ABSTRACT

Title of Dissertation:	Impact of Stress on the Prefrontal Cortex: A View of How Socioeconomic Status Impacts Executive Function
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By the time they reach kindergarten, children from low Socioeconomic (SES) backgrounds lag behind their high SES peers in a host of cognitive abilities including executive function. The mechanism of how SES impacts executive function is still unclear; however, recent research eludes to the effects of stress regulation of the Hypothalamus-Pituitary-Adrenal (HPA) axis on cortical development as a promising explanation. Children raised in low SES backgrounds are exposed to a multitude of environmental stressors that can impact the child's development of their stress response and regulation within the HPA axis. Alterations within the HPA axis, particularly cortisol levels, are shown to impact brain development especially the prefrontal cortex (PFC) which is a major region supporting executive function. Although the stress regulation mechanism seems valid, the influence of early life stress on the PFC and subsequent executive function outcomes have not been directly tested. The current study aimed to

examine how earlier and concurrent responses to stress, as reflected in measures of cortisol reactivity, relate to neural and behavioral measures of executive function within the framework of how SES impacts executive function. This longitudinal study consisted of two waves of data collection, the first wave was collected when the children were 3-5 years old and the second wave when the children were 7-10 years old. Measures of executive functioning and cortisol stress response were collected during both waves, whereas structural and functional magnetic resonance imaging (MRI) of the brain were collected at the second wave. Although multiple analyses were conducted and numerous nonsignificant results were present, the significant results suggest variations in cortisol reactivity relate to executive function, overall brain volume, and regional differences in cortical thickness within the PFC including middle frontal cortex, inferior frontal cortex, insula, and anterior cingulate cortex. Within the bigger SES framework, SES was related to cortisol reactivity and executive function. SES differences were found in total grey matter and regional cortical thickness within the PFC including the insula and anterior cingulate cortex. The cortical thickness of the right inferior frontal cortex mediated the association between SES and executive function. The inferior frontal cortex and the anterior cingulate cortex were associated with both cortisol reactivity and SES suggesting these regions may contribute to the mechanism of how SES impacts executive function via stress regulation or dysregulation. Although future studies are necessary to replicate findings on a larger scale, the current study is an encouraging step towards understanding how differential stress responses along the socio-economic ladder impact brain and cognitive development.

THE IMPACT OF STRESS ON THE PREFRONTAL CORTEX: A VIEW OF HOW SOCIOECONOMIC STATUS IMPACTS EXECUTIVE FUNCTION

by

Brandee Feola

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Advisory Committee:

Professor Donald J. Bolger, Chair
Professor Lea Dougherty
Professor Brenda Jones Harden
Professor Colleen O'Neal
Professor Tracy Riggins

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Chapter 1: Introduction

Significance

The impact of poverty, particularly on early childhood development, is a major issue in the United States and across the globe. Research has shown poverty and low Socioeconomic Status (SES), a measure of status including income, education, and profession (McLoyd, 1998), are associated with numerous negative health outcomes including lower immune function, poor nutrition, increases in substance abuse, and an increased chance of exposure to toxic substances such as lead (Brooks-Gunn & Duncan, 1997; Bradley & Corwyn, 2002; Adler & Rehkopf, & 2008). Children raised in low SES environments throughout development are far more likely to experience multiple negative cognitive outcomes. One primary example of this is the "achievement gap" between children from low SES backgrounds relative to middle and high SES backgrounds. The term achievement gap is used to describe the persistent SES differences in academic achievement visible in grade point averages, standardized tests, and even the highest level of educational attainment (Brooks-Gunn & Duncan, 1997). For instance, at the outset of kindergarten, children from low SES backgrounds lag behind their high SES peers in language (Rowe, 2008), mathematics (Siegler & Ramani, 2008), and general intelligence (Lupien et al., 1998) measures.

While closing the achievement gap remains the top priority for federal, state, and local governments, the identification of the dynamic relationship between the environment and cognitive/affective processes is critical to revealing potential pathways to amelioration or remediation. One avenue of research suggests that children raised in low SES backgrounds have lower executive function, the core set of cognitive abilities critical for daily activities including planning, decision making, problem solving,

reasoning, and learning (Blanchard, Chamberlain, Roiser, Robbins, & Muller 2011; Diamond, 2013). Hence, it has been argued that the effect of SES on early achievement and academic abilities is mediated by the cognitive construct of executive function (Nesbitt, Baker-War, & Willoughby, 2013; Lawson & Noble, 2015). Executive function (EF) is suggested to be a better predictor of school readiness than IQ (Diamond, 2007) and is a positive predictor for current math and literacy achievement along with future achievement in these areas (Blair & Razza, 2007; Bull, Espy, Weibe, Sheffield, & Nelson, 2011; Bull, Espy, & Wiebe, 2008). Therefore, variation in the developmental trajectory of executive function in relation to low SES environments in early childhood is hypothesized to be a primary contributor to the achievement gap. Yet, the question of mechanisms underlying such differences in EF development remain somewhat elusive leading researchers to consider factors of impoverished environments that may impact cortical development.

Beyond the inherent health factors associated with a low SES environment, the social environment of the home and community is a major contributor to the achievement gap. Such factors include exposure to violence, low mobility, experiences of homelessness, crowding, instability, higher levels of parental stress, fewer resources, and substance abuse often resulting in less engaged parenting (Brooks-Gunn & Duncan, 1997; Bradley & Corwyn, 2002; Adler & Rehkopf, 2008). Along with environmental risks, aspects of the home and family dynamics can be protective factors with respect to the emotional and cognitive development of the child such as cultural context, language enrichment, parental responsiveness, dispositional optimism, and beliefs on achievement (Taylor & Seeman, 1999; Garmezy, 1993; Luby et al., 2013).

As previously highlighted, a child growing up in a low SES environment is likely to have exposure to a multitude of adverse experiences relative to a child raised in a family from a high SES background. Repeated stressful events early in life have been shown to have long-term consequences with respect to emotional and cognitive processing (Mezzacappa, 2004; Noble et al., 2005; Farah et al., 2006; Hackman & Farrah, 2010; Kim et al., 2013; Blair, Berry, Mills-Koonce, & Granger, 2013; Finn et al., 2016). The impact of such stressful events and the child's response to and regulation of stress have been suggested to play a primary role in altering the trajectory of brain development (Teicher et al., 2003; McEwen, 2007; Mackey, Raizada, & Bunge, 2012; McEwen & Morrison, 2013). Linking this new research on the effects of stress on brain development with the consequences of living in impoverished conditions provides broader insight into the systematic relationship between poverty and negative life outcomes including the development of EF and the subsequent achievement gap.

Introduction

A major focus of current research is identifying the mechanisms of how the environment affect the cognitive development of children. When considering different SES backgrounds and upbringings, many factors contribute to the environment especially in the home, including poor nutrition, low environmental stimulation, or quality of the parent-child interaction (Brooks-Gunn & Duncan, 1997; Bradley & Corwyn, 2002; Adler & Rehkopf, & 2008). Realistically, no single element in the environment is the sole contributor to the developing child, but it is more likely that the accumulation and interaction of multiple adverse events and conditions influence development. However,

these various factors may share a common mechanism of influencing development in the long-term by shaping the development of the child's stress-response system.

The Biodevelopmental Framework (Shonkoff, 2010) suggests the environment of the child can impact the development of the child's stress regulation system. A stressful environment can cause high levels of stress in the child resulting in high levels of cortisol. Long-term, chronic high levels of glucocorticoids have damaging effects on the neural development of the child (Shonkoff, 2010). Given the altered neural trajectory as a result of environmental stress, the skills and processing that rely on the neural system responsible for stress reactivity will also be negatively impacted. Recent research applying the Biodevelopmental Framework to children from different SES backgrounds suggests that low SES influences the development of the child's stress response and regulation, which in turn affects the physical and cognitive development of the child (Hackman & Farrah, 2009; Blair & Raver, 2012).

Although there are multiple systems involved with the body's overall response to stress, the peripheral responses of the sympathetic nervous system are primarily driven by the central nervous system's hypothalamus-pituitary-adrenal (HPA) axis. The amygdala, hippocampus, prefrontal cortex, and hypothalamus aid in the detection of stress, activation, and regulation of the HPA axis (Lupien, McEwen, Gunnar, & Haim, 2009). The HPA axis produces a neuroendocrine reaction to stress by means of the release of corticosteroids including the end product cortisol. Elevations in cortisol level in the short-term enable appropriate initiation of the fight-or-flight response from stressful events such as increasing alertness and arousal. However, chronic activation of this stress-response system may have adverse effects on the body and on the cortical systems. High

levels of glucocorticoids in the system have been shown to cause neural changes in hippocampus, amygdala, and prefrontal cortex (PFC) (McEwen, 2007; McEwen, 2012; McEwen & Morrison, 2013). Thus, a negative feedback loop is engaged in which these cortical systems responsible for regulating the neuroendocrine stress response are precisely those that are impacted by the prolonged and repeated release of the stress hormones.

The developing brain is particularly sensitive to elevations in cortisol levels especially long-term, repeated exposures to stressful events (McEwen & Seeman, 1999). More importantly, the specific regions or networks of the brain impacted by chronic levels of stress are those associated with executive function such as the prefrontal cortex (PFC) (Hackman & Farrah, 2009; Kim et al., 2013; McEwen, 2013). The protracted development of the PFC creates a unique situation that can be beneficial for learning and plasticity. However, this also makes the PFC vulnerable throughout development to negative influences such as early life stress (Anderson, 2003; Pechtel & Pizzagalli, 2011). Children raised in low SES backgrounds are at risk for the neural consequences of chronic stress as children from low SES backgrounds show heightened activation of the HPA axis with increased levels of cortisol and may lack the regulation necessary for executive function and learning (Blair, Berry, Mills-Koonce, & Granger, 2013). Considering the converging lines of evidence, the SES differences in executive function may be an outcome of highly stressful environments and the child's repeated and prolonged response to those events (Blair & Raver, 2012). Therefore, it is postulated that, due to the various risks associated with poverty, a child being raised in a low SES environment develops an altered stress regulatory system, which affects neural networks

including the PFC, which in turn affects the differential behaviors manifested in executive function.

The specific factors and relations of how adversity, stress hormones, genetic variation, and the quality of parent-child interaction all dynamically converge to explain the influence of poverty on cognitive development and achievement are still speculative. The stress mechanism of the HPA axis has been shown to be a promising explanation; however, the influence of early life stress on the PFC and the network supporting executive function and subsequent behavioral outcomes has not been directly tested. The current study aims to integrate previous behavioral, physiological, and neural research to support a model of stress regulation and its relation to brain development as an underlying mechanism of how different SES environments influence the development of executive function. The overall aim of the current study is to examine how stress reactivity and regulation impact executive function development in children from various socioeconomic status backgrounds. The primary aim of the study is to better understand the relation between cortisol reactivity and executive function using both behavioral executive function tasks and cortical thickness measures of structural development in the Prefrontal Cortex (PFC). The secondary goal of the study is to examine the impact of abnormal stress regulation on the neural development of the PFC a potential mechanism underlying SES differences in executive function. The data used for the current study was collected as part of a larger study examining biomarkers of child psychopathology systems (Dougherty, Tolep, Smith, & Rose, 2013). The longitudinal study design involved two waves of data collection during early preschool age and early elementary

age. Cortisol reactivity and behavioral executive function assessments were collected at both waves whereas structural neural data was collected at the second wave.

The overall theme of the predicted results falls under the framework of Shonkoff's Biodevelopmental model as early life adversity can "get under the skin" through biological embedding (Shonkoff, 2010). According to this framework, early life adversity is biologically embedded through gene-environment interactions and influencing the development of multiple systems in the body including stress regulation, immune function, and metabolic processes (Shonkoff, 2010). The body adapts to environment to be beneficial for the individual. Exposure to high levels of glucocorticoids, as a result of toxic stress, alters the regulatory mechanisms of the stress response system to be beneficial short term but can have detrimental long-term implications. The early life adversity can lead to aberrant levels of cortisol release and subsequent changes to synapse formation and dendritic arborization in the PFC (McEwen, 2007; Teicher et al., 2003; Mackey, Raizada, & Bunge 2012). Therefore, atypical cortisol reactivity is predicted to be related to smaller volumes of the development of specific regions within the PFC, a major component of the network supporting executive function. Executive function, supported by the PFC, will also be negatively impacted by the damaging high levels of stress with lower executive function being associated with atypical cortisol reactivity.

Although research on cortisol reactivity has been inconsistent with respect to the direction of aberrant cortisol release, studies have suggested low SES or high environmental stress is associated with higher overall cortisol levels and atypical changes in cortisol levels in response to stress (Lupien, King, Meaney, & McEwen, 2000; Blair et

al., 2011; Blair & Raver, 2012; Blair, Berry, Mills-Koonce, & Granger, 2013). Given the distribution of SES is somewhat limited in the current sample in this investigation, the SES research questions will be framed as more exploratory. However, it is predicted that the cortisol reactivity of the child will partially mediate the association between SES and executive function with both the neural and behavioral measures as outcomes.

Chapter 2: Literature Review

The Role of Executive Function

The construct of executive function, also referred to as cognitive control, is positively associated with long-term academic outcomes, socialization, and life achievement in general (Blanchard et al., 2011; Diamond, 2013). Executive function supports multiple daily activities such as decision-making, planning, problem solving, social interactions, and reading (Diamond, 2012). Thus, the development of executive function is crucial for a child's development especially in terms of social adaptation and academic performance. Although there has been a great excitement in the literature with respect to executive function, a coherent operational definition has been sorely lacking (see for example, Baggetta & Alexander, 2016). One approach has been to treat executive function as a unitary construct of cognitive control such as in Baddeley's homoncular "central executive" (e.g. Baddeley, 1992). An alternative approach has been to define executive function as multiple interacting components typically including aspects of inhibition, cognitive flexibility, and maintenance or working memory (Diamond, 2012). Although executive function can be thought of as these three separate and independent constructs for older children (Miyake et al., 2000), for younger children especially in preschool, executive function is suggested to be one unitary umbrella process

(Willoughby, Blair, Wirth, & Greenberg, 2010). Whereas we favor the multiple components approach, it is important to note that recent theories about the components of executive function such as working memory and attentional control have been viewed as arising from a singular construct of selective attention (Cowan, 1995) and that many of these multiple "functions" rely on a common neural system (Gazzaley & Nobre, 2012). Although there are multiple terms and components associated with executive function, for the sake of simplicity, executive function will be defined as the overarching construct of conscious, effortful cognition typically engaged when there is competition between stimuli in the environment or responses to that stimuli. Executive function is often necessary to override prevalent or automatic behaviors. The specific components will be discussed in relation to previous studies examining the impact of SES.

Independent of the definition of executive function, researchers agree that executive function relies on a common neural architecture. The overwhelming consensus in the literature is that the prefrontal cortex (PFC) is a key player in executive functioning (Fuster, 1980; Goldman-Rakic, 1988; Miller & Cohen, 2001; Diamond, 2006). The PFC is argued to have a hierarchical organization that enables increasing abstraction or elaboration of rule formation that forms the basis of executive control of behavior (Badre & Wagner, 2007; Koechlin & Summerfield, 2007). Moreover, the neural development of this region coincides with the development of executive function (Zelazo, Carlson, & Kesek, 2008). The development of executive function is thought to emerge around the age two or three (Rothbart & Michel, 1989) and continues to develop into the mid-twenties; however, the roots of early control behaviors have been shown in infancy with the onset of agency (Keen, 2003) and maintenance behaviors (Munakata, 2001).

Coinciding with the behavioral trajectory, the PFC has a protracted development in which the region continues to develop into young adulthood (Casey, Giedd, & Thomas, 2000; Fuster, 2000).

The protracted development of the PFC is visible throughout multiple stages of development. Infancy and early childhood are marked by a large increase in the creation of new neurons (neurogenesis) and connections (synaptogenesis) followed by the refining of these connections by synaptic pruning, which is driven by competitive elimination—use it or lose it—resulting in fewer, more efficient networks (Hebb, 1955). In most regions of the brain including the somatosensory cortex, synaptic pruning peaks between 4-9 months. However, pruning in the PFC occurs between 30-36 months (Thompson-Schill, Ramscar, & Chrysikou, 2009). Another marker of the protracted development in childhood is grey matter thickness which is generally associated with dendritic arborization. In the PFC, grey matter thickness peaks between 7-9 years of age and continues to develop into early adulthood (Geidd et al., 1999; Gogtay et al., 2004). Lastly, myelination of long range cortico-cortico axons, reflected in measurements of "white matter" fiber tracts, appears to peak in the early 20s (Casey, Jones, & Hare, 2008; Schmithorst & Yuan, 2010). The protracted development of the PFC creates a unique situation that can be beneficial for learning and plasticity. On the other hand, the protracted development also makes the PFC vulnerable throughout development to negative influences such as early life stress (Anderson, 2003; Pechtel & Pizzagalli, 2011).

As the field of cognitive neuroscience has evolved beyond a simple structure-function mapping, a model of a Cognitive Control Network has emerged (Cabeza & Nyberg, 2000; Fair et al., 2009; Schneider & Chein, 2003; Chein & Schneider, 2005;

Dosenbach et al., 2007; Cole & Schneider, 2007). The Cognitive Control Network (Cole & Schneider, 2010) includes cortical regions such as prefrontal, parietal, insula, striatum, and anterior cingulate cortex (Cole & Schneider, 2010). Several sub-networks in this broad architecture have been shown to underlie different aspects of task performance (Dosenbach et al., 2006; 2007), suggesting that such sub-networks may reflect the different components of executive functioning. However, several brain systems are critical to the overall functioning of the executive function including the striatum. The striatum has belt-like projections that loop through PFC out to sensorimotor regions and the cerebellum and is important for learning, response regulation, and constant updating and resetting to process new stimuli in the environment (Blanchard, Chamberlain, Roiser, Robbins, & Müller, 2011). Therefore, our understanding of the neural basis of executive functioning begins with PFC but extends to the vast dynamic network that enables complex, goal-driven behavior.

SES Differences in Executive Function

Given the "window of opportunity" or protracted development of the PFC in coordination with regions of the Cognitive Control Network, it becomes apparent that the development of executive function is subject to environmental influences. A prominent example of the impact of the environment is the differences in executive function in children from different SES backgrounds. Lower executive function and language abilities are found in children from low SES backgrounds in comparison to children from middle or high SES backgrounds (Noble et al., 2005). From a behavioral standpoint, multiple studies show skills associated with executive function including working memory, conflict monitoring, self-regulation, inhibition, and attention in children differ

on the basis SES backgrounds with children from low SES backgrounds having generally poorer performance (Mezzacappa, 2004; Noble et al., 2005; Farrah et al., 2006; Noble et al., 2007; Stevens, Lauinger, & Neville, 2009). In measures of attentional control, children from lower SES backgrounds showed a reduced effect of alerting cues, which is suggested to be a result of an overall heighted alertness and had a harder time with inhibiting the distracters of the task (Mezzacappa, 2004; Stevens, Lauinger, & Neville, 2009). Specifically, the children from lower SES backgrounds in comparison to their higher SES peers have slower reaction times for the executive component, derived from a modified flanker paradigm in which subjects must selectively attend to a central stimulus by inhibiting the flanking stimuli that often conflict (Mezzacappa, 2004). Based on these attentional and inhibition differences, some researchers argue against the deficit model and that the higher "distractibility" may be environmentally adaptive for children in poverty who have to be aware of threatening cues in the environment (Stevens, Lauinger, & Neville, 2009).

Differences associated with SES are present in brain structure, function, and connections of regions supporting executive function and learning in general. Children from different SES backgrounds have overall brain volume differences as children from high income backgrounds have greater cortical thickness and cortical grey matter in comparison to children from low income backgrounds (Mackey et al., 2015; Piccolo, Merz, He, Sowell, & Noble, 2016). Differences in the developmental trajectory of children from different economic backgrounds was highlighted by Hanson et al. (2013) by following a group of economically diverse 5 months olds' brain growth until the children were 4 years old. Children from low SES backgrounds had a slower trajectory of

overall brain volume during infancy and early childhood (Hanson et al., 2013). When the specific lobes of the brain were compared separately, the frontal and parietal lobes grey matter volume had significant differences with children from low SES backgrounds showing reduced grey matter in these lobes (Hanson et al., 2013). There was no difference in total brain volume or regional differences in volume of the infants at the 5-month assessment, which suggests the SES environment plays a large role during early brain development. The authors suggest that synaptic remodeling rather than neurogenesis underlie the differences grey matter because of the experiences of the SES environment (Hanson et al., 2013). Researchers suggest children from low SES backgrounds may endure a developmental lag in brain development in comparison to the children from higher SES backgrounds. Along with reduced volumes in specific regions of children from low SES backgrounds, local gyrification differences in anterior frontal regions are also present in children from low SES backgrounds (Jednorog et al., 2012).

Along with overall brain differences, there are SES differences in specific regional volumes as children from low SES families have reduced brain volumes within the networks associated with executive function in comparison to the children from high SES families. Smaller grey matter volumes of bilateral hippocampi, middle temporal gyri, left fusiform, and right inferior occipito-temporal gyri were associated with children from lower SES backgrounds (Jednorog et al., 2012). However, individuals from low SES backgrounds had greater amygdala volumes in comparison to individuals from higher SES background (Noble, Houston, Kane, & Sowell, 2012). Some counter-intuitive findings in developmental brain differences associated with SES have also been shown. For instance, higher levels of education were associated with decreased white matter

integrity from seed regions in PFC (the cingulum bundle and the superior longitudinal fasiculus) for young adults (Noble et al., 2013); whereas Jednorog et al. (2012) did not find significant SES white matter differences in 8-10-year-old children.

Along with SES as a general construct, different components including parental education and income have been suggested to separately influence structural development in specific regions as well. In a recent study, Noble et al. (2015) examined the association between SES and brain structure in individuals whose age ranged from 3 to 20 years old. When SES was broken down into parental education and income, differences in parental education was linearly related to surface area in multiple regions involved in executive function, language, and learning including inferior frontal cortex, medial frontal cortex, orbital frontal cortex, cingulate, inferior and middle temporal cortex, and insula (Noble et al., 2015). Family income was logarithmically related to surface area in numerous regions including inferior frontal, inferior temporal/insula, right medial frontal, and right occipital cortex (Noble et al., 2015). The logarithmic association suggests larger differences in surface area were associated with differences in income in families from lower SES backgrounds compared to higher SES families as increases in smaller amounts of money may influence brain development more extremely for families from low SES backgrounds.

Differences in functional activation and connectivity within the Cognitive Control Network have been shown in children from different SES backgrounds, likely stemming from the structural variations related to SES. A handful of studies have suggested differences in the recruitment of the Cognitive Control Network have been associated with SES (D'Angiulli, Herdman, Stapells, & Hertzman, 2008). Sheridan et al. (2012)

found differences in the areas recruited for the stimulus response learning task in children from 8-12 years old were associated with SES. Children from lower SES background showed increases in multiple regions associated with executive function including supplementary motor area, basal ganglia, bilateral inferior frontal gyrus, ACC, and right middle frontal gyrus (Sheridan, Sarsour, Jutte, D'Esposito, & Boyce, 2012). In a more recent study, children from higher income groups showed higher working memory capacity, math achievement, and greater activation of the frontal-parietal network as a result of working memory load (Finn et al., 2016). More specifically to the PFC, childhood income at age 9 was also related to later PFC activation during an emotion regulation task completed at age 24 (Kim et al., 2013).

Electroencephalogram (EEG) studies also support SES differences in brain activity associated with executive function. SES differences in resting EEG brain activity in a longitudinal study of children from Mexico (Otero, 1997; Otero, Pliego-Rivero, Fernández, & Ricardo, 2003). A group of studies used event-related potentials (ERP) to examine selective attention differences in children from different SES backgrounds. Overall, the studies suggest even when there are no apparent behavioral differences, children from different SES backgrounds may recruit different neural processes when using selective attention. More specifically, children from lower SES backgrounds use more attentional resources to process irrelevant information in the environment (Stevens, Lauinger, & Neville, 2009; D'Anguilli et al., 2008; Kishiyama, Boyce, Jimenez, Perry, & Knight, 2008). Stevens, Lauinger, & Neville (2009) examined ERP processing during a selective attention task in children from different SES backgrounds (as measured by maternal educational attainment). The selective attention task required the children to

listen to the story in one ear and ignore the story presented in the other ear. There were no behavioral differences between the children from families with higher educational attainment versus the children from families with lower maternal education. However, neural differences were present specifically in the ability to suppress or ignore the irrelevant information. In children, a positivity (P1) between 100-300 ms is associated with attention. In the attended stimuli channels, both groups of children showed broad positivity around 100 ms. However, the children from mothers with lower educational achievement had a larger P1 around 150ms for the unattended information whereas the children with mothers with higher educational achievement showed no P1 (Stevens, Lauinger, & Neville, 2009). This difference suggests the children of mothers with lower educational attainment were worse using attentional resources to process the unattended stimuli suggesting these children have difficulty ignoring irrelevant information in the environment (Stevens, Lauinger, & Neville, 2009). D'Anguilli et al. (2008) showed similar patterns of ERP results when examining SES differences in selective attention using a non-spatial auditory selective attention task that required 12-14-year-old children to attend to two tones and ignore two other tones. Although there were no behavioral differences, children from lower SES backgrounds showed the positive waveform around 100ms after the presentation of attended and unattended tones whereas the children from higher SES backgrounds only showed the P1 for the attended tones. Children from lower SES backgrounds also showed decreased recruitment of attentional resources during a target detection task (Kishiyama, Boyce, Jimenez, Perry, & Knight, 2008). More specifically, 7-12-year-old children from lower SES backgrounds had decreased P1, N1, and a novelty (N2) responses but there were no behavioral differences in task

performance. This study also adds to the literature suggesting SES differences in the allocation of neural processes associated with selective attention (Kishiyama, Boyce, Jimenez, Perry, & Knight, 2008).

In summary, numerous studies support the association between SES and executive function and the neural substrates underlying the components of this ability. Children from low SES backgrounds appear to have lower executive function abilities. More specifically, children from low SES backgrounds perform poorly in assessments of selective attention, working memory, and conflict monitoring/inhibition. When considering neural evidence, differences arise in children from different SES backgrounds. Children from lower SES backgrounds show decreases in grey matter within various regions of the Cognitive Control network. Along with structural differences, there appears to be less overall activation and functional connectivity of the Cognitive Control Network in children from low SES backgrounds compared to children from high SES backgrounds. While we cannot presume causality with respect to brain-behavior associations, one primary assumption is that chronic poverty is driving changes in the brain that are associated with executive functioning. The fundamental question again is what is responsible for these neural changes that occur from economic factors.

