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Infants of mothers with higher physiological stress show alterations in brain function

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Abstract

Chronic stress has been increasingly linked with aberrations in children's behavioral, cognitive, and social development, yet the effect of chronic physiological stress on neural development during the first year of life is largely unknown. The present study aims to link a physiological index of chronic stress (maternal hair cortisol concentration) to maturational differences in infant functional brain development during the first year of life. Participants were 94 mother-infant dyads. To index chronic physiological stress, maternal hair samples were assayed for the previous three months' cortisol output. To examine the development of brain function during the first year of life, six-to-twelve-month-old infants (N = 94) completed a resting electroencephalography (EEG) recording. Infants of mothers with evidence of higher physiological stress showed increased relative low-frequency (theta) power and reduced relative high-frequency (alpha, high-gamma) power, compared to infants of mothers with evidence of low physiological stress. This pattern of findings is consistent with other studies suggesting that early life stress may lead to alterations in patterns of infant brain development. These findings are important given that maturational lags in brain development can be long-lasting and are associated with deficits in cognitive and emotional development. The present research also suggests that reducing maternal physiological stress may be a useful target for future interventions aiming to foster neurodevelopment during the first year of life.

KEYWORDS

cortisol, EEG, infancy, memory, neurodevelopment, stress

1 | INTRODUCTION

Chronic environmental stress has deleterious effects on the developing child. While the type and degree of stress that children experience can vary widely, the downstream influence of varying stressors may impact child development similarly. Of particular interest is building an understanding of how chronic stress impacts brain functioning early in life, as both environmental stress and alterations in patterns of infant brain development have been related to a constellation of subsequent negative developmental outcomes.

Among typically developing children, studies using electroencephalography (EEG) have shown that the relative contribution of low-frequency resting EEG power decreases with age, whereas the relative contribution of high-frequency resting EEG power increases with age (Marshall, Bar-Haim, & Fox, 2002). A variety of highly stressful environments have been linked to alterations

in this typical pattern of functional brain development (Harmony et al., 1988; Marshall, Reeb, Fox, Nelson, & Zeanah, 2008). Specifically, children raised in chronically stressful environments tend to show an overabundance of low-frequency brain power and a relative paucity of high-frequency power, compared to their peers raised in lower-stress environments. This pattern has been postulated to reflect a "maturational lag" in neural development (Coming, Steffy, & Chaprin, 1982).

Several studies have identified stress-related maturational lags in brain activity development in early childhood, across different circumstances. One hallmark study showed that institutionalized children showed increased theta power, as well as reduced alpha and beta power, by 22 months of age, when compared to never-institutionalized children (Marshall, Fox, & BEIP Core Group, 2004). Another study found that higher maternal reports of stress were associated with decreased beta and gamma power in 3-month-old infants (Pierce et al., 2019). Such altered patterns of EEG activity can persist throughout childhood and early adolescence (Otero, 1994, 1997; Otero, Pliego-Rivero, Fernández, & Ricardo, 2003; Vanderwert, Marshall, Nelson, Zeanah, & Fox, 2010), suggesting that the study of how early adversity affects patterns of brain electrical activity may be of importance for understanding the impact of stress on neurodevelopmental functioning, with implications for prevention and intervention research.

This pattern of increased low-frequency brain power and reduced high-frequency brain power has been associated with numerous negative sequelae, such as perturbations in working memory and vocabulary (Maguire & Schneider, 2019), developmental delays, and problems with learning and attention (Corning, Steffy, Anderson, & Bowers, 1986; Harmony et al., 1990; McLaughlin et al., 2010). This emerging evidence suggests that maturational lags have important downstream effects on neurocognitive functioning.

Notably, previous studies of maturational lag have relied on *parent report* of persistent stressors (e.g. poverty, food insecurity, social deprivation). However, the heterogeneity in early life environments that create stress, in concert with the reliance on parental perception of stress, makes it difficult to develop a mechanistic understanding of chronic stress. In addition to parental report, there is increased interest in the assessment and characterization of *physiological stress* as linked to early neural development, given that physiological stress has been related to brain function and development (McEwen, 2004; St. John, Kao, Liederman, Grieve, & Tarullo, 2017).

