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Maternal HPA Axis Function During Parenting is Associated with Reduced Brain Activation to Infant Cry and More Intrusive Parenting Behavior

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Abstract

Previous research indicated that maternal cortisol function and maternal brain response to infant stimuli are separately related to differences in parenting behavior. Evidence from animal models have demonstrated that chronically high cortisol concentration alters brain structure and function, suggesting that studying these two mechanisms together may further improve understanding of parental behavior in human mothers. First time mothers of infants aged 1-7 months old (M age = 3 months) were recruited to participate. Mother's cortisol concentration was measured during a naturalistic interaction with their infant and their behavior was coded for maternal sensitivity and nonintrusiveness. In a separate session using fMRI, mothers listened to their own infant and a control infant crying. We demonstrated an association between mother's average cortisol concentration and nonintrusive maternal behavior, but not maternal sensitivity, such that higher cortisol concentration was associated with more intrusive behavior. In the brain, we found in the right precentral gyrus, the left culmen extending into the left inferior temporal gyrus and fusiform, two clusters in the superior temporal gyrus, and in the medial frontal gyrus, greater cortisol concentration was associated with decreased activation to infant cry. We also found that activation in these regions to cry sounds was associated with maternal nonintrusiveness such that greater activation in these regions was associated with less intrusive behavior.

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ABSTRACT

Previous research indicated that maternal cortisol function and maternal brain response to infant stimuli are separately related to differences in parenting behavior. Evidence from animal models have demonstrated that chronically high cortisol concentration alters brain structure and function, suggesting that studying these two mechanisms together may further improve understanding of parental behavior in human mothers. First time mothers of infants aged 1-7 months old (M age = 3 months) were recruited to participate. Mother's cortisol concentration was measured during a naturalistic interaction with their infant and their behavior was coded for maternal sensitivity and nonintrusiveness. In a separate session using fMRI, mothers listened to their own infant and a control infant crying. We demonstrated an association between mother's average cortisol concentration and nonintrusive maternal behavior, but not maternal sensitivity, such that higher cortisol concentration was associated with more intrusive behavior. In the brain, we found in the right precentral gyrus, the left culmen extending into the left inferior temporal gyrus and fusiform, two clusters in the superior temporal gyrus, and in the medial frontal gyrus, greater cortisol concentration was associated with decreased activation to infant cry. We also found that activation in these regions to cry sounds was associated with maternal nonintrusiveness such that greater activation in these regions was associated with less intrusive behavior.

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And finally, thank you to my family. My parents, Tom and Anne, who instilled in me early and often the importance of education and a curiosity for how the world works, and my sibling Hannah, who has always had my back.

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CHAPTER ONE: INTRODUCTION

Neuroendocrine signaling and the brain mechanisms that govern them are important for supporting effective parenting behavior. Maternal cortisol function (Finegood, Blair, Granger, Hibel, Mills-Koonce, 2016) and maternal brain response to infant stimuli (Musser, Kaiser-Laurent, Ablow, 2012) both separately predict differences in parenting behavior. Many areas of the brain that are highly engaged in responding to infant stimuli are also important regulators of the hypothalamic-pituitary-adrenal (HPA) axis (Herman, Ostrander, Mueller, Figueiredo, 2005) and animal models show that chronically high cortisol concentration alters brain structure and function (Brummelte and Galea, 2010; Pawluski, Lambert, Kinsley, 2016), suggesting that studying these two mechanisms together may improve understanding of how maternal biology can influence parenting behavior. Despite the links between these two biological mechanisms, there has been relatively little study of how these two aspects of maternal biology together support parenting behavior. This current study examines the dual influences of maternal HPA axis function during a normal parenting interaction and maternal brain response to infant stimuli to understand differences in parenting behavior.

There is an ideal level of basal cortisol that supports effective parenting behaviors. In animal models, adrenalectomized rats that are unable to produce cortisol show significantly lower levels of time spent with pups and reduced licking and

grooming behaviors in the postpartum period (Rees, Panesar, Steiner, Fleming, 2004). In these animals, cortisol replacement via exogenous administration increased the amount of these behaviors. Other studies of animal models have observed that greater basal cortisol levels are associated with reduced time spent with young and reduced arched-back nursing. Importantly, this was observed in contexts when exogenous administration of cortisol increased fluctuating cortisol levels, and for naturally high concentrations observed in a sample. This finding was observed both in rats (Brummelte, Gaela, 2010; Leuner, Fredericks, Nealer, Albin-Brooks, 2014) and primates (Bahr, Martin, Pryce, 2001; Bardi, Shimizu, Barrett, Borgognini-Tarli, Huffman, 2003). In humans, a similar pattern has been observed using correlational studies. In multiple studies of mothers of infants aged 3-6 months, higher basal cortisol levels were associated with less sensitive and appropriate caregiving and more intrusive caregiving behaviors (Gordon, Zagoory-Sharon, Leckman, Feldman, 2010; Mills-Koonce, Propper, Gariepy, Barnett, Moore, Calkins, Cox, 2009). This finding has been replicated in the largest study of maternal cortisol and parenting behavior; a study looking at 1,180 mothers found that basal salivary cortisol was negatively associated with sensitive maternal behavior at both 15 and 24 months postpartum (Finegood et al., 2016). Taken together, this is evidence that basal cortisol associated with less sensitive and engaged parenting starting 3-6 months postpartum.

Immediately postpartum, increased basal cortisol is associated with more positive parenting behaviors, which suggests a more complicated relation across infant age. Greater basal cortisol was associated with more attraction to infant's body odor (Fleming,

Steiner, Corter, 1997) and higher levels of affection and contact with their infant (Fleming, Steiner, Anderson, 1987). In a sample of new primiparous mothers, greater basal cortisol was associated with more positive interactions and more affection towards their infant (Krpan, Coombs, Zinga, Steiner, Fleming, 2005). This is evidence that studies of mothers postpartum spanning a relatively wide age range may need to test age effects, as when the relation between cortisol and behavior shifts between immediately postpartum and three months is still unclear. Additionally, more study is needed to understand how maternal cortisol concentration during a naturalistic parenting context is associated with parenting behavior.

The few existing studies that examined maternal cortisol changes during parenting contexts indicate that during naturalistic interactions with one's infant, cortisol tends to decrease. Studies of more naturalistic contexts with newborns have demonstrated that for mothers breastfeeding, diaper changing, or experiencing skin to skin contact with their newborns, these mothers show reduced cortisol concentrations after these interactions (Handlin, Jonas, Petersson, Edjebäck, Ransjö-Arvidson, Nissen, Uvnäs-Moberg, 2009; Mörelius, Nelson, Gustafsson, 2007; Mörelius, Theodorsson, Nelson, 2005). Researchers hypothesize that these experiences were typically positive for mothers and served to reduce their psychological feelings of stress. This would indicate that interactions with one's newborn may typically serve to reduce cortisol concentrations in mothers. This also suggests that mothers who feel more stressed during an interaction with their infant would not show as much of a decrease in cortisol. These studies, however, did not measure parenting behavior differences as a result of differences in HPA axis function.

In order to appropriately measure HPA axis function, the proper variable must be selected. Average cortisol concentration refers to the mean cortisol level across a number of samples. Other measures of HPA axis function, such as cortisol area under the curve, are more related to cortisol patterns or rates of change over time, which does not reflect an accurate measure of basal cortisol (Fekedulegn, Andrew, Burchfiel, Violanti, Hartley, Charles, Miller, 2007; Gordon et al, 2010). Using average cortisol concentration has the benefit of creating a more stable estimate of mothers' HPA axis function at rest, at the expense of collapsing across time and not measuring directly in response to a particular stimulus. This technique has been used to measure average plasma cortisol (Halbreich, Asnis, Zumoff, Nathan, Shindledecker, 1984; Kurina, Schneider, Waite, 2004; Zumoff, Fukushima, Weitzman, Kream, Hellman, 1974) and average salivary cortisol (Cacioppo, Ernst, Burleson, McClintock, Malarkey, Hawkley, Kowaleski, Paulsen, Hobaon, Hugdahl, Spiegel, Berntson, 2000; Smider, Essex, Kalin, Buss, Klein, Davidson, Goldsmith, 2002; Viau, Arsenault-Lapierre, Fecteau, Champagne, Walker, Lupien, 2010). Given that in some studies of mothers with their infants, cortisol tends to decrease (Handlin et al., 2009; Mörelius et al., 2007; Mörelius et al., 2005) and lower basal cortisol is generally considered more adaptive for parenting, we would hypothesize that mothers with lower average cortisol concentrations would show more positive parenting behaviors.

Another important biological mechanism that supports parenting behaviors is the brain's responses to infant cues. Specific networks of brain regions respond strongly to infant cues in ways that are associated with behavior. Frontal regions, particularly in the

pre-SMA and SMA, are reliably activated in response to infant distress cues (Witteman, Van IJzendoorn, Rilling, Bos, Schiller, Bakermans-Kranenburg, 2019). This area was demonstrated to be reliably activated in response to infant cries in the only cross-cultural study of this paradigm conducted to date (Bornstein, Putnick, Rigo, Esposito, Swain, Suwalsky, 2017) and activation of this region is believed to represent auditory perception of the cry and motor planning to support effective parenting behavior (Lee & Quessy, 2003; Witteman et al., 2019). Another region that is reliably activated to infant cues is the amygdala. It has been shown to be activated in response to infant emotional faces (Barrett, Wonch, Gonzalez, Ali, Steiner, Hall, Fleming, 2012; Kim, Capistrano, Erhart, Gray-Schiff, Xu, 2017) and infant cries (Kim et al., 2011; Swain, Ho, Rosenblum, Morelen, Dayton, Muzik, 2017; Witteman et al., 2019). The relation between amygdala activation and positive parenting behaviors appears to be context-dependent, with activation to negative infant faces being associated with more intrusive behavior (Kim et al., 2017), activation to positive infant faces associated with more positive maternal experiences (Barrett et al., 2012), and greater activation to infant cry sounds being associated with more maternal sensitivity (Kim et al., 2011). In addition to subcortical regions, temporal regions appear to be highly engaged by infant stimuli in ways that are associated with differences in parenting behavior.

Activation of temporal regions to infant stimuli has been associated with more engaged parenting behavior. Multiple studies of maternal brain response to infant cry stimuli have identified temporal regions, particularly the superior temporal gyrus (STG), as reliably activated to infant cry (Kim et al., 2011; Swain et al., 2017; Witteman et al.,

2019). Activation of temporal regions have been related to maternal behavior – a study of high compared to low sensitivity mothers found that high sensitivity mothers showed greater activation to their infant's neutral and happy faces (Elmadih, Wan, Downey, Elliott, Swain, Abel, 2016). Conversely, a study of mothers responding to infant cries found that more intrusive mothers had greater activation to infant cry (Musser et al., 2012). Taken together, these studies indicate that SMA, amygdalar, and STG regions are highly responsive to infant cry stimuli in ways that may be important for parenting behavior.

There is also preliminary evidence that differences in amygdala functional connectivity (FC), particularly to motor regions such as the SMA, further help explain differences in parenting behavior. Factors known to be associated with disrupted parenting behavior, such as maternal depression (Ho & Swain, 2017) and child maltreatment experiences (Swain et al., 2017), are associated with altered amygdala FC. Of particular importance for parenting behavior is the FC between the amygdala and motor planning regions like the SMA. Studies of mothers experiencing childhood maltreatment had greater amygdala-SMA FC (Olsavsky, Stoddard, Erhart, Tribble, Kim, 2021). In this sample, greater amygdala-SMA FC was associated with less intrusive parenting behavior. In a community sample of mothers, greater amygdala-SMA FC was associated with greater intrusive parenting behavior (Atzil et al., 2011). More research is necessary to disentangle these results and determine to what extent amygdala-SMA FC is adaptive for parenting. Additionally, despite evidence from studies of nonmothers demonstrating that cortisol concentration was associated with differences in amygdalar

FC during resting state scans (Kogler, Mueller, Seidel, Boubela, Kalcher, Moser, Derntl, 2016; Veer, Oei, Spinhoven, van Buchem, Elzinga, Rombouts, 2012; Vaisvaser, Lin, Admon, Podlipsky, Greenman, Stern, Hendler, 2013), no study has investigated whether maternal cortisol concentration is associated with amygdala-SMA FC in ways that are maladaptive for parenting behavior. Given that amygdala-SMA FC in a community sample was associated with more intrusive behavior, we hypothesize that greater maternal cortisol will be associated with greater amygdala-SMA FC.

When considering the dual influence of cortisol and maternal brain on maternal behavior, it is important to consider how maternal brain function may be altered by cortisol. In animal models, greater fluctuating levels of corticosterone was associated with altered brain structure in multiple regions. Studies of rats given exogenous cortisol treatment in the postpartum period found reduced cell proliferation in the dentate gyrus of the hippocampus (Brummelte and Galea, 2010). This altered hippocampal structure was observed in other studies showing decreased dendritic remodeling in the hippocampus in postpartum rats with greater corticosterone (Pawluski et al., 2016). Similar findings of reduced neurogenesis and cell proliferation and reduced dendritic branching and spine density was also observed in the nucleus accumbens (Haim, Sherer, Leuner, 2014) and in the medial prefrontal cortex (Leuner et al, 2014). These studies also identified that these alterations in brain structure were associated with altered maternal care. Reduced cell proliferation in the hippocampus and reduced dendritic branching and density in the medial prefrontal cortex were both associated with reduced time spent nesting and reduced arched-back nursing (Brummelte and Galea, 2010; Leuner et al, 2014). It is still

unclear whether these alterations are specific to the brain regions in these studies or whether we would expect similar findings across the entire brain. Regardless, this is evidence that cortisol concentration can directly alter brain structure and function. In humans, only one study to our knowledge has investigated how maternal cortisol is related to differences in brain activation to infant cry in a sample of mothers of 18-month-olds. This study examined maternal cortisol change in response to a stressful infant paradigm (the Strange Situation) and then related that cortisol change to differences in maternal brain activation to infant cry sound. They found that mothers who were less reactive to the stressful infant paradigm showed increased activation to their own infant cry in both frontal and subcortical networks including the periaqueductal grey, insula, bilateral orbitofrontal cortex, and the anterior cingulate and medial prefrontal cortex (Laurent, Stevens, Ablow, 2011). Researchers interpret this finding as demonstrating how mothers who were less reactive to the stressful paradigm were better able to engage neural circuits underlying empathy and emotion regulation and engage with the infant stress cues with greater empathetic attunement. However, this paper did not measure parenting behavior, and measured maternal cortisol during a stressful context, which limits the generalizability of these results to the current study and does not reflect the natural variations in HPA axis function during a naturalistic parenting context. Extending this work to a naturalistic parenting interaction and examining how differences in maternal brain activation to infant distress cues relate to parenting behavior would extend the literature on biological mechanisms underlying parenting behavior.