SES and Development of the Stress Response

The studies covered in the previous section highlight SES differences in the processes and neural networks that support executive function. However, a major question that remains is how differences in environment, such as SES, affect the neural and cognitive development of children. When considering different SES backgrounds and upbringings, many factors contribute to the environment especially in the home,

including poor nutrition, low environmental stimulation, or quality of the parent-child interaction (Brooks-Gunn & Duncan, 1997; Bradley & Corwyn, 2002; Adler & Rehkopf, & 2008). Realistically, no single element in the environment is the sole contributor to the developing child, but it is more likely that the accumulation and interaction of multiple adverse events and conditions influence development. However, a common mechanism through the multiplicity of factors may emerge to shape the development of the child's stress-response system.

The Biodevelopmental Framework suggests the environment impacts the child positively and negatively through the biological embedding of physiological and neurological processes (Shonkoff, 2010). An impoverished environment can cause high levels of stress and over activation of the stress systems (Shonkoff, 2010). Long-term, chronic levels of stress can have damaging effects on the mental health, physical health, and neural development of the child. However, there are protective factors in the environment, such as maternal warmth or family stability, which can buffer these negative effects (Shonkoff, 2010).

Multiple systems are involved with the body's overall response to stress. The specific peripheral responses of the sympathetic nervous system are driven by the central nervous system's hypothalamus-pituitary-adrenal (HPA) axis. The HPA axis is a negative feedback loop involving a cascade of hormones and glucocorticoids with cortisol as the end product. In response to a stressor, the amygdala signals hypothalamus to synthesize and release corticotrophin-releasing hormone (CRH). The levels of CRH activates synthesis and secretion of the adrenocorticotrophin hormone (ACTH) in the pituitary gland. In the adrenal cortex, the levels of ACTH induce the production of glucocorticoids

including cortisol (Lupien, McEwen, Gunnar, & Heim, 2009). Under normal stress, cortisol is released by the kidneys in response to a stressor and the levels of cortisol are monitored by a homeostatic mechanism which generally provides negative feedback for the continued release of cortisol (Smith & Vale, 2006). High cortisol levels increase arousal and alertness, commonly described at the fight or flight response. This neuroendocrine response to stress directly impacts cortical regions which is beneficial in the context of the immediate response to a stressful situation however can be detrimental long term. Chronic activation of this stress-response system resulting from chronic stress has adverse effects on the regulation of the stress system, the body, and cortical systems (McEwen & Seeman, 1999; McEwen 2003; McEwen 2007). Chronic high levels of cortisol can cause neural remodeling, dendritic reorganizing, and dendritic shortening in regions crucial for executive function and learning including the hippocampus, amygdala, PFC, and ACC (McEwen, 2007; Teicher et al., 2003; Mackey, Raizada, & Bunge 2012). Even more concerning, the developing brain is particularly sensitive to elevations in cortisol levels, particularly long-term, repeated exposures to stressful events (McEwen & Seeman, 1999; McEwen 2003; McEwen 2007; McEwen 2013).

How a child responds to stress and the ability to regulate responses develops throughout childhood and is impacted by early life experience (Holochwost, Propper, Mills-Koone, & Granger, 2017). The body is thought to possible adapt to the environment of the child. Granted, this ability to adapt is not necessarily deleterious as a heightened state of arousal may be better suited for a child's environment (Ellis & Boyce, 2008; Blair & Raver, 2012). However, the chronicity of elevated stress reactivity has direr effects in the long-term. McEwen & Seeman (1999) termed this cumulative,

maladaptive, toxic stress as allostatic load that is associated with negative long-term outcomes biologically and behaviorally. Allostatic load is different from the normal, healthy levels of stress, which results in the body maintaining a healthy balance of cortisol and catecholamines referred to as allostatis (McEwen & Seeman, 1999). Within the more recent Biodevelopmental Framework, Shonkoff (2010) classifies stress into three different categories: positive, tolerable, and toxic. Positive stress represents the increased arousal of short term increases in cortisol that can be beneficial for learning and performing. Tolerable stress is borderline toxic stress that can be repetitive and have the potential to be damaging but the effects are buffered by a positive support system for the child (Shonkoff, 2010). Toxic stress is similar to the allostatic load definition in which chronic, long-term high levels of stress that results in long-term elevations in cortisol (Shonkoff, 2010). The long-term elevations in cortisol have damaging effects on the neural development of the child as well as a magnitude of other negative effects on the child's body and immune system. Higher chronic or toxic stress is associated with lower SES backgrounds as higher allostatic load is associated with lower education levels and vice versa (Seeman, Epel, Gruenewald, Karlamangla, & McEwen, 2010). With chronic stress, the body must adapt in order to protect itself against the damaging high levels of cortisol and other hormones of the stress response, for instance by altering the stress response system. The deleterious effects of continuous stress and associated heightened levels of cortisol generate a homeostatic response in the brain's HPA axis that results in down-regulation of critical systems for attention and memory (Blair, Berry, Mills-Koonce, & Granger, 2013). Although recent research supports SES differences in cortisol levels and cortisol reactivity, the directions of the results have been mixed.

Nevertheless, a relatively consistent set of studies show children from low SES backgrounds have higher diurnal and baseline levels of cortisol along with altered cortisol responses for tasks that are designed to evoke stress responses in children from low SES background (Lupien, King, Meaney, & McEwen, 2000; Blair et al., 2011, Blair & Raver, 2012; Blair, Berry, Mills-Koonce, & Granger, 2013). In the few studies that have examined cortisol reactivity in children from different SES backgrounds, the cortisol reactivity response in children from low SES backgrounds is suggested to be "blunted" (Blair et. al, 2013) and is suggested to support the mechanism of the adapting to chronic stress as down regulation of children facing early adversity (Blair et. al, 2013). Lupien, King, Meaney, & McEwen (2000) examined basal cortisol levels, the average of two morning cortisol assessments collected within the first hour of school, of six to ten-year-old children from all SES backgrounds. Children from low/middle SES backgrounds showed higher basal cortisol levels than children from high SES backgrounds at all ages. The difference between children from low, middle, and high SES families arose when the children were 10 year olds (Lupien, King, Meaney, & McEwen, 2000). Another study by Blair et al. (2013) found differences in cortisol reactivity related to poverty exposure in 48-month-old children. Higher cumulative poverty was associated with less change in cortisol before and after completing the EF battery (Blair et al., 2013). The cortisol reactivity was assessed by measuring cortisol once before and two following a challenging battery of EF tasks which was thought to evoke a cortisol response (Blair et al., 2013).

Although this line of work is promising, a concern is the consistency and replication of cortisol findings. Not all studies show differences in cortisol associated

with SES. Although developmental trends of the HPA axis and cortisol levels are being established, methodological differences and age of the children makes it challenging to interpret the literature as a whole. Various measures of cortisol such as (diurnal, waking response, and reactivity) are compared within the literature, while each of these cortisol responses have different developmental trajectories with age and pubertal status (Gunnar, Wewerka, Frenn, Long, & Griggs, 2009). As an explanation of the inconsistency in the SES literature, Ursache, Noble, and Blair (2015) suggest young children from low SES backgrounds show hypercortisolism and adolescents/adults from lower SES backgrounds show hypocortisolism. The flip in the direction of the relationship is suggested to be related to the impact of puberty on the developmental trajectory of the cortisol response (Ursache, Noble, & Blair, 2015). Although the SES cortisol literature is somewhat mixed, research suggests there is an association between SES and the HPA axis needs more attention to clarify the specific findings.

Chronic stress impacts the body at the macro and micro levels as cortisol is one indicator of adaptation of the HPA axis. At the systems level, the stress response system is constantly interacting and influencing other systems in the body especially the peripheral and central nervous system, the cardiac and respiratory system, and the immune system (McEwen & Stellar, 1993). At the physiological level, there are multiple hormones, catecholamines, proteins, and other components of the stress response constantly interacting, regulating, and mediating each other (McEwen, 1999). These physiological interactions of neuroendocrinology, which are popularly assessed by shifts in baseline cortisol levels or cortisol reactivity (to stress), have been associated with

changes in neural connections such as neurogenesis, dendritic remodeling, and long-term potentiation (McEwen, 2007).

At the macro level, variations across the multiple components of the stress response system affect brain networks in unique ways. Structural and functional neural differences have been associated with chronic stress as assessed by animal and human models. In general, the prefrontal cortex, hippocampus, anterior cingulate cortex, and amygdala have all been implicated in studies of exposure to chronic stress (McEwen, 2007; Teicher et al., 2003; Mackey, Raizada, & Bunge 2012) and are all regions crucial for everyday cognitive and emotional processing. The prefrontal cortex plays a higher-level role in the HPA axis as it aids to limit the response to stress. The PFC has monoamine projection to subcortical regions that can be inhibited and limit the stress response by decreasing the production of the hormones within the HPA axis (Diori, Viau, & Meaney; Brake et al., 2000; Teicher et al, 2003). However, the interactions between the PFC and HPA axis can become altered as a result of chronic stress. In the case of chronic stress, the levels of cortisol and other stress related hormones influence the function of glucocorticoid receptors and dopamine projecting neurons within the PFC. Therefore, the PFC may not be able to correctly regulate or limit stress responses even when it would be beneficial.

The alterations in the HPA axis and elevated levels of glucocorticoids from chronic stress results in dendritic shortening and remodeling in the PFC (Teicher et al., 2003; McEwen, 2007; Mackey, Raizada, & Bunge, 2012). In children with posttraumatic stress symptoms, increases in bedtime cortisol levels were associated with decreases in cortical volume of the PFC (Carrion, Weems, Richert, Hoffman, & Reiss, 2010). This

pattern of changes in the structure and function of the PFC are also suggested by clinical studies of chronic early life stress such as maltreatment, neglect, and PTSD (Teicher et al., 2003; McEwen, 2007; McEwen, 2013).

The impact of chronic stress on the PFC is particularly worrisome in younger children as the protracted development of the PFC creates a longer window of vulnerability. As previously discussed, the PFC is still developing during childhood and adolescence until around age 25 (Casey, Jones, & Hare, 2008). Therefore, chronic exposure to stress any time during this developmental period can strongly affect the neural attributes of the PFC. Early chronic stress exposure is thought to cause the PFC to mature at a faster rate which results in an altered trajectory of the PFC with growth peaking earlier and having a lower overall plasticity than normal (Teicher, Ito, Glod, Schiffer & Gelbard, 1996; Teicher et al., 2003). Neural changes as a result of chronic stress has also been shown in adolescence. For instance, exposure to abuse occurring between 14-16 years old has been associated with changes in frontal grey matter volumes (Anderson et al., 2008). Therefore, it is likely that the impact of SES is dependent on the age of the child and may suggest that the impact of stress response on the association between SES and cognitive development may become visible at an older age.

Although the PFC is of interest when considering executive function, previous chronic stress research focused primarily on the hippocampus and amygdala. Overall, decreases in hippocampal dependent circuits processing have been associated with high levels of cortisol and stress in general (McKittrick et al., 2000; McEwen, 2007; Frodl & O'Keane, 2013; Sudheimer et al., 2014). However, the association between cortisol and hippocampal development may differ depending on the age of the child as there is a

positive relationship between cortisol and hippocampal development in young adults (Pruessner, Pruessner, Hellhammer, Pike, & Lupien, 2007). Overall, chronic stress is shown to cause decreases in hippocampal neural connections which are thought to underlie the behavioral differences in abilities supported by the hippocampus including learning and memory (Lupien et al., 2002; Goosens and Sapolsky, 2007; Frodl & O'Keane, 2013). The decreases in neural connections of the hippocampus is thought to occur through neurogenesis, dendritic regression, and dentate gyrus Long Term Potentiation (LTP) (McEwen, 2007). Neuromodulators of the hippocampus are highly impacted by changes in levels of corticosteroids associated with a stress response. For example, serotonin is a crucial neuromodulator that appears to be directly impacted by elevated cortisol levels (Chalmers, Kwak, Akil, &Watson, 1993). There is a high density of serotonin receptors in the hippocampus and chronic stress has been shown to cause a down-regulation of these receptors, which is associated with dendritic remodeling of the hippocampus (McKittrick et al., 2000; McEwen, 2007).

Although chronic stress is associated with decreases in synapse formation in the PFC and hippocampus, the opposite effect is shown in the amygdala. Within the amygdala, chronic stress is associated with increases in structure and volume. The enlargement of the amygdala occurs through dendritic growth and remodeling as a result of chronic stress. (Conrad, Magarino, LeDoux, McEwen, 1999; Corodimas, LeDoux, Gold, Schulkinm, 1994; McEwen 2007). These structural increases are associated with heightened stress response and sensitivity. Individuals with stress-related neural disorders including depression, anxiety, borderline personality, and Post Traumatic Stress Disorder (PTSD) show aberrant processing of stress that appear to be associated with increases in

the structure and function of the amygdala (Driessen et al., 2000; Frodl et al., 2003; Vermetten, Schmahl, Linder, Lowenstein, & Brem, 2006; McEwen, 2007; Teicher, Anderson, & Polcari, 2012).

More evidence for physiological changes in feedback system of the HPA derives from epigenetic studies on the impact of early life stress on the function of the glucocorticoid receptor (GR) gene. Epigenetics research examines the impact of the environment on gene expression rather than the actual change of genetic code (Meaney, 2010). Although DNA is normally wound tightly in a double helix configuration, DNA must be unwound for gene expression to occur. The general idea is the environment causes change in the structure of the DNA which affects aspects of transcription by altering the efficiency of the promoters binding. Two common methods of epigenetic changes include methylation and the modification of histone proteins (Meaney, 2010). Epigenetic changes as a result of the environment are shown in rat models as early licking and grooming behavior of the mother pup to the rat pup influences the expression of GR gene (Meaney, 2010). However, more recently this framework has been applied to human research examining whether early life stress such as maltreatment and anxiety (McEwen, Eiland, Hunter, & Miller, 2012), influences the GR gene expression and has been found even infants. Three-month-old infants of mothers with symptoms prenatal maternal depressive/anxious mood have greater methylation of the promoter and exon regions of the GR gene. The higher methylation was also associated with increased stress reactivity as assessed by salivary cortisol (Oberlander et al., 2014). Long-term epigenetics effects are also suggested as early maltreatment in 11-14-year-old children is associated with greater methylation within a promoter region of glucocorticoid receptor

gene (Romens et al., 2015). Even within a healthy adult population, differences in early life nurturing and parental care are associated with methylation of the GR gene. (Tyrka, Price, Marsit, Walters, & Carpenter, 2012). In the adult population, the methylation of the GR gene was associated with an attenuated stress response (Tyrka, Price, Marsit, Walters, & Carpenter, 2012) which also highlights the body's adaptation to high levels of stress.

In summary, research suggests the development of the systems supporting stress regulation are highly sensitive to the environment. At times when stress is "normal", it can be beneficial and adaptive for certain situations and environments. However, when stress is chronic, stress can be harmful to the body at multiple levels. In this situation, the body will adapt to protect itself from the harmful toxins associated with high levels of stress. One suggested mechanism of protection is the down regulation of stress response. The exposure and adaptation to the harmful chronic stress impacts specific neural connections especially within the PFC, the hippocampus, and amygdala. Although previous research has identified and defined some of the negative consequences of chronic stress, which can be associated with SES differences, there are still numerous questions that need to be addressed. First, the neural research has focused mainly on the hippocampus and amygdala while the PFC and striatum have not been researched as extensively. Future research should aim to examine and quantify the differences in the PFC and striatum which are areas highly involved in important high-level functions such as executive function and learning in general. Research has also begun to address how the dysregulation of the stress response in children from low SES backgrounds affects neural networks and functioning however findings are still mixed. Although research suggests differences in stress responses and regulation affect neural development, further research

needs to clarify the association between stress and neural development and what this means cognitively. To address the behavioral implications, future research needs address the network differences associated with SES and how this related to behavioral differences in cognitive processes such as executive functioning.

SES, Stress, and Executive Function

The previous sections highlighted socioeconomic differences in behavioral and neural assessments of executive function and the impact of chronic stress on the brain. However, these two bodies of research may not be as distinct as presented. Research suggests a child's stress response and regulation impacts the neural development of the child. An interesting point to consider when examining the regions and networks of the brain that are impacted by chronic levels of stress, is that these regions are highly overlapping with the regions associated with SES differences in with executive function such as the PFC. Considering the two converging lines of evidence, the SES differences in executive function may be an outcome of highly stressful environments and how the child's response to those events (Hackman & Farrah, 2010; Blair & Raver, 2012). Due to the various risks associated with poverty, a child being raised in a low SES environment develops an altered stress regulatory system, which affects neural development of the PFC, which in turn affects the behavior manifested in executive function differences (Denase & McEwen, 2012).

Children from low SES backgrounds have increased basal levels of cortisol and have been suggested to lack the regulation necessary for executive function and learning (Blair, Berry, Mills-Koonce, & Granger, 2013). High executive function is associated with an increase in cortisol in response to a stressor followed by a decrease while low

executive function, particularly in children from low SES backgrounds, is associated with higher basal levels and a flatter trajectory of cortisol change before and after being stressed (Blair, Granger, & Razza, 2004; Blair et al., 2011). Higher basal cortisol levels have also been associated with low executive function at 7, 15, and 24 month assessments in a large sample of children from predominantly low-income backgrounds, (Blair et al., 2011). In children 8-12 years old, the percent of change in cortisol levels assessed before and after scanning were related to PFC activation in a stimulus response learning task (Sheridan et al., 2012).

As discussed in the previous section, chronic stress is associated with changes in various regions in the brain including the PFC which supports executive function and learning. Further support for the converging of these two lines of research is found at the lower level when the neuromodulators involved in stress and executive function or learning in general are considered. Cortisol and catecholamines (e.g. epinephrine, norepinephrine, and dopamine) are associated with the stress response system that in a chronic stress or high allostatic load situation, the levels of multiple neuromodulators and neurotransmitters are impacted. Two dominant neuromodulators of executive function and learning in general are dopamine and serotonin. Dopamine is one of the dominant neuromodulators in the PFC as a part of Cognitive Control Network (Seamans &Yang, 2004) that underlie executive function. Along with other neuromodulators, glucocorticoids, serotonin, and dopamine levels all interact to support healthy brain functioning. An imbalance arises when there is a change in the levels of a neuromodulator. In the case of chronic stress as high levels of glucocorticoids influence dopamine and serotonin levels and receptors (McEwen 2007; McEwen 2013). The PFC

has high levels of glucocorticoid receptors and there are numerous dopamine neurons that project to this region which are both impacted by high levels of stress (Diorio, Vaiu, & Meaney, 1993; Teicher et al., 2003).

In support of this stress-dopamine relationship, studies have suggested an association between stress reactivity and the genetic polymorphisms of Catechol-O-methyltransferase (COMT) (Munakata, Casey, & Diamond, 2004). COMT is expressed at higher levels in the PFC and variations of COMT been related to executive function. The COMT gene encodes an enzyme that degrades dopamine within the synaptic gap to facilitate efficient neuronal firing. The Val allele is associated with a higher level of expression of the dopamine-degrading enzyme that leaves less dopamine available synaptic transmission in comparison to individuals homozygous for the Met allele. The less efficient synaptic function associated with the Val allele hampers the communication of neurons and brain regions supporting learning and cognitive control in comparison to individuals homozygous for the Met allele (Blanchard et al., 2011). COMT polymorphisms are related to executive function with the general trend of individuals homozygous for the Val allele performing worse than individuals homozygous for the Met allele (Blanchard et al., 2011).

A handful of current studies have aimed to examine different components of the complex question of how SES influences the cognitive and emotional development of children. In a longitudinal study by Kim et al. (2013), low income was associated with reduced activation in frontoparietal regions in the Cognitive Control Network including the dlPFC, vlPFC, precentral gyrus, inferior parietal lobe, insula, and superior temporal lobe (Kim et al., 2013). In regards to how income related to emotional regulation, the

reduced activation in the PFC was related to a failure of suppression of the amygdala during an emotional regulation task. The lack of regulation and connection between PFC and amygdala was supported by their functional connectivity analysis of vlPFC, dlPFC, and the amygdala.

Barch et al. (2016) examined the impact of preschool poverty on functional connectivity and school age depression. Lower income to needs ratio at preschool was associated with reduced connectivity in multiple regions supporting learning including hippocampus, amygdala, superior frontal cortex, lingual gyrus, posterior cingulate and putamen. More specifically, lower SES was negatively related to connectivity between amygdala and lingual gyrus as well as between hippocampus and prefrontal connectivity (Barch et al., 2016). Demir et al. recently examined the impact of early-life stress on later school aged prefrontal resting-state fMRI connectivity (Demir et al., 2016). The results suggested higher early life stress, rather than concurrent, was related to differences in regional homogeneity in the left prefrontal cortex and right middle temporal (Demir et al., 2016). In another study of healthy males, early life stress was associated with elevated cortisol waking response and impaired executive function (Butler, Klaus, Edward, & Pennington, 2017).

The bigger question of how SES impacts academic achievement via the neural substrates of executive function was examined by Finn et al. (2016). More specifically the study examined the associations between income, neural measures of working memory, behavioral measures of working memory, and math achievement (Finn et al., 2016). Higher income groups showed higher working memory capacity, math achievement, and greater activation of the frontal-parietal network as a result of working

memory load. Along with lower working memory capacity and math achievement, children from the low-income group did not have the increases in activation as working memory load increased but showed the greatest activation at the lowest load when the task should have been the easiest. Brain-behavior correlations between the prefrontal cortex and math achievement were significant in the children from high SES backgrounds but not in children from low SES backgrounds. This study suggests behavioral and neural SES differences in working memory ability and math achievement (Finn et al., 2016).

Differences associated with children raised in low SES backgrounds highlight the potential impact of chronic stress on child development (Blair & Raver, 2012). Another factor to consider in the complicated picture of how SES impacts executive function is timing. Early experience is thought to "get under the skin" through biological embedding by influencing the development of the HPA axis and its regulation (Danese & McEwen, 2012). Previous research suggests the association between SES and health exists at young ages and becomes more pronounced as individual's age (Case, Lubotsky, & Paxon, 2001). The increase in visible manifestations of SES differences throughout development could be a result of individuals continuously receiving "health shocks" throughout life. These cumulative shocks have negative impact on an individual's health (Currie & Stabile, 2001). This has been shown as differences in basal cortisol levels in children from different background becomes more distinct in older children as high versus low children show a difference at age six but the differences between low, middle, and high SES children arise at age ten (Lupien, King, Meaney, & McEwen, 2000).

Early childhood stress is shown to impact hippocampal development while the window of opportunity or risk for chronic stress impacting the PFC is larger. Yu et al.

(2017) found early childhood SES was negatively associated with hippocampus volume however this association was not present when SES was measured in adulthood (Yu et al., 2017). Along with early childhood, chronic stress that occurs in late childhood and adolescence has been shown to alter PFC development (Lupien et al., 2009). For example, Teicher (2006) showed sexual abuse occurring in younger children was associated with changes in the hippocampus while sexual abuse during adolescence was associated with frontal cortex differences (Teicher, 2006; Lupien et al., 2009). The impact of a child being raised in a low SES environment has long lasting implication on neural development in the PFC as well (Boyce, Sokolowski, & Robinson, 2012; McEwen, 2012). Exposure to poverty before age 9, was related to later chronic stress when the same children were 17 years old. More specifically, the proportion of the child's life spent in poverty was related to a physiological allostatic load when the children were 17 years old (Evans & Kim, 2012). Childhood income at age 9 was also related to later PFC activation during an emotion regulation task completed at age 24. However, adult income at age 24 was not related to the neural activation during the emotional task which highlights the long-term implications to early exposure to poverty (Kim et al., 2013).

Early exposure to stressful environments has long-term implications for emotion regulation and executive function (Evans & Kim, 2012; Kim et al., 2013). Younger children's brains have more plasticity than adolescence and adults. Early experience and development lay the foundation for these networks and the connections are continually strengthened and modified as the child develops. Therefore, it is more beneficial to create strong neural connections and networks earlier on rather than attempt to improve modify

these circuits later in life. There is much more research to be done on the PFC especially in relation to how stress and cortisol affects this crucial brain region at different stages of development.

Although most of this review discussed children from different SES backgrounds as homogeneous groups, there are various individual differences in how resilient a child is to their environment. The classic example of these individual differences is the highly resilient dandelion and the less resilient orchid. The orchid or the less resilient child needs a lot of care and a specific high-quality environment to thrive and develop to their full potential. On the other hand, the dandelion can survive and thrive in any environment (Luthar, 2006; Boyce & Ellis, 2008). This analogy applies to poverty and stressful environments in general with individual differences arising in how a child responds and adapts to high stress exposure (Boyce & Ellis, 2008; Shonkoff, 2010; Hughes, 2012). Specific individuals may be better adept at handling a specific environment, which can be due to many factors including genetics, parenting, temperament, sex, and cognitive abilities. Differences in the genetics of the major components of the stress response and executive function including GR, COMT, and a serotonin transporter (5HTTP) have been suggested to impact individual differences in adaptation and executive function abilities (Kuningas, et al., 2007; Blanchard et al., 2011; Canli, & Lesch, 2007). Along with individual differences in the child, different protective factors can influence the impact of a stressful environment on a child such as warm, responsive parenting (Luby et al., 2013). Neural evidence also supports the relation to the environmental factors that influence the impact of poverty on neural development (Luby et al., 2013). Luby et al., (2013) examined the structural differences associated with poverty. Children from lower SES

backgrounds showed decreased grey and white matter in regions associated with executive function and learning including the hippocampus and amygdala. However, these associations were moderated by environmental factors such as relationship with caregivers and stressful events (Luby et al., 2013). In essence, more specific individual differences in stress response in low-SES environments may predict the severity of cognitive impact and conversely resiliency.

Study Overview

Although research on the impact of a low SES environment on a child's stress regulation and executive function is growing there is still a long road ahead. The specific details of how adversity, stress hormones, genetics, and quality of parent-child interaction all dynamically converge to explain the influence of SES on executive function are still unclear. Numerous studies aimed to address different components and associations but much of this complex framework has yet to be shown empirically. One major question that remains is how exactly stress relates to PFC and executive function development within the theoretical framework of how SES impacts executive function. The current study aimed to merge the converging lines of research of chronic stress impacting the PFC and environmental causes of chronic stress such as poverty impact executive function to address these research questions.

