6-2021

Early Emotion Regulation in the Children of Superstorm Sandy

Jessica L. Buthmann
The Graduate Center, City University of New York

EARLY EMOTION REGULATION IN THE CHILDREN OF SUPERSTORM SANDY

by

JESSICA BUTHMANN

A dissertation submitted to the Graduate Faculty in Psychology in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York

2021

Early Emotion Regulation in the Children of Superstorm Sandy

by

Jessica Buthmann

This manuscript has been read and accepted for the Graduate Faculty in Psychology in satisfaction of the dissertation requirement for the degree of Doctor of Philosophy

_____	_____
Date	Yoko Nomura Chair of Examining Committee
_____	_____
Date	Richard Bodnar Executive Officer

Supervisory Committee:

Joshua Brumberg

Patrizia Casaccia

Kerstin Unger

Ahmed Duke Shereen

THE CITY UNIVERSITY OF NEW YORK

ABTRACT

Early Emotion Regulation in the Children of Superstorm Sandy

by

Jessica Buthmann

Advisor: Yoko Nomura

Rising prevalence of childhood psychopathology mandate investigation into the antecedents of symptom onset. Growing evidence shows prenatal maternal stress experienced in utero is a strong contributor to offspring neurodevelopmental deficits, including emotion dysregulation, a core feature of many types of psychopathology. This dissertation summarizes a body of work studying children prenatally exposed to maternal stress related to a natural disaster, Superstorm Sandy (i.e., storm stress). This work includes six experiments conducted in the framework of the Developmental Origins of Health and Disease (DOHaD) hypothesis. The DOHaD hypothesis posits that developmental disruptions, like storm stress exposure, during a critical period of developmental, like gestation, can have long term influences on health. The first experiment explores infant behavioral temperament and shows correlations between objective stressors related to the storm and poor regulation and negative affect. Experiment 2 demonstrates that associations between temperament and a sympathetic nervous system measure, electrodermal activity (EDA), vary by child sex. Experiment 3 shows that prenatal storm stress is associated with increased EDA in girls, and decreased EDA in boys. Experiment 4 describes an interaction between prenatal storm stress and maternal depression predicting blunted offspring EDA in early childhood. Experiments 5 and 6 present preliminary findings that children prenatally exposed to storm stress exhibit differential prefrontal-limbic structure and amygdala function, respectively. Future work should expand the current sample, which was hampered by the Covid-19 pandemic, consider maternal mental health history in more depth, and

continue to follow the trajectory of neurodevelopment of children affected by Superstorm Sandy. The vulnerability of pregnant people and their children, and how they can best be supported in the face of widespread disasters, needs to be more thoroughly studied as well. This knowledge may inform public health officials and mental health professionals in best practices to mitigate the impact of stressors, especially during pregnancy, and improve psychological wellbeing and optimal neurodevelopment in vulnerable people.

ACKNOWLEDGEMENTS

This dissertation was made possible by the support of my loving parents, my sister, Caitlin, Yoko Nomura, Duke Shereen, Tingting Wu, lab members past and present, and my friends, especially Jackie Finik – who is as wonderful a friend as she is a statistician. I am also grateful to the families who let us into their lives to participate in this research and the CUNY administration at Queens College and the Graduate Center.

This work was funded in part by the PSC CUNY and National Institute of Mental Health (R01MH102729, PI Yoko Nomura).

Portions of this dissertation have been published in the following:

Buthmann, J., Ham, J., Davey, K., Finik, J., Dana, K., Pehme, P., Zhang, W., Glover, V., & Nomura, Y. (2019). Infant temperament: Repercussions of Superstorm Sandy-related maternal stress. *Child Psychiatry & Human Development, 50*(1), 150–162

Buthmann, J., Finik, J., & Nomura, Y. (2018). Sex differences in the relations between infant temperament and electrodermal responses in early childhood. *International Journal of Behavioral Development, 42*(6), 535–542.

Buthmann, J., Finik, J., Ventura, G., Zhang, W., Shereen, A. D., & Nomura, Y. (2019). The children of Superstorm Sandy: Maternal prenatal depression blunts offspring electrodermal activity. *Biological Psychology*, *146*, 107716.

Contents

TABLES

FIGURES

Chapter 1: An Introduction to Prenatal Stress

Mental health in American youth is in decline. One in six children aged 2-8 is estimated to have a mental, behavioral, or developmental disorder, with children from low income households at even greater risk for a disorder (Cree et al., 2018). Anxiety and depression diagnoses in particular have increased among children aged 6-17 (Bitsko et al., 2018). Further, an estimated 60% of all American youth are classified as not thriving on the basis of interest in new things, ability to complete tasks, and the ability to regulate emotions (Bethell et al., 2019). Emotion regulation, the capacity to alter the intensity or expression of an emotion, is irregular in many psychopathological disorders and may cue risk of a clinical disorder or subclinical impairment (Aldao et al., 2016; Beauchaine, 2015). Internalizing disorders such as anxiety and depression are characterized by sadness, shame, and over-regulation of emotion. Externalizing disorders such as oppositional defiant disorder and conduct disorder are characterized by impulsivity, aggression, and under-regulation of emotion. Moreover, emotion dysregulation below the threshold of a psychopathological diagnosis may contribute to clinically significant levels of distress and functional impairment. Early signs of emotion dysregulation may signal global yet significant risk for development of psychopathology and provide an opportunity for intervention and prevention to mitigate worsening of symptoms.

Researchers have identified prenatal maternal stress as a contributor to the development of psychopathology in children by way of maladaptive emotion regulation and stress response patterns (Eichler et al., 2017; Curt A Sandman & Davis, 2010). During gestation, the accelerated pace of development makes the fetus susceptible to disruption from environmental insults that may elicit structural and functional changes that can impact the offspring's developmental trajectory of neurobehaviors (Barker, 1998). David Barker first posited that conditions occurring before birth can impact wellbeing later in life. He developed the fetal programming hypothesis after discovering a relationship between poor maternal nutrition during pregnancy and poor adult offspring cardiovascular health (Barker, 1998). This phenomenon has been reformulated more recently as the Developmental Origins of Health and Disease (DOHaD) paradigm (Gluckman et al., 2007) to encompass the study of the spectrum of early life factors that can influence health across the lifespan, not just cardiovascular and endocrine-related disorders in adulthood. Gestation and infancy are thought to be the two most critical time periods for developmental

disruption due to increased plasticity in the brain, allowing for environmental insults to become "stamped in" via epigenetic alterations (Gluckman et al., 2007). Importantly, researchers have incorporated an evolutionary perspective that views the outcomes of prenatal disruption (e.g., offspring psychopathology) as a result of a poor match between the prenatal and postnatal environments (Glover, 2011). One of the most prominently studied examples of this phenomenon is an apparent link between prenatal maternal stress and offspring mental health outcomes. Briefly, it is proposed that the maternal physiological stress response cues the developing fetus to stressful environmental conditions, leading to a cascade of epigenetic programming to make the offspring more anxious, aggressive, etc. to succeed in the anticipated postnatal environment, even though the prior stressor may no longer be present, and the postnatal environment is completely different (Gluckman et al., 2007; Glover 2011).

Human and animal models have documented relationships between prenatal maternal stress and increased offspring fear and anxiety behaviors (McLean et al., 2018), maladaptive stress response (Field et al., 2004), depressive symptoms (Van den Hove et al., 2014), and social deficits (Ehrlich & Rainnie, 2015). Cortisol, a hormone produced by the maternal hypothalamo-pituitary-adrenal (HPA) axis, is secreted in response to experienced stressors and in association with psychological conditions, including anxiety (Sandman et al., 1999). In times of stress the paraventricular nucleus of the hypothalamus releases corticotropin releasing hormone (CRH), which stimulate the release of adrenocorticotropic hormone (ACTH) from the anterior lobe of the pituitary gland. This, in turn, cues the secretion of cortisol from the adrenal gland (for review see Smith & Vale, 2006). Maternal cortisol can cross the placenta to the fetal compartment and activate epigenetic, hormonal, and immune responses with the potential to alter the development of the rapidly developing brain (Chrousos, 1992; Glover, 2011; Van den Bergh et al., 2005; Wadhwa et al., 2001). Fetal oxygen deprivation, inflammation, and fetal growth restriction have been well-studied as mediators to understand the roles of prenatal maternal stress on offspring neurodevelopment (Lipner et al., 2019).

Animal models

The impact of prenatal maternal stress on offspring development has been studied in both human and animal models. Animal models afford the ability to experimentally manipulate the timing, type,

and intensity of stressors during pregnancy in a tightly controlled experimental setting. In a rat model, unpredictable electric shocks administered to pregnant subjects were associated with reduced amygdala neuron excitability, fewer social behaviors, and decreased anxiety-like behaviors in offspring (Ehrlich & Rainnie, 2015). Reduced social interaction and altered epigenetic expression of brain-derived neurotrophic factor (BDNF), glutamate, and GABA suggestive of a schizophrenia-like profile were also found in adult rats prenatally exposed to maternal stress (Dong et al., 2015). Mice prenatally exposed to stress caused by noise had significantly higher pre- and post-stress test blood corticosterone levels (Faraji et al., 2017). Increased anxiety-like behaviors were found in another rat model of unpredictable prenatal maternal stress, as well as increased depression-like behaviors and corticosterone levels in male offspring (Van den Hove et al., 2014). Depression-like symptoms were further found in male and female rat offspring exposed to chronic prenatal maternal stress, but only males exhibited abnormal patterns of glutamate receptor subunit expression in the prefrontal cortex (Y. Wang et al., 2015). Sex differences were also found in pre-pubertal rats exposed to prenatal restraint stress, wherein only male offspring demonstrated decreased corticosterone response, anxiety-like behaviors, and depression-like behaviors (Iturra-Mena et al., 2018). In contrast, no sex differences were found among the increased anxiety-like behaviors, depression-like behaviors, corticosterone levels, or hippocampal and bed nucleus of stria terminalis structural alterations in another rat model of unpredictable prenatal maternal stress (Soares-Cunha et al., 2018). Cognitive, memory, and dietary effects have also been observed in animal models of prenatal maternal stress (for review see Weinstock, 2016). While animal models have considerable strength in their ability to manipulate stress ethically and evaluate the molecular effects, thus far, no clear consensus on sex effects, stressor type, or age of onset of developmental deficits has been reached. Lack of consensus might be due to the difference in gestational period length, development rate, and offer only an approximation of the nuance and complexity of human emotional experiences.

Human models

Prenatal maternal stress research in human models relies on the occurrence of stressors that are not manipulated, such as stressful life events, daily hassles, and maternal psychopathology. Outcome measures in these models include psychopathology diagnosis, behavioral assessment, and physiological

measurements including autonomic nervous system function, hormone levels, gene expression, and brain structure and function. Temperament is one such widely used behavioral measure, especially in early childhood. It refers to an individual's patterns of behavior and emotion, including factors such as fearfulness, activity level, and social tendencies (Gartstein & Rothbart, 2003). Although subject to the influence of environmental factors, temperament is thought to have a genetic basis and be relatively stable over the life course (Saudino, 2005), giving it value as a predictor of future behavior and emotion patterns, which are linked to vulnerability for psychopathology (Sayal et al., 2014).

To briefly summarize findings regarding prenatal maternal stress and temperament, researchers have largely linked prenatal maternal stress with suboptimal offspring temperament. For example, infant temperament was more likely to be rated as "difficult," reflecting poor mood and adaptability, if the mother of the child experienced late gestation anxiety (Austin, Hadzi-Pavlovic, et al., 2005) or depression (McGrath et al., 2008). Infants of mothers who experienced a stressful life event in the first trimester were rated as displaying greater attention and less distress at having limitations in one study (Zhu et al., 2014). However, in another, it was found that female infants whose mother experienced a stressful life event during pregnancy had increased methylation of the 1F exon of the gene encoding the cortisol receptor, *NR3C1*, which in turn predicted increased fearfulness (Ostlund et al., 2016). This association was not significant in male infants. In lieu of asking pregnant women about mental health symptoms or stressful life events, researchers have also evaluated maternal cortisol during gestation. Maternal second trimester cortisol levels were negatively correlated with offspring birthweight, which was negatively correlated with levels of fear and distress at having limitations at three months of age (Baibazarova et al., 2013). The temperament of two month old offspring of mothers with higher late-gestation cortisol, anxiety, and depression symptoms was rated as displaying more negative emotion (E. P. Davis et al., 2007). Lastly, maternal cortisol responses to a social stressor in mid-late gestation predicted offspring ability to self-soothe at 6 months of age (Bolten et al., 2013). Experiment 1 of this dissertation elaborates on the association between prenatal maternal stress and offspring temperament.

Natural disaster models

Despite the advantages of human models, they are often limited by their reliance on pre-existing mental health conditions or the occurrence of common stressful life events. These stressors may lack

acute negative emotional valence or be confounded by other biopsychosocial factors that can also affect offspring neurodevelopment. In recent years researchers have turned to the rising occurrence of natural disasters to study the impact of stressful events that cast a shadow on a large population of people at once. These acute stressors allow for the assessment of objective stress through measures of residential displacement, financial loss, injury, etc. and subjective stress through measures of fear and anxiety related to the disaster. Studying natural disasters as a model of prenatal maternal stress offers the advantages of a) the event being quasi-experimental, in that the occurrence of the storm is somewhat random, b) a large population is impacted by the same event, and c) multiple types of aspects of stress can be assessed related to the one event. Additional benefit to studying natural disasters as a model of prenatal maternal stress stems from a growing body of research called "solastalgia," which examines the impact of climate change on human psychological well-being (Warsini et al., 2014). Mental health changes related to natural disasters, changing landscapes, resource depletion, and displacement must be better understood, particularly as the number of natural disasters and other climate change-related events are expected to increase in frequency and intensity (Grinsted et al., 2013; Khan, 2017). Indeed, early research already points to disproportionate suffering in low income populations and women (Obradovich et al., 2018), indicating that pregnant women may be especially vulnerable.

A number of research groups have begun characterizing the neurodevelopment of children prenatally exposed to a natural disaster, although outcomes have been mixed. For example, maternal mental health but not prenatal exposure to Hurricane Katrina in 2005 was associated with offspring temperament at two months and one year of age (Tees et al., 2010). In contrast, temperament was linked with prenatal maternal stress related to the 1998 Quebec Ice Storm, with infant offspring being rated as more temperamentally difficult and needing more attention than unexposed infants (Laplante et al., 2016). Interestingly, an interaction was found between maternal prenatal depression and prenatal exposure to Superstorm Sandy, such that natural disaster exposure seemed to amplify infant temperament difficulties related to maternal depression (Nomura et al., 2019). Prenatal maternal stress related to the 2011 Queensland Flood has been linked with increased childhood anxiety symptoms (McLean et al., 2018) and maladaptive interpersonal skills (Simcock et al., 2017). Experiments 1 and 2 of this dissertation focus in

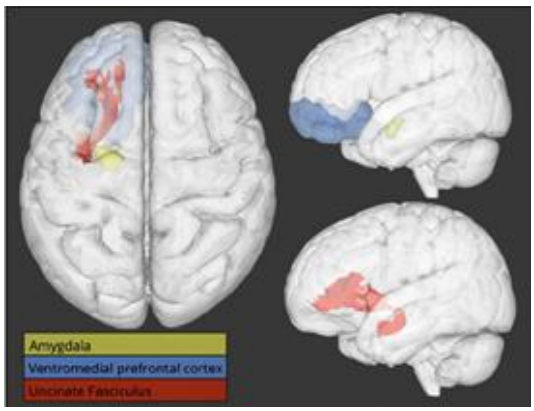
more detail on temperament and its relation to sex, other aspects of emotion regulation, and prenatal storm stress related to Superstorm Sandy.

Physiological alterations related to prenatal maternal stress have been observed as well. Prenatal exposure to the 2008 Iowa Flood has been associated with salivary cortisol response to a stressor in offspring aged two and a half years old (Yong Ping et al., 2015). Sympathetic nervous system (SNS) reactivity has been correlated with prenatal exposure to Superstorm Sandy, with interactions between prenatal storm stress and maternal prenatal mental health (Buthmann, Finik, et al., 2019) and prenatal storm stress and offspring sex (Buthmann, unpublished data). These findings will be elaborated upon in Experiments 3 and 4 of this dissertation. Lastly, the Quebec Ice Storm was linked with increased externalizing symptoms, which was partially mediated by amygdala volume in adolescent female offspring (Jones et al., 2019), suggesting the neural development of children prenatally exposed to a natural disaster may help explain observed behavioral and emotional deficits.

Neural development

A number of studies have begun the work of investigating the relationship between prenatal maternal stress and offspring neural development, although, to date the aforementioned Quebec Ice Storm study is the only one to have published results in a natural disaster model. Maternal prenatal depression, anxiety, and stressful life events have been used to model the association between prenatal maternal stress and offspring structural and functional measures. The primary target of interest is the prefrontal-limbic circuit, depicted in Figure 1.1 (from Hanson et al., 2015). The prefrontal cortex and limbic system have high concentrations of glucocorticoid receptors, making them a potential target of excess maternal prenatal cortisol, and play an active role in regulating the HPA-axis stress response system (for review see Smith & Vale, 2006). As characterized by Gee, Humphreys, et al. (2013), the functional

Figure 1.1. *The prefrontal-limbic circuit*.



A diagram of the prefrontal-limbic circuit that helps modulate emotion regulation, from: Hanson, J. L., Knodt, A. R., Brigidi, B. D., & Hariri, A. R. (2015). Lower structural integrity of the uncinate fasciculus is associated with a history of child maltreatment and future psychological vulnerability to stress. *Development and Psychopathology*, *27*, 1611–1619. https://doi.org/10.1017/S0954579415000978

connectivity between the prefrontal and the limbic regions is positive until age ten, indicating the areas increase and decrease in activity at the same rate. However, this correlation becomes increasingly negative after age ten, indicating an increase in prefrontal activity is accompanied by a decrease in amygdala activity (Gee, Humphreys, et al., 2013). A mature negative correlation is thought to reflect a stronger ability to regulate emotions, making this circuit an important marker for emotional wellbeing.

In prenatal maternal stress studies maternal prenatal depressive symptoms have been linked to various changes in different brain morphology that indicate different level of emotion regulation. For example, prenatal maternal stress is associated with reduced cortical thickness and white matter structural integrity in the inferior frontal region of 2-5 year old offspring (Lebel et al., 2016), increased thickness of the amygdala and the insula in four year old female offspring (Lee et al., 2019), and negative resting functional connectivity (FC) and decreased structural connectivity between the prefrontal cortex (PFC) and amygdala in six week old offspring (Posner et al., 2016). Maternal prenatal anxiety symptoms have been linked with increased left amygdala volume in four-year-old female offspring, which was further correlated with emotional and behavioral difficulties (Acosta et al., 2019), decreased PFC, premotor cortex, temporal lobe, and postcentral gyrus volume in 6-9 year old offspring (Buss et al., 2010), and decreased frontal and temporal cortical thickness in offspring at age seven and with increased depression symptoms at age 12 (E. P. Davis et al., 2020). The occurrence of stressful life events during pregnancy has been associated with increased white matter structural integrity of the uncinate fasciculus in infants who were also born preterm (Lautarescu et al., 2020), increased gray matter in 11-14 year old offspring in several subareas of the parietal cortex (McQuaid et al., 2019), and increased white matter integrity of the uncinate fasciculus of 6-9 year old offspring (Sarkar et al., 2014). In sum, although maternal prenatal stress is consistently linked with brain aberrations, the level of aberration varies from study to study. The wide range of results reported may be related to both the array of ages studied and the subjective measures of maternal stress and mental health used.

Researchers have also used more objective biological measures of maternal stress via measures of glucocorticoid and inflammation markers in the body and their link with brain morphology. Elevated maternal prenatal cortisol levels have been correlated with weaker hippocampal-cingulate resting state FC and stronger hippocampal-temporal lobe FC (Scheinost et al., 2020), increased frontal lobe cortical

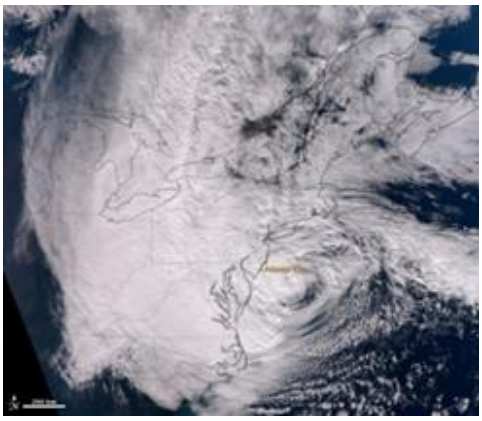
thickness and cognitive performance in 6-9 year old children (Davis et al., 2017), and increased neural network connectivity and internalizing symptoms in 6-9 year old female offspring only (Kim et al., 2017). Further, elevated prenatal cortisol was associated with neonatal amygdala connectivity that was decreased in boys and increased in girls; amygdala connectivity in turn mediated the link between maternal cortisol and internalizing symptoms in girls at two years of age (Graham et al., 2019). In the same cohort, higher levels of maternal prenatal interleukin-6 (IL-6) was positively correlated with neonatal larger right amygdala volume and stronger bilateral amygdala connectivity, which mediated a correlation between IL-6 and impulse control at two years of age (Graham et al., 2018). Maternal prenatal IL-6 levels were also inversely related to white matter integrity of the uncinate fasciculus and the rate of white matter myelination across the first year of life (Rasmussen et al., 2019).

The structure and function of the prefrontal-amygdala brain circuitry may be particularly revealing in understanding how prenatal maternal stress impacts neurodevelopment. Although this circuit, which undergoes a shift in connectivity around ten years of age that enhances the ability to regulate emotions (Gee, Humphreys, et al., 2013), is vulnerable to early life stress in the postnatal period (Callaghan & Tottenham, 2016) it is unknown if this trajectory is vulnerable to prenatal maternal stress. It is therefore crucial to unravel this relationship in children under ten years of age to clarify the risk posed by prenatal storm stress and identify potential targets for clinical intervention. Identification of aberrations in brain structure and function related to prenatal storm stress and emotion regulation may improve understanding of these processes and better inform intervention efforts. Experiments 5 and 6 of this dissertation present pilot data on the link between natural disaster-related prenatal maternal stress and offspring neurodevelopment of this circuit.

Superstorm Sandy

Hurricane Sandy formed in the Atlantic Ocean near the Caribbean in late October 2012 (see Figure 1.2, from NOAA, 2017). At its peak strength, the storm was a category-3 hurricane. It reached the New Jersey shore of

Figure 1.2. *Hurricane Sandy 10/29/12*



Hurricane Sandy approaches the northeast coast on 10/29/12 (NOAA, 2017).

the United States on October 29th, when it went from a category-2 hurricane to a post-tropical cyclone (NOAA, 2017), or more colloquially, a “superstorm.” In New York City, the storm brought a nine-foot storm surge and 79 miles per hour winds at John F. Kennedy Airport (NOAA, 2017). Significant losses brought by the storm include the historic two-day shut down of the New York Stock exchange, nearly eight million customers without electricity across 15 states, New York City public schools closed for five days, the Metropolitan Transit Authority in New York City incurred nearly five billion dollars in infrastructure damage, and nearly 150 people died, including 53 in the state of New York (CNN Library, 2018).

The current study

Two years prior to this devastating natural disaster, a longitudinal birth cohort study led by Dr. Yoko Nomura began recruiting pregnant women from their prenatal care clinic in New York City. The goal was to evaluate maternal mental health during pregnancy and chart child development postnatally. Dr. Nomura secured funding from the National Institute of Mental Health (NIMH) to expand recruitment from Manhattan to affected areas in Queens (for full cohort profile see (Finik & Nomura, 2017). The total sample of 416 mother-child dyads that continue to be followed up with postnatally is heterogeneous with respect to race, marital status, and education level.

Data on maternal characteristics that have been collected include demographic information, substance use, family history of psychopathology, maternal history and current psychopathology, stressful life event history, perceived stress, and medical history. Maternal blood and urine were collected during pregnancy, and placenta tissue, umbilical cord blood, and meconium microbiome were collected at birth. Postnatally, questionnaires measuring parent-child bond, social support, the home environment, and environmental exposure were added.

To gauge maternal experience during Superstorm Sandy, self-report questionnaires were administered assessing posttraumatic symptoms and objective stressors related to the storm, including financial loss and injury. Child annual assessments include medical history, temperament, psychopathology symptoms, behavioral difficulties, cognitive development, socio-emotional development, and motor skills. Assessments also include the recording of sympathetic and parasympathetic nervous system activity during periods of rest and a period of startling sounds both from mother and child. Samples of hair, toenails, and saliva are also collected from mother and child.

The following experiments outline research findings that explore some of the outcomes of prenatal exposure to Superstorm Sandy. Experiments 1 and 2 focus on temperament, its measurement, sex differences, and links to prenatal maternal stress. The primary finding of interest relates to correlations between infant temperament and objective maternal stress related to Superstorm Sandy (Buthmann, Ham, et al., 2019). Additional findings discussed include an interaction between maternal mental health and prenatal storm stress predicting infant temperament (Nomura et al., 2019), trajectories of temperament development over the first two years of life in relation to prenatal storm stress exposure (Zhang, Rajendran, et al., 2018), and the association between temperament and sympathetic nervous system function (Buthmann et al., 2018). Experiments 3 and 4 focus on sympathetic nervous system function as measured by electrodermal activity (EDA). Specific findings include an interaction between prenatal storm stress and maternal mental health predicting offspring EDA in early childhood (Buthmann, Finik, et al., 2019) and an interaction between prenatal storm stress and offspring sex predicting early childhood EDA. Experiments 5 and 6 reviews the relationship between prenatal maternal stress and child brain development and details preliminary findings from a pilot study of prenatal storm stress and child prefrontal-limbic structure and function.

Chapter 2: Prenatal Storm Stress and Temperament

Note: This chapter contains excerpts from:

Buthmann, J., Ham, J., Davey, K., Finik, J., Dana, K., Pehme, P., Zhang, W., Glover, V., & Nomura, Y. (2019). Infant Temperament: Repercussions of Superstorm Sandy-Related Maternal Stress. *Child Psychiatry & Human Development, 50*(1), 150–162

Buthmann, J., Finik, J., & Nomura, Y. (2018). Sex differences in the relations between infant temperament and electrodermal responses in early childhood. *International Journal of Behavioral Development, 42*(6), 535–542.

Temperament is a broad term that refers to an individual's general patterns of emotionality, reactivity, and sociability (Bates et al., 1979). There is a long history of the study of temperament, its measurement, stability over time, basis in biology, and utility as a predictor of future mental health. Several factors contribute to the widespread study of temperament. It is readily observable through behavior, and therefore, measurable. Many questionnaires have been developed to evaluate the temperament of self and other. Indeed, parent-report measures are widely used to assess the temperament of children, as these characteristics are already observable in infancy. The multifaceted nature of temperament is also appealing, in that several domains of function can be evaluated under the umbrella of temperament. For example, the seminal work of Chess and Thomas (1977) identified nine traits relevant to temperament (activity level, rhythmicity, approach/withdrawal, adaptability, sensory threshold, quality of mood, intensity of mood expression, distractibility, and persistence/attention span) that formed three different profiles: easy, difficult, or slow to warm up temperament. Later work that culminated in the Infant Behavior Questionnaire identified fourteen traits (distress to limitations, sadness, fear, falling reactivity, duration of orientation, cuddliness, soothability, low-pleasure seeking, high-pleasure seeking, activity level, smiling and laughter, approach perceptual sensitivity, and vocal reactivity), which cluster under three higher order traits of negative affect/withdrawal, regulation/effortful control, and surgency/extraversion (Gartstein & Rothbart, 2003; Putnam et al., 2014). Thus, the study of temperament yields a rich and comprehensive approach to understanding many aspects of emotional health and mental wellbeing.

Longitudinal studies have demonstrated the predictive utility of temperament measures, particularly in predicting symptoms of psychopathology. Aspects of temperament including adaptability, emotional reactivity, and activity level at two years of age has been found to predict onset of a psychotic disorder at seven years of age (Sayal et al., 2014). Externalizing symptoms include traits reflecting under-

regulation of emotion such as aggression, hyperactivity, and impulsivity, encompassing psychopathy, and attention deficit-hyperactivity disorder. Internalizing, on the other hand, includes traits reflecting overregulation such as fearfulness, sadness, and inhibition, encompassing depression and anxiety disorders. Negative affect is a temperament measure derived from the Infant Behavior Questionnaire (Gartstein & Rothbart, 2003; Putnam et al., 2014) comprised of traits representing poor emotionality, such as sadness, fearfulness, and distress to limitations. Both internalizing and externalizing symptoms in preschool aged children were predicted by higher levels of negative affect in infancy (Gartstein et al., 2012). Decreased fearfulness and inhibition at three years of age has been found to predict psychopathy in adults (Glenn et al., 2007). Internalizing symptoms have also been associated with less impulsivity and more sadness than control children and children with higher externalizing symptoms (Eisenberg et al., 2001). Surgency/extraversion is also derived from the Infant Behavior Questionnaire, reflecting openness to new stimuli, activity level, and tendency to smile. This measure is predictive of good cognitive and social skills, and low internalizing symptoms (Davis & Suveg, 2014). Effortful control is another measure derived from the Infant Behavior Questionnaire reflecting good attentional control and ability to be soothed. This has been linked with lower externalizing symptoms in school-aged children, a correlation that strengthened with age (Valiente et al., 2003). Assessing temperament early in life may therefore serve as a useful predictor of future symptoms of psychopathology.

There is mixed evidence that sex differences in child temperament may exist. For example, a meta-analysis by Else-Quest, Hyde, Goldsmith, and Van Hulle (2006) found that girls have higher regulation scores and lower surgency scores than boys ages three months to thirteen years. Other studies have found that the age of the child can affect results. Gartstein and Rothbart (2003) reported that after infancy boys have higher activity level scores and lower fearfulness scores than girls. Similarly, others have found girls rated as having a “difficult” temperament, as defined as more irritable and reactive, were more likely to grow out of this categorization than boys by age four (Maziade et al., 1989). Further, another group found that shyness predicted internalizing symptoms in both boys and girls from early childhood to eight and half years of age; however, boys with high activity levels did not demonstrate this trend (Karevold et al., 2011). Others still have found no sex differences (e.g., Schipper et al., 2008). As a whole, early measures of temperament may help researchers and clinicians to identify children at risk for

behavioral problems or psychopathology risk. Early detection efforts are key to improving well-being and preventing or delaying psychopathology onset.

Experiment 1. Infant Temperament: Repercussions of Superstorm Sandy-Related Maternal Stress

One way in which the study of temperament has proven fruitful is in research of the impact of prenatal maternal stress on offspring development. As reviewed in Chapter 1, many researchers have identified maladaptive outcomes, including altered stress response, increased anxiety symptoms, and abnormal social behaviors in offspring prenatally exposed to maternal stress. The ease of data collection via mother's self-report and early emergence of temperament characteristics has made it a widely used measure of signs of dysregulated neurodevelopment in offspring as early as infancy. More stressful life events occurring during pregnancy was associated with 16–18-month-old child temperament, characterized by abnormal regularity, attention, and persistence scores (Zhu et al., 2014). Prenatal maternal anxiety symptoms were associated with elevated emotion dysregulation at four years of age (O'Connor et al., 2002). Independent of maternal history of abuse and anxiety symptoms, McGrath et al. (2008) found that maternal prenatal depression symptoms were associated with significantly worse temperament in offspring at 2-6 months of age. Looking at more objective biological measures, maternal prenatal cortisol indirectly predicted three-month-old infant fearfulness and distress to limitations via low birth weight (Baibazarova et al., 2013). Researchers have also examined the effects of stressors occurring in the postnatal period as having a potential impact on offspring temperament. Maternal stress related to bereavement was associated with lifetime risk of completed suicide if it occurred in the first postnatal year, and with risk of autism spectrum disorder if it occurred in second postnatal year (Class et al., 2014). Pagliaccio et al. (2014) found a negative correlation between stressful life events experienced in the first 3-5 years of life and cortisol levels. Further, that early life stress interacted with variation in polymorphisms in genes related to the HPA-axis system to predict altered hippocampal and amygdala volumes in the left hemisphere at 7-12 years of age (Pagliaccio et al., 2014). Early life institutional rearing and maltreatment have also been associated with emotion dysregulation and amygdala volume (Tottenham et al., 2010) and uncinate fasciculus structural integrity (Hanson et al., 2015), respectively.