Taken together, the evidence from animal models supports the idea that high levels of maternal cortisol can alter brain structure in function in ways that are associated with less effective parenting behaviors (Brummelte and Galea, 2010; Leuner et al, 2014). Converging human evidence has demonstrated that differences in maternal cortisol function is related to differences in brain response to infant stimuli (Laurent, Stevens, Ablow, 2011) in regions that have been shown to be important for directing maternal behavior. Separately, studies have shown that greater maternal cortisol in humans is associated with less effective parenting behaviors (Gordon, et al. 2010; Mills-Koonce, Propper, Gariepy, Barnett, Moore, Calkins, Cox, 2009). This suggests that in humans, maternal cortisol concentration may alter maternal brain structure and function in ways that are related to differences in parenting behavior. No study to our knowledge has investigated maternal cortisol, maternal brain response to infant stimuli, and subsequent parenting behavior, which obscures a full mechanistic understanding of how biological mechanisms support parenting behavior.

Thus, the current study seeks to examine two biological mechanisms thought to support effective parenting behaviors – maternal HPA axis function and maternal brain response to infant distress cues—and their relation to sensitive and intrusive parenting behaviors. Mother's cortisol concentration was measured during a naturalistic interaction with their infant, which was coded for sensitive and intrusive behaviors, and then this cortisol concentration was related to differences in brain activation to infant distress cues. The current study will include first-time mothers ranging from 1 month to 7 months postpartum, with an average postpartum age of 3 months. We hypothesize that on

average, higher maternal cortisol concentration during parenting will be related to less sensitive and more intrusive parenting behaviors. We hypothesize that greater maternal cortisol concentration during parenting will be associated with reduced activation to infant cry sounds in the SMA, the amygdala, and the STG, and that reduction of activation in these regions will likewise be associated with less sensitive and more intrusive parenting. We hypothesize that greater maternal cortisol concentration will be associated with greater amygdala-SMA FC.

CHAPTER TWO: METHODS

1. Participants

A socioeconomically diverse sample of participants was recruited through cooperation with WIC (Women, Infant, and Children) centers, Colorado state Prenatal Plus programs, and midwifery clinics in the Denver metro area. Participants were eligible to participate if they were between the ages of 18 and 40, primiparous, English-speaking, had an IQ greater than 70, an income-to-needs ratio (INR; see section 2.1.3) of less than 8 and no pregnancy-related or infant medical illnesses as well as no current or historical psychiatric illness other than depression or anxiety diagnosis, as well as having no metal in their body that would prevent MRI scanning. Mothers who were 3-4 months postpartum were targeted for recruitment. The research protocol was approved by the University of Denver IRB, and informed consent was administered to all participants. Thus, all analysis focused on participants (N = 59) with useable cortisol and fMRI data. This subset was mothers with a mean age of 25.24 years (SD 5.5) with children (% Female = 57.6) having a mean age of 3.47 (SD 1.74). 44.1% of this sample identified as Hispanic. Racially, 50.8% identified as White, 6.8% Black, 1.7% Asian, and 40.7% other (a mix of Hispanic, Latino, and Biracial).

A portion of this sample has been analyzed and published in other papers. 47.45% of the sample was published in a study examining socioeconomic disadvantage and

maternal brain response to infant stimuli (Kim, Capistrano, Congleton, 2016), 66.10% was published in a further study of socioeconomic disadvantage (Kim et al., 2017), 77.9% was published in a study of maternal functional connectivity (Dufford, Erhart, Kim, 2019), and 88.14% was published in a study of cumulative risk (Kim, Tribble, Olsavsky, Dufford, Erhart, Hansen, Grande, Gonzalez, 2020). The analysis involved in maternal cortisol levels presented in this paper is novel and has not been published before.

2. Procedure

Potential participants were contacted by a member of the research staff and their eligibility was assessed over the phone. For those participants who were eligible, a home visit was scheduled. At this home visit, an fMRI visit was scheduled.

2.1 Home Visit

Two trained researchers visited the home of each participant. Visits began at either 4:00pm (81.4% of visits), 4:15pm (1.7% of visits), or 4:30pm (13.6% of visits). Participants were consented prior to starting the visit. At this home visit, structured interviews were conducted with the mother and questionnaires were administered. At this visit cortisol samples were collected from the mother and infant (although only maternal cortisol was analyzed for this project), and a mother child interaction occurred. All visits had the same timeline; four cortisol samples were collected from mother immediately upon arrival and then 40 minutes, an hour and 25 minutes, and an hour and 50 minutes after arrival. At the visit, a mother child interaction began 55 minutes after arrival.

2.1.1 Mother Child Interaction

Mothers were instructed to interact naturally with their infant without the use of toys. These interactions were recorded for 15 minutes. Two trained coders watched these videos and coded them according to the Emotional Availability scales (Biringen, Robinson, Emde, 2000) for maternal sensitivity and maternal nonintrusiveness.

Maternal Sensitivity A global rating of the congruence and appropriateness of the mother's affect and behavior. This scale ranges from 1-7, with 7 being a highly sensitive parent, 1 being highly insensitive, and mid-range scores representing 'apparent' sensitivity (i.e. incongruent affect and behavior).

Maternal Nonintrusiveness A global rating of the degree to which the mother follows the child's lead and waits for non-interruptive ports of entry into the interaction. This scale ranges from 1-7, with 7 being optimally nonintrusive but still emotionally present and available, 1 being intrusive, and mid-range scores representing 'benign' intrusiveness where the parent is too frequently leading but the child is still responding appropriately.

Crying During Interaction During the maternal video coding procedure, trained coders also attended to whether infants cried or not during the interaction. Crying was defined as any extended distress vocalization that persisted for more than several seconds. Total length of time spent crying during the interaction was recorded for each video and "crying during interaction" was recorded as yes if the infant cried for more than 1 minute during the 15-minute interaction.

2.1.2 Saliva Sampling

Participants withheld consuming all food and liquids ≥30 minutes before sampling. Participants provided saliva samples via passive drool procedure at 4 time points during the visit. Samples were collected at time 0:00 (sample 1), 0:40 (sample 2), 1:25 (sample 3), and 1:50 (sample 4) of each visit, with each visit occurring at either 4:00pm, 4:15pm, or 4:30pm. Samples were capped and refrigerated on-site with a portable cooler, then transported to the laboratory, centrifuged and frozen at −20° Celsius. Cortisol samples were shipped to Trier, Germany and analyzed using a time resolved fluorescence immunoassay (Dressendörfer, Kirschbaum, Rohde, Stahl, Strasburger, 1992). The test sensitivity was 6.27× 10−3 µg/dl with an intra-assay coefficient of variation for duplicates of the same sample of 3.26% and inter-assay coefficients of variation for known cortisol concentrations of 6.21% for low, 6.56% for medium and 7.56% for high concentrations.

Data Quality Check and Data Cleaning Cortisol values were checked for high values in each sample but also for trends across participants, so participants that had consistently higher cortisol sample values would not be identified as spurious outliers, but a single high value would be more likely to be identified as an outlier. A priori, it was decided that biologically implausible outliers would be removed and biologically plausible outliers would be winsorized. Cortisol values that were more than 3 standard deviations above the mean for a given sample were winsorized to be 3SD above the mean (Allwood, Handwerger, Kivlighan, Granger, Stroud, 2011; Wilcox, 1994). 4 samples were winsorized in this way.

Average Cortisol Concentration During Parenting To calculate the average cortisol concentration during the parenting interaction, the cortisol concentration for samples 2, 3 and 4 were averaged. These samples were all highly correlated (see Results) and represent the cortisol concentration immediately before and after the mother-child interaction. Sample 1 was not included because it does not capture cortisol during the parenting task and may instead capture the anticipatory stressor of having researchers in the home (Gunnar, Talge, Herrera, 2009; Hardie, Moss, Vanyukov, Yao, Kirillovac, 2002).

2.1.3 12-Month INR

An interview was conducted with each participant to collect a month-by-month index of the family's income for the past 12 months. An INR was constructed for each month by dividing total family income by the poverty threshold defined by the US Census Bureau at each month, and these were averaged for the last 12 months to construct a 12-month INR.

2.1.4 Cortisol and Parenting Behavior

To assess the degree to which maternal cortisol concentration was associated with parenting behavior, partial correlations were used. A priori control variables for these correlations were maternal age and visit start time. Maternal age was included as a control variable because cortisol function has been demonstrated to differ by age (Carpenter, Tyrka, Ross, Khoury, Anderson, Price, 2009). Visit start time was included as a control variable to control for diurnal cortisol patterns (Edwards, Clow, Evans,

Hucklebridge, 2001; Adam, Quinn, Tavernier, McQuillan, Dahlke, Gilbert, 2017). 12-month INR was included as a control variable because of its association with average cortisol concentration. Mothers breastfeeding status was included as a control variable because of its association with average cortisol concentration and theoretical association with parenting behaviors (Dunn & Richards, 1977; Kuzela, Stifter, & Worobey, 1990; Lavelli & Poli, 1998).

Child Age Posthoc

Given that the relation between maternal cortisol and maternal behavior appear to change in the first three months postpartum (Almanza-Sepulveda et al., 2020; Fleming et al., 1987; Krpan et al., 2005) and our sample includes a wide range of child age (1-7 months) we tested the degree to which child age moderates any maternal cortisol and parenting behavior findings in our sample.

Maternal IQ, Maternal Education, and Gestational Weeks Posthocs In order to ensure our findings are generalizable to mothers in general and not driven by outliers in our sample, analysis will be repeated without these outliers.

2.2 fMRI Visit

Participants traveled to the Center for Innovation and Creativity scanning center at UC Boulder for the fMRI Visit. Participants were trained on the tasks they would be completing and changed into MRI safe clothing. In the scanner, participants completed an infant cry task, an infant picture task, an adult faces task, a T1W structural scan, an emotion regulation task, and a resting state scan. For this analysis, only cry task and

structural scan were used. For all participants, cry task was completed before the structural scan.

2.2.1 Cry Task

The infant cry task has been used in a number of previous studies of postpartum women, with brain activation during this task associated with a range of maternal factors including behavioral and mood outcomes (Guo, Moses-Kolko, Phillips, Swain, Hipwell, 2018; Ho & Swain, 2017; Kim et al., 2016, 2011, 2010, 2020; Laurent et al., 2011; Musser et al., 2012). Participant's own baby cry was collected during the home visit. The cry was a natural cry occurring during a diaper change, when a baby was seeking mother's attention, or when feeding time was approaching. The control cry was collected using a similar home visit protocol, but from an infant not enrolled in the current study. Non-cry noise and background sounds for both cries were removed from the recordings using sound editing software (Cool Edit Pro Version 2.0, Syntrillium Software, Phoenix, AZ.). Control cry and own baby cry matched to have equal volumes. These cries were also used to make white noise by generating a spectral average of the cry and matching this white noise to the temporal envelope of the own infant and control infant cry sounds.

The infant cry task involved 2 runs of approximately 10 minutes each. A crosshair was shown on the screen and mothers were instructed to listen to the sounds presented and keep their eyes open. The task consisted of mothers passively listening to 4 types of stimuli, own cry, other cry, own noise, and other noise. Sounds were presented in random order. Each stimulus was presented for 20 seconds each and each block was repeated five

times per run. In between each block there was a rest period that varied from 8-12 seconds with an average 10 seconds of rest following each block.

2.2.2 fMRI Acquisition

High-resolution T1-weighted magnetization prepared rapid gradient-echo (MPRAGE) images were acquired. Midway through the study the scanner was upgraded—women were first scanned using a 3T Siemens Magnetom Tim Trio scanner and later participants were scanned on a 3T Siemens Prismafit scanner. Anatomical data was acquired using the 3D magnetization-prepared rapid gradient-echo (MPRAGE) protocol were also acquired. For the Trio scanner, the parameters were 192 sagittal slices, TR = 2530 ms, TE = 1.64 ms, flip angle = 7°, FOV = 256 mm2 and voxels = 1 mm3. For the Prisma scanner, the parameters were 224 sagittal slices, TR = 2400 ms, TE = 2.07 ms, flip angle = 8°, FOV = 256 mm2 and voxels = 0.8 mm3. Functional data was acquired using a 32-channel phased array coil collecting sagittal planes with the following parameters: 192 sagittal slices, TR=2530 ms, TE=1.64 ms, flip angle=7°, FOV =256 mm2 and voxel size 1×1×1 mm. 61.01% of analyzed participants (N = 36) were scanned on the old Tim Trio and the remainder (N = 23) were scanned on the Prismafit. There was no significant difference between participants on any demographic or study variable (all p's > .125) based on which scanner they were scanned with.

2.2.3 fMRI Preprocessing

Participant's images were processed according to a standard preprocessing pipeline. Images were analyzed using Analysis of Functional Neuroimages (AFNI 18.3.12, Cox,

1996) using these steps: remove 4 pre-steady-state volumes, slice-timing correction, registration to Talairach template, non-linear warping and smoothing with a FWHM kernel of 6mm). Volumes with greater than 0.5mm displacement or >10% voxel outliers were censored. Subjects with more than 20% of TRs removed would not be used in analysis, however no subjects were removed due to this metric. Anatomical images were skull-stripped using FreeSurfer (Segonne, Dale, Busa, Glessner, Salat, Hahn, Fischl, 2004), followed by non-linear co-registration to AFNI TT_N27 template. Single-subject GLMs were constructed by modeling the hemodynamic response function as a block function with length equivalent to stimuli presentation length (20 seconds) and an amplitude of 1.0. Each condition (own cry, other cry, own noise, other noise) was modeled as its own regression as well as a cubic polynomial regressor for drift and 6 framewise motion regressors.

3. Analysis Plan

To investigate the degree to which demographic and study variables were associated with whether mothers were reported breastfeeding their infant and whether the infant was crying during the mother-child interaction, simple correlations were used.