The primary question of this thesis regarding how early life stress relates to PFC and executive function development was addressed by examining the associations between cortisol reactivity, structural PFC volumes, and behavioral measures of executive function. The bigger theoretical picture of how SES impacts executive function was also investigated by considering the associations between SES, cortisol reactivity,

PFC development, and executive function. The data used for the current study was collected as part of a larger research project examining potential early identifiers of later psychopathology particularly in children of women with depression (Dougherty, Tolep, Smith, & Rose, 2013; Kushner, Barrios, Smith, & Dougherty, 2016; Blankenship et al., In Prep). The longitudinal study included two waves of data collection. The first wave was collected when the children were an average of 4.2 (±0.82, range = 3.0-5.9) years old and the second wave was collected when the children were an average of 7.3 (±0.96, range = 5.5-10) years old. The first wave included two sessions of data collection with behavioral tasks completed on one day and the cortisol reactivity task another day scheduled close to the first session. The second wave of data collected about three years after the first assessment with a mean time of 2.96 years between the two waves. The second wave of data collection included two sessions with a day of behavioral executive function tasks and cortisol reactivity collection and a day of neural assessments.

A composite of income and average parental education was used as a measure of SES. To include the highest sample numbers for the SES analyses, the composite of the income and average parental education was used as the primary SES measure. A risk composite including family income, average parental education, and whether the child lived in a single parent household was also examined as a secondary measure of SES. The cortisol response was evoked by the child completing age appropriate stress inducing tasks at each wave of data collection. Cortisol was collected at five different time points with one prior to the task and four following task completion. Two measures of the Area Under the Curve (AUC) of the five different time points of cortisol levels was calculated and used as the outcome of the cortisol reactivity. Cortical thickness was used as

measure of structural volume within the PFC. Cortical thickness is thought to represent growth of dendrites, dendritic arborization, synaptic pruning, and atrophy (Giedd, 2004; Shaw et al., 2008; Jeon, Mishra, Ouyang, Chen, & Huang, 2015). Chronic stress is shown to alter dendritic arborization, growth of dendrites, and atrophy (Teicher et al., 2003; McEwen, 2007; Mackey, Raizada, & Bunge, 2012; McEwen, 2013) in the PFC. Therefore, cortical thickness was selected as the best way to capture structural variation within the PFC.

Research Aims

The broader aim of the study was to examine how SES impacts executive function by examining if cortisol reactivity mediates the association between SES and differences in executive function assessed at the behavioral and neural level. The more specific goal of the study was to better understand the relationship between cortisol reactivity and executive function using both behavioral executive function tasks and strucutral assessments of the PFC. Although the distribution of SES in the data set is somewhat limited, the associations were still explored using the range of SES available.

The overall predictions for the current study was chronic stress would be associated with decreased executive function at a neural and behavioral level. Based on the biological embedding of the early environment through the adaptation of HPA axis to the environment within the Biodevelopmental Framework (Shonkoff, 2010), we hypothesized the early differences in the cortisol reactivity would relate to the development of the PFC. In a high stress environment, it has been suggested that the body protects itself from the damaging high levels of glucocorticoids results by altering the cortisol response to stressor. Four-year-old children from low SES backgrounds have

been shown to have higher basal cortisol levels and have an altered cortisol reactivity response with less change in cortisol production which has been thought of as "blunted" (Blair et al., 2011; Blair et al., 2013). The high levels of glucocorticoids have been shown to cause dendritic shortening and remodeling of the PFC (McEwen, 2007; Teicher et al., 2003; Mackey, Raizada, & Bunge 2012). The PFC contains a high number of glucocorticoid receptors that interact with multiple neuromodulators that are altered when exposed to high levels of glucocorticoids (McEwen, 2007; McEwen; 2013). The protracted development of the PFC creates a larger window of opportunity or vulnerability to the environment including exposure to high levels of stress. Therefore, we hypothesized that early and concurrent stress would impact the development of the PFC. More specifically, we predicted cortisol reactivity would be related to executive function and cortical thickness of the regions of interest within the PFC.

As a natural analogue of chronic stress, SES was predicted to be positively related to executive function as previously shown (Mezzacappa, 2004; Noble et al., 2005; Farrah et al., 2006; Hackman & Farrah, 2010; Kim et al., 2013; Finn et al., 2016). Based on previous studies showing SES differences in the function and structure of the PFC (D'Angiulli, Herdman, Stapells, & Hertzman, 2008; Sheridan et al., 2012; Hanson et al., 2013), lower SES was predicted to be associated with smaller cortical thickness in the PFC. Given chronic stress is associated with low SES environments, SES differences in cortisol reactivity were also predicted. The effects of SES on executive function were predicted to be mediated by neural changes in the PFC as low SES environments impact the development of the PFC which in turn executive function that is predominantly supported by this region. However, the timing of these differences is unclear especially in

regards to cortisol reactivity. Lupien, King, Meaney, and McEwen (2000) present differences in basal cortisol levels in 6 year olds between high SES versus low/middle SES however the differences between low, middle, and high SES in basal cortisol levels become apparent at age 10. Therefore, it was hypothesized that the more specific differences in cortisol reactivity may arise in the older population and not the younger as the cumulative stress occurs.

Although the PFC was previously spoken of as whole, specific regions of the PFC are more associated with executive function than others including dlPFC, IFG, and mPFC (Cole & Schneider; Doesenbach et al., 2007). The OFC is normally more associated with the reward system and has been found to show opposite effects in response to stress than other regions of the PFC. Although studies are somewhat mixed due to specificity of animal and human correlated of the OFC, the OFC has been suggested to follows a similar pattern to the amygdala as higher chronic is associated with greater development of the OFC (McEwen, 2007). A *priori* regions of the PFC associated with executive function were selected for regions of interest in the current study.

Research Aim 1: How does cortisol reactivity (wave 1 or wave 2) relate to behavioral assessments of executive function (wave 1 or wave 2)?

Differences in cortisol reactivity (AUC) were predicted to be related to performance on executive function tasks. We hypothesized the impact of earlier AUC differences would become more apparent in later EF composite from the second wave due to the long-term implications of alterations in the stress response system.

Research Aim 2: How does cortisol reactivity (wave 1 or wave 2) relate to neural measures of executive function (wave 2)?

High chronic stress, especially early in development, can alter the response and regulation of stress systems including the HPA axis. The PFC has high levels of glucocorticoid receptors which are impacted by altered stress responses within the HPA axis. The high levels of glucocorticoids in the system are associated with neural changes in the brain including dendritic remodeling and shortening (Teicher et al., 2003; McEwen, 2007; Mackey, Raizada, & Bunge, 2012; McEwen, 2013). Therefore, the AUCs were predicted to be associated with cortical thickness of the selected PFC regions.

Research Aim 3: How does SES (wave 1) relate to behavioral measures of executive function (wave 1 or wave 2)?

SES differences in executive function have been previously established with lower SES being associated with lower executive function (Mezzacappa, 2004; Noble et al., 2005; Farrah et al., 2006; Hackman & Farrah, 2010; Kim et al., 2013; Finn et al., 2016). Therefore, we predicted lower SES would be related to lower executive function. Hackman et al. (2015) showed SES differences in EF arise in early childhood and persist throughout middle childhood (Hackman, Gallop, Evans, & Farah, 2015). Therefore, we predicted the association to be present at both waves of data collection, however, SES differences may become more apparent in the later measure executive function.

Research Aim 4: How does SES (wave 1) relate to neural measures of executive function (wave 2)?

Given the neural effects associated with high levels of stress, the impact of high stress is predicted to be visible in children from low SES backgrounds. Even by the age of three, children from low SES backgrounds have less grey matter development in the frontal cortex (Hanson et. al., 2013) and specifically the PFC (Noble et al., 2015). SES differences in the recruitment of the PFC have also been shown (D'Anguilli, Herdman, Stapells, & Hertzman, 2008**;** Sheridan et al., 2012; Finn et al., 2016). Therefore, lower SES was predicted to be related to smaller values of cortical thickness of the PFC regions supporting executive function.

Research Aim 5: Does SES (wave 1) relate to differences in cortisol reactivity (wave 1 or wave 2)?

As previously discussed, low SES environments are associated with high levels of chronic stress which can impact a child's stress response and regulation. Previous studies have shown SES relates to cortisol levels of the child as children from low SES backgrounds are suggested to have higher basal levels of cortisol and atypical cortisol reactivity (Lupien, Meaney, King, & McEwen, 2000; Blair, Granger, & Razza, 2005; Blair et al., 2011). Therefore, the SES of the child was predicted to be related to the cortisol reactivity of the child.

Research Aim 6: Do the structural difference in PFC (wave 2) mediate the association between cortisol reactivity (wave 1 or 2) and executive function (wave 2)?

As previously discussed, research suggests exposure to high chronic stress results in high levels of glucocorticoids in the system which are harmful long term. The PFC, a major component of the network that supports executive function, has a magnitude of

glucocorticoid receptors that can be altered as a result of high chronic stress. If differences in AUC arise as a result of chronic stress which relate to structural differences in the PFC, then the abilities that relay on these regions are predicted to be impacted as well. Therefore, we predicted that the structural differences in the PFC would partially mediate the associations between cortisol reactivity and executive function. The mediation was predicted to partial because of other environmental factors that can contribute to the association between cortisol reactivity and executive function including temperament, parenting, and genetics.

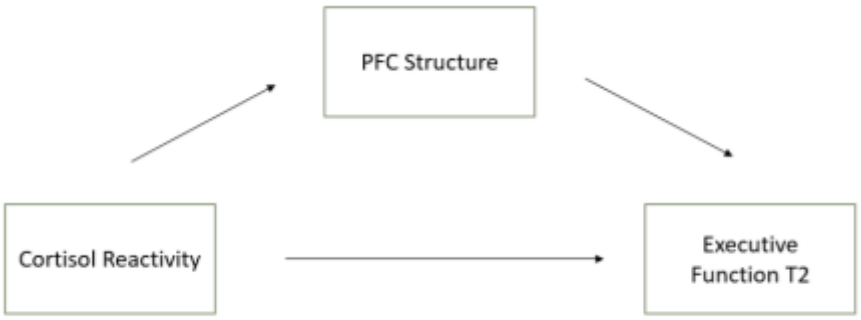


Figure 1. Mediation Model of Cortisol Reactivity, PFC structure, and Executive Function

Research Aim 7: Do the structural differences in PFC (wave 2) mediate the association between SES (wave 1) and executive function (wave 2)?

Children raised in lower SES environments have lower executive function in comparison to children from higher SES backgrounds (Noble et al., 2005; Farrah et al., 2006). SES differences have been found in the structure and function of the PFC with children from lower SES backgrounds having smaller volumes and less recruitment of the PFC (D'Angiulli, Herdman, Stapells, & Hertzman, 2008; Sheridan et al., 2012; Hanson et al., 2013; Kim et al., 2013; Finn et al., 2013). The abilities that rely on PFC are likely to be impacted by the neural changes of the region. Therefore, we predicted the PFC cortical thickness would partially mediate the association between SES and executive function. The mediation was predicted to be partial because there are other factors that influence the association between SES and executive function including language abilities, maternal warmth, and other brain regions.

Figure 2. Mediation Model of SES, PFC structure, and Executive Function

Research Aim 8: Does cortisol reactivity (wave 1 or wave 2) mediate the association between SES (wave 1) and PFC cortical thickness (wave 2)?

As previously discussed, low SES environments are associated with high levels of chronic stress which can impact a child's stress response and regulation. The body, especially the HPA axis, can adapt to the high exposure of stress by altering the stress response and/or regulation as atypical cortisol reactivity is associated with low SES. Differences in cortisol reactivity have been shown in children from different SES background. Children from low SES backgrounds have been suggested to have higher basal levels of cortisol and atypical cortisol reactivity (Lupien, Meaney, King, & McEwen, 2000; Blair, Granger, & Razza, 2005; Blair et al., 2011). The altered cortisol levels and reactivity can impact the neural development in the PFC as structural differences in the PFC are associated with high levels of chronic stress (Teicher et al., 2003; McEwen, 2007, McEwen 2013) and low SES environments (Hanson et al., 2013; Noble et al., 2015). Therefore, we predicted the impact of low SES environments on the development of the PFC would be partially mediated by cortisol reactivity. The mediation was predicted to be partial because there are other factors that may influence the association between SES and the structure of the PFC including genetics, exposure to toxins, and nutrition.

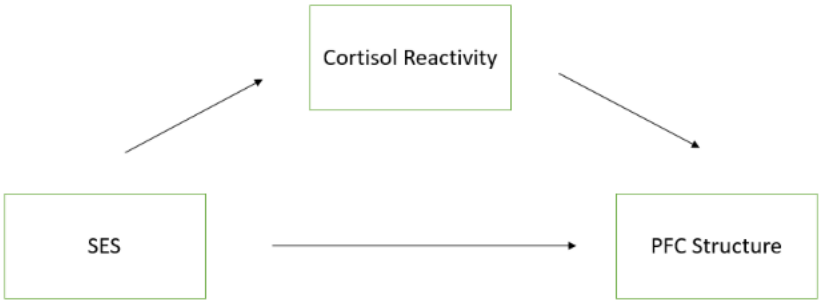


Figure 3. Mediation Model of SES, Cortisol Reactivity, and PFC Structure

Research Aim 9: Does cortisol reactivity (wave 1 or wave 2) mediate the association between SES (wave 1) and executive function (wave 2)?

Although the relationship between structure and function is not always clear cut, the effect of the high stress of the lower SES environments on executive function was predicted to be partially mediated by cortisol reactivity. This mediation was suggested within the Biodevelopmental Model framework. Low SES environments are associated with high levels of chronic stress and the body may adjust to handle chronic stress by adapting the stress response system. However, chronic stress has damaging impact on the development of the PFC which is highly involved in executive function. As cortisol reactivity mediates the association between SES and structural differences in the PFC, then the abilities that rely on these regions should be impacted as well. Therefore, we predicted the association between SES and executive function would be partially mediated by cortisol reactivity.

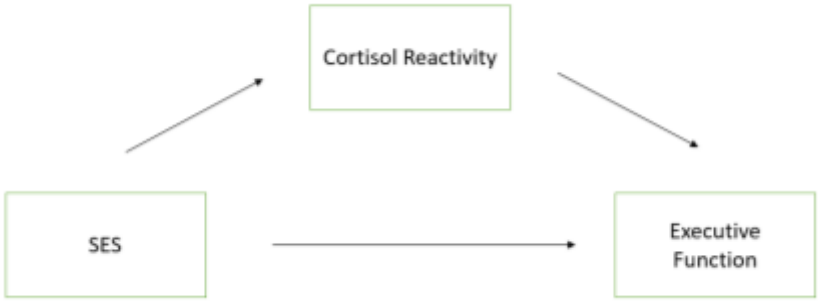


Figure 4. Mediation Model of SES, Cortisol Reactivity, and Executive Function

Chapter 3: Methods

Participants

The sample was recruited from the Washington D.C. greater metropolitan area through flyers (73.1%) and a commercial mailing list (26.9%). The data was collected as part of a larger study aiming to identify early risk for psychopathology, specifically of young children with a parent with a lifetime history of depression (Dougherty, Tolep, Smith, & Rose, 2013; Kushner, Barrios, Smith, & Dougherty, 2015). The study protocol was approved by the University of Maryland's Institutional Review Board (IRB) including informed consent at both waves of data collection. The eligible children recruited were between three to five years old, had an English-speaking biological parent with at least 50% custody, no parent reported history of significant medical conditions or developmental disorders, and had biological parents without a history of bipolar or psychotic disorders. Children were excluded if the ability to comprehend English was not sufficient to complete the behavioral tasks in the laboratory. Given the aims of the larger study, the initial recruitment specifically targeted parents with a lifetime history of depression. Therefore, the presence of the mother's lifetime depressive disorder (major

depressive disorder and/or dysthymic disorder) as assessed with the Structured Clinical Interview for DSM-IV-TR Disorders, (SCID) (First, Spitzer, Gibbon, & Williams, 1996), was examined as a potential covariate for all analyses.

The sample size of the first wave of data collection began with 175 preschool age children; 156 of the 175 children completed the cortisol reactivity assessment in the laboratory during wave 1. Of the 156 children who completed wave 1, 117 children returned (67%) for wave 2. Of the 117, 104 children completed the cortisol reactivity assessment at wave 2. Cortisol reactivity data was excluded if the child was sick with a fever, had taken antibiotic medication, or if the values of cortisol provided were greater than 3 standard deviations above the mean. Cortisol reactivity was excluded for five children at wave 1 and one child at wave 2. Local families that completed the behavioral and cortisol components of wave 2 were invited to return for the MRI portion of the study. Of the 104 families invited back for the MRI visit, 64 chose to participate and 61 of the children completed the assessments. One child did not scan due to claustrophobia and different scanning parameters were used for two children. The sample size for each analysis will differ as not all children provided usable data for the different measures and are presented in Table 1.

Table 1: Sample sizes for behavioral and neural analyses

		1	2	3	4	5
1.	SES	107	-	-	-	-
2.	Cortisol Reactivity W1	98	151	-	-	-
3.	EF Composite W1	106	149	172	-	-
4.	Cortisol Reactivity W2	94	94	94	103	-
5.	EF Composite W2	95	94	101	101	103

Sample sizes (n) for structural analyses

		1	2	3	4	5
1.	SES	60	-	-	-	-
2.	Cortisol Reactivity W1	51	58	-	-	-
3.	EF Composite W1	56	56	62	-	-
4.	Cortisol Reactivity W2	55	56	60	58	-
5.	EF Composite W2	56	56	60	60	62

W1: Wave 1 W2: Wave 2

Demographics

The demographics for the 175 children who participated in the first wave of data collected are reported in Table 2. Eighty-six (49.1%) of the 175 children had a mother with a lifetime depressive disorder. The average age of the 175 children at the first wave of data collection was 4.14 (±0.81, range = 3.0-5.9) years and the average age of 104 children that participated in the second wave of data collection 7.28 (±0.96, range = 5.5-10.0) years at the second wave. The overall sample included 89 (51.1%) females and 85 (48.9%) males. The sample was racially diverse: 44.6% White, 34.9% African American, 1.7% Asian, 5.7% Multi-Racial, 9.1% other, and 3.4% did not report. The total family

income of the sample varied with 13 (7.4%) less than $20,000; 17 (9.4%) ranged from $20,001 to $40,000; 34 (19.4%) ranged from $40,001 to $70,000; 45 (25.7%), ranged from $70,000 to $100,000; 58 (33.1%) was greater than $100,000; and 8 families did not report. The maternal education of the sample was varied: 4 (2.3%) some high school, 11 (6.3%) high school graduate or GED, 55 (31.4%) some college or two-year degree, 55 (31.4%) four -year college degree, 36 (20.6) master's degree, and 11 (6.3%) doctoral degree, and 3 families did not report. The paternal education of the sample was varied: 1 (0.6%) 8th grade or less; 3 (1.7%) some high school, 24 (13.7%) high school graduate or GED, 44 (25.1%) some college or two-year degree, 44 (25.1%) four -year college degree, 29 (16.6) master's degree, and 18 (10.3%) doctoral degree, and 12 families did not report.

Table 2: Demographic characteristics of behavioral sample (n=175)

Demographic variable	
Child age (in years) at W1 Executive Function, [Mean (SD)]	4.14 (0.81)
Child age (in years) at W1 Cortisol Assessment, [Mean (SD)]	4.15 (0.81)
Child age (in years) at W2, [Mean (SD)]	7.28 (0.95)
Child sex, (*n=174*) [*n* (%)]	
Male	85 (48.6%)
Child race (*n=168*) [*n* (%)]	
White, European-American	78 (44.6%)
African-American	61 (34.9)
Asian	3 (1.7%)
Multi-Racial/Other	26 (14.8%)
Child ethnicity (*n*=168) [*n* (%)]	
Hispanic/Latino descent	31 (17.7%)
Single parent household [*n* (%)]	
Lives with only one parental figure	27 (15.4%)
Family income (*n=167*) [*n* (%)]	
<$20,000	13 (7.4%)
$20,001 to $40,000	17 (9.7%)
$40,001 to $70,000	34 (19.4%)
$70,001 to $100,000	45 (25.6%)
>$100,000	58 (33.1%)
Maternal education (n=172) [*n* (%)]	
Some high school	4 (2.3%)
High school graduate (or GED)	11 (6.3%)
Some college (or two-year degree)	55 (31.4%)
Four-year college degree	55 (31.4%)
Master's degree	36 (20.6%)
Doctoral degree	11 (6.3%)
Paternal education (n=163) [*n* (%)]	
Eighth grade or less	1 (0.6%)
Some high school	3 (1.7%)
High school graduate (or GED)	24 (13.7%)
Some college (or two-year degree)	44 (25.1%)
Four-year college degree	44 (25.1%)
Master's degree	29 (16.6%)
Doctoral degree	18 (10.3%)
Maternal lifetime history of depressive disorders	86 (49.1%)

Note. *n*=175 unless otherwise noted; W1: Wave 1; W2: Wave 2

Sixty-three children completed the structural scan as one child did not complete the scan due to claustrophobia. Thirty-eight (60.3%) of the 63 children had a mother with a lifetime depressive disorder. The average age at first wave of data collection was 4.2 (±0.84, range = 3.0-5.9) years and 7.2 (±0.89, range = 5.5-10) years at the second wave. The sample consisted of 31 (49.1%) females and 32 (50.8%) males. The sample was racially diverse: 47.6% White, 34.9% African American, 6.3% Multi-Racial, and 7.9% other. Total family income of the sample varied with 3 (4.8%) less than $20,000, 4 (6.3%) ranged from $20,001 to $40,000, 17 (27.0%) ranged from $40,001 to $70,000, 17 (27.0%) ranged from $70,000 to $100,000, 20 (31.7%) above $100,000, and 2 families did not report income. Maternal education of the sample varied: 2 (3.2%) some high school, 2 (3.2%) high school graduate or GED, 21 (33.3%) some college or two-year degree, 17 (27.0%) four-year college, 17 (27.0%) degree master's degree, and 4 (6.3%) doctoral degree. Paternal education of the sample varied: 3 (4.8%) some high school, 6 (9.5%) high school graduate or GED, 12 (19.0%) some college or two-year degree, 18 (28.6%) four-year college, 14 (22.2%) degree master's degree, and 6 (9.5%) doctoral degree.

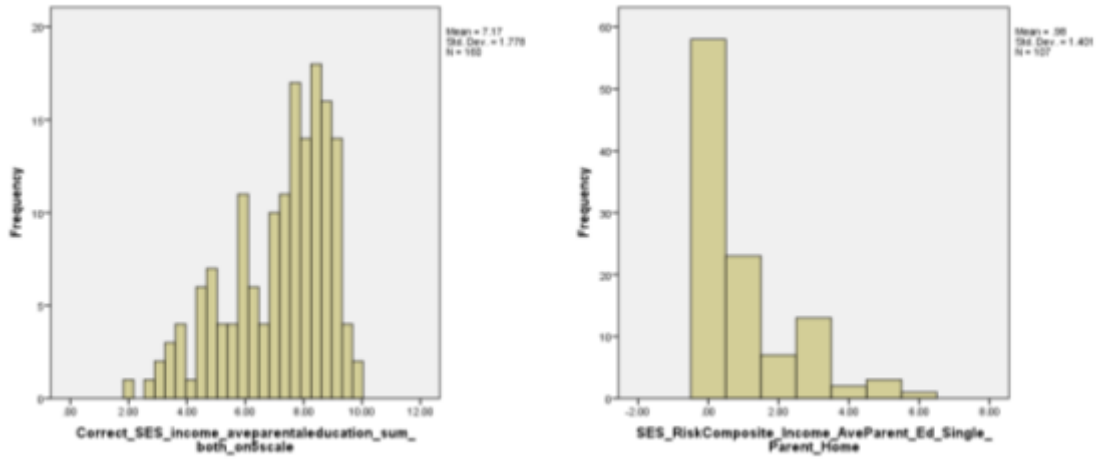
First Wave of Data Collection

Socioeconomic Status

Given the complexity of SES, two composites were calculated as a proxy for SES. To include the highest number of participants, the composite of average parental education and income will be used as the main proxy for SES. The family income was collected on a scale of 1-5. Average parental education was calculated by taking the average of maternal and parental education on a scale from 0-7. To ensure equal weights

of income and average parental education within the composite, the average education was then transformed from a 0-7 scale to a 1-5 scale. The SES composite was calculated by summing the level of income on a scale of 1-5 and the average parental education on a scale of 1-5. Therefore, the SES composite is on a scale of 1-10 with higher numbers representing higher SES. A SES risk composite composed of income, average parental education, and living in single family household was also calculated. A risk value was assigned to the lower levels of income with a 3 for less than $20,000; 2 for $20,000-$40,000; and 1 for $40,000-$70,000. A higher risk value was assigned to the lower levels of average education including a 3 for both parents completing some high school, 2 for both parents graduating high school, 1 for both parents completing some college on average; and 0 for both parents graduating college or any education above. A risk value of 1 was assigned to a single parent home and 0 was assigned for a non-single parent home. The distributions for the SES composites are shown below in Figure 5.

a



b

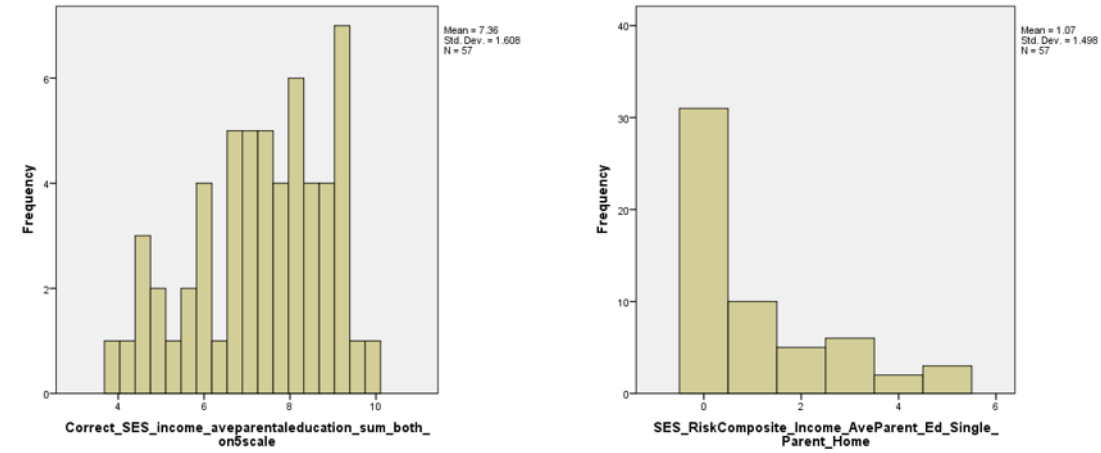


Figure 5: Distribution of SES variables
(a) Distribution of the behavioral sample for SES composed of the sum of family income and average parental education and the SES Risk Composite (b) Distribution of the neural sample for SES composed of the sum of family income and average parental education and the SES Risk Composite

Executive Function

At wave 1, executive function was assessed by the child completing two tasks including a day/night task and a snack delay task. Although the components of executive function are highly overlapping and tasks normally tap into more than one component, the two tasks used at wave 1 are used to assess different aspects of inhibition. The day/night task assess response inhibition whereas the snack delay task assesses emotion regulation (Diamond, 2013). The day/night task required the child to point to the picture of the moon when the experimenter says "day" and to point to the picture of the sun when the experimenter says "night". The child's performance was recorded for correct and incorrect responses. The child's performance was recorded and scored for total number of trials correct. The number of correct trials was divided by the total number of trials to produce the proportion of trials correct out of the number of trials the child completed. The higher score of proportion of correct trials suggests higher inhibitory control. Children were excluded if they did not complete more than one of the 16 trials which resulted in 55 children being excluded.

