether maternal stress at 3 months was concurrently related to infant negative affect. Number of children in the home as an imperfect proxy for parity was also considered, as previous research has demonstrated links between parity and prenatal stress and infant emotional reactivity (Grant et al., 2010; Katus et al., 2022). Finally, prenatal anxious and depressive symptoms have been linked to prenatal stress and infant emotional problems (Brown et al., 2021; Davis et al., 2007), thus we included correlations with the State-Trait Anxiety Inventory Trait sum score (Spielberger, 1983) and the PROMIS Depression Short Form *T* scores (Pilkonis et al., 2011).

3 | RESULTS

Descriptive statistics for all study variables are presented in Table 1, and correlations of variables relevant to research questions are presented in Table 2.

Preliminary Analyses. Independent samples *t*-tests revealed no difference in baseline age between the 72 women in the analytic sample ($M = 33.10$, SD = 4.60) and the 27 women excluded from the analyses ($M = 33.37$, SD = 4.92), $t(97) = -0.26$, $p = 0.80$. There was no difference in baseline stress between the women in the analytic sample ($M = 4.61$, SD = 3.08) and those excluded ($M = 5.37$, SD = 2.80), $t(97) = -1.12$, $p = 0.27$. Women excluded from these analyses had a higher income-to-needs ratio ($M = 9.07$, SD = 4.65) than those included ($M = 7.09$, SD = 3.62), $t(93) = -2.19$, $p < 0.05$.

Given the wide recruitment window, we also examined whether there were differences between mothers who completed the baseline assessment in the first trimester ($n = 20$) and those who completed the baseline assessment in the second trimester ($n = 52$). Baseline stress may be different in the first compared to the second trimester, and mean stress and stress lability across the 14 weeks may follow different patterns when measured across the second and third trimesters. There was no difference in baseline stress between those who completed the baseline assessment in the first trimester ($M = 4.30$, SD = 3.42) and those who completed it in the second trimester ($M = 4.73$, SD = 2.97), $t(70) = -0.53$, $p = 0.60$. Additionally, there was no difference in mean stress for those who completed the baseline assessment in the first trimester ($M = 3.62$, SD = 2.30) and those who completed it in the second trimester ($M = 3.80$, SD = 2.32), $t(70) = -0.30$, $p = 0.76$. Finally, there was no difference in stress lability for those who completed the baseline assessment in the first trimester ($M = 6.10$, SD = 4.04) and those who completed it in the second trimester ($M = 6.70$, SD = 5.85), $t(70) = -0.42$, $p = 0.67$. Therefore, we did not control for the trimester in which mothers completed the baseline assessment in the Aim 2 regression model.

Aim 1A: *Does baseline stress differ depending on whether mothers completed the baseline assessment before or during the pandemic?* Results from the independent samples *t*-test demonstrated that there was no difference in baseline stress between the 37 pregnant women whose baseline stress measurement was taken pre-pandemic ($M = 4.51$, SD = 2.88) and the 35 pregnant women whose baseline stress measurement was taken during the pandemic ($M = 4.71$, SD = 3.32), $t(70) = -0.27$, $p = 0.78$.

Aim 1B. *Do average stress levels and stress lability across the 14-week period relate to the timing of the EMA data collection period relative to the onset of the pandemic?* Table 2 shows that EMA timing relative to the pandemic was not related to the mean stress levels ($r = 0.14$, $p = 0.24$) or stress lability ($r = 0.16$, $p = 0.17$) across the 14-week EMA period during pregnancy.

Aim 2: *Do prenatal stress exposure patterns (baseline, mean, lability) predict infant temperamental negative affect at 3 months of age?* We first explored bivariate associations between potential covariates and the outcome (i.e., infant temperamental negative affect at 3 months) (Table 2). Female infant sex ($r = 0.37$, $p < 0.01$) and EMA timing ($r = -0.30$, $p < 0.01$) were correlated with the outcome of infant temperamental negative affect, and thus were included in the regression model. The total number of EMAs participants completed, gestational age at baseline, maternal age at baseline, maternal stress at 3 months, number of children in the home, and maternal symptoms of anxiety and depression were not associated with infant negative affect (Table 2), thus they were not included in the regression model.