3.1 Group Level Analysis

Whole brain analysis was performed using AFNI 3dLME command. Fixed effects were cry (vs noise), identity (own vs other), and average cortisol concentration for each subject. Mother's age, child's age, home visit start time, and scanner type were added as covariates in this model. Child's age was included to control for parental experience

differences—mothers of older babies have spent more time with their infant and may have a different response to infant cues (Mascaro, Hackett, Gouzoules, Lori, Rilling, 2014). Home visit start time was included in the model to control for any diurnal differences in maternal cortisol concentration due to timing differences (Adam & Gunnar, 2001; Tu, Lupien, Walker, 2006). 12-month INR was included in the model because of its association with average cortisol concentration. Mothers breastfeeding status was included because of its association with average cortisol concentration and theoretical links with differences in brain response to infant cry (Kim, Feldman, Mayes, Eicher, Thompson, Leckman, Swain, 2011).

Activation was masked to only areas where all participants anatomical and EPI images overlapped by 80% or more. Activation maps were thresholded at $p < .001$ and were cluster corrected with NN=1 and a cluster extent threshold k=28, equivalent to a FWCE of $p < .05$. To decompose interactions and to examine post-hoc associations with parenting measures, the activation in these regions was extracted using AFNI's 3dROIStats command and each subject's activation was brought into another statistics package (SPSS 25; IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) for further analysis.

3.2 Amygdala ROI

The amygdala ROI was defined anatomically using the Desai DKD Atlas (Desikan, Segonne, Fischl, Quinn, Dickerson, Blacker, Killiany, 2006; Destrieux, Fischl, Dale, Halgren, 2010). Activation in this ROI was extracted using AFNI's 3dROIStats and analyzed in SPSS 25. To test the degree to which it is associated with average cortisol

concentration, a 2x2x2 ANCOVA (side [left vs. right]*sound [cry vs. noise]*actor[own vs. other]) with average cortisol concentration as a between subjects variable of interest, controlling for visit start time, postpartum months, scanner type, 12 month INR, mothers breastfeeding status, and child age will be constructed.

3.3 Decomposition Analysis

In order to determine the degree to which activation in regions significantly associated with cortisol concentration is related to parenting behavior, beta weights from those clusters will be extracted and analyzed in IBM SPSS Version 20 (IBM Corp, 2011). First, interaction effects will be decomposed using these extracted clusters to determine how these regions are related to cortisol concentration (i.e. under which condition is this region *more* or *less* activated as a consequence of cortisol concentration). Simple correlations will determine the degree to which activation in these clusters is associated with parenting behaviors associated with maternal cortisol concentration behaviorally.

3.4 Psychophysiological interaction (PPI) analyses

Generalized PPI analyses (McLaren, Ries, Xu, Johnson, 2012) were utilized to assess amygdala FC. Left and right amygdala seeds were defined anatomically using the Desai DKD Atlas (Desikan et al, 2006; Destrieux et al, 2010). For each run, amygdala time series were extracted without censoring to prevent temporal discontinuity from interfering with the modeling of amygdala time series and task regression interactions. Amygdalar time series were deconvolved and interaction regressors were created including task parameters x seed time-series interaction. Single-subject models were

generated in AFNI and included six motion regressors, task condition parameters, and PPI regressors for condition x time-series interaction. Group models were constructed using AFNI's 3dLME with task conditions (sound x identity), average maternal cortisol concentration, and mother's age, child's age, home visit start time, and scanner type as covariates. FC analysis was masked to only areas where all participants anatomical and EPI images overlapped by 80% or more. Activation maps were thresholded at $p < .001$ and were cluster corrected with NN=1 and a cluster extent threshold k=28, equivalent to a FWCE of $p < .05$.

3.4.1 Exploratory PPI Analysis

We also will conduct exploratory PPI analysis with brain regions identified in whole brain activation analysis that may benefit from increased understanding. These regions will be analyzed using the PPI pipeline described above using atlas-defined anatomical seeds for those regions. Anatomical seeds are chosen rather than the functionally-masked ROIs to ensure anatomical uniformity across participants and increase generalizability (Etzel, Gazzola, Keysers, 2009). In our study, we examined the FC of the right SMA to better understand it's functional activation patterns. Right SMA seed was defined anatomically using the Desai DKD Atlas (Desikan et al, 2006; Destrieux et al, 2010). SMA time series were extracted without censoring to prevent temporal discontinuity from interfering with the modeling of SMA time series and task regression interactions. SMA time series were deconvolved and interaction regressors were created including task parameters x seed time-series interaction. Single-subject models were generated in AFNI and included six motion regressors, task condition

parameters, and PPI regressors for condition x time-series interaction. Group models were constructed using AFNI's 3dLME with task conditions (sound x identity), average maternal cortisol concentration, and mother's age, child's age, home visit start time, 12-month INR, mothers breastfeeding status, and scanner type as covariates. FC analysis was masked to only areas where all participants anatomical and EPI images overlapped by 80% or more. Activation maps were thresholded at $p < .001$ and were cluster corrected with NN=1 and a cluster extent threshold k=28, equivalent to a FWCE of $p < .05$.

CHAPTER THREE: RESULTS

1. *Demographic Characteristics*

Mothers (N = 59, mean age = 25) and their infants (% female = 57.6, mean age = 3.5 months) were relatively socioeconomically and racially diverse, demonstrating a representative community sample of mothers in the postpartum period (see Table 1). Most mothers did not show signs of current depression or anxiety based on questionnaire measures, and most were not using antidepressants. 42.37% of the sample was classified based on their INR as living in poverty. The majority of mothers were breastfeeding.

Table 1. *Demographic Table*

	Minimum	Maximum	Mean	SD
Child Age (in months)	.46	7	3.50	1.71
Mother's Age	18	36	25.22	5.50
Average Cortisol Concentration	0.46	5.00	2.019	1.019
12 Month INR	.43	6.24	2.55	1.53
Mother's IQ	73	125	98.16	12.02
Pregnancy Term	35	42	39.35	1.52
Highest Year School Completed	9	20	14.02	2.43
Maternal Sensitivity	3	7	5.31	1.24
Maternal Nonintrusiveness	2	7	5.55	1.32
BDI	0	22	7.32	4.95
STAI (Trait)	20	60	36.17	10.11
	%			
Breastfeeding	64.4			
Child Sex (% Female)	57.6			
Mental Health History (% Yes)	40.7			
Antidepressant Usage (% No)	91.5%			
Mother Ethnicity (N)	White = 30	Black = 4	Hispanic = 11	Other = 14

Note. INR = Income to Needs Ratio, BDI = Beck's Depression Inventory, STAI = State Trait Anxiety Inventory

1.2 *Cortisol Sample*

Cortisol samples ranged from 0.800 to 6.939 nmol/L for Sample 2, from 0.140 to 5.911 nmol/L for Sample 3, and from 0.220 to 4.577 nmol/L for Sample 4. Mean cortisol concentration was 2.431 nmol/L for Sample 2, 2.008 nmol/L for Sample 3, and 1.616 nmol/L for Sample 4. Four total outliers were identified, one in Sample 2 values, two in Sample 3 values, and one in Sample 4 values. All outliers were from different participants and these outlier values were all less than 4 standard deviations from the mean of their sample. Cortisol samples 2-4 were all highly correlated with each other, Sample 2 and Sample 3 $r(59) = .536$, $p < .001$, Sample 2 and Sample 4 $r(59) = .604$, $p < .001$, Sample 3 and Sample 4 $r(59) = .776$, $p < .001$. The mean Average Cortisol Concentration (the average of samples 2-4) was 2.019 nmol/L with a range from 0.46 to 5.00 nmol/L.

1.3 *Potential Control Variables*

Examining correlations between demographic and parenting variables, there was no association between child's age, mother's age, 12-month INR, and parenting variables (all p's greater than .236) (see Table 2).

Maternal sensitivity and maternal nonintrusiveness were associated with maternal IQ, $r(58) = .38$ and $r(58) = .28$, p's $< .05$. Maternal sensitivity was also associated with maternal years of schooling, $r(58) = .31$, $p < .05$.

Average maternal cortisol concentration was associated with 12 month INR, $r(59) = -.263$, $p < .05$. Levene's test indicated that the variances for average cortisol were not

equal based on mothers' breastfeeding status, $F(1,58) = 4.845$, $p < .05$. Average maternal cortisol concentration was significantly higher for mothers who were breastfeeding, $t(56.437) = 2.044$, $p < .05$ (M Cortisol of Breastfeeding = 2.1910, M Cortisol of Not Breastfeeding = 1.7062). No other demographic variables were associated with average cortisol concentration (all p's greater than .166).

Maternal sensitivity and maternal nonintrusiveness was not associated with breastfeeding status, whether the infant was crying during the interaction, child sex, mother's mental health history and antidepressant useage, and mother's ethnicity, all p's greater than .25.

2. *Maternal Cortisol and Parenting Behavior*

Average maternal cortisol concentration was associated with maternal nonintrusiveness controlling for maternal age, breastfeeding status, 12-month INR, and visit start time, $r(52) = -.306$, $p = .023$. No association was found between maternal cortisol concentration and maternal sensitivity, $p = .322$.

Table 2. *Correlations of Characteristics*

	1	2	3	4	5	6	7	8	9	10
1. Child Age	--									
2. Mother Age	.20	--								
3. Mother IQ	.00	.40**	--							
4. Pregnancy Term	-.02	.31*	.25	--						
5. 12 Month INR	-.13	.50**	.38**	.22	--					
6. Years Schooling	.15	.74**	.48**	.30*	.54**	--				
7. Average Cortisol Concentration	.11	-.16	-.14	-.18	-.26*	-.09	--			
8. Maternal Sensitivity	-.08	.16	.38**	.17	.09	.31*	-.13	--		
9. Nonintrusiveness	-.14	.06	.28*	.12	-.05	.18	-.27*	.59**	--	
10. BDI	.01	.01	.25	.01	-.02	.05	-.16	.06	.14	--
11. STAI Trait	.01	.01	.01	-.11	-.16	-.07	-.12	-.01	.10	.66**

* = Correlation is significant at the 0.05 level (2 tailed)
** = Correlation is significant at the 0.01 level (2 tailed)
Note. INR = Income-to-Needs Ratio, BDI = Beck's Depression Inventory, STAI = State Trait Anxiety Inventory.

2.1 *Child Age Posthoc*

In order to assess the degree to which the relation between average maternal cortisol concentration and maternal nonintrusiveness was related to child's age, a regression model predicting maternal nonintrusiveness based on average cortisol concentration, child's age, and a cortisol concentration x child's age interaction was constructed. Both linear and quadratic child age predictors were included separately to test the possibility of a nonlinear child age effect. The quadratic child age model was a better fit for the data but both models had R-squared values less than 0.1. In these models, neither child's age nor the interaction effect were significant, p's > .192.

2.2 Maternal IQ Posthoc

When removing one participant with a maternal IQ value that was a low outlier (a mother with an IQ of 73) and another participant with missing IQ data, there was still a trend level association between average maternal cortisol concentration and maternal nonintrusiveness controlling for visit start time, maternal age, 12-month INR, and breastfeeding status, $r(51) = -.305$, $p < .05$.

2.3 Gestational Weeks Posthoc

When removing one participant with a gestational week value that was a low outlier (a mother with a gestational weeks value of 36), there was still an association? between average maternal cortisol concentration and maternal nonintrusiveness controlling for visit start time, maternal age, 12-month INR, and breastfeeding status, $r(51) = -.306$, $p < .05$.

2.4 Maternal Education Posthoc

Including the number of years of schooling completed by mothers as an additional covariate did not change the directionality or significance of the finding, $r(52) = -.333$, $p < .05$.

3. *fMRI Analysis*

A significant three-way Average Cortisol Concentration*Identity*Sound interaction ($F(1,57) = 22.288$, $p < .001$) was found with a center of mass in the right Precuneus with activation extending into left precuneus (see Table 2). Post-hoc decomposition of this activation showed that average cortisol concentration was associated with reduced activation to own cry $F(1, 57) = 8.210$, $p < .05$, beta = -.355 and other noise $F(57) = 4.710$, $p < .05$, beta = -.276.

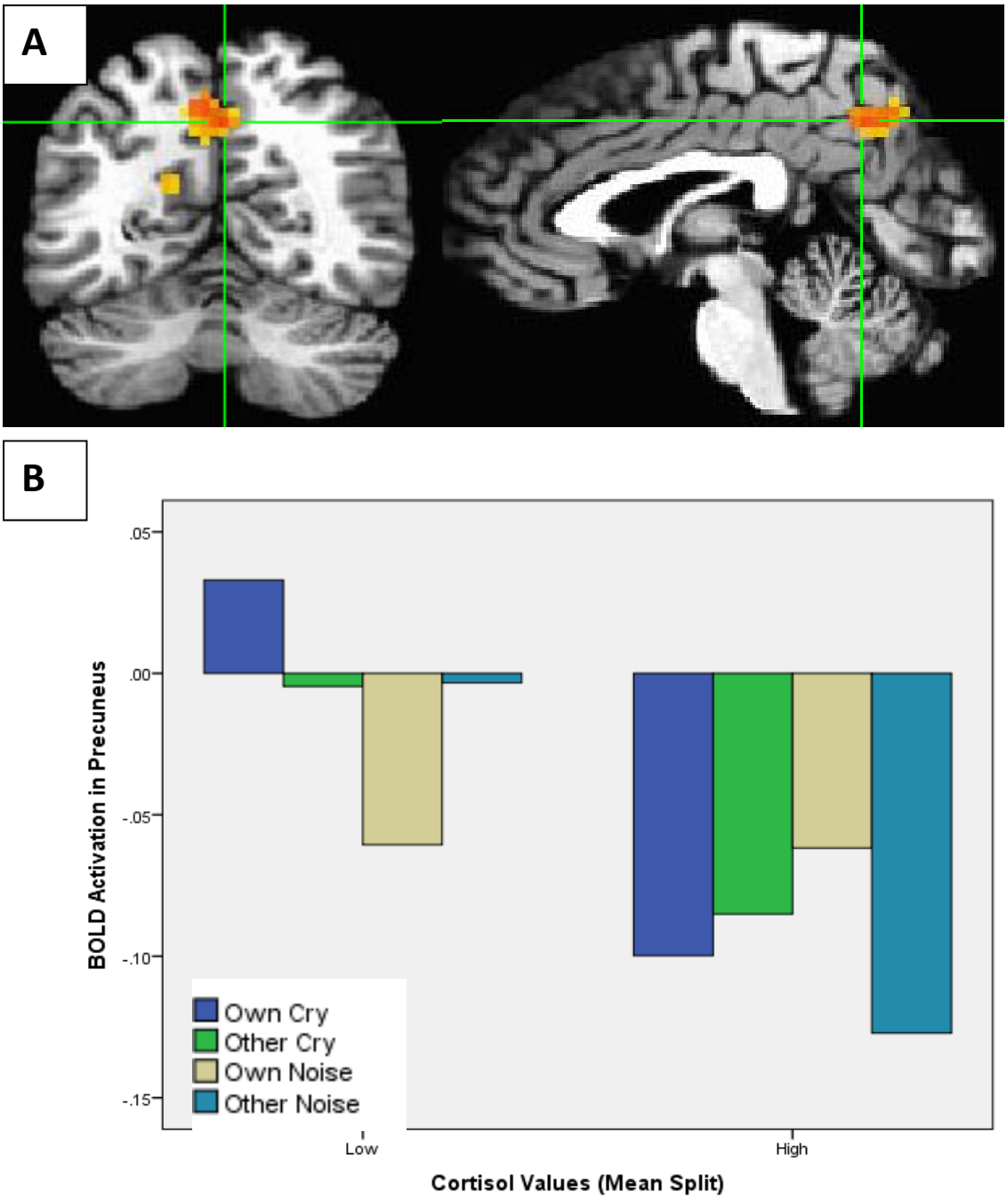
A significant Sound*Average Cortisol Concentration was observed in five clusters: the right precentral gyrus ($F(1,57) = 18.432$, $p < .001$), the left culmen ($F(1,57) = 22.524$, $p < .001$), two clusters in the superior temporal gyrus with one extending into medial temporal gyrus and ($F(1,57) = 13.905$, $p < .001$), and the other squarely in the superior temporal gyrus ($F(1,57) = 15.938$, $p < .001$), and medial frontal gyrus/BA8 ($F(1,57) = 18.814$, $p < .001$). (see Figures 2-5). Activation in these clusters to cry sounds was significantly associated with average cortisol concentration; precentral $r(59) = -.426$, $p = .001$, culmen $r(59) = -.409$, $p = .001$, MTG $r(59) = -.408$, $p = .001$, STG $r(59) = -.429$, $p = .001$, and MFG $r(59) = -.362$, $p = .005$. There was no association between average cortisol concentration and activation in any of these regions to noise.