In the snack delay task, the experimenter put a cracker under a cup and instructs the child not to eat the cracker until the experimenter rang the bell. The pause between the experimenter placing the cracker under the cup and ringing the bell varied including 5 seconds, 10 seconds, 20 seconds, 30 seconds and no pause. The behavior of the child was coded to indicate if the child waited until the experimenter rang the bell for each trial. The total amount of times the child failed to wait for the bell was summed and reverse scored. Higher values of the reverse score of the failure to wait indicate higher inhibitory control. Three children did not complete the snack delay task and were excluded. An

average executive function score for wave 1 was calculated for each child by the average Z score of the proportion of correct trials score on the day/night task and Z score of reverse scored total failure to wait in the snack delay task. The higher composite executive function score indicated higher executive function.

Cortisol Reactivity

The child's cortisol levels were assessed using a developmentally appropriate acute stressor paradigm (Kryski et al., 2011; Dougherty, Tolep, Smith, & Rose, 2013; Kushner, Barrios, Smith, & Dougherty, 2016; Blankenship et al., in prep). The child was presented with a board full of bears and frogs and told they were playing a matching game. For the matching game, the child was told different colored balls go with different animals as the bear has a blue ball and the frog has a red ball. Then the child was instructed to match all of the correct colored balls with the animals within a short time period and the "yacker tracker" would indicated the amount of time the child has left. The yacker tracker looked like a stop light with red, yellow, and green lights. The color of the light corresponded to the amount of time the child has remaining. The child was told when the light is green there is a great deal of time, the yellow light indicates there is a short amount of time, and the red light signifies there is no time left to complete the matching game. Also, the child was told that younger children have been able to finish this game easily. The yacker tracker is controlled by the experimenter and always runs out of time before the child finishes the game. When the time is running low, the experimenter also prompts the child to rush by stating "Uh oh, you're running out of time." The laboratory stressor paradigm includes components shown to evoke a cortisol response such as uncontrollability and social evaluation (for review Gunner, Talge, &

Herrera, 2009). After the three trials are completed the child is debriefed and the experimenter explains there was a problem with the timer and the child should have had more time to complete the task. Then the experimenter and the child went through the matching game without a timer and the experimenter praised the child's performance.

Children's cortisol reactivity was assessed through the analysis of cortisol levels in the child's saliva (further described in Dougherty, Tolep, Smith, & Rose, 2013; Kushner, Barrios, Smith, & Dougherty, 2016; Blankenship et al., in prep). The child's saliva was collected using a cotton roll and placing a tiny amount (approximately 0.025 mg) of Kool-Aid® on the cotton roll. Then the child chewed on the roll until all of the cool-aid was dissolved or for the duration of one minute. The cotton roll was then put into a syringe and the saliva was extracted into a plastic tube. Although the use of Kool-Aid is shown to influence salivary concentrations with a small effect, this method increases cooperation of young participants and is suggested to be beneficial for research with children (Talge, Donzella, Kryzer, Gierens, & Gunnar, 2005). Five samples of cortisol were collected from each child. The first sample was a baseline which was collected after a 30-minute play session with the child and prior to the stressor task. Four other samples were collected following the stress-inducing task at 20, 30, 40, 50 minutes. To address prior research stating consumption of food and caffeine influence cortisol levels (Gunnar & Talge, 2007), parents were instructed not to give food to the child an hour prior the laboratory visit nor any caffeine to the child two hours prior to the visit. Data was excluded if the child was sick with a fever, had taken antibiotic medication, or if the values of cortisol provided were greater than 3 standard deviations above the mean. Cortisol reactivity was excluded for 5 children at wave 1.

After collection, cortisol vials were frozen at -20º Celsius until assayed using a time-resolved fluorescence immunoassay with fluorometric end-point detection (DELFIA). Salivary cortisol samples were assayed at the Biochemical Laboratory at the University of Trier, Germany. Two measures of the area under the curve (AUC) were calculated based on the trapezoid formula (Pruessner, Kirschbaum, Meinlschmid, & Hellhammer, 2003). The area under the curve with respect to increase (AUCi), a measure of total cortisol change over the 5 samples, and the area under the curve with respect to ground (AUCg) which is a measure of the magnitude of total cortisol secretion were calculated.

Second Wave of Data Collection

Executive Function

At wave 2, children completed three tasks assessing different component of executive function including working memory, inhibition, and attention shifting. The task to assess working memory, color span, presented a series of 8 colored triangles to the child one at a time. For the forward condition, the child was instructed to repeat the colors in the order that was presented. For the backwards conditions, the child was instructed to repeat the colors in the reverse order that was presented. There were two backward and two forward trials all with 8 colors. The number of correct colors was recorded for each trial. The color span forward was the sum of the two forward trials which had a max score of 16. The color span forward was the sum of the two backward trials which had a max score of 16. The total color span was the sum of the color span forward and color span backwards measures. Higher scores on the forward and backward color span represent higher working memory.

To assess inhibitory control the child played a “Simon Says” game. The child was instructed to perform the exercises when the experimenter says “Simon says” before stating the exercise and not to perform the exercise if the experimenter does not say “Simon says” before stating the exercise. There was a practice trial and then 16 trials of different exercises with 8 “Simon says” trials and 8 trials without the Simon says command. The trials without Simon says was scored on a 0-3 scale with 0 representing full commanded movement and 3 indicated no movement. The scores of all the trials were summed to indicate a total Simon Says score higher values indicate higher inhibition.

Attention shifting was assessed with Trails, a task similar to connect the dots. In part A, the experimenter showed the child a piece of paper with dots filled with numbers and instructed to connect the dots in numerical order. In part B, the experimenter showed the child a second piece of paper of dots filled with numbers and letters. The experimenter explained to the child that they must connect the dots in numerical and alphabetical order switching between numbers and letters. The total number of errors during Part B was summed to compute a total score which was reversed. Higher reverse-scored total number of errors represent higher attention shifting. An average executive function composite was calculated by computing an average of the Z scores of the Total Color Span, Simon Says, and the reverse-scored Trails errors. The higher composite executive function score indicated higher executive function.

Cortisol Reactivity

Cortisol reactivity of the children was measured using an acute stressor paradigm with the same cortisol collection methods used in wave 1. The task aimed to evoke a

cortisol response at the second wave was an adapted version of the Trier Social Stress Task for Children (TSST-C) and an impossible-solvable puzzle for the child to complete. TSST-C has previously been shown to evoke a cortisol response in children (Gunner, Talge, & Herrera, 2009; Kushner, Barrios, Smith, & Dougherty, 2016). The experimenter first presented the child with four different prizes and the child picked their favorite and least favorite prizes. The child was told they will be judged on their performance of the games and might receive their favorite prize. The child was first told to tell a story to the judge using a picture book for 4.5 minutes. Then the child was told to complete a puzzle within 3 minutes; however, the puzzle is impossible to complete because it was missing multiple pieces. Then the child was left alone for 5 minutes and told the judge was going to decide which prize the child will receive. After the waiting period, the experimenter returned and stated the child would receive their favorite prize. Then the child was debriefed about the impossible puzzle stating pieces of the puzzle were accidently not included. The task had similar components to the stressor task completed in the first wave including social evaluation and inability to complete the task which have previously been shown to evoke a cortisol response in children and adults (Gunner, Talge, & Herrera, 2009).

Children's cortisol reactivity was assessed through the analysis of cortisol levels in the child's saliva (further described in Dougherty, Tolep, Smith, & Rose, 2013; Kushner, Barrios, Smith, & Dougherty, 2016; Blankenship et al., in prep). The child's saliva was collected using a cotton roll. The method of collection was adapted to be child friendly and has been shown not to by first placing a tiny amount (approximately 0.025 mg) of Kool-Aid® on the cotton roll. The child then chewed on the roll until all of the

Kool-Aid was dissolved or for the duration of one minute. The cotton roll was then put into a syringe and the saliva was extracted into a plastic tube. Five samples were collected from each child. The first sample was a baseline which was collected after a 30-minute play session with the child and prior to the stressor task. Four other samples were collected following the stress-inducing task at 20, 30, 40, 50 minutes. To address prior research stating consumption of food and caffeine influence cortisol levels (Gunnar & Talge, 2007), parents were instructed to not give food to the child an hour prior the laboratory visit nor any caffeine to the child two hours prior to the visit. Data was excluded if the child was sick with a fever, had taken antibiotic medication, or if the values of cortisol provided were greater than 3 standard deviations above the mean. Cortisol reactivity of one child at wave 2 was excluded. After collection, cortisol vials were frozen at -20º Celsius until assayed using a time-resolved fluorescence immunoassay with fluorometric end-point detection (DELFIA). Salivary cortisol samples were assayed at the Biochemical Laboratory at the University of Trier, Germany. Two measures of the area under the curve (AUC) were calculated based on the trapezoid formula (Pruessner, Kirschbaum, Meinlschmid, & Hellhammer, 2003). The area under the curve with respect to increase (AUCi), a measure of total cortisol change over the 5 samples, and the area under the curve with respect to ground (AUCg) which measures of the magnitude of total cortisol secretion were calculated.

Neural Assessments

Structural scans were collected on a 3T Siemen's scanner with a 12-channel coil. For the structural scan, the child watched a video of their choice as a way to foster engagement and limit motion during the scan. The data was collected using a high

resolution T1 magnetization-prepared rapid gradient-echo (MPRAGE) sequence. There was 176 adjacent sagittal slices collection with 1.0 x 1.0 x 1.0 voxel size, TR of 1900ms, TE of 2.52ms, Inversion time of 900ms, flip angle 9^{o}, and pixel matrix = 256 x 256.

The structural scans were analyzed using Freesurfer (Version 5.1.0; surfer.nmr.mgh.harvard.edu). The automated segmentation package was used for preprocessing. The images checked for overall correct segmentation and manual edits (*n*=7) were made if large errors were present. First, an overall brain analysis was conducted to examine the relative effects of SES and cortisol reactivity at the whole brain level using total grey matter. Second, cortical thick analyses were conducted for the regions of interest (ROI) within the PFC.

The Freesurfer ROIs were selected from the Desikan atlas were the regions that best correspond to the *a priori* regions associated with executive function particularly proposed by Doesenbach et al. (2007). A cross analysis study of executive function determined 10 frontal ROIs including bilateral frontal cortex, dorsolateral (dlPFC), bilateral anterior insula/frontal operculum (aI/fO), medial superior frontal cortex (dACC), anterior Prefrontal cortex (aPFC), and ventromedial prefrontal cortex (vmPFC) (Doesenbach et al., 2007). The Freesurfer regions selected that best corresponded with *a prior* regions included bilateral superior frontal gyrus, rostral and caudal divisions of the middle frontal gyrus, pars opercularis, pars triangularis, and pars orbitalis divisions of the inferior frontal gyrus, frontal pole, precentral gyrus, and insula. Cortical thickness of the PFC regions was used in subsequent analyses. Cortical thickness is thought to represent dendritic growth, dendritic arborization, and synaptic pruning/atrophy (Giedd, 2004; Shaw et al., 2008; Jeon, Mishra, Ouyang, Chen, & Huang, 2015). The altered levels of

cortisol during development, as a result of chronic stress, are shown to reduce dendritic arborization and decrease growth of dendrites (Teicher et al., 2003; McEwen, 2007; Mackey, Raizada, & Bunge, 2012; McEwen, 2013). Therefore, the measure of cortical thickness was used to capture the cortical variation in the in the PFC.

Chapter 4: Results

Data Analysis

The overall goal of the data analysis was to better understand the association between cortisol reactivity and executive function using both behavioral and neural measures of regions in the PFC. Mediation models were also conducted to determine if cortical thickness differences in the PFC mediate the association between cortisol reactivity and EF. The secondary, more theoretical, goal of the study was to examine if the impact of cortisol reactivity on the PFC was the mechanism underlying the association between SES and executive function. The relations between SES, cortisol reactivity, neural development, and executive function were independently examined. Then multiple mediations were conducted to examine if the PFC cortical thickness mediates the association between SES and executive function. To address the mechanism of stress reactivity as a way of the SES environment impacting brain development, the mediations examining if cortisol reactivity mediates the association between SES and PFC cortical thickness were also conducted. Although the distribution of SES in the data set is somewhat limited, the relations were explored using the range of SES variables available. The decriptive statistics for all of the independent and dependent variables are shown in Table 3.

Table 3: Descriptive statistics for primary study variables. (N = 175)

	n	Mean[a]	*SD*[a]	Min[a]	Max[a]
Independent Variables					
W1 SES	160	7.17	1.78	2.00	10.00
W1 SES Risk Composite	107	0.98	1.40	0.00	6.00
W1 Executive Function Composite	120	-0.28	0.63	-1.58	1.21
Day/Night Proportion Score	120	1.24	0.49	0.25	2.00
Snack Delay Failure to Wait	172	0.35	0.2	0.00	5.00
T2 Executive Function	103	-0.03	0.63	-1.58	1.21
Color Span Total Score	102	8.76	2.51	2.00	14.00
Trails Time to Complete B (<180)	103	149.55	39.92	50.78	180.00
Simon Says Total Score	103	14.71	0.85	12.00	15.00
W1 AUC_g (log_{10})[b]	151	1.05	0.23	0.56	1.98
W1 AUC_i (log_{10})	151	1.89	0.09	1.05	2.07
W2 AUC_g (log_{10})	103	1.06	0.27	0.42	2.36
W2 AUC_i (log_{10})	103	1.30	0.12	0.59	1.66
Dependent Measures[c]					
Total Grey Matter Volume	63	757236.38	59983.28	607181.85	895304.80
Right Superior Frontal	63	3.27	0.19	2.72	3.66
Right Rostral Middle Frontal	63	2.82	0.23	2.08	3.32
Right Rostral Anterior Cingulate	63	3.48	0.21	3.06	3.87
Right Precentral	63	2.84	0.15	2.53	3.28
Right Pars Triangularis	63	3.05	0.20	2.52	3.45
Right Pars Orbitalis	63	3.34	0.30	2.49	3.90
Right Pars Opercularis	63	3.13	0.19	2.63	3.50
Right Insula	63	3.60	0.18	3.21	3.97
Right Frontal Pole	63	3.32	0.42	2.02	4.43
Right Caudal Middle Frontal	63	3.03	0.26	1.97	3.64
Right Caudal Anterior Cingulate	63	3.06	0.24	2.62	3.80
Left Superior Frontal	63	3.39	0.18	2.78	3.81
Left Rostral Middle Frontal	63	2.95	0.18	2.42	3.14
Left Rostral Anterior Cingulate	63	3.62	0.26	3.04	4.24
Left Precentral	63	2.89	0.16	2.45	3.20
Left Pars Triangularis	63	3.03	0.18	2.63	3.45
Left Pars Orbitalis	63	3.40	0.31	2.54	4.17
Left Pars Opercularis	63	3.14	0.17	2.63	3.48
Left Insula	63	3.60	0.16	3.29	3.94
Left Frontal Pole	63	3.50	0.44	2.32	4.41
Left Caudal Middle Frontal	63	3.04	0.21	2.47	3.46
Left Caudal Anterior Cingulate	63	3.25	0.29	2.41	4.06

[a]Means, standard deviations, and ranges are reported for the subsample included in the present analyses [b] Cortisol measured in nmol/L [c]Volumes measured in mm^3

Maternal depressive disorders, age, and sex are all shown to impact cortisol levels and reactivity (Seeman, Singer, Wilkinson, & McEwen, 2001). Therefore, to determine the appropriate covariates for subsequent analyses, bivariate correlations for all of the variables with age, gender, and maternal depression were conducted (Table 4). To further examine the effects of the covariates, ANOVAs were conducted with maternal depressive disorders, age, and sex with each of the variables in the study (Table 5). If the association was significant, then the factor was included as a covariate for the subsequent analyses with that variable. The bivariate correlations for all of the variables were also conducted. Results are reported in Supplementary Table 1. The associations between each of the variables (SES, cortisol reactivity, PFC volumes, and EF scores) were examined within the same wave of data collection and between waves. Once the necessary covariates and main associations were established, the mediation models of interest were conducted.

Table 4: Correlations between variables and potential covariates

Variable	Maternal Depression	Gender	Age
W1 Executive function	-.02	.05	**.24***
W2 Executive function	-.29	.06	**.43****
R superior frontal	-.15	**.33****	.11
R rostral middle frontal	-.06	.23	<.01
R rostral anterior cingulate	-.05	.19	.01
R precentral	-.22	**.33****	**.39****
R pars triangularis	.11	.23	-.03
R pars orbitalis	-.05	.21	.10
R pars opercularis	.02	-.03	**-.24***
R insula	-.07	.03	.03
R frontal pole	-.01	.22	-.15
R caudal middle frontal	-.16	**.27***	**.28***
R caudal anterior cingulate	-.09	.08	-.08
L superior frontal	-.18	.23	-.02
L rostral middle frontal	-.16	.06	.03
L rostral anterior cingulate	-.09	.08	-.08
L precentral	-.18	.23	-.02
L pars triangularis	-.16	.06	.03
L pars orbitalis	**-.28***	**-.29***	.05
L pars opercularis	-.20	**.26***	**.26***
L insula	-.19	.23	.20
L frontal pole	-.16	.19	-.22
L caudal middle frontal	-.17	.29	-.04
Left caudal anterior cingulate	-.08	.05	.14
W1 AUC_g (log_{10})	.05	-.04	.01
W1 AUC_i (log_{10})	-.19	.15	.20
W2 AUC_g (log_{10})	-.18	.19	-.03
W2 AUC_i (log_{10})	.01	.01	-.10
SES	.06	-.09	-.06
SES Risk Composite	-.12	**-.23***	.03

*Significant <.05 **Significant <.01 W1:Wave 1 W2: Wave 2 R:Right L:Left

Table 5: Effects of potential covariates on all variables

Dependent Variable	Predictor (IV)	IV β	IV b(SE)	IV *t*	IV *p*
EF W1	Gender	.054	.095(.134)	.706	.481
EF W1	Age	.236	.021(.007)	3.173	**<.01**
EF W1	MD	-.021	-.038(.138)	-.274	.784
EF W2	Gender	.062	.007(.124)	.623	.535
EF W2	Age	.433	.027(.006)	4.826	**<.01**
EF W2	MD	-.192	-.242(.123)	-1.968	***.052***
W1AUCi	Gender	-.086	-.015(.014)	-1.046	.297
W1AUCi	Age	-.061	-.001(.001)	-.748	.455
W1AUCi	MD	.058	.010(.014)	.701	.484
W1AUCg	Gender	.005	.002(.038)	.065	.948
W1AUCg	Age	-.095	-.002(.002)	-1.164	.246
W1AUCg	MD	.009	.004(.038)	.115	.908
W2AUCi	Gender	-.135	-.033(.024)	-1.367	.175
W2AUCi	Age	.079	.001(.001)	.793	.430
W2AUCi	MD	-.157	-.038(.024)	-1.601	.112
W2AUCg	Gender	-.231	-.123(.051)	-2.391	**.019**
W2AUCg	Age	.031	.001(.003)	.311	.757
W2AUCg	MD	-.123	-.066(.053)	-1.246	.216
TGM	Gender	-.218	-25916.97(14874.01)	-1.742	.086
TGM	Age	.096	571.12(756.48)	.755	.453
TGM	MD	-.021	-2584.11(15569.39)	-.166	.869
Right Hemisphere					
Superior Frontal	Gender	.329	.122(.045)	2.723	**<.01**
Superior Frontal	Age	.109	.002(.002)	.857	.395
Superior Frontal	MD	-.150	-.057(.048)	-1.185	.241
Rostral Middle Frontal	Gender	.227	.105(.058)	1.822	***.073***
Rostral Middle Frontal	Age	.004	.008(.002)	.029	.977
Rostral Middle Frontal	MD	-.064	-.030(.060)	-.505	.616
Rostral Anterior Cingulate	Gender	.186	.079(.054)	1.482	.144
Rostral Anterior Cingulate	Age	.006	.000(.003)	.044	.965
Rostral Anterior Cingulate	MD	-.048	-.021(.056)	-.372	.711
Precentral	Gender	.326	.096(.036)	2.697	**<.01**
Precentral	Age	.394	.006(.002)	3.345	**<.01**
Precentral	MD	-.215	-.065(.038)	-1.723	***.090***

Pars Triangularis	Gender	.230	.090(.049)	1.848	***.069***
Pars Triangularis	Age	-.027	-.001(.002)	-.209	.836
Pars Triangularis	MD	.109	.044(.051)	.858	.394
Pars Orbitalis	Gender	.213	.126(.074)	1.705	***.093***
Pars Orbitalis	Age	.101	.003(.004)	.795	.430
Pars Orbitalis	MD	-.053	-.032(.077)	-.414	.681
Pars Opercularis	Gender	.301	.111(.045)	2.462	**.017**
Pars Opercularis	Age	.136	.003(.002)	1.073	.287
Pars Opercularis	MD	-.131	-.050(.048)	-1.036	.304
Insula	Gender	.026	.009(.045)	.201	.841
Insula	Age	.026	.000(.002)	.205	.838
Insula	MD	-.067	-.024(.046)	-.521	.604
Frontal Pole	Gender	.221	.182(.103)	1.766	***.082***
Frontal Pole	Age	-.153	-.006(.005)	-1.213	.230
Frontal Pole	MD	-.008	-.007(.108)	-.062	.951
Caudal Middle Frontal	Gender	.266	.137(.064)	2.155	**.035**
Caudal Middle Frontal	Age	.278	.007(.003)	2.256	**.028**
Caudal Middle Frontal	MD	-.238	-.125(.065)	-1.917	***.060***
Caudal Anterior Cingulate	Gender	.078	.037(.060)	.615	.541
Caudal Anterior Cingulate	Age	-.079	-.002(.003)	-.618	.539
Caudal Anterior Cingulate	MD	-.150	-.071(.060)	-1.181	.242
Left Hemisphere					
Superior Frontal	Gender	.233	.084(.045)	1.871	***.066***
Superior Frontal	Age	-.015	.000(.002)	-.115	.909
Superior Frontal	MD	-.183	-.068(.046)	-1.458	.150
Rostral Middle Frontal	Gender	.055	.019(.045)	.428	.670
Rostral Middle Frontal	Age	.034	.002(.002)	.268	.790
Rostral Middle Frontal	MD	-.160	-.058(.046)	-1.269	.209
Rostral Anterior Cingulate	Gender	.294	.150(.062)	2.405	**.019**
Rostral Anterior Cingulate	Age	.053	.001(.003)	.411	.683
Rostral Anterior Cingulate	MD	-.279	-.145(.064)	-2.268	**.027**
Precentral	Gender	.260	.085(.040)	2.107	**.039**
Precentral	Age	.257	.004(.002)	2.074	**.042**
Precentral	MD	-.200	-.067(.042)	-1.593	.116

Pars Triangularis	Gender	.229	.080(.044)	1.835	***.071***
Pars Triangularis	Age	.028	.000(.002)	.218	.828
Pars Triangularis	MD	-.191	-.069(.045)	-1.520	.134
Pars Orbitalis	Gender	.194	.120(.078)	1.547	.127
Pars Orbitalis	Age	-.217	-.007(.004)	-1.734	***.088***
Pars Orbitalis	MD	-.157	-.099(.080)	-1.240	.220
Pars Opercularis	Gender	.189	.064(.043)	1.502	.138
Pars Opercularis	Age	-.037	-.001(.002)	-.292	.772
Pars Opercularis	MD	-.173	-.060(.044)	-1.368	.176
Insula	Gender	.051	.016(.041)	.399	.692
Insula	Age	.135	.002(.002)	1.061	.293
Insula	MD	-.079	-.026(.042)	-.618	.539
Frontal Pole	Gender	-.038	-.033(.111)	-.298	.767
Frontal Pole	Age	.006	.000(.006)	.050	.960
Frontal Pole	MD	.047	.041(.113)	.366	.716
Caudal Middle Frontal	Gender	.194	.113(.073)	1.546	.127
Caudal Middle Frontal	Age	.201	.004(.003)	1.604	.114
Caudal Middle Frontal	MD	-.191	-.078(.052)	-1.516	.135
Caudal Anterior Cingulate	Gender	.194	.113(.073)	1.546	.127
Caudal Anterior Cingulate	Age	-.031	-.001(.004)	-.243	.809
Caudal Anterior Cingulate	MD	-.180	-.107(.075)	-1.427	.159

Significant <.05 are shown in bold and marginal results <.10 are shown in bold italic font; W1: Wave 1 W2: Wave 2 MD: Maternal Depression

Research Aim 1: How does cortisol reactivity (wave 1 or wave 2) relate to behavioral assessments of executive function (wave 1 or wave 2)?

The longitudinal relation between earlier cortisol reactivity and later executive function was examined. A multiple regression was conducted with the AUCs from wave 1 and executive function composite from wave 2 with the appropriate covariates. The association between cortisol reactivity (AUCi or AUCg) at wave 1 and executive function at wave 2 was not significant. The relation between cortisol reactivity and executive function within waves was examined using the wave 1 AUCs and executive function composite from wave 1 along with the appropriate covariates. The associations between wave 2 AUCs and wave 2 executive function were also examined. Results are presented in Table 6 and Table 7. The association between wave 2 AUCg was significantly related to executive function at wave 2. When controlling for AUCg at wave 1, the association between wave 2 AUCg and wave 2 executive function was significant. When controlling for wave 1 executive function and wave 1 AUCg, the association between wave 2 AUCg and executive function at wave 2 was only marginally significant. The associations between wave 1 cortisol reactivity (AUCi or AUCg) and wave 1 executive function were not significant.