Both prenatal and postnatal events appear to have in influence on child temperament and emotion regulation abilities.

Natural disaster studies have also related prenatal storm stress with infant temperament. Tracking children prenatally exposed to the Quebec Ice Storm of 1998, Laplante et al. (2016) found that subjective maternal stress predicted characteristics of difficult temperament, including fussiness, dullness, and need for attention, at six months of age. They also found that maternal illness during pregnancy was associated with infant temperament, but in a manner independent from storm-related stress. A research group following children prenatally exposed to the Queensland Flood of 2011 found that objective including property damage and financial loss, rather than subjective stressors, was associated with increased anxiety symptoms at four years of age (McLean et al., 2018). The group also found that male offspring of mothers that encountered more objective and subjective stressors during pregnancy exhibited more behavioral problems than female offspring (Lequertier et al., 2019). In contrast, 2–12-month-old children displayed more difficult temperament traits in correlation with maternal posttraumatic stress disorder, depression, and hostility, rather than in correlation with prenatal exposure to 2005's Hurricane Katrina (Tees et al., 2010).

Superstorm Sandy, as described in Chapter 1, affected the New York metropolitan area, which is a culturally and ethnically diverse region. We endeavored to examine the relationship between prenatal storm stress and offspring temperament in a racially heterogenous sample. Objective and subjective measures of maternal storm stress were collected prospectively via questionnaire data. The timing of the pregnancy in relation to the occurrence of the storm was also prospectively recorded. At six months postpartum mothers reported on child temperament. We hypothesized that both objective and subjective stress measures would be related to child temperament, specifically that higher levels of both would correlate with high levels of negative affective and low levels of surgency and regulation. As an exploratory aim, we analyzed individual subscales of our objective stress measure to determine if specific aspects of storm-related stress (e.g., injury, financial loss) were more closely related to offspring temperament. Further, we hypothesized that the timing of the storm in relation to the pregnancy would be associated with temperament, such that prenatal exposure would be more closely related than exposure before the pregnancy or after birth.

Experiment 1 Methods

Participants

The study included 380 mother–child dyads part of an ongoing birth cohort study at two New York metropolitan area prenatal obstetrics and gynecological (OB/GYN) clinics. Participating mothers were originally recruited from the prenatal OB/GYN clinic at Mt. Sinai Hospital, which draws patients from East Harlem and the South Bronx in New York City. In 2012, the study expanded recruitment to women in the OB/GYN Department at New York Presbyterian Queens, which draws patients from Queens and Long Island, New York. Mount Sinai Hospital is located approximately 1 mile from the East River, which surged and flooded major roadways in Manhattan. New York Presbyterian Queens is located approximately 2.5 miles from Flushing Bay, which also surged and resulted in flooding, and 15 miles from the Rockaway Beach area that was severely damaged by the storm. Criteria for exclusion included HIV infection, maternal psychosis, maternal age < 15 years, or life-threatening medical complications of the fetus. The study was approved by the institutional review board at Mt. Sinai Hospital, New York Presbyterian Queens Hospital, and CUNY Queens College. Written informed consent was obtained from all eligible women for all study procedures. Detailed information can be found in the study's cohort profile (Finik & Nomura, 2017).

Measures

Temperament. The 91-item Infant Behavior Questionnaire-Revised (IBQ-R; Gartstein & Rothbart, 2003; Putnam et al., 2014) was the primary outcome measure. It is a widely used, reliable, and validated parent-report measure of infant temperament. At 6 months postpartum mothers reported the relative frequency of specified infant behaviors in the past week on a seven-point Likert scale from 1 (never) to 7 (always), with an option to indicate that she had not observed her child in the situation in question. The mean age of the infants at the time the IBQ-R was completed was 6.96 months (SD = 2.71, range = 11.9). The IBQ-R consists of 14 subscales which yield three composite scores (negative affect, emotion regulation, and surgency/extraversion), according to the formula prepared by the creators of the instrument. Negative affect consists of distress to limitations, sadness, fear, and reverse coded falling reactivity. Regulation consists of duration of orientation, cuddliness, soothability, and low pleasure seeking. Surgency consists of high pleasure seeking, activity level, smiling and laughter, approach,

perceptual sensitivity, and vocal reactivity. These composite scales were reported to have high internal reliability, with a reported Cronbach's alpha of 0.91 for negative affect, 0.91 for emotion regulation, and 0.92 for surgency (Putnam et al., 2014).

Superstorm Sandy exposure measures. Our main predictors included objective and subjective measures of Superstorm Sandy related stressors. Specifically, data assessing objective hardship, subjective distress, and timing of the pregnancy in relation to Superstorm Sandy (before, during, or after Superstorm Sandy) were collected immediately after the storm or at the time of enrollment. Each of these measures are described in detail below.

The specific gestational timing during which Superstorm Sandy occurred was calculated based on the date of birth of the child and the day the storm hit the metropolitan New York area (October 29, 2012). They were grouped in three categories: children born before the storm who experienced it early in life (postnatal group, 46% of the sample), children *in utero* during the storm (*in utero* group, 44% of the sample), and children who were not exposed to the storm (preconception group, 10% of the sample).

Objective hardship due to Superstorm Sandy was assessed with the Storm32 measure developed by King and Laplante (2005) based on Bromet and Dew's (1995) review. The questionnaire produces four dimensions of hardship as objectively and systematically as possible. Those four dimensions include threat, loss, scope, and change. Threat measures the degree to which life or injury to self or others was threatened by the event. Financial loss refers to loss of income and property damage. Scope measures amount of time without electricity and telephone. Change is the degree of disruption to living arrangements. Each dimension was weighted equally on a scale of 0 to 8, ranging from no to high hardship due to the disaster. Convergent validity is demonstrated in the correlations among these four scales and with the subjective distress scale described below (all $p < .01$).

The Impact of Event Scale-Revised (IES-R) was used to measure maternal subjective distress related to Superstorm Sandy (Weiss & Marmar, 1997). Questions asked how respondents felt about the disaster in the seven days after the event. The 22-item IES-R, which has a high internal consistency (Cronbach's $\alpha = .92$), assesses three dimensions of post-traumatic stress disorder (intrusion, hyperarousal, and avoidance). Items are responded to on a five-point Likert scale (0 - 4), producing a theoretical range of 0 to 88. Convergent validity is demonstrated in the correlations between this scale

and all four subscales of objective hardship described above and the state anxiety measure described below (all $p < .01$).

Potential confounders. A host of variables potentially related to child temperament or experience during Superstorm Sandy were collected, including demographic characteristics, pregnancy and birth outcomes, and maternal physical and mental health.

Self-reported maternal age, education, parity (i.e., number of lifetime pregnancy including miscarriages and abortions), and marital status were collected at the time of enrollment in the study. Traditional indicators of pregnancy outcomes (e.g., birth weight, gestational age), history of birth complications (e.g., C-section, forceps delivery, premature rupture of membrane), and neonatal problems (jaundice, neonatal intensive care unit admission, shoulder dystocia) were collected at birth via electronic medical records. The number of birth complications formed a birth complication index used for analysis.

Information on two common forms of maternal medical illness during pregnancy, endocrine disorders and infection, was collected both via medical chart reviews and maternal self-report. Endocrine disorders included gestational diabetes mellitus, preeclampsia, and gestation-induced hypertension. Infection included vaginal infection and sexually transmitted infection such as chlamydia, herpes simplex, group B streptococcus, and human papillomavirus.

The Edinburgh Postnatal Depression Scale (EPDS; Murray & Carothers, 1990), a widely utilized self-report inventory of pre- and postnatal depression, measured depression symptomatology during pregnancy. Mothers reported how they felt in the past seven days on a four-point Likert scale. Response options included "*yes, all the time*," "*yes, most of the time*," "*no, not very often*," and "*no, not at all*." The total score on all items, after certain items were reverse scored, yielded the "maternal depression" scale. The inventory has acceptable reliability (Cronbach's $\alpha = .74$ during pregnancy, Cronbach's $\alpha = .79$ after pregnancy), satisfactory sensitivity (79%) and specificity (85%). Depression symptomatology was assessed during the second trimester and repeated at postpartum when infants were assessed at 6 months of age. These two scores are highly correlated with each other and the maternal state anxiety and negative life events measures described below (all $p < 01$.)

The State-Trait Anxiety Inventory (STAI; Spielberger, 1983) measures the temporary condition of state anxiety and long-standing quality of trait anxiety. Each type is assessed by 20 statements that may or

may not describe the participants, responded to on a 4-point Likert scale ranging from 1 "*not at all*" to 4 "*very much so*." The current study used state anxiety to measure of anxiety during the second trimester (Cronbach's α = .92). Convergent validity is demonstrated in the significant correlations between this measure and stressful life events (described below), maternal depression, and subjective storm distress measures described above (all $p < .01$).

The Psychiatric Epidemiology Research Interview Life Events Scale (PERI; Dohrenwend et al., 1978) assessed the occurrence of stressful events in five major areas of life: relationships, health, legal matters, work and financials, and friendships. Mothers reported their experiences with stressful life events in those five areas of life during the second trimester. They endorsed for specific events and reported the valence (i.e., positive or negative) associated with each. This measure is widely used, has been shown to have good validity with narrative reports of life events, and has low intra-category variability (Dohrenwend, 2006). We used the total number of negative life events reported by the mothers as our measure of stressful life events. Convergent validity is demonstrated in the significant correlations between this measure and maternal depression and state anxiety measures (all $p < .01$).

Data analysis

All analyses were conducted using SPSS version 23 (IBM, Inc.). First, descriptive statistics were calculated to evaluate the correlation, mean, and standard deviation (SD) among the three composite temperament scores (i.e., negative affect, emotion regulation, and surgency), nine measures of maternal characteristics, (i.e., state anxiety, stressful life events, prenatal depression, postnatal depression, the number of birth complications, maternal age, parity, education attainment, endocrine disorders and infections), three child characteristics, (i.e., birthweight gestational age at birth, and sex), and objective and subjective Sandy-related stress, and gestational timing of exposure (before, during, or after gestation).

Prior to the analysis, the three temperament subscales were evaluated for normality by examining univariate indices of skewness. These subscales were normally distributed and consequently no transformation was applied. The frequency of missing data in this sample was negligible (less than 0.6%) for all variables except temperament variables (5.2%). No substitutions or imputations were used. Subjects with missing data did not significantly differ from the rest of the sample. Followed by the initial

descriptive statistics, multivariable analysis was conducted using a general linear model (GLM) to examine the main effects of Sandy-related stress variables (i.e., threat, loss, scope, change, subjective distress, and exposure timing) simultaneously on each of the three temperament outcomes separately. All analyses were performed first without potential confounders (Model 1), then with potential confounders, including *a priori* determined maternal and child demographic confounders and prenatal problems (i.e., maternal age, parity, obstetric complication, maternal education, birthweight, gestational age, endocrine illness, and infection during pregnancy; Model 2), and finally with additional normative, non-Sandy related stress (i.e., stressful life events, state-anxiety, prenatal and postnatal depression symptomatology; Model 3). In order to control for Type I errors due to multiple testing (3 models), we made an adjustment using the Benjamini–Hochberg procedure (Benjamini & Hochberg, 1995; Benjamini & Yekutieli, 2001). The model specifications for each temperament dimension are as follows:

Model 1: $Y(\text{temperament})_i = \beta_0 + \beta_1 \text{Threat}_i + \beta_2 \text{Loss}_i + \beta_3 \text{Scope}_i + \beta_4 \text{Change}_i + \beta_5 \text{SubjectiveStress}_i + \beta_6 \text{Timing}_i + \varepsilon$

Model 2: $Y(\text{temperament})_i = \beta_0 + \beta_1 \text{Threat}_i + \beta_2 \text{Loss}_i + \beta_3 \text{Scope}_i + \beta_4 \text{Change}_i + \beta_5 \text{SubjectiveStress}_i + \beta_6 \text{Timing}_i + \beta_7 \text{MotherAge}_i + \beta_8 \text{Parity}_i + \beta_9 \text{ObstetricComplication}_i + \beta_{10} \text{MaternalEdu}_i + \beta_{11} \text{BirthWeight}_i + \beta_{12} \text{GestationalAge}_i + \beta_{13} \text{Endocrine}_i + \beta_{14} \text{Infection}_i + \varepsilon$

Model 3: $Y(\text{temperament})_i = \beta_0 + \beta_1 \text{Threat}_i + \beta_2 \text{Loss}_i + \beta_3 \text{Scope}_i + \beta_4 \text{Change}_i + \beta_5 \text{SubjectiveStress}_i + \beta_6 \text{Timing}_i + \beta_7 \text{MotherAge}_i + \beta_8 \text{Parity}_i + \beta_9 \text{ObstetricComplication}_i + \beta_{10} \text{MaternalEdu}_i + \beta_{11} \text{BirthWeight}_i + \beta_{12} \text{GestationalAge}_i + \beta_{13} \text{Endocrine}_i + \beta_{14} \text{Infection}_i + \beta_{15} \text{NegativeEvents}_i + \beta_{16} \text{PrenatalDepression}_i + \beta_{17} \text{Anxiety}_i + \beta_{18} \text{PostnatalDepression}_i + \varepsilon$

Experiment 1 Results

Demographic Characteristics of Participants

The mean age of mothers was 27. Mothers had, on average, approximately three pregnancies prior to the index pregnancy in the present study. The majority of participants were Hispanic (50%) or Black (24%), then White (15%) or Asian (10%). Slightly more than half of the mothers were single (55%), and 44% were either married or in a common law marriage. Approximately 50% were girls and 50% were boys. Approximately 46% of the total sample was pregnant prior to Superstorm Sandy and their offspring experienced the storm in the postnatal period. Of the postnatal group, a majority were Hispanic (45%) or Black (38%), 66% had single mothers, 53.7% were male, and the mean age of the mother was 27.7 (*SD* = 6.2). Forty-four percent of participants were pregnant at the time of Superstorm Sandy with offspring experiencing the storm in utero. Of the in utero group, more than half were Hispanic (56%), 44.4% had

single mothers, 52% were male, and the mean age of the mother was 27.49 (*SD* = 5.67). The remaining 10% were conceived after the storm. Of the pre-conception group, nearly half were Hispanic (47%), nearly half had single mothers (47.2%), 25% were male, and the mean age of the mother was 26.29 (*SD* = 6.3). The mean age of the infants at the time the IBQ-R was completed was 6.96 months (*SD* = 2.71, range = 11.9). Additional demographic characteristics can be found in Table 2.1.

Correlations and Mean (SD) among Predictors and Child Temperament Scales

Means and standard deviations (SDs) of the outcome variables are as follows: negative affect *M* = 3.42, *SD* = 0.86; regulation *M* = 5.32, *SD* = 0.69; and surgency *M* = 5.26, *SD* = 0.86. Means and standard deviations of the main predictors, Superstorm Sandy related stress, are as follows: threat *M* = 0.44, *SD* = 1.00; loss *M* = 0.68, *SD* = 1.29; scope *M* = 0.43, *SD* = 1.25; change *M* =1.08, *SD* = 1.05; and subjective distress *M* = 7.85, *SD* = 12.88. Means, SDs, and ranges of all variables used in the study can be found in Table 2.2.

Table 2.3 shows the correlations among predictors and the outcomes: the three composite temperament scores of negative affect, emotion regulation, and surgency/extraversion. The three temperament dimensions were correlated with each other. Surgency was positively correlated with regulation and negative affect, and regulation was negatively correlated with negative affect. Surgency was negatively correlated with postnatal maternal depression, maternal age, and maternal education, indicating fewer surgency/extraversion tendencies as those variables increased. Regulation was negatively correlated with prenatal maternal anxiety and depression and postnatal maternal depression, indicating poorer regulation abilities as those variables increased. Negative affect was negatively correlated with prenatal maternal anxiety, indicating more negative affect tendencies as anxiety increased. Negative affect was positively correlated with number of maternal stressful life events, prenatal and postnatal depression, and subjective storm stress, indicating more negative affect tendencies as those variables increased. Exposure timing was correlated with regulation and negative affect such that postnatal exposure to the storm was associated with poorer regulation abilities and more negative affect tendencies.

General Linear Model Predicting Temperament

Results of the conducted multivariable general linear models predicting infant temperament dimensions of negative affect, emotion regulation, and surgency/extraversion are found in Table 2.4.

Timing of storm exposure. As hypothesized, the timing of the occurrence of Superstorm Sandy in relation to the timing of the pregnancy (i.e., before, during, or after the pregnancy) predicted negative affect after controlling for confounders in Model 2 (p = .03) and Model 3 (p = .02, partial η^2 = .01), such that children exposed to these factors postnatally had the greatest negative affect scores. Exposure timing was also marginally associated with regulation in Model 1 (p = .06) and significantly associated in Model 2 (p = .05) and in Model 3 (p = .03, partial η^2 = .02). Similar to negative affect, this suggested a decline in regulation among offspring if they were exposed to the storm during pregnancy or shortly after the birth of the infants. Exposure timing was not significantly associated with surgency.

Table 2.1. *Demographic Characteristics of the Sample Population.*

	Total sample (*N* = 380)		Postnatal (*N* = 175)		*In utero* (*N* = 169)		Preconception (*N* = 36)	
Parents' age	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Mother's age	27.45	5.97	27.67	6.24	27.49	5.67	26.09	6.3
Father's age	29.84	7.20	30.03	8.05	29.94	6.39	6.34	1.05
Parity	2.78	2.01	3.23	2.25	2.43	1.62	2.31	2.07
Race	*N*	%	*N*	%	*N*	%	*N*	%
Hispanic	189	49.7	78	44.6	94	55.6	17	47.2
Black	92	24.2	59	33.7	25	14.8	8	22.2
White	55	14.5	19	10.9	29	17.2	7	19.4
Asian	37	9.7	17	9.7	18	10.7	2	5.6
Other	7	1.8	2	1.1	3	1.8	2	5.6
Marital status	*N*	%	*N*	%	*N*	%	*N*	%
Single	207	54.5	115	65.7	75	44.4	17	47.2
Married	147	38.7	50	28.6	79	46.7	18	50.0
Common Law Marriage	21	5.5	8	4.6	12	7.1	1	2.8
Divorced/separated	3	0.8	1	0.6	2	1.2	0	0.0
Widowed	2	0.5	1	0.6	1	0.6	0	0.0
Education level	*N*	%	*N*	%	*N*	%	*N*	%
Primary school	13	3.4	4	2.3	7	4.1	2	5.6
Some high school	48	12.6	31	17.7	13	7.7	4	11.1
High school GED	84	22.1	47	26.9	30	17.8	7	19.4
Some college	100	26.3	39	22.3	47	27.8	14	38.9
Associate degree	39	10.3	15	8.6	22	13.0	2	5.6
Bachelor's degree	54	14.2	22	12.6	27	16.0	5	13.9
Graduate/professional	42	11.1	17	9.7	23	13.6	2	5.6
Child Sex	*N*	%	*N*	%	*N*	%	*N*	%
Boys	190	50.0	94	53.7	87	51.5	9	25
Girls	190	50.0	81	46.3	82	48.5	27	75

Table 2.2. *Means and Standard Deviations for Outcomes and Predictors.*

	Total sample (*N* = 380)			Postnatal (*N* = 175)		*In utero* (*N* = 169)		Preconception (*N* = 36)	
Child characteristics	Mean	SD	Range	Mean	SD	Mean	SD	Mean	SD
Surgency	5.26	0.86	4.33	5.17	0.89	5.29	0.80	5.21	0.83
Regulation	5.32	0.69	3.30	5.32	0.68	5.15	0.67	5.11	0.57
Negative affect	3.42	0.86	4.86	3.44	0.92	3.60	0.77	3.67	0.72
Birth complications	0.17	0.37	1.00	0.20	0.40	0.15	0.36	0.10	0.30
Birthweight (kg)	3.19	0.61	4.56	3.15	0.57	3.30	0.56	3.09	0.66
Gestational age (wks)	38.93	2.02	18.34	38.92	1.98	39.06	1.98	38.55	2.42
Maternal characteristics	Mean	SD	Range	Mean	SD	Mean	SD	Mean	SD
Postpartum depression	5.7	5.2	24	5.6	5.2	6.1	5.1	6.3	4.8
State anxiety	38.3	11.7	54	37.8	11.9	37.9	11.7	42.3	10.5
Negative life events	1.5	2.0	10	1.6	2.0	1.4	2.0	2.1	2.9
Endocrine illness, N (%)	48	13%	--	30	17%	16	10%	2	6%
Infection, N (%)	77	20%	--	39	22%	31	18%	7	19%
Disaster related factors	Mean	SD	Range	Mean	SD	Mean	SD	Mean	SD
Threat	0.46	1.02	8	0.43	0.08	0.53	0.08	0.31	0.13
Loss	0.73	1.31	8	0.61	0.09	0.85	0.11	0.80	0.22
Scope	0.45	1.28	8	0.44	0.09	0.48	0.12	0.38	0.12
Change	1.20	1.01	8	1.01	0.08	1.18	0.08	1.20	0.23
Subjective distress	7.85	12.89	88	7.04	0.91	8.52	0.98	8.62	3.26

SD = standard deviation

Table 2.3. *Correlation Coefficients for Outcomes and Predictor Variables.*

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Temperament Dimension																					
1. Surgency	--	.52**	.16**	-.07	.06	-.06	-.16**	-.04	-.15**	-.02	-.11*	.02	-.02	-.11	-.02	-.01	-.08	-.06	-.05	-.06	.04
2. Regulation		--	-.26**	-.15**	-.01	-.15**	-.22**	.02	.02	.06	-.05	.04	-.02	-.04	-.01	.01	-.05	.01	-.03	-.06	-.13*
3. Negative affect			--	-.18**	.14*	.18**	.24**	-.06	-.05	-.05	-.01	.03	.01	-.04	-.01	.09	.07	-.08	.04	.11*	.11*
Maternal Characteristics																					
4. State anxiety				--	.29**	.66**	.37**	-.01	-.07	.05	-.05	.03	.13*	-.09	-.07	.14**	.11*	.02	.06	.20**	.08
5. Stressful life events					--	.39**	.19**	.01	-.19**	.14*	-.15**	.05	.16**	-.04	.05	.13*	.03	-.04	-.06	.09	-.01
6. Prenatal depression						--	.49**	.05	.01	.01	-.04	.09	.13*	-.05	.02	.15**	.10	-.04	.18**	.24	.04
7. Postnatal depression							--	--	.07	.05	.17**	-.01	.03	.07	-.01	.02	.02	-.06	-.03	.23**	.05
8. Birth complications								--	.14**	.04	.02	.84**	.01	-.10	-.08	.01	.04	.04	.02	.06	-.09
9. Mother's age									--	.19**	.39**	.13*	-.12*	.08	-.06	.01	.11*	.12*	.07	.06	-.06
10. Parity										--	-.18**	.04	.02	-.06	-.17**	-.01	-.01	-.07	-.12*	-.05	-.19**
11. Education											--	.03	-.16**	.13*	-.02	-.09	.11*	.14**	.06	.03	.07
12. Endocrine illness												--	.01	-.09	-.09	.03	.03	.03	.03	.04	-.12*
13. Infection													--	-.08	.06	.06	-.05	-.09	-.07	.08	-.04
Child Characteristics at Birth																					
14. Birthweight (kg)														--	.58**	-.05	.07	-.02	.07	.03	.06
15. Gestational age															--	-.01	.05	-.05	.08	-.03	-.01
Disaster-related Factors																					
16. Threat																--	.34**	.29**	.19**	.28**	-.01
17. Loss																	--	.40**	.40**	.24**	.07
18. Scope																		--	.33**	.18**	.01
19. Change																			--	.07	.07
20. Subjective distress																				--	.05
21. Exposure timing																					--

Note: See Table 2 for means and standard deviations for each variable.
*$p < .05$, **$p < .01$

Table 2.4. *Summary of Multivariable General Linear Model.*

	A) Negative Affect						B) Emotion Regulation						C) Surgency/Extraversion					
	Model 1[a]		Model 2[b]		Model 3[c]		Model 1[a]		Model 2[b]		Model 3[c]		Model 1[a]		Model 2[b]		Model 3[c]	
	B	*SE*	*B*	*SE*	*B*	*SE*	*B*	*SE*	*B*	*SE*	*B*	*SE*	*B*	*SE*	*B*	*SE*	*B*	*SE*
Threat	0.06	.05	0.09^{+}	.05	0.07	.06	-0.05	.05	-0.11**	.04	-0.12	.04**	0.05	0.05	0.08	.06	0.10^{+}	.06
Loss	0.04	.04	0.11*	.05	0.10*	.05	-0.06+	.04	-0.06**	.04	-0.09**	.04	-0.05	0.04	-0.22	-.04	-0.02	.05
Scope	-0.06^{+}	.04	-0.11*	.05	-0.13**	.05	0.15	.03	-0.02	.04	0.02	.04	-0.02	0.04	0.01	.05	-0.03	.06
Change	0.01	.05	0.06	.06	0.06	.06	-0.08	.04	-0.02	.05	-0.01	.05	-0.01	0.05	-0.03	.06	-0.04	.07
Distress	0.02^{+}	.01	-0.01	.08	-0.01	.02	0.01	.01	0.01	.01	0.01	.01	-0.01	0.01	-0.01	.01	-0.01	.02
Exposure timing	0.09	.07	0.12**	.03	0.15^{+}	.08	-0.16*	.05	-0.13**	.06	-0.16**	.07	0.04	0.07	0.07	.08	0.02	.09
Maternal age	--	--	-0.01	.01	0.01	.01	--	--	-0.01	.01	-0.01	.01	--	--	-0.01	.01	-0.01	.01
Parity	--	--	0.01	.03	-0.01	.03	--	--	-0.01	.02	0.02	.02	--	--	0.02	.03	0.01	.03
Complication	--	--	0.31	.27	0.38	.29	--	--	0.13	.21	-0.01	.22	--	--	-0.58*	.26	-0.65*	.29
Education	--	--	-0.01	.04	-0.04	.04	--	--	0.02	.03	0.40	.03	--	--	-0.04	.03	-0.06	.04
Birthweight	--	--	-0.01	.11	-0.15	.11	--	--	0.04	.08	0.01	.09	--	--	-0.16	.10	-0.14	.12
Gestational age	--	--	-0.01	.03	0.01	.03			-0.01	.08	-0.04	.03	--	--	0.01	.03	-0.14	.11
End illness[d]	--	--	-0.27	.29	0.32	.03			-0.26	.23	-0.40^{+}	.24	--	--	0.63	.28*	0.77	.32*
Infection	--	--	0.04	.13	0.14	.02			-0.03	.09	-0.10	.10	--	--	0.01	.12	-0.02	.14
Life events[e]	--	--	--	--	0.04	.03			--	--	-0.04	.02	--	--	--	--	-0.04	.03
State anxiety	--	--	--	--	0.01	.02			--	--	0.01^{+}	.01	--	--	--	--	-0.01	.02
Pre depression[f]	--	--	--	--	0.01	.01			--	--	-0.01^{+}	.01	--	--	--	--	-0.01	.01
Post depression[g]	--	--	--	--	0.03*	.01			--	--	0.02^{+}	.01	--	--	--	--	-0.01	.02

Note: $^{+}$p < .1, *p < .05, **p < .01. [a]Model 1 includes only Superstorm Sandy related trauma, including threat, loss, scope, change, distress, and the time the participant was exposed to the disaster (prenatal, during, and postnatal); [b]Model 2 includes all predictors in Model 1 after adjusting for maternal age, parity, pregnancy complication, maternal education, birth weight, gestational age, endocrine illness and infection (in pregnancy); and [c]Model 3 additionally include stressful life events, state anxiety, and depression during pregnancy and postnatal depression. [d] End illness denotes endocrine illness; [e] Life events denote stressful life events; [f] Pre depression denotes prenatal depression; and [g] post depression denotes postnatal depression

Disaster related hardship. As hypothesized, objective measures of hardship related to the storm correlated with negative affect and emotion regulation. More time without phone or electricity was associated with an increase in negative affect tendencies ($p = .05$). This association remained significant when other demographics, obstetric, and maternal illness risks were controlled for in Model 2 ($p = .04$), and with further adjustment of prenatal stress unrelated to the storm in Model 3 ($p = .02$, partial $\eta^2 = .03$). More financial loss was also ($p < .01$) associated with increased negative affect. The association remained significant in both Model 2 ($p = .02$) and Model 3 ($p = .05$, partial $\eta^2 = .01$).

More financial loss was associated with decreased regulation abilities in Model 1 ($p = .05$). The association remained significant in both Model 2 ($p = .01$) and Model 3 ($p < .01$, partial $\eta^2 = .01$). Threat of injury was only marginally ($p = .06$) associated with decreased regulation in Model 1, until confounders were adjusted, and the associations became significant in Model 2 ($p = .01$) and Model 3 ($p < .01$, partial $\eta^2 = .01$). There was no notable association with surgency and disaster related hardship.

Subjective distress. Subjective distress related to Superstorm Sandy was not significantly associated with any of the three temperament dimensions.

Experiment 1 Summary

In this study we examined the effects of maternal hardship and subjective distress during Superstorm Sandy and its timing in relation to the index pregnancy on infant temperament. Four findings are notable. First, in line with our hypotheses, aspects of hardship including financial loss and scope of time without electricity or phone access were associated with more negative affect in infancy. Further, decreased emotion regulation was associated with financial loss and threat of injury to self or others. Second, the timing of the exposure to Superstorm Sandy (i.e., before, during, or shortly after birth) was associated with increased negative affect and decreased emotion regulation, such that infants who experienced the storm early in the postnatal period had the highest negative affect and lowest emotion regulation scores. Third, these associations remained significant after adjusting the statistical model for other risk factors, including demographic information, obstetrics, maternal stress unrelated to the storm, maternal health problems during pregnancy, and maternal prenatal and postnatal depression. Fourth,

contrary to expectations, we found no notable associations with the temperament dimension of surgency and storm variables, nor was subjective storm stress related to any dimension of infant temperament.

Our findings are largely consistent with the results of Laplante et al. (2016) who studied a cohort of mothers and children exposed to the 1998 Quebec Ice Storm and unlike the results of Tees et al. (2010) who found that maternal mental health, but not exposure to Hurricane Katrina, predicted infant temperament. Interestingly, we found that maternal subjective distress related to Superstorm Sandy did not predict any of the temperament dimensions (emotion regulation, negative affect, surgency), whereas Laplante et al. found that subjective distress predicted all three dimensions that they measured, namely fussiness/difficulty, dullness, and need for attention. Similarly, a group studying the 2011 Queensland Flood found that subjective maternal distress predicted interpersonal skills in offspring (Yong Ping et al., 2015). Laplante et al. measured infant temperament via the parent-report Infant Characteristics Questionnaire (ICQ; Bates et al., 1979), whereas we used the parent-report Infant Behavior Questionnaire-Revised (IBQ-R; Gartstein & Rothbart, 2003; Putnam et al., 2014). The IBQ-R is thought to encompass a broader range of temperament traits than the ICQ, and is more closely correlated with the Revised Infant Temperament Questionnaire (RITQ), which follows the nine temperament dimensions identified by the New York Longitudinal Study, a defining study on infant temperament (Chess & Thomas, 1977). Furthermore, it is notable that Laplante et al. only assessed children exposed in utero, Tees et al., assessed children exposed in utero or shortly before conception, and we assessed children exposed in utero, shortly before conception, or in the early postnatal period. Our finding that children exposed in the early postnatal period displayed the highest negative affect and lowest emotion regulation scores is therefore unique, as that exposure was not included in prior studies.