Table 3. *Brain Areas Showing Significant Activation by Condition*

Region	**BA**	**Side**	**x**	**y**	**z**	**Cluster Size**	**F**
*Cortisol Concentration*Sound*Identity*							
Precuneus	7	R/L	-1.5	-58.5	38.5	134 vox	22.288
*Cortisol Concentration*Sound*							
Precentral gyrus	4	L	-43.5	-22.5	35.5	171 vox	18.432
Culmen extending into fusiform gyrus	n/a	R	37.5	49.5	-1.5	81 vox	22.524
MTG/STG	21/22	R	-64.5	19.5	-3.5	43 vox	13.905
STG	41/42	L	61.5	19.5	-0.5	38 vox	15.938
MFG	8	L	25.5	-34.5	41.5	28 vox	18.814
*Sound*Identity*							
IPL/LOC	39/19/40	R	43.5	-58.5	-3.5	124 vox	22.4
IPL	39/40	L	-43.5	-67.5	2.5	74 vox	18.59
SPL	5/7	R	31.5	-46.5	47.5	47 vox	20.34
Postcentral Gyrus	2/1/3/5		49.5	-31.5	44.5	40 vox	28.53
Hippocampus/Fusiform	37	L	-37.5	-22.5	-18.5	38 vox	17.67

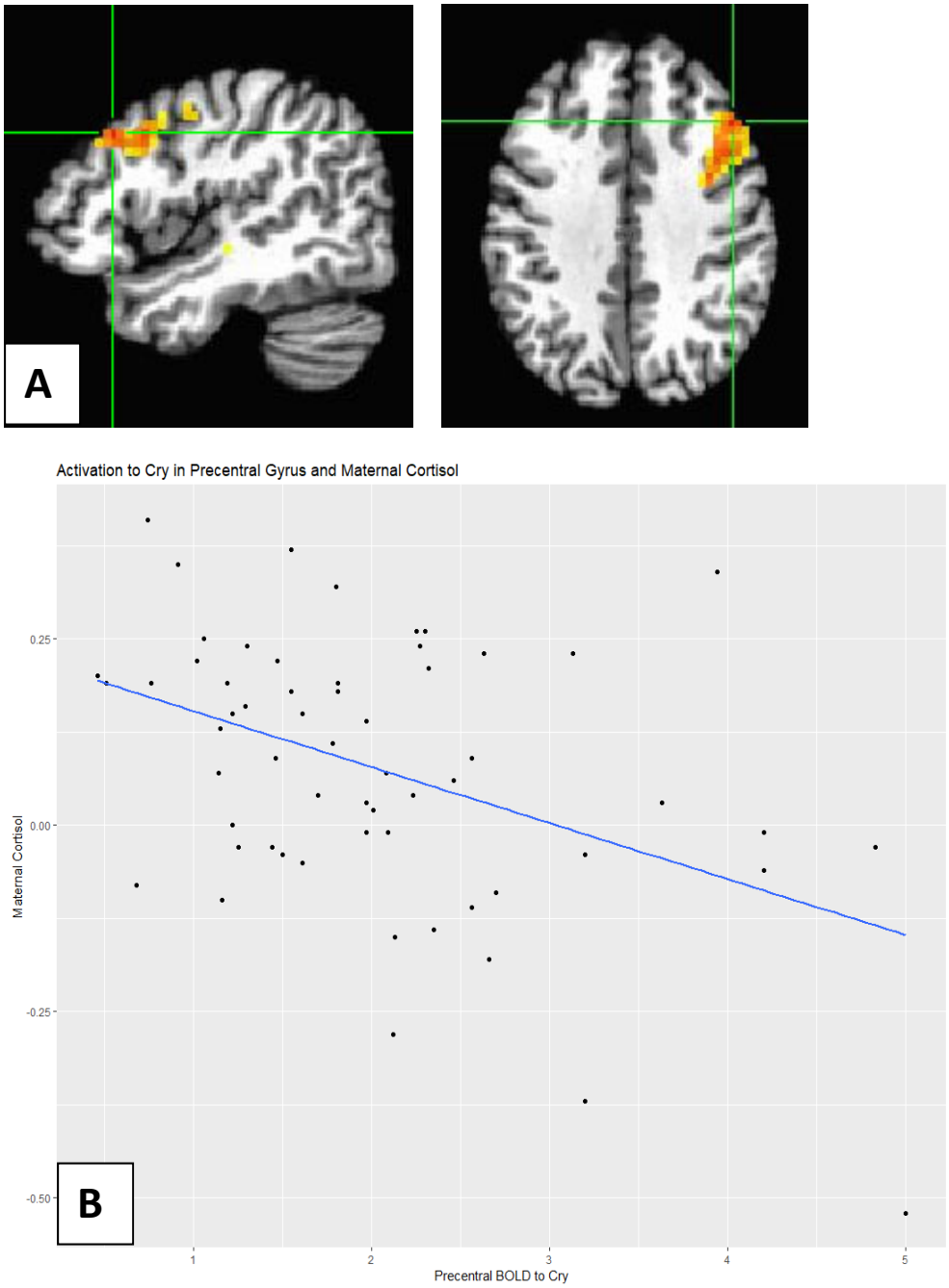
Note. MTG = Medial Temporal Gyrus, STG = Superior Temporal Gyrus, MFG = Medial Frontal Gyrus, IPL = Inferior Parietal Lobule, LOC = Lateral Occipital Cortex, SPL = Superior Parietal Lobule

Figure 1. *Precuneus Activation (Sound*Identity*Average Cortisol) Map and Decomposition of Interaction Effects. (A) Activation in the Precuneus at coordinates -2, 59, 43. (B) Differences in precuneus activation based on task parameters and maternal cortisol*



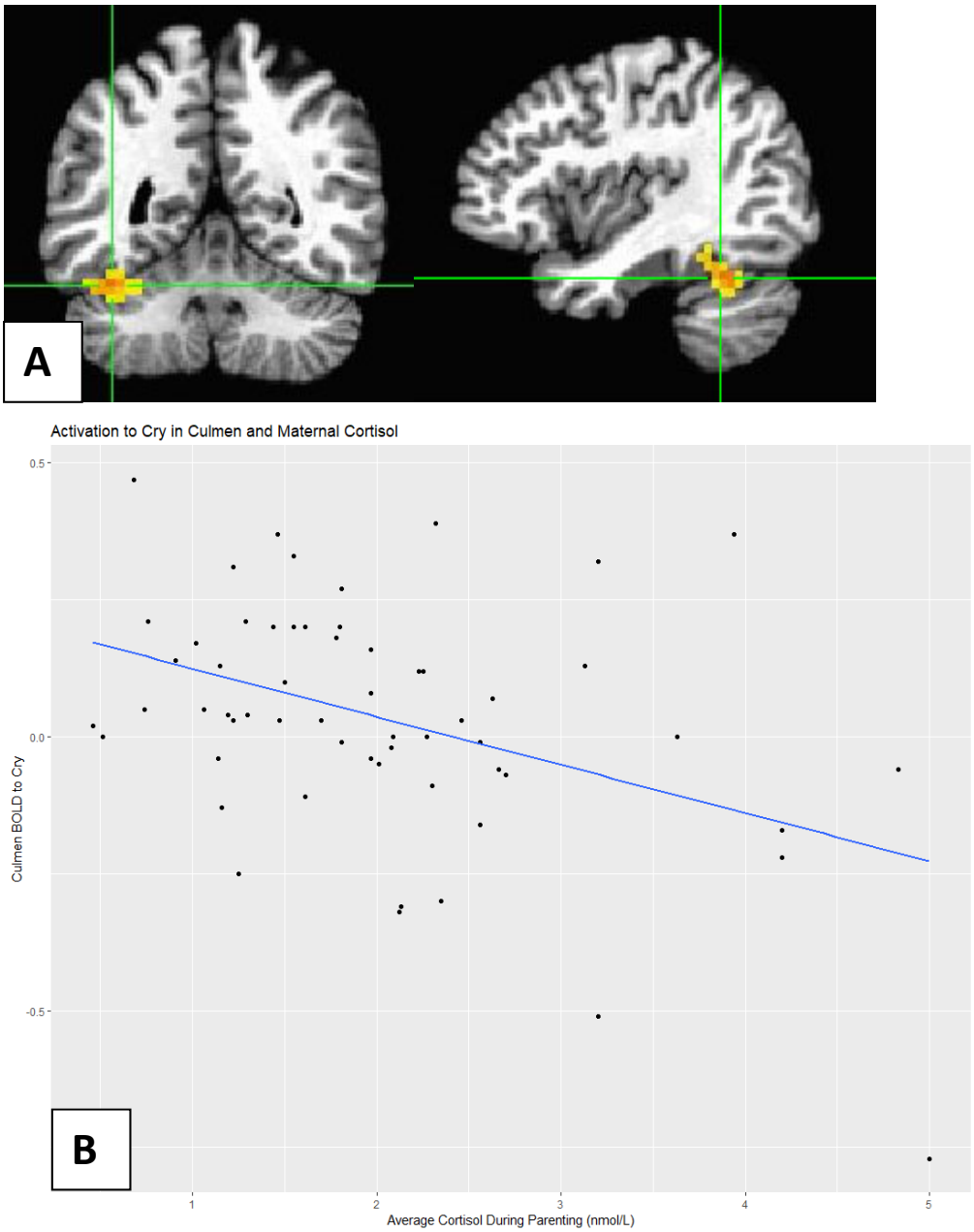
Note. BOLD = Blood Oxygen Level Dependent signal.

Figure 2. *Precentral Gyrus Activation Map (Sound*Cortisol) Map and Decomposition of Interaction Effect. (A) Activation in the Precentral gyrus at coordinates -47, -29, 34. (B) Linear relation between Maternal Cortisol and Precentral Brain Activation*



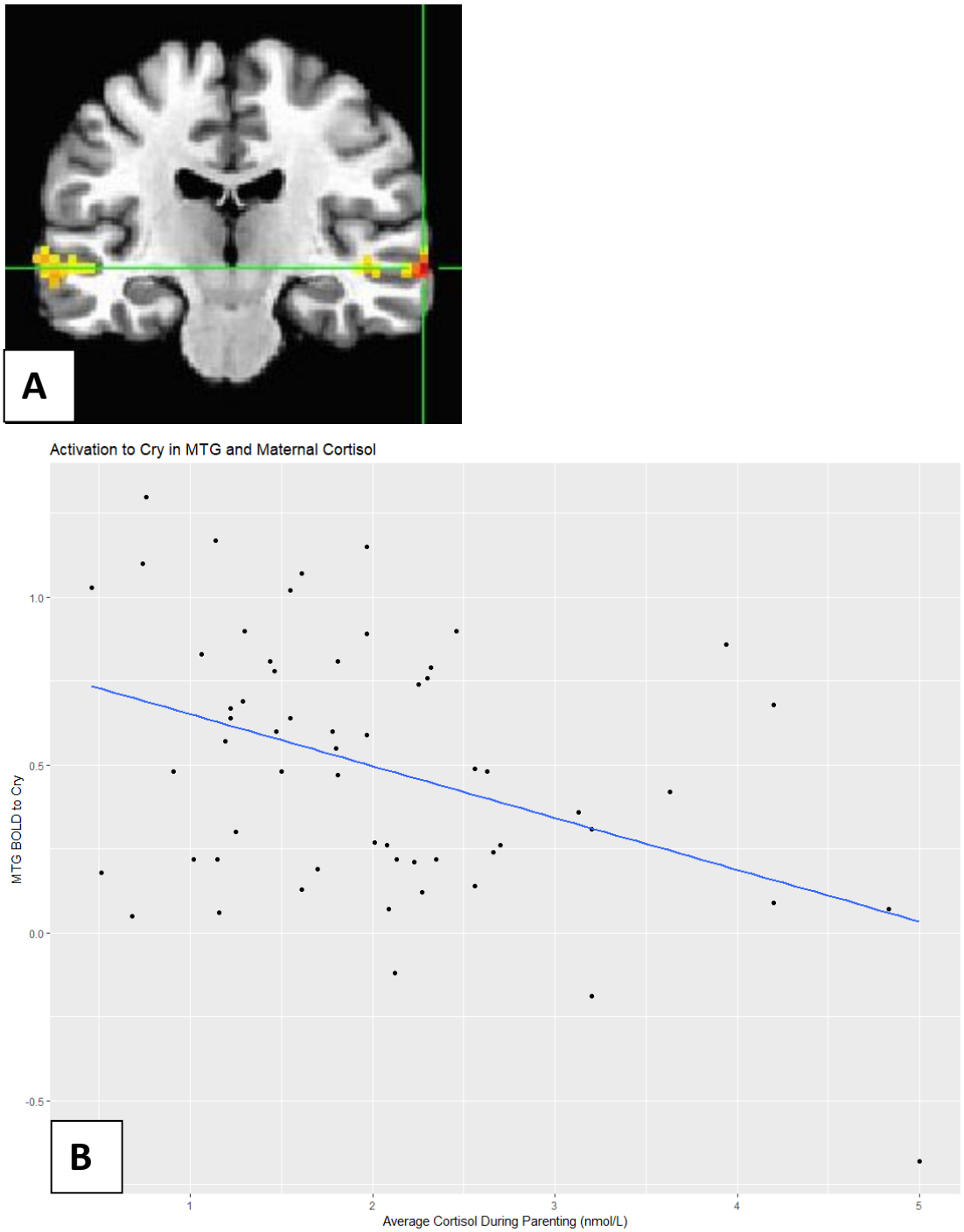
Note. BOLD = Blood Oxygen Level Dependent signal.