The final model included stress lability, baseline stress, mean stress, infant sex, EMA timing, and intervention group status predicting infant negative affect (Table 3). Maternal prenatal stress lability was associated with infant negative affect ($b = 0.05$, $t = 2.55$, $p < 0.05$), indicating that mothers with greater variation in stress from moment to moment across the 14-week period during pregnancy had infants with higher levels of temperamental negative affect early in life. In contrast, stress measured at

TABLE 1 Descriptive statistics

	N (%) or *M* (SD)	Min.	Max.
Mother age at baseline, *M* (SD)	33.10 (4.60)	19.00	44.00
Infant age at outcome in months, *M* (SD)	3.45 (0.63)	2.20	6.80
Infant sex—Female, *n* (%)	39 (54.17)		
Mother race, *n* (%)			
White	52 (72.22)		
Black/African American	7 (9.72)		
Asian	7 (9.72)		
More than one race/Other	5 (6.94)		
Unknown race	1 (1.39)		
Mother ethnicity, *n* (%)			
Hispanic or Latina	9 (12.50)		
Infant race, *n* (%)			
White	38 (52.78)		
Black/African American	5 (6.94)		
Asian	3 (4.17)		
More than one race/Other	9 (12.50)		
Unknown race	17 (23.61)		
Infant ethnicity, *n* (%)			
Hispanic or Latino	7 (9.72)		
Mother education level, *n* (%)			
High school diploma or GED, or less	3 (4.17)		
College degree or beyond	24 (33.33)		
Graduate or professional degree, or higher	44 (61.11)		
Prefer not to answer	1 (1.39)		
Mother employment status, *n* (%)			
Full-Time	55 (76.39)		
Part-Time	8 (11.11)		
Unemployed	9 (12.50)		
Mother marital status, *n* (%)			
Married	62 (86.11)		
Single	2 (2.78)		
Living with partner	4 (5.56)		
Engaged	4 (5.56)		
Number of children in the home, *M* (SD)	0.51 (0.92)	0	6
Income to need ratio, *M* (SD)	7.09 (3.62)	0.86	17.40
EMA timing, *M* (SD)	0.54 (0.48)	0.00	1.00
RCT group status—treatment, *n* (%)	36 (50.00)		
Count of EMAs completed, *M* (SD)	293.86 (100.35)	22	391
Gestational age at baseline in weeks, *M* (SD)	16.24 (3.50)	9.43	22.71
Baseline anxiety—STAI-TAI sum score, *M* (SD)	16.26 (9.55)	1.00	44.00

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TABLE 1 (Continued)

	N (%) or M (SD)	**Min.**	**Max.**
Baseline depression—PROMIS *T* score, *M* (SD)	48.30 (7.02)	37.10	69.30
Baseline stress, *M* (SD)	4.61 (3.08)	0.00	12.00
Stress at 3 months, *M* (SD)	5.24 (2.53)	0.00	11.00
Stress lability, *M* (SD)	6.53 (5.39)	0.65	28.07
Mean stress over time, *M* (SD)	3.75 (2.30)	0.10	9.45
Infant negative affect, *M* (SD)	3.52 (0.83)	1.73	5.57

Note: $N = 72$. Only numeric variables will have a minimum (Min.) and maximum (Max.) value.

Abbreviations: EMA, ecological momentary assessment; M, mean; RCT, randomized control trial; SD, standard deviation; STAI-TAI, State-Trait Anxiety Inventory-Trait Anxiety Inventory. EMA timing corresponds to the proportion of EMAs participants completed during the pandemic.

the baseline assessment ($b = -0.01$, $t = -0.31$, $p = 0.76$) and mean stress across 14 weeks ($b = -0.03$, $t = -0.61$, $p = 0.54$) were unrelated to infant negative affect. Turning to the covariates, we found an effect of sex, such that girls had higher levels of negative affect than boys ($b = 0.57$, $t = 2.99$, $p < 0.01$). Additionally, EMA timing was negatively related to infant negative affect, such that mothers who completed more of their EMAs during the pandemic had infants with lower levels of temperamental negative affect at 3 months of age ($b = -0.41$, $t = -2.05$, $p < 0.05$).