Other findings from our research group support the results from this study. An initial analysis found that prenatal maternal depression as measured by a cutoff score of twelve or higher on the Edinburgh Postnatal Depression Scale (EPDS; Murray & Carothers, 1990) predicted decreased smiling and laughter, soothability, recovery from distress, cuddliness, and increased sadness scores at six months of age (Nomura et al., 2019). When stratified by prenatal Superstorm Sandy exposure, children exposed to both prenatal maternal depression and storm-related stress displayed increased activity levels, distress to limitations, approach, and sadness scores. Although this analysis did not include the

higher order temperament dimensions of emotion regulation, negative affect, and surgency, the results point to a similar trend: maternal stress related to the storm predicts poor temperament profiles in offspring as early as infancy. A second study conducted by our research group also supports this. To evaluate the impact of prenatal Superstorm Sandy stress from infancy through early childhood, we examined trajectories of temperament in relation to storm exposure at six, twelve, eighteen, and twenty-four months of age. At six months old, children prenatally exposed exhibited higher scores on high-intensity stimulus pleasure, approach, perceptual sensitivity, and fearfulness, as well as lower cuddliness and duration of orientation/attention scores (Zhang, Rajendran, et al., 2018). The trajectories of children exposed vs. unexposed to the storm prenatally was different as well, such that exposed children has greater increases in activity level and greater decreases in high-intensity stimulus pleasure, approach, and fearfulness from six to twenty-four months of age. Further analysis revealed an interaction between objective and subjective maternal storm stress, such that children exposed to both in utero had greater increases in activity level than all other subjects (Zhang et al., 2018).

These two studies in conjunction with the current study show a clear relationship between maternal stress related to Superstorm Sandy and alterations in infant offspring temperament. Zhang et al.'s findings in particular allude to longer lasting aberrant temperament profiles. The current results that financial adversity and the occurrence of the disaster in the early postnatal period correlated with poor temperament outcomes underscore the importance of psychosocial stability for mother and child. Importantly, this was found in a racially heterogenous sample while statistically covarying for other important factors, including prior stress. Although the stress caused by natural disasters might now be preventable, mental health services and other support for new and expectant mothers who experience natural disasters and other stressful events may mitigate their impact. Increased awareness that maternal stress related to natural disasters may have a negative impact on infant temperament, which has been repeatedly linked to risk for development of future neurodevelopmental problems (Lahey et al., 2008; Rettew & McKee, 2005), is warranted. Taken together, our findings add to the growing body of literature suggesting that periods of early development, both pre- and postnatal, are especially vulnerable to stressors.

Limitations of the current study highlight several areas for future investigation. Mothers are typically considered the best informant of her child's temperament, especially in infancy; however, multiple informants or independent observation of infant temperament could have strengthened our findings. Importantly, we controlled for maternal depressive symptomatology, a known confounder of child temperament reporting. Readers should nonetheless be mindful that maternal perception could have influenced her temperament reporting. Future studies may consider collecting biological samples of child steroid hormones, inflammation markers, and autonomic nervous system function as an objective measure of stress response to bolster temperament score interpretation. Samples of maternal cortisol during pregnancy would have validated our measures of stress. Additionally, it is also possible that being pregnant or having an infant during a natural disaster makes the event more stressful. This is a possibility that was not factored into our analyses. Moreover, identification of trimester-specific vulnerability to prenatal maternal stress was not the focus of this study but would greatly improve understanding of sensitive period for neurodevelopment during gestation. Lack of data about the father of the child constitutes a further limitation. Roughly half of the mothers in the sample were single and unable to provide information about paternal stress of mental health, which would have helped form a more comprehensive picture of factors contributing to the child's development. We must also cautiously interpret our findings in relation to other types of stressors expecting mothers face. Press coverage, environmental cues, and other lasting consequences of natural disasters may make associated stressors substantially different. Similarly, we also would like to acknowledge that reliability of change, one of the disaster-specific scales, was poor. We considered removing this subscale from the analysis, however, as it is one of the four scales of the objective hardship instrument and contains important information about evacuation and change of residence during the storm, we felt the benefits of keeping it in the analysis outweighed the limitation it presented. Nevertheless, findings with those specific question items should be carefully interpreted. Lastly, we must take into account the small effect sizes of the associations reported in this study. However, while interpretation of the results needs to be cautious, it is important to note that a small effect size may still have an angle of trajectory such that the difference grows as children ages.

Despite limited generalizability to pre- and postnatal stressors other than natural disasters (as discussed above), this evidence is a part of a growing body of literature of human and animal models

pointing to the existence of critical periods for neurodevelopment. It is notable that we included children exposed to the storm in the early postnatal period. Although Laplante et al (2016) and Tees et al., (2010) did not, this was the group with the negative temperament characteristics most strongly correlated with Superstorm Sandy. Further investigation of potential mediators and moderators of the relationship between early life and gestational stress and poor infant temperament traits will aid the development of strategies to prevent this outcome in the face of unavoidable, widespread stressful events like natural disasters. These factors may include epigenetics, mother-child bond, or presence of social support structures such as therapeutic intervention.

Compounded importance of the present findings stem from recent calls to increase replication of research from the National Institutes of Health (Collins & Tabak, 2014). Psychological science has suffered from a lack of reproducibility, calling the validity of the results of many studies into questions. This has been particularly difficult in natural disaster research, which presents the unique challenge of collecting data in a timely manner and accurately quantifying participants' disaster experience. Additionally, from the similarities between our findings and that of Laplante et al., (2016) we are able to infer that natural disasters with difference characteristics, e.g., ice versus rain, may have similar effects on offspring. Replication extending these findings to other extraordinary events such as earthquakes and wildfires will further our understanding of the ways in which these occurrences can be passed on from one generation to the next.

The next experiment details electrodermal activity as a measure of sympathetic nervous system function, validity as a neurodevelopment biomarker, and relation with prenatal stress exposure.

Experiment 2. Sex differences in the relations between infant temperament and electrodermal responses in early childhood

Temperament is a valuable measure of child neurodevelopment, predictor of future risk for psychopathological impairment, and relatively stable trait across the lifespan. It is, however, a subjective measure with no one agreed upon method of evaluation. Physiological measures offer a more objective assessment of neurodevelopment with standardized methodologies and clearer links to behavior, personality, and psychopathology. Electrodermal activity (EDA) is one such measure. EDA, also referred

to as skin conductance or galvanic skin response, is a direct measure of sympathetic nervous system (SNS) function. The SNS, thought of as the “fight or flight” system, becomes more active in times of fear, threat, and general stress. It is also known to be irregular in several types of psychopathologies related to the under or over regulation of emotion (Chen et al., 2015; Dieleman et al., 2015). EDA has a moderate to large genetic basis and is somewhat stable over time (Tuvblad et al., 2012). The SNS is intrinsically linked to the stress response system, the HPA axis. Corticotropin releasing hormone stimulates cortisol production from the adrenal glands via adrenocorticotropic hormone, which in turn stimulates the release of norepinephrine from the locus coeruleus (Curtis et al., 2002). Norepinephrine is the primary neurotransmitter driving SNS function, especially in times of stress. EDA measures activity in primarily glabrous skin stemming from eccrine sweat glands stimulated by sympathetic nerves.

EDA is considered a direct measure of the SNS because it is uninfluenced by the parasympathetic nervous system. Cardiac measures of SNS, however, are entangled by vagal influence. However, it is important to note that no one measure of SNS can present a comprehensive portrait of its function (Jänig & Häbler, 2000). Directional fractionation of the autonomic nervous system leads to variability in measures of SNS taken throughout the body (Lacey, 1967). Therefore, the research findings presented below should be interpreted cautiously.

Temperament and other behavioral indices of neurodevelopment have consistently been linked with EDA. Behaviorally inhibited temperaments characterized by high trait fearfulness and inhibitory control has been linked with elevated EDA measures across participants of different ages (Fowles et al., 2000; Scarpa et al., 1997). For example, Fowles et al. (2000) found a positive correlation between fearfulness and inhibitory control and skin conductance level in four-year-old children. A similar trend was found in temperamentally inhibited three-year-old children by Scarpa et al. (1997). Additionally, self-report anxiety symptoms were positively correlated with skin conductance in older 6–17-year-old children (Weems et al., 2005). On the other hand, decreased EDA measures have been associated with features of psychopathy and aggression (Baker et al., 2013; Gao et al., 2015). Proactive – but not reactive – aggression from ages 10-18 years old has been linked with decreased EDA fear conditioning at 18 years of age, indicating deficient learning about the avoidance of stimuli with unpleasant consequences (Gao et al., 2015). Four-six year-old children with both attention deficit hyperactivity disorder (ADHD) and

oppositional defiant disorder (ODD) had fewer skin conductance responses (SCRs) while playing a reward-based game than controls (Crowell et al., 2006), suggesting hyporeactive EDA may underlie impulsive behavior. Further, in a longitudinal model, skin conductance at one year of age predicted aggressive behavior at three years of age (Baker et al., 2013). In sum, a body of literature shows a clear relationship between EDA and temperament traits, such that hyper-responsive EDA is linked with internalizing symptoms and hypo-responsive EDA is linked with externalizing symptoms.

One aspect of the relationship between EDA and temperament that remains unresolved is the role of sex differences. Variability in results may be attributed to men have a higher resting skin conductance level (SCL) than women, and women having higher amplitude SCRs in response to stimuli than men (Boucsein, 1992). This has been supported in one sample of children in which boys had higher SCLs than girls at age eight; however, this trend did not remain after the age of eight, suggesting puberty may affect EDA (El-Sheikh et al., 2010). This is in line with other research that has found that EDA measures increase after puberty in women, but not men (Venables & Mitchell, 1996), making it important to account for the age of subjects in interpreting research results. Studies examining the relationship between EDA, temperament, and sex in prepubertal children are relatively scarce. In one sample of four-year-olds, fearfulness and SCL were more strongly correlated in girls than in boys (Fowles et al., 2000), whereas no sex difference was found in another sample of three-year-old children (Scarpa et al., 1997). The nature of the relationship between sex, EDA and temperament, two measures with predictive value for psychopathology risk, in prepubertal children therefore remains unclear.

We endeavored to clarify the relationship between sex, EDA, and temperament in young children in order to elucidate the early beginnings of children's mental health. EDA was recorded from 18–60-month-old children during a startle probe paradigm designed to elicit SCRs. We hypothesized that internalizing characteristics of temperament including high negative affect, low surgency/extraversion, and high regulation scores would predict greater SCR response rates to startling stimuli. Conversely, we hypothesized that externalizing temperament characteristics including low negative affect, high surgency/extraversion, and low regulation scores would predict lower SCR response rates. We further hypothesized that girls would be more electrodermally reactive to the startling stimuli than boys,

regardless of temperament. Lastly, we hypothesized that sex would moderate the relationship between temperament and EDA, such that girls with high negative affect, low surgency/extraversion, and high regulation scores would have higher rates of SCR responses than their male counterparts.

Experiment 2 Methods

Participants

A total of 150 subjects drawn from a larger longitudinal study of neurodevelopment were recruited from prenatal obstetrics and gynecological clinics (OB/GYN), as described in Experiment 1. Data was collected during the second trimester (baseline), throughout the pregnancy, and at a follow-up assessment with their children (ranging from 18-60 months in age, M = 35.1, SD =13.6). Child's infant temperament was collected via mother-report (M = 7.6 months of age, SD = 3.6) using the Infant Behavior Questionnaire (IBQ-R). When a child reached 18 months of age (ranging from 18 to 60 months, M = 35.14, SD = 13.6), the family was invited to the assessment center for a follow-up assessment of several neurodevelopmental indices. At this time, each child completed a psychophysiological assessment of startle response. Informed consent was obtained from the mothers of the children prior to participation and all study procedures were approved by the institutional review board at the assessment center in accordance with the standards set forth by the 1964 Declaration of Helsinki. Of these 150 mothers, 15 were excluded for lack of completed temperament questionnaires. An additional 10 were excluded due to child movement artifact resulting in distorted signal during at least half of the psychophysiological recording period, leaving 125 participants for this current study. Approximately 32.8% of mothers are white Hispanic, 20.8% Black, 17.6% mixed-Hispanic, 11.2% Caucasian, 9.6% Asian, 6.4% Black-Hispanic, 1.6% identified as "other." 51% of children were female. Independent samples t test indicated that children missing data did not significantly differ from children with complete data in terms of sex, age, behavioral startle response, skin conductance response rate, or the temperament dimensions of negative affect, surgency, or regulation. A full description of the parent study can be found elsewhere (Finik & Nomura, 2017).

Materials

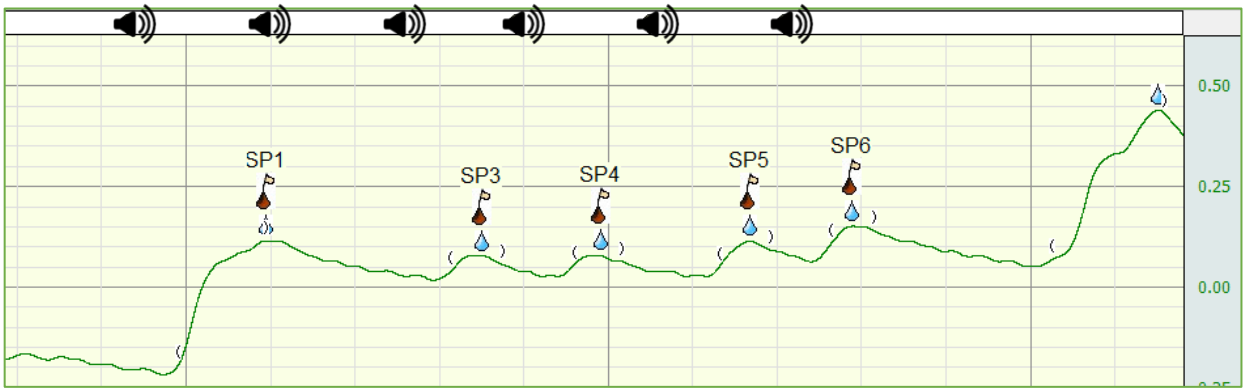
Temperament. Mothers completed the Infant Behavior Questionnaire-Revised (IBQ-R, Gartstein & Rothbart, 2003) at around 6 months postpartum (M = 7.6 months of age, SD = 3.6). See Experiment 1 for more information on the measure. Cronbach's alpha = .75 for surgency, .56 for negative affect, and .45 for regulation.

Electrodermal activity. A BioNomadix Wireless EDA transmitter connected to two pre-gelled disposable Ag/AgCl electrodes via snap connection transmitted electrodermal activity data at 2000 Hz to the BioPac MP150 acquisition system and a computer running AcqKnowledge software. Electrodes were placed on the left side of the left foot of the children, with .05 molar NaCl electrode gel added to better conduct the signal between skin and electrode. Mothers were present in the room with the child during recording to mitigate any distress unrelated to stimulus presentation. 60 Hz and 1 Hz noise were filtered from the signal. A skin conductance response (SCR) specific to a startle stimulus was defined as an increase in sweat production of at least 0.02 μS occurring 1–7 seconds after the auditory stimulus. Figure 2.1 is a representation of a raw recording of the signal collected. Each of the increases in the signal marked with a water droplet above it indicates an SCR has been identified.

Procedure

Children were seated next to their mothers for the duration of the experiment in a room kept at 71.6–75.2F, as per Braithwaite, Watson, Jones, and Rowe (2013). In order to keep background sound to a minimum, the door to the experiment room was kept shut throughout, with another empty room and shut door between the experiment room and a communal hallway. Participants were asked to remain still and passively watch the computer monitor in front of them. The startling stimuli were presented on a computer running E-Prime 2.0 while psychophysiological signals were recorded. A period of approximately 1 minute of a series of six 90 dB auditory stimuli 1 second in duration with varying inter-stimulus intervals of 6–12 seconds was preceded and followed by 3-minute baseline period videos with no startling stimuli depicting nature scenes. Each of the speaker icons in Figure 2.1 represents one of the startling stimuli.

Figure 2.1. *EDA signal recording during startle probe paradigm*



Note: The signal is measured in μS. Each speaker icon represents one of six startle probes, SP1-6. The water droplet icons represent a skin conductance response (SCR) has been identified. The flags labeled SP1, 3-6 indicate the SCR is specific to that startle probe.

Analysis

SCR analysis. The percentage of startle probes that successfully elicited a skin conductance response (SCR), is referred to as SCR rate and each of the three temperament dimensions from the IBQ (surgency, negative affect, regulation) were dichotomized using median splits to determine high and low scores within the current sample. Nonspecific skin conductance responses occurring during the baseline period were also quantified as a continuous variable. Two trained research assistants visually inspected the raw signal for each subject and reached a consensus about whether or not the file should be excluded due to artifact (n = 15). Independent samples t tests indicated that there were no differences between data with artifact and data without artifact with respect to child sex, age, behavioral startle response, or the three temperament dimensions (all $p > .17$).

Behavioral data. A trained research assistant reviewed video recorded of the experiment to code for overall behavioral response to the startling stimuli. Behavior was coded on a scale from 0–3. A score of 0 represented a total lack of behavioral startle response, whereas a score of 3 represented an extreme startle response characterized by movement, facial expression, or vocalization indicating intense surprise.

Statistical analysis. Analysis of descriptive statistics and Pearson correlation analysis was conducted for the whole sample and for each sex to observe associations between child sex, age, behavioral startle response, baseline nonspecific skin conductance occurrence, number of skin conductance responses specific to the startling stimuli, and the three temperament dimensions of interest

(see Table 2.5). Pearson chi square analysis was used to examine the association between SCR rate (low vs. high) and three temperament dimensions (low vs. high). Odds ratios (OR) were calculated. This was followed by the same chi square analysis with additional Breslow Day procedure. This procedure tests the differential magnitude of association between the two factors, that is, temperament and EDA, by the third factor, that is, sex, serving as a formal test of interaction. ORs for each stratum (boys and girls) were separately calculated. In order to adjust for potential confounders, binomial logistic regressions were performed, predicting a binary measure of SCR rate. Age, race of the child, number of nonspecific skin conductance responses (NSSCRs) occurring during the baseline period, and behavioral startle response were a priori determined as confounders of sex. To correct for multiple testing, the Benjamini-Hochberg procedure was followed with a 15% false discovery rate (Benjamini & Hochberg, 1995). The model specifications are as follows:

$$Y(\text{SCR rate})_i = \beta_0 + \beta_1 \text{Temperament}_i + \beta_2 \text{Age}_i + \beta_3 \text{Race}_i + \beta_4 \text{NSSCRs}_i + \beta_5 \text{BehavioralStartle}_i + \varepsilon_i$$

Table 2.5. *Pearson's correlations between variables of interest.*

	1	2	3	4	5	6	7	8	*Mean*	*SD*	Range
1. Gender	–	−.12	.14	−.12	−.08	.18*	.20*	.08			
2. Child age		–	.12	−.04	.12	−.07	−.15	.23**	34.56	13.40	48.26
3. Behavioral startle			–	−.04	−.06	.05	.20*	−.02	0.72	0.98	3.00
4. Baseline nonspecific skin conductance responses				–	.37**	.13	.07	.09	2.70	4.03	19.00
5. Skin conductance response rate					–	.02	.03	.08	30.93%	31.23	100%
6. Surgency						–	.09	.37**	5.42	0.83	4.77
7. Negative affect							–	−.32**	3.69	0.84	4.77
8. Regulation								–	5.38	0.68	3.64
Boys	**1**	**2**	**3**	**4**	**5**	**6**	**7**		***Mean***	***SD***	**Range**
1. Child age	–	−.09	−.01	.22	−.08	−.17	.23		36.19	13.71	45.21
2. Behavioral startle		–	−.03	−.04	−.03	.20	−.26*		0.58	4.46	3.00
3. Baseline nonspecific skin conductance responses			–	.27*	.19	.25	.06		3.19	4.46	19.00
4. Skin conductance response rate				–	.01	.11	−.002		33.33%	32.36	100%
5. Surgency					–	−.02	.46**		5.27	0.92	4.77
6. Negative affect						–	−.38**		3.52	0.80	3.85
7. Regulation							–		5.32	0.75	3.64
Girls	**1**	**2**	**3**	**4**	**5**	**6**	**7**		***Mean***	***SD***	**Range**
1. Child age	–	.32*	−.12	.00	−.02	−.08	.26*		33.01	13.00	44.91
2. Behavioral startle		–	−.00	−.05	.06	.16	.15		0.86	1.06	3.00
3. Baseline nonspecific skin conductance responses			–	.49**	.11	−.09	.16		2.22	3.53	19.00
4. Skin conductance response rate				–	.07	−.02	.20		28.57%	30.15	83.33%
5. Surgency					–	.14	.22		5.56	0.71	2.95
6. Negative affect						–	−.30*		3.85	0.85	4.17
7. Regulation							–		5.44	0.61	2.94

Note. Boys $n = 62$, Girls $n = 63$. Item anchors: behavioral startle (0 = *no visible startle*, 3 = *extreme startle response*), surgency, , negative affect, and regulation (1 = *behavior never occurs*, 7 = *behavior always occurs*).
*$p < .05$; **$p < .01$.

Experiment 2 Results

Pearson Correlations

As seen in Table 2.5, behavioral startle was positively correlated with negative affect. The rate of skin conductance responses to the startling stimuli was positively correlated with the number of nonspecific skin conductance responses that occurred during the baseline period. Lastly, regulation was positively correlated with child age and surgency, and negatively correlated with negative affect.

Main effects predicting SCR rate

Temperament. There was no sex difference in surgency, $X^2(81) = 1.4$, p = .23, OR = 0.6, negative affect, $X^2(1) = 1.2$, p = .28, OR = 1.5, or regulation, $X^2(1) = 1.8$, p = .84, OR = 1.7.

Sex. Pearson Chi-square between sex and SCR rate was not significant, $X^2(1) = 0.1$, p = .75, OR = 0.9, suggesting there were no notable sex differences in SCR rate.

Table 2.6. *Chi-square test of association between temperament and skin conductance response rate by sex.*

			Skin conductance response rate					
Scale			Low (*n*)	High (*n*)	$X^2(1)$	*p* value	OR	Homogeneity test of OR
Positive affect	Boys	low	7	26	6.45	.01	4.17	
		high	13	13				$p = .016$
	Girls	low	11	14	.70	.40	1.56	
		high	11	25				
Negative affect	Boys	low	13	20	2.20	.14	2.33	
		high	6	18				$p = .32$
	Girls	low	10	15	.01	.91	1.07	
		high	12	22				
Surgency	Boys	low	9	19	.30	.59	.74	
		high	11	20				$p = .04$
	Girls	low	15	14	5.73	0.02	3.71	
		high	7	25				

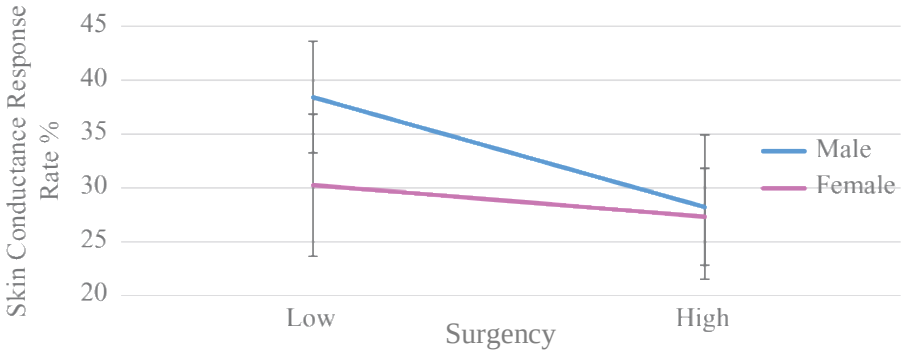
Note. OR = odds ratio; Boys $n = 55$, Girls $n = 53$.

Interactions between temperament and sex on SCR rate

Chi-square and OR between each of the three temperament dimensions were computed. The IBQ and the SCR rate were stratified by sex and a formal test of interaction, Breslow-Day tests, was used to determine whether the ORs for SCR rate by temperament was homogeneous for each sex, or stratum. See Table 2.6 for full results.

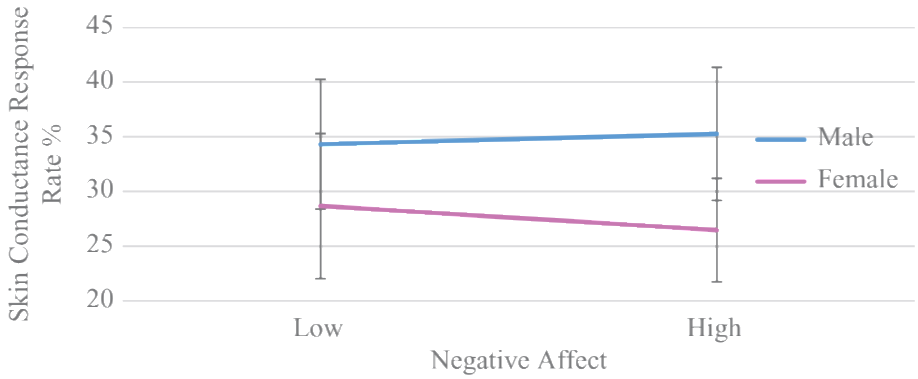
Surgency. There was a significant association between surgency and SCR rate among boys [X^2(1, n = 62) = 6.5, p = .01, OR = 4.2] but not among girls, X^2(1, n = 63) = .7, p = .40, OR = 1.6] (see Fig. 2.2). The mean surgency score for boys with low SCR rates (M = 5.5, SE = .21) was greater than boys with higher skin conductance response rate (M = 5.2, SE = .14). Boys with lower surgency scores had greater SCR rates (M = 37.0%, SE = 5.2) than boys with higher surgency scores (M = 28.2%, SE = 6.7). Overall, low surgency temperament scores were associated with an over 4-fold greater rate of SCR for boys. No notable association between SCR rate and surgency was found among girls. Breslow-Day tests indicated that the magnitude of risk for low SCR rate posed by surgency significantly differed by sex, X^2(1) = 5.8, p = .016. This suggests the strata were heterogeneous, providing evidence for interaction such that low surgency boys were at greater odds for high SCR rate, or sympathetic reactivity, and girls' odds for SCR rate unaffected by surgency.

Figure 2.2 *Surgency and sex predicting skin conductance response rate.*



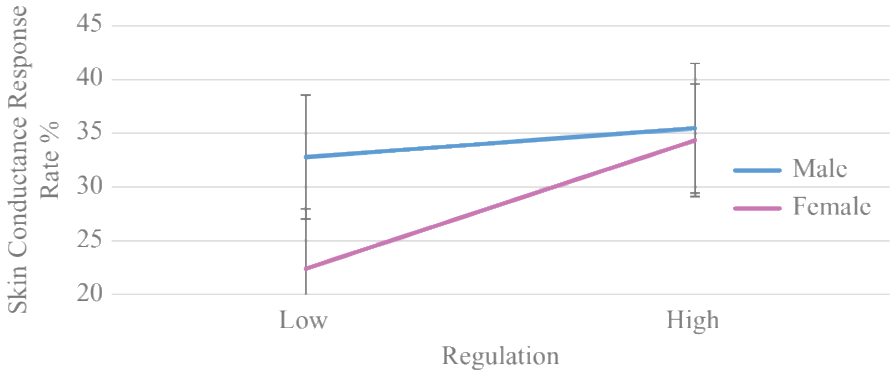
Negative affect. Pearson Chi-square between temperament dimension of negative affect and SCR rate by sex was not significant for boys, X^2(1, n = 62) = 2.2, p = .14, OR = 2.3, or girls, X^2(1, n = 63) = .01, p = .91, OR = 1.1 (see Figure 2.3). Further, Breslow-Day tests indicated that the difference in risk for high or low SCR rate posed by negative affect did not significantly differ by sex, X^2(1) = 1.0, p = .32.

Figure 2.3 *Negative affect and sex predicting skin conductance response rate.*



Regulation. Pearson Chi-square between temperament dimension of regulation and SCR rate by sex was significant among girls, $X^2(1, n = 63) = 5.7$, p = .017, OR = 3.8, but not among boys, $X^2(1, n = 62) = .3$, p = .59, OR = 0.7 (see Figure 2.4). The mean regulation score for girls with low SCR rate was lower (M = 5.2, SE = .1) than that of girls with higher SCR rates (M = 5.6, SE = .1). Girls with lower regulation scores had lower SCR rates (M = 22.2%, SE = 5.4) than girls with higher regulation scores (M = 34.4%, SE = 5.2). Overall, higher regulation scores were associated with a nearly 4-fold greater rate of SCR rate for girls. No observable differences were found for boys. Breslow-Day tests indicated that the magnitude of risk for low-SCR rate posed by regulation significantly different by sex, $X^2(1) = 4.3$, p = .04. This suggests the strata were heterogeneous, with an interaction indicating that low regulation increased odds of low SCR rate, or low sympathetic reactivity, in girls. The odds for boys were unaffected by regulation.

Figure 2.4. *Regulation and sex predicting skin conductance response rate.*



Logistic regression. Logistic regression analysis after controlling for age, race of the child, behavioral startle response, and number of baseline nonspecific skin conductance responses revealed that the observed associations between SCR rate and temperament were almost identical. Specifically, high surgency predicted greater SCR rate, or sympathetic reactivity, in boys (OR = 3.8, p = .04), but not in girls. There were no significant results related to negative affect in boys or girls. High regulation predicted lower SCR rate, or sympathetic reactivity, in girls (OR = 4.2, p = .03), but not in boys. These results remained significant following the Benjamini-Hochberg procedure for multiple testing with a false discovery rate of 15%. See Table 2.7 for full results.

Table 2.7. *Age and race adjusted binomial logistic regression predicting skin conductance response rate by sex.*

	B [95% CI]	*df*	OR	*p*
Surgency				
Boys	1.3 [1.04, 14.03]	1	3.8	.04*
Girls	−.36 [0.20, 2.44]	1	0.7	.57
Negative affect				
Boys	−.73 [0.12, 1.98]	1	0.5	.31
Girls	.18 [0.33, 4.33]	1	1.2	.78
Regulation				
Boys	0.1 [0.27, 4.83]	1	1.1	.86
Girls	−1.4 [0.07, 0.86]	1	4.2	.03*

Note. OR = Odds Ratio; Boys $n = 55$, Girls $n = 53$.
*$p < .05$

Experiment 2 Summary

This study had three main findings. First, we found no main effect of sex or temperament predicting SCR rate, contrary to our hypotheses that girls would be more electrodermally reactive than boys and that in boys and girls internalizing characteristics of temperament including high negative affect, low surgency/extraversion, and high regulation scores would predict greater SCR response rates. Second, we found that boys with low surgency scores had greater SCR rates than those with high scores. Third, we found that girls with high regulation scores had greater SCR rates than those with low scores.

This is the first study to document an interaction between sex and temperament on a measure of SNS reactivity. The presence of an interaction but lack of main effects of sex or temperament predicting EDA may indicate that the two are intrinsically linked in young children. Our finding that boys with low surgency traits were more sympathetically reactive to startling stimuli than other boys, has some support in the literature. Surgency has a negative correlation with internalizing symptoms (Davis & Suveg, 2014), which have been correlated with higher EDA measures (Weems et al., 2005). These boys with low positive affect scores and high EDA reactivity may therefore be at risk for the development of internalizing symptoms. Contrary to prior research (Gartstein & Rothbart, 2003), we did not find that boys had higher positive affect score than girls. It is possible that this sex difference emerges later in life. Our last finding was that girls with high regulation traits were more sympathetically reactive to startling stimuli than girls with low regulation traits. This may indicate that girls who tightly regulate their emotions are at risk for internalizing symptoms.

Women disproportionately develop internalizing disorders such as depression and anxiety disorders and men disproportionately develop externalizing and neurodevelopmental disorders (Rutter et al., 2003). Examining potential developmental trajectories of sex differences in temperament and psychophysiological reactivity could help to explain the origins of this phenomenon. For example, a female tendency to over-regulate emotions may predispose women toward behavioral inhibition, and, in some cases, develop internalizing disorders. Indeed, researchers have associated traits such as behavioral inhibition and low impulsivity with internalizing (Eisenberg et al., 2001). Similarly, low regulation in boys relative to girls reported in the literature may predispose them to develop disorders

such as ADHD. Identifying early risk via temperament and autonomic function could allow for intervention before symptom onset.