Figure 3. *Culmen Activation Map (Sound*Cortisol) and Decomposition of Interaction Effect. (A) Activation in the Culmen at coordinates 40, -54, -26 (B) Linear relation between Maternal Cortisol and Culmen Brain Activation*



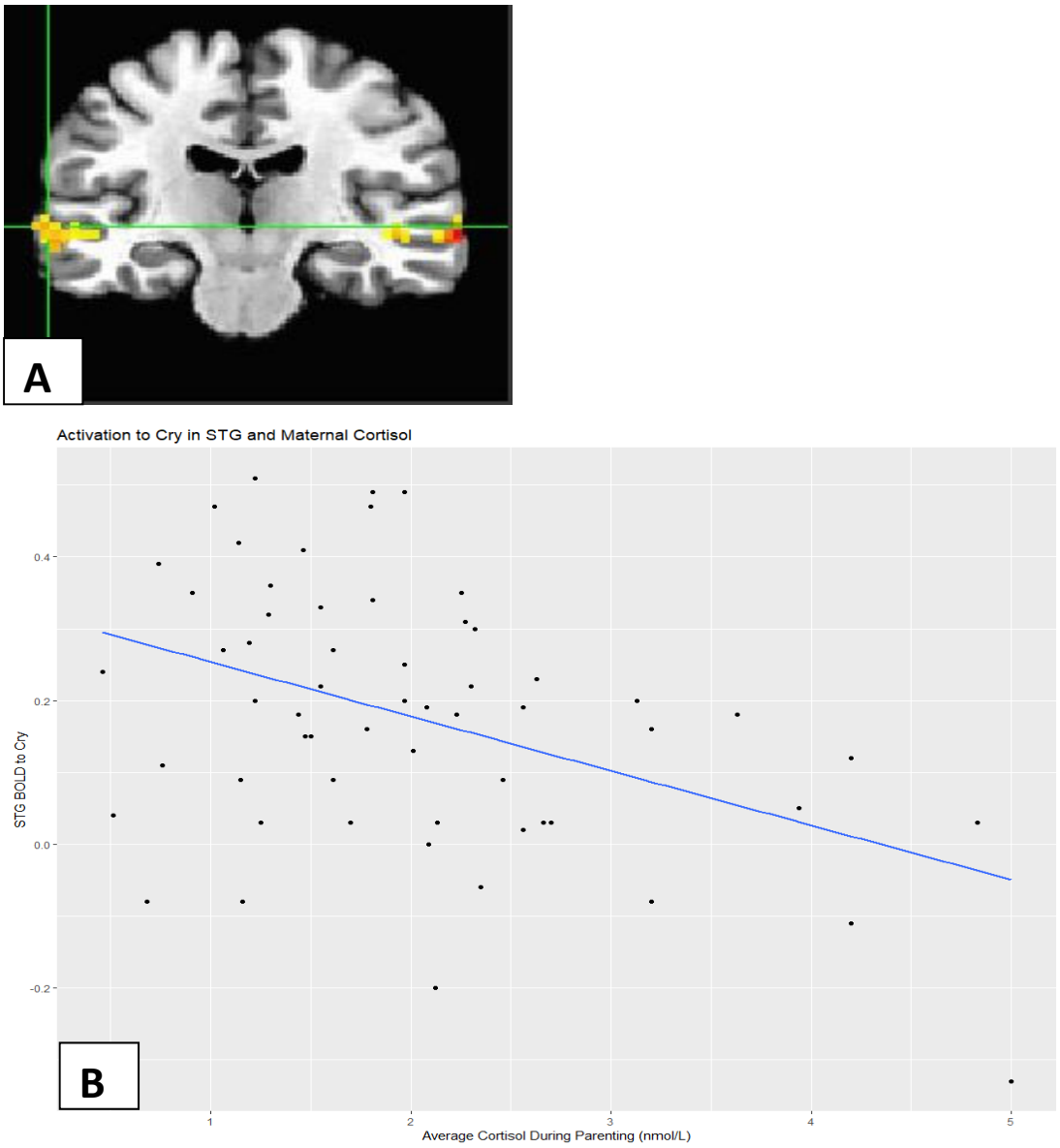
Note. BOLD = Blood Oxygen Level Dependent signal.

Figure 4. *MTG Activation Map (Sound*Cortisol) and Decomposition of Interaction Effect. (A) Activation in the MTG at coordinates -69, 20, -8 (B) Linear relation between Maternal Cortisol and MTG Brain Activation*



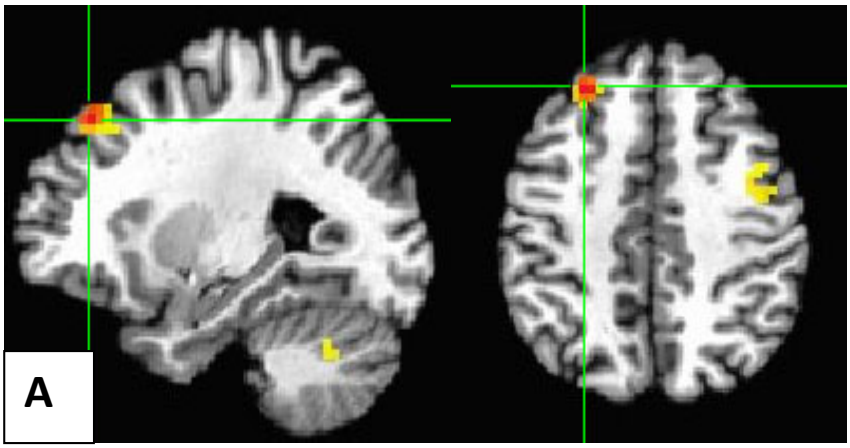
Note. MTG = Medial Temporal Gyrus, BOLD = Blood Oxygen Level Dependent signal.

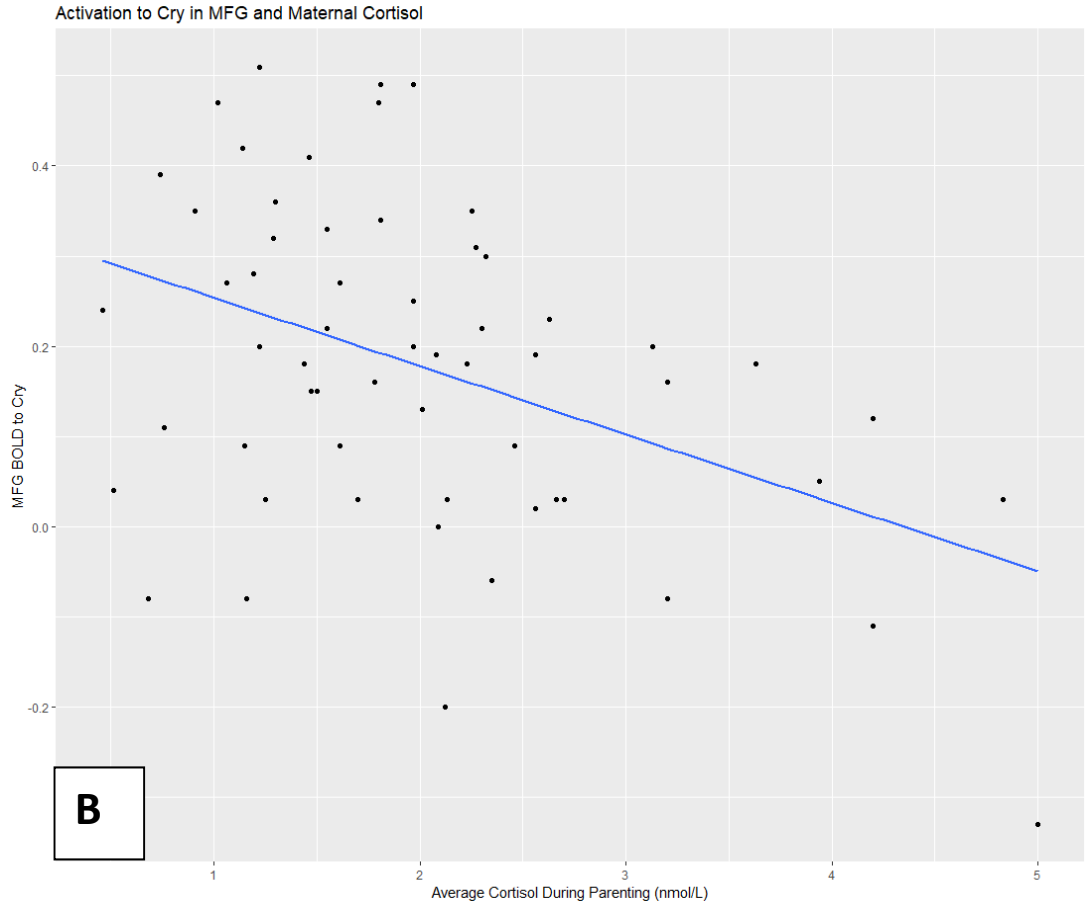
Figure 5. *STG Activation Map (Sound*Cortisol) and Decomposition of Interaction Effect. (A) Activation in the STG at coordinates 65, -20, -4 (B) Linear relation between Maternal Cortisol and STG Brain Activation*



Note. BOLD = Blood Oxygen Level Dependent signal, STG = Superior Temporal Gyrus.

Figure 6. *MFG Activation Map (Sound*Cortisol) and Decomposition of Interaction Effect. (A) Activation in the MFG at coordinates 27, -41, 40 (B) Linear relation between Maternal Cortisol and MFG Brain Activation*





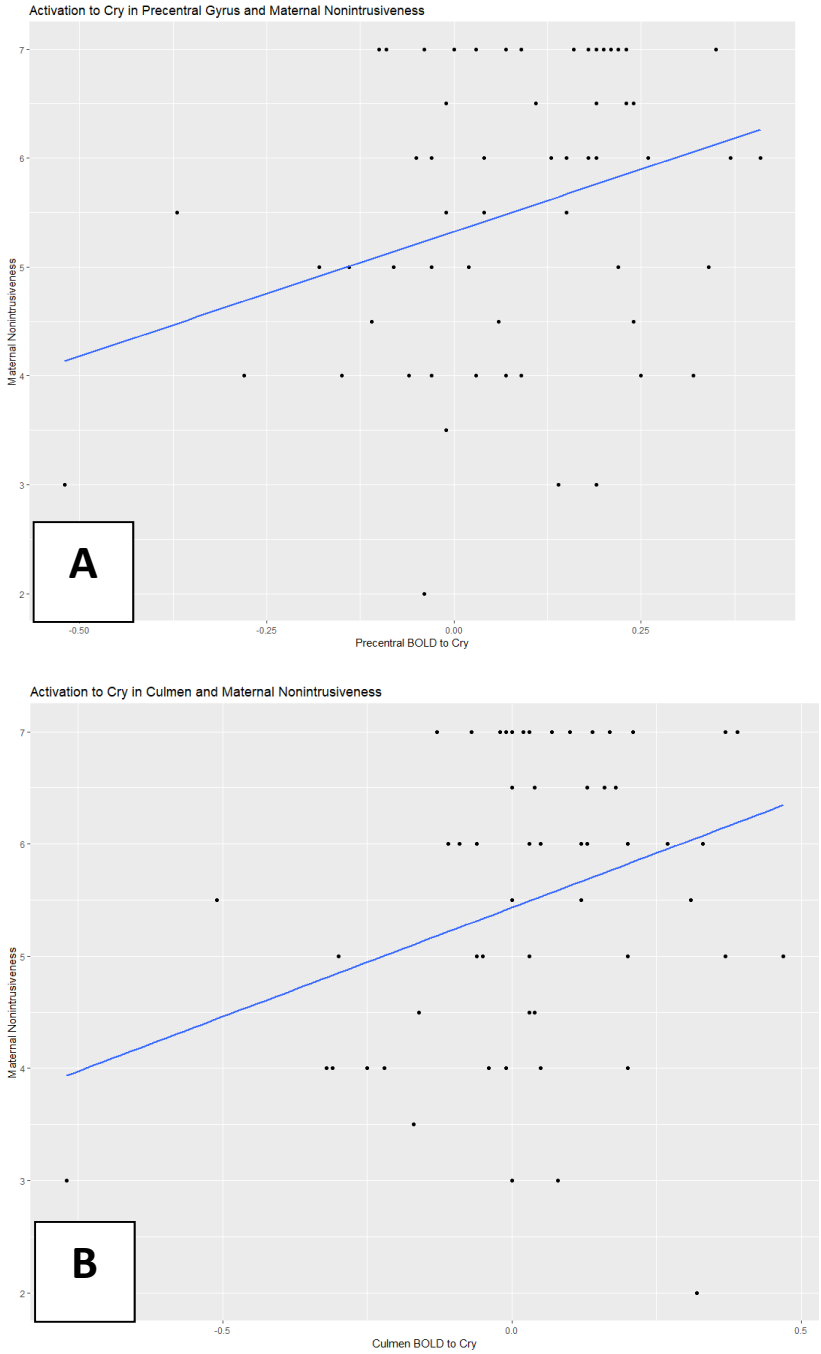
Note. BOLD = Blood Oxygen Level Dependent signal, MFG = Medial Frontal Gyrus.

