

ABSTRACT

Title of dissertation: PSYCHOLOGICAL AND NEUROBIOLOGICAL
OUTCOMES OF PARENT-CHILD
ADRENOCORTICAL CONCORDANCE

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Emerging work has examined parent-child concordance of hypothalamic-pituitary-adrenal (HPA) axis functioning (i.e., adrenocortical concordance) which reflects the attunement or association of the stress hormone cortisol between the parent and child. The cortisol awakening response (CAR) is a critical aspect of HPA axis functioning that is sensitive to environmental factors and uniquely predicts psychopathology in youth. HPA axis functioning has also been linked to alterations in brain structure, specifically the hippocampus. The hippocampus is a critical brain region involved in learning and emotional processing and is sensitive to the parenting context, and undergoes change across early childhood. Despite these critical links between the parent-child dyad, HPA axis functioning, and hippocampal structure, no study has examined the longitudinal outcomes of adrenocortical concordance.

The current study examined early parent-child adrenocortical concordance and its concurrent and longitudinal associations with parenting and children's psychopathology and psychosocial functioning, as well as its longitudinal associations with children's hippocampal structure in middle childhood. Participants included 142 parent-child dyads. Parents and children provided cortisol at Wave 1 when children were 3-5 years-old, and 98 dyads returned for the Wave 2 assessment three years later when children were 5-9 years-old. At Wave 1, parents and children provided salivary cortisol samples at waking, and 30 and 45 minutes post-waking across two days to assess the CAR. At Waves 1 and 2, child psychopathology and functioning were assessed through a parent-report clinical interview, and the parenting context was assessed through a laboratory-based parent-child interaction task. At Wave 2, a subsample of 51 children completed an anatomical magnetic resonance imaging assessment to measure hippocampal structure.

Stronger parent-child concordance was associated with children's poorer outcomes, namely increases in parental hostility from early to middle childhood, and children's greater psychiatric symptoms and poorer psychosocial functioning in early and middle childhood. Moreover, parent- and child-level risk factors moderated several associations between stronger concordance and children's poor outcomes. Parent-child concordance was not related to children's hippocampal volumes in middle childhood. Importantly, our findings highlight adrenocortical concordance as a process underlying the parent-child relationship that plays a role in the development of psychopathology and functional impairment in children.

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ADRENOCORTICAL CONCORDANCE

by

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Chapter 1: Introduction

Evidence consistently documents the widespread effects of the parent-child relationship on children's developmental outcomes, including social, emotional, behavioral, and even neural development (e.g., Belsky & de Haan, 2011; Belsky, Putnam, & Crnic, 2006; Maccoby & Martin, 1983). Moreover, parent-child relationship quality predicts the development and course of psychological problems and has been linked to neurological changes across development (Belsky & de Haan, 2011; Little et al., 2015; Luby et al., 2012; Rao et al., 2010a; Whittle et al., 2014). The parent-child dyad is a dynamic system that involves bidirectional and transactional processes that begin in the first months of an infant's life and evolve over time (Belsky, 1984; Collins, Maccoby, Steinberg, Hetherington, & Bornstein, 2000; Sameroff, 2009). Many complex factors influence this relationship, including parenting, parent and child regulatory mechanisms, and parent and child personality/temperament, but little is known about the biological mechanisms impacting the dyad or their predictive validity on child outcomes. Investigating the underlying biological mechanisms that influence the parent-child relationship is critical to identifying children at risk and informing the development of interventions.

Behavioral and Biological Synchrony

One aspect of the parent-child dyad significant to children's development is *synchrony*, or the matching of parent and child behavior and biological rhythms (Feldman, 2007a; Feldman & Greenbaum, 1997). Behavioral synchrony reflects the temporal matching of discrete events (e.g., eye-gaze, vocalizations, touch, affective states) within the parent-child dyad. This matching of behaviors involves a repetitive

rhythm or sequence in which a behavioral change in one partner of the dyad is paralleled by the other partner engaging in a similar behavioral change (Feldman, 2012; Tronick, 1989). Concurrent synchronous behaviors refer to coordinated and simultaneous act, such as shared gaze, touch, or matched facial expression; whereas sequential synchronous behaviors indicate that the behavior in one partner is then followed by a similar behavior in the other member of the dyad (Feldman, Gordon, & Zagoory-Sharon, 2011).

Behavioral synchrony emerges in early infancy and spans across early child development (Feldman, 2012; Harrist & Waugh, 2002). Beginning in infancy, behavioral synchrony involves a coordinated exchange between the parent and child during social interactions in which the parent focuses vocal and tactile stimulation toward the infant (Feldman, 2007b). As the child develops throughout the first year of life, parent-child behavioral synchrony also evolves to include coordination of social cues and affect, and the sharing of symbolic play (Feldman, 2007b). This coordination is related to increased attachment security and mutual affiliation within the parent-child relationship (Feldman, 2012; Harrist & Waugh, 2002).