Consideration of the limitations of this experiment are important for the interpretation of its findings. Although statistical adjustment for age did not alter results the age range in the sample was large, and future work should examine narrower age windows. Further, although race was not a significant predictor in the logistic regressions, there are known race effects of EDA in the literature, and a more nuanced analysis of race within our racially heterogenous sample may reveal important differences (El-Sheikh et al., 2010). Moreover, we broadly dichotomized the temperament domains and electrodermal reactivity as “high” and “low” using median splits. This dichotomy does not necessarily represent pathological levels of each measure but allowed for an examination of general tendencies of each. Future analysis with more than two categories or with diagnostic cutoffs may be more clinically informative.

Discussion

Experiments 1 and 2 explored the nature of temperament. Experiment 1 evaluated temperament in infants prenatally exposed to Superstorm Sandy. We found that higher negative affect scores were associated with exposure to financial damages and loss of electricity and phone related to the storm. Poor emotion regulation scores were associated with both financial damages and threat or actual injury to self or other. Further, experiencing the storm as an infant was associated with high negative affect and low emotion regulation scores. These findings remained significant after introducing potentially confounding variables including obstetrics, maternal stress unrelated to the storm, maternal health problems during pregnancy, and maternal prenatal and postnatal depression.

In Experiment 2 we delved deeper into temperament to investigate its relationship with a more objective biological measure of reactivity, EDA. We found no main effect of sex or temperament predicting SCR rate. We had hypothesized that girls would be more electrodermally reactive than boys, which was not supported. We had also hypothesized that internalizing characteristics of temperament including high negative affect, low surgency, and high regulation scores would predict greater SCR response rates, which was not supported either. We did, however, find interactions between temperament

and sex. Boys with low surgency scores had greater SCR rates than those with high scores. Lastly, girls with high regulation scores had greater SCR rates than those with low scores.

Taken together, these studies illuminate the nature of temperament in young children. Based on the results observed, temperament is both influenced by prenatal and early postnatal stressors and intrinsically linked with sex and SNS function. Better understanding of these factors and their trajectories may help to unravel mental health in young children and identifying when abnormality arises.

As rates of childhood psychopathology increase (Bitsko et al., 2018), it becomes imperative to develop better indicators of risk earlier in life. Identifying precursors for psychopathology early in life, such as atypical behavioral and physiological reactivity, provides mental health practitioners the opportunity for early intervention. It also lends insight into the ways through which psychopathology develops. The National Institute of Mental Health's Research Domain Criteria (RDoC) initiative emphasizes the need to integrate pathophysiological consideration in our understanding of mental illnesses (Insel et al., 2010). Knowledge of biomarkers of risk, like electrodermal reactivity, as well as risk factors such as prenatal maternal stress exposure, can improve efforts into psychopathology intervention and prevention.

Electrodermal reactivity and the ways in which it is associated with prenatal maternal stress is the focus of Experiments 3 and 4. Guided by the findings presented in this chapter and the National Institute of Mental Health's call for the integration of pathophysiology, we endeavored to evaluate the relationship between prenatal maternal stress and offspring electrodermal activity. If prenatal/early postnatal maternal storm stress is associated with altered temperament profiles, and the relationship between temperament and electrodermal reactivity is moderated by sex, then the association between prenatal maternal stress and offspring electrodermal reactivity may in fact be a complicated one to unravel. The following experiments endeavor to do so.

Chapter 3: Prenatal Storm Stress and Electrodermal Activity

Note: This chapter contains excerpts from:

Buthmann, J., Finik, J., Ventura, G., Zhang, W., Shereen, A. D., & Nomura, Y. (2019). The children of Superstorm Sandy: Maternal prenatal depression blunts offspring electrodermal activity. *Biological Psychology*, *146*, 107716.

Experiment 3. Sex moderates link between electrodermal reactivity and prenatal stress exposure

Experiments 1 and 2 of this dissertation showed that maternal experience during Superstorm Sandy in the prenatal and early postnatal periods were associated with infant temperament characterized by higher negative affect and lower emotion regulation scores. Experiment 1 uncovered a complicated relationship between temperament, electrodermal activity, and sex in young children. Experiment 2 added another layer to these questions and explored the relationship between electrodermal activity, and sex in young children. These findings guide the expectations in the analyses presented in this chapter regarding prenatal maternal stress and offspring electrodermal reactivity.

Uncertainty remains as to whether sex differences in offspring outcomes differ with prenatal maternal stress exposure, including natural disaster related prenatal maternal stress. Although a number of studies have found no differences between male and female offspring (Austin, Hadzi-Pavlovic, et al., 2005; Class et al., 2014; McLean et al., 2018), many others have documented such differences. In a rat model, prenatal maternal stress led to increased anxiety-like behaviors and social behaviors in females, but not males, who exhibited memory deficits not apparent in females (Schulz et al., 2011). Maternal daily life stress was found to predict symptoms of schizophrenia spectrum disorders in male, but not female offspring (Fineberg et al., 2016). In a large birth cohort study, high maternal prenatal cortisol levels predicted greater negative emotionality at five weeks of age in girls and lower negative emotionality in boys (Braithwaite et al., 2017). Three-year-old girls of mothers who reported high levels of mental health symptoms during pregnancy had higher cortisol levels than girls of mothers reporting lower levels of symptoms, whereas no effects were seen among boys (de Bruijn et al., 2009). Looking specifically at natural disaster related prenatal maternal stress, maternal traumatic stress was linked with more behavior problems in girls than boys in studies of both the 1998 Quebec Ice Storm and the 2011 Queensland Flood (Jones et al., 2019; Lequertier et al., 2019). Similarly, prenatal maternal stress from the 2008 Iowa Flood correlated with increased HPA axis reactivity in girls (Yong Ping et al., 2015). Overall, the literature

points to heightened reactivity in girls exposed to prenatal maternal stress and little to no significant effects in males.

Impairments in emotion regulation, expression, and processing are prominently featured in an array of psychological disorders (e.g., anxiety, attention-deficit hyperactivity disorder, depression, see Beauchaine, 2012 and Keenan, 2000) and correlate closely with measures of ANS function. The parasympathetic (PNS) and sympathetic (SNS) divisions of the ANS have both been studied in this context. For example, Calkins and colleagues found that patterns of parasympathetic control of the heart during emotionally challenging tasks characterized by withdrawal of the vagus nerve were associated with better social skills and lower negativity and externalizing problems (Calkins et al., 2007). Looking specifically at links with prenatal maternal stress, Tibu and colleagues found a correlation between maternal prenatal anxiety and lower vagal reactivity in infant boys, as well as a correlation between low birth weight for gestational age and higher vagal reactivity in girls (Tibu et al., 2014).

The SNS also correlates with neurodevelopmental indices. Elevated electrodermal activity (EDA), reflecting greater SNS activity, is typically associated with internalizing, anxiety, inhibition, and fearfulness (Fowles et al., 2000; Scarpa et al., 1997; Weems et al., 2005). Externalizing symptoms, attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder (Crowell et al., 2006), and aggression (Baker et al., 2013) have been linked with lower levels of EDA. Sex differences in the EDA of children are not clear. Prior research findings range from no significant differences (Scarpa et al., 1997), sex differences as a function of age (El-Sheikh et al., 2010), and sex differences moderated by behavioral differences (see Experiment 2 and Fowles et al., 2000). Specifically, Fowles et al. found that the association between EDA and fearfulness was stronger in girls than boys, whereas in Experiment 2 we found that greater EDA reactivity was linked with low surgency in boys and high emotion regulation in girls.

Few studies have investigated the relation between prenatal maternal stress and offspring autonomic reactivity. With prenatal maternal stress defined as maternal mental health and psychosocial stress, van Dijk et al. found no significant differences in resting cardiac sympathetic and parasympathetic measures between exposed and unexposed children (van Dijk et al., 2012). Trajectories of cardiac sympathetic and parasympathetic reactivity from six months to five years of age have been associated

with prenatal maternal lack of social support and socioeconomic adversity, respectively (Alkon et al., 2014). Maternal prenatal mental health and adversity was also linked with reactivity to emotional challenge, via greater SNS activity and lower PNS in infants, (Suurland et al., 2017) and greater cardiovascular reactivity to stressors in children 7-9 years of age (Fan et al., 2016). Since sex differences in the autonomic response function of children exposed to prenatal maternal stress have not been reported thus far, the aim of the current study was to examine whether the impact of natural disaster related prenatal maternal stress on SNS reactivity differed across sex in a sample of children exposed to prenatal storm stress.

We examined whether the relation between prenatal storm stress on EDA reactivity differed between girls and boys. EDA reactivity to startling auditory stimuli was measured in 2–5-year-old children who either were or were not exposed to the storm prenatally. We hypothesized that (1) girls would have greater EDA reactivity than boys independent of prenatal storm stress status, (2) children exposed to prenatal storm stress would have greater EDA reactivity than unexposed children independent of sex, and (3) the EDA reactivity of children exposed to prenatal storm stress would differ by sex, such that girls would be more reactive than boys. We expected that the results of these analyses will shed light on vulnerability to prenatal insults and sex differences in neurodevelopment and psychopathology risk in early childhood.

Experiment 3 Methods

Participants

Participants were recruited at prenatal clinics in the New York City metropolitan area as part of a longitudinal birth cohort study, as described in Experiment 1. 330 mother-child dyads completed at least one follow up assessment. Children were excluded if they were born more than nine months after Superstorm Sandy hit the New York area (n = 45). There were no significant differences in age, race, sex, maternal marital status, or maternal education level between those who were and were not excluded (all $p < .10$). Another 86 were excluded due to excess artefact from movement or equipment malfunction during EDA recording. There were no significant differences in age, race, sex, maternal marital status, or maternal education level between those who were and were not excluded (all $p < .25$).

Procedures

As described in Experiment 2, electrodermal activity was recorded from mother-child dyads during a startle probe paradigm. The dyads watched a three-minute, non-arousing, child-friendly video of zoo animals to establish baseline autonomic function. This was followed by a series of six 90 dB auditory stimuli occurring at varying interstimulus intervals of six-twelve seconds. All stimuli were presented via E-Prime 2.0.

Measures

Electrodermal activity. Electrodermal activity was recorded via a Biopac MP150 acquisition system and a Dell computer running AcqKnowledge 4.4 software (Biopac, Goleta, CA) as described in Experiment 2. The skin conductance response magnitude was calculated by the software as the average amplitude of each skin conductance response specific to a startle probe multiplied by the percentage of the startle probes that elicited a response. Skew and kurtosis of the skin conductance magnitude was reduced by adding one to the magnitude and taking the log, a commonly used transformation.

Superstorm Sandy exposure. Prenatal exposure to Superstorm Sandy was calculated based on date of birth in relation to the date the storm hit the New York City area (October 28, 2012). Children in utero at that time were categorized as exposed, and children who were not were categorized as unexposed.

Maternal depression. The widely used Edinburgh Postnatal Depression Scale (EPDS) was administered to mothers during the second trimester (Murray & Carothers, 1990). The ten question self-report scale screens mothers for depressive symptoms. Each question has four answer choices which refer to the frequency of the mothers' depressive feelings within the prior seven days. Any endorsement of self-harm was immediately reported to the primary investigator and proper referrals were issued.

Maternal anxiety. The 40 question State-Trait Anxiety Inventory (STAI, Spielberger, 1983) was administered during the second trimester to measure transient state anxiety and trait, or dispositional, anxiety. Twenty statements address each type of anxiety and participants indicated whether the statement was applicable using a four-point Likert scale: one being "not at all" and four being "very much

so." The STAI is the most widely used anxiety scale among pregnant populations, though it has been validated for use amongst individuals who are not pregnant (Newham et al., 2012). In the current sample Cronbach's Alpha was .90 for state anxiety and .90 for trait anxiety, indicating excellent internal consistency.

Child race and other demographic information was self-reported upon recruitment. Maternal age was self-reported during yearly follow-ups and verified using their self-reported date of birth.

Statistical analyses

Initial analyses were conducted in SPSS 25. Independent samples t-tests evaluating differences in skin conductance response magnitude between boys and girls or between prenatally exposed and prenatally unexposed children were conducted. A grouping variable was created to form four groups: boys not prenatally exposed (n = 54), boys prenatally exposed (n = 48), girls not prenatally exposed (n = 43), and girls prenatally exposed (n = 54), with a total N = 199. Demographic information by group is provided in Table 3.1. General Linear Models with the grouping variable predicting skin conductance response were run with and without covariates. Child age, race, maternal marital status, and maternal education were included as covariates.

To account for the hierarchical structure of the data, of children nested within the same family unit (i.e., siblings), we subsequently ran additional statistical analyses in R software. No significant differences were detected across demographic characteristics between those who did and did not complete the electrodermal startle paradigm. We ran Linear Mixed Effects Models to account for statistical dependency of children nested within the same family unit (i.e., siblings) and further examine potential sex differences. This methodology also provides accurate estimates under the assumption that data is missing at random. We first built an empty model to compute the interclass correlation coefficient (ICC) (Shrout & Fleiss, 1979) to assess the degree of clustering by family unit. In the subsequent models we included 1) exposure to prenatal stress, and 2) sex, and 3) the interaction (Prenatal stress*Sex). Finally, we included maternal age, race, depression, and anxiety identified a priori to our final model. To account for potential inflated type-I error due to multiple comparisons the Benjamini-Hochberg procedure with a 5% false discovery rate was applied (Benjamini & Hochberg, 1995). See the model specifications below, where the

ij subscript denotes the nesting of the individual within the family unit, SCR is skin conductance response magnitude, and PNMS is Superstorm Sandy exposure timing:

Model 1: $(SCR)_{ij} = \beta_{00} + b_{0j} + \varepsilon_{ij}$

Model 2: $(SCR)_{ij} = \beta_{00} + \beta_{10}PNMS_{ij} + \beta_{20}Sex_{ij} + b_{0j} + \varepsilon_{ij}$

Model 3: $(SCR)_{ij} = \beta_{00} + \beta_{10}PNMS_{i} + \beta_{20}Sex_{ij} + \beta_{30}PNMS*Sex_{ij} + b_{0j} + \varepsilon_{ij}$

Model 4: $(SCR)_{ij} = \beta_{00} + \beta_{10}PNMS_{i} + \beta_{20}Sex_{ij} + \beta_{30}PNMS*Sex_{ij} + \beta_{40}Depression_{ij} + \beta_{50}Anxiety_{ij} + \beta_{60}Age_{ij} + \beta_{1j}Age_{ij} + b_{0j} + \varepsilon_{ij}$

Where SCR is skin conductance response magnitude and PNMS is prenatal Superstorm Sandy exposure timing.

We obtained simple effects (differences of the predicted skin conductance magnitude values across total sample) using the emmeans package in R to examine the interaction. We have included the results of the final unadjusted and adjusted models, based on an ordinary least squares regression method, below.

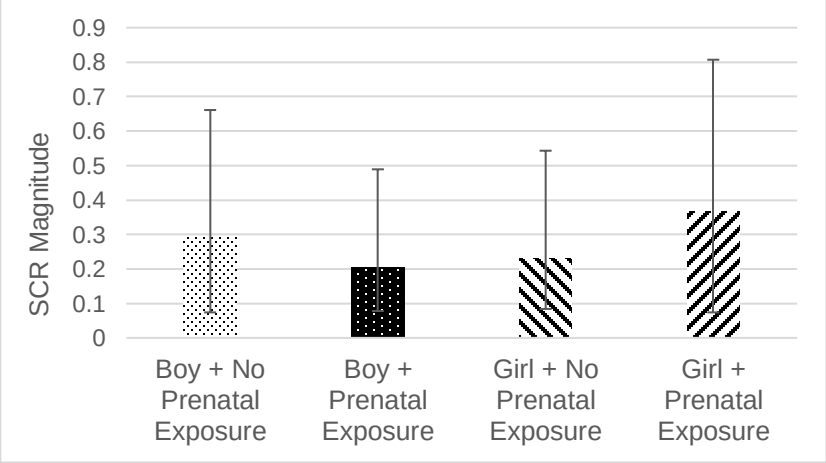
Table 3.1. *Demographic information by sex and prenatal storm exposure group.*

	Boy + No Prenatal Exposure, n = 54	Boy + Prenatal Exposure, n = 48	Girl + No Prenatal Exposure, n = 43	Girl + Prenatal Exposure, n = 54
Child Age M (SD)	49.32 (1.15)	37.68 (1.73)	49.04 (1.76)	39.76 (1.93)
Race				
Black	35.20%	16.70%	41.90%	20.40%
Latinx	37.10%	43.80%	39.50%	59.20%
White	18.50%	22.90%	7%	11.10%
Other	9.20%	16.60%	11.60%	9.30%
Maternal Marital Status				
Single	64.90%	41.70%	65.10%	46.30%
Married	35.20%	58.40%	34.90%	53.70%
Maternal Education Level				
No High School Degree	20.40%	18.80%	25.60%	11.10%
High School/GED	22.20%	16.70%	23.30%	16.70%
Some College	20.40%	18.80%	27.90%	37%
College Degree	24.10%	31.30%	16.30%	18.50%
Graduate Degree	13.00%	14.60%	7.00%	16.70%

Experiment 3 Results

Independent samples t-tests indicated no significant differences in skin conductance magnitude between boys and girls or between prenatally exposed and prenatally unexposed children. A general linear model of sex/prenatal exposure group predicting skin conductance response magnitude without covariates was significant ($p = .018$, partial $\eta^2 = .050$). The model run with child age, race, maternal marital status, and maternal education as covariates was also significant ($p = .029$, partial $\eta^2 = .046$). Bonferroni post hoc analyses indicated a significant difference between boys prenatally exposed to the storm ($M = 0.21$, $SE = .04$) and girls prenatally exposed to the storm ($M = 0.37$, $SE = .04$), $p = .028$, 95% confidence interval (-.305, -.011). Girls prenatally exposed to the storm were significantly more electrodermally reactive than boys prenatally exposed to the storm. Results are shown in Figure 3.1.

Figure 3.1. *Sex and prenatal storm exposure groups predicting skin conductance response magnitude.*



Note: Results of Bonferroni post hoc tests adjusted for child age, race, maternal marital status, and maternal education.

Results of the intercept-only linear mixed effects model indicated that 24.7% of the variance in skin conductance response magnitude was explained by between family differences. As this is a substantial degree of clustering, the family unit identifier was retained as a clustering variable in the analysis. Although linear mixed effects modelling indicated no significant main or interaction effects (see Table 3.2), guided by the results of our preliminary analyses we further examined potential dimorphism in skin conductance response magnitude via simple contrast. Estimated skin conductance response magnitude means by sex and prenatal exposure are shown in Table 3.3. Table 3.4 shows a contrast on the value of mean skin conductance response magnitude between boys and girls, where girls prenatally exposed to the storm were significantly more reactive than girls postnatally exposed to the storm ($p = 0.021$), whereas boys had no difference between the two groups. Consistent with our initial hypothesis, the simple effects indicated that mean skin conductance response magnitude was higher among girls irrespective of prenatal exposure status, and that this difference was greater particularly among those exposed.

Table 3.2. *Adjusted and unadjusted linear mixed effects models.*

N = 330	Model 1		Model 2		Model 3		Model 4 †	
	β (SE)	p	β (SE)	p	β (SE)	p	β (SE)	p
Intercept	3.66 (0.21)	<.001	3.45 (0.25)	<.001	3.64 (0.28)	<.001	0.38 (2.90)	0.908
Prenatal exposure	--	--	0.25 (0.32)	0.421	-0.21 (0.44)	0.630	-0.12 (0.46)	0.791
Sex	--	--	0.47 (0.31)	0.130	0.06 (0.41)	0.890	0.07 (0.41)	0.864
*Sex*Prenatal Exposure*	--	--	--	--	0.96 (0.63)	0.130	1.03 (0.63)	0.102

Note: †Adjusted for age, race, depression (EPDS), anxiety (STAI-S,T). P-values calculated using Kenward-Roger standard errors and df.

Table 3.3. *Estimated skin conductance response magnitude means by sex & prenatal exposure.*

	Estimated Means within Strata	
Adjusted	**M (SE)**	**95%CI**
Males		
Prenatal exposure: 0	2.97 (0.50)	(1.99, 3.95)
Prenatal exposure: 1	2.85 (0.55)	(1.77, 3.93)
Females		
Prenatal exposure: 0	3.04 (0.53)	(1.99, 4.09)
Prenatal exposure: 1	3.95 (0.55)	(2.87, 5.04)

Note: Estimated marginal means, standard error (SE), and 95% confidence intervals (CI).

Table 3.4. *Simple contrasts of skin conductance response magnitude in girls by prenatal exposure.*

Simple contrast	Model 1	
Adjusted	**β (SE)**	**P**
*Female*Prenatal exposure: 0*	0.07 (0.41)	0.861
*Female*Prenatal exposure: 1*	1.10 (0.48)	**0.021**

Note: Simple contrasts analysis comparing skin conductance response magnitude of girls who were versus were not exposed to prenatal storm stress.

Experiment 3 Summary

In an effort to better understand the role of sex in the relation between prenatal maternal stress and offspring SNS reactivity, we tested for interaction effects in children prenatally exposed to Superstorm Sandy. We found that child sex moderates the association between prenatal exposure and SNS reactivity, as measured by skin conductance response magnitude. The lack of significant main effects in skin conductance magnitude by sex or storm exposure suggest that the results were driven by the differential effect of the storm on the two sexes. Specifically, male offspring who were prenatally exposed were significantly less electrodermally reactive to startling stimuli than female offspring who were exposed. These findings are largely in line with and help clarify prior research. In one study, the salivary cortisol response of young girls, but not boys, prenatally exposed to high levels of maternal psychosocial stress was higher than in their low prenatal stress counterparts (de Bruijn et al., 2009). In another, a trend linked maternal prenatal stress with increased methylation of the glucocorticoid receptor encoding gene NR3C1, which was further correlated with fearfulness, in infant girls but not boys (Ostlund et al., 2016). These studies had smaller sample sizes than the present study and relied on the occurrence of normative stressors but support the idea that prenatal stress may affect boys and girls differently, with the potential to set them on trajectories toward different psychopathology. While the formal test of interaction between prenatal Sandy stress and sex was not significant, in our stratified analysis, we found that only girls had significantly higher skin conductance response magnitude when exposed to Superstorm Sandy-related stress in the womb. Those finding add to the existing literature that provide warning that girls might be

more vulnerable to the subsequent normative threat during childhood if they were programmed to be vigilant and alert by being exposed to traumatic stress in the womb.

The observed sexually dimorphic sympathetic nervous system reactivity in children exposed to prenatal stress reflects the general rates of psychopathology symptomatology developed by males and females. For example, females tend to develop internalizing symptoms (e.g., anxiety), whereas males tend to develop externalizing symptoms (e.g., aggression). In a review, Glover & Hill (2012) hypothesize that in species in which female members are more stationary than males (e.g., caregiving activities), female offspring exposed to prenatal stress may benefit from heightened arousal and stress responsiveness, whereas more mobile males (e.g., hunting) may benefit from a blunted stress response. Evidence in animal studies reviewed by Bale (2011) points to placental epigenetic changes linked with prenatal stress as a potential progenitor of this sexual dichotomy.

These findings should be interpreted in light of several notable limitations. First, had we accounted for subjective feelings about the storm, we may have been able to draw conclusions about the impact of variable psychological responses to stress, including resilience. Our measure of SNS, electrodermal activity, is not influenced by the parasympathetic nervous system as some cardiac measures are. However, directional fractionation of the nervous system prevents any one measure from fully encompassing the function of the SNS (Jänig & Häbler, 2000; Lacey, 1967). Additionally, without prenatal or placental biological tissue we cannot draw conclusions about mechanisms (e.g., inflammation, stress hormones, epigenetics) underlying the observed sympathetic nervous system differences.

The potential for prenatal maternal stress will continue to rise with the observed increase in the frequency and intensity of natural disasters related to climate change. The findings presented here need to be replicated and expanded upon to determine the full extent to which these acutely stressful events may contribute to sexually dimorphic reactivity in offspring. The utility of autonomic reactivity as a predictor for future psychopathology onset, particularly for the stereotypical disorders developed by males and females, should also be explored. Further, neurological underpinnings of the relationships between prenatal stress and altered reactivity should be investigated.

Experiment 4: Maternal depression blunts offspring electrodermal activity

Prenatal maternal stress exposure is a risk factor for abnormal emotion regulation and psychopathology risk. Although studies have documented behavioral problems in offspring, studies of autonomic dysfunction related to prenatal stress exposure of any kind are limited. The lack of findings on correlations between offspring autonomic function and maternal prenatal depression in is particularly concerning due to recent statistics showing that one in seven women now experience a depressive episode during pregnancy (Curry et al., 2019). Indeed, the most recent Diagnostic and Statistical Manual of Mental Disorder includes a peripartum onset specifier for depressive disorder diagnosis, noting that half of all postpartum episodes begin *during* pregnancy (American Psychiatric Association, 2013). Of the studies that have examined children exposed to prenatal maternal depression, outcomes have largely consisted of poor temperament profiles (McGrath et al., 2008; Nomura et al., 2019; Zhang, Rajendran, et al., 2018), high neonatal cortisol levels, low vagal tone, and poor habituation (Davis et al., 2004). Sympathetic nervous system (SNS) function, a correlate of stress response and psychopathology risk, remains largely unexplored.

The literature also suffers from a lack of investigation into the interaction of prenatal maternal stress and depression. The term “stress” has been operationalized across studies to refer to daily hassles, social conflict, chronic or acute stress, natural or manmade disasters, and psychopathological symptoms or diagnosis (Glover, 2014). Focusing on mental health issues, one group found that prenatal maternal anxiety interacted with prenatal maternal depression to predict poor infant temperament, but not depression number of stressful life events independently (Austin, Hadzi-Pavlovic, et al., 2005). As discussed previously, Nomura et al. (2019) found that prenatal maternal stress from Superstorm Sandy interacted with prenatal depression to predict poor temperament outcomes. While these studies are important for our understanding of the unfortunate conjunction of stress and mental health struggles, these behavioral temperament outcomes are not without bias and would benefit from more object outcome measures.

Although the literature features some biological measures of offspring outcomes after prenatal depression exposure, these outcomes are seldom collected after infancy or toddlerhood. Early childhood is in important period of transition, maturation, and when psychopathology symptoms can begin to emerge. To

date, one other study has examined the interaction between prenatal maternal stress and depression on autonomic nervous system function in five-six-year-old children. van Dijk et al., who operationalized stress as psychosocial stressors, found no correlation between the two conditions and offspring cardiac measures of resting para- and sympathetic nervous system function. The current experiment operationalizes stress as maternal exposure to a natural disaster and measures sympathetic reactivity rather than resting function to attempt to fill that gap.

We aimed to address three main points. First, we evaluated the electrodermal reactivity of young children prenatally exposed to an acute, specific, non-normative stressful event, i.e., Superstorm Sandy. Second, we observed the electrodermal reactivity of offspring as a function of exposure to prenatal maternal depression. Third, we investigated the nature of the interplay between maternal prenatal stress and depression on offspring electrodermal reactivity. Following reports that prenatal maternal stress is associated with more fearfulness (Austin, Hadzi-Pavlovic, et al., 2005; Austin, Leader, et al., 2005) and elevated stress response (Davis et al., 2007), we hypothesized that children prenatally exposed to Superstorm Sandy would be more electrodermally reactive to startling stimuli as indicated by greater SCR magnitude. Following research connecting depression with hyporeactive electrodermal reactivity (Sarchiapone et al., 2018), we further hypothesized that children prenatal exposed to maternal depression would have lower SCR magnitudes than controls. Our third aim is exploratory, and we therefore made no hypothesis regarding the electrodermal pattern of children exposed to both prenatal maternal stress and depression.

Experiment 4 Methods

Participants

Participants for this study were drawn from an ongoing prospective birth cohort study, as described in Experiment 1. At 3–4 years postpartum the mother and child were invited to CUNY Queens College for a comprehensive follow-up assessment. Of the 329 children who completed a follow up assessment, 104 had EDA data that was not usable due to excess artefact in the raw signal or technical malfunction. A further 29 children were missing maternal mental health data, yielding N = 196. Younger children were more likely to have data with artefact or technical malfunction (age in months of children

with artefact M = 38.75, SD = 13.95; children without artefact M = 42.85, SD = 12.43, p = .013). No other significant differences were found with respect to child sex, in utero storm exposure, prevalence of maternal depression, or skin conductance response magnitude (all p > .52). The attrition rate from infant assessments to postnatal follow up was 32%. See Finik and Nomura (2017) for further details.

Procedure

As described in Experiment 2, electrodermal activity was recorded from mothers and children during a startle probe paradigm A three-minute baseline period was followed by a one-minute period of six90 dB auditory stimuli one second in duration with varying inter-stimulus intervals of 6–12 seconds was presented with E-Prime 2.0.

Measures

Electrodermal activity. Electrodermal activity was recorded via a Biopac MP150 acquisition system and a Dell computer running AcqKnowledge 4.4 software (Biopac, Goleta, CA) as described in Experiment 2. The skin conductance response magnitude was calculated by the software as the average amplitude of each skin conductance response specific to a startle probe multiplied by the percentage of the startle probes that elicited a response. Skew and kurtosis of the skin conductance magnitude was reduced by adding one to the magnitude and taking the log, a commonly used transformation.

Superstorm Sandy exposure. Acute prenatal storm stress was determined based on timing of the index pregnancy (0 = not pregnant during the storm, 1 = pregnant during the storm). The storm impacted the metropolitan New York area (October 29, 2012). Based on this calculation, 44.3% of the sample were exposed to the storm in utero (n = 87) and 55.6% (n = 109) were not. Timing of index pregnancy was not available for 2 cases (.006% of the sample).

Maternal depression. Prenatal maternal depression was measured with the Edinburgh Postnatal Depression Scale (EPDS) (Murray & Carothers, 1990), as described in Experiment 2. The items were summed and the recommended cutoff score of 12 was used to determine presence of major depression based on depressive symptoms. Within the sample 22% (n = 44) met this threshold. The high portion of participants who met the threshold compared to the prevalence of depression in pregnant women in the

population (6%) may be due to people with depression being more likely to join the study, either for mental health or financial resources.

Race. Maternal ethnicity was collected via self-report. Mothers were asked to identify their race/ethnicity as one of the following: White Hispanic, Black Hispanic, Mixed Hispanic, Black (non-Hispanic), White (non-Hispanic), Asian, or Other.

Confounders. Following a review of the literature, a directed acyclic graph (DAG) was diagrammed to represent the theorized causal pathway between acute prenatal storm stress, prenatal maternal depression and offspring ANS function (as represented by EDA measures) (Textor et al., 2016). Of the measured variables available to the present analysis, maternal anxiety, trauma, and ethnicity were identified as confounders, which have been strongly associated with prenatal stress and child neurodevelopment in previous research, which required adjustment in order to capture the total effect of acute prenatal storm stress and depression on childhood EDA. These potential confounders were measured as follows.

The State-Trait Anxiety Inventory (STAI) (Spielberger, 1983), as described in Experiment 1 measures current “state anxiety” and typical “trait anxiety.” Anxiety was determined based on presence of "state anxiety" or "trait anxiety" according to the suggested thresholds of a sum score of 40 or greater (Dennis et al., 2013). Cronbach’s alpha was .90 for state anxiety and .90 for train anxiety, indicating excellent reliability.

The Posttraumatic Diagnostic Scale (PDS) (Foa, 1995) is a self-report measure used to determine severity of symptoms related to posttraumatic stress disorder (PTSD) using 49 items related to the DSM-IV criteria for PTSD. When a traumatic event is reported, symptom frequency is reported on a scale of 0 (Not at all or only one time) to 3 (5 or more times a week/almost always). This was administered following the storm or at the time of enrollment into the study. A sum score was used as a measure of prior trauma before pregnancy. Cronbach’s alpha for the scale was .93, indicating excellent reliability.