Table 6: Associations between cortisol reactivity and executive function

Model	Covariates	IV *β*	IV b(SE)	IV *t*	IV *p*
DV: W1 Executive Function					
W1 AUCg	Age	-.068	-.249(.289)	-.860	.391
W1 AUCi	Age	.053	.514 (.772)	.666	.507
DV: W2 Executive Function					
W1 AUCg	Age, MD	-.040	-.108(.253)	-.427	.671
W1 AUCi	Age, MD	-.041	-.413(.944)	-.438	.663
W2 AUCg	Age,Gender, MD	-2.10	-.491(.206)	-2.388	**.019**
W2 AUCi	Age, MD	-.080	-.413(.466)	-.885	.378

Significant <.05 are shown in bold and marginal results <.10 are shown in bold italic font; W1: Wave 1 W2: Wave 2 MD: Maternal Depression

Table 7: Longitudinal associations of cortisol reactivity and executive function

Model	IV β	IV b(SE)	IV *t*	IV *p*
DV: W2 Executive Function				
W1 AUCg	.018	.049(.252)	1.97	.845
W2 AUCg	-.245	-.565(.214)	-2.642	**.010**
Age	.452	.028(.006)	4.976	**<.01**
MD	-.101	-.123(.110)	-1.117	.267
Gender	.071	.086(.111)	.771	.443
DV: W2 Executive Function				
W1 AUCg	.011	.029(.256)	.113	.910
W2 AUCg	-.240	-.554(.216)	-2.568	**.012**
W1 Executive Function	-.025	-.018(.070)	-.262	.794
Age	.463	.029(.006)	4.821	**<.01**
MD	-.170	-.130(.111)	-1.170	.245
Gender	.078	.095(.112)	.842	.402
DV: W2 Executive Function				
W1 AUCi	-.039	-.398(.949)	-.420	.676
W2 AUCi	-.069	-.332(.456)	-.728	.468
Age	.461	.028(.006)	4.902	**<.01**
MD	-.099	-.120(.115)	-1.050	.297
DV: W2 Executive Function				
W1 AUCi	-.044	-.448(.960)	-.467	.642
W2 AUCi	-.071	-.344(.459)	-.749	.456
W1 Executive Function	-.028	-.020(.072)	-.281	.779
Age	.475	.029(.006)	4.762	**<.01**
MD	-.106	-.129(.116)	-1.110	.270
DV: W2 Executive Function				
SES	.135	.039(.026)	1.455	.149
W1 Executive Function	-.040	-.029(.069)	-.417	.677
Age	.432	.028(.006)	4.440	**<.01**
MD	-.132	-.169(.119)	-1.417	.160
DV: W2 Executive Function				
SES Risk Composite	-.159	-.072(.042)	-1.726	***.088***
W1 Executive Function	-.036	-.026(.069)	-.371	.712
Age	.432	.028(.006)	4.460	**<.01**
MD	-.135	-.173(.119)	-1.459	.148

Significant <.05 are shown in bold and marginal results <.10 are shown in bold italic font; W1: Wave 1 W2: Wave 2 MD: Maternal Depression

Research Aim 2: How does cortisol reactivity (wave 1 or wave 2) relate to neural measures of executive function (wave 2)?

The associations between earlier cortisol reactivity at wave 1 and later structural volumes at wave 2 were examined. The associations between the wave 2 cortisol reactivity and the twenty-two PFC regions cortical thickness at wave 2 were examined as well. Multiple regressions were conducted with the volume of the regions selected in the PFC and the AUCs from each wave of data collection along with the appropriate covariates. Results are shown in Table 8. The between wave analyses revealed wave 1 AUCg was significantly related to total grey matter at wave 2. For the specific prefrontal regions of interest, wave 1 AUCg was significantly related to right frontal pole cortical thickness and marginally related right caudal middle frontal cortical thickness. The associations between PFC cortical thickness at wave 2 and wave 1 AUCi were not significant. The associations between cortisol reactivity at wave 2 and neural assessments at wave 2 revealed wave 2 AUCi was related to total grey matter. For the specific regions of interest within the PFC, wave 2 AUCg was significantly related to the cortical thickness of the insula bilaterally and right pars triangularis. Wave 2 AUCg was marginally related to the left caudal middle frontal and left pars triangularis cortical thickness. Wave 2 AUCi was significantly related to the left rostral anterior cingulate and left insula cortical thickness.

The timing effects were examined by including both wave 1 and wave 2 AUCs in the regression. Results are presented in Table 9. The overall association between total grey matter at wave 2 and AUCg at wave 1 was significant when accounting for wave 2 AUCg. Wave 1 AUCg was significantly related to right insula and significantly related to caudal right middle frontal, left pars opercularis, and left insula cortical thickness when controlling

for wave 2 AUGg. On the other hand, wave 2 AUCg was significantly related to left insula and marginally related to left pars triangularis cortical thickness when accounting for wave 1 AUCg. Wave 2 AUCi was significantly related to the left insula cortical thickness when accounting for wave 1 AUCi.

Table 8: Associations between cortisol reactivity and PFC cortical thickness

Dependent Variable	Predictor (IV)	Covariates	IV β	IV b(SE)	IV t	IV p
TGM	W1 AUCi	Gender	-.121	-105420.62(112324.27)	-9.39	.352
	W1 AUCg	Gender	.255	67849.189(33314.90)	2.037	**.047**
	W2 AUCi	Gender	-.210	-123429.74(72559.71)	-1.701	***.094***
	W2 AUCg	Gender	-.185	39044.24(26362.20)	-1.481	.144
Right Superior Frontal	W1AUCi	TGM, Gender	.025	.063(.293)	.216	.830
	W1 AUCg	TGM, Gender	-.007	-.007(.125)	-.054	.957
	W2 AUCi	TGM, Gender	.071	.131(.205)	.638	.526
	W2 AUCg	TGM, Gender	.025	.017(.074)	.226	.822
Right Rostral Middle Frontal	W1 AUCi	TGM, Gender	-.109	-.344(.394)	-.872	.387
	W1 AUCg	TGM, Gender	.095	.092(.129)	.714	.478
	W2AUCi	TGM, Gender	.037	.086(.273)	.316	.753
	W2 AUCg	TGM, Gender	.008	.007(.098)	.071	.943
Right Rostral ACC	W1 AUCi	TGM	.017	.052(.412)	.126	.900
	W1 AUCg	TGM	.082	.077(.128)	.598	.552
	W2 AUCi	TGM	-.014	-.029(.276)	-.107	.915
	W2 AUCg	TGM	.094	.072(.099)	.726	.471
Right Precentral	W1 AUCi	TGM, Age	.003	.007(.253)	.028	.978
	W1 AUCg	TGM, Age	.083	.052(.079)	.657	.514
	W2 AUCi	TGM, Age	.048	.070(.173)	.403	.688
	W2 AUCg	TGM, Age, Gender	.124	.065(.056)	1.154	.254
Right Pars Triangularis	W1 AUCi	TGM	-.009	-.024(.361)	-.067	.947
	W1 AUCg	TGM	-.031	-.026(.112)	-.237	.814
	W2 AUCi	TGM	.025	.049(.249)	.199	.843
	W2 AUCg	TGM, Gender	.292	.114(.050)	2.296	**.025**
Right Pars Orbitalis	W1 AUCi	TGM, Gender	.061	.247(.510)	.484	.630
	W1 AUCg	TGM, Gender	.014	.017(.160)	.103	.918
	W2 AUCi	TGM, Gender	.020	.059(.359)	.164	.871
	W2 AUCg	TGM, Gender	.065	.069(.129)	.536	.594
Right Pars Opercularis	W1 AUCi	TGM, Gender	-.116	-.298(.313)	-.952	.345
	W1 AUCg	TGM, Gender	-.114	-.089(.098)	-.907	.368
	W2 AUCi	TGM, Gender	-.179	-.332(.207)	-1.603	.114
	W2 AUCg	TGM, Gender	-.054	-.036(.076)	-.471	.639

Right Insula	W1 AUCi	TGM	.054	.139(.319)	.435	.665
	W1 AUCg	TGM	-.112	-.088(.098)	-.894	.375
	W2 AUCi	TGM, Gender	.098	.171(.212)	.805	.424
	W2 AUCg	TGM, Gender	.021	.013(.077)	.172	.864
Right Frontal Pole	W1 AUCi	TGM, Gender	.016	.092(.633)	.145	.885
	W1 AUCg	TGM, Gender	.335	.269(.091)	2.966	**.004**
	W2 AUCi	TGM, Gender	-.068	-.278(.439)	-.634	.529
	W2 AUCg	TGM, Gender	-.010	-.015(.158)	-.097	.923
Right Caudal Middle Frontal	W1 AUCi	TGM, Age, Gender, MD	-.201	-.636(.381)	-1.67	.101
	W1 AUCg	TGM, Age, Gender, MD	.221	.212(.121)	1.745	***.087***
	W2 AUCi	TGM, Age, Gender, MD	.088	.228(.301)	.758	.452
	W2 AUCg	TGM, Gender	.048	.045(.109)	.412	.682
Right Caudal ACC	W1 AUCi	TGM	.112	.387(.429)	.903	.370
	W1 AUCg	TGM	.067	.070(.134)	.524	.602
	W2 AUCi	TGM	.039	.092(.292)	.315	.754
	W2 AUCg	TGM, Gender	.020	.017(.107)	.157	.876
Left Superior Frontal	W1 AUCi	TGM, Gender	.089	.222(.315)	.703	.485
	W1 AUCg	TGM, Gender	.012	.009(.099)	.095	.925
	W2 AUCi	TGM, Gender	.029	.053(.218)	.243	.809
	W2 AUCg	TGM, Gender	-.019	-.012(.078)	-.153	.879
Left Rostral Middle Frontal	W1 AUCi	TGM	.143	.362(.316)	1.145	.257
	W1 AUCg	TGM	-.152	-.117(.098)	-1.191	.239
	W2 AUCi	TGM	.052	.092(.216)	.424	.673
	W2 AUCg	TGM, Gender	.076	.048(.078)	.619	.539
Left Rostral ACC	W1 AUCi	TGM, Gender, MD	.034	.128(.487)	.263	.794
	W1 AUCg	TGM, Gender, MD	.154	.177(.151)	1.169	.248
	W2 AUCi	TGM, Gender, MD	.226	.576(.318)	1.812	***.075***
	W2 AUCg	TGM, Gender	.196	.179(.114)	1.572	.121
Left precentral	W1 AUCi	TGM, Age, Gender	.095	.213(.244)	.871	.388
	W1 AUCg	TGM, Age, Gender	-.131	-.090(.079)	-1.139	.260
	W2 AUCi	TGM, Age, Gender	.076	.123(.166)	.741	.462
	W2 AUCg	TGM, Age, Gender	.129	.075(.059)	1.267	.210

Left Pars Triangularis	W1 AUCi	TGM, Gender	.026	.068(.335)	.202	.841
	W1 AUCg	TGM, Gender	.185	.146(.103)	1.413	.163
	W2 AUCi	TGM, Gender	.185	.319(.221)	1.441	.155
	W2 AUCg	TGM, Gender	.250	.155(.078)	1.976	***.053***
Left Pars Orbitalis	W1 AUCi	TGM, Age	.078	.352(.600)	.587	.560
	W1 AUCg	TGM	.036	.049(.189)	.261	.795
	W2 AUCi	TGM, Gender	.094	.290(.400)	.723	.473
	W2 AUCg	TGM, Gender	.204	.225(.141)	1.590	.117
Left Pars Opercularis	W1 AUCi	TGM	.100	.252(.319)	.788	.434
	W1 AUCg	TGM	-.125	-.095(.099)	-.966	.338
	W2 AUCi	TGM	-.025	-.043(.210)	-.204	.839
	W2 AUCg	TGM, Gender	.057	.035(.073)	.475	.636
Left Insula	W1 AUCi	TGM	.067	.160(.280)	.570	.571
	W1 AUCg	TGM	-.108	-.078(.086)	-.896	.374
	W2 AUCi	TGM	.237	.380(.180)	2.106	**.039**
	W2 AUCg	TGM, Gender	.300	.172(.063)	2.729	**<.01**
Left Frontal Pole	W1 AUCi	TGM	.111	.713(.724)	.984	.329
	W1 AUCg	TGM	-.058	-.114(.226)	-.504	.617
	W2 AUCi	TGM	-.100	-.422(.469)	-.900	.372
	W2 AUCg	TGM, Gender	-.095	-.144(.171)	-.841	.404
Left Caudal Middle Frontal	W1 AUCi	TGM	.144	.390(.330)	1.181	.243
	W1 AUCg	TGM	-.054	-.045(.104)	-.433	.667
	W2 AUCi	TGM	.117	.236(.239)	.990	.326
	W2 AUCg	TGM, Gender	.197	.142(.082)	1.730	***.089***
Left Caudal ACC	W1 AUCi	TGM	-.122	-.499(.553)	-.902	.371
	W1 AUCg	TGM	.117	.146(.172)	.848	.400
	W2 AUCi	TGM	-.013	-.036(.387)	-.094	.925
	W2 AUCg	TGM, Gender	.043	.045(.138)	.323	.748

Significant <.05 are shown in bold and marginal results <.10 are shown in bold italic font; W1: Wave 1 W2: Wave 2 MD: Maternal Depression

Table 9: Longitudinal associations between cortisol reactivity and PFC cortical thickness

Model	IV β	IV b(SE)	IV *t*	IV *p*
DV: TGM				
W1 AUCi	-.108	-92993.35(110016.80)	-.845	.402
W2 AUCi	-.220	-127101.75(74604.95)	-1.704	***.095***
Age	.314	1820.29(1509)	1.206	.233
MDD	-.246	-1350.91(1430.71)	-.944	.350
Gender	-.328	-39249.78(15242.51)	-2.575	**.013**
DV: Right Superior Frontal				
W1 AUCi	.026	.065(.299)	.218	.828
W2 AUCi	.024	.040(.205)	.194	.847
TGM	.475	<.01(<.01)	3.661	**<.01**
Gender	.390	.134(.044)	3.073	**<.01**
DV: Right Rostral Middle Frontal				
W1 AUCi	-.113	-.356(.403)	-.882	.328
W2 AUCi	.017	.035(.276)	.128	.899
TGM	.375	<.01 (<.01)	2.725	**<.01**
Gender	.233	.102(.059)	1.726	***.090***
DV: Right Rostral ACC				
W1 AUCi	.027	.083(.419)	.197	.844
W2 AUCi	-.034	-.069(.286)	-.242	.809
TGM	.177	<.01(<.01)	1.205	.234
Gender	.174	.074(.061)	1.212	.231
DV: Right Precentral				
W1 AUCi	-.007	-.014(.256)	-.055	.956
W2 AUCi	.061	.084(.174)	.482	.632
TGM	.224	<.01(<.01)	1.750	***.086***
Age	.367	.005(.002)	-2.939	**<.01**
DV: Right Pars Triangularis				
W1 AUCi	-.017	-.046(.366)	-.125	.901
W2 AUCi	.014	.026(.249)	.104	.918
TGM	.252	<.01(<.01)	1.850	***.070***
DV: Right Pars Orbitalis				
W1 AUCi	.068	.275(.520)	.528	.600
W2 AUCi	-.034	-.091(.356)	-.257	.798
TGM	.376	<.01(<.01)	2.715	**<.01**
Gender	.263	.174(.076)	1.943	***.057***
DV: Right Pars Opercularis				
W1 AUCi	-.096	-.248(.311)	-.798	.429
W2 AUCi	-.195	-.337(.213)	-1.585	.119
TGM	.348	<.01 (<.01)	2.689	**.010**
Gender	.341	.122(.045)	2.690	**.010**
DV: Right Insula				
W1 AUCi	.051	.132(.326)	.404	.688
W2 AUCi	.098	.168(.223)	.756	.453
TGM	.464	<.01(<.01)	3.414	**<.01**
Gender	.118	.042(.048)	.887	.379

DV: Right Frontal Pole				
W1 AUCi	.022	.124(.643)	.193	.848
W2 AUCi	-.095	-.366(.440)	-.831	.410
TGM	.580	<.01(<.01)	4.822	**<.01**
Age	.339	.271(.094)	2.882	**<.01**
DV: Right Caudal Middle Frontal				
W1 AUCi	-.205	-.648(.388)	-1.670	.101
W2 AUCi	.084	.177(.271)	.654	.516
TGM	.348	<.01(<.01)	2.611	**.012**
Gender	.260	.114(.058)	1.954	***.056***
Age	.210	.004(.003)	1.719	***.092***
MD	-.093	-.041(.056)	-.730	.469
DV: Right Caudal ACC				
W1 AUCi	.111	.382(.441)	.867	.390
W2 AUCi	.010	.024(.304)	.080	.937
TGM	-.377	<.01(<.01)	-2.908	**<.01**
MD	-.071	-.034(.062)	-.550	.584
DV: Left Superior Frontal				
W1 AUCi	.093	.231(.322)	.717	.477
W2 AUCi	-.023	-.039(.221)	-.177	.860
TGM	.376	<.01(<.01)	2.716	**<.01**
Gender	.261	.091(.047)	1.925	***.060***
DV: Left Rostrial Middle Frontal				
W1 AUCi	.137	.340(.321)	.137	.294
W2 AUCi	.039	.066(.218)	.039	.764
TGM	.369	<.01 (<.01)	.369	**<.01**
DV: Left Rostral ACC				
W1 AUCi	.014	.052(.485)	.110	.913
W2 AUCi	.213	.541(.339)	1.595	.117
TGM	.028	<.01(<.01)	.200	.842
Gender	.258	.136(.073)	1.864	***.068***
MD	-.211	-.112(.070)	-1.594	.117
DV: Left Precentral				
W1 AUCi	.094	.210(.249)	.845	.402
W2 AUCi	.065	.098(.170)	.576	.567
TGM	.586	<.01(<.01)	4.874	**<.01**
Gender	.376	.117(.036)	3.212	**<.01**
Age	.173	<.01(<.01)	1.556	.126
DV: Left Pars Triangularis				
W1 AUCi	.005	.012(.332)	.035	.972
W2 AUCi	.207	.354(.228)	1.558	.125
TGM	.250	<.01(<.01)	1.784	***.080***
Gender	.325	.115(.049)	2.365	**.022**
DV: Left Pars Orbitalis				
W1 AUCi	.070	.315(.600)	.525	.602
W2 AUCi	.105	.315(.411)	.767	.447
TGM	.231	<.01(<.01)	1.606	.114
Gender	.273	.170(.088)	1.938	***.058***

DV: Left Pars Opercularis				
W1 AUCi	.103	.258(.326)	.790	.433
W2 AUCi	-.031	-.053(.222)	-.239	.812
TGM	.342	<.01 (<.01)	2.594	**.012**
DV: Left Insula				
W1 AUCi	.047	.111(.275)	.405	.687
W2 AUCi	.242	.382(.187)	2.043	**.046**
TGM	.528	<.01(<.01)	4.441	**<.01**
DV: LeftFrontal Pole				
W1 AUCi	.116	.721(.726)	.116	.325
W2 AUCi	-.113	-.474(.493)	-.113	.340
TGM	.516	<.01(<.01)	.516	**<.01**
DV: Left Caudal Middle Frontal				
W1 AUCi	.137	.371(.336)	1.105	.274
W2 AUCi	.098	.179(.228)	.785	.436
TGM	.448	<.01(<.01)	3.560	**<.01**
DV: Left Caudal ACC				
W1 AUCi	-.121	-.498(.566)	-.881	.382
W2 AUCi	-.015	-.041(.384)	-.106	.916
TGM	-.040	<.01(<.01)	-.289	.774
DV: TGM				
W1 AUCg	.355	96302.50(32559.72)	2.958	**<.01**
W2 AUCg	-.217	-45941.79(25435.91)	-1.806	***.077***
Gender	-.380	-45424.99(14441.50)	-3.145	**<.01**
DV: Right Superior Frontal				
W1 AUCg	-.009	-.007(.102)	-.066	.948
W2 AUCg	-.012	-.007(.076)	-.096	.924
TGM	.467	<.01(<.01)	3.371	**<.01**
Gender	.385	.133(.046)	3.371	**<.01**
DV: Right Rostral Middle Frontal				
W1 AUCg	.007	.007(.138)	.052	.958
W2 AUCg	-.003	-.003(.103)	-.026	.980
TGM	.384	<.01 (<.01)	2.600	**.012**
Gender	.235	.103(.062)	1.660	.103
DV: Right Rostral ACC				
W1 AUCg	.087	.084(.141)	.592	.557
W2 AUCg	.079	.059(.105)	.561	.577
TGM	.165	<.01(<.01)	1.062	.293
Gender	.171	.073(.063)	1.147	.256
DV: Right Precentral				
W1 AUCg	.009	.006(.080)	.070	.944
W2 AUCg	.110	.055(.059)	.939	.352
TGM	.360	<.01(<.01)	2.738	**<.01**
Gender	.429	.112(.035)	3.430	**<.01**
Age	.347	.005(.002)	3.024	**<.01**

DV: Right Pars Triangularis				
W1 AUCg	-.049	-.042(.122)	-.344	.732
W2 AUCg	-.014	-.010(.091)	-.106	.916
TGM	.344	<.01(<.01)	2.289	**.026**
Gender	.261	.099(.055)	1.814	***.075***
DV: Right Pars Orbitalis				
W1 AUCg	-.019	-.024(.177)	-.137	.892
W2 AUCg	.029	.029(.132)	.221	.826
TGM	.387	<.01(<.01)	2.616	**.012**
Gender	.274	.153(.079)	1.931	***.059***
DV: Right Pars Opercularis				
W1 AUCg	-.167	-.136(.107)	-1.265	.212
W2 AUCg	-.037	-.024(.080)	-.297	.768
TGM	.461	<.01 (<.01)	3.296	**<.01**
Gender	.408	.146(.048)	3.044	**<.01**
DV: Right Insula				
W1 AUCg	-.142	-.115(.110)	-1.039	.304
W2 AUCg	.040	.025(.082)	.305	.761
TGM	.494	<.01(<.01)	3.422	**<.01**
Gender	.143	.051(.049)	1.030	.308
DV: Right Frontal Pole				
W1 AUCg	.129	.223(.217)	1.071	.289
W2 AUCg	-.074	-.105(.162)	-.648	.520
TGM	.537	<.01(<.01)	4.213	**<.01**
Gender	.306	.244(.097)	2.511	**.015**
DV: Right Caudal Middle Frontal				
W1 AUCg	.230	-.229(.134)	1.704	***.095***
W2 AUCg	-.019	-.014(.009)	-.145	.885
TGM	.266	<.01(<.01)	1.857	***.069***
Gender	.197	.086(.061)	1.418	.162
Age	.245	.005(.003)	1.968	***.055***
MDD	-.110	-.048(.055)	-.877	.385
DV: Right Caudal ACC				
W1 AUCg	.121	.131(.150)	.877	.385
W2 AUCg	-.007	-.006(.112)	-.050	.960
TGM	-.462	<.01(<.01)	-3.166	.427
Gender	-.112	-.054(.067)	-.801	**<.01**
DV: Left Superior Frontal				
W1 AUCg	.012	.009(.110)	.083	.934
W2 AUCg	-.060	-.037(.082)	-.451	.654
TGM	.352	<.01(<.01)	2.376	**.021**
Gender	.244	.085(.049)	1.723	***.091***
DV: Left Rostrial Middle Frontal				
W1 AUCg	-.164	-.129(.110)	-1.175	.245
W2 AUCg	.118	.072(.082)	.885	.380
TGM	.443	<.01 (<.01)	3.001	**<.01**
Gender	.110	.038(.049)	.774	.443

DV: Left Rostral ACC				
W1 AUCg	.176	.209(.163)	1.286	.204
W2 AUCg	.165	.153(.122)	1.256	.215
TGM	-.056	<.01(<.01)	-.387	.700
Gender	.211	.111(.075)	1.487	.143
MDD	-.230	-.112(.068)	-1.787	***.080***
DV: Left Precentral				
W1 AUCg	-.179	-.126(.084)	-1.496	.141
W2 AUCg	.144	.079(.062)	1.277	.207
TGM	.655	<.01(<.01)	5.179	**<.01**
Gender	.433	.134(.037)	3.598	**<.01**
Age	.147	<.01(<.01)	1.327	.190
DV: Left Pars Triangularis				
W1 AUCg	.225	.180(.108)	1.662	.103
W2 AUCg	.237	.148(.081)	1.835	***.072***
TGM	.167	<.01(<.01)	1.167	.248
Gender	.285	.101(.048)	2.077	**.043**
DV: Left Pars Orbitalis				
W1 AUCg	-.012	-.017(.201)	-.083	.934
W2 AUCg	.217	.239(.150)	1.596	.116
TGM	.245	<.01(<.01)	1.624	.111
Gender	.296	.185(.090)	2.051	**.045**
DV: Left Pars Opercularis				
W1 AUCg	-.230	-.182(.105)	-1.737	***.088***
W2 AUCg	.096	.060(.078)	.763	.449
TGM	.527	<.01 (<.01)	3.752	**<.01**
Gender	.358	.125(.047)	2.665	**.010**
DV: Left Insula				
W1 AUCg	-.202	-.149(.088)	-1.701	***.095***
W2 AUCg	.347	.217(.065)	3.312	**<.01**
TGM	.666	<.01(<.01)	5.308	**<.01**
Gender	.249	.081(.039)	2.068	**.044**
DV: LeftFrontal Pole				
W1 AUCg	-.013	-.025(.252)	-.098	.922
W2 AUCg	-.090	-.138(.188)	-.733	.467
TGM	.523	<.01(<.01)	3.855	**<.01**
Gender	.030	.026(.113)	.233	.817
DV: Left Caudal Middle Frontal				
W1 AUCg	-.155	-.132(.110)	-1.197	.237
W2 AUCg	.216	.144(.082)	1.748	***.086***
TGM	.582	<.01(<.01)	4.243	**<.01**
Gender	.300	.113(.049)	2.284	**.026**
DV: Left Caudal ACC				
W1 AUCg	.088	.114(.193)	.590	.557
W2 AUCg	.058	.059(.144)	.409	.684
TGM	.005	<.01(<.01)	.030	.976
Gender	.144	.082(.086)	.955	.344

Significant <.05 are shown in bold and marginal results <.10 are shown in bold italic font; W1: Wave 1 W2: Wave 2 MD: Maternal Depression

Research Aim 3: How does SES (wave 1) relate to behavioral measures of executive function (wave 1 or wave 2)?

The association between SES and the behavioral assessments of executive function was examined through multiple regressions with the appropriate covariates. Separate multiple regressions were conducted with either SES (income and average education) or the SES risk composite from the wave 1 and the executive function composites from each wave of data. Results are presented in Table 10. The association between the wave 1 SES risk composite and the executive function composite at wave 2 was marginally significant. This association was not significant with the SES composite of average parental education and income. The associations between SES and wave 1 executive function composite were not significant.