A growing body of research suggests that measures of physiological stress are related to both the structural and functional child brain development (e.g. Merz et al., 2019; St. Johnet al., 2017). To our knowledge, only one study has examined how maternal stress physiology may alter task-related infant brain functioning (St. John et al., 2017). This study found that maternal point-in-time salivary cortisol (collected at infant age 6 months) predicted later infant brain function (6–9 Hz power). Critically, this study also found that maternal perceptions of stress were not associated with infant brain

Research Highlights

- Chronic stress has been linked with aberrations in children's neurocognitive development, yet the effect of maternal *physiological* stress on infant neural development is largely unknown
- Results suggest that infants of mothers with higher physiological stress (hair cortisol) showed increased relative low-frequency electroencephalography power and reduced relative high-frequency power
- Maternal *physiological* stress predicted patterns consistent with maturational lags in brain activity development over and above maternal perceived stress and socioeconomic circumstance

function, suggesting that maternal physiological stress may provide important, independent contributions to infant functional brain development. While an important first study, point-in-time salivary collection only gives a snapshot of maternal stress, rather than assessing chronic maternal physiological stress (e.g. physiological stress output over weeks or months). Traditionally, assessing chronic physiological stress has been difficult, due to the need to repeatedly collect saliva, blood, or urine over long periods. Fortunately, new methodology that enables a reliable physiological characterization of chronic stress may aid in the characterization of the neurodevelopmental responses to early stress exposure.

Recent advances in cortisol extraction from hair have created new opportunities to characterize chronic physiological stress (Flom, St. John, Meyer, & Tarullo, 2017; Meyer, Novak, Hamel, & Rosenberg, 2014). Hair cortisol is a valid measure of chronic stress (Flom et al., 2017) and has been associated with common stressors such as poverty (Ursache, Merz, Melvin, Meyer, & Noble, 2017). Indeed, validation studies have found that hair cortisol provides a reliable estimate of free cortisol production and it correlates with salivary cortisol production over time (Short et al., 2016). Leveraging hair cortisol methodology enables us to explore links between chronic physiological stress in parents and the development of their infants' brain function.

The present study seeks to examine whether the infants of mothers with higher levels of physiological stress exhibit a pattern of brain activity consistent with a maturational lag during the first year of life, compared to infants of mothers with lower levels of physiological stress. To this end, we examined absolute and relative EEG power in five frequency bands: theta, alpha, beta, low-gamma, and high-gamma. We hypothesized that infants of mothers with higher hair cortisol concentrations would show proportionally more low-frequency power (i.e. theta) and proportionally less high-frequency power (i.e. alpha, beta, gamma) when compared to infants of mothers with lower hair cortisol concentrations. We also examined whether maternal reports of perceived stress would relate to infant brain function. Finally, given increasing interest in understanding

how differences in resting brain activity relate to cognitive functioning, we investigated exploratory relations between resting EEG power and concurrent infant memory skill.

2 | MATERIALS AND METHODS

2.1 | Experimental design

2.1.1 | Participants

Participants were recruited from the New York metropolitan area. This sample of convenience was recruited from flyers in the community, a WIC clinic, community events, and the laboratory website. Families were intentionally recruited across a wide range of maternal educational attainment. Inclusionary criteria for children were the following: (a) between 5 and 13 months of age, (b) born at or after 36 weeks of gestation, and (c) without neurological or developmental complications. Participants were invited to participate when they were 6, 9, or 12 months of age. A total of 94 infants (65% male) and their mothers were enrolled in the study (32 six-month-olds, 31 nine-month-olds, 31 twelve-month-olds). While the influence of chronic maternal stress on EEG power has not been examined, sample size was determined to be sufficient the basis of the observed effect and sample sizes of other EEG studies examining the influence of stress on infant and child EEG power (Otero, 1994; Pierce et al., 2019; Tomalski et al., 2013). Sample statistics appear in Table 1.

2.1.2 | Demographic & education information

Participants' age, race, sex, parental educational attainment, and household income were collected via questionnaire (see Figure 1). Household income-to-need ratios (ITN) were computed by dividing the household income by the federal poverty line for the year the family visited the lab or the most recent year available. The ITN for the sample ranged from 0 to 25, with a median ITN value of 2.26

(IQR = 5.03). Thirty percent (30.9%) of the sample reported an ITN below the poverty line. Due to the expected positive skew, ITN values were log transformed. One participant reported receiving no income, thus the log-transformed value was not valid. As such, their ITN value was Winsorized to the next lowest valid ITN value.