Analysis

The raw signal for each subject was visually inspected to determine whether or not the recording should be excluded due to artefact or technical malfunction (n = 104). Independent samples t-tests indicated that there were no differences between data with artefact and data without artefact with respect to child sex, in utero storm exposure status, prevalence of maternal depression, or SCR magnitude (all p > .52). Younger children were, however, more likely to have data with artefact or malfunction (age in months of children excluded M = 38.75, SD = 13.95; children not excluded M = 42.85, SD = 12.43, p = .013). Electrodermal reactivity to the startling stimuli was quantified as the SCR magnitude specific to the stimuli. As per AcqKnowledge 4.4 software, the SCR magnitude is calculated based on the amplitude of each specific SCR and the SCR frequency, or percentage of the 6 startle probes that elicited a response.

Storm severity, as measured by the PDS, was weakly correlated with state anxiety (r = .20), trait anxiety, (r = .22), and maternal depression (r = .27); while maternal anxiety was moderately correlated with maternal depression (r = .38). The variance inflation factor (VIF) did not exceed 2.0 for the final model, indicating minimal model distortion due to multicollinearity. There were no significant differences between participants based on the OB/GYN clinic of recruitment with respect to SCR magnitude, baseline SCR frequency, storm severity, depression, or anxiety (p > .26). Further, there were no significant differences among prenatal exposure groups and baseline SCR frequency [F(3, 191) = .83, p = .5].

All statistical tests specified an alpha level of .05 and were performed in SAS version 9.4 (SAS Institute, Cary, NC). Descriptive statistics, including kurtosis (8.9) and skew (2.65), for the sample were obtained. As both kurtosis and skewness were greater than 2, we transformed SCR magnitude values via square root to reduce the positive skew, a method commonly used in studies using EDA (Braithwaite et al., 2013). After transformation, kurtosis and skew were 0.81 and 0.88, respectively. To address missing data, multiple imputation was used for key variables (SCR magnitude = 31.3%, prenatal depression = 12.5%, postnatal depression = 26.1%, anxiety = 16.1%, trauma = 16.7%). Multiple imputation procedures followed those outlined by Liu and De using the fully conditional specification (FCS) method in SAS (Liu & De, 2015). Results of the multivariable models with and without imputation indicated no notable differences in estimates or significance; only results from the imputed models are reported.

Following a review of the literature, a Directed Acyclic Graph (DAG) was made to represent the theorized causal pathway between prenatal storm stress, prenatal maternal depression and offspring ANS function (as represented by EDA measures) (Textor et al., 2016). Of the measured variables available to the present analysis, maternal anxiety, trauma, and ethnicity were identified as confounders requiring adjustment in order to capture the direct effect of prenatal storm stress and prenatal maternal depression on childhood EDA. Maternal education and marital status, proxies for socioeconomic status in women who are pregnant or new mothers, were identified as intermediate variables along the theoretical causal pathway from Superstorm Sandy experience, maternal depression, and childhood physiological reactivity. These variables were therefore not included to reduce the likelihood of overfitting and bias via unnecessary adjustment.

Intrafamilial correlation due to multiple children within one family (n = 30) was evaluated and the clustering effect was adjusted as follows. First, an empty model (Model 1) was carried out to compute the interclass correlation coefficient (ICC) (Shrout & Fleiss, 1979) due to clustering at the family level. Results of the empty model indicated that 24.9% (ICC = 0.249) of the variation in SCR magnitude was due to between family differences. As this represents a substantial amount of clustering, a random intercept for family was included in all models. Subsequently, univariable models predicting SCR magnitude were carried out with acute prenatal storm stress (PNMS; Model 2) and prenatal maternal depression (PNMD; Model 3) as predictors. Finally, multivariable models predicting SCR magnitude (unadjusted and unadjusted, Model 4–5) were carried out. Model 4 tested the interaction between prenatal storm and depression exposure (PNMS*PNMD). Model 5 tested the interaction while adjusting for maternal anxiety (Anx), prior trauma (Tma), and race (R). The model specifications are as follows, where the ij subscript denotes the nesting of the individual within the family unit:

Model 1: $Y_i = \beta_{00} + b_{0i} + \varepsilon_{ij}$

Model 2: $Y_i = \beta_{00} + b_{0i} + \beta_{10}PNMS_i + \varepsilon_i$

Model 3: $Y_i = \beta_{00} + b_{0i} + \beta_{10}PNMD_i + \varepsilon_i$

Model 4: $Y_i = \beta_{00} + b_{0i} + \beta_{10}PNMS_i + \beta_{20}PNMD_i + \beta_{30}PNMS*PNMD_i + \varepsilon_i$

Model 5: $Y_i = \beta_{00} + b_{0i} + \beta_{10}PNMS_i + \beta_{20}PNMD_i + \beta_{30}PNMS*PNMD_i + \beta_{40}Anx_i + \beta_{50}Tma_i + \beta_{60}R_i + \varepsilon_i$

To explore the potential interaction effect of prenatal storm stress * prenatal maternal depression on SCR magnitude, post hoc analyses were conducted using Tukey's HSD test to compare means of SCR magnitude across group status (no prenatal exposure = 0, prenatal maternal depression only = 1, prenatal storm stress only = 2, both prenatal maternal depression and prenatal storm stress = 3).

Experiment 4 Results

Table 3.5 displays descriptive statistics for the sample stratified by prenatal maternal depression and prenatal storm stress. Of the sample 42.3% (n = 85) were not exposed to acute prenatal storm stress or prenatal maternal depression in utero. 35.2% (n = 69) were exposed to acute prenatal storm stress but not prenatal maternal depression in utero, 13.3% (n = 26) were exposed to prenatal maternal depression but not acute prenatal storm stress, and 9.2% (n = 18) were exposed to both acute prenatal storm stress and prenatal maternal depression.

Table 3.5. *Descriptive Statistics*

	Full Sample N = 198		No Exposure N = 85, 42.3%		PNMS Only N = 69, 35.2%		PNMD Only N = 26, 13.3%		PNMS + PNMD N = 18, 18%	
Child Characteristics	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Age (months)	42.54	12.76	47.19	11.23	36.71	12.14	48.86	10.55	33.80	11.06
% Female	n = 102	51.5%	n = 41	48.2%	n = 39	56.5%	n = 14	53.8%	n = 8	44.4%
Ethnicity	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Asian	20	10.1	10	11.8	7	10.1	1	3.8	2	11.1
Black	58	29.3	27	31.8	13	18.8	14	53.9	4	22.2
Hispanic	86	43.4	34	40.0	37	53.6	8	30.8	7	38.9
White	30	15.2	14	16.5	10	14.5	2	7.7	4	22.2
Other	4	2.0	0	0	2	2.9	1	3.8	1	5.6
Marital Status	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Married	78	39.4	29	34.1	33	47.8	8	30.8	8	44.4
Common-law	12	6.1	4	4.7	8	11.6	0	0	0	0
Never Married	106	53.5	51	60.0	28	40.6	18	69.2	9	50.0
Widowed	1	0.5	1	1.2	0	0	0	0	0	0
Divorced/Separated	1	0.5	0	0	0	0	0	0	1	5.6
Maternal Education	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Primary School	5	2.5	0	0	3	4.3	1	3.8	1	5.6
Some High School	29	14.6	16	18.8	4	5.8	6	23.1	3	16.7
High School/GED	39	19.7	17	20.0	16	23.2	6	23.1	0	0
Some College	57	28.8	26	30.6	20	29.0	5	19.2	6	33.3
Associate's Degree	14	7.1	5	5.9	4	5.8	3	11.5	2	11.1
Bachelor's Degree	26	13.1	11	12.9	10	14.5	3	11.5	2	11.1
Graduate Degree	28	14.1	10	11.8	12	17.4	2	7.7	4	22.2
Mental Health	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Prior Trauma Score	4.82	9.1	3.6	6.9	5.14	9.8	10.00	13.7	2.29	4.9
State Anxiety	37.93	11.8	34.8	10.7	34.78	8.7	46.48	12.2	52.47	10.6
Trait Anxiety	38.42	10.6	35.0	8.8	34.74	7.7	49.35	9.8	52.65	6.1
Psychophysiology	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Raw SCR Magnitude	0.40	0.5	0.41	0.5	0.5	0.7	0.23	0.3	0.21	0.2
SCR Frequency	50.09	27.1	54.42	28.6	48.79	27.0	43.59	22.6	44.44	24.3

Note: SCR = Skin conductance response

Linear mixed effects models

Results of Models 1–5 can be found in Table 3.6. The initial intercept only model (Model 1) indicated that a substantial amount of the variation in SCR magnitude was explained by between family differences (29%). Results from our univariable models (2, 3) indicate that acute prenatal storm stress did not predict SCR magnitude (B_{PNMS} = 0.01, p > .05), whereas prenatal maternal depression did significantly predict SCR magnitude (B_{PNMD} = −0.14, p <.001), such that reactivity was decreased in those exposed to prenatal depression.

Acute prenatal storm stress remained non-significant and prenatal maternal depression remained a significant predictor in our unadjusted multivariable model (4), while the interaction of the two was non-significant (B_{PNMS} = −0.03, p > 0.05; B_{PNMD} = 0.12, p = .005; $B_{PNMSxPNMD}$ = 0.03, p > 0.05). No changes in significance were noted following adjustment for confounders (maternal anxiety, trauma and race/ethnicity) in Model 5 (B_{PNMS} = −0.004, p > 0.05; B_{PNMD} = 0.17, p = .002; $B_{adjusted}$ = 0.01, p > 0.05).

Table 3.6. *Summary of linear fixed effects models.*

	Model 1[a]	Model 2[b]	Model 3[c]	Model 4[d]	Model 5[e]
Intercept	0.50 (0.01)***	0.50 (0.01)***	0.53 (0.01)***	0.41 (0.30)***	0.19 (0.04)***
Storm Exposure	–	0.01 (0.02)	–	−0.03 (0.04)	−0.01 (0.04)
Depression	–	–	−0.14 (0.02)***	0.12 (0.03)**	0.17 (0.04)**
Storm*Depression	–	–	–	0.03 (0.04)	0.01 (0.04)
Postnatal Depression	–	–	–	–	−0.06 (0.03)*
Trauma	–	–	–	–	0.02 (0.04)
Anxiety	–	–	–	–	0.08 (0.02)***
Ethnicity	–	–	–	–	0.04 (0.01)

Note: p < .05; p ** < .01; p *** < .001.
Number outside parentheses reflects unstandardized beta, number in parentheses reflects standard error.

[a] Empty Model, ICC = 0.21.
[b] Superstorm Sandy exposure.
[c] Prenatal maternal depression.
[d] Prenatal storm stress x Prenatal depression.
[e] Model 4 adjusted for postnatal depression, ethnicity, anxiety, and other trauma.

Tukey post hoc analyses

Tukey's post hoc analysis further indicated that SCR magnitude of children exposed to both prenatal maternal depression and acute prenatal storm stress was lower than in children exposed to neither condition in utero (p = .002), prenatal maternal depression only (p = .046), and acute prenatal storm stress only (p = .002). SCR magnitude was also lower in children exposed to prenatal maternal

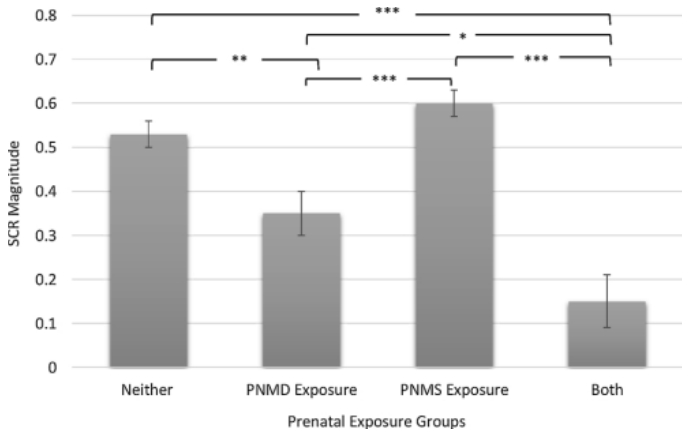
depression only as compared to children exposed to neither in utero (p = .008) and children exposed to acute prenatal storm stress only (p = .002). Reported p-values have been adjusted for multiple comparisons using the Benjamini-Hochberg procedure with a 5% false discovery rate. Full results are available in Table 3.7. The mean and standard error per group are represented in Figure 3.2.

Table 3.7. *Post hoc contrasts linear mixed effects model (Tukey)*

(I) Group	(J) Group	Mean Difference (I-J)	SE	t-ratio	*p value*	(95% CI)	*Cohen's d*
Control	PNMD	0.18	0.06	3.30	0.0081	(0.04 to 0.33)	0.09
	PNMS	−0.07	0.03	−1.96	0.2051	(−0.15 to 0.02)	0.05
	Both	0.38	0.06	5.98	0.0002	(0.22 to 0.55)	0.16
PNMD	Control	−0.18	0.06	3.30	0.0081	(0.04 to 0.33)	0.09
	PNMS	−0.25	0.06	−4.28	0.0002	(−0.40 to −0.10)	0.11
	Both	0.20	0.07	2.67	0.0457	(0.01 to 0.39)	0.07
PNMS	Control	0.07	0.03	−1.96	0.2051	(−0.15 to 0.02)	0.05
	PNMD	0.25	0.06	−4.28	0.0002	(−0.40 to −0.10)	0.11
	Both	0.45	0.06	7.10	0.0002	(0.28 to 0.61)	0.19
Both	Control	−0.38	0.06	5.98	0.0002	(0.22 to 0.55)	0.16
	PNMD	−0.20	0.07	2.67	0.0457	(0.01 to 0.39)	0.07
	PNMS	−0.45	0.06	7.10	0.0002	(0.28 to 0.61)	0.19

Note: SE = standard error, CI = confidence interval.
All significance values were corrected for multiple testing using the Benjamini-Hochberg procedure with a 5% false discovery rate.
PNMS = Prenatal Maternal Storm Stress.
PNMD = Prenatal Maternal Depression.

Figure 3.2. *Skin conductance response magnitude by prenatal exposure groups*



Note: *p < .05, **p < .01, ***p < .001.
SCR = Skin Conductance Response. SCR Magnitude values are normalized by square root transformation.
Bars reflect the standard error of the mean.

Experiment 4 Summary

The aim of this study was to evaluate the independent and joint contributions of prenatal maternal stress and depression on offspring electrodermal reactivity in early childhood. Contrary to our initial hypotheses, prenatal exposure to Superstorm Sandy was not related to SCR magnitude. Prenatal exposure to maternal depression was associated with lower SCR magnitude to startling stimuli than that of children unexposed to prenatal maternal depression. Post hoc analyses revealed that those exposed to prenatal maternal depression only and those exposed to both prenatal maternal depression and acute prenatal storm stress had lower SCR magnitude than those only exposed to Superstorm Sandy. Despite finding no interaction between prenatal storm stress and prenatal maternal depression, those exposed to both were significantly less electrodermally reactive than those exposed to prenatal maternal depression only, suggesting acute stress may exacerbate the impact of prenatal maternal depression.

Although van Dijk et al. (2012) found no correlations between prenatal maternal depression, psychosocial stress, and cardiac autonomic function at rest, evaluation of the impact of one specific and acute prenatal stressor in conjunction with prenatal maternal depression on offspring SCR magnitude in response to startling stimuli was previously uninvestigated. Further, van Dijk et al. used a cardiac measure of autonomic function, which may have been subject to vagal influence, unlike EDA. We did not anticipate the null findings between prenatal storm stress and offspring EDA given the literature documenting this relation (Austin, Hadzi-Pavlovic, et al., 2005; Baibazarova et al., 2013; Davis et al., 2007). We have previously reported increased temperament measures of emotional reactivity within the same sample of children prenatally exposed to Superstorm Sandy (Zhang, Rajendran, et al., 2018). Potential factors explaining this null finding include directional fractionation on the autonomic nervous system (Lacey, 1967), individual variation in electrodermal reactivity, or postnatal factors such as mother-child bond or socioeconomic factors that may mask the effect. Importantly, prior research, including our own, has identified effect of sex (see Experiment 2) and trimester of exposure to stress (Mueller & Bale, 2008; Sandman et al., 2012). Had we examined these factors, we may have uncovered a more nuanced understanding of the relationship between prenatal storm stress and electrodermal reactivity. Future research would do well to consider these factors.

Our hypothesis that children exposed prenatal maternal depression would be less electrodermally reactive to startling stimuli was confirmed. The SCR magnitude was even lower for children exposed to both prenatal storm stress and prenatal maternal depression, suggesting SNS activity was further blunted by the conjunction of the two factors. Several mechanisms may underlie these findings. First, it is also possible that blunted electrodermal reactivity has a genetic component related to depression that may be heritable from the mother, since depression is associated with low electrodermal activity (Sarchiapone et al., 2018). Second, longer term exposure to depression than to an acute stressor such as a natural disaster may result in greater alteration in fetal development, which may in turn contribute to the blunted SNS reactivity observed in children exposed to both conditions. These alterations may be a result of exposure to excess cortisol, increased inflammation, or decreased oxytocin influencing epigenetic mechanisms leading to blunted SNS function. Although no prenatal measure of cortisol is available, support for this mechanism comes from work by our colleagues' finding that placental gene expression of three genes known to modulate cortisol levels moderated the relationship between prenatal maternal depression and increased negative affect at six months of age (Zhang, Finik, et al., 2018).

These findings should be interpreted cautiously in light of several limitations. First, one or more measures of cortisol, oxytocin, or inflammation throughout pregnancy would have shed light on an underlying mechanism. While we were unable to examine the specific trimester(s) in which the acute prenatal storm stress and prenatal maternal depression were experienced, this line of inquiry could have helped clarify critical windows of susceptibility to this aspect of SNS dysregulation. Further, our measure of SNS reactivity is limited, in that electrodermal activity is only one measure of the SNS, and directional fractionation of the autonomic nervous system and individual differences in reactivity may lead to variation in skin conductance responses (Jänig & Häbler, 2000; Lacey, 1967). We therefore urge caution in generalizing our findings to other measures of SNS function. Moreover, we quantified skin conductance responses as a 0.02 μS amplitude increase as compared to the period immediately preceding the stimulus, and does not reflect the skin conductance level, which is likely to have been much lower during baseline. We were also unable to examine potential paternal contribution in this analysis, as half of all participating mothers were single and did not provide information regarding the father of their child. In addition, a majority of measures used in the present analysis consisted of self-report questionnaires

(maternal depression, anxiety, trauma history) which are subject to bias. We also quantified storm exposure based on whether or not the child was in utero or not at the time and were not able to further examine our results according to level of storm severity experienced. We did not examine which aspects of the storm experience (e.g., power loss, home evacuation, injury) most strongly correlated with electrodermal activity, nor did we examine the variability of the magnitude of stress experienced. Lastly, it is possible that natural disasters are fundamentally different from other forms of prenatal stress (e.g., financial or interpersonal difficulties) because of media coverage, sustained damage, etc., limiting the generalizability of these findings.

Acknowledging these limitations, these results extend the literature on prenatal storm stress, prenatal maternal depression, and child development in a prospective longitudinal study. We used a more objective measure of stress reactivity than parent or observer temperament ratings, as is commonly used in the literature. We also differentiated between acute stress and depression, which may differentially impact underlying biological systems across different time scales (i.e., short term versus long term). Further, we adjusted our statistical model for anxiety, prior trauma, and race/ethnicity in order to parse out the total effect of acute prenatal storm stress and prenatal maternal depression on SCR magnitude.

The US Preventive Services Task Force on Interventions to Prevent Perinatal Depression recently recommended that doctors refer pregnant women for counseling to prevent depression onset if at least one risk factor is present, including history of depression or abuse, presence of depression or anxiety symptoms, low socioeconomic status, or lack of social support (Curry et al., 2019). Our findings underscore the importance of this recommendation and point to the occurrence of a natural disaster or similar stressor as additional factors for consideration.

Discussion

Our aim in these experiments was to elucidate any link between prenatal maternal stress related to Superstorm Sandy and offspring electrodermal reactivity. The goal of Experiment 3 was to evaluate the role of the sex of the child, if any. No significant differences in SCR magnitude were found with respect to sex or prenatal exposure status independently. Although the literature has some support for a lack of sex differences in EDA before puberty, null results were unexpected with respect to prenatal storm exposure.

However, an interaction between sex and exposure status was found, such that boys who were exposed had a lower average SCR magnitude than girls who were exposed. These results may help to disentangle the mechanisms underlying sexually dimorphic rates of psychopathology onset.

The goal of Experiment 4 was to investigate the influence of maternal mental health, specifically prenatal depression, on the link between storm exposure and EDA. We confirmed that prenatal storm exposure was not associated with SCR magnitude, as in Experiment 3. We further found that a) maternal prenatal depression correlated with lower SCR magnitude than control children and children exposed to the storm and b) prenatal exposure to both depression and the storm correlated with lower SCR magnitude than control children, children exposed to depression alone, and children exposed to the storm alone. Although prenatal exposure to Superstorm Sandy on its own did not significantly predict higher SCR magnitude as expected, the addition of maternal mental health to the equation was correlated with lower SCR magnitude than prenatal maternal depression alone.

These results help illuminate the link between prenatal maternal mental health and offspring SNS reactivity. Both sex and mental health other than stress seemed to play an important role. Stress related to a natural disaster seemed to differentially impact reactivity on the basis of sex and maternal depression seemed to be exacerbated by disaster stress. The blunted reactivity correlated with male exposure in Experiment 3 and the combination of depression and storm exposure in Experiment 4 suggests potential risk for the development of symptoms including oppositional defiant disorder, impulsivity, and inattention.

Electrodermal activity is a useful marker of SNS function by virtue of its noninvasive measurement and stability overtime but is not an all-encompassing indicator of neurodevelopment. Until such an indicator is developed, neuroimaging techniques may provide further insight into the impact of prenatal disaster-related stress. SNS function, part of the peripheral nervous system, represents only one of several systems in the body that influence mental health and behavior. Structural, functional, and diffusion-weight magnetic resonance imaging (MRI) techniques can give evidence as to the health of the central nervous system, which influence not only the SNS, but the parasympathetic nervous system, the HPA axis, and the enteric nervous system as well. The next chapter presents a review of the literature on

the association between prenatal maternal stress and offspring neuroimaging and the results of a pilot study conducted on fourteen children, eight of whom were prenatally exposed to Superstorm Sandy.

Chapter 4: Prenatal Storm Stress and the Prefrontal-Limbic Circuit

Experiments 1-4 examined the associations between prenatal maternal stress and subsequent behavioral and autonomic outcome measures to try to get to the core of the question: what happens to children prenatally exposed to natural disasters? These outcome measures are readily obtainable and informative as to the general emotional function of the child but are not direct measures of brain structure and function. Deeper understanding of the brain, especially early in childhood while plasticity is still high, may help to elucidate which areas are most vulnerable to prenatal stress and therefore potential targets for intervention before downstream consequences emerge. This chapter presents an overview of the field to date and results from a pilot study of fourteen 5–8-year-old children, eight of whom were prenatally exposed to Superstorm Sandy.

The primary neural circuit of interest to the current study is the connection between the prefrontal cortex and the limbic system. The prefrontal cortex (PFC) serves many purposes and is generally thought to be the seat of executive functions such as judgment, planning, and critical thinking. It takes up about 30% of human brain volume (Carlén, 2017) and can be divided into several areas: the dorsolateral (dlPFC), dorsomedial PFC (dmPFC), ventromedial PFC (vmPFC), ventrolateral PFC (vlPFC), and the rostral anterior cingulate cortex (rACC). The limbic system is composed of multiple structures including the amygdala, hippocampus, and hypothalamus (Rajmohan & Mohandas, 2007). Each of these structures has its own function, but as a whole the system is thought to be the seat of emotion in humans. The amygdala in particular is known as a center for threat detection and fear behavior (Feinstein et al., 2011).

The PFC and limbic system are connected by a white matter tract called the uncincate fasciculus (Hanson et al., 2015). The function of this tract is to facilitate communication between these two areas, although it is not the only means of communication between the regions. That communication is critical to the process of emotion regulation. Studies of functional connectivity between the two have demonstrated that increased medial PFC (mPFC) and ACC activity is correlated with decreased amygdala activity in healthy adults, particularly when regulating emotions (Hariri et al., 2003). Research has shown that this reciprocal relationship between the two regions does not develop until around ten years of age in healthy children (Gee, Humphreys, et al., 2013). Prior to this age activity in the two is positively correlated rather

than negative. However, early childhood maternal deprivation has been linked with earlier maturation of the emergence of the negative correlation between the prefrontal and limbic areas. The literature currently lacks functional neuroimaging data in prepubertal children prenatally exposed to natural disaster stress, but many other studies shed some light on what we can expect to find in these critical parts of the brain. No one measure of the brain perfectly encompasses central nervous system (CNS) function (Suárez et al., 2020). Experiment 5 will examine the link between prenatal stress exposure and the structure of the PFC and limbic system, and Experiment 6 will examine the functional connectivity.

Experiment 5: Prenatal stress and the structure of the prefrontal-limbic circuit

The gray matter of the brain is composed of the cell bodies of neurons. Gray matter volume of a given structure is often correlated with its function, but the relationship between structure and function is now understood to be more nuanced due in part to direct and indirect synapses throughout the brain (for review see Suárez et al., 2020). Studying the gray matter volume of regions of interest is therefore an important part of evaluating the degree of neurodivergence.

Young people who experienced firsthand stress in the early postnatal period have been shown to have structural differences in the prefrontal-limbic circuit in comparison with typically developing controls. For example, children who were maltreated had decreased gray matter volume in the OFC and left middle temporal gyrus in one sample of twelve year old children (De Brito et al., 2013) and decreased volume in the vmPFC, right OFC, right inferior frontal gyrus, and bilateral parahippocampal gyri in another sample of 13-20 year olds (Gold et al., 2016). Gold et al. (2016) further found that decreased parahippocampal gyrus volume was related to higher externalizing symptoms. Moreover, anxiety and depression symptoms were correlated with reduced vmPFC volume in children younger than nine years of age, and then increased volume in the same region after twelve years of age, suggesting a development shift. Further, more time spent in a rearing institution was correlated with increased amygdala volume, lower emotion regulation capacity, and increased anxiety symptoms as compared to children who spent less time in a rearing institution (Tottenham et al., 2010).

Several studies have investigated the question of prenatal stress and offspring neural health by using maternal mental health, stressful life events, or glucocorticoids levels as a measure of stress. In

one such study prenatal maternal depression was correlated with increased amygdala volume in 4-5-year-old girls, but not boys (Wen et al., 2017). The same research group also found that in girls prenatally exposed to maternal prenatal depression there was a positive correlation between amygdala volume and insula thickness and a negative correlation between amygdala volume and inferior frontal cortical thickness (Lee et al., 2019). In a small sample of 24 four-year-old children, second trimester pregnancy-related anxiety was correlated with increased left amygdala volume in female offspring (Acosta et al., 2019). Further, prenatal anxiety exposure was associated with increased emotional and behavioral problems – however, in children with a larger left amygdala volume, fewer emotional and behavioral problems were observed, suggesting a kind of resiliency compensation (Acosta et al., 2019). Another group found that second trimester pregnancy-specific anxiety was correlated with decreased volume in the PFC, premotor cortex, medial temporal lobe, lateral temporal cortex, and postcentral gyrus in 6-9-year-old children (Buss et al., 2010). Only one study to date has evaluated offspring development in relation to prenatal exposure to a natural disaster. The group following children prenatally exposed to the Quebec Ice Storm of 1998 found that late gestation exposure to high levels of maternal objective stress related to the storm was correlated with increased amygdala and total brain volume. This in turn mediated the link between prenatal stress and increased externalizing symptoms in eleven-year-old girls (Jones et al., 2019). While informative, the Quebec brain scans were conducted past the age that Gee and colleagues identified a developmental shift occurs, leaving open the question of brain structure related to prenatal natural disaster stress prior to that age (Gee, Humphreys, et al., 2013).

These studies consistently show aberrations in areas involved in emotion processing and regulation, i.e., the prefrontal-limbic circuit. Others have also identified emotional and behavioral deficits in offspring related to these brain aberrations. Prenatal maternal perceived stress was associated with decreased frontal and temporal cortical thickness at seven years of age, as well as increased depression symptoms at 12 years of age (Davis et al., 2020). Stressful life events during pregnancy was correlated with increased volume in the posterior parietal cortex, bilateral intraparietal sulcus, left superior parietal lobule, inferior parietal lobule, and increased risk for psychiatric symptoms in 11-14-year-old children (McQuaid et al., 2019). Using a more objective measure, Davis et al. (2017) found that third trimester maternal glucocorticoid levels correlated with increased frontal cortical thickness and cognitive

performance in 6-9-year-old offspring. The same research group also found that glucocorticoid levels correlated with a thinner rACC, which in turn was associated with more affective problems (Davis et al., 2013).

We conducted a pilot study of eight children who were prenatally exposed to Superstorm Sandy and six children who were not. Based on the literature, we hypothesized that children prenatally exposed to the storm would have larger volumes in limbic system structures and smaller PFC and ACC volumes. Our sample size was small due to COVID-19 restrictions, and we therefore anticipated that some of the analyses would be under powered to detect the differences. Thus, we will evaluate the trend when necessary.

Experiment 5 Methods

Participants

Participants were drawn from the parent study as described in Experiment 1. Families were contacted with permission, given information about the neuroimaging procedure, and asked if they were interested in participating. The participant and family needed to speak English well enough to provide informed consent and complete the study assessments. Children were asked to provide assent to document willingness to participate at the time of the neuroimaging procedure. Exclusion criteria included 1) head injury that caused overt focal brain damage; 2) psychotropic medication within 3 months of the study or on asthma inhaler during the study; 3) pre-existing condition which precludes scanning (e.g., epileptic seizures in the past 3 years, cannot tolerate narrow closed spaces); and 4) metal in the body that cannot be removed including neurostimulators, implanted drug infusion devices, aneurysm clips, metal dental work, cochlear implants, cardiac defibrillators and pacemakers, metal joint prostheses or artificial limbs, metal fragments, pins, screws, plates, catheters, stents, or surgical staples. A description of the demographic information for each of the fourteen subjects is provided in Table 4.1. A majority of participants were female and of Hispanic descent.

Table 4.1. *Demographic information of neuroimaging subjects.*

Subject	Case/Control	Age (months)	Sex	Race
1	Case	71.63	Female	White/Hispanic
2	Case	71.63	Female	White/Hispanic
3	Case	69.63	Female	White/Hispanic
4	Case	75.40	Female	Black
5	Case	81.06	Male	Hispanic
10	Case	79.83	Female	Black/Hispanic
13	Case	78.37	Female	White/Hispanic
14	Case	79.97	Female	White/Hispanic
6	Control	93.77	Male	Black
7	Control	87.77	Male	Hispanic
8	Control	87.63	Female	Black
9	Control	94.00	Female	White/Black
11	Control	90.13	Female	Asian/Hispanic
12	Control	97.50	Male	White/Hispanic

Procedure

Before entering the scan room, the parent and child were informed that participation was voluntary, and the child could be withdrawn at any time during the study. To promote compliance and reduce motion artifact, we followed the "submarine protocol" described by Theys, Wouters, and Ghesquière (2014). This procedure includes informational, child-friendly video explanations of the scan session, showing the child the difference between a clear and blurry picture, and practicing balancing objects on the nose to teach them to stay still. Earplugs and headphones were provided during MRI acquisition. Padding was carefully placed under the knees, between the head and coil, and under the forearm to maximize comfort, minimize muscle strain, and physically restrict head motion. A parent was allowed to stay with the child in the scan room during the entire procedure to reduce the child's anxiety. We communicated with the child during every break in scanning (every 4-7 minutes) to make sure the child was happy to continue and were prepared to discontinue the scan immediately if there was any sign of discomfort or distress. All were able to tolerate the MRI.