Table 10: Associations between SES, cortisol reactivity, and executive function

Model	Covariates	IV β	IV b(SE)	IV *t*	IV *p*
DV: W1 Executive Function					
SES	Age	.005	.002(.036)	.057	.954
SES Risk Composite	Age	.022	.013(.057)	.232	.817
DV: W2 Executive Function					
SES	Age, MD	.135	.039(026)	1.461	.147
SES Risk Composite	Age, MD	-.160	-.072(.041)	-1.746	***.084***
DV: W1 AUCi					
SES	Age	.078	.002(.003)	.767	.445
SES Risk Composite	Age	-.025	-.001(.004)	-.242	.810
DV: W1 AUCg					
SES	Age	.071	.007(.010)	.700	.486
SES Risk Composite	Age	-.058	-.009(.017)	-.571	.569
DV: W2 AUCi					
SES	Age	-.184	-.010(.006)	-1.806	***.074***
SES Risk Composite	Age	.235	.020(.009)	2.331	**.022**
DV: W2 AUCg					
SES	Age, Gender	.049	.005(.011)	.480	.632
SES Risk Composite	Age, Gender	-.023	-.004(.017)	-.225	.823

Significant <.05 are shown in bold and marginal results <.10 are shown in bold italic font; W1: Wave 1 W2: Wave 2 MD: Maternal Depression

Research Aim 4: How does SES (wave 1) relate to neural measures of executive function (wave 2)?

The relation between SES and cortical thickness of the PFC regions were examined by multiple regressions with the appropriate covariates. The association between wave 1 SES and total grey matter at wave 2 was examined. Then, multiple regressions were conducted for regions selected in the PFC and wave 1 SES as measured average parental education and family income or the SES risk composite. Results are presented in Table 11. Wave 1 SES was significantly related to total grey matter volume at wave 2. As for the specific twenty-two PFC regions at wave 2, the SES composite was significantly related to right pars triangularis and marginally related to right rostral anterior cingulate cortical thickness. The SES Risk composite was significantly related to the cortical thickness of the right rostral anterior cingulate cortex.

Table 11: Associations between SES and PFC cortical thickness

Dependent Variable	Predictor (IV)	Covariates	IV β	IV b(SE)	IV *t*	IV *p*
TGM	SES IE	Gender	.340	8893.71	2.709	**<.01**
	SES Risk	Gender	-.383	-15455.58(5035.47)	-3.069	**<.01**
Right Superior Frontal	SES IE	TGM, Gender	.039	.003(.010)	.325	.746
	SES Risk	TGM, Gender	-.096	-.012(.016)	-.779	.439
Right Rostral Middle Frontal	SES IE	TGM, Gender	-.203	-.021(.013)	-1.618	.112
	SES Risk	TGM, Gender	.117	.019(.021)	.890	.377
Right Rostral ACC	SES IE	TGM, Gender	.255	.024(.013)	1.894	***.064***
	SES Risk	TGM, Gender	-.281	-.041(.020)	-2.050	**.045**
Right Precentral	SES IE	TGM, Age, Gender, MD	-.009	-.001(.008)	-.077	.939
	SES Risk	TGM, Age, Gender, MD	-.042	-.004(.012)	-.360	.720
Right Pars Triangularis	SES IE	TGM, Age, Gender, MD	-.233	-.020(.011)	-1.800	***.078***
	SES Risk	TGM, Age, Gender, MD	.160	.022(.018)	1.187	.241
Right Pars Orbitalis	SES IE	TGM, Gender	-.198	-.026(.017)	-1.541	.129
	SES Risk	TGM, Gender	.155	.032(.027)	1.166	.249
Right Pars Opercularis	SES IE	TGM, Gender	.014	.001(.010)	.106	.916
	SES Risk	TGM, Gender	-.094	-.011(.016)	-.716	.477
Right Insula	SES IE	TGM, Gender	-.129	-.011(.010)	-1.036	.305
	SES Risk	TGM, Gender	.182	.022(.016)	1.330	.189
Right Frontal Pole	SES IE	TGM, Gender	-.021	-.004(.021)	-.178	.859
	SES Risk	TGM, Gender	.026	.007(.003)	.214	.832
Right Caudal Middle Frontal	SES IE	TGM, Age, Gender, MD	-.127	-.015(.014)	-1.038	.304
	SES Risk	TGM, Age, Gender, MD	.016	.003(.023)	.125	.901
Right Caudal ACC	SES IE	TGM, Gender	.141	.015(.014)	1.052	.298
	SES Risk	TGM, Gender	-.128	-.021(.022)	-.926	.358

Left Superior Frontal	SES IE	TGM, Gender	-.052	-.004(.011)	-.399	.692
	SES Risk	TGM, Gender	.028	.004(.017)	.210	.834
Left Rostral Middle Frontal	SES IE	TGM	-.074	-.006(.010)	-.563	.576
	SES Risk	TGM	-.012	-.001(.016)	-.090	.929
Left Rostral ACC	SES IE	TGM, Gender, MD	.075	.008(.015)	.554	.582
	SES Risk	TGM, Gender, MD	-.077	-.013(.024)	-.556	.581
Left Precentral	SES IE	TGM, Age, Gender	.054	.004(.008)	.489	.627
	SES Risk	TGM, Age, Gender	-.073	-.008(.013)	-.644	.522
Left Pars Triangularis	SES IE	TGM, Gender	-.064	-.005(.011)	-.454	.652
	SES Risk	TGM, Gender	.047	.006(.017)	.329	.743
Left Pars Orbitalis	SES IE	TGM, Gender	-.047	-.007(.020)	-.334	.740
	SES Risk	TGM, Gender	.017	.004(.031)	.117	.907
Left Pars Opercularis	SES IE	TGM	-.036	-.003(.010)	-.265	.792
	SES Risk	TGM	.005	.001(.015)	.038	.970
Left Insula	SES IE	TGM	-.139	-.010(.009)	-1.112	.271
	SES Risk	TGM	.092	.010(.014)	.728	.470
Left Frontal Pole	SES IE	TGM	-.074	-.014(.022)	-.631	.530
	SES Risk	TGM	.013	.004(.034)	.108	.914
Left Caudal Middle Frontal	SES IE	TGM, Gender	.056	.005(.011)	.446	.657
	SES Risk	TGM, Gender	-.117	-.016(.018)	-.906	.369
Left Caudal ACC	SES IE	TGM	.134	.017(.018)	.943	.350
	SES Risk	TGM	-.182	-.035(.028)	-1.276	.207

Significant <.05 are shown in bold and marginal results <.10 are shown in bold italic font; W1: Wave 1 W2: Wave 2 MD: Maternal Depression

Research Aim 5: How does SES (wave 1) relate to cortisol reactivity (wave 1 or wave 2)?

The longitudinal and concurrent relations between SES and cortisol reactivity were examined. Multiple regression were conducted with SES measures from wave 1 and AUC measures from wave 1 or wave 2 with the appropriate covariates. Results are presented in Table 10. The wave 1 SES risk composite was significantly related to the AUCi at wave 2. The wave 1 SES measure of income and average parental education was marginally related to wave 2 AUCi. Neither of the SES measures were significantly related to either of the AUC measures at wave 1. When examining the timing effects of the AUCi effects, the association between wave 1 SES and wave 2 AUCi was no longer significant when wave 1 AUCi was included in the model. The same pattern of results was found when the risk composite was used as a measure of SES. The association between the wave 1 SES risk composite and AUCi at wave 2 when controlling for AUCi at wave 1 was still marginally significant. The associations between SES and AUCg were not significant at either wave.

Research Aim 6: Does PFC cortical thickness (wave 2) mediate the association between cortisol reactivity (wave 1 or wave 2) and executive function (wave 2)?

Multiple mediations were conducted to examine if wave 2 PFC cortical thickness mediated the association between the AUCs from wave 1 or wave 2 and the wave 2 executive function composite (see Figure 1). The mediation models examining the longitudinal relations were conducted with using the wave 1 AUCs, wave 2 PFC cortical thickness, and wave 2 executive function composite. Then the mediation models within wave 2 were conducted with wave 2 AUCs, wave 2 PFC cortical thickness, and wave 2 EF composite. The mediations were conducted using Hayes SPSS macro using bootstrapping (Hayes, 2009) for each of the twenty-two PFC regions. This mediation approach examines the indirect effects

of the mediator (X) on the association between A and B even if there is not a significant association between A and B. An empirical representation of the sampling distribution is generated and repeatedly resampled throughout the analysis. The variables and path coefficients are estimated with each resampling *k* number of times which creates an empirical distribution of path coefficients that can produce confidence intervals and determine if an indirect effect is present (Hayes, 2009). If the value zero is not contained within the confidence interval of the indirect effect, then the indirect effect is significant using an alpha criteria of $p<.05$. Results are presented in Supplementary Table 2. None of the Hayes bootstrapping models of the PFC regions cortical thickness mediating the association between AUC and executive function were significant.

Research Aim 7: Does PFC cortical thickness (wave 2) mediate the association between SES (wave 1) and executive function (wave 2)?

To determine if PFC cortical thickness mediated the association between SES and executive function (see Figure 2), multiple mediations were conducted. The mediations included a wave 1 SES measure, wave 2 PFC cortical thickness, and wave 2 executive function composite. Mediation models were examined using Hayes SPSS macro with bootstrapping (Hayes, 2009) for each of the twenty-two PFC regions. Results are presented in Supplementary Table 3. The cortical thickness of the right pars triangularis mediated the association between SES and executive function at wave 2 (Direct Effect= .042; Indirect Effect= .0247; Boot SE= .0151; Lower Boot CI= .0015; Boot Upper CI= .0608). The cortical thickness of the other twenty-one regions in the PFC at wave 2 did not significantly mediate the association between wave 1 SES and wave 2 executive function.

Research Aim 8: Does cortisol reactivity (wave 1 or wave 2) mediate the association between SES (wave 1) and PFC cortical thickness (wave 2)?

Mediation models were conducted via Hayes SPSS macro using bootstrapping (Hayes, 2009) to examine if cortisol reactivity at wave 1 or wave 2 mediates the association between SES at wave 1 and PFC cortical thickness at wave 2 (see Figure 3). Mediation models included SES measure of income and education, AUCs from either wave 1 or wave 2, and one of the twenty-two PFC regions cortical thickness at wave 2. Results are presented in Supplementary Table 4. Mediation models were also conducted with the SES Risk Composite, AUCs from either wave 1 or wave 2, and wave 2 PFC cortical thickness. Results are shown in Supplementary Table 5. None of the models of the AUCs mediating the association between SES and PFC cortical thickness were significant.

Research Aim 9: Does cortisol reactivity (wave 1 or wave 2) mediate the association between SES (wave 1) and executive function (wave 1 or wave 2)?

Mediation models were conducted to examine if cortisol reactivity (wave 1 or wave 2) mediates the association between wave 1 SES and executive function (wave 1 or wave 2). Mediations were conducted using bootstrapping from Hayes SPSS macro with the AUCs from wave 1 or wave 2 mediating the association between SES from wave 1 and the executive function composite scores from wave 1 or wave 2 (see Figure 4). The results are presented in Supplementary Table 6. None of the models of the AUCs mediating the association between SES executive function at wave 2.

Chapter 5: Discussion

The current study aimed to examine how stress reactivity, reflected in evoked cortisol response, in early childhood (3-5 years of age) and later childhood (7-10 years), predicts neural and behavioral measures of executive function. This secondary question was framed within the context of the impact of SES on cognition and executive function to investigate the specific role of alterations in stress regulation in neural differences within the PFC. Overall, the results suggest concurrent cortisol reactivity is related to overall brain (with respect to total grey matter) as well as regional differences in development of cortical thickness within the PFC including middle frontal cortex, inferior frontal cortex, insula, and anterior cingulate cortex. Within the bigger SES framework, SES at wave 1 was related to wave 2 cortisol reactivity (AUCi) and executive function. Lower SES was associated with lower executive function, replicating previous studies (Mezzacappa, 2004; Noble et al., 2005; Farrah et al., 2006; Hackman & Farrah, 2010; Kim et al., 2013; Finn et al., 2016). SES was positively related to the change in cortisol in response to a stressor, AUCi, aligning with previous studies showing less of an increase in cortisol in response to stressors in children from low SES backgrounds (Blair, Granger, & Razza; 2005; Blair & Raver, 2012; Blair et al., 2013). SES was correlated with overall brain volume with respect to total grey matter and regionally within the PFC cortical thickness including the inferior frontal cortex and anterior cingulate cortex which are two areas associated with executive function. Although the associations between SES, cortisol reactivity, PFC cortical thickness, and behavioral executive function were significant, only one mediation path for one of twenty-two PFC regions was found to be significant. Specifically, the association between SES at wave 1 and executive function wave 2 was mediated by the cortical thickness of the right inferior frontal

pars triangularis. Multiple analyses were conducted and numerous nonsignificant results were present, which should be taken into consideration when interpreting the results of the present study. Although other mediations were predicted, they were not statistically confirmed, likely due to a lack of power of the analyses. We believe that larger sample sizes including increased distribution of SES would render other mediations significant.

Cortisol Reactivity and Executive Function

Research Aim 1: How does cortisol reactivity (wave 1 or wave 2) relate to behavioral assessments of executive function (wave 1 or wave 2)?

Changes in cortisol levels can impact the development of the PFC along with cognitive abilities associated with this region. Previous studies suggest differences in cortisol relate to executive function as higher basal levels and blunted cortisol reactivity are related to worse performance (Lupien, King, McEwen, & Meaney, 2000; Blair, Granger, & Razza, 2005; Blair et al., 2011). Thus, our first research aim was to test this association, and we predicted that alterations in cortisol reactivity would be related to differences in executive function performance. Current findings support this prediction, as the magnitude of the total cortisol secreted in response to a stressor (AUCg) at wave 2 related negatively to executive function at wave 2. Since the AUCg measure includes all area under the curve of the cortisol response is a measure of total magnitude of cortisol secreted, this association supports the work suggesting higher levels of cortisol secretion are related to worse executive function.

The second part of this research aim was to examine how the association between cortisol reactivity and executive function changes over development and when this association first arises. The current study suggests cortisol reactivity is strongly related to executive function around age 7, but that the association may not be as strong earlier in childhood. However, the association between cortisol reactivity and executive function may be present when the children are younger but not at a statistically significant level. When the wave 1 AUCg and wave 1 executive function were accounted for in the model, the association between wave 2 AUCg and wave 2 executive function decreased to only marginal significance. That is, even though the association between cortisol and executive

function in four year olds did not reach significance, cortisol may have still been impacting executive function abilities.

A potential confound in these comparisons is the variation in the measures of executive function at the different ages. At wave 1, tasks comprising the executive function composite were snack delay and day/night tasks. Although the components of executive function are highly overlapping, these tasks tend to assess more inhibition aspects of executive function in comparison to working memory or cognitive flexibility. However, the tasks used to assess executive function at the wave 2 were a more well-rounded representation of executive function, including a measure of working memory (color span), a measure of cognitive flexibility (trails), and a measure of inhibition (Simon Says). Therefore, the different composites of executive function may relate differently to cortisol reactivity.

Research Aim 2: How does cortisol reactivity (wave 1 or wave 2) relate to neural measures of executive function (wave 2)?

To understand the association between cortisol reactivity and executive function, the question of how cortisol reactivity impacts the regions of the brain that support executive function has to be addressed. The measures of cortisol reactivity (AUCg, AUCi) at wave 1 and wave 2 were both predicted to be related to overall brain volume and regional differences within the PFC. The results of the current study support the main hypothesis, specifically, cortisol reactivity at wave 1 (AUGg) and wave 2 (AUCi) were related to overall total grey matter volumes at wave 2. Interestingly, the AUCg at wave 1 was positively related to total grey matter and at wave 2, the change of cortisol secretion in response to stressor (AUCi) was negatively related to total grey matter at wave 2. For the specific prefrontal regions of interest, there was a positive association between wave 1 cortisol reactivity (AUCg) and right

frontal pole cortical thickness and a marginal positive association with right caudal middle frontal cortical thickness at wave 2. This pattern of results was shown at wave 2 as well, as the magnitude of cortisol secreted in response to a stressor (AUCg) was positively related to cortical thickness at wave 2 in multiple regions involved in executive function including inferior frontal cortex, insula, and middle frontal cortex. There was also a positive association between the change in cortisol levels in response to a stressor (AUCi) at wave 2 and the left rostral anterior cingulate and left insula cortical thickness at wave 2.

Four major regions of the PFC associated with cortisol reactivity are regions that are highly involved in executive function including the middle frontal cortex, ACC, inferior frontal cortex, and insula. The middle frontal cortex includes the dorsolateral prefrontal cortex (dlPFC) a major component of the Cognitive Control Network. The dlPFC supports numerous aspects of executive function. The dlPFC is engaged when attention is needed to learn something new, especially when holding goal-relevant information in mind (Miller & Cohen, 2001; Kane & Engle; 2002; Diamond, 2002; Diamond 2013). The middle frontal cortex is suggested to be impacted by acute and chronic levels of stress. In rodents, the mPFC (thought to be a close representation of the human dlPFC) is impacted by acute and chronic stress, with chronic stress causing dendritic shrinkage (see McEwen, 2013 for review). Although numerous rodent studies have shown this, the impact of stress on the PFC is not examined in humans as often. The current study shows that as the magnitude of cortisol released in response to a stressor (AUCg) at wave 2 decreased, the cortical thickness of middle frontal cortex at wave 2 also decreased. These results support research suggesting a low or blunted cortisol response is related to worse executive function (Blair, Granger, & Razza, 2005; Blair et al., 2013;), and can negatively impact neural development (Teicher et

al., 2003; McEwen, 2007; Mackey, Raizada, & Bunge, 2012; McEwen, 2013; Mackey et al., 2015). This is important because development of this region promotes healthy development of executive function in children. Previous studies show alterations in neural functioning of the dlPFC in various mental disorders as well as in children from low SES backgrounds. For example, Kishyama (2009) showed decreases in neural activity (similar to adults with lesions) in the lateral PFC when the child completed an attention task, and Sheridan et al. (2012) showed SES and change in cortisol reactivity related to PFC activation during an executive function task. Other evidence suggests that individuals from low SES backgrounds showed decreases in the recruitment of the middle frontal cortex, and specifically the dlPFC during executive function tasks (Kim et al., 2013; Finn et al., 2016).

The anterior cingulate cortex (ACC) is another region involved in executive function, specifically engaged during conflict monitoring and error-related feedback. Botvinick et al. (2001), proposed the ACC and dlPFC work together as two major components handling conflicting or competing processes occurring within the brain. Specifically, the ACC is thought to be involved in monitoring cognitive conflict, whereas the dlPFC relates to detecting conflict and top down regulation to modulate attention (Botvinick et al., 2001). The stress literature suggests the ACC is one of the major regions involved in down-regulations of the stress response (McEwen & Giananos, 2010). The development and function of the ACC is linked to the regulation of the HPA axis. For example, Eisenberger et al. (2007) found that cortisol reactivity responses during a social stress test were associated with the activation in the ACC (Eisenberg et al., 2007). Our findings suggest that increases in the change in cortisol response (AUCi) in response to a stressor at wave 2 relate to larger cortical thickness within the ACC at wave 2. These findings align with previous studies that show

the dysregulation of the HPA axis is associated with decreases in development of the ACC (Gianaros, et al., 2007; McEwen & Gianaros, 2010 for review). These results suggest the dysregulation of the HPA axis impacts the development of the ACC and may undermine the development of abilities that rely on this region such as inhibition, self-regulation, and learning in general.

The inferior frontal cortex is another major component of the Cognitive Control Network and implicated in executive function. Previous work by Aron et al. examining behavioral inhibition suggests the inferior frontal cortex functions within a right lateralized fronto-striatal network, including the right inferior frontal cortex, subthalamic nucleus (STN), supplementary motor cortex, and ACC (Aron, Behrens, Smith, Frank, & Poldrack, 2007; Aron, 2007; Aron & Poldrack, 2006). Research suggests that the inferior frontal cortex, particularly the pars triangularis, is activated by the environmental cue to stop the response, which in turn signals the STN to inhibit the motor response (Aron & Poldrack, 2006; Aron, Durston, Eagle, Logan, et al., 2007). The inferior frontal cortex is divided into three regions: pars triangularis, pars orbitalis, and pars opercularis. In the current study, results show that as the magnitude of cortisol in response to a stressor (AUCg) at wave 2 increased, the cortical thickness of the pars triangularis inferior frontal cortex at wave 2 increased. This association seems plausible, as a stress response could be initiated by the processing of cues in the environment to stop behaviors or thought especially to cues in different high stress, higher violence, crowded, and noisy environments.

The insula is involved in numerous cognitive and emotional processes (Kurth, Zilles, Fox, Laird, & Eickhoff, 2010; Menon & Uddin, 2010). Menon & Uddin (2010) suggest the insula has major roles in self-regulation as part of the saliency network. The saliency network

is a group of brain regions that support the detection of behaviorally relevant information in the environment. Within the saliency network, the insula detects which areas are in need of extra processing and aid in switching major processing between different systems (Menon & Uddin, 2010). Threatening or stressful events are salient to survival, and activate the insula. Neuroscience fMRI studies provide support the role of the insula in perceived stressful or threating events as higher insula activation is associated with threat processes (van Wingen, Geuze, Vermetten, and Fernandez, 2011). The current study showed that as the change in cortisol levels in response to a stressor (AUCi) at wave 2 increased, the cortical thickness of the insula at wave 2 increased. This pattern of results fits into a larger framework suggesting a detection of threatening or salient information in the environment would be related to the stress response and regulation. It goes without saying that the ability to detect salient events and to respond accordingly is beneficial for healthy child development.

The second part of this research aim was to examine the timing of neural differences associated with cortisol reactivity. In the current study, the results suggest the influence of cortisol reactivity on the development of PFC regions may occur at different time points in a child's life. For the cortisol reactivity at wave 1, the total amount of cortisol secreted in response to the stressor (AUCg) at wave 1 was positively related to total grey matter at wave 2. The wave 1 AUCg was positively related to right insula cortical thickness and marginally related to caudal right middle frontal, and left insula cortical thickness when controlling for wave 2. On the other hand, the wave 2 (AUCg) was positively related to left insula cortical thickness and marginally related to left pars triangularis cortical thickness when accounting for wave 1. The change in cortisol in response to the stressor (AUCi) at wave 2 was positively related to the left insula cortical thickness when accounting for wave 1 AUCi.

Although the development of the PFC is normally discussed as protracted as it continues to develop until early adulthood, the developmental trajectory of the individual regions within the PFC is not always addressed. Different regions of the brain develop at different time points in a child's life. Even within the PFC, various regions may have different developmental trajectories (Shaw et al., 2008) which may make them differentially susceptible to environmental influences, such as stress, in positive or negative ways. From a developmental standpoint, it is necessary to understand the "typical" development of the regions of the PFC. However, more research is necessary to understand the development of the PFC, environmental influences impact the development, and the windows of opportunities or timeframes of sensitivity in these regions.

SES, Cortisol Reactivity, and Executive Function

Research Aim 3: How does SES (wave 1) relate to behavioral measures of executive function (wave 1 or wave 2)?

SES was predicted to be positively related to executive function as previous research shows children from lower SES backgrounds have lower executive function in comparison to children from higher SES backgrounds (Mezzacappa, 2004; Noble, Norman, & Farrah, 2005; Farrah et al., 2006; Noble, McCandliss, & Farrah; 2007; Hackman & Farrah, 2010; Kim et al., 2013; Finn et al., 2016). Although we predicted that this association would be present in both waves, we found only a marginal negative association between the SES risk composite at wave 1 and the wave 2 executive function composite.

The lack of strong significant results may be due to the distribution of the SES of the children in the current study, as there were not many children from low SES backgrounds. The actual measure of SES used in the current study may play a role as well. SES is a

complex factor and the measures of SES selected not be ideal given the scales and variation. SES measures used in previous studies are not always consistent as some researchers approach SES as a whole whereas others examine the independent factors of SES such as education and income. Noble et al. suggest parental education and family income may have different impact on the child as income is more strongly associated with brain and executive function development whereas maternal education is more associated with language development (Nobel, Sowell, & Houston, 2012; Noble et al., 2015). Moving forward, consistency in the selection of SES measures would be ideal. Future studies should be aware of the importance of choosing a measure of SES and the potential impact on the interpretation of results.

Research Aim 5: Does wave 1 SES relate to differences in cortisol reactivity (wave 1 or wave 2)?

Lower SES environments are highly stressful and can impact the way a child responds and regulates stress. Therefore, we predicted that SES at wave 1 would be related to the cortisol reactivity of the child. In the current study, earlier SES was related to cortisol reactivity of the child but only at wave 2. The pattern of results suggest lower SES is related to smaller changes in cortisol levels in response to a stressor (AUCi) at wave 2. There was a marginal positive association between SES at wave 1 and wave 2 AUCi. The relation between SES risk composite at wave 1 and wave 2 AUCi was significant in the negative direction. Both of these associations support previous studies suggesting children from low SES backgrounds have a blunted response or have less of a response to stressors than children from higher SES backgrounds (Blair, Granger, & Razza; 2005; Blair & Raver, 2012; Blair et al., 2013).

Previous studies of SES differences in cortisol reactivity have been somewhat mixed with some studies showing lower whereas others showing higher levels of cortisol associated with lower SES. One of the major factors that could contribute to the inconsistencies is the age of the child. As an explanation of the inconsistency in the literature, the authors suggest young children from low SES backgrounds show hypercortisolism and in adolescents/adults from lower SES backgrounds show hypocortisolism. The flip in the direction of the association is suggested to be related to the impact of puberty on the developmental trajectory of the cortisol response, as (Ursache, Noble, & Blair, 2015) showed that in younger children the association between SES and cortisol reactivity is negative, whereas in older children/adolescents the association is positive.

The question of timing arises again whilst considering when SES is "getting under the skin" and impacting stress regulation in children. Previous studies show the effect of SES on cortisol arises more clearly as children grow older. The difference in basal cortisol levels in 6-10 year olds gradually become more apparent (Lupien, King, Meaney, & McEwen, 2001). In the current study, there was not a significant association between SES at wave 1 and cortisol reactivity at wave 1. However, the association between SES at wave 1 and cortisol reactivity at wave 2 was impacted when accounting for wave 1 cortisol reactivity. This suggests the SES environment may be impacting the stress regulation system at a younger age but it is not significant until the child is older. The cumulative stress or chronicity of a low SES environment may be playing a role as the amount of time a child is exposed to a low SES environment could determine the impact of stress on neural development and executive function. The chronicity of poverty is shown to relate to 4 year olds executive function ability (Raver, Blair, & Willoughby, 2013). Therefore, the amount of time spent in a low SES

environment, particularly in the current sample, may not be large enough to have detectable differences until wave 2.

Research Aim 4: How does SES relate to neural measures of executive function?