2.1.3 | Perceived maternal stress

Perceived maternal stress was assessed using the perceived stress scale (PSS; Cohen, Kamarck, & Mermelstein, 1983; Cohen & Williamson, 1988). The PSS is a 14-question self-report questionnaire that assesses the degree to which the respondent has perceived situations as stressful within the last month. For participants with less than 10% missing data in total (i.e. a participant skipped one item), the missing value was mean-replaced with their mean for the other 13 items.

2.1.4 | Hair cortisol collection and analysis

Each mother-infant dyad attended a single laboratory visit. A research staff member cut a small section of hair proximal to the posterior vertex of the mother's scalp. Each hair sample weighed at least 15 mg and was trimmed to be approximately 3 cm long (measured from the end closest to the root), thereby containing cortisol deposited during roughly the past three months. Samples were stored at −40°C until being sent to the University of Massachusetts for analysis. Samples were processed and analyzed using methods previously validated and described in detail (Davenport, Tiefenbacher, Lutz, Novak, & Meyer, 2006; Meyer et al., 2014) Briefly, each sample was weighed, washed twice in isopropanol to remove external contaminants, ground to a fine powder, and extracted with methanol. The methanol extract was evaporated, re-dissolved in assay buffer, and analyzed in duplicate along with standards and quality controls by a sensitive and specific enzyme-linked immunosorbent assay (Salimetrics). Assay readout was converted to pg cortisol per mg dry

TABLE 1 Demographics. Descriptive statistics for each age group (mean and standard deviation [where appropriate] in parentheses)

	6 month (N = 32)	9 month (N = 31)	12 month (N = 31)
Age (in months)	6.26 (0.42)	9.12 (0.43)	12.18 (0.34)
Parental education	15.08 (3.89)	14.66 (3.71)	15.04 (3.65)
Race (%)			
White	28.1%	38.7%	28.6%
Black	21.9%	19.4%	33.3%
Other	37.5%	19.4%	25.7%
Refused	12.5%	22.5%	32.3%
Ethnicity (%)			
Hispanic	50.0%	41.9%	41.9%
Not Hispanic	43.8%	48.4%	32.3%
Refused	6.3%	9.7%	25.8%

FIGURE 1 Timeline of assessment

Laboratory Visit Data:
-Infant age (6, 9, or 12 months)
-Demographic Information
-Maternal Hair Sample
-Resting EEG
-Family income and composition
-Parental Education
-Perceived Stress Scale

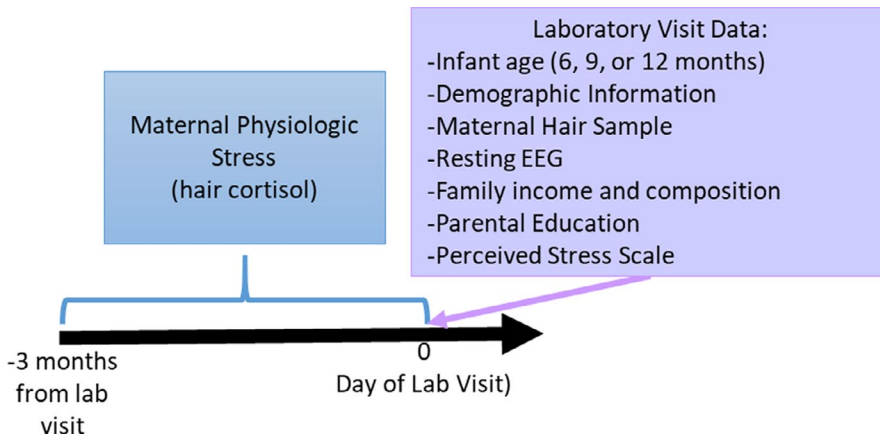Maternal Physiologic Stress (hair cortisol)