3.1 *Analysis of Associations with Maternal Behaviors*

Activation in left precuneus for own cry r(59) = .375 p=.003, other cry r(59) = .314 p = .015, and other noise r(59) = .286, p = .028 were associated with nonintrusiveness (see Figure 2).

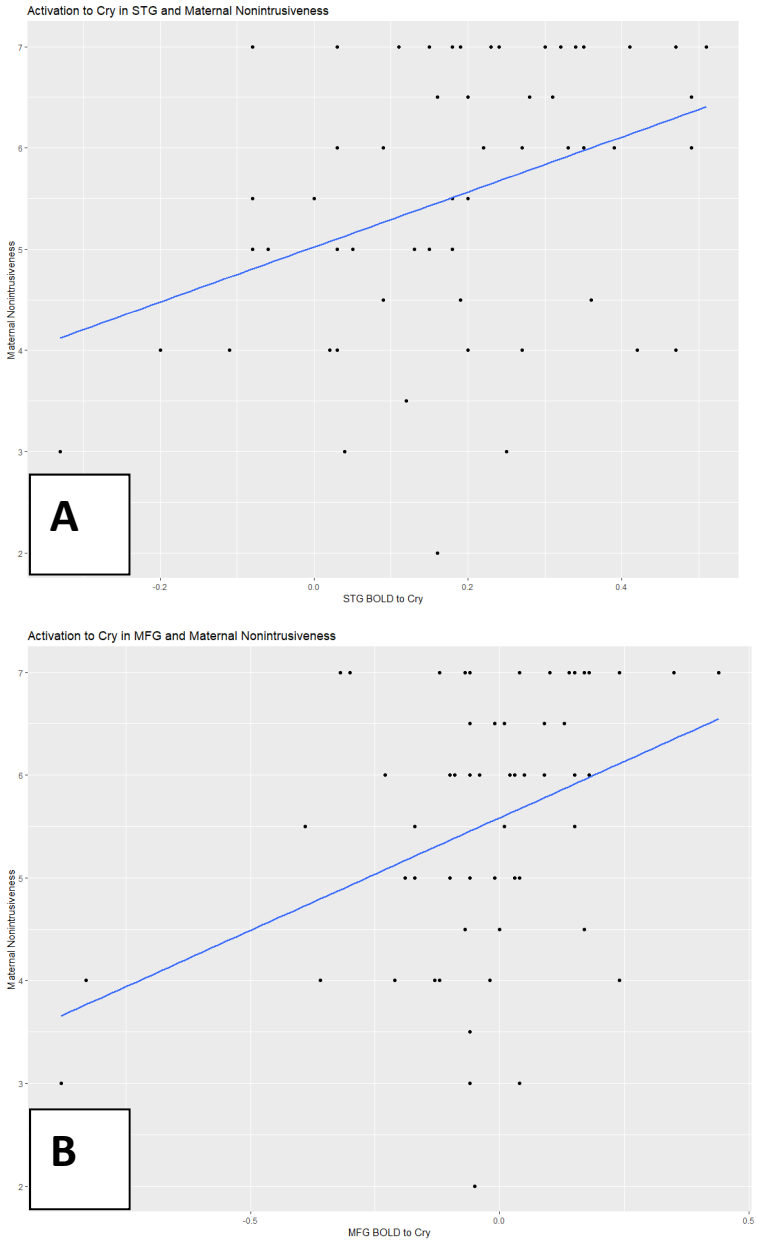
Activation in the precentral gyrus r(59) = .308 p = .018, culmen r(59) = .321 p = .013, STG r(59) = .367 p = .004, and MFG r(59) = .369, p = .004 to cry sounds were associated with nonintrusiveness (see Figures 7 and 8). Associations with sensitivity were not tested because there was no behavioral association between maternal cortisol and maternal sensitivity.

Figure 7. *Association between Maternal Brain Activation and Maternal Nonintrusiveness (A) Association Between Precentral Gyrus Activation to Cry Sounds and Maternal Nonintrusiveness (B) Association Between Culmen Activation to Cry Sounds and Maternal Nonintrusiveness*



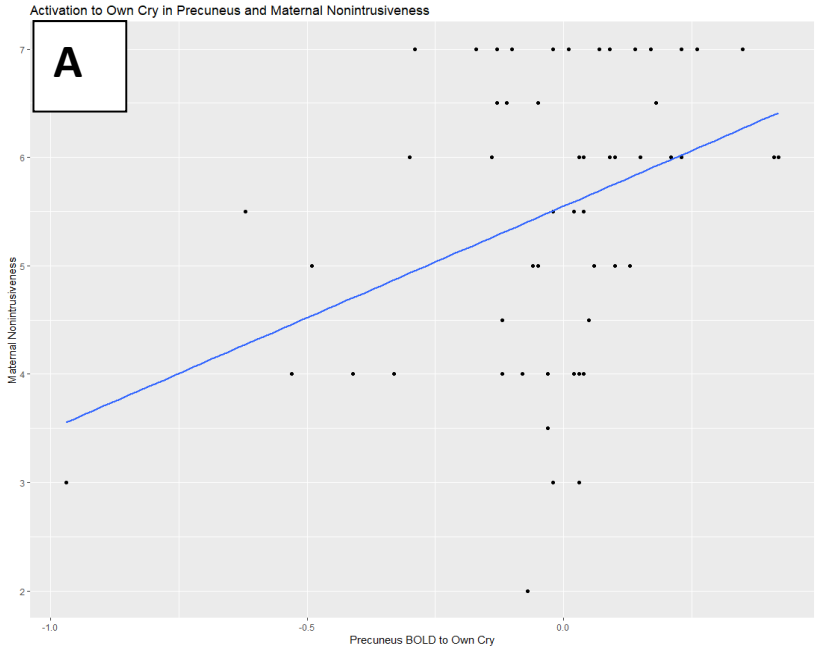
Note. BOLD = Blood Oxygen Level Dependent Signal

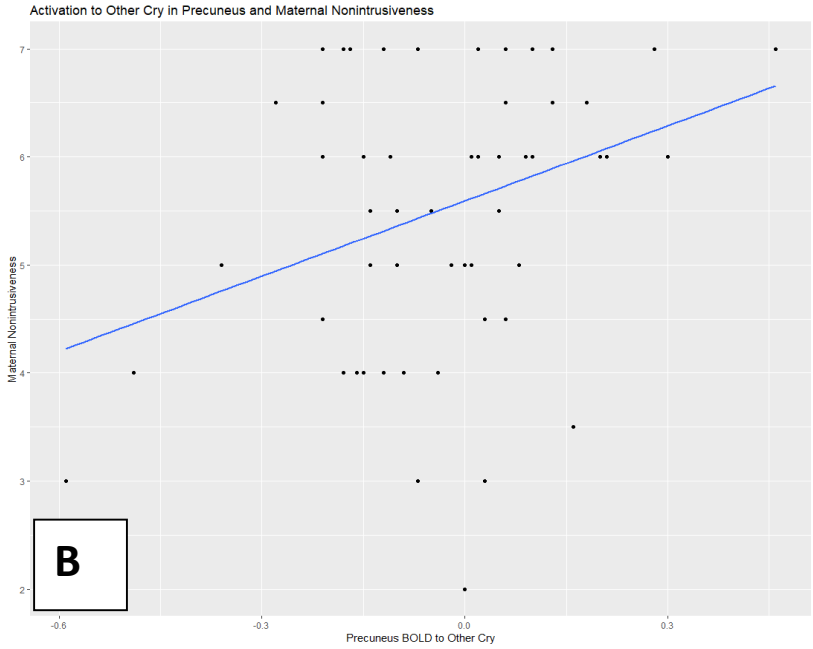
Figure 8. *Association between Maternal Brain Activation and Maternal Nonintrusiveness*
(A) Association Between STG Activation to Cry Sounds and Maternal Nonintrusiveness
(B) Association Between MFG Activation to Cry Sounds and Maternal Nonintrusiveness



Note. BOLD = Blood Oxygen Level Dependent Signal, STG = Superior Temporal Gyrus, MFG = Medial Frontal Gyrus

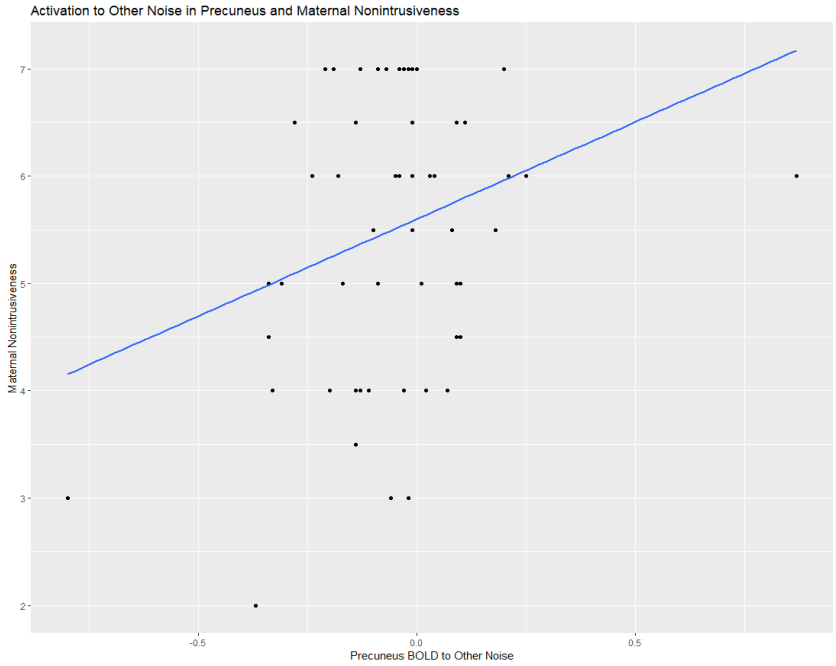
Figure 9. *Association between Maternal Brain Activation to Task in the Precuneus and Maternal Nonintrusiveness. (A) Activation to Own Cry in the Precuneus and Maternal Nonintrusiveness. (B) Activation to Other Cry in the Precuneus and Maternal Nonintrusiveness.*





Note. BOLD = Blood Oxygen Level Dependent Signal

Figure 10. *Association between Maternal Brain Activation to Other Noise in the Precuneus and Maternal Nonintrusiveness*



Note. BOLD = Blood Oxygen Level Dependent Signal

3.2 *Maternal IQ*

In investigating whether our results were driven by differences in maternal IQ, all previous analyses were run including maternal IQ as an additional covariate.

In the brain, all whole-brain analysis was tested again using models that included maternal IQ as an additional covariate and the same clusters were observed.

3.3 *Gestational Weeks*

In the brain, all whole-brain analysis was tested again using models that included gestational weeks as an additional covariate and the same clusters were observed.

3.6 *Amygdala ROI Analysis*

Amygdalar activation was not associated with average cortisol concentration, p's > .376. Activation in the amygdala to cry sounds was not associated with sensitivity nor nonintrusiveness, p's > .588. Activation in the amygdala to noise sounds was negatively associated with maternal sensitivity, $r(59) = -.260$ $p = .047$, but not nonintrusiveness, $p > .536$.

4. *PPI Analysis*

Using a left amygdala seed, two significant clusters were identified that showed FC with Sound*Own. The first was a region of the left posterior cingulate ($F(1,58) = 18.773$, $p < .001$). This region showed greater FC during own cry (95% CI: .069 - .165) and other noise (95% CI: .041-.114) conditions. The second was a region in the left superior parietal lobule ($F(1,58) = 17.153$, $p < .001$). This region showed greater FC during own cry (95% CI: 029 - .143) and other noise (95% CI: .007 - .142) conditions.

Using the right amygdala as a seed, there were no findings.

In order to better understand the function of the SMA activation identified in the whole brain analysis, a right SMA seed was utilized for PPI analysis. Group generalized PPI analysis of right SMA seed revealed an Cortisol Concentration*Identity interaction in the R Triangular Inferior Frontal Gyrus, $F(1,57) = 33.871$. Greater average cortisol concentration was associated with reduced FC to the IFG during own baby stimuli, both cries and noise, ($r(59) = -.377$, $p < .05$), but increased FC to the IFG during control stimuli, both cries and noise ($r(59) = .303$, $p < .05$).

The second region showing significant FC with the right SMA seed was a Cortisol Concentration*Sound interaction observed in the L Postcentral gyrus, $F(1,57) = 10.669$. Greater average cortisol concentration was associated with greater FC to the Pre/Postcentral gyrus during noise trials, $r(59) = .356$, $p < .05$.

Table 4. *Generalized PPI Analysis Results*

Region	**Side**	**x**	**y**	**z**	**Cluster Size**	**F**
L Amygdala seed						
*Sound*Own*						
Posterior Cingulate	L	4.5	-31.5	32.5	77 vox	18.773
Superior Parietal Lobule	L	7.5	-79.5	41.5	37 vox	17.153
R SMA seed						
*Cortisol*Identity*						
Inferior Frontal Gyrus	R	-59	-36	2	73 vox	33.871
*Cortisol*Sound*						
Precentral Gyrus	L	40	-23	54	48 vox	10.669

Note. PPI = Psychophysiological Interaction, SMA =Supplementary Motor Area

CHAPTER FOUR: DISCUSSION

This study investigated the relation between maternal cortisol, maternal brain, and maternal parenting behavior. We demonstrated an association between mother's average cortisol concentration and maternal nonintrusive behavior, but not maternal sensitivity, such that higher cortisol concentration was associated with more intrusive behavior. In the brain, we found that in the right precentral gyrus, the left culmen extending into the left inferior temporal gyrus and fusiform, two clusters in the superior temporal gyrus, and in the medial frontal gyrus, greater cortisol concentration was associated with decreased activation to infant cry. We also found that activation in these regions to cry sounds, was associated with maternal nonintrusiveness, such that greater activation in these regions was associated with less intrusive behavior. Additionally, a three-way interaction was observed in the precuneus, whereby greater average maternal cortisol concentration during parenting was associated with reduced activation to own cry and other noise. In this cluster, greater activation to own cry and other noise were associated with less intrusive maternal behaviors. Using psychophysiological interaction, greater average cortisol concentration was associated with differences in functional connectivity (FC) between the SMA and two regions. Greater maternal cortisol was associated with reduced SMA-rIFG FC during own baby stimuli and increased SMA-rIFG FC during control stimuli. Greater maternal cortisol was also associated with increased SMA-Precentral Gyrus FC during noise trials.