It is important to note that we identified one outlier (3 SD above the mean) in stress lability. As a test of robustness, we compared a model removing the outlier to the regression model in Table 3. The results did not change significantly between the models, and stress lability remained a significant predictor of infant negative affect. Therefore, we retained the outlier and the original regression model.

4 | DISCUSSION

Using the COVID-19 pandemic as a natural experiment, the current study examined whether lability in stress across a 14-week period during pregnancy, mean levels of stress during the 14 weeks, and baseline levels of stress were related to timing of the stress assessment relative to the pandemic. As a secondary aim, we examined whether these prenatal stress exposure patterns were associated with 3-month-old infants' temperamental negative affect. This study is unique in that our characterization of prenatal stress exposure during the pandemic includes dense real-time measurement of changes in perceived stress over time, that is, stress lability. Its measurement as a dynamic, within-person construct may more accurately reflect the natural variation in stress occurring during pregnancy. The current study is one of the first to examine dynamic fluctuations in prenatal stress, leveraging hundreds of repeated assessments, as well as how such fluctuations are associated with infant emotion dysregulation in the context of the pandemic.

The first aim of the study was to examine whether baseline stress differed for pregnant women prior to versus during the pandemic, as well as whether stress lability and mean stress across the 14-week EMA period were correlated with EMA timing (i.e., proportion of EMAs completed during the pandemic given the timing of participant study enrollment). The results suggest that baseline stress does not differ depending on whether mothers completed the assessment before or during the pandemic, and that mean stress and stress lability are not related to EMA timing. The lack of significant associations between stress patterns and the pandemic was surprising, given that several prior

TABLE 2 Pearson correlations of relevant study variables

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.
1. Gestational age at baseline	1.00	0.05	0.10	0.15	−0.03	−0.17	−0.13	0.08	0.03	0.07	0.08	0.00	0.10	−0.04	0.08
2. Infant age at outcome		1.00	−0.09	0.13	0.00	0.02	0.03	−0.16	0.02	0.15	−0.18	−0.12	−0.10	0.25*	0.22†
3. Infant sex[a]			1.00	0.00	−0.18	−0.31**	0.03	0.18	−0.12	0.01	0.00	0.13	0.37**	0.10	−0.04
4. Mother age at baseline				1.00	0.26*	−0.05	0.17	−0.04	−0.13	0.14	−0.11	0.02	0.07	0.06	0.07
5. Number of children in the home					1.00	−0.15	0.11	−0.19	0.20†	0.14	0.21†	0.12	−0.04	0.17	0.16
6. EMA timing						1.00	−0.08	0.02	0.16	0.10	0.15	0.14	−0.30**	0.12	0.07
7. RCT group status[b]							1.00	−0.18	−0.18	0.07	−0.20†	−0.12	−0.03	0.18	0.11
8. Count of EMAs completed								1.00	−0.52***	−0.33**	−0.09	−0.20†	−0.13	−0.08	−0.35**
9. Stress lability									1.00	0.38***	0.34**	0.21†	0.17	0.10	0.27*
10. Baseline stress										1.00	0.44***	0.62***	−0.01	0.55***	0.80***
11. Stress at 3 months											1.00	0.50***	0.15	0.19	0.32**
12. Mean stress over time												1.00	−0.02	0.31**	0.47***
13. Infant negative affect													1.00	0.00	−0.04
14. PROMIS Depression T-score														1.00	0.69***
15. STAI-TAI sum score															1.00

Abbreviations: EMA, ecological momentary assessment; RCT, randomized control trial; STAI-TAI, State-Trait Anxiety Inventory-Trait Anxiety Inventory. EMA timing corresponds to the proportion of EMAs participants completed during the pandemic.

[a]Infant sex was converted from a categorical variable to numeric values, 0 = Male and 1 = Female.

[b]RCT group status was converted from a categorical variable to numeric values, 0 = control group and 1 = treatment group.