Each subject was scanned using a Siemens Prisma 3T whole-body scanner (Erlangen, Germany) with a 32-channel head coil at the CUNY ASRC MRIF. High-resolution, T1-weighted anatomical images will be collected for each subject using an MPRAGE sequence (TR = 2500 ms, TE = 2.9 mm, FOV = 256 mm, FA = 8.0 deg, matrix size = 256 x 256, slices = 176, slice thickness = 1 mm, voxel size = 1.0 x 1.0 x 1.0 mm). Data acquisition lasted approximately seven minutes while the child watched a video of their choosing.

Analysis

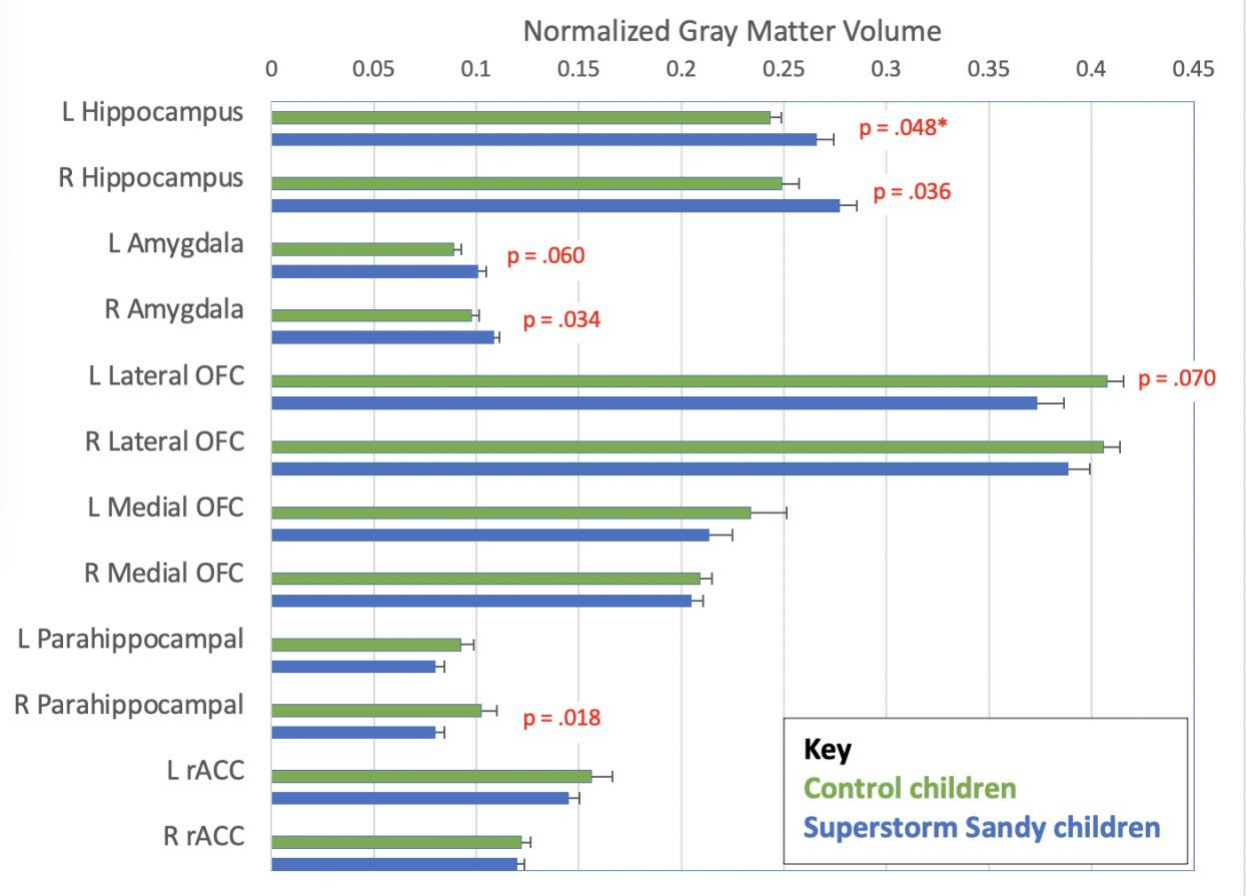
We converted all DICOM files to NIfTI format using the command “dcm2niix -o” in Python. Outliers were calculated and despiked. A de-oblique of the data was performed to correct for any tilt. The motion sensor parameter was set to 2mm displacement. We further processed the structural MRI (sMRI) data with Freesurfer to create a mask using segmentation. Anatomical segments were resampled to the resolution of the fMRI data. Data was segmented and parcellated using Freesurfer for each subject.

Data was imported into SPSS 25 (IBM Inc.) and normalized by total intracranial brain volume to correct for individual differences in brain size. Independent sample t-tests were conducted to determine significant differences between the children who were and the children who were not prenatally exposed to Superstorm Sandy in the following bilateral regions of interest: hippocampus, amygdala, lateral and medial orbitofrontal cortex (OFC, a proxy for the PFC), parahippocampal gyrus, and rACC. The Benjamini-Hochberg procedure was then used to correct for multiple comparisons with a false discovery rate of 15% (Benjamini & Hochberg, 1995).

Experiment 5 Results

Independent sample t-tests indicated gray matter volume was greater bilaterally in the hippocampus of children prenatally exposed to Superstorm Sandy as compared with children who were not, as seen in Figure 4.1. The volume of the amygdala was also significantly larger in the right amygdala of the prenatal exposure group, although in the left amygdala this only approached significance. The right parahippocampal gyrus of control children was significantly larger than prenatally exposed children. Further, a nonsignificant trend indicated that the left lateral orbitofrontal cortex (OFC), a proxy for the lateral PFC, was smaller in prenatally exposed children than control children. All findings remained significant after correcting for multiple comparisons using the Benjamini-Hochberg procedure with a 15% false discovery rate.

Figure 4.1. *Group comparisons of normalized gray matter volume in regions of interest.*



Note: *indicates equal variances in the independent sample t-test were not assumed. “L” and “R” indicate left or right hemisphere, respectively.

Experiment 5 Summary

We assessed the gray matter volume of several areas of the prefrontal-limbic circuit in eight children who were and six children who were not prenatally exposed to Superstorm Sandy. As expected, the amygdala was larger in children with prenatal exposure, although this trend was nonsignificant in the left hemisphere. Prior research into the impact of maternal prenatal mental health has also found this in children (Acosta et al., 2019; Lee et al., 2019; Wen et al., 2017). The hippocampus was also bilaterally larger in children with prenatal storm exposure. A trend approaching significance indicated the left lateral OFC was smaller in storm exposed children was also expected, as others have found reductions in prefrontal gray matter (Buss et al., 2010; Davis et al., 2020). However, there were no differences in the rACC. Lastly, the right hippocampal gyrus was significantly smaller in storm exposed children than

controls. This was unexpected, given that it is part of the limbic system and the hippocampus was larger than controls in these children.

The contradictory findings with regard to the hippocampus and parahippocampal gyrus are interesting in light of the literature. Human studies have had mixed results, with Buss et al. (2012) finding no differences in the hippocampal volume of children prenatally exposed to higher levels of maternal cortisol. Wang et al. (2018) uncovered a complex relationship between prenatal maternal depression and offspring hippocampal volume that was mediated by *FKBP5* genetic risk, such that high depression symptoms and genetic risk predicted increased volume. Further, animal studies have found decreased hippocampal volume in rhesus monkeys (Coe et al., 2003) and rat models (Mychasiuk et al., 2012) subsequent to prenatal maternal stress. Few studies have reported findings in the parahippocampal gyrus, which is highly connected to the mPFC and ACC, in relation to prenatal stress. In one such study Buss et al., (2010) found that 6-9-year-old children exposed to high levels of maternal pregnancy anxiety in the second trimester had reduced gray matter volume in this region. Child abuse in the postnatal period has also been linked with reduced volume, which in turn was correlated with increased externalizing symptoms (Gold et al., 2016). Lack of consistency across studies with regard to this critical region of the brain mandates further investigation in larger sample sizes.

This experiment was preliminary in nature and has notable limitations. First among these is the small sample size of eight prenatal storm exposed and six non-prenatal storm exposed children. Second, the composition of age and sex is uneven between the two groups. Subject recruitment was halted due to Covid-19 considerations, and we will aim to correct this when recruitment resumes. Third, prenatal Superstorm Sandy exposure was determined based on date of birth in relation to the occurrence of the storm, rather than degree of maternal stress related to the storm. The small sample size necessitated this simplistic grouping mechanism, but an assessment that takes maternal perceived stress into account would be more informative. A larger sample size would also allow for consideration of postnatal maternal mental health as well. A measure of maternal cortisol would also provide more insight into the level of stress most closely associated with brain structure aberrations.

Despite these limitations, we have demonstrated significant structural differences in brain regions key to emotion experience and regulation on the basis of prenatal Superstorm Sandy experience. Importantly, the statistical analyses remained significant after correction for multiple testing. These findings support the need to expand the current sample size to increase statistical power and enable more nuanced analyses of maternal subjective storm experience, sex effects, and potential behavioral problems related to these structural differences.

Experiment 6: Prenatal stress and the function of the prefrontal-limbic circuit

Evaluating the gray matter volume of brain structures is an important piece in understanding the health of a neural circuit, but not all encompassing on its own. Functional MRI (fMRI) provides important information about the degree of neural activity inferred from oxygenated blood flow to the structure. fMRI can be measured while the subject is at rest or performing a task thought to engage specific neural circuits. Activity relative to other tasks or other subjects provides context as to whether structures are hyper- or hypoactive. Further, functional connectivity, or the degree of synchronization between two brain structures is inferred from the temporal coincidence of activity in those structures. A commonly used task for investigating prefrontal-limbic circuit function was developed by Hariri et al. (2002) and displays faces with different emotional expressions, including happy, sad, angry, or fearful. Viewing negative emotions in particular is known to activate the prefrontal-limbic circuit, giving an approximation of the health of the circuit. This methodology has been used to address the question of the impact of stress on offspring neurodevelopment, although the issue of prenatal natural disaster-related stress on early childhood neurodevelopment remains unresolved.

The relation between stress experienced firsthand in the postnatal period and the function of the prefrontal-limbic system lends some insight into what can be expected of the impact of prenatal stress. One such study found that prior institutional rearing (i.e., time in an orphanage) was associated with greater amygdala activation in response to images of fearful faces compared to control children (Gee, Gabard-Durnam, et al., 2013). Another found that amygdala activation was greater in response to faces displaying fearful, sad, and happy expressions in 7-12-year-old children exposed to early life stress than control children (Suzuki et al., 2014). They further found that children with higher levels of depression

symptoms had a correlation between early life stress and activation in the left hippocampus and globus pallidus. Increased early life trauma was also correlated with increased activation in the bilateral amygdalae and cingulate in response to sad facial expressions (Suzuki et al., 2014). Pagliaccio et al., (2015) observed that the number of negative life events experienced was correlated with weaker functional connectivity between the amygdala and ACC, increased anxiety symptoms, and decreased externalizing symptoms in children 9-14 years old. Although some results are mixed, most of these studies report relative amygdala hyperactivity in subjects who experienced stressful life events. Evaluating neural circuitry in relation to postnatal stressors is important in its own right and provides some data from which to hypothesize about the outcomes of prenatal stressors. However, the vulnerability of the prenatal period may make results different from those of postnatal stressors.

Understanding the neural function of the prefrontal-limbic circuit in children who have psychopathological symptoms or diagnoses may also give vital insight, as it is thought that prenatal stress may put offspring at risk for psychopathology. For example, pediatric post-traumatic stress disorder (PTSD) has been associated with increased dorsal ACC activity and decreased amygdala-mPFC functional connectivity in response to stimuli signaling threat (Wolf & Herringa, 2016). Among 8-16-year old subjects looking at faces with happy, sad, or fearful expressions, amygdala-vPFC/ACC functional connectivity was positive in youths with bipolar disorder and negative in healthy controls and youths with ADHD (Hafeman et al., 2017). The same study also found that amygdala-subgenual ACC functional connectivity was positive in youths with bipolar disorder, negative in healthy controls, and neutral in youths with ADHD. In another small sample of 8-16-year old subjects viewing fearful facial expressions, the presence of an anxiety disorder was correlated with exaggerated amygdala response whereas depression was associated with blunted amygdala response (Thomas et al., 2001), suggesting the need to differentiate between these two clusters of internalizing symptoms. Among twelve-year-old children with high externalizing symptoms and a paternal family history of substance use, mPFC, precuneus, and occipital lobe activation in response to facial expressions with emotional valence was higher than that of healthy controls (Hulvershorn et al., 2013). Lastly, among young adults with conduct disorder viewing angry and fearful facial expressions, having high levels of both oxytocin receptor methylation and callous-unemotional traits was associated with weak functional connectivity between the centromedial nucleus of

the amygdala and vmPFC/OFC, as well as between the bilateral amygdalae and precuneus/temporoparietal area(Aghajani et al., 2018). These studies largely found hyperactive amygdala responses and poor coordination between frontal and limbic areas. We would expect to see similar outcomes in children at risk for these disorders by virtue of prenatal maternal stress exposure.

A recent wave of studies has shed more light on the impact of prenatal maternal stress on child prefrontal-limbic circuit function. In one sample of six-week-old infants exposed to maternal prenatal depression, resting state functional connectivity between the amygdala and dPFC was negative compared to unexposed infants (Posner et al., 2016). In another sample of offspring exposed to prenatal depression, symptoms were associated with altered amygdala resting state functional connectivity in four-year-old girls, such that left hemisphere connectivity with the subgenual ACC and caudate was weaker and right hemisphere connectivity with the left OFC, insula, and temporal pole was weaker (Soe et al., 2018). In another sample of 6-9-year-old children exposed to prenatal maternal depression, amygdala response to negative facial expressions was greater than that of control children (van der Knaap et al., 2018). Other studies have relied on more objective, biological indicators of stress during pregnancy. For example, Graham et al. (2018) found that higher levels of the inflammatory cytokine interleukin-6 (IL-6) during pregnancy were associated with a larger right amygdala *and* stronger left amygdala resting connectivity with sensory, salience, and learning and memory areas of the brain at birth. This, in turn, mediated a correlation between prenatal IL-6 levels and decreased impulse control at two years of age (Graham et al., 2018). In the same sample, the relationship between prenatal maternal cortisol levels and increased internalizing symptoms in girls was also mediated by stronger amygdala connectivity to sensory and integration areas of the brain and the default mode network (Graham et al., 2019). In the same study, the correlation between prenatal cortisol and resting state amygdala connectivity was weaker in boys. Another study further found an association between elevated maternal glucocorticoid levels at 31 weeks gestation and increased general neural network connectivity and internalizing symptoms in 6-9-year-old female, but not male offspring (Kim et al., 2017). These findings point to alterations in the prefrontal-limbic circuit related to prenatal maternal stress exposure, but the studies lack task-based fMRI data outcomes (with the exception of van der Knaap et al.) and exposure to a common stressor.

Experiment 6 attempted to fill this gap in knowledge by investigating the function of the prefrontal-limbic circuit during an emotion-based task in 5-8-year-old children prenatally exposed to Superstorm Sandy in comparison with children who were not prenatally exposed. Children underwent an fMRI scan while viewing facial expressions displaying negative facial expressions. We hypothesized that the prenatal exposure group would display increased limbic system activity during an emotion-based task compared to controls, based on these results in children with anxiety disorders (Thomas et al., 2001) and children exposed to early life stress (Gee, Gabard-Durnam, et al., 2013; Suzuki et al., 2014). Our hypothesis regarding prefrontal and rACC activity was exploratory, as prior studies have only reported resting state activity of prefrontal areas in relation to limbic activity.

Experiment 6 Methods

Participants

As described in Experiment 1, participants were drawn from the parent. Exclusion criteria included 1) head injury that caused overt focal brain damage; 2) psychotropic medication within 3 months of the study or on asthma inhaler during the study; 3) pre-existing conditions that preclude scanning (e.g., epileptic seizures in the past 3 years, claustrophobia); and 4) metal in the body that cannot be removed. The same fourteen subjects as in Experiment 5 underwent the fMRI scan, however subject 9 and 12 from Table 4.1 were excluded for falling asleep during the scan, leaving seven who were prenatally exposed to the storm, and five who were not.

Procedure

As described in Experiment 5, parents and children gave their informed consent before all study procedures. To promote compliance and reduce motion artifact, we followed the “submarine protocol” described by Theys, Wouters, and Ghesquière (2014), including child-friendly video explanations, demonstrating difference between a clear and blurry picture, and practicing balancing objects on the nose. The task performed in the scanner (described below) was practiced before entering the scanner to ensure the child understood how to respond to the stimuli. Earplugs and headphones were provided during MRI acquisition. Padding was placed to maximize comfort, minimize muscle strain, and physically restrict head motion. A parent was allowed to stay with the child in the scan room during the entire

procedure to reduce the child's anxiety. We communicated with the child during every break in scanning (every 4-7 minutes) to make sure the child was happy to continue and were prepared to discontinue the scan immediately if there was any sign of discomfort or distress. All were able to tolerate the MRI.

Each subject was scanned using a Siemens Prisma 3T whole-body scanner (Erlangen, Germany) with a 32-channel head coil and response box at the CUNY ASRC MRIF. Functional data was collected using a multi-echo EPI sequence (TR=800ms, TE=30ms, GRAPPA=3, 66 near axial slices, FoV=216mm, slice thickness=2.4, local shimming to the field of view, matrix size = 90 x 90, voxel size = 2.4 x 2.4 x 2.4 mm, FA = 52 deg, acceleration factor = 6).

Data acquisition lasted approximately four minutes while the child engaged in a task designed to evoke emotion regulation processes (Hariri et al., 2000; Hariri et al., 2002; Somerville et al., 2018). Participants viewed one image at the top of the screen and two at the bottom, one of which matched the top image. Participants were instructed to press a button corresponding to the image (i.e., left or right) that matched the top image. There are five blocks of six trials in which these images are shapes, and five alternating blocks in which these images are faces displaying either angry or fearful expressions. The stimuli were presented, and responses were recorded via E-prime 2.0 (Psychology Software Tools, Pittsburgh, PA, USA). This task is known to increase blood-oxygen-level-dependent (BOLD) signal in the amygdala (Manuck et al., 2007), fusiform gyrus, occipital cortex, and right prefrontal cortex (Geuter et al., 2018). The task has also been shown predict symptoms of internalizing emotion dysregulation (Gard et al., 2018).

Analysis

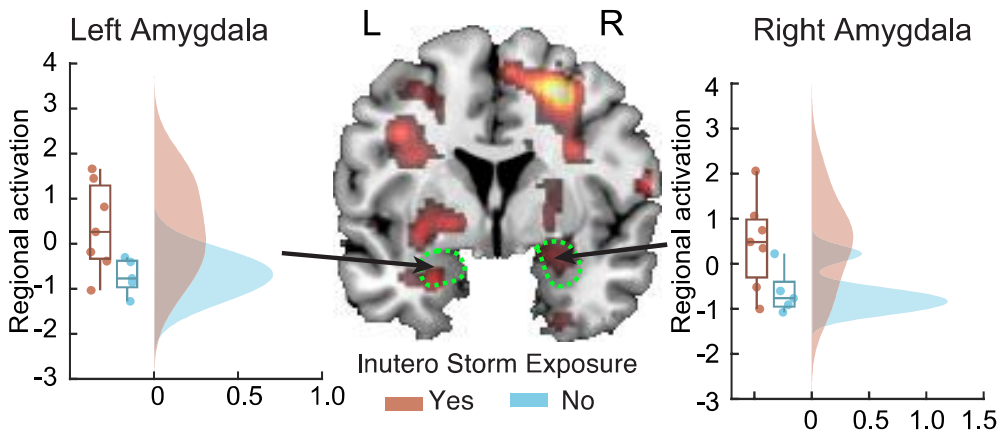
Functional MRI preprocessing and statistical modeling was conducted using the statistical parametric mapping package (SPM12, Wellcome Trust Centre for Neuroimaging, London, UK). Preprocessing included bias correction for intensity inhomogeneities, realignment, co-registration, normalization to an age-specific template, and spatial smoothing. Subject-level general linear modeling (GLM) was conducted to localize brain regions associated with the processing of faces expressing negative emotion. Psychophysiological interaction analysis was conducted to identify regions with connectivity to the seed region (e.g., amygdala) modulated by the processing of angry faces. Independent

samples t-test was conducted to compare the activity between participants with prenatal versus postnatal storm exposure.

Experiment 6 Results

Preliminary results showed that the group prenatally exposed to the storm (n = 7) showed significant or marginally significant higher activation in both left and right amygdala (left: p = 0.043, right: p = 0.054), compared to the group that was not prenatally exposed (n = 5). Figure 4.2 illustrates the clusters of the amygdalae (areas in red within the green dashed contours) that showed significant between-group difference under the voxel-wise threshold of p = .05 or less, and raindrop plots of amygdala activation for the two groups by hemisphere. Negative values represent decreased activity relative to the shaping matching blocks. No significant differences were found in the prefrontal areas or other limbic system areas.

Figure 4.2. *Amygdala response to negative facial expressions by prenatal exposure*



Note: The green contours encircle the left and right amygdala. Raindrop plots for each hemisphere show the magnitude of difference in regional amygdala activation by prenatal exposure group.

Experiment 6 Summary

In a preliminary investigation of prenatal stress and the prefrontal-limbic circuit we demonstrated hyperactive amygdala response to negative facial expressions in children prenatally exposed to maternal prenatal stress related to a natural disaster, Superstorm Sandy. This is in line with reports of hyperactive amygdala responses in children exposed to postnatal stress (Gee, Gabard-Durnam, et al., 2013; Suzuki et al., 2014) and children with anxiety disorders (Thomas et al., 2001). Our hypothesis regarding prefrontal activity was exploratory and we found no significant differences between groups.

Despite the small sample size presented here, we were able to detect differences in amygdala response among children prenatally exposed and unexposed to maternal stress. Abnormality of the amygdala has been the one consistent finding in children with postnatal stress exposure, psychopathology, or prenatal stress exposure. Dysfunction of the amygdala has been implicated in numerous forms of psychopathology, including anxiety (e.g. Li et al., 2016; Thomas et al., 2001; Williams et al., 2015), depression (e.g., Young et al., 2017), bipolar disorder (e.g., Hafeman et al., 2017; Paret et al., 2016), PTSD (e.g., Nicholson et al., 2017; Wolf & Herringa, 2016), autism (e.g., Guo et al., 2016), conduct disorder (e.g., Aghajani et al., 2018; Holz et al., 2017), psychosis (e.g., Jalbrzikowski et al., 2019), and schizophrenia (e.g., Escartí et al., 2010). That we have found a similar trend in young children prenatally exposed to natural disaster-related stress suggests that they may indeed have an increased risk for psychopathology onset.

Although this study was highly preliminary in nature, it is a significant first step and appear to be consistent with the hypothesis. Nevertheless, findings require an expanded sample to replicate these results before many conclusions can be drawn. The small number of subjects in first among the limitations, which also include the lack of balance with regard to the age and sex of subjects in the two groups. We will aim to achieve greater balance post Covid-19. Another limitation includes the rudimentary method of determining case versus control (i.e., by date of birth in relation to the occurrence of Superstorm Sandy). Further consideration of maternal mental health during the prenatal and postnatal periods is also required. Finally, although our task is widely used in similar studies, it does not require

participants to actively regulate their emotions. This would be difficult to ask of participants at this age but would more accurately test the emotion regulation capability of the prefrontal-limbic circuit.

Despite the limitations of this preliminary experiment, the data compel an expansion of the sample. With a greater sample size, and therefore greater statistical power, we may uncover group differences in prefrontal regions of the brain and incorporate more variables related to maternal prenatal and postnatal mental health. Linking the mental health of the children with neural function will also help shed light on the relation between prenatal stress, risk for the development of psychopathology, and overall impairment.

Discussion

The goal of this chapter was to evaluate the health of the prefrontal-limbic circuit in young children who were prenatally exposed to natural disaster-related stress in comparison with children who were not. The prefrontal-limbic circuit was the focus of interest because it subserves emotion regulation processes and has been implicated many different forms of psychopathology. We evaluated the circuit in two ways: structurally and functionally. For the latter method, a widely used task involving the viewing of faces with negative expressions was employed.

With regard to the structure of the circuit, we had several notable findings in Experiment 5. First, the gray matter volume of the right amygdala of children prenatally exposed to Superstorm Sandy was significantly larger and the left amygdala was marginally larger than control children. Second, the bilateral hippocampi of these children were significantly larger than children who were not prenatally exposed. Third, the right parahippocampal gyrus of children prenatally exposed was smaller than control children. Lastly, the left lateral orbitofrontal cortex of the exposure group was marginally smaller than the control group. Taken together, these results suggest that there are structural differences in this circuit related to prenatal stress from a natural disaster. Although the relationship between brain structure and function is complicated, these differences may speak to the basic makeup of these critical brain regions.

One main finding, greater amygdala activation among cases versus controls, emerged from our analysis of the function of the prefrontal-limbic circuit in Experiment 6, has both biological and clinical implications. While viewing negative facial expressions, children who were prenatally exposed to

Superstorm Sandy had greater amygdala activation than control children. This effect was significant in the left hemisphere and marginally significant in the right hemisphere. Amygdala differences have been discovered across many different types of psychopathology and emotion regulation abilities. Note no other significant differences were detected. These findings may suggest that children prenatally exposed to traumatic events are at risk for emotion dysregulation and the development of psychopathology, particularly when also considering the findings of Experiments 3-5.

Children prenatally exposed to traumatic events may also be vulnerable to future stressors including natural disasters, pandemics, or other traumatic events. Another research group studying Superstorm Sandy has demonstrated how postnatal exposure to the storm interacted with preexisting neural function to predict increased emotion dysregulation. Meyer et al. (2017) found that children with elevated internalizing symptoms at three years of age, who then demonstrated an exaggerated error-related negativity (ERN) in an electroencephalogram (EEG) experiment at six years of age and also experienced a high level of Superstorm Sandy-related stressors, had even more internalizing symptoms at age nine in comparison with other children. The ERN is a known neural biomarker of anxiety and related disorders, as is hyperactive amygdala activity. The children prenatally exposed to Superstorm Sandy with aberrant prefrontal-limbic structure and function may be particularly at risk for postnatal stressful events, such as a pandemic.

Although our findings need to be replicated and linked to behavioral indices of emotion regulation, future work could reveal that a generation of children pre- or postnatally exposed to these kinds of stressful events should be closely monitored for signs of psychopathology development. In light of the Covid-19 pandemic, social injustice, and record-breaking hurricane seasons, advocates for child mental health may especially focus on the needs of children who also experienced maternal prenatal stress.

Chapter 5: Conclusions and Future Directions

This preceding chapters document neurodevelopmental outcomes in children prenatally exposed to prenatal maternal stress related to a natural disaster, Superstorm Sandy. Although much is unique about these children, from the storm itself to the cultural makeup of New York City residents, commonalities have been found between the outcomes described here and research into children affected by similarly stressful events. Experiments 1-2 described correlations between infant temperament and objective maternal stress related to Superstorm Sandy. This is discussed in the context of other findings by our research group, including maternal prenatal mental health predicting infant temperament and trajectories of temperament development over the first two years of life. Experiment 2 further explored the association between temperament and sympathetic nervous system function. Experiments 3-4 described an interaction between prenatal storm stress and maternal mental health predicting offspring EDA in early childhood and an interaction between prenatal storm stress and offspring sex predicting early childhood EDA. Experiments 5-6 reviewed current literature that investigates the associated between prenatal/postnatal stress and child brain development and presented preliminary findings from a pilot study of prenatal stress related to Superstorm Sandy and child prefrontal-limbic structure and function. A picture emerges from these data that suggest prenatal exposure to Superstorm Sandy may contribute to neurodevelopmental aberrations, but other factors such as maternal mental health and offspring sex may interact with the prenatal stress to influence the trajectory of neurobehavioral and neural development.

In addition to expanding the sample size and conducting functional connectivity analyses of the prefrontal-limbic circuit, continuing to follow this sample of subjects may reveal key information about trajectories of neurodevelopment in children vulnerable by virtue of prenatal stress. In two cross-sectional studies of neurotypically developing children, functional connectivity between the PFC and limbic system while viewing faces with emotional expressions was found to undergo a shift from a positive correlation to a negative correlation around puberty (Gee, Humphreys, et al., 2013; Wu et al., 2016). Cross-sectional studies have also found that age correlated with decreased amygdala activity (Gee, Humphreys, et al., 2013) and increased resting functional connectivity between the amygdala and mPFC (Gabard-Durnam et al., 2014). In another cross-sectional study of 6–23-year-old

neurotypically developing subjects, children had a greater amygdala response to neutral and adverse stimuli than older subjects (Silvers et al., 2017). Further, an age-related shift in mPFC response to aversive stimuli occurred, such that activation was more ventral in younger subjects and dorsal in older subjects. In the same sample, Silvers et al. (2016) found that cognitive reappraisal of aversive stimuli was associated with a) negative correlation between age and amygdala response mediated by vlPFC activity, b) a connective correlation between vmPFC-amygdala functional connectivity and age, and c) the relationship between the vmPFC and amygdala modulated the effect of the vlPFC on the amygdala, with negative vmPFC-amygdala functional connectivity linked with stronger influence of the vlPFC on the amygdala. Prefrontal-limbic connectivity is well-documented in neurotypically developing children, but the trajectories in children impacted by stress are still emerging.

Prior research indicates a unique pattern of prefrontal-limbic development in children exposed to early life stress. In a cross-sectional study of 6–17-year-olds viewing faces with emotional expressions, subjects who spent time in a rearing institution (i.e., orphanage) displayed more mature amygdala-PFC functional connectivity, such that the correlation in activation between the two regions was more negative than neurotypically developing subjects (Gee, Gabard-Durnam, et al., 2013). Researchers hypothesize that accelerated maturation of this circuit may be an adaptation to lack of emotional support from a caregiver that can put children at risk for psychopathology, stating “anxiety is a common long-term outcome associated with ‘growing up quickly’” (Callaghan & Tottenham, 2016, p. 79). Children with psychological disorders have also been studied in this context. In a large cross-sectional sample of 7–25-year-olds viewing faces with emotional expressions, functional connectivity between the amygdala and ACC switched from positive to negative around fifteen years of age in neurotypically developing subjects, whereas in subjects with an anxiety disorder this correlation switched from negative to positive around fifteen years of age (Kujawa et al., 2016)\. In the same sample, right inferior frontal gyrus and orbitofrontal gyrus response to facial expressions was negatively correlated with age, with no observed significant differences on the basis of anxiety disorder diagnosis (Bunford et al., 2018). In another cross-sectional sample of 8–18-year-olds viewing stimuli signaling threat or neutrality, the correlation between age and amygdala-vmPFC functional connectivity and between age and dmPFC response to threat was negative in subjects with PTSD and positive in neurotypically developing subjects (Wolf & Herringa, 2016). The

trajectory of prefrontal-limbic development seems altered in children exposed to early life stress and those with early onset psychopathology but remains unstudied in children exposed to prenatal stress.

With rates of childhood psychopathology on the rise, including one in six children aged 2-8 having a mental, behavioral, or developmental disorder, and an estimated 60% of American youth classified as not thriving (Bethell et al., 2019), both the sources and outcomes of impactful stressors need to be examined. The latest agenda set forth by the National Academy of Medicine emphasizes the role of promoting mental wellbeing at a societal level in reducing the incidence of psychopathology (National Academy of Medicine, 2019). One source of increased stress at the societal level may stem from climate change events, including natural disasters. According to the most recently published Intergovernmental Panel on Climate Change, frequency and intensity of extreme weather events is predicted to continue to increase in North America in the years to come (IPCC, 2019). On the heels of the most active hurricane season on record in the Atlantic Ocean (NOAA, 2020), the psychological suffering associated with these events is coming into focus. As reviewed by Hayes et al. (2018), changes to climate and extreme weather events have been linked to a wide spectrum of mental health problems including trauma, anxiety, depression, grief, and despair. “Solastalgia,” or distress related to environmental changes including natural disasters, changing landscapes, and resource depletion, is a growing field of research (Warsini et al., 2014). Children, women, and socioeconomically disadvantaged people are believed to be particularly vulnerable to these effects . The vulnerability of pregnant people and their children, and how they can best be supported in the face of climate change, needs to be more thoroughly studied as well.