Low SES environments are associated with chronic stress which can cause neural changes within the PFC such as dendritic shortening and remodeling (Teicher et al., 2003; McEwen, 2007; Mackey, Raizada, & Bunge, 2012; McEwen, 2013). Children from low SES backgrounds are shown to have less grey matter development overall and specifically less grey matter in the frontal cortex (Hanson et. al., 2013; Noble et al., 2015). Therefore, higher SES was predicted to be associated with higher overall total grey matter and larger cortical thickness within the PFC. Results of the current study confirmed these predictions as higher SES was related to higher total grey matter. When examining the association between SES and the cortical thickness of the specific PFC regions, SES was positively related to the right rostral anterior cingulate cortical thickness. Although the SES income and average parental education measure was marginally related to the right rostral anterior cingulate cortical thickness, the SES risk composite was significantly related to the right rostral anterior cingulate cortical thickness. There was a marginal positive association between SES and the cortical thickness of the right pars triangularis as well.

Research Aims 6-9: Mediations of the associations between SES (wave 1), cortisol reactivity (wave 1 or 2), PFC (wave 2), and executive function (wave 2).

Considering the bigger picture of these research questions, a low SES environment is stressful and can alter a child's stress response and regulation as well as have damaging effects on neural development. These neural changes were predicted to impact the processes that rely on the PFC such as executive function. Therefore, the effect of the high stress of the

lower SES environments at wave 1 on the wave 2 executive function was predicted to be partially mediated by the PFC volumes at wave 2. When the actual mediations were examined, only one mediation was significant. The association between SES and executive function was significantly mediated by the right pars triangularis cortical thickness. As previously discussed, the pars triangularis is component of the inferior frontal cortex which is a major component of the Cognitive Control Network supporting executive function. Previous neural studies examining SES differences suggest children from lower SES environments have less activation within the inferior frontal cortex when performing executive function tasks which relates to worse executive function abilities (Finn et al., 2016). The significant mediation of the right pars triangularis within the inferior frontal cortex supports the claim that the alterations in the PFC mediate the association between SES and executive function. However, it must be noted that multiple mediations models and analyses were conducted, which raises the issue of multiple comparisons and Type I error. Although other mediations were predicted, we believe the issue may be related to the power of the analyses given the multiple variables in each model and not a large enough sample size. The distribution of the sample and the variables may also have been a contributing factor. A larger, more diverse sample would likely result in more significant mediations, as we found significant associations between each of the variables independently.

Two regions that were significantly related to both cortisol reactivity and SES were the ACC and inferior frontal cortex. These results suggest the ACC and inferior frontal cortex may be part of the network that is impacted by stress regulation as a result of the SES environment which in turn impacts the processes that rely on these regions such as executive function. As previously discussed, these two regions are major components of the Cognitive

Control Network. The current study is one of the first to show associations between SES, cortisol reactivity, and executive function in specific prefrontal regions. More specifically, the current study showed in the ACC, the change in levels of cortisol in response to a stressor (AUCi) at wave 2 positively related to cortical thickness. SES was also positively related to increases in cortical thickness in these regions. Overall the results suggest a child raised in a higher SES background have a larger change of cortisol levels in response to a stressor which may promote neural development within the ACC. As previously discussed, the dysregulation of the HPA axis is associated with decreases in development of the ACC (Gianaros, et al., 2007; McEwen & Gianaros, 2010 for review). These results suggest the dysregulation of the HPA axis impacts the development of the ACC. Potentially, the chronic stress of a low SES environment may cause dysregulation of the HPA axis and undermine the development of the ACC which in turn impacts the abilities that rely on this region such as inhibition and conflict monitoring.

In regards to the inferior frontal cortex, the current study found the total magnitude of cortisol released in response to a stressor (AUCg) at wave 2 was positively related to cortical thickness of the right inferior frontal cortex. These results suggest the overall higher response to a stressor may promote neural development of the inferior frontal cortex while a smaller magnitude of cortisol response to a stressor may hamper development. As previously discussed the inferior frontal cortex is a major component of the network supporting executive function especially inhibition. Given the importance of IFC in inhibition, not surprisingly altered functioning of the inferior frontal cortex has been associated with impulsivity (Arons, 2007). Within the current study, the cortical thickness of the inferior frontal cortex also mediated the association between SES and EF. Validating the link of

inferior frontal cortex and executive function while highlighting the association with SES. However, the models examining cortisol reactivity mediating the association between SES and cortical thickness in the inferior frontal cortex were not significant, again likely due to the distribution of the SES measure and sample size on the power of these analyses. However, the association between each of those variables was significant, SES and cortisol reactivity, cortisol reactivity and inferior frontal cortex cortical thickness, and SES and inferior frontal cortex cortical thickness. Although these relations and mediations need to be replicated and explored with larger data sets, these results are a step in the right direction of understanding if SES is impacting the inferior frontal cortex via stress regulation differences as previous research suggesting children from lower SES backgrounds have a blunted response or less secretion of cortisol in response to a stressor which is detrimental to neural development (Blair, Granger, & Razza, 2005; Blair et al., 2011; McEwen & Gianaros, 2011; McEwen & Morrison, 2013).

One main point to consider is the definition of stress and level of stress captured in the current study. We showed a positive association between the total magnitude of cortisol secreted in response to a stressor (AUCg) and cortical thickness in multiple regions. However, this highlights a major question when examining the association between stress and development, that is, what is considered toxic stress? In a general sense, there is a certain level of stress that is optimal for learning as described originally by the Yerkes-Dodson curve (Yerkes & Dodson, 1908) and more specifically adapted to arousal and performance with by Hebb (1955). The association between arousal and performance is suggested to be an inverted-U shape curve as a certain amount of stress or arousal is beneficial for learning; however, at some point the level of stress is detrimental to learning and performance (Yerkes

& Dodson, 1908; Hebb, 1955). Given the sample of the participants of the current study, numerous children may fall under a healthy stress regulation and cortisol reactivity response promoting development. Multiple researchers and theories agree that a certain level of high stress is damaging to the brain and body such as allostatic load. Within the Biodevelopmental Framework (Shonkoff, 2010) there are three levels of stress: positive, tolerable, and toxic. Positive stress is the short-term increase in arousal that can be beneficial for the body and learning. Tolerable stress is stress that has the potential to impact neural development but may not impact every individual if protective factors are present. On the other hand, toxic stress has damaging effects on the body and brain. It is possible that the current study is capturing more of the positive and tolerable stress rather than the toxic stress. A major component this study fails to consider is protective factors and resilience of the child. Thus, individual differences, along with the effect of moderating protective factors should be addressed in future studies.

Although the current study was a step in the right direction to better understanding how cortisol reactivity relates to the PFC cortical thickness and executive function, there are various lines of research that should be considered for future studies. First, replicating this study on a larger level with larger sample sizes would allow the complex picture of SES impacting the brain and cognitive functioning to be better understood. Second, bigger picture studies considering other factors that are important for relationship between SES and cognitive abilities including the parent-child dynamic, language abilities, academic measures, and stress levels of the parents would be helpful to better address the complex model of SES. Third, children are not all impacted by an SES environment in the same way as there are various factors that puts a child more at risk or more resilient to environments. Future studies

should also address these factors and examine how and what factors moderate the relationship between SES and cognitive abilities.

A broader understanding of how SES impacts the brain and executive function is crucial to inform better interventions and prevention of the negative outcomes associated with lower SES environments. In the bigger picture, a better understanding of the mechanism of how environmental stress gets under the skin of children and impacts their development would inform prevention of various risks associated with chronic environmental stress including physical and mental health. To create effective interventions or preventions, a greater understanding of the mechanism is crucial to understand what the causes of the issues is which eventually can lead to better prevention tactics. The greater understanding of the neuroscience underlying SES differences in EF and the role of stress regulation could inform caregivers and teachers to prioritize healthy stress regulation or a possible level of intervention to teach children stress coping mechanisms. At the policy level, this knowledge could inform policy makers to better understand the differences in children from low SES backgrounds and influence policies impacting these children and their environment.

Limitations

Several limitations in the current study should be considered for future studies. 1) The length of time a child is exposed to a low SES environment could determine the impact of stress on neural development and executive function. The chronicity of poverty is shown to relate to 4 year olds executive function ability (Raver, Blair, & Willoughby, 2013). Future studies should include this to better understand the impact of the environment on the child. 2) Numerous analyses and mediation models were conducted within the current study. There was no correction for multiple comparisons within the current analyses which increases the

likelihood of erroneous findings and type 1 errors. Therefore, the audience should take the risk of multiple comparisons into account when interpreting the findings from the current study. To truly determine if these associations and mediations are present within a larger model, future studies need to address these complex questions with larger sample sizes. 3) SES is a complex factor and the measure of SES selected in the current study may not be ideal. A more specific measure of SES, such as the income to needs ratio, may have better captured the SES construct. Moving forward, future studies should be aware of choosing a measure of SES and how the measure may change the interpretation of results. 4) Within the current study the distribution of SES is also a concern as there were not very many low SES families. To address external validity, these research questions need to be replicated with a different sample with more children from low SES backgrounds. 5) To truly understand the developmental effects of how the environment impacts stress regulation and neural development, a neural measures at an earlier wave of data collection is necessary. The results of the current study cannot truly decipher when the neural changes occurred. These neural differences could be arising as early as prenatal periods and it would be beneficial to have earlier neural measures to determine the developmental trajectories of children from different SES backgrounds. 6) The measures of executive function used in the current study appeared to tap into different components of executive function and may not have been the most consistent measure of executive function over development. Ideally, a group of developmentally appropriate task that tap into the same components of executive function would be used to keep the measure of executive function consistent. 7) A larger sample size would be beneficial for examining the larger picture mediation models and allow a clearer picture of these complex models to arise. 8) Although this study was motivated by the initial

question of how SES impacts academic achievement, there were no academic measures available but would be beneficial moving forward.

General Conclusions

The current study examined how stress regulation impacts neural development and executive function. This association was addressed as a potential mechanism of how SES impacts executive function. In general, the results support the hypothesis that early differences in SES environments relate to differences in stress regulation. Individual differences in cortisol reactivity were related to executive function, neural development overall, and regional cortical thickness differences within the PFC. SES was related to differences in cortisol reactivity, executive function, overall brain volume, and regional cortical thickness differences within the PFC. The ACC and inferior frontal cortex were separately related to cortisol reactivity and SES. These results suggest the inferior frontal cortex and ACC may potentially underlie the mechanism of how SES impacts executive function via stress regulation or dysregulation impacting the development of these regions. The current study was one of the first to show data to support a low SES environment may impact neural and executive function through alterations in stress response and regulation. This study was just a first step toward better understanding how SES environments get under the skin of children. Future studies should continue to examine the details and caveats of these complex associations as well as aim to replicate these findings on a larger scale.

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Supplementary Table 1: Correlation matrix of all variables

Variables																												
EFT1																												
EFT2	.12																											
R superior frontal	.10	-.09																										
R rostral mF	.09	-.19	.78**																									
R rostral ACC	.16	.04	.51**	.48**																								
R precentral	.28*	.15	.61**	.61**	.43**																							
R pars triangularis	.08	-.28*	.64**	.70**	.39**	.49**																						
R pars orbitalis	.15	.03	.47**	.56**	.36**	.42**	.51**																					
R pars opercularis	.19	.06	.56**	.60**	.49**	.58**	.49**	.46**																				
R insula	.24	.05	.29*	.25**	.27**	.31*	.39**	.24	.31*																			
R frontal pole	.03	-.10	.51**	.61**	.46**	.35**	.43**	.41**	.45**	.20																		
R caudal mF	.03	.04	.73**	.62**	.32**	.61**	.42**	.45**	.49	.18	.33**																	
R caudal ACC		.06	.16	-.01	.30**	.13	.06	-.02	.02	-.02	-.06	.18																
L superior frontal	.13	-.15	.87**	.76**	.51**	.57**	.69**	.49**	.50**	.36**	.55**	.60**	.20															
L rostral mF	.18	-.18	.63**	.79**	.33**	.56*	.60**	.42**	.48**	.32**	.47**	.45**	-.02	.69**														
L rostral ACC	.12	.00	.29**	.24	.37**	.20	.08	.14	.02	.16	.26*	.23	.07	.30**	.18													
L precentral	.23	.13	.69**	.56**	.38**	.78**	.53**	.45**	.56**	.47**	.40**	.56**	.11	.68**	.60**	.21												
L pars triangularis	.01	.07	.19	.24	.11	.30**	.32*	.32*	.13	.26*	.22	.09	.05	.15	.23	.11	.24											
L pars orbitalis	.07	-.18	.28*	.35**	.22	.30*	.47**	.36**	.17	.28*	.36**	.17	.17	.39**	.47**	.29*	.33**	.41**										
L pars opercularis	.23	-.08	.51**	.50**	.28*	.50**	.41**	.42**	.55**	.33**	.49**	.35**	.12	.56**	.65**	.01	.60**	.12	.38**									
L insula	.20	-.07	.49**	.48**	.31*	.43**	.51**	.40**	.39**	.56**	.35**	.48**	-.03	.48**	.48**	.22	.60**	.26*	.44**	.47**								
L frontal pole	.05	.06	.46**	.51**	.23	.35**	.35**	.36**	.36**	.35**	.51**	.37**	-.17	.48**	.60**	.19	.45**	.07	.29	.52**	.47**							
L caudal mF	.21	.02	.68**	.55**	.39**	.58**	.47**	.48**	.52**	.38**	.25*	.65**	.14	.63**	.58**	.19	.75**	.18	.41**	.51**	.63**	.45**						
Left caudal ACC	.17	.08	.39**	.22	.39**	.24	.20	.61	.19	.26*	.20	.30*	.47*	.38**	.20	.43**	.21	.08	.20	.20	.13	.22	.17					
T1 AUC_a (log_{10})	-.09	-.08	.14	.11	.14	.08	.03	.12	.02	-.10	.26*	.28*	-.03	.12	-.06	.19	.02	.25	.07	-.04	.01	.07	.04	.11				
T1 AUC_i (log_{10})	.04	.00	-.04	-.16	.00	-.01	-.04	.01	-.17	.01	-.06	-.24	.16	.04	.10	.02	.03	-.01	.05	.06	.01	.05	.09	-.12	-.32**			
T2 AUC_a (log_{10})	.09	-.18	-.11	-.10	.02	.02	-.11	-.04	-.18	-.06	-.15	-.07	.07	-.12	-.01	.17	-.01	.18	.14	-.05	.18	-.18	.07	.01	.16	-.01		
T2 AUC_i (log_{10})	.05	-.02	-.05	-.07	-.07	.01	-.03	-.08	-.28*	.02	-.20	.01	.10	-.07	-.02	.24	-.06	.13	.04	-.09	.14	-.20	.03	-.01	.04	.06	.22*		
SES	.01	.12	.22	-.01	.32*	.16	-.06	-.02	.17	.02	.20	.06	.01	.11	.06	.11	.28**	.01	.05	.07	.03	.12	.23	.11	.07	.07	.04	-.19	
SES Risk Composite	.02	-.14	-.308*	-.10	-.35**	-.23	-.04	-.05	-.27*	-.01	-.23	-.18	.02	-.17	-.14	-.12	-.33*	-.05	-.10	-.11	-.08	-.18	-.31*	-.15	-.06	-.02	<.01	.24*	-.93*

Supplementary Table 2: Mediations of the association between cortisol reactivity and executive function by PFC cortical thickness

Dependent Measure	Predictor	Covariate	Mediator	Direct Effect	Indirect Effect	Boot SE	Boot Lower CI	Boot Upper CI
W2 Executive Function	W1 AUCi	TGM, Age, Gender, MD	Right Superior Frontal	-.8006	-.0788	.5451	-1.4817	.6033
	W1 AUCg	TGM, Age, Gender, MD		.3183	.0006	.1138	-.2524	.2081
	W2 AUCi	TGM, Age, Gender, MD		-.9078	-.1234	.3399	-.8722	.4259
	W2 AUCg	TGM, Age, Gender, MD		-.3378	-.0103	.1102	-.2136	.2470
W2 Executive Function	W1 AUCi	TGM, Age, Gender, MD	Right Rostral Middle Frontal	-1.2085	.3292	.4594	-.6629	1.0917
	W1 AUCg	TGM, Age, Gender, MD		.2988	.0200	.1102	-.1757	.2729
	W2 AUCi	TGM, Age, Gender, MD		-.9699	-.0613	.3334	-.7449	.5987
	W2 AUCg	TGM, Age, Gender, MD		-.3451	-.0030	.1182	-.1893	.2943
W2 Executive Function	W1 AUCi	TGM, Age, MD	Right Rostral Anterior Cingulate	-.9476	-.0004	.1541	-.2842	.3039
	W1 AUCg	TGM, Age, MD		.3907	-.0048	.0550	-.1631	.0799
	W2 AUCi	TGM, Age, MD		-1.1203	.0033	.1087	-.2223	.2473
	W2 AUCg	TGM, Age, Gender, MD		-.3446	-.0035	.0528	-.1641	.0723
W2 Executive Function	W1 AUCi	TGM, Age, Gender, MD	Right Precentral	-.7934	-.0860	.4451	-1.079	.6804
	W1 AUCg	TGM, Age, Gender, MD		.3194	-.0006	.1176	-.2672	.1992
	W2 AUCi	TGM, Age, Gender, MD	-	-.9200	-.1111	.2458	-.8705	.1705

	W2 AUCg	TGM, Age, Gender, MD		-.2919	-.0562	.0971	-.3382	.0666
W2 Executive Function	W1 AUCi	TGM, Age, Gender, MD	Right Pars Triangularis	-.8696	-.0098	.6145	-1.6662	.7382
	W1 AUCg	TGM, Age, Gender, MD		.2519	.0669	.1290	-.1269	.3994
	W2 AUCi	TGM, Age, Gender, MD		-.7980	-.2331	.3933	-1.1886	.4408
	W2 AUCg	TGM, Age, Gender		-.3469	-.0012	.1477	-.2107	.3891
W2 Executive Function	W1 AUCi	TGM, Age, Gender, MD	Right Pars Orbitalis	-.8042	-.0751	.1965	-1.1589	.0803
	W1 AUCg	TGM, Age, Gender, MD		.3244	-.0055	.0624	-.1914	.0929
	W2 AUCi	TGM, Age, Gender, MD		-1.0076	-.0235	.1643	-.4723	.2269
	W2 AUCg	TGM, Age, Gender, MD		-.3296	-.0184	.0671	-.2526	.0626
W2 Executive Function	W1 AUCi	TGM, Age, Gender, MD	Right Pars Opercularis	-1.1032	.2239	.3903	-.3322	1.0471
	W1 AUCg	TGM, Age, Gender, MD		.2641	.0548	.1009	-.0582	.4105
	W2 AUCi	TGM, Age, Gender, MD		-1.2878	.2567	.2777	-.0531	1.1367
	W2 AUCg	TGM, Age, Gender, MD		-.3718	.0237	.0593	-.0360	.2435
W2 Executive Function	W1 AUCi	TGM, Age, MD	Right Insula	-.9820	.0340	.3647	-.3119	1.4642
	W1 AUCg	TGM, Age, MD		.4139	-.0280	.0803	-.3285	.0621
	W2 AUCi	TGM, Age, MD		-1.1079	-.0091	.1631	-.4512	.2616
	W2 AUCg	TGM, Age, Gender, MD		-.3466	-.0015	.0581	-.1682	.0907
W2 Executive Function	W1 AUCi	TGM, Age, Gender, MD	Right Frontal Pole	-.8381	-.0412	.2521	-1.1295	.1926
	W1 AUCg	TGM, Age, Gender, MD		.3547	-.0359	.0744	-.3048	.0437

	W2 AUCi	TGM, Age, Gender, MD		-1.1007	.0695	.1962	-.1890	.6504
	W2 AUCg	TGM, Age, Gender, MD		-.3438	-.0043	.0746	-.1992	.1000
W2 Executive Function	W1 AUCi	TGM, Age, Gender, MD	Right Caudal Middle Frontal	-1.5771	.6978	.6649	-.5046	1.9580
	W1 AUCg	TGM, Age, Gender, MD		.5552	-.2364	.1717	-.6903	.0061
	W2 AUCi	TGM, Age, Gender, MD		-.8834	-.1478	.2016	-.7294	.0977
	W2 AUCg	TGM, Age, Gender, MD		-.3327	-.0154	.0842	-.1999	.1302
W2 Executive Function	W1 AUCi	TGM, Age, MD	Right Caudal Anterior Cingulate	-1.1097	.1617	.2429	-.1046	.9401
	W1 AUCg	TGM, Age, MD		.3697	.0162	.0677	-.0549	.2874
	W2 AUCi	TGM, Age, MD		-1.1350	.0180	.1415	-.1811	.4317
	W2 AUCg	TGM, Age, Gender, MD		-.3494	.0013	.0651	-.1227	.1434
W2 Executive Function	W1 AUCi	TGM, Age, Gender, MD	Left Superior Frontal	-.5466	-.4014	.6211	-2.2483	.2953
	W1 AUCg	TGM, Age, Gender, MD		.3070	.0118	.1004	-.1733	.2328
	W2 AUCi	TGM, Age, Gender, MD		-.9978	-.0333	.3253	-.8176	.4649
	W2 AUCg	TGM, Age, Gender, MD		-.3694	.0213	.1014	-.1260	.3299
W2 Executive Function	W1 AUCi	TGM, Age, MD	Left Rostral Middle Frontal	-.3972	-.3684	.6507	-2.3019	.3419
	W1 AUCg	TGM, Age, MD		.2423	.1436	.1395	-.0419	.5202
	W2 AUCi	TGM, Age, MD		-1.1001	-.0169	.3346	-.7838	.5030
	W2 AUCg	TGM, Age, Gender, MD		-.3103	-.0378	.1215	-.3117	.1834
W2 Executive Function	W1 AUCi	TGM, Age, Gender, MD	Left Rostral Anterior Cingulate	-.8504	-.0289	.2160	-.7535	.1057

	W1 AUCg	TGM, Age, Gender, MD		.3749	-.0560	.0782	-.3313	.0315
	W2 AUCi	TGM, Age, Gender, MD		-.9248	-.1063	.1995	-.7577	.1353
	W2 AUCg	TGM, Age, Gender, MD		-.3131	-.0350	.0808	-.3336	.0472
W2 Executive Function	W1 AUCi	TGM, Age, Gender, MD	Left Precentral	-.6800	-.1993	.6054	-1.9820	.5694
	W1 AUCg	TGM, Age, Gender, MD		.2392	.0797	.1153	-.0648	.4278
	W2 AUCi	TGM, Age, Gender, MD		-.9781	-.0530	.1906	-.6155	.2083
	W2 AUCg	TGM, Age, Gender, MD		-.3015	-.0465	.0753	-.2632	.0437
W2 Executive Function	W1 AUCi	TGM, Age, Gender, MD	Left Pars Triangularis	-.8951	.0157	.3660	-.3471	1.4582
	W1 AUCg	TGM, Age, Gender, MD		.3034	.0155	.0984	-.1189	.3112
	W2 AUCi	TGM, Age, Gender, MD		-1.0432	.0120	.1950	-.2737	.5299
	W2 AUCg	TGM, Age, Gender, MD		-.3630	.0150	.0888	-.1109	.2695
W2 Executive Function	W1 AUCi	TGM, Age, MD	Left Pars Orbitalis	-.8973	-.0507	.2152	-.8365	.1761
	W1 AUCg	TGM, Age, MD		.3820	.0039	.0511	-.0852	.1287
	W2 AUCi	TGM, Age, MD		-1.0678	-.0492	.1484	-.5274	.1420
	W2 AUCg	TGM, Age, MD, Gender		-.2776	-.0705	.0801	-.3073	.0216
W2 Executive Function	W1 AUCi	TGM, Age, MD	Left Pars Opercularis	-.8079	-.1401	.2306	-.9106	.0982
	W1 AUCg	TGM, Age, MD		.3271	.0588	.0842	-.0356	.3231
	W2 AUCi	TGM, Age, MD		-1.1827	.0657	.2158	-.2531	.7111
	W2 AUCg	TGM, Age, Gender, MD		-.3293	-.0189	.0902	-.2974	.0906
W2 Executive Function	W1 AUCi	TGM, Age, MD	Left Insula	-.8161	-.1319	.3461	-1.0849	.3471

	W1 AUCg	TGM, Age, MD		.3240	.0619	.0894	-.0477	.3181
	W2 AUCi	TGM, Age, MD		-.8077	-.3094	.2270	-.9486	-.0062
	W2 AUCg	TGM, Age, Gender, MD		-.1776	-.1705	.1102	-.4817	-.0216
W2 Executive Function	W1 AUCi	TGM, Age, MD	Left Frontal Pole	-.9348	-.0132	.1738	-.4941	.2781
	W1 AUCg	TGM, Age, MD		.3828	.0031	.0444	-.0641	.1354
	W2 AUCi	TGM, Age, MD		-1.1498	.0328	.1286	-.1036	.5068
	W2 AUCg	TGM, Age, Gender, MD		-.3601	.0120	.0385	-.0294	.1554
W2 Executive Function	W1 AUCi	TGM, Age, MD	Left Caudal Middle Frontal	-.6390	-.3090	.6322	-2.1199	.3696
	W1 AUCg	TGM, Age, MD		.3426	.0433	.1027	-.1368	.2822
	W2 AUCi	TGM, Age, MD		-1.0474	-.0697	.1680	-.5630	.1668
	W2 AUCg	TGM, Age, Gender, MD		-.2672	-.0809	.0752	-.3072	.0157
W2 Executive Function	W1 AUCi	TGM, Age, MD	Left Caudal Anterior Cingulate	-.8605	-.0875	.1481	-.5845	.0852
	W1 AUCg	TGM, Age, MD		.3631	.0227	.0445	-.0259	.1820
	W2 AUCi	TGM, Age, MD		-1.1091	-.0079	.0831	-.2717	.1035
	W2 AUCg	TGM, Age, Gender, MD		-.3512	.0031	.0420	-.0481	.1455

Significant <.05 are shown in bold and marginal results <.10 are shown in bold italic font; W1: Wave 1 W2: Wave 2 MD: Maternal Depression

Supplementary Table 3: Mediation of the association between SES and executive function by PFC cortical thickness