†$p < 0.10$; *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

TABLE 3 Linear regression model predicting infant negative affect at 3 months of age

Variable	Estimate	SE	t	F	df	R^2	p
Overall model				3.74	6, 65	0.26	0.0029
Intercept	**3.39*****	**0.25**	**13.52**				
Infant sex[a] (Female)	**0.57****	**0.19**	**2.99**				
EMA timing	**−0.41***	**0.20**	**−2.05**				
Stress lability	**0.05***	**0.02**	**2.55**				
Baseline stress	−0.01	0.04	−0.31				
Mean EMA levels	−0.03	0.05	−0.61				
RCT group (Treatment)	−0.20	0.18	−1.08				

Note: Bolded values are significant.

Abbreviations: EMA, ecological momentary assessment; SE, standard error; RCT, randomized control trial. EMA timing corresponds to the proportion of EMAs participants completed during the pandemic.

[a]For Infant Sex, Male is the reference.

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

studies have found significant effects of COVID-19 on mental health (e.g., Rajkumar, 2020; Torales et al., 2020) and on stress during pregnancy (e.g., Hessami et al., 2020; López-Morales et al., 2021).

One potential reason why we did not find pandemic-related differences in stress could be that the majority of current sample was highly educated, partnered, and middle to upper class—indeed, many of the participants agreed to participate in a research study that included receiving daily EMAs for 14 weeks during an extremely tumultuous time. These mothers may have had more financial and social support than most individuals during the pandemic, as well as more opportunities to protect themselves from infection (e.g., work from home). Such resources and opportunities may have allayed fears surrounding job loss, unstable social support or care, and disease exposure. Some prior research has shown that participants with lower socioeconomic status (SES) report higher levels of pandemic-related fear than higher SES participants (Bitan et al., 2020). Further, longitudinal studies during the pandemic in Poland and Israel found that most individuals did not show increases in anxious and depressive symptoms across the study periods (Gambin et al., 2021; Kimhi et al., 2021). However, those individuals considered "resilient" had fewer economic difficulties (Kimhi et al., 2021), and the smaller group of individuals that had chronic symptoms over the period had several risk factors, including poorer financial situations (Gambin et al., 2021). A systematic review and meta-analysis on mental health in pregnant and postpartum women during the pandemic saw contrasting findings, such that anxiety was more prevalent in women with a university degree than those without. Anxiety was also more prevalent in women who were employed than those were unemployed (Yan et al., 2020). Other work suggests that social supports may buffer against the effect of pandemic-related worries on psychological health (Szkody et al., 2021). Therefore, we would expect that higher levels of sociode-mographic variability and a larger sample could result in more evident differences in pandemic-related stress. Other possible reasons why we did not find these pandemic-related differences were our rela-tively small sample size and the fact that the larger study from which these data were derived was not designed a priori to answer questions related to the pandemic.

A secondary aim of the study was to examine whether stress lability over the 14-week EMA period was related to 3-month-old infants' temperamental negative affect. The results provide some initial evidence that higher levels of stress lability during pregnancy, accounting for baseline and mean stress, are related to higher levels of infant negative affect. Heightened stress lability, or more intense fluctuations in stress from one moment to the next, reflects inconsistencies in perceived stress during

pregnancy that may have negative implications for young infants' burgeoning regulatory abilities. Despite associations between prenatal stress and infant development evidenced in the prior literature, the mechanisms driving these associations, and the levels or patterns at which stress becomes harmful, have remained unclear (Huizink & de Rooij, 2018; Monk et al., 2013). These preliminary findings suggest that a prenatal environment characterized by heightened fluctuations in stress may program a greater vulnerability to negative affect in the young infant, over and above overall levels of stress.

Thus far, there has been very little research on stress or overall mood lability during pregnancy and infant temperament, despite existing literature arguing the potential importance of fluctuations in stress during pregnancy for maternal well-being and infant outcomes (Huizink et al., 2002; Racine et al., 2019). A study measuring self-reported general mood instability at two points in pregnancy found no relation between instability and neonatal outcomes (Apgar scores and physical outcomes) (Li et al., 2021). However, research examining mood entropy across five time points during pregnancy found significant associations with infant negative affect at 6 and 12 months of age (Glynn et al., 2018). The measure of entropy was also correlated with mood lability across 3 days. The current study examined instability by statistically capturing change from one occasion to the next across multi-day reports over 14 weeks during pregnancy using MSSDs. Measuring stress across multiple measurement occasions can capture the naturally-occurring variations in stress during pregnancy, which may be an index mothers' own emotion dysregulation (Glynn et al., 2018; Howland et al., 2021). Further, Howland et al. (2021) discuss that predictability in maternal signals can play a role increasing organization in the developing brain, whereas instability or unpredictability may contribute to disorganization, as evidenced by maternal behavior in rodents and humans in the postnatal period (Davis et al., 2017; Singh-Taylor et al., 2018). More research is needed to understand why large fluctuations in stress may matter for infants' socioemotional development in the prenatal period. Because the mechanisms underlying stress lability are unknown and postnatal stress lability could not be estimated in the current study, the association between prenatal stress lability and infant negative affect should be interpreted with caution.