-3 months from lab visit
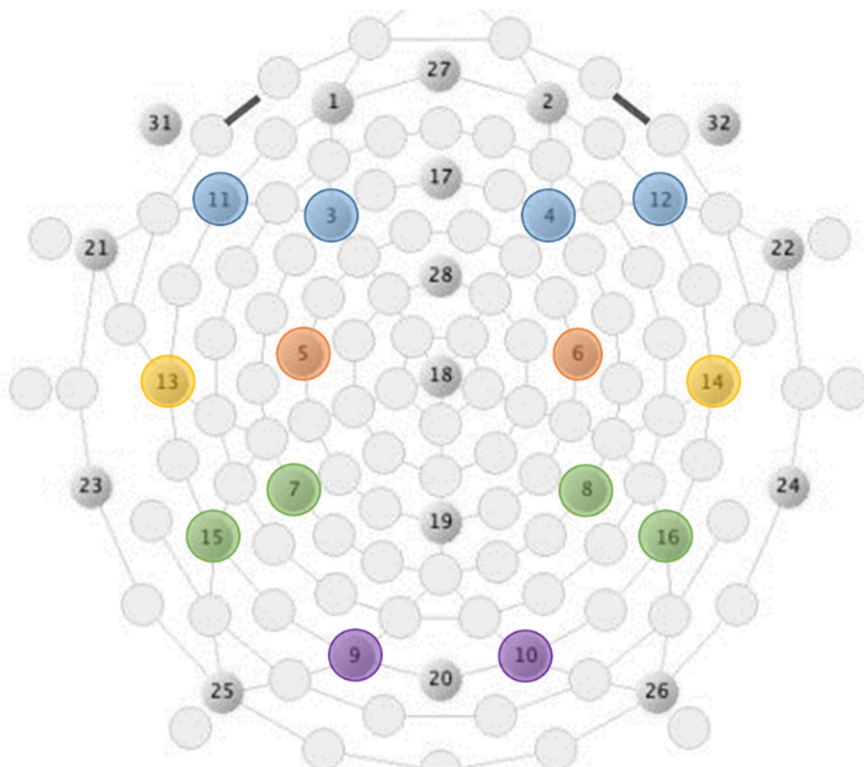
0
Day of Lab Visit)

FIGURE 2 Electrode groupings by region

hair weight (pg/mg). Intra- and inter-assay coefficients of variation for this assay are <10%. Hair cortisol values were log-transformed to correct for skew, similar to previous methods (Chen et al., 2016). Additionally, parents currently using steroid medications were excluded from analysis (n = 9). In total, 60 parents provided usable hair cortisol data. There were no significant associations between hair cortisol and potential confounds, including hair washing frequency, use of oral contraceptives, and use of hair dye.

2.1.5 | EEG collection and analysis

EEG was recorded using a 28-channel HydroCel Geodesic Sensor Net (Electrical Geodesic, Inc.) and on a GEM 100 amplifier (Electrical Geodesic, Inc.; EB NEURO S.p.A., Firenze, Italy). The GEM system is a high input-impedance system, and electrode impedances were kept below 50 kΩ whenever possible. The sampling rate was 250 Hz and data were online referenced to the vertex (Cz) electrode. During collection, infants were seated on their mothers' laps in a dimmed room while watching soundless videos of infant toys. Mothers were instructed to keep their infant facing the video, to not talk to the infant, and to interact with the infant as little as possible. Data collection lasted approximately 5 min unless the infant rejected collection before that time.

Electroencephalography was analyzed using the EEGLAB toolbox (Delorme & Makeig, 2004), MATLAB scripts (The MathWorks), and the MADE pipeline (Debnath et al., 2020). Data were high-pass filtered at 0.3 Hz and low-pass filtered at 50 Hz. Bad channels were identified and removed using the EEGLAB plug-in FASTER (Nolan, Whelan, & Reilly, 2010). Consistent with the approach used by other developmental studies (e.g. Debnath, Salo, Buzzell, Yoo, & Fox, 2019), ocular artifacts and generic noise removal were completed by creating a copy of the dataset and performing independent component

TABLE 2 Means and correlations for variables of interest. Correlations (Pearson *r*) between measures of interest, means, and standard deviations

	1.	2.	3.	4.	5.
1. Age (in months)	1				
2. Family ITN (log transformed)	−0.043	1			
3. Parental education	−0.031	0.691***	1		
4. Perceived stress scale	0.146	0.043	0.042	1	
5. Maternal hair cortisol (log transformed; pg/mg)	0.028	−0.151	−0.127	−0.056	1
Mean	9.156	0.293	14.931	20.534	0.664
SD	2.467	0.581	3.713	7.729	0.458