The vulnerability of children exposed to prenatal stress to postnatal stressors experienced first-hand should also be studied. Early research into the immediate mental health impact of the COVID-19 pandemic indicate rises in anxiety, depression, PTSD, and general stress symptoms in populations across the globe (Xiong et al., 2020), although the long term effects remain to be seen. Families facing financial instability due to the pandemic in particular in the United States are facing high rates of mental health problems in parents and adults (Patrick et al., 2020). The impact of these factors on pregnant people and their offspring will become clearer in the coming years. If leaders had a better understanding of the mental health cost related to the pandemic, especially for vulnerable populations, better care could

have been taken early on to protect people. Studying the shared stressors and consequences of natural disasters and pandemics, such as financial loss, food and housing insecurity, and mental strain, can shed light on how to best care for those most at risk.

This dissertation presents data that scratches the surface of the question as to the impact of natural disaster stress during pregnancy on the psychological wellbeing of offspring. Continuing to study the children prenatally exposed to Superstorm Sandy and other disasters to determine rates of psychopathology development, resilience, and overall health will be key to understanding the full impact of climate change on human suffering. Public health policy and mental health professionals may benefit from this knowledge to best support children and pregnant people during times of crisis. Improved intervention and prevention strategies could promote adaptive coping mechanisms to mitigate stress and curb the rise of psychopathology across a generation.

References

Acosta, H., Tuulari, J. J., Scheinin, N. M., Hashempour, N., Rajasilta, O., Lavonius, T. I., Pelto, J., Saunavaara, V., Parkkola, R., Lähdesmäki, T., Karlsson, L., & Karlsson, H. (2019). Maternal pregnancy-related anxiety is associated with sexually dimorphic alterations in amygdala volume in 4-year-old children. *Frontiers in Behavioral Neuroscience*, *13*. https://doi.org/10.3389/fnbeh.2019.00175

Aghajani, M., Klapwijk, E. T., Colins, O. F., Ziegler, C., Domschke, K., Vermeiren, R. R. J. M., & van der Wee, N. J. A. (2018). Interactions between oxytocin receptor gene methylation and callous-unemotional traits impact socioaffective brain systems in conduct-disordered offenders. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *3*(4), 379–391. https://doi.org/10.1016/j.bpsc.2017.12.010

Aldao, A., Gee, D. G., Reyes, A. D. L., & Seager, I. (2016). Emotion regulation as a transdiagnostic factor in the development of internalizing and externalizing psychopathology: Current and future directions. *Development and Psychopathology*, *28*(4pt1), 927–946. https://doi.org/10.1017/S0954579416000638

Alkon, A., Boyce, W. T., Tran, L., Harley, K. G., Neuhaus, J., & Eskenazi, B. (2014). Prenatal adversities and Latino children's autonomic nervous system reactivity trajectories from 6 months to 5 years of age. *PLoS ONE*, *9*(1), e86283. https://doi.org/10.1371/journal.pone.0086283

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders (DSM-5®)*. American Psychiatric Pub.

Austin, M.-P., Hadzi-Pavlovic, D., Leader, L., Saint, K., & Parker, G. (2005). Maternal trait anxiety, depression and life event stress in pregnancy: Relationships with infant temperament. *Early Human Development*, *81*(2), 183–190. https://doi.org/10.1016/j.earlhumdev.2004.07.001

Austin, M.-P., Leader, L. R., & Reilly, N. (2005). Prenatal stress, the hypothalamic–pituitary–adrenal axis, and fetal and infant neurobehaviour. *Early Human Development*, *81*(11), 917–926. https://doi.org/10.1016/j.earlhumdev.2005.07.005

Baibazarova, E., van de Beek, C., Cohen-Kettenis, P. T., Buitelaar, J., Shelton, K. H., & van Goozen, S. H. M. (2013). Influence of prenatal maternal stress, maternal plasma cortisol and cortisol in the

amniotic fluid on birth outcomes and child temperament at 3 months. *Psychoneuroendocrinology*, *38*(6), 907–915. https://doi.org/10.1016/j.psyneuen.2012.09.015

Baker, E., Shelton, K. H., Baibazarova, E., Hay, D. F., & van Goozen, S. H. M. (2013). Low skin conductance activity in infancy predicts aggression in toddlers 2 years later. *Psychological Science*, *24*(6), 1051–1056. https://doi.org/10.1177/0956797612465198

Bale, T. L. (2011). Sex differences in prenatal epigenetic programming of stress pathways. *Stress (Amsterdam, Netherlands)*, *14*(4), 348–356. https://doi.org/10.3109/10253890.2011.586447

Barker, D. J. P. (1998). In utero programming of chronic disease. *Clinical Science*, *95*(2), 115. https://doi.org/10.1042/CS19980019

Bates, J. E., Freeland, C. A. B., & Lounsbury, M. L. (1979). Measurement of infant difficultness. *Child Development*, *50*(3), 794–803. https://doi.org/10.2307/1128946

Beauchaine, T. P. (2012). Physiological markers of emotion and behavior dysregulation in externalizing psychopathology. *Monographs of the Society for Research in Child Development*, *77*(2), 79–86. https://doi.org/10.1111/j.1540-5834.2011.00665.x

Beauchaine, T. P. (2015). Future directions in emotion dysregulation and youth psychopathology. *Journal of Clinical Child & Adolescent Psychology*, *44*(5), 875–896. https://doi.org/10.1080/15374416.2015.1038827

Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: A practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society. Series B (Methodological)*, *57*(1), 289–300.

Benjamini, Y., & Yekutieli, D. (2001). The control of the false discovery rate in multiple testing under dependency. *The Annals of Statistics*, *29*(4), 1165–1188.

Bethell, C. D., Gombojav, N., & Whitaker, R. C. (2019). Family resilience and connection promote flourishing among US children, even amid adversity. *Health Affairs*, *38*(5), 729–737. https://doi.org/10.1377/hlthaff.2018.05425

Bitsko, R. H., Holbrook, J. R., Ghandour, R. M., Blumberg, S. J., Visser, S. N., Perou, R., & Walkup, J. T. (2018). Epidemiology and impact of health care provider–diagnosed anxiety and depression

among US children. *Journal of Developmental and Behavioral Pediatrics : JDBP*, *39*(5), 395–403. https://doi.org/10.1097/DBP.0000000000000571

Bolten, M., Nast, I., Skrundz, M., Stadler, C., Hellhammer, D. H., & Meinlschmidt, G. (2013). Prenatal programming of emotion regulation: Neonatal reactivity as a differential susceptibility factor moderating the outcome of prenatal cortisol levels. *Journal of Psychosomatic Research*, *75*(4), 351–357. https://doi.org/10.1016/j.jpsychores.2013.04.014

Boucsein, W. (1992). Electrodermal activity. In I. Martin & P. H. Venables (Eds.), *Techniques in psychophysiology* (Vol. 3, pp. 3–67).

Braithwaite, E. C., Pickles, A., Sharp, H., Glover, V., O'Donnell, K. J., Tibu, F., & Hill, J. (2017). Maternal prenatal cortisol predicts infant negative emotionality in a sex-dependent manner. *Physiology & Behavior*, *175*, 31–36. https://doi.org/10.1016/j.physbeh.2017.03.017

Braithwaite, J. J., Watson, D., Jones, R., & Rowe, M. (2013). A guide for analysing electrodermal activity (EDA) & skin conductance responses (SCRs) for psychological experiments. *Psychophysiology*, *49*, 1017–1034.

Bromet, E., & Dew, M. (1995). Review of psychiatric epidemiologic research on disasters | Epidemiologic Reviews | Oxford Academic. *Epidemiologic Reviews*, *17*, 113–119.

Bunford, N., Kujawa, A., Fitzgerald, K. D., Monk, C. S., & Phan, K. L. (2018). Convergence of BOLD and ERP measures of neural reactivity to emotional faces in children and adolescents with and without anxiety disorders. *Biological Psychology*, *134*, 9–19. https://doi.org/10.1016/j.biopsycho.2018.02.006

Buss, C., Davis, E. P., Shahbaba, B., Pruessner, J. C., Head, K., & Sandman, C. A. (2012). Maternal cortisol over the course of pregnancy and subsequent child amygdala and hippocampus volumes and affective problems. *Proceedings of the National Academy of Sciences*, *109*(20), E1312–E1319. https://doi.org/10.1073/pnas.1201295109

Buss, C., Davis, E. P., Muftuler, L. T., Head, K., & Sandman, C. A. (2010). High pregnancy anxiety during mid-gestation is associated with decreased gray matter density in 6-9 year-old children. *Psychoneuroendocrinology*, *35*(1), 141–153. https://doi.org/10.1016/j.psyneuen.2009.07.010

Buthmann, J., Finik, J., Ventura, G., Zhang, W., Shereen, A. D., & Nomura, Y. (2019). The children of Superstorm Sandy: Maternal prenatal depression blunts offspring electrodermal activity. *Biological Psychology*, *146*, 107716. https://doi.org/10.1016/j.biopsycho.2019.107716

Buthmann, J., Finik, J., & Nomura, Y. (2018). Sex differences in the relations between infant temperament and electrodermal responses in early childhood. *International Journal of Behavioral Development*, *42*(6), 535–542. https://doi.org/10.1177/0165025418757705

Buthmann, J., Ham, J., Davey, K., Finik, J., Dana, K., Pehme, P., Zhang, W., Glover, V., & Nomura, Y. (2019). Infant temperament: Repercussions of Superstorm Sandy-related maternal stress. *Child Psychiatry & Human Development*, *50*(1), 150–162. https://doi.org/10.1007/s10578-018-0828-2

Calkins, S. D., Graziano, P. A., & Keane, S. P. (2007). Cardiac vagal regulation differentiates among children at risk for behavior problems. *Biological Psychology*, *74*(2), 144–153. https://doi.org/10.1016/j.biopsycho.2006.09.005

Callaghan, B. L., & Tottenham, N. (2016). The Stress Acceleration Hypothesis: Effects of early-life adversity on emotion circuits and behavior. *Current Opinion in Behavioral Sciences*, *7*, 76–81. https://doi.org/10.1016/j.cobeha.2015.11.018

Carlén, M. (2017). What constitutes the prefrontal cortex? *Science*, *358*(6362), 478–482. https://doi.org/10.1126/science.aan8868

Chen, F. R., Raine, A., Glenn, A. L., & Granger, D. A. (2015). Hypothalamic pituitary adrenal activity and autonomic nervous system arousal predict developmental trajectories of children's comorbid behavior problems. *Developmental Psychobiology*, *58*(3), 393–405. https://doi.org/10.1002/dev.21379

Chess, S., & Thomas, A. (1977). Temperament and the Parent-Child Interaction. *Pediatric Annals*, *6*(9), 26–45.

Chrousos, G. P. (1992). The concepts of stress and stress system disorders. Overview of physical and behavioral homeostasis. *JAMA: The Journal of the American Medical Association*, *267*(9), 1244–1252. https://doi.org/10.1001/jama.267.9.1244

Class, Q. A., Abel, K. M., Khashan, A. S., Rickert, M. E., Dalman, C., Larsson, H., Hultman, C. M., Långström, N., Lichtenstein, P., & D'Onofrio, B. M. (2014). Offspring psychopathology following

preconception, prenatal and postnatal maternal bereavement stress. *Psychological Medicine*, *44*(1), 71–84. https://doi.org/10.1017/S0033291713000780

CNN Library. (2018, March 13). *Hurricane Sandy Fast Facts*. CNN. https://www.cnn.com/2013/07/13/world/americas/hurricane-sandy-fast-facts/index.html

Coe, C. L., Kramer, M., Czéh, B., Gould, E., Reeves, A. J., Kirschbaum, C., & Fuchs, E. (2003). Prenatal stress diminishes neurogenesis in the dentate gyrus of juvenile Rhesus monkeys. *Biological Psychiatry*, *54*(10), 1025–1034. https://doi.org/10.1016/S0006-3223(03)00698-X

Collins, F. S., & Tabak, L. A. (2014). NIH plans to enhance reproducibility. *Nature*, *505*(7485), 612–613.

Cree, R. A., Bitsko, R., Robinson, L., Holbrook, J., Danielson, M., Smith, C., Kaminski, J., Kenney, M. K., & Peacock, G. (2018). Health care, family, and community factors associated with mental, behavioral, and developmental disorders and poverty among children aged 2–8 Years—United States, 2016. *MMWR. Morbidity and Mortality Weekly Report*, *67*. https://doi.org/10.15585/mmwr.mm6750a1

Crowell, S. E., Beauchaine, T. P., Gatzke-Kopp, L., Sylvers, P., Mead, H., & Chipman-Chacon, J. (2006). Autonomic correlates of attention-deficit/hyperactivity disorder and oppositional defiant disorder in preschool children. *Journal of Abnormal Psychology*, *115*(1), 174–178. https://doi.org/10.1037/0021-843X.115.1.174

Curry, S. J., Krist, A. H., Owens, D. K., Barry, M. J., Caughey, A. B., Davidson, K. W., Doubeni, C. A., Epling, J. W., Grossman, D. C., Kemper, A. R., Kubik, M., Landefeld, C. S., Mangione, C. M., Silverstein, M., Simon, M. A., Tseng, C.-W., & Wong, J. B. (2019). Interventions to prevent perinatal depression: US Preventive Services Task Force recommendation statement. *JAMA*, *321*(6), 580–587. https://doi.org/10.1001/jama.2019.0007

Curtis, A. L., Bello, N. T., Connolly, K. R., & Valentino, R. J. (2002). Corticotropin-releasing factor neurones of the central nucleus of the amygdala mediate locus coeruleus activation by cardiovascular stress. *Journal of Neuroendocrinology*, *14*(8), 667–682. https://doi.org/10.1046/j.1365-2826.2002.00821.x

Davis, E. P., Glynn, L. M., Schetter, C. D., Hobel, C., Chicz-Demet, A., & Sandman, C. A. (2007). Prenatal exposure to maternal depression and cortisol influences infant temperament. *Journal of*

the American Academy of Child & Adolescent Psychiatry, *46*(6), 737–746. https://doi.org/10.1097/chi.0b013e318047b775

Davis, E. P., Hankin, B. L., Glynn, L. M., Head, K., Kim, D. J., & Sandman, C. A. (2020). Prenatal maternal stress, child cortical thickness, and adolescent depressive symptoms. *Child Development*, *91*(2), e432–e450. https://doi.org/10.1111/cdev.13252

Davis, E. P., Head, K., Buss, C., & Sandman, C. A. (2017). Prenatal maternal cortisol concentrations predict neurodevelopment in middle childhood. *Psychoneuroendocrinology*, *75*, 56–63. https://doi.org/10.1016/j.psyneuen.2016.10.005

Davis, E. P., Sandman, C. A., Buss, C., Wing, D. A., & Head, K. (2013). Fetal glucocorticoid exposure is associated with preadolescent brain development. *Biological Psychiatry*, *74*(9), 647–655. https://doi.org/10.1016/j.biopsych.2013.03.009

Davis, E. P., Snidman, N., Wadhwa, P. D., Glynn, L. M., Schetter, C. D., & Sandman, C. A. (2004). Prenatal maternal anxiety and depression predict negative behavioral reactivity in infancy. *Infancy*, *6*(3), 319–331. https://doi.org/10.1207/s15327078in0603_1

Davis, M., & Suveg, C. (2014). Focusing on the positive: A review of the role of child positive affect in developmental psychopathology. *Clinical Child and Family Psychology Review*, *17*(2), 97–124. https://doi.org/10.1007/s10567-013-0162-y

De Brito, S. A., Viding, E., Sebastian, C. L., Kelly, P. A., Mechelli, A., Maris, H., & McCrory, E. J. (2013). Reduced orbitofrontal and temporal grey matter in a community sample of maltreated children: Reduced in maltreated children grey matter. *Journal of Child Psychology and Psychiatry*, *54*(1), 105–112. https://doi.org/10.1111/j.1469-7610.2012.02597.x

de Bruijn, A. T. C. E., van Bakel, H. J. A., Wijnen, H., Pop, V. J. M., & van Baar, A. L. (2009). Prenatal maternal emotional complaints are associated with cortisol responses in toddler and preschool aged girls. *Developmental Psychobiology*, *51*(7), 553–563. https://doi.org/10.1002/dev.20393

Dennis, C.-L., Coghlan, M., & Vigod, S. (2013). Can we identify mothers at-risk for postpartum anxiety in the immediate postpartum period using the State-Trait Anxiety Inventory? *Journal of Affective Disorders*, *150*(3), 1217–1220. https://doi.org/10.1016/j.jad.2013.05.049

Dieleman, G. C., Huizink, A. C., Tulen, J. H. M., Utens, E. M. W. J., Creemers, H. E., van der Ende, J., & Verhulst, F. C. (2015). Alterations in HPA-axis and autonomic nervous system functioning in childhood anxiety disorders point to a chronic stress hypothesis. *Psychoneuroendocrinology*, *51*, 135–150. https://doi.org/10.1016/j.psyneuen.2014.09.002

Dohrenwend, B. P. (2006). Inventorying stressful life events as risk factors for psychopathology: Toward resolution of the problem of intracategory variability. *Psychological Bulletin*, *132*(3), 477–495. https://doi.org/10.1037/0033-2909.132.3.477

Dohrenwend, B. S., Askenasy, A. R., Krasnoff, L., & Dohrenwend, B. P. (1978). Exemplification of a Method for Scaling Life Events: The PERI Life Events Scale. *Journal of Health and Social Behavior*, *19*(2), 205–229. https://doi.org/10.2307/2136536

Dong, E., Dzitoyeva, S. G., Matrisciano, F., Tueting, P., Grayson, D. R., & Guidotti, A. (2015). Brain-derived neurotrophic factor epigenetic modifications associated with schizophrenia-like phenotype induced by prenatal stress in mice. *Biological Psychiatry*, *77*(6), 589–596. https://doi.org/10.1016/j.biopsych.2014.08.012

Ehrlich, D. E., & Rainnie, D. G. (2015). Prenatal stress alters the development of socioemotional behavior and amygdala neuron excitability in rats. *Neuropsychopharmacology*, *40*(9), 2135–2145. https://doi.org/10.1038/npp.2015.55

Eichler, A., Walz, L., Grunitz, J., Grimm, J., Doren, J. V., Raabe, E., Goecke, T. W., Fasching, P. A., Beckmann, M. W., Kornhuber, J., Kratz, O., Heinrich, H., & Moll, G. H. (2017). Children of prenatally depressed mothers: Externalizing and internalizing symptoms are accompanied by reductions in specific social-emotional competencies. *Journal of Child and Family Studies*, *26*(11), 3135–3144. https://doi.org/10.1007/s10826-017-0819-0

Eisenberg, N., Cumberland, A., Spinrad, T. L., Fabes, R. A., Shepard, S. A., Reiser, M., Murphy, B. C., Losoya, S. H., & Guthrie, I. K. (2001). The relations of regulation and emotionality to children's externalizing and internalizing problem behavior. *Child Development*, *72*(4), 1112–1134. https://doi.org/10.1111/1467-8624.00337

Else-Quest, N. M., Hyde, J. S., Goldsmith, H. H., & Van Hulle, C. A. (2006). Gender differences in temperament: A meta-analysis. *Psychological Bulletin*, *132*(1), 33–72. https://doi.org/10.1037/0033-2909.132.1.33

El-Sheikh, M., Keiley, M., & Hinnant, J. B. (2010). Developmental trajectories of skin conductance level in middle childhood: Sex, race, and externalizing behavior problems as predictors of growth. *Biological Psychology*, *83*(2), 116–124. https://doi.org/10.1016/j.biopsycho.2009.11.009

Escartí, M. J., de la Iglesia-Vayá, M., Martí-Bonmatí, L., Robles, M., Carbonell, J., Lull, J. J., García-Martí, G., Manjón, J. V., Aguilar, E. J., Aleman, A., & Sanjuán, J. (2010). Increased amygdala and parahippocampal gyrus activation in schizophrenic patients with auditory hallucinations: An fMRI study using independent component analysis. *Schizophrenia Research*, *117*(1), 31–41. https://doi.org/10.1016/j.schres.2009.12.028

Fan, F., Zou, Y., Tian, H., Zhang, Y., Zhang, J., Ma, X., Meng, Y., Yue, Y., Liu, K., & Dart, A. M. (2016). Effects of maternal anxiety and depression during pregnancy in Chinese women on children's heart rate and blood pressure response to stress. *Journal of Human Hypertension*, *30*(3), 171–176. https://doi.org/10.1038/jhh.2015.64

Faraji, J., Soltanpour, N., Lotfi, H., Moeeini, R., Moharreri, A.-R., Roudaki, S., Hosseini, S. A., Olson, D. M., Abdollahi, A.-A., Soltanpour, N., Mohajerani, M. H., & Metz, G. A. S. (2017). Lack of social support raises stress vulnerability in rats with a history of ancestral stress. *Scientific Reports*, *7*(1), 5277. https://doi.org/10.1038/s41598-017-05440-8

Feinstein, J. S., Adolphs, R., Damasio, A. R., & Tranel, D. (2011). The human amygdala and the induction and experience of fear. *Current Biology : CB*, *21*(1), 34–38. https://doi.org/10.1016/j.cub.2010.11.042

Field, T., Diego, M., Dieter, J., Hernandez-Reif, M., Schanberg, S., Kuhn, C., Yando, R., & Bendell, D. (2004). Prenatal depression effects on the fetus and the newborn. *Infant Behavior and Development*, *27*(2), 216–229. https://doi.org/10.1016/j.infbeh.2003.09.010

Fineberg, A. M., Ellman, L. M., Schaefer, C. A., Maxwell, S. D., Shen, L., Chaudhury, N. H., Cook, A. L., Bresnahan, M. A., Susser, E. S., & Brown, A. S. (2016). Fetal exposure to maternal stress and

risk for schizophrenia spectrum disorders among offspring: Differential influences of fetal sex. *Psychiatry Research*, *236*, 91–97. https://doi.org/10.1016/j.psychres.2015.12.026

Finik, J., & Nomura, Y. (2017). Cohort Profile: Stress in Pregnancy (SIP) Study. *International Journal of Epidemiology*, *46*(5), 1388–1388k. https://doi.org/10.1093/ije/dyw264

Foa, E. (1995). *PDS: Posttraumatic Stress Diagnostic Scale: Manual*. Pearson.

Fowles, D. C., Kochanska, G., & Murray, K. (2000). Electrodermal activity and temperament in preschool children. *Psychophysiology*, *37*(6), 777–787.

Gabard-Durnam, L. J., Flannery, J., Goff, B., Gee, D. G., Humphreys, K. L., Telzer, E., Hare, T., & Tottenham, N. (2014). The development of human amygdala functional connectivity at rest from 4 to 23years: A cross-sectional study. *NeuroImage*, *95*, 193–207. https://doi.org/10.1016/j.neuroimage.2014.03.038

Gao, Y., Tuvblad, C., Schell, A., Baker, L., & Raine, A. (2015). Skin conductance fear conditioning impairments and aggression: A longitudinal study. *Psychophysiology*, *52*(2), 288–295. https://doi.org/10.1111/psyp.12322

Gard, A. M., Waller, R., Swartz, J. R., Shaw, D. S., Forbes, E. E., & Hyde, L. W. (2018). Amygdala functional connectivity during socioemotional processing prospectively predicts increases in internalizing symptoms in a sample of low-income, urban, young men. *NeuroImage*, *178*, 562–573. https://doi.org/10.1016/j.neuroimage.2018.05.079

Gartstein, M. A., Putnam, S. P., & Rothbart, M. K. (2012). Etiology of preschool behavior problems: Contributions of temperament attributes in early childhood. *Infant Mental Health Journal*, *33*(2), 197–211. https://doi.org/10.1002/imhj.21312

Gartstein, M. A., & Rothbart, M. K. (2003). Studying infant temperament via the Revised Infant Behavior Questionnaire. *Infant Behavior and Development*, *1*(26), 64–86.

Gee, D. G., Humphreys, K. L., Flannery, J., Goff, B., Telzer, E. H., Shapiro, M., Hare, T. A., Bookheimer, S. Y., & Tottenham, N. (2013). A Developmental shift from positive to negative connectivity in human amygdala-prefrontal circuitry. *Journal of Neuroscience*, *33*(10), 4584–4593. https://doi.org/10.1523/JNEUROSCI.3446-12.2013

Gee, D. G., Gabard-Durnam, L. J., Flannery, J., Goff, B., Humphreys, K. L., Telzer, E. H., Hare, T. A., Bookheimer, S. Y., & Tottenham, N. (2013). Early developmental emergence of human amygdala–prefrontal connectivity after maternal deprivation. *Proceedings of the National Academy of Sciences*, *110*(39), 15638–15643. https://doi.org/10.1073/pnas.1307893110

Geuter, S., Qi, G., Welsh, R. C., Wager, T. D., & Lindquist, M. A. (2018). Effect size and power in fMRI group analysis. *BioRxiv*. https://doi.org/10.1101/295048

Glenn, A. L., Raine, A., Venables, P. H., & Mednick, S. A. (2007). Early temperamental and psychophysiological precursors of adult psychopathic personality. *Journal of Abnormal Psychology*, *116*(3), 508–518. https://doi.org/10.1037/0021-843X.116.3.508

Glover, V. (2011). Prenatal stress and the origins of psychopathology: An evolutionary perspective. *Journal of Child Psychology and Psychiatry*, *52*(4), 356–367. https://doi.org/10.1111/j.1469-7610.2011.02371.x

Glover, V. (2014). Maternal depression, anxiety and stress during pregnancy and child outcome; what needs to be done. *Best Practice & Research Clinical Obstetrics & Gynaecology*, *28*(1), 25–35. https://doi.org/10.1016/j.bpobgyn.2013.08.017

Glover, V., & Hill, J. (2012). Sex differences in the programming effects of prenatal stress on psychopathology and stress responses: An evolutionary perspective. *Physiology & Behavior*, *106*(5), 736–740. https://doi.org/10.1016/j.physbeh.2012.02.011

Gluckman, P. D., Hanson, M. A., & Beedle, A. S. (2007). Early life events and their consequences for later disease: A life history and evolutionary perspective. *American Journal of Human Biology*, *19*(1), 1–19. https://doi.org/10.1002/ajhb.20590

Gold, A. L., Sheridan, M. A., Peverill, M., Busso, D. S., Lambert, H. K., Alves, S., Pine, D. S., & McLaughlin, K. A. (2016). Childhood abuse and reduced cortical thickness in brain regions involved in emotional processing. *Journal of Child Psychology and Psychiatry*, *57*(10), 1154–1164. https://doi.org/10.1111/jcpp.12630

Graham, A. M., Rasmussen, J. M., Entringer, S., Ben Ward, E., Rudolph, M. D., Gilmore, J. H., Styner, M., Wadhwa, P. D., Fair, D. A., & Buss, C. (2019). Maternal Cortisol concentrations during pregnancy and sex-specific associations with neonatal amygdala connectivity and emerging

internalizing behaviors. *Biological Psychiatry*, *85*(2), 172–181. https://doi.org/10.1016/j.biopsych.2018.06.023

Graham, A. M., Rasmussen, J. M., Rudolph, M. D., Heim, C. M., Gilmore, J. H., Styner, M., Potkin, S. G., Entringer, S., Wadhwa, P. D., Fair, D. A., & Buss, C. (2018). Maternal Systemic interleukin-6 during pregnancy is associated with newborn amygdala phenotypes and subsequent behavior at 2-years-of-age. *Biological Psychiatry*, *83*(2), 109–119. https://doi.org/10.1016/j.biopsych.2017.05.027

Grinsted, A., Moore, J. C., & Jevrejeva, S. (2013). Projected Atlantic hurricane surge threat from rising temperatures. *Proceedings of the National Academy of Sciences*, *110*(14), 5369–5373. https://doi.org/10.1073/pnas.1209980110

Guo, X., Duan, X., Long, Z., Chen, H., Wang, Y., Zheng, J., Zhang, Y., Li, R., & Chen, H. (2016). Decreased amygdala functional connectivity in adolescents with autism: A resting-state fMRI study. *Psychiatry Research: Neuroimaging*, *257*, 47–56. https://doi.org/10.1016/j.pscychresns.2016.10.005

Hafeman, D., Bebko, G., Bertocci, M. A., Fournier, J. C., Chase, H. W., Bonar, L., Perlman, S. B., Travis, M., Gill, M. K., Diwadkar, V. A., Sunshine, J. L., Holland, S. K., Kowatch, R. A., Birmaher, B., Axelson, D., Horwitz, S. M., Arnold, L. E., Fristad, M. A., Frazier, T. W., … Phillips, M. L. (2017). Amygdala-prefrontal cortical functional connectivity during implicit emotion processing differentiates youth with bipolar spectrum from youth with externalizing disorders. *Journal of Affective Disorders*, *208*, 94–100. https://doi.org/10.1016/j.jad.2016.09.064

Hanson, J. L., Knodt, A. R., Brigidi, B. D., & Hariri, A. R. (2015). Lower structural integrity of the uncinate fasciculus is associated with a history of child maltreatment and future psychological vulnerability to stress. *Development and Psychopathology*, *27*(4pt2), 1611–1619. https://doi.org/10.1017/S0954579415000978

Hariri, A., Bookheimer, S., & Mazziotta, J. (2000). Modulating emotional responses: Effects of a neocortical network on the limbic system. *Neuroreport*, *11*(1), 43–48.

Hariri, A. R., Mattay, V. S., Tessitore, A., Fera, F., & Weinberger, D. R. (2003). Neocortical modulation of the amygdala response to fearful stimuli. *Biological Psychiatry*, *53*(6), 494–501. https://doi.org/10.1016/S0006-3223(02)01786-9

Hariri, A. R., Tessitore, A., Mattay, V. S., Fera, F., & Weinberger, D. R. (2002). The amygdala response to emotional stimuli: A comparison of faces and scenes. *NeuroImage*, *17*(1), 317–323. https://doi.org/10.1006/nimg.2002.1179

Hayes, K., Blashki, G., Wiseman, J., Burke, S., & Reifels, L. (2018). Climate change and mental health: Risks, impacts and priority actions. *International Journal of Mental Health Systems*, *12*(1), 28. https://doi.org/10.1186/s13033-018-0210-6

Holz, N. E., Boecker-Schlier, R., Buchmann, A. F., Blomeyer, D., Jennen-Steinmetz, C., Baumeister, S., Plichta, M. M., Cattrell, A., Schumann, G., Esser, G., Schmidt, M., Buitelaar, J., Meyer-Lindenberg, A., Banaschewski, T., Brandeis, D., & Laucht, M. (2017). Ventral striatum and amygdala activity as convergence sites for early adversity and conduct disorder. *Social Cognitive and Affective Neuroscience*, *12*(2), 261–272. https://doi.org/10.1093/scan/nsw120

Hulvershorn, L. A., Finn, P., Hummer, T. A., Leibenluft, E., Ball, B., Gichina, V., & Anand, A. (2013). Cortical activation deficits during facial emotion processing in youth at high risk for the development of substance use disorders. *Drug and Alcohol Dependence*, *131*(3), 230–237. https://doi.org/10.1016/j.drugalcdep.2013.05.015

Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D. S., Quinn, K., Sanislow, C., & Wang, P. (2010). Research Domain Criteria (RDoC): Toward a new classification framework for research on mental disorders. *American Journal of Psychiatry*, *167*(7), 748–751. https://doi.org/10.1176/appi.ajp.2010.09091379

IPCC. (2019). *IPCC Special Report on the Ocean and Cryosphere in a Changing Climate*. https://www.ipcc.ch/srocc/

Iturra-Mena, A. M., Arriagada-Solimano, M., Luttecke-Anders, A., & Dagnino-Subiabre, A. (2018). Effects of prenatal stress on anxiety- and depressive-like behaviours are sex-specific in prepubertal rats. *Journal of Neuroendocrinology*, *30*(7), e12609. https://doi.org/10.1111/jne.12609

Jalbrzikowski, M., Murty, V. P., Tervo-Clemmens, B., Foran, W., & Luna, B. (2019). Age-associated deviations of amygdala functional connectivity in youths with psychosis spectrum disorders: relevance to psychotic symptoms. *American Journal of Psychiatry*, *176*(3), 196–207. https://doi.org/10.1176/appi.ajp.2018.18040443

Jänig, W., & Häbler, H. J. (2000). Specificity in the organization of the autonomic nervous system: A basis for precise neural regulation of homeostatic and protective body functions. *Progress in Brain Research*, *122*, 351–367.