It is critical to note that the influence of *chronic* stress on infant outcomes may differ from the impact of fluctuations in *daily* stress (Rieger et al., 2004). Prior research has shown that variations in prenatal stress are likely due to social determinants of health, including experiences of poverty, discrimination, and racism (Kingston et al., 2012). Notably, chronic stress is often measured at a single time point via maternal questionnaire or interview (e.g., Trier Inventory for the Assessment of Chronic Stress; Prenatal Distress Questionnaire). Here, we included a measure of perceived stress at baseline, as well as mean levels of stress over the 14-week period, which were not associated with infant emotion dysregulation. Although the current study examined three unique aspects of stress throughout the prenatal period, stress was operationalized at a general level, and future research should consider different types of stress including fluctuations in pregnancy- and COVID-specific stress. However, it should be noted that previous research has suggested that stress, regardless of type, may result in similar neurodevelopmental outcomes (Huizink & De Rooiji, 2018).

We also controlled for proportion of EMAs completed during the pandemic in our regression model as a proxy for stress captured during the pandemic. We were surprised to find that mothers who completed more of their EMAs during the pandemic, due to their timing of enrollment in the study, reported their infants to have lower levels of negative affect. Again, this finding may be explained by the characteristics of the current sample, in that highly resourced mothers may have experienced reduced work stress, had more time to sleep, had more time in quarantine, etc. In turn, they may have had more time to complete the EMAs during a pandemic. More time to complete EMAs during a pandemic may also be related to several adaptive behaviors during the perinatal period that would increase the likelihood for better emotion regulation skills in infants. For instance, higher SES parents

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may have a greater understanding about infant temperament and/or resources to manage difficult temperaments, which may potentially mitigate stress and negative affect (Bornstein et al., 2015). Lower SES has been related to higher levels of difficult temperament in infants (Jansen et al., 2009). Alternatively, completing more EMAs during the pandemic, and therefore spending more time pregnant during the pandemic, could reflect an adaptive or resilience process. More specifically, these well-resourced mothers may have been better able to adapt to the demands of a changing environment, which may have had a positive effect on infant development. Using a larger and more diverse sample, future research should examine whether stress during pregnancy, measured at different periods of the pandemic, relate to infant outcomes. For example, we might expect stress patterns to look different (e.g., heightened, more variable) around the first stay-at-home order than later on in the pandemic and when vaccines became available.

4.1 | Limitations and conclusions

The findings of the current study should be viewed in the context of study limitations. First, the sample was small and relatively homogenous in terms of SES, thus findings may not generalize across populations. Findings should be replicated in a larger and more socioeconomically diverse sample. Relatedly, due to the small sample size, we were limited in the number of predictors we could include in the regression model. Because prior research has shown that variations in prenatal stress may be due to maternal individual differences and unique social experiences, an important future direction for research is to take into consideration social determinants of health in assessing the extent to which stress lability affects infant emotion dysregulation (Evans et al., 2001).

Second, the timing of enrollment was wide, spanning several phases of the pandemic. The large enrollment window was in part a result of the pandemic, which placed a universal strain on human subjects research, and the focus of the larger study from which these data were collected was not on pandemic-related outcomes. It is plausible that stress was higher in both the general population and in pregnant individuals during the onset of the pandemic compared to other phases, such as when the vaccine roll-out began. EMAs spanning 14 weeks added further complexity, such that this time period may have spanned more than one phase during the pandemic, thus requiring the examination of several between-group differences. Therefore, the large enrollment window may have impacted study results.