***p < .001.

analysis (ICA) on the copied dataset. This copied dataset was high-pass filtered at 1-Hz and segmented into arbitrary 1,000 ms epochs. Epochs were removed from this copied dataset if the amplitude was ±1,000 μV or if power in the 20–40 Hz band (after Fourier analysis) was greater than 30 dB (Harrewijn et al., 2019). Additionally, if more than 20% of the epochs in a given channel were removed, that channel was excluded from both the ICA-copied dataset and the original dataset (Debnath et al., 2019; Troller-Renfree, Nelson, Zeanah, & Fox, 2016). Additionally, if a child had more than six electrodes (>20%) deemed globally bad, that child was then removed from all future processing (*N* = 8). Then, ICA (Comon, 1994; Makeig, Jung, Bell, Ghahremani, & Sejnowski, 1997) was performed on the copied dataset and the ICA weights were copied back to the original continuous dataset (high-pass filtered at 0.3 Hz). The ADJUST toolbox (Mognon, Jovicich, Bruzzone, & Buiatti, 2011) was used to automatically identify artifactual independent components (ICs) in the original dataset, and, as is common in developmental work, ICs were also visually inspected (Buzzell et al., 2019; Debnath et al., 2019). All artifactual ICs were removed from the data. Then, data were epoched in segments of 2 s with 50% (1 s) overlap. Similar to other infant work (Debnath et al., 2019), epochs where any of the frontal electrodes (electrode numbers 1, 2, 11, 12, 27) exceeded a voltage threshold of ±100 μV were rejected from all further analyses to ensure ocular artifacts were removed. For the remaining epochs, remaining bad channels were identified if the electrode exceeded a voltage threshold of ±100 μV. Epochs were rejected when more than 20% of channels were interpolated (Harrewijn et al., 2019). Finally, all rejected channels were interpolated using a spherical spline (Perrin, Pernier, Bertrand, & Echallier, 1989). Participants needed to have at least ten artifact-free epochs (DeBoer, Scott, & Nelson, 2007) to be included for analysis (removed *N* = 7). The average number of used epochs was 176.42 (*SD* = 125.98, range: 12–452). Finally, data were re-referenced to an average reference.

A fast fourier transformation (FFT) with a 2-s Hamming window was applied to the epoched data. Consistent with other infant studies (Tomalski et al., 2013), spectral power (μV^2) was computed for theta (3–5 Hz), alpha (6–9 Hz), beta (13–19 Hz), and two gamma frequency ranges (21–30 Hz, 31–45 Hz). Average absolute power was computed separately for each hemisphere across electrodes in

five electrode groups (see Figure 2 for a grouping diagram). Finally, given that there were no significant differences in absolute power by hemisphere or region for any of the frequency bands (see Supporting information S1), each frequency band was averaged across all included electrodes to create whole-brain measures of theta, alpha, beta, low-gamma, and high-gamma power. Additionally, whole-brain relative power was computed by dividing the absolute power within one frequency band (e.g. theta) by total absolute power from all frequency bands (e.g. theta, alpha, beta, low-gamma, and high-gamma). Given that past findings relating early life stress to differences in brain function have been more commonly found in relative power (e.g. Vanderwert, Zeanah, Fox, & Nelson III, 2016), relative power results are reported below. Examination of absolute power is provided in the Supporting Information (see Supporting information S2 and Table S1).

2.1.6 | Memory measurement

A subset of 70 children completed the visual paired comparison (VPC) task (Morgan & Hayne, 2006), of whom 44 children also had EEG data. See Supporting information S3 for further details on exploratory analyses.