Jones, S. L., Dufoix, R., Laplante, D. P., Elgbeili, G., Patel, R., Chakravarty, M. M., King, S., & Pruessner, J. C. (2019). Larger amygdala volume mediates the association between prenatal maternal stress and higher levels of externalizing behaviors: Sex specific effects in Project Ice Storm. *Frontiers in Human Neuroscience*, *13*. https://doi.org/10.3389/fnhum.2019.00144

Keenan, K. (2000). Emotion dysregulation as a risk factor for child psychopathology. *Clinical Psychology: Science and Practice*, *7*(4), 418–434. https://doi.org/10.1093/clipsy.7.4.418

Khan, A. (2017, September 10). Fires, droughts and hurricanes: What's the link between climate change and natural disasters? *Los Angeles Times*. http://www.latimes.com/science/sciencenow/la-sci-sn-climate-change-natural-disasters-20170907-htmlstory.html

Kim, D. J., Davis, E. P., Sandman, C. A., Sporns, O., O'Donnell, B. F., Buss, C., & Hetrick, W. P. (2017). Prenatal maternal cortisol has sex-specific associations with child brain network properties. *Cerebral Cortex*, *27*(11), 5230–5241. https://doi.org/10.1093/cercor/bhw303

King, S., & Laplante, D. P. (2005). The effects of prenatal maternal stress on children's cognitive development: Project Ice Storm. *Stress*, *8*(1), 35–45. https://doi.org/10.1080/10253890500108391

Kujawa, A., Wu, M., Klumpp, H., Pine, D. S., Swain, J. E., Fitzgerald, K. D., Monk, C. S., & Phan, K. L. (2016). Altered development of amygdala-anterior cingulate cortex connectivity in anxious youth and young adults. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *1*(4), 345–352. https://doi.org/10.1016/j.bpsc.2016.01.006

Lacey, J. (1967). Somatic response patterning and stress: Some revisions of activation theory. *Psychological Stress: Issues in Research*, 14–37.

Lahey, B. B., Van Hulle, C. A., Keenan, K., Rathouz, P. J., D'Onofrio, B. M., Rodgers, J. L., & Waldman, I. D. (2008). Temperament and parenting during the first year of life predict future child conduct problems. *Journal of Abnormal Child Psychology*, *36*(8), 1139–1158. https://doi.org/10.1007/s10802-008-9247-3

Laplante, D. P., Brunet, A., & King, S. (2016). The effects of maternal stress and illness during pregnancy on infant temperament: Project Ice Storm. *Pediatric Research*, *79*(1–1), 107–113. https://doi.org/10.1038/pr.2015.177

Lautarescu, A., Pecheva, D., Nosarti, C., Nihouarn, J., Zhang, H., Victor, S., Craig, M., Edwards, A. D., & Counsell, S. J. (2020). Maternal prenatal stress is associated with altered uncinate fasciculus microstructure in premature neonates. *Biological Psychiatry*, *87*(6), 559–569. https://doi.org/10.1016/j.biopsych.2019.08.010

Lebel, C., Walton, M., Letourneau, N., Giesbrecht, G. F., Kaplan, B. J., & Dewey, D. (2016). Prepartum and postpartum maternal depressive symptoms are related to children's brain structure in preschool. *Biological Psychiatry*, *80*(11), 859–868. https://doi.org/10.1016/j.biopsych.2015.12.004

Lee, A., Poh, J. S., Wen, D. J., Guillaume, B., Chong, Y.-S., Shek, L. P., Fortier, M. V., & Qiu, A. (2019). Long-term influences of prenatal maternal depressive symptoms on the amygdala–prefrontal circuitry of the offspring from birth to early childhood. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *4*(11), 940–947. https://doi.org/10.1016/j.bpsc.2019.05.006

Lequertier, B., Simcock, G., Cobham, V. E., Kildea, S., & King, S. (2019). Infant behavior and competence following prenatal exposure to a natural disaster: The QF2011 Queensland Flood Study. *Infancy*, *24*(3), 411–432. https://doi.org/10.1111/infa.12286

Li, W., Cui, H., Zhu, Z., Kong, L., Guo, Q., Zhu, Y., Hu, Q., Zhang, L., Li, H., Li, Q., Jiang, J., Meyers, J., Li, J., Wang, J., Yang, Z., & Li, C. (2016). Aberrant functional connectivity between the amygdala and the temporal pole in drug-free generalized anxiety disorder. *Frontiers in Human Neuroscience*, *10*. https://doi.org/10.3389/fnhum.2016.00549

Lipner, E., Murphy, S. K., & Ellman, L. M. (2019). Prenatal maternal stress and the cascade of risk to schizophrenia spectrum disorders in offspring. *Current Psychiatry Reports*, *21*(10), 99. https://doi.org/10.1007/s11920-019-1085-1

Liu, Y., & De, A. (2015). Multiple imputation by fully conditional specification for dealing with missing data in a large epidemiologic study. *International Journal of Statistics in Medical Research*, *4*(3), 287–295. https://doi.org/10.6000/1929-6029.2015.04.03.7

Manuck, S. B., Brown, S. M., Forbes, E. E., & Hariri, A. R. (2007). Temporal stability of individual differences in amygdala reactivity. *American Journal of Psychiatry*, *164*(10), 1613–1614. https://doi.org/10.1176/appi.ajp.2007.07040609

Maziade, M., Côté, R., Bernier, H., Boutin, P., & Thivierge, J. (1989). Significance of extreme temperament in infancy for clinical status in preschool years: Value of extreme temperament at 4–8 months for predicting diagnosis at 4.7 years. *The British Journal of Psychiatry*, *154*(4), 535–543. https://doi.org/10.1192/bjp.154.4.535

McGrath, J. M., Records, K., & Rice, M. (2008). Maternal depression and infant temperament characteristics. *Infant Behavior and Development*, *31*(1), 71–80. https://doi.org/10.1016/j.infbeh.2007.07.001

McLean, M. A., Cobham, V. E., Simcock, G., Elgbeili, G., Kildea, S., & King, S. (2018). The role of prenatal maternal stress in the development of childhood anxiety symptomatology: The QF2011 Queensland Flood Study. *Development and Psychopathology*, *30*(3), 995–1007. https://doi.org/10.1017/S0954579418000408

McQuaid, G. A., Darcey, V. L., Avalos, M. F., Fishbein, D. H., & VanMeter, J. W. (2019). Altered cortical development and psychiatric symptom risk in adolescents exposed to maternal stress in utero. *Neuroscience*. https://doi.org/10.1101/540930

Meyer, A., Danielson, C. K., Danzig, A. P., Bhatia, V., Black, S. R., Bromet, E., Carlson, G., Hajcak, G., Kotov, R., & Klein, D. N. (2017). Neural biomarker prospectively predicts increases in anxiety symptoms in children after Hurricane Sandy. *Journal of the American Academy of Child and Adolescent Psychiatry*, *56*(5), 410–416. https://doi.org/10.1016/j.jaac.2017.02.005

Mueller, B. R., & Bale, T. L. (2008). Sex-specific programming of offspring emotionality after stress early in pregnancy. *Journal of Neuroscience*, *28*(36), 9055–9065. https://doi.org/10.1523/JNEUROSCI.1424-08.2008

Murray, L., & Carothers, A. D. (1990). The validation of the Edinburgh Post-natal Depression Scale on a community sample. *The British Journal of Psychiatry: The Journal of Mental Science*, *157*, 288–290.

Mychasiuk, R., Gibb, R., & Kolb, B. (2012). Prenatal stress alters dendritic morphology and synaptic connectivity in the prefrontal cortex and hippocampus of developing offspring. *Synapse*, *66*(4), 308–314. https://doi.org/10.1002/syn.21512

National Academy of Medicine. (2019). *Fostering Healthy Mental, Emotional, and Behavioral Development in Children and Youth: A National Agenda*. https://doi.org/10.17226/25201

Newham, J. J., Westwood, M., Aplin, J. D., & Wittkowski, A. (2012). State–trait anxiety inventory (STAI) scores during pregnancy following intervention with complementary therapies. *Journal of Affective Disorders*, *142*(1), 22–30. https://doi.org/10.1016/j.jad.2012.04.027

Nicholson, A. A., Rabellino, D., Densmore, M., Frewen, P. A., Paret, C., Kluetsch, R., Schmahl, C., Théberge, J., Neufeld, R. W. J., McKinnon, M. C., Reiss, J. P., Jetly, R., & Lanius, R. A. (2017). The neurobiology of emotion regulation in posttraumatic stress disorder: Amygdala downregulation via real-time fMRI neurofeedback. *Human Brain Mapping*, *38*(1), 541–560. https://doi.org/10.1002/hbm.23402

NOAA, U. D. of C. (2017). *Sandy 5th Anniversary*. NOAA's National Weather Service. https://www.weather.gov/phi/sandy_5th_anniversary

NOAA, U. D. of C. (2020). *2020 Atlantic Hurricane Season takes infamous top spot for busiest on record*. https://www.noaa.gov/news/2020-atlantic-hurricane-season-takes-infamous-top-spot-for-busiest-on-record

Nomura, Y., Davey, K., Pehme, P., Finik, J., Glover, V., Zhang, W., Huang, Y., Buthmann, J., Dana, K., Yoshida, S., Tsuchiya, K., Li, X., & Ham, J. (2019). Influence of in-utero exposure to maternal depression and natural disaster-related stress on infant temperament at 6 months: The children of Superstorm Sandy. *Infant Mental Health Journal*, *40*(2), 204–216. https://doi.org/DOI: 10.1002/imhj.21766

Obradovich, N., Migliorini, R., Paulus, M. P., & Rahwan, I. (2018). Empirical evidence of mental health risks posed by climate change. *Proceedings of the National Academy of Sciences of the United States of America*, *115*(43), 10953–10958. https://doi.org/10.1073/pnas.1801528115

O'Connor, T. G., Heron, J., Golding, J., Beveridge, M., & Glover, V. (2002). Maternal antenatal anxiety and children's behavioural/emotional problems at 4 years. Report from the Avon Longitudinal Study of Parents and Children. *The British Journal of Psychiatry: The Journal of Mental Science*, *180*, 502–508.

Ostlund, B. D., Conradt, E., Crowell, S. E., Tyrka, A. R., Marsit, C. J., & Lester, B. M. (2016). Prenatal stress, fearfulness, and the epigenome: Exploratory analysis of sex differences in dna methylation of the glucocorticoid receptor gene. *Frontiers in Behavioral Neuroscience*, *10*. https://doi.org/10.3389/fnbeh.2016.00147

Pagliaccio, D., Luby, J. L., Bogdan, R., Agrawal, A., Gaffrey, M. S., Belden, A. C., Botteron, K. N., Harms, M. P., & Barch, D. M. (2014). Stress-system genes and life stress predict cortisol levels and amygdala and hippocampal volumes in children. *Neuropsychopharmacology*, *39*(5), 1245–1253. https://doi.org/10.1038/npp.2013.327

Pagliaccio, D., Luby, J. L., Bogdan, R., Agrawal, A., Gaffrey, M. S., Belden, A. C., Botteron, K. N., Harms, M. P., & Barch, D. M. (2015). Amygdala functional connectivity, HPA axis genetic variation, and life stress in children and relations to anxiety and emotion regulation. *Journal of Abnormal Psychology*, *124*(4), 817–833. https://doi.org/10.1037/abn0000094

Paret, C., Kluetsch, R., Zaehringer, J., Ruf, M., Demirakca, T., Bohus, M., Ende, G., & Schmahl, C. (2016). Alterations of amygdala-prefrontal connectivity with real-time fMRI neurofeedback in BPD patients. *Social Cognitive and Affective Neuroscience*, *11*(6), 952–960. https://doi.org/10.1093/scan/nsw016

Patrick, S. W., Henkhaus, L. E., Zickafoose, J. S., Lovell, K., Halvorson, A., Loch, S., Letterie, M., & Davis, M. M. (2020). Well-being of parents and children during the COVID-19 pandemic: A national survey. *Pediatrics*, *146*(4). https://doi.org/10.1542/peds.2020-016824

Posner, J., Cha, J., Roy, A. K., Peterson, B. S., Bansal, R., Gustafsson, H. C., Raffanello, E., Gingrich, J., & Monk, C. (2016). Alterations in amygdala–prefrontal circuits in infants exposed to prenatal

maternal depression. *Translational Psychiatry*, *6*(11), e935–e935. https://doi.org/10.1038/tp.2016.146

Putnam, S. P., Helbig, A. L., Gartstein, M. A., Rothbart, M. K., & Leerkes, E. (2014). Development and assessment of short and very short forms of the Infant Behavior Questionnaire–Revised. *Journal of Personality Assessment*, *96*(4), 445–458. https://doi.org/10.1080/00223891.2013.841171

Rajmohan, V., & Mohandas, E. (2007). The limbic system. *Indian Journal of Psychiatry*, *49*(2), 132–139. https://doi.org/10.4103/0019-5545.33264

Rasmussen, J. M., Graham, A. M., Entringer, S., Gilmore, J. H., Styner, M., Fair, D. A., Wadhwa, P. D., & Buss, C. (2019). Maternal Interleukin-6 concentration during pregnancy is associated with variation in frontolimbic white matter and cognitive development in early life. *NeuroImage*, *185*, 825–835. https://doi.org/10.1016/j.neuroimage.2018.04.020

Rettew, D. C., & McKee, L. (2005). Temperament and its role in developmental psychopathology. *Harvard Review of Psychiatry*, *13*(1), 14–27. https://doi.org/10.1080/10673220590923146

Rutter, M., Caspi, A., & Moffitt, T. E. (2003). Using sex differences in psychopathology to study causal mechanisms: Unifying issues and research strategies. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *44*(8), 1092–1115. https://doi.org/10.1111/1469-7610.00194

Sandman, C. A., Wadhwa, P. D., Chicz-DeMet, A., Porto, M., & Garite, T. J. (1999). Maternal corticotropin-releasing hormone and habituation in the human fetus. *Developmental Psychobiology*, *34*(3), 163–173.

Sandman, Curt A, & Davis, E. P. (2010). Gestational stress influences cognition and behavior. *Future Neurology*, *5*(5), 675–690. https://doi.org/10.2217/fnl.10.35

Sandman, Curt A., Davis, E. P., Buss, C., & Glynn, L. M. (2012). Exposure to prenatal psychobiological stress exerts programming influences on the mother and her fetus. *Neuroendocrinology*, *95*(1), 8–21. https://doi.org/10.1159/000327017

Sarchiapone, M., Gramaglia, C., Iosue, M., Carli, V., Mandelli, L., Serretti, A., Marangon, D., & Zeppegno, P. (2018). The association between electrodermal activity (EDA), depression and suicidal behaviour: A systematic review and narrative synthesis. *BMC Psychiatry*, *18*, 1–27. https://doi.org/10.1186/s12888-017-1551-4

Sarkar, S., Craig, M. C., Dell'Acqua, F., O'Connor, T. G., Catani, M., Deeley, Q., Glover, V., & Murphy, D. G. M. (2014). Prenatal stress and limbic-prefrontal white matter microstructure in children aged 6-9 years: A preliminary diffusion tensor imaging study. *The World Journal of Biological Psychiatry: The Official Journal of the World Federation of Societies of Biological Psychiatry*, *15*(4), 346–352. https://doi.org/10.3109/15622975.2014.903336

Saudino, K. J. (2005). Behavioral genetics and child temperament. *Journal of Developmental and Behavioral Pediatrics : JDBP*, *26*(3), 214–223.

Sayal, K., Heron, J., Maughan, B., Rowe, R., & Ramchandani, P. (2014). Infant temperament and childhood psychiatric disorder: Longitudinal study. *Child: Care, Health and Development*, *40*(2), 292–297. https://doi.org/10.1111/cch.12054

Scarpa, A., Raine, A., Venables, P. H., & Mednick, S. A. (1997). Heart rate and skin conductance in behaviorally inhibited Mauritian children. *Journal of Abnormal Psychology*, *106*(2), 182–190.

Scheinost, D., Spann, M. N., McDonough, L., Peterson, B. S., & Monk, C. (2020). Associations between different dimensions of prenatal distress, neonatal hippocampal connectivity, and infant memory. *Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology*, *45*(8), 1272–1279. https://doi.org/10.1038/s41386-020-0677-0

Schipper, J. C. D., Tavecchio, L. W. C., & IJzendoorn, M. H. V. (2008). Children's attachment relationships with day care caregivers: Associations with positive caregiving and the child's temperament. *Social Development*, *17*(3), 454–470. https://doi.org/10.1111/j.1467-9507.2007.00448.x

Schulz, K. M., Pearson, J. N., Neeley, E. W., Berger, R., Leonard, S., Adams, C. E., & Stevens, K. E. (2011). Maternal stress during pregnancy causes sex-specific alterations in offspring memory performance, social interactions, indices of anxiety, and body mass. *Physiology & Behavior*, *104*(2), 340–347. https://doi.org/10.1016/j.physbeh.2011.02.021

Shrout, P. E., & Fleiss, J. L. (1979). Intraclass correlations: Uses in assessing rater reliability. *Psychological Bulletin*, *86*(2), 9.

Silvers, J. A., Insel, C., Powers, A., Franz, P., Helion, C., Martin, R. E., Weber, J., Mischel, W., Casey, B. J., & Ochsner, K. N. (2017). vlPFC–vmPFC–amygdala interactions underlie age-related

differences in cognitive regulation of emotion. *Cerebral Cortex*, *27*(7), 3502–3514. https://doi.org/10.1093/cercor/bhw073

Silvers, J. A., Lumian, D. S., Gabard-Durnam, L., Gee, D. G., Goff, B., Fareri, D. S., Caldera, C., Flannery, J., Telzer, E. H., Humphreys, K. L., & Tottenham, N. (2016). Previous institutionalization is followed by broader amygdala–hippocampal–PFC network connectivity during aversive learning in human development. *The Journal of Neuroscience*, *36*(24), 6420–6430. https://doi.org/10.1523/JNEUROSCI.0038-16.2016

Simcock, G., Kildea, S., Elgbeili, G., Laplante, D. P., Cobham, V., & King, S. (2017). Prenatal maternal stress shapes children's theory of mind: The QF2011 Queensland Flood Study. *Journal of Developmental Origins of Health and Disease*, *8*(4), 483–492. https://doi.org/10.1017/S2040174417000186

Smith, S. M., & Vale, W. W. (2006). The role of the hypothalamic-pituitary-adrenal axis in neuroendocrine responses to stress. *Dialogues in Clinical Neuroscience*, *8*(4), 383. https://doi.org/10.31887/DCNS.2006.8.4/ssmith

Soares-Cunha, C., Coimbra, B., Borges, S., Domingues, A. V., Silva, D., Sousa, N., & Rodrigues, A. J. (2018). Mild prenatal stress causes emotional and brain structural modifications in rats of both sexes. *Frontiers in Behavioral Neuroscience*, *12*. https://doi.org/10.3389/fnbeh.2018.00129

Soe, N. N., Wen, D. J., Poh, J. S., Chong, Y.-S., Broekman, B. F., Chen, H., Shek, L. P., Tan, K. H., Gluckman, P. D., Fortier, M. V., Meaney, M. J., & Qiu, A. (2018). Perinatal maternal depressive symptoms alter amygdala functional connectivity in girls. *Human Brain Mapping*, *39*(2), 680–690. https://doi.org/10.1002/hbm.23873

Somerville, L. H., Bookheimer, S. Y., Buckner, R. L., Burgess, G. C., Curtiss, S. W., Dapretto, M., Elam, J. S., Gaffrey, M. S., Harms, M. P., Hodge, C., Kandala, S., Kastman, E. K., Nichols, T. E., Schlaggar, B. L., Smith, S. M., Thomas, K. M., Yacoub, E., Van Essen, D. C., & Barch, D. M. (2018). The Lifespan Human Connectome Project in Development: A large-scale study of brain connectivity development in 5–21 year olds. *NeuroImage*, *183*, 456–468. https://doi.org/10.1016/j.neuroimage.2018.08.050

Spielberger, C. D. (1983). *Manual for the State-Trait Anxiety Inventory STAI*. Mind Garden.

Suárez, L. E., Markello, R. D., Betzel, R. F., & Misic, B. (2020). Linking structure and function in macroscale brain networks. *Trends in Cognitive Sciences*, *24*(4), 302–315. https://doi.org/10.1016/j.tics.2020.01.008

Suurland, J., Van der Heijden, K., Smaling, H., Huijbregts, S., van Goozen, S. H. M., & Swaab, H. (2017). Infant autonomic nervous system response and recovery: Associations with maternal risk status and infant emotion regulation. *Development and Psychopathology*, *29*(3), 759–773.

Suzuki, H., Luby, J. L., Botteron, K. N., Dietrich, R., McAvoy, M. P., & Barch, D. M. (2014). Early life stress and trauma and enhanced limbic activation to emotionally valenced faces in depressed and healthy children. *Journal of the American Academy of Child & Adolescent Psychiatry*, *53*(7), 800-813.e10. https://doi.org/10.1016/j.jaac.2014.04.013

Tees, M. T., Harville, E. W., Xiong, X., Buekens, P., Pridjian, G., & Elkind-Hirsch, K. (2010). Hurricane Katrina-related maternal stress, maternal mental health, and early infant temperament. *Maternal and Child Health Journal*, *14*(4), 511–518. https://doi.org/10.1007/s10995-009-0486-x

Textor, J., van der Zander, B., Gilthorpe, M. S., Liśkiewicz, M., & Ellison, G. T. (2016). Robust causal inference using directed acyclic graphs: The R package 'dagitty.' *International Journal of Epidemiology*, *45*(6), 1887–1894. https://doi.org/10.1093/ije/dyw341

Theys, C., Wouters, J., & Ghesquière, P. (2014). Diffusion tensor imaging and resting-state functional MRI-scanning in 5- and 6-year-old children: training protocol and motion assessment. *PLOS ONE*, *9*(4), e94019. https://doi.org/10.1371/journal.pone.0094019

Thomas, K. M., Drevets, W. C., Dahl, R. E., Ryan, N. D., Birmaher, B., Eccard, C. H., Axelson, D., Whalen, P. J., & Casey, B. J. (2001). Amygdala response to fearful faces in anxious and depressed children. *Archives of General Psychiatry*, *58*(11), 1057–1063. https://doi.org/10.1001/archpsyc.58.11.1057

Tibu, F., Hill, J., Sharp, H., Marshall, K., Glover, V., & Pickles, A. (2014). Evidence for sex differences in fetal programming of physiological stress reactivity in infancy. *Development and Psychopathology*, *26*(4pt1), 879–888. https://doi.org/10.1017/S0954579414000194

Tottenham, N., Hare, T. A., Quinn, B. T., McCarry, T. W., Nurse, M., Gilhooly, T., Millner, A., Galvan, A., Davidson, M. C., Eigsti, I.-M., Thomas, K. M., Freed, P. J., Booma, E. S., Gunnar, M. R., Altemus,

M., Aronson, J., & Casey, B. J. (2010). Prolonged institutional rearing is associated with atypically large amygdala volume and difficulties in emotion regulation: Previous institutionalization. *Developmental Science*, *13*(1), 46–61. https://doi.org/10.1111/j.1467-7687.2009.00852.x

Tuvblad, C., Gao, Y., Isen, J., Botwick, T., Raine, A., & Baker, L. A. (2012). The heritability of the skin conductance orienting response: A longitudinal twin study. *Biological Psychology*, *89*(1), 47–53. https://doi.org/10.1016/j.biopsycho.2011.09.003

Valiente, C., Eisenberg, N., Smith, C. L., Reiser, M., Fabes, R. A., Losoya, S., Guthrie, I. K., & Murphy, B. C. (2003). The relations of effortful control and reactive control to children's externalizing problems: A longitudinal assessment. *Journal of Personality*, *71*(6), 1171–1196. https://doi.org/10.1111/1467-6494.7106011

Van den Bergh, B. R. H., Mulder, E. J. H., Mennes, M., & Glover, V. (2005). Antenatal maternal anxiety and stress and the neurobehavioural development of the fetus and child: Links and possible mechanisms. A review. *Neuroscience & Biobehavioral Reviews*, *29*(2), 237–258. https://doi.org/10.1016/j.neubiorev.2004.10.007

Van den Hove, D. L. A., Leibold, N. K., Strackx, E., Martinez-Claros, M., Lesch, K. P., Steinbusch, H. W. M., Schruers, K. R. J., & Prickaerts, J. (2014). Prenatal stress and subsequent exposure to chronic mild stress in rats; interdependent effects on emotional behavior and the serotonergic system. *European Neuropsychopharmacology*, *24*(4), 595–607. https://doi.org/10.1016/j.euroneuro.2013.09.006

van der Knaap, N. J. F., Klumpers, F., El Marroun, H., Mous, S., Schubert, D., Jaddoe, V., Hofman, A., Homberg, J. R., Tiemeier, H., White, T., & Fernández, G. (2018). Maternal depressive symptoms during pregnancy are associated with amygdala hyperresponsivity in children. *European Child & Adolescent Psychiatry*, *27*(1), 57–64. https://doi.org/10.1007/s00787-017-1015-x

van Dijk, A. E., van Eijsden, M., Stronks, K., Gemke, R. J. B. J., & Vrijkotte, T. G. M. (2012). Prenatal stress and balance of the child's cardiac autonomic nervous system at age 5-6 years. *PLoS ONE*, *7*(1), e30413. https://doi.org/10.1371/journal.pone.0030413

Venables, P. H., & Mitchell, D. A. (1996). The effects of age, sex and time of testing on skin conductance activity. *Biological Psychology*, *43*(2), 87–101. https://doi.org/10.1016/0301-0511(96)05183-6

Wadhwa, P. D., Sandman, C. A., & Garite, T. J. (2001). The neurobiology of stress in human pregnancy: Implications for prematurity and development of the fetal central nervous system. *Progress in Brain Research*, *133*, 131–142.

Wang, C., Shen, M., Guillaume, B., Chong, Y.-S., Chen, H., Fortier, M. V., Meaney, M. J., & Qiu, A. (2018). FKBP5 moderates the association between antenatal maternal depressive symptoms and neonatal brain morphology. *Neuropsychopharmacology*, *43*(3), 564–570. https://doi.org/10.1038/npp.2017.232

Wang, Y., Ma, Y., Hu, J., Cheng, W., Jiang, H., Zhang, X., Li, M., Ren, J., & Li, X. (2015). Prenatal chronic mild stress induces depression-like behavior and sex-specific changes in regional glutamate receptor expression patterns in adult rats. *Neuroscience*, *301*, 363–374. https://doi.org/10.1016/j.neuroscience.2015.06.008

Warsini, S., Mills, J., & Usher, K. (2014). Solastalgia: Living with the environmental damage caused by natural disasters. *Prehospital and Disaster Medicine; Cambridge*, *29*(1), 87–90. http://dx.doi.org/10.1017/S1049023X13009266

Weems, C. F., Zakem, A. H., Costa, N. M., Cannon, M. F., & Watts, S. E. (2005). Physiological response and childhood anxiety: Association with symptoms of anxiety disorders and cognitive bias. *Journal of Clinical Child & Adolescent Psychology*, *34*(4), 712–723. https://doi.org/10.1207/s15374424jccp3404_13

Weinstock, M. (2016). Prenatal stressors in rodents: Effects on behavior. *Neurobiology of Stress*, *6*, 3–13. https://doi.org/10.1016/j.ynstr.2016.08.004

Weiss, D., & Marmar, C. (1997). The Impact of Event Scale-Revised. In *Assessing psychological trauma and PTSD* (pp. 399–411). Guilford Press.

Wen, D. J., Poh, J. S., Ni, S. N., Chong, Y.-S., Chen, H., Kwek, K., Shek, L. P., Gluckman, P. D., Fortier, M. V., Meaney, M. J., & Qiu, A. (2017). Influences of prenatal and postnatal maternal depression on amygdala volume and microstructure in young children. *Translational Psychiatry*, *7*(4), e1103. https://doi.org/10.1038/tp.2017.74

Williams, L. E., Oler, J. A., Fox, A. S., McFarlin, D. R., Rogers, G. M., Jesson, M. A., Davidson, R. J., Pine, D. S., & Kalin, N. H. (2015). Fear of the unknown: Uncertain anticipation reveals amygdala

alterations in childhood anxiety disorders. *Neuropsychopharmacology*, *40*(6), 1428–1435. https://doi.org/10.1038/npp.2014.328

Wolf, R. C., & Herringa, R. J. (2016). Prefrontal–amygdala dysregulation to threat in pediatric posttraumatic stress disorder. *Neuropsychopharmacology*, *41*(3), 822–831. https://doi.org/10.1038/npp.2015.209

Wu, M., Kujawa, A., Lu, L. H., Fitzgerald, D. A., Klumpp, H., Fitzgerald, K. D., Monk, C. S., & Phan, K. L. (2016). Age-related changes in amygdala–frontal connectivity during emotional face processing from childhood into young adulthood. *Human Brain Mapping*, *37*(5), 1684–1695. https://doi.org/10.1002/hbm.23129

Xiong, J., Lipsitz, O., Nasri, F., Lui, L. M. W., Gill, H., Phan, L., Chen-Li, D., Iacobucci, M., Ho, R., Majeed, A., & McIntyre, R. S. (2020). Impact of COVID-19 pandemic on mental health in the general population: A systematic review. *Journal of Affective Disorders*, *277*, 55–64. https://doi.org/10.1016/j.jad.2020.08.001

Yong Ping, E., Laplante, D. P., Elgbeili, G., Hillerer, K. M., Brunet, A., O'Hara, M. W., & King, S. (2015). Prenatal maternal stress predicts stress reactivity at 2½ years of age: The Iowa Flood Study. *Psychoneuroendocrinology*, *56*, 62–78. https://doi.org/10.1016/j.psyneuen.2015.02.015

Young, K. D., Siegle, G. J., Zotev, V., Phillips, R., Misaki, M., Yuan, H., Drevets, W. C., & Bodurka, J. (2017). Randomized clinical trial of real-time fMRI amygdala neurofeedback for major depressive disorder: Effects on symptoms and autobiographical memory recall. *American Journal of Psychiatry*, *174*(8), 748–755. https://doi.org/10.1176/appi.ajp.2017.16060637

Zhang, W., Finik, J., Dana, K., Glover, V., Ham, J., & Nomura, Y. (2018). Prenatal depression and infant temperament: The moderating role of placental gene expression. *Infancy*, *23*(2), 211–231. https://doi.org/10.1111/infa.12215

Zhang, W., Rajendran, K., Ham, J., Finik, J., Buthmann, J., Davey, K., Pehme, P. M., Dana, K., Pritchett, A., Laws, H., & Nomura, Y. (2018). Prenatal exposure to disaster-related traumatic stress and developmental trajectories of temperament in early childhood: Superstorm Sandy pregnancy study. *Journal of Affective Disorders*, *234*, 335–345. https://doi.org/10.1016/j.jad.2018.02.067

Zhu, P., Sun, M.-S., Hao, J.-H., Chen, Y.-J., Jiang, X.-M., Tao, R.-X., Huang, K., & Tao, F.-B. (2014). Does prenatal maternal stress impair cognitive development and alter temperament characteristics in toddlers with healthy birth outcomes? *Developmental Medicine & Child Neurology*, *56*(3), 283–289. https://doi.org/10.1111/dmcn.12378