Third, all variables in the current study were measured via maternal report, thus the findings are subject to shared rater variance. Future research should consider observations of infant negative affect to reduce this potential bias. Further, given the evidence that prenatal exposure to elevated cortisol is related to affective problems in offspring, examining repeated measures of both maternal perceived stress and physiological correlates might be particularly helpful for further unpacking the link between stress lability and infant negative affect (Buss et al., 2012). Such an investigation leveraging electrocardiogram biosensing data is currently underway (Wakschlag et al., 2021).

Fourth, stress lability was only assessed during the prenatal period, and we acknowledge that infants in the current study were born during a global pandemic that may have influenced the stability of their postnatal environment. Mothers with higher stress lability during pregnancy may continue to experience daily fluctuations in stress postpartum, which in turn, may impact their early parenting and infant negative affect. Longitudinal follow-up beyond the first months of life is needed to understand the impact of the pandemic and its related stressors on neurodevelopmental trajectories, particularly the development of emotion dysregulation and anxiety, given the large body of existing research on negative affect as an early predictor (Clauss & Blackford, 2012; Fox et al., 2001; Fox & Pine, 2012).

Fifth, the current study focused on the negative affect dimension of temperament as the outcome of interest, although stress patterns may also impact the other temperament dimensions of positive affect/surgency and orienting and regulation capacity. Given the previous literature on relations between prenatal stress and infant negative affect, as well as the small sample size of the current study and need to limit predictors, we chose to solely investigate the relations with negative affect in our secondary aim. Modeling relations between stress patterns across pregnancy and other dimensions of temperament would be an interesting exploratory line of future research.

Finally, this study focused specifically on perceived stress, but other mental health conditions that are common during pregnancy, such as depressive symptoms and anxiety, may have unique or additive effects on early infant outcomes and should be considered in future studies, particularly given the known benefits of interventions related to these conditions (Tandon et al., 2018). Because the larger study asked mothers about their depression and anxiety levels at the baseline assessment, we were able to test their correlations with negative affect. Although depression and anxiety were not correlated with infant negative affect, they were highly related to all levels of stress (baseline, mean, lability). These findings suggest pregnant individuals with higher baseline depression and anxiety may also have higher levels of initial stress, stress over time, and fluctuations in stress over time. Prevention and intervention programs may therefore benefit from targeting anxiety, depression, and stress patterns in early pregnancy, or ideally before, to enhance maternal well-being (Brown et al., 2021). The finding that more stress lability during pregnancy is associated with more negative affect in infants may help to inform prenatal stress management interventions by working toward a "steady calm". Such interventions would ideally be responsive to the variability in stress over time. For instance, adapting prenatal interventions with personalized just-in-time adaptive intervention content during periods of pronounced stress lability may be advantageous for modifying perceived stress as it is happening in real time, which may in turn, impact infants' vulnerability to mental health problems (Muñoz et al., 2007; Tandon et al., 2018; Wakschlag et al., 2021).

We join a chorus of research examining stress in pregnancy during the pandemic (e.g., Lebel et al., 2020; López-Morales et al., 2021) and argue for an increasing focus on the relation between different patterns of prenatal stress and infant neurodevelopmental outcomes, particularly given how the mechanisms linking the two are largely unknown. Using innovations in measurement to gain a richer view of prenatal stress via a focus on lability sheds light on how daily fluctuations that occur prior to delivery may influence a pathway toward infant negative affect. Although collecting data during a global pandemic presented many challenges, the intensive longitudinal assessment of stress presented here reflects the study team's flexibility, even if it limited our use of more intensive methods (e.g., behavioral observation; Krogh-Jespersen et al., 2022). Studies that take a transdisciplinary approach to measuring both maternal and infant outcomes will provide further insight into the trajectories of development, including a focus on innovative methods, biological mechanisms, and repeated measurement of constructs (Provenzi et al., 2021; Wakschlag et al., 2021). Infant temperament has shown relative stability in longitudinal observations across infancy, yet the environment is a clear factor influencing development over time, with a particular focus on social interactions (Rothbart, 1986; Rothbart & Putnam, 2002). As the pandemic continues to disrupt daily living, unfortunately we are tasked with learning in real-time the fluctuating influences on caregivers and their infants.

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