2.2 | Statistical analyses

2.2.1 | Participant inclusion and analysis

To examine associations between reported maternal stress and infant EEG findings, initial descriptive statistical analyses were conducted in SPSS (Version 25.0, IBM Corp). Multivariable linear regressions were performed in Mplus statistical software (Muthén & Muthén, 2010). The sample size was maximized using Full Information Maximum Likelihood Estimation to account for missing data, which were missing at random (Little's MCAR: χ^2 = 11.59, *p* = .710). All regressions described below took the following format: Infant EEG power (relative power in each of the five frequency bands) served as the dependent variable; demographic factors (infant age, average parental educational
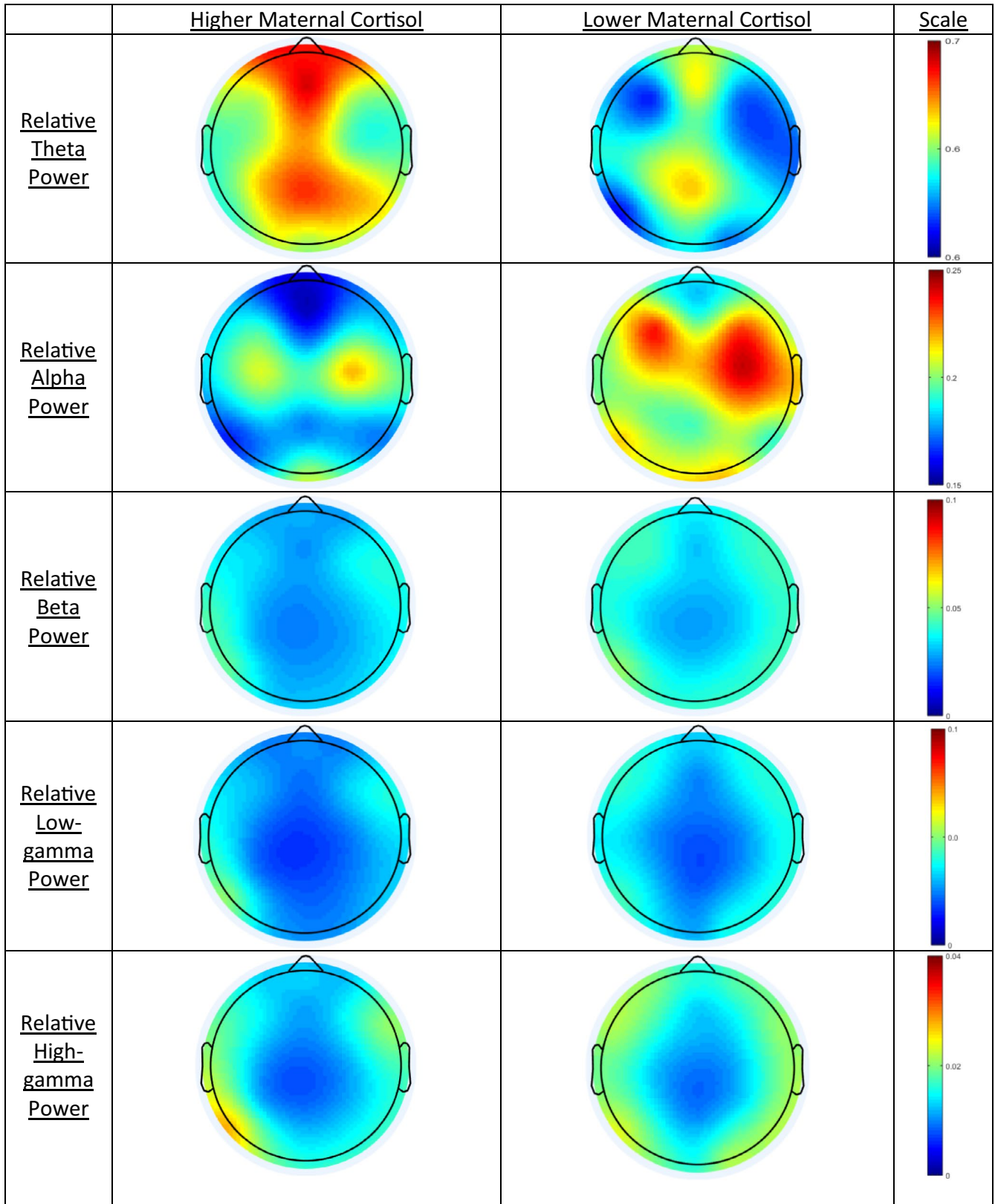
	Higher Maternal Cortisol	Lower Maternal Cortisol	Scale
Relative Theta Power			
Relative Alpha Power			
Relative Beta Power			
Relative Low-gamma Power			
Relative High-gamma Power			

FIGURE 3 Power topoplots by group. False-color topographic maps indicating the distribution of relative power across the scalp for the higher maternal cortisol and lower maternal cortisol using a median split for visualization only

attainment, and family income-to-needs ratio) served as covariates; and maternal stress measures (hair cortisol and PSS scores) together served as independent variables (see Table 2 for correlations between measures of interest). As expected, mean parental educational attainment and family income-to-needs ratio were significantly associated, but they did not violate assumptions of multicollinearity (VIF < 2.5).

3 | RESULTS

3.1 | Relations between maternal stress and infant relative theta power

Regression analyses indicated that higher maternal hair cortisol concentration was associated with significantly greater relative (β = 0.470, p < .001) theta power, whereas maternal report of perceived stress was not associated with infant relative theta (β = 0.134, p = .243; see Figure 3 for false-color topographic maps. See Table 3 for regression effects).