Behaviorally, it was identified that mothers who had greater cortisol concentrations during parenting showed more intrusive parenting behaviors. To our knowledge, the relation between maternal cortisol during a naturalistic interaction and parenting behavior has not been tested previously, however these results comport with previous literature. Studies of naturalistic parenting interactions show that cortisol tends to decrease (Handlin et al., 2009; Mörelius et al., 2007; Mörelius et al., 2005), suggesting that mothers who decrease less or increase their cortisol concentration during the interaction are exhibiting less adaptive HPA axis function. Literature examining HPA reactivity and parenting behavior later in the postpartum period indicates that greater reactivity to infant distress cues (considered to be adaptive and appropriate HPA axis function) is associated with more positive maternal behaviors (Stallings et al., 2001; Thompson & Trevathan, 2008). Likewise, greater basal cortisol is associated with more negative and intrusive parenting behaviors (Finegood et al., 2016; Gonzalez et al., 2012; Gordon et al., 2010; Mills-Koonce et al., 2009). Together, this can be taken as preliminary evidence that relatively lower average maternal cortisol concentrations during naturalistic parenting may be adaptive, and that deviations in maternal HPA axis during these interactions may be another marker for biological risk of maladaptive parenting.

This effect was found regardless of infant age. Our sample had a relatively wide age range (0-6 months), and there was evidence from studies of mothers immediately postpartum that cortisol was associated with beneficial maternal behaviors in a way that would be unexpected later in the postpartum period (Fleming, Steiner, Anderson, 1987;

Krpan, Coombs, Zinga, Steiner, Fleming, 2005). For this reason, we tested infant age effects both linearly and nonlinearly. There was no evidence in our sample that either our behavior or neuroimaging effects were different across infant age, as the relation between maternal cortisol and parenting behavior did not differ by infant age, nor did the regions identified in our neuroimaging analysis differ when infant age was included as a covariate.

We confirmed our hypothesis that the SMA and STG would show reduced activation to infant cry sounds with greater maternal cortisol concentration during parenting. Consistent with our hypothesis, reduced activation in these regions was associated with more intrusive parenting behavior. The SMA has been demonstrated to be highly activated to infant distress cues, including cross-culturally (Bornstein et al., 2017; Witteman et al., 2019). Maternal cortisol may be related to difference in SMA function due to the high density of projections to the adrenal medulla. In nonhuman primates, the SMA has been identified as the cortical region most densely projecting to the adrenal medulla (Picard & Strick, 2001). Researchers have highlighted control of the adrenal medulla via the SMA as being important for sympathetic nervous system function (Dum, Levinthal, Strick, 2016), suggesting that the SMA may serve to regulate HPA axis function. Regarding maternal behavior, literature has highlighted this region as important for auditory perception of the cry as well as motor planning of parenting behaviors (Lee & Quessy, 2003; Olsavsky et al., 2021). Accurate perception of infant cues and appropriate actions are important components of effective parenting behavior, so disruptions of regions that serve these functions are plausible influences of maladaptive

parenting behavior. Evidence linking SMA activation and parenting behavior is still limited; Bornstein et al., 2017 study examined both parenting behavior and parental brain response to infant distress cues and have suggested that activation of the SMA (among other regions) is involved in supporting culturally common parenting behaviors such as picking up and comforting a crying infant. This was not tested explicitly, however. The current study adds to the initial literature supporting a link between SMA activation to infant distress cues and parenting behavior by adding the additional mechanism of maternal HPA axis.

Similarly, in the STG we confirmed our hypothesis that greater maternal cortisol would be associated with reduced activation and that this reduction activation would be further associated with parenting behavior. Multiple studies have the highlighted the relation between STG activity in response to infant distress cues and sensitive parenting. One study comparing high sensitivity and low sensitivity mothers found that mothers with high maternal sensitivity showed greater STG activity (Elmadih et al., 2016), while another found that sensitive mothers (compared to intrusive ones) had greater amygdala-STG functional connectivity (Atzil et al., 2011). Our finding that greater STG activation is associated with less intrusive behaviors is consistent with this previous literature. One possible explanation is direct relationship between the HPA axis and STG. The STG has direct connections with the hypothalamus (a main component of the HPA axis), both structurally (Risold, Thompson, Swanson, 1997), and functionally (Kullman, Heni, Linder, Zipfel, Haring, Veit, Preissl, 2014), as well as structural connections with the subcortical HPA axis regulator the amygdala (Abivardi & Bach, 2017). This indicates

that there may be regulation of the HPA axis via STG function or vice-versa. A study using a stress induction paradigm found that following stress induction, participants showed reduced STG activation to pictures of all valences (van Leeuwen, Vink, Fernandez, Hermans, Joels, Kahn, Vinkers, 2018). This was interpreted as representing abnormal functional activation following stress. Again, the described study is quite different from the current study in terms of study population and study methods but shows evidence that differences in stress exposure can alter functional activation of the STG.

We observed an association between maternal cortisol concentration and activation to cry sounds in the culmen. This was an unexpected finding but considering the function of the culmen itself and the cluster's projection into fusiform gyrus its activation to infant cry it is consistent with previous literature. Research has identified the culmen as part of the 'auditory cerebellum', a network of cerebellar regions that respond strongly to auditory information and is believed to be responsible for early auditory processing (Oertel & Young, 2004; Petacchi, Laird, Fox, Bower, 2005). The cluster extends into the fusiform gyrus, which has been associated with social cognition in a variety of contexts (Adolphs, 2001; Schultz, Grelotti, Klin, Kleinman, Van der Gaag, Marois, Skudlarski, 2003), including auditory modality (Kawase, Yamaguchi, Ogawa, Suzuki, Suzuki, Itoh, Fujii, 2005). Culmen activation to cry sounds may be part of a broader network of auditory processing of cry information. Given that the cerebellum has connections to the hypothalamus and is dense in glucocorticoid receptors, it is plausible that it is involved in HPA axis function (Schutter, 2012). Importantly, a previous study of

maternal cortisol and brain response to infant stimuli observed cerebellar activation associations as well (Laurent et al., 2011). More research is needed to understand the role of the cerebellum in supporting effective parenting behavior.

A cluster in the precuneus was found to be more functionally deactivated to own cry and other noise with greater cortisol concentration during parenting. The functional deactivation observed was unexpected but consistent with previous literature. Researchers have identified the precuneus as a central hub of the Default Mode Network (DMN), a network of brain regions that are more active during rest compared to when doing a task (Rigo, De Pisapia, Bornstein, Putnick, Serra, Esposito, Venuti, 2017; Utevsky, Smith, Huettel, 2014). This functional deactivation was also observed for new mothers listening to infant cries (Rigo, Esposito, Bornstein, De Pisapia, Manzardo, Venuti, 2019). In this context, the functional deactivation of the precuneus in response to task may represent task engagement. It may be that mothers who are more stressed need to engage the DMN more (as evidenced by greater functional deactivation of the precuneus) in order to engage with the task.

Cortisol concentration has also been shown in animal models to alter maternal brain structure and function in the postpartum period. Exogenous cortisol treatment in the postpartum period was related to reduced cell proliferation in the dentate gyrus of the hippocampus (Brummelte and Galea, 2010), and decreased dendritic remodeling in the hippocampus in postpartum rats with greater corticosterone (Pawluski et al, 2016). Reduced neurogenesis and cell proliferation and reduced dendritic branching and spine density was also observed in the nucleus accumbens (Haim et al., 2014) and in the medial

prefrontal cortex (Leuner et al., 2014). While the findings in these papers were in different regions than the regions identified in the current study, it is possible that similar mechanisms are at work. Further study of animal models are needed in other regions to untangle this mechanism.

It must be understood that maternal cortisol concentration was not associated with different brain activation to own infant cry vs. other infant cry sounds in any region other than the precuneus. The majority of regions identified that were associated with maternal cortisol concentration responded to infant cry regardless of the identity of the infant. This is consistent with other studies of maternal brain response to infant cry and the association to environmental exposures. Kim et al., 2016 found that lower income-to-needs ratio was associated with reduced brain activation to infant cry sounds (across own and other baby stimuli) in the PFC and STG (Kim et al., 2016). This same research group found that exposure to cumulative risk, including socioeconomic, environmental, and psychological risk, was associated with reduced activation to infant cry sounds in the insula, inferior frontal gyrus, and STG (Kim et al., 2020). There is evidence across multiple studies that mothers show increased neural and physiological responses to unfamiliar cries compared to nonmothers (Boukydis & Burgess, 1982; Seifritz, Esposito, Neuhoff, Luthi, Mustovic, Dammann, Di Salle, 2003; Stallings et al., 2001). Additionally, multiple studies have identified brain responses that are common to familiar and unfamiliar infant cries in many of the regions identified in our study (Bornstein et al., 2017; Witteman et al., 2019). Taken together this evidence highlights the fact that there may be neural mechanisms that are highly responsive to infant distress cues regardless of

context, but that are more selective in their response to infant images. Regardless, we have identified areas of the maternal brain that respond strongly to infant cries and are associated with maternal cortisol concentration.

We found an association between maternal cortisol concentration and nonintrusive parenting behavior, but not maternal sensitivity. This may be because of how each of these parenting behaviors are operationalized in our sample. In our study, the construct of maternal sensitivity is associated more with affect, while the construct of maternal nonintrusiveness is more associated with behavior (Biringen et al., 2008). It may be possible that maternal cortisol alters motor processes and perceptions related to infant need more so than altering maternal displays of affect. Cortisol is associated with enhanced negative perception of ambiguous facial expressions (Brown, Raio, Neta, 2017) and heightened arousal ratings of nonarousing stimuli (Abercrombie, Kalin, Davidson, 2005). Cortisol concentration is also associated with inhibition of neuroplasticity in motor cortex and motor cortex excitability (Milani, Piu, Popa, della Volpe, Bonifazi, Rossi, Mazzocchio, 2010; Sale, Ridding, Nordstrom, 2008). Taken together, this may indicate that with greater cortisol, mothers' perception of infant need is altered, and their motor control is also disrupted.

Mother's breastfeeding status was associated with differences in average cortisol concentration, with mothers who were breastfeeding having higher average levels. This is consistent with previous literature showing differences in HPA axis function by breastfeeding status (Neelon, Stroo, Mayhew, Maselko, Hoyo, 2015; Simon, Adam, McKinney, Krohn, Shalowitz, 2016; Tu, Lupien, Walker, 2006). In our sample, this was

not associated with either parenting variable nor confounded the behavioral or neuroimaging results. Maternal mood was not associated with average cortisol concentration or either parenting variable in our sample and thus not an explanation for our findings. This is surprising given previous research showing that maternal depression and anxiety is associated with maternal cortisol (Orta, Gelaye, Bain, Williams, 2017; Sarkar, Bergman, Fisk, Glover, 2006; Seth, Lewis, Galbally, 2016) and parenting behavior (Drake, Ginsburg, 2011; Gerdes, Hoza, Arnold, Pelham, Swanson, Wigal, Jensen, 2007; Lovejoy, Graczyk, O'Hare, Neuman, 2000; Seymour, Giallo, Cooklin, Dunning, 2015). Given that our sample was a community sample and average scores on the mood measures were relatively low, it may be that there are not enough mothers with severe mood symptoms to show an effect. Additionally, given the relatively involved and demanding study procedure, which included a home visit and travel to another city for an fMRI visit, it is likely that a self-selection for relatively higher functioning and non-clinically affected mothers occurred. Further research in this area should also include subsamples of mothers with clinical depression and anxiety to better understand underlying mechanisms.

Measures of socioeconomic status (SES) including maternal IQ and maternal education predicted differences in parenting behavior as well. In our study, greater maternal IQ predicted both greater sensitivity and greater nonintrusiveness, while greater maternal education predicted greater sensitivity only. This is consistent with previous literature showing that parents of lower SES tend to exhibit more control and less warmth (Anton, Jones, Youngstrom, 2015; Pomerleau, LaCroix, Malcuit, and Seguin, 1999;

Tudge, Hogan, Snezhkova, Kulakova, and Etz, 2000). In our sample, however, we did not observe a direct association between 12-month INR and differences in parenting behavior. Previous studies of family income have shown a relation between income and parenting (Dooley and Stewart, 2007; Lee, Anderson, Horowitz, August, 2009), but studies have indicated that this is unlikely to be directly causal and likely mediated by other factors (Gershoff, Aber Raver, Lennon, 2007; Lee et al., 2009). In our study a similar pattern may be at play – an indirect relationship of family income to differences in average cortisol, and differences in average cortisol to parenting behavior. Future studies should seek to investigate these indirect pathways in more detail.

We failed to confirm our hypothesis that maternal cortisol concentration would be associated with reduced amygdala activation to infant cry sounds. Despite the amygdala being involved in regulation of the HPA axis (Herman et al., 2003) and activated in response to infant distress cues (Kim et al., 2011; Swain et al., 2017; Witteman et al., 2011), there was no association between maternal cortisol concentration and amygdala response to infant cry sounds. This was unexpected, especially considering the relation between amygdalar activation and maternal sensitivity (Kim et al., 2011). It may be that cortisol concentration does not impact the function of the amygdala in this context or that the timescale of fMRI is too limited to capture this relationship.

Examining the functional connectivity of the amygdala, two regions were identified that showed FC with the left amygdala seed region. The first, the posterior cingulate cortex (PCC) had greater FC with the left amygdala during own cry and other noise conditions. The second, the superior parietal lobule (SPL), showed the same FC

pattern. These regions were relatively unexpected given previous literature in this space that found amygdala being functionally connected to regions such as the SMA and STG (Atzil et al., 2011; Olsavsky et al., 2021; Swain et al., 2017), however there is meta-analytic evidence showing both resting state and task-based FC between the amygdala and PCC in other contexts (Robinson, Laird, Glahn, Lovallo, Fox, 2010). The PCC is believed to be involved in both function of the default mode network (DMN), particularly self-referential aspects of the DMN (Buckner, Andrews-Hanna, Schacter, 2008), as well as theory of mind (Mars, Neubert, Nooan, Sallet, Toni, Rushworth, 2012) and social and emotional processing (Adolphs, 2003). In a parenting context, a study of depressed and nondepressed mothers found that only for mothers with postpartum depression, there was inverse FC between the amygdala-PCC (Chase, Moses-Kolko, Zevallos, Wisner, Phillips, 2014). These studies highlight that generally amygdala-PCC FC is adaptive. In our study, mothers may show greater amygdala-PCC engagement to own cry as a signal of task engagement and personal relevance signaling. In explaining the increased coupling during other noise condition, this is consistent with a study of nonparents listening to infant cry and control sounds, who showed greater PCC activation to control stimuli than infant cry (Sander, Frome, Scheich, 2007). In this instance, PCC engagement is thought to represent cognitive modulation of affective processing (Pessoa, Padmala, Morland, 2005).