Dependent Measure	Predictor	Covariate	Mediator	Direct Effect	Indirect Effect	Boot SE	Boot Lower CI	Boot Upper CI
W2 Executive Function	SES	TGM, Age, Gender, MD	Right Superior Frontal	.0714	-.0046	.0173	-.0388	.0279
	SES Risk Composite	TGM, Age, Gender, MD		-.0904	.0188	.0272	-.0281	.0796
W2 Executive Function	SES	TGM, Age, Gender, MD	Right Rostral Middle Frontal	.0492	.0176	.0159	-.0039	.0564
	SES Risk Composite	TGM, Age, Gender, MD		-.0548	-.0168	.0238	-.0761	.0146
W2 Executive Function	SES	TGM, Age, MD	Right Rostral Anterior Cingulate	.0795	-.0080	.0121	-.0418	.0094
	SES Risk Composite	TGM, Age, MD		-.0948	.0126	.0212	-.0200	.0672
W2 Executive Function	SES	TGM, Age, Gender, MD	Right Precentral	.0662	.0006	.0107	-.0204	.0254
	SES Risk Composite	TGM, Age, Gender, MD		-.0763	.0047	.0176	-.0194	.0592
W2 Executive Function	SES	TGM, Age, Gender, MD	Right Pars Triangularis	**.0421**	**.0247**	**.0151**	**.0015**	**.0608**
	SES Risk Composite	TGM, Age, Gender, MD		-.0438	-.0278	.0239	-.0822	.0101
W2 Executive Function	SES	TGM, Age, Gender, MD	Right Pars Orbitalis	.0625	.0043	.0115	-.0065	.0418
	SES Risk Composite	TGM, Age, Gender, MD		-.0647	-.0069	.0193	-.0721	.0087
W2 Executive Function	SES	TGM, Age, Gender, MD	Right Pars Opercularis	.0675	-.0007	.0090	-.0276	.0136
	SES Risk Composite	TGM, Age, Gender, MD		-.0790	.0074	.0172	-.0104	.0787

W2 Executive Function	SES	TGM, Age, MD	Right Insula	.0704	.0011	.0086	-.0088	.0260
	SES Risk Composite	TGM, Age, MD		-.0799	-.0023	.0141	-.0472	.0156
W2 Executive Function	SES	TGM, Age, Gender, MD	Right Frontal Pole	.0657	.0011	.0098	-.0158	.0261
	SES Risk Composite	TGM, Age, Gender, MD		-.0685	-.0031	.0157	-.0457	.0228
W2 Executive Function	SES	TGM, Age, Gender, MD	Right Caudal Middle Frontal	.0569	.0099	.0184	-.0120	.0590
	SES Risk Composite	TGM, Age, Gender, MD		-.0695	-.0021	.0295	-.0732	.0455
W2 Executive Function	SES	TGM, Age, MD	Right Caudal Anterior Cingulate	.0667	.0047	.0084	-.0043	.0367
	SES Risk Composite	TGM, Age, MD		-.0749	-.0073	.0137	-.0559	.0070
W2 Executive Function	SES	TGM, Age, MD, Gender	Left Superior Frontal	.0625	.0043	.0174	-.0285	.0435
	SES Risk Composite	TGM, Age, MD, Gender		-.0689	-.0027	.0277	-.0627	.0512
W2 Executive Function	SES	TGM, Age, MD	Left Rostral Middle Frontal	.0654	.0061	.0129	-.0148	.0362
	SES Risk Composite	TGM, Age, MD		-.0843	.0021	.0215	-.0431	.0434
W2 Executive Function	SES	TGM, Age, Gender, MD	Left Rostral Anterior Cingulate	.0700	-.0032	.0084	-.0296	.0070
	SES Risk Composite	TGM, Age, Gender, MD		-.0767	.0051	.0143	-.0126	.0523
W2 Executive Function	SES	TGM, Age, Gender, MD	Left Precentral	.0707	-.0039	.0111	-.0369	.0106
	SES Risk Composite	TGM, Age, Gender, MD		-.0800	.0084	.0181	-.0122	.0722
W2 Executive Function	SES	TGM, Age, Gender, MD	Left Pars Triangularis	.0672	-.0004	.0064	-.0178	.0086
	SES Risk Composite	TGM, Age, Gender, MD		-.0719	.0002	.0101	-.0166	.0222

W2 Executive Function	SES	TGM, Age, MD	Left Pars Orbitalis	.0719	-.0004	.0063	-.0159	.0106
	SES Risk Composite	TGM, Age, MD		-.0859	.0036	.0119	-.0114	.0422
W2 Executive Function	SES	TGM, Age, MD	Left Pars Opercularis	.0700	.0015	.0094	-.0141	.0272
	SES Risk Composite	TGM, Age, MD		-.0822	-.0001	.0159	-.0338	.0349
W2 Executive Function	SES	TGM, Age, MD	Left Insula	.0634	.0081	.0086	-.0019	.0360
	SES Risk Composite	TGM, Age, MD		-.0734	-.0089	.0135	-.0508	.0089
W2 Executive Function	SES	TGM, Age, MD	Left Frontal Pole	.0712	.0002	.0042	-.0067	.0122
	SES Risk Composite	TGM, Age, MD		-.0821	-.0002	.0065	-.0176	.0111
W2 Executive Function	SES	TGM, Age, MD	Left Caudal Middle Frontal	.0777	-.0062	.0076	-.0289	.0042
	SES Risk Composite	TGM, Age, MD		-.1015	.0192	.0159	-.0023	.0643
W2 Executive Function	SES	TGM, Age, MD	Left Caudal Anterior Cingulate	.0719	-.0004	.0057	-.0160	.0092
	SES Risk Composite	TGM, Age, MD		-.0832	.0009	.0110	-.0180	.0291

Significant <.05 are shown in bold and marginal results <.10 are shown in bold italic font; W1: Wave 1 W2: Wave 2 MD: Maternal Depression

Supplementary Table 4: Mediation of the association between SES and PFC cortical thickness by cortisol reactivity.

Dependent Measure	Predictor	Covariate	Mediator	Direct Effect	Indirect Effect	Boot SE	Boot Lower CI	Boot Upper CI
TGM	SES IE	-	W1 AUCi	8297.51	-561.35	626.35	-2543.13	164.95
		-	W1 AUCg	7578.22	157.95	1012.33	-1306.46	3157.86
		-	W2 AUCi	7486.07	779.84	1400.75	-496.02	5537.99
		Gender	W2 AUCg	8750.01	184.25	844.18	-758.90	2738.20
Right Superior Frontal	SES IE	TGM, Gender	W1 AUCi	.0062	.002	.0031	-.0033	.0078
		TGM, Gender	W1 AUCg	.0063	.0002	.0016	-.0020	.0054
		TGM, Gender	W2 AUCi	.0038	-.0010	.0023	-.0092	.0019
		TGM, Gender	W2 AUCg	.0029	.0000	.0015	-.0038	.0026
Right Rostral Middle Frontal	SES IE	TGM, Gender	W1 AUCi	-.0211	-.0012	.0031	-.0077	.0050
		TGM, Gender	W1 AUCg	-.0226	.0003	.0019	-.0019	.0072
		TGM, Gender	W2 AUCi	-.0221	.0010	.0036	-.0039	.0121
		TGM, Gender	W2 AUCg	-.0208	-.0002	.0021	-.0061	.0025
Right Rostral Anterior Cingulate	SES IE	TGM	W1 AUCi	.0257	-.0005	.0022	-.0049	.0042
		TGM	W1 AUCg	.0255	-.0003	.0025	-.0081	.0028
		TGM	W2 AUCi	.0297	-.0008	.0031	-.0107	.0034
		TGM, Gender	W2 AUCg	.0239	.0004	.0025	-.0033	.0079
Right Precentral	SES IE	TGM, Gender, Age, MD	W1 AUCi	-.0054	.0007	.0025	-.0021	.0071
		TGM, Gender, Age, MD	W1 AUCg	-.0049	.0002	.0014	-.0015	.0051
		TGM, Gender, Age, MD	W2 AUCi	-.0001	-.0001	.0017	-.0042	.0030
		TGM, Gender, Age, MD	W2 AUCg	-.0002	.0000	.0012	-.0026	.0029

Right Pars Triangularis	SES IE	TGM, Gender	W1 AUCi	-.0149	.0007	.0032	-.0026	.0089
		TGM, Gender	W1 AUCg	-.0152	.0010	.0031	-.0027	.0114
		TGM, Gender	W2 AUCi	-.0205	.0007	.0031	-.0032	.0104
		TGM, Gender	W2 AUCg	-.0194	-.0004	.0022	-.0062	.0029
Right Pars Orbitalis	SES IE	TGM, Gender	W1 AUCi	-.0371	.0034	.0034	-.0001	.0121
		TGM, Gender	W1 AUCg	-.0342	.0005	.0033	-.0032	.0109
		TGM, Gender	W2 AUCi	-.0286	.0011	.0041	-.0035	.0163
		TGM, Gender	W2 AUCg	-.0275	.0000	.0026	-.0059	.0051
Right Pars Opercularis	SES IE	TGM, Gender	W1 AUCi	-.0029	-.0019	.0028	-.0096	.0029
		TGM, Gender	W1 AUCg	-.0054	.0006	.0022	-.0018	.0085
		TGM, Gender	W2 AUCi	-.0026	.0028	.0030	-.0007	.0127
		TGM, Gender	W2 AUCg	.0003	-.0001	.0015	-.0045	.0021
Right Insula	SES IE	TGM	W1 AUCi	-.0052	.0008	.0033	-.0032	.0093
		TGM	W1 AUCg	-.0048	.0004	.0027	-.0026	.0081
		TGM	W2 AUCi	-.0064	-.0021	.0030	-.0120	.0006
		TGM, Gender	W2 AUCg	-.0108	.0003	.0019	-.0021	.0058
Right Frontal Pole	SES IE	TGM, Gender	W1 AUCi	.0133	-.0001	.0040	-.0079	.0092
		TGM, Gender	W1 AUCg	.0140	-.0008	.0043	-.0173	.0032
		TGM, Gender	W2 AUCi	-.0066	.0030	.0054	-.0033	.0219
		TGM, Gender	W2 AUCg	-.0035	-.0002	.0032	-.0083	.0039
Right Caudal Middle Frontal	SES IE	TGM, Gender, Age, MD	W1 AUCi	-.0237	-.0035	.0046	-.0148	.0043
		TGM, Gender, Age, MD	W1 AUCg	-.0258	-.0013	.0035	-.0131	.0031
		TGM, Gender, Age, MD	W2 AUCi	-.0153	-.0005	.0029	-.0102	.0034
		TGM, Gender, Age, MD	W2 AUCg	-.0156	-.0002	.0020	-.0061	.0028

Right Caudal Anterior Cingulate	SES IE	TGM	W1 AUCi	.0081	.0019	.0023	-.0008	.0076
		TGM	W1 AUCg	.0101	-.0001	.0024	-.0064	.0039
		TGM	W2 AUCi	.0157	-.0003	.0025	-.0072	.0036
		TGM, Gender	W2 AUCg	.0156	-.0002	.0021	-.0063	.0030
Left Superior Frontal	SES IE	TGM, Gender	W1 AUCi	-.0013	.0014	.0047	-.0032	.0138
		TGM, Gender	W1 AUCg	-.0001	.0002	.0022	-.0030	.0072
		TGM, Gender	W2 AUCi	-.0045	-.0001	.0026	-.0063	.0046
		TGM, Gender	W2 AUCg	-.0045	-.0001	.0016	-.0054	.0018
Left Rostral Middle Frontal	SES IE	TGM	W1 AUCi	-.0099	.0025	.0046	-.0014	.0140
		TGM	W1 AUCg	-.0079	.0005	.0028	-.0030	.0102
		TGM	W2 AUCi	-.0054	-.0001	.0026	-.0057	.0053
		TGM, Gender	W2 AUCg	-.0076	.0001	.0019	-.0030	.0049
Left Rostral Anterior Cingulate	SES IE	TGM, Gender, MD	W1 AUCi	.0072	.0008	.0026	-.0027	.0082
		TGM, Gender, MD	W1 AUCg	.0091	-.0011	.0037	-.0148	.0030
		TGM, Gender, MD	W2 AUCi	.0157	-.0071	.0076	-.0316	.0010
		TGM, Gender, MD	W2 AUCg	.0075	.0015	.0052	-.0100	.0115
Left Precentral	SES IE	TGM, Gender, Age	W1 AUCi	.0006	.0015	.0042	-.0026	.0127
		TGM, Gender, Age	W1 AUCg	.0013	.0009	.0025	-.0017	.0105
		TGM, Gender, Age	W2 AUCi	.0040	-.0004	.0017	-.0061	.0019
		TGM, Gender, Age	W2 AUCg	.0034	.0001	.0014	-.0020	.0040
Left Pars Triangularis	SES IE	TGM, Gender	W1 AUCi	-.0005	.0006	.0030	-.0052	.0081
		TGM, Gender	W1 AUCg	.0010	-.0008	.0029	-.0117	.0019
		TGM, Gender	W2 AUCi	-.0022	-.0015	.0026	-.0100	.0017

		TGM, Gender	W2 AUCg	-.0042	.0004	.0025	-.0030	.0073
Left Pars Orbitalis	SES IE	TGM, Age	W1 AUCi	.0103	.0020	.0062	-.0045	.0184
		TGM, Age	W1 AUCg	.0123	.0001	.0034	-.0062	.0082
		TGM, Age	W2 AUCi	.0049	-.0023	.0045	-.0175	.0028
		TGM, Age, Gender	W2 AUCg	-.0051	.0007	.0047	-.0067	.0130
Left Pars Opercularis	SES IE	TGM	W1 AUCi	-.0055	.0015	.0025	-.0008	.0081
		TGM	W1 AUCg	-.0043	.0003	.0021	-.0025	.0069
		TGM	W2 AUCi	-.0026	.0000	.0028	-.0051	.0063
		TGM, Gender	W2 AUCg	-.0065	.0003	.0024	-.0030	.0071
Left Insula	SES IE	TGM	W1 AUCi	-.0106	.0015	.0033	-.0019	.0100
		TGM	W1 AUCg	-.0094	.0003	.0022	-.0026	.0070
		TGM	W2 AUCi	-.0070	-.0026	.0025	-.0104	.0003
		TGM, Gender	W2 AUCg	-.0127	.0006	.0028	-.0051	.0067
Left Frontal Pole	SES IE	TGM	W1 AUCi	-.0225	.0046	.0044	.0000	.0159
		TGM	W1 AUCg	-.0182	.0003	.0038	-.0051	.0116
		TGM	W2 AUCi	-.0148	.0025	.0058	-.0049	.0202
		TGM, Gender	W2 AUCg	-.0158	-.0001	.0035	-.0102	.0053
Left Caudal Middle Frontal	SES IE	TGM	W1 AUCi	-.0007	.0025	.0056	-.0030	.0167
		TGM	W1 AUCg	.0214	-.0003	.0027	-.0089	.0028
		TGM	W2 AUCi	.0105	-.0016	.0024	-.0098	.0011
		TGM, Gender	W2 AUCg	.0041	.0004	.0023	-.0034	.0065
Left Caudal Anterior Cingulate	SES IE	TGM	W1 AUCi	.0253	-.0041	.0035	-.0133	.0001
		TGM	W1 AUCg	.0171	.0000	.0026	-.0050	.0063
		TGM	W2 AUCi	.0181	-.0010	.0041	-.0152	.0034
		TGM, Gender	W2 AUCg	.0103	.0003	.0029	-.0035	.0102

Significant <.05 are shown in bold and marginal results <.10 are shown in bold italic font; W1: Wave 1 W2: Wave 2 MD: Maternal Depression

Supplementary Table 5: Mediation of the association between SES Risk Composite and PFC cortical thickness by cortisol reactivity

Dependent Measure	Predictor	Covariate	Mediator	Direct Effect	Indirect Effect	Boot SE	Boot Lower CI	Boot Upper CI
TGM	SES Risk Composite	-	W1 AUCi	-13339.00	206.65	769.94	-531.83	2687.64
		-	W1 AUCg	-12349.38	-782.98	1604.35	-6535.68	826.99
		-	W2 AUCi	-12428.60	-1191.05	2144.14	-7975.40	807.36
		Gender	W2 AUCg	-15357.27	-238.68	1397.48	-4270.25	1687.73
Right Superior Frontal	SES Risk Composite	TGM, Gender	W1 AUCi	-.0160	-.0002	.0033	-.0074	.0026
		TGM, Gender	W1 AUCg	-.0161	-.0001	.0024	-.0063	.0042
		TGM, Gender	W2 AUCi	-.0136	.0020	.0038	-.0028	.0148
		TGM, Gender	W2 AUCg	-.0117	.0001	.0026	-.0043	.0071
Right Rostral Middle Frontal	SES Risk Composite	TGM, Gender	W1 AUCi	.0201	.0014	.0031	-.0028	.0089
		TGM, Gender	W1 AUCg	.0216	-.0001	.0026	-.0076	.0043
		TGM, Gender	W2 AUCi	.0200	-.0013	.0057	-.0191	.0066
		TGM, Gender	W2 AUCg	.0181	.0006	.0037	-.0033	.0134
Right Rostral Anterior Cingulate	SES Risk Composite	TGM	W1 AUCi	-.0435	.0001	.0021	-.0041	.0043
		TGM	W1 AUCg	-.0430	-.0004	.0032	-.0100	.0038
		TGM	W2 AUCi	-.0526	.0019	.0049	-.0042	.0175
		TGM, Gender	W2 AUCg	-.0407	-.0009	.0043	-.0151	.0046
Right Precentral	SES Risk Composite	TGM, Age, Gender, MD	W1 AUCi	.0008	-.0004	.0028	-.0077	.0020
		TGM, Age, Gender, MD	W1 AUCg	.0005	-.0001	.0021	-.0057	.0033
		TGM, Age, Gender, MD	W2 AUCi	-.0054	.0003	.0026	-.0036	.0076
		TGM, Age, Gender, MD	W2 AUCg	-.0052	.0000	.0022	-.0049	.0047

Right Pars Triangularis	SES Risk Composite	TGM, Gender	W1 AUCi	.0115	-.0003	.0043	-.0108	.0042
		TGM, Gender	W1 AUCg	.0094	-.0003	.0041	-.0118	.0061
		TGM, Gender	W2 AUCi	.0210	.0004	.0050	-.0085	.0126
		TGM, Gender	W2 AUCg	.0205	.0010	.0037	-.0029	.0156
Right Pars Orbitalis	SES Risk Composite	TGM, Gender	W1 AUCi	.0519	-.0021	.0045	-.0149	.0012
		TGM, Gender	W1 AUCg	.0498	-.0001	.0050	-.0113	.0074
		TGM, Gender	W2 AUCi	.0359	-.0016	.0070	-.0280	.0063
		TGM, Gender	W2 AUCg	.0343	.0000	.0050	-.0106	.0110
Right Pars Opercularis	SES Risk Composite	TGM, Gender	W1 AUCi	-.0038	.0016	.0027	-.0018	.0112
		TGM, Gender	W1 AUCg	-.0020	-.0002	.0032	-.0094	.0046
		TGM, Gender	W2 AUCi	-.0053	-.0045	.0047	-.0212	.0006
		TGM, Gender	W2 AUCg	-.0102	.0003	.0028	-.0034	.0091
Right Insula	SES Risk Composite	TGM	W1 AUCi	.0117	-.0005	.0033	-.0095	.0023
		TGM	W1 AUCg	.0105	.0007	.0035	-.0040	.0101
		TGM	W2 AUCi	.0126	.0035	.0049	-.0010	.0208
		TGM, Gender	W2 AUCg	.0221	-.0007	.0032	-.0119	.0030
Right Frontal Pole	SES Risk Composite	TGM, Gender	W1 AUCi	-.0254	-.0001	.0044	-.0127	.0064
		TGM, Gender	W1 AUCg	-.0257	.0003	.0059	-.0081	.0164
		TGM, Gender	W2 AUCi	.0123	-.0053	.0094	-.0395	.0057
		TGM, Gender	W2 AUCg	.0066	.0004	.0058	-.0069	.0162
Right Caudal Middle Frontal	SES Risk Composite	TGM, Age, Gender, MD	W1 AUCi	.0243	.0033	.0047	-.0028	.0206
		TGM, Age, Gender, MD	W1 AUCg	.0271	.0006	.0062	-.0092	.0175
		TGM, Age, Gender, MD	W2 AUCi	.0030	.0015	.0049	-.0039	.0192

		TGM, Age, Gender, MD	W2 AUCg	.0040	.0005	.0039	-.0046	.0124
Right Caudal Anterior Cingulate	SES Risk Composite	TGM	W1 AUCi	-.0107	-.0018	.0033	-.0110	.0010
		TGM	W1 AUCg	-.0097	-.0001	.0033	-.0089	.0056
		TGM	W2 AUCi	-.0220	.0006	.0042	-.0063	.0118
		TGM, Gender	W2 AUCg	-.0225	.0004	.0037	-.0047	.0124
Left Superior Frontal	SES Risk Composite	TGM, Gender	W1 AUCi	-.0010	-.0011	.0056	-.0159	.0018
		TGM, Gender	W1 AUCg	-.0020	-.0001	.0030	-.0077	.0050
		TGM, Gender	W2 AUCi	.0041	.0003	.0043	-.0085	.0100
		TGM, Gender	W2 AUCg	.0040	.0004	.0028	-.0029	.0098
Left Rostral Middle Frontal	SES Risk Composite	TGM	W1 AUCi	.0034	-.0016	.0047	-.0150	.0009
		TGM	W1 AUCg	.0009	.0009	.0039	-.0047	.0112
		TGM	W2 AUCi	-.0028	.0006	.0040	-.0072	.0093
		TGM, Gender	W2 AUCg	-.0022	.0000	.0036	-.0064	.0071
Left Rostral Anterior Cingulate	SES Risk Composite	TGM, Gender, MD	W1 AUCi	-.0100	-.0008	.0031	-.0119	.0019
		TGM, Gender, MD	W1 AUCg	-.0110	.0003	.0054	-.0086	.0158
		TGM, Gender, MD	W2 AUCi	-.0263	.0118	.0119	-.0015	.0490
		TGM, Gender, MD	W2 AUCg	-.0108	-.0039	.0084	-.0203	.0147
Left Precentral	SES Risk Composite	TGM, Age, Gender	W1 AUCi	-.0043	-.0012	.0052	-.0159	.0017
		TGM, Age, Gender	W1 AUCg	-.0051	-.0004	.0040	-.0134	.0046
		TGM, Age, Gender	W2 AUCi	-.0083	.0008	.0028	-.0028	.0096
		TGM, Age, Gender	W2 AUCg	-.0071	-.0004	.0026	-.0082	.0029

Left Pars Triangularis	SES Risk Composite	TGM, Gender	W1 AUCi	-.0050	-.0004	.0037	-.0155	.0034
		TGM, Gender	W1 AUCg	-.0057	.0003	.0042	-.0057	.0122
		TGM, Gender	W2 AUCi	.0007	.0027	.0046	-.0028	.0188
		TGM, Gender	W2 AUCg	.0046	-.0011	.0046	-.0147	.0049
Left Pars Orbitalis	SES Risk Composite	TGM, Age	W1 AUCi	-.0193	-.0020	.0089	-.0252	.0031
		TGM, Age	W1 AUCg	-.0210	-.0003	.0064	-.0160	.0104
		TGM, Age	W2 AUCi	-.0013	.0031	.0071	-.0054	.0286
		TGM, Age, Gender	W2 AUCg	.0037	.0019	.0079	-.0243	.0081
Left Pars Opercularis	SES Risk Composite	TGM	W1 AUCi	.0037	-.0009	.0026	-.0090	.0005
		TGM	W1 AUCg	.0021	.0006	.0031	-.0038	.0095
		TGM	W2 AUCi	.0004	.0002	.0045	-.0096	.0090
		TGM, Gender	W2 AUCg	.0104	-.0008	.0046	-.0141	.0045
Left Insula	SES Risk Composite	TGM	W1 AUCi	.0106	-.0009	.0032	-.0105	.0015
		TGM	W1 AUCg	.0091	.0006	.0030	-.0036	.0100
		TGM	W2 AUCi	.0051	.0046	.0043	-.0001	.0186
		TGM, Gender	W2 AUCg	.0171	-.0015	.0049	.0127	.0079
Left Frontal Pole	SES Risk Composite	TGM	W1 AUCi	.0134	-.0029	.0048	-.0164	.0013
		TGM	W1 AUCg	.0099	.0006	.0056	-.0083	.0171
		TGM	W2 AUCi	.0048	-.0036	.0095	-.0049	.0202
		TGM, Gender	W2 AUCg	.0218	-.0038	.0066	-.0206	.0020
Left Caudal Middle Frontal	SES Risk Composite	TGM	W1 AUCi	-.0088	-.0017	.0061	-.0187	.0019
		TGM	W1 AUCg	-.0109	.0005	.0035	-.0042	.0107
		TGM	W2 AUCi	-.0276	.0034	.0042	-.0012	.0176
		TGM, Gender	W2 AUCg	-.0142	-.0011	.0041	-.0115	.0054

Left Caudal Anterior Cingulate	SES Risk Composite	TGM	W1 AUCi	-.0428	.0027	.0037	-.0014	.0132
		TGM	W1 AUCg	-.0397	-.0005	.0034	-.0117	.0039
		TGM	W2 AUCi	-.0381	.0023	.0071	-.0049	.0279
		TGM, Gender	W2 AUCg	-.0211	-.0007	.0050	-.0191	.0051

Significant <.05 are shown in bold and marginal results <.10 are shown in bold italic font; W1: Wave 1 W2: Wave 2 MD: Maternal Depression

Supplementary Table 6: Mediation of the association between SES and executive function by cortisol reactivity

Dependent Measure	Predictor	Covariate	Mediator	Direct Effect	Indirect Effect	Boot SE	Boot Lower CI	Boot Upper CI
W2 Executive Function	SES	Age, MD	W1 AUCi	.0309	-.0016	.0045	-.0167	.0022
		Age, MD	W1 AUCg	.0295	-.0003	.0044	-.0114	.0067
		Age, MD	W2 AUCi	.0366	.0020	.0079	-.0104	.0234
		Age, Gender, MD	W2 AUCg	.0408	-.0030	.0076	-.0238	.0082
W1 Executive Function	SES	Age	W1 AUCi	.0202	.0009	.0044	-.0028	.0151
		Age	W1 AUCg	.0244	-.0033	.0081	-.0384	.0041
W2 Executive Function	SES Risk Composite	Age, MD	W1 AUCi	-.0566	.0013	.0057	-.0038	.0201
		Age, MD	W1 AUCg	-.0553	.0000	.0063	-.0139	.0134
		Age, MD	W2 AUCi	-.0696	-.0027	.0154	-.0407	.0213
		Age, Gender, MD	W2 AUCg	-.0726	.0026	.0126	-.0170	.0376
T1 Executive Function	SES Risk Composite	Age	W1 AUCi	-.0245	-.0005	.0053	-.0130	.0058
		Age	W1 AUCg	-.0292	.0042	.0126	-.0074	.0536

Significant <.05 are shown in bold and marginal results <.10 are shown in bold italic font; W1: Wave 1 W2: Wave 2 MD: Maternal Depression