3.2 | Relations between maternal stress and infant relative alpha power

Analyses indicated that higher maternal hair cortisol concentration was associated with significantly lower relative alpha power (β = −0.463, p < .001). Maternal report of perceived stress was not associated with infant relative (β = −0.035, p = .762) alpha power when controlling for covariates.

3.3 | Relations between maternal stress and infant relative high-gamma power

Analyses indicated that higher maternal hair cortisol concentration was associated with significantly lower relative high-gamma power (β = −0.300, p = .029). Higher maternal perceived stress was associated with marginally reduced relative high-gamma power (β = −0.214, p = .067).

3.4 | Relations between maternal stress and infant beta power and low-gamma power

Analyses indicated that higher maternal hair cortisol concentration (β = −0.257, p = .066) and higher maternal perceived stress (β = −0.234, p = .050) were each marginally associated with reduced relative beta power. Neither maternal hair cortisol concentration

(β = −0.073, p = .612) nor perceived stress (β = −0.174, p = .159) were significantly associated with either relative low-gamma power.

3.5 | Relations between resting EEG and infant memory

Models for relative theta, alpha, and high-gamma power did not reach significance (all ps > .165); see Supporting information S3 for further details.

4 | DISCUSSION

The present study suggests that infants being raised by mothers with chronic higher physiological stress have altered patterns of neural activity. Specifically, infants whose mothers have higher hair cortisol concentrations tend to have both increased low-frequency brain activity (i.e. higher relative theta power), as well as decreased high-frequency brain activity (i.e. less relative alpha and high-gamma power and marginally less relative beta power). Importantly, these links between maternal stress physiology and child brain function are seen over and above the effects of parental report of perceived stress, family ITN, mean parental education, and infant age. Parental report of stress was also marginally related to decreased beta and decreased high-gamma power, after controlling for covariates. Furthermore, because hair cortisol concentration represents an average cortisol level from the *preceding* three months, our chronic stress measure temporally predates our measure of infant brain function. These findings are thus most consistent with prior work suggesting that early life stress impacts functional brain development in a pattern suggestive of a maturational lag in brain activity (Marshall et al., 2008; Pierce et al., 2019; Tomalski et al., 2013).

This study adds to a growing body of literature suggesting that neurodevelopmental lags may be a consequence of early life stress, with patterns emerging as early as the first year of life (e.g. Marshall et al., 2004; Vanderwert et al., 2010). Similar patterns have been observed in environments characterized by chronic stressors such as neglect (Marshall et al., 2004; Vanderwert et al., 2010) and poverty

TABLE 3 Regression coefficients. Standardized effects reported with standard errors reported parenthetically for relative EEG power

	Age (in months)	Family ITN (log transformed)	Parental education	Perceived stress scale	Maternal hair cortisol (log transformed; pg/mg)
Theta	−0.218 (0.122)	0.204 (0.171)	−0.128 (0.163)	0.134 (0.114)	0.470 (0.120)***
Alpha	0.262 (0.121)*	−0.166 (0.171)	0.091 (0.164)	−0.035 (0.114)	−0.463 (0.122)***
Beta	0.032 (0.137)	0.019 (0.188)	0.022 (0.179)	−0.234 (0.120)	−0.257 (0.140)
Low-gamma	−0.072 (0.141)	−0.113 (0.193)	0.083 (0.184)	−0.174 (0.124)	−0.073 (0.144)
High-gamma	0.105 (0.130)	−0.337 (0.176)	0.219 (0.169)	−0.214 (0.117)	−0.300 (0.137)*

*p < .05;
***p < .001.

(Otero et al., 2003; Tomalski et al., 2013) as well as in environments characterized by more "garden variety" stressors (e.g. Pierce et al., 2019). As the present sample was not specifically recruited for stress exposure, these findings provide important evidence that *stressors encountered in everyday life* may alter neurodevelopmental patterns. Further, an effort was made to recruit a socioeconomically and racially diverse sample, extending the generalizability of these findings.

Maturational lags in brain function similar to those reported here have been linked to a variety of negative developmental outcomes, including deficits in language development (Maguire & Schneider, 2019), cognitive functioning (Coming et al., 1982; Corning et al., 1986; Maguire & Schneider, 2019) and psychopathology (Harmony et al., 1990; McLaughlin et al., 2010). While a limitation of this study is that we did not see direct relations between brain activity and neurocognitive functioning (see Supporting information S3), understanding the mechanisms by which stressors impact neurocognitive and psychiatric development in infancy has crucial implications for preventive and intervention efforts, and should be a priority for future research.