Conversely, the SPL has been identified as being involved in audio-visual multisensory processing (Molholm, Sehatpour, Mehta, Shpaner, Gomez-Ramirez, Ortigue, Foxe, 2006) and sensory-motor integration in a wide variety of contexts

(Andersen, Snyder, Bradley, Xing, 1997; Cohen & Andersen 2004; Iacoboni, Woods, Mazziotta, 1998; Lacquaniti & Caminiti 1998; Stricanne, Andersen, Mazzoni, 1996; Nakashita, Saito, Kochiyama, Honda, Tanabe, Sadato, 2008). This may suggest that amygdala-SPL FC is an artefact of concurrent salience, emotion, and motor processing to engage with the sounds presented in the task. This may represent approach behaviors when listening to own baby cry and avoidance behaviors when listening to control noise. Another study has identified the role of amygdala-parietal FC during emotion regulation, which is another potential explanation for the FC in this context (Banks, Eddy, Angstadt, Nathan, Phan, 2007).

Despite hypothesizing that maternal cortisol would be related to amygdala FC, we did not observe this relation. While the current study used a novel methodology that makes direct comparison to other studies difficult, the only other study of maternal cortisol and brain response to infant stimuli did not find amygdala activation as a function of cortisol either (Laurent et al., 2011) and did not test amygdala FC. Previous studies have found that cortisol is associated with altered amygdala connectivity to a number of different regions (Kogler et al., 2016; Vaisvaser et al., 2013; Veer et al., 2012), however no study have examined amygdala FC in mothers listening to infant stimuli. To our knowledge, only a small number of studies have investigated maternal amygdala FC and found amygdala FC with SMA and STG regions (Atzil et al., 2011; Olsavsky et al., 2021; Swain et al., 2017), however none of these studies examined maternal cortisol concentration. More research is needed to replicate findings for amygdala-PCC FC and identify what it indicates for parental behavior.

In our exploratory analysis, SMA FC was found to differ based on maternal cortisol concentration in two regions, the rIFG and the left precentral gyrus. The right IFG has been identified as an important region for motor inhibition, and alterations in the function of the IFG have been highlighted in impulse control problems (Aron, Robbins, Poldrack, 2014). The right IFG and SMA are structurally and functionally connected, and functional connectivity between them has been shown to be important for the control of motor actions, particularly motor inhibition (Swann, Cai, Conner, Pieters, Claffey, George, Tandon, 2012). This would suggest that greater cortisol interrupts motor inhibition processes that may signal a desire to act and engage with infant stimuli. Indeed, acute stress has been shown to reduced neural responses to motor inhibition tasks in both the IFG and SMA (Westwater, Mancini, Gorka, Shapleske, Serfontein, Grillon, Fletcher, 2020). Further interpretation is difficult given that SMA-IFG FC was found across both cry and noise stimuli. The precentral gyrus has been identified as the location of primary motor cortex (Penfield & Boldrey, 1937; Meier, Aflalo, Kastner, Graziano, 2008) and there exist direct structural and functional connections between these regions (Narayana, Laird, Tandon, Franklin, Lancaster, Fox 2012). Cortisol has been shown to modify neuroplasticity of M1 circuits and increase excitability (Sale et al., 2008; Milani et al., 2010). It may be that mothers with greater cortisol are responding more strongly with avoidance motor signals to the noise sounds.

It is important to consider several explanations for how individual differences in maternal cortisol concentration may emerge. The first is differing early caregiving experiences. Animal models have shown that particularly high- or low- maternal care

environments (have been demonstrated in animal models to alter stress response in adulthood – evidenced by altered corticosterone levels, altered expression of markers of neural plasticity, and altered brain circuitry (Lovic, Belay, Walker, Burton, Meaney, Sokolowski, Fleming, 2007; Fleming and Korsmit, 1996; Klampfl and Bosch, 2019). Similar findings have been observed in humans, with early life adversity is associated with disrupted HPA axis function in postpartum women (Gonzalez, Jenkins, Steiner, Fleming, 2009), indicating that these early life experiences may also impact cortisol concentration as well. Likewise, evidence showing early life experiences such as abuse (Choi, Jeong, Rohan, Polcari, Teicher, 2009; De Bellis, Keshavan, Shifflett, Iyengar, Beers, Hall, Moritz, 2002) and high maternal care (Kim, Leckman, Mayes, Newman, Feldman, Swain, 2010) have been related to alterations in brain function. Another explanation may be that chronic stress, either experienced prenatally or after birth, may drive differences in cortisol concentration and brain structure and function. In animals, stress experienced prenatally (Belay, Burton, Lovic, Meaney, Sokolwski, Fleming, 2011) has been demonstrated in animal models to alter stress response in adulthood – evidenced by altered corticosterone levels, altered expression of markers of neural plasticity, and altered brain circuitry. Similar patterns have been observed for chronic stress exposure in adult animal models, even when that stressor is relatively mild (Herzog, Czeh, Corbach, Wuttke, Schulte-Herbruggen, Hellweg, Fuchs, 2009; Pardon, Gerardin, Joubert, Perez-Diaz, Cohen-Salmon, 2000). Studies of animal models have demonstrated that chronic peripartum stress was associated with increased basal corticosterone and less attenuation in response to stressors than would be during normal peripartum adaptations to parenting

(Hillerer, Neumann, Slattery, 2012; Hillerer, Reber, Neumann, Slattery, 2011). In humans, mothers who are exposed to chronic stress may be more likely to have altered HPA axis function (Hellhammer, Wust, Kudielka, 2009; Fecteau, Boivin, Trudel, Corbett, Harrell, Viau, Champagne, Picard, 2017) and show differences in brain function (Kim, Evans, Angstadt, Ho, Sripada, Swain, Phan, 2013; Sripada, Swain, Evans, Welsh, Liberzon, 2014). Chronic stress is also related to less adaptive parenting behavior (Crnic, Gaze, Hoffman, 2005; Scaramella, Neppl, Ontai, Conger, 2008), indicating that cortisol may be a marker for chronic stress processes at the brain and behavioral level. In our study, mother's 12-month INR, an index of family income, was negatively associated with maternal cortisol concentration, lending initial evidence that financial stress may be a contributing factor to individual differences in maternal cortisol concentration. Further research should seek to separate the impact of each of these potential explanations on maternal HPA axis function.

Our study is not without limitations. The first is that our study used a cross-sectional design. We observed natural variations in cortisol concentration only, without examining direct causes of those variations. Additionally, despite demonstrating associations between cortisol and behavior, cortisol and brain, and brain and behavior, we are unable to assess directionality or causality of these associations (Maxwell & Cole, 2007), limiting our understanding to merely correlational analysis. It is unclear whether differences in brain function drive differences in HPA axis function via top-down dysregulation or whether individual differences in cortisol concentration over time alter the function of maternal brain circuitry. Further research should asses the directionality of

association between maternal cortisol and maternal brain function. The second limitation of the current study is that maternal cortisol was assessed in a different context and at a different time from when maternal brain response was assessed. The measurement of cortisol changes during a naturalistic parenting interaction necessitates using different stimuli and a different context than how maternal brain response is assessed. This study extends the literature on the biological mechanisms underlying parenting, but future studies should continue to assess maternal cortisol changes during naturalistic parenting as well as study cortisol changes during fMRI contexts. Relatedly, our study only assessed maternal cortisol concentration on one day, which means that it may be a noisy estimate of mother's typical HPA axis function. A third limitation of the study is the nature of our cortisol variables includes measurements before *and* after parenting, so drawing conclusions about whether our finding reflects a broad cortisol concentration effect or a more specific cortisol concentration during parenting effect is impossible. Future studies should attempt to disentangle these two aspects. A fourth limitation of this study is that only one neuroendocrine marker was assessed. Research has suggested that multiple neuroendocrine systems, including the HPA axis and the oxytocin system, may interact with each other as unique biological mechanisms supporting parenting (Gordon et al., 2010). Indeed, oxytocin has been shown to be associated with differences in brain activation in humans (Grace, Rossell, Heinrichs, Kordsachia, Labuschange, 2018), although this association is understudied in mothers. Examining only one neuroendocrine system associated with parenting limits our understanding of the biological mechanisms underlying parenting behavior. The last limitation is our study is a focus on mothers only.

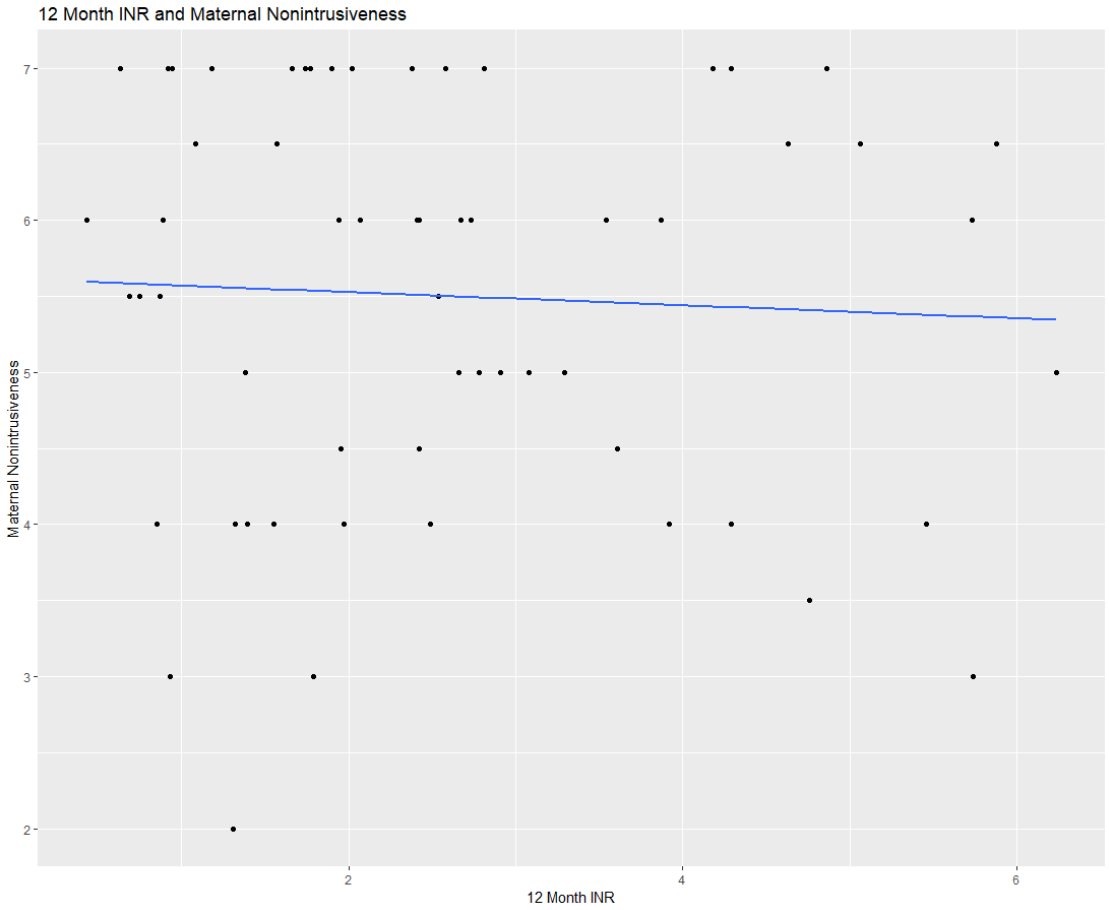
While mothers represent the majority of parents in the United States (US Census), fathers and non-biological caregivers are an important part of the parental ecosystem and undergo many of the same biological changes new mothers do to support effective parenting behavior (Abraham & Feldman, 2018; Feldman, Braun, Champagne, 2019; Kim, Rigo, Leckman, Mayes, Cole, Feldman, Swain, 2015; Li, Horta, Mascaro, Bijanki, Arnal, Adams, Rilling, 2018; Rajhans, Goin-Kochel, Strathearn, Kim, 2019). Preliminary evidence has demonstrated an association between fatherhood and cortisol concentration (Burke & Bribiescas, 2018), particularly in ways that are associated with caregiving quality (Bos, Hechler, Beijers, Shinohara, Esposito, de Weerth, 2018). Future studies can expand this research to assess cortisol and other biological mechanisms in all caregivers to improve generalizability of our research.

Conclusion

Overall, this study demonstrated—for the first time--associations between maternal cortisol concentration during a naturalistic parenting task, maternal nonintrusiveness, and maternal brain response to infant distress cues. We identified a number of motor planning and auditory processing regions that showed decreases in activation to infant cry with increased cortisol concentration and demonstrated that reduced activation in those regions was associated with more intrusive maternal behaviors. We found that greater maternal cortisol concentration during parenting was associated with more intrusive maternal behaviors. This study was the first to our knowledge to investigate maternal cortisol during a naturalistic parenting interaction and connect it to maternal brain response to infant stimuli and subsequent intrusive parenting

behaviors. This study extended the literature on maternal cortisol during the postpartum period to demonstrate a similar finding as previous studies across a wider infant age range and synthesize across biological and behavioral levels of analysis. This study has several implications for applied research and intervention work. The first is that high maternal cortisol may be a biomarker for mothers at risk for intrusive parenting behaviors. Salivary cortisol sampling is relatively simple, making it a useful biomarker if our findings are replicated. Additionally, our study has demonstrated the importance of cortisol levels during the postpartum period, making it a promising target for intervention work. Our finding that maternal cortisol was associated with alterations in the function of motor planning and auditory processing regions indicate the potential physiological processes that may be affected by maternal cortisol. Interventions targeting motor control and auditory processing may be promising inflection points to improve neural sensitivity to infant cues in ways that would support more effective parenting behavior.

Figure 11. *Association Between 12 month INR and Maternal Nonintrusiveness*



Note. INR = Income to Needs Ratio.

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