To our knowledge, this study is the first to tie infant brain function to a measure of chronic maternal *physiological* stress. Interestingly, this effect held above and beyond maternal report of perceived stress—indeed, maternal report and measures of physiological stress were not even correlated in this sample. While on its face this finding is surprising, there is a growing body of work showing that physiological and perceived stress levels are frequently unrelated, even in some of the most common stress paradigms, and therefore provide independent information (for review see Schlotz et al., 2008). However, in the present study, the time scales for the assessment of physiological stress (previous 3 months) and perceived stress (previous 1 month) were slightly different, which could also account for the lack of correlation between these two measures. Interestingly, in both animal and human models, the effects of stress hormone on neurocognitive development have been well documented (Koss & Gunnar, 2018; Lupien, McEwen, Gunnar, & Heim, 2009; Talge, Neal, & Glover, 2007). However, the maternal transmission of stress to the infant and subsequent neurodevelopmental consequences is less well understood.

Several mechanisms could explain how maternal stress hormone may get "under the skin" of offspring, potentially accounting for the present results. One of the most direct ways mothers may pass stress hormone to their offspring is through the gestational environment or via breast milk following birth (Grey, Davis, Sandman, & Glynn, 2013; Lupien et al., 2009). Second, maternal physiological stress may impact brain development through HPA axis synchrony (via touch, shared gaze, vocalization, etc.) between mother and child (Stenius et al., 2008; Williams et al., 2013). Third, it is plausible that environmental stressors such as noise, pollution, or crowding may impact mothers and infants similarly, such that maternal physiological stress serves as a proxy for infant physiological stress (Ursache et al., 2017). Finally, work has suggested that higher maternal stress may lead to reductions in warm,

contingent caregiving, which in turn can impact infant neurodevelopment (Twardosz & Lutzker, 2010; Ursache et al., 2017). While linking maternal physiological stress to infant brain function is an important advancement, future research should aim to further identify the particular pathways and mechanisms through which maternal stress impacts the child. Such research would aid in the development of interventions targeting stress-related deficits and delays in infant neurodevelopment.

While the present study provides important evidence concerning the potentially deleterious effects of chronic maternal physiological stress on infant neurodevelopment, we acknowledge several limitations. First, this study is limited by a relatively small sample size, and thus replication is of great importance. Second, although hair cortisol concentration represents an average cortisol level from the *preceding* three months, and thus our chronic stress measure temporally predates our measure of infant brain function, the present research is nonetheless cross-sectional and correlational and cannot determine causation. Indeed, an alternate explanation could be that any pattern consistent with a maturational lag in the infant was present earlier in development and led to higher stress for the mother. As such, future research should aim to look at longitudinal relations between maternal physiological stress and neurodevelopment. Another limitation is an inability to assess if differences are caused by prenatal stress or genetic susceptibility to stress. It is possible that neurodevelopmental differences observed are gestational or genetic rather than being rooted in postnatal experience. Future studies should further examine the specific time course on which early neurodevelopmental differences emerge and whether stress during pregnancy predicts early brain function. Third, while our findings suggest that elevated maternal cortisol is related to a pattern consistent with a maturational lag in brain activity, populations that experience significant early stressors (particularly neglect) sometimes show a diminished stress response (e.g. Fisher, Gunnar, Dozier, Bruce, & Pears, 2006; Fries, Hesse, Hellhammer, & Hellhammer, 2005). While we did not expect this association in our sample, it is important to consider for future research since relations between maternal physiological stress and infant brain function may not be linear, but rather an inverted-U shaped function, in more diverse samples. Finally, while the EEG data are presented as resting brain activity, infant attention to our visual stimuli was not coded. It is possible that individual differences in the allocation of visual attention during EEG data collection could be related to individual differences in the EEG power ratios. Without behavioral data being gathered during EEG collection, contributions of infant state to the EEG patterns observed are unknown.

Altogether, the present study provides the first evidence that chronic maternal physiological stress negatively impacts developmental patterns of infant brain activity during the first year of life. These findings are important given that maturational lags in brain development can be long-lasting and are associated with deficits in cognitive and emotional development (Harmony et al., 1990; Otero et al., 2003; Vanderwert et al., 2010). The present research also suggests that reducing maternal physiological stress may be a useful

target for future interventions aiming to foster neurodevelopmental trajectories.

CONFLICT OF INTEREST

The authors declare no competing financial interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

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