Importantly, behavioral synchrony is not only critical to the bond between parent and child, but also impacts children's later social and emotional development. Previous research has demonstrated that behavioral synchrony within the parent-child dyad, such as affect attunement during play, predicts children's positive outcomes, including increased self-regulation, cognitive development, complexity of symbolic play, use of words that reflect internal state (e.g., "I feel"), and fewer behavior problems (Feldman & Greenbaum, 1997; Feldman, 2007b; Feldman, Greenbaum, & Yirmiya, 1999; Harrist & Waugh, 2002). Moreover, the beneficial effects of behavioral synchrony have been

shown to last into adolescence such that early parent-child behavioral synchrony is related to adolescents' capacity for empathy (Feldman, 2007a; 2012) and emotional adjustment (Barber, Bolitho, & Bertrand, 2001). There are also important factors within the dyad that disrupt parent-child behavioral synchrony that may put children at risk for adverse outcomes. For example, mothers with depression often display flat affect and do not often share frequent eye-gazes with their infants, and mothers with anxiety show more frequent social behaviors at times when the child is not receptive to this maternal stimulation (e.g., the child is in need of rest) (Feldman 2007a; Granat, Gadassi, Gilboa-Schechtman, & Feldman, 2017). Consequently, mothers with psychopathology may be at greater risk of demonstrating low synchrony with their child putting these children at risk for adverse outcomes. These findings highlight the critical role of synchrony within the parent-child relationship and its significant impact during these formative years of children's development.

Research has also recently begun to investigate the biological and physiological underpinnings of behavioral synchrony. During pregnancy, biological rhythms emerge between the mother and fetus (Feldman, 2007a). Specifically, the development of oscillator systems such as the biological clock and cardiac vagal tone prepare the mother and child for interactive synchrony (Feldman, 2006, 2007a, b). These biological processes appear to provide the foundation for the development of social coordination and engagement, preparing the child to detect social cues after birth (Feldman, 2006, 2012; Feldman & Eidelman, 2007). In addition, recent work has also linked parent-child behavioral synchrony (e.g., gaze, affect) to biological synchrony (e.g., heart rate) and other measures of biological outcomes (e.g., autonomic response, hormone levels)

(Feldman, 2012; Feldman Magori-Cohen, Galili, Singer, & Louzoun, 2011). For example, one study demonstrated that after engaging in synchronous play with their parent, infants showed greater vagal-tone suppression in response to a still-face paradigm, which indicates an adaptive autonomic response to a stressor (Moore & Calkins, 2004). In addition, Feldman and colleagues (2011) observed mothers and their 3-month old infants during face-to-face interactions while also measuring cardiac output. During moments of gaze and affect synchrony, mother-child biological synchrony of their heart rhythms increased significantly (Feldman et al., 2011). Previous work has also demonstrated reciprocal relations between biological processes and behavioral synchrony (Feldman, 2012). Specifically, maternal and paternal levels of oxytocin, a hormone associated with bond formation, were related to the matching of parent affectionate touch with parent-child gaze when the infant was six months old (Gordon, Zagoory-Sharon, Leckman, & Feldman, 2010), and parent affectionate and stimulatory contact with their infant also predicted parental oxytocin levels (Feldman, Gordon, Schneiderman, Weisman, & Zagoory-Sharon, 2010). These studies demonstrate that synchrony and parent-child interactions are related to biological processes. However, no study has expanded upon these findings to examine links between these processes and child outcomes. These biological processes involved in the parent-child relationship may play an important role influencing children's social and emotional development.

Hypothalamic-Pituitary-Adrenal (HPA) Axis and Parent-Child Adrenocortical Concordance

The hypothalamic-pituitary-adrenal (HPA) axis is one of the body's primary stress response systems activated by either internal or external events (McEwen, 1998).

Once activated by a stressor, the paraventricular nucleus of the hypothalamus releases corticotropin-releasing hormone (CRH), and the presence of this hormone leads to the release of adrenocorticotropin hormone (ACTH) by the anterior pituitary gland, which stimulates the release of the primary stress hormone cortisol from the adrenal glands (Miller, Chen, & Zhou, 2007). Cortisol influences a number of important mental and physical regulatory capacities (Miller et al., 2007). Specifically, cortisol plays a critical role in learning, memory, and emotion via the central nervous system and significantly impacts the body's metabolic system and immune system functioning (Miller et al., 2007; Sapolsky, Romero, & Munck, 2000). While HPA axis functioning provides an adaptive response to stressors, exposure to extreme or chronic stress can lead to inefficient inactivation of this system and overexposure to cortisol (McEwen, 1998). Abnormalities in HPA axis functioning have been linked to a number of adverse outcomes, including physical health problems and risk for depression and other stress-related disorders (Chrousos & Gold, 1998; Gunnar & Vazquez, 2001; McEwen, 1998), highlighting the critical role of the stress response system in influencing human functioning and development.

Research has examined parent-child adrenocortical concordance as an aspect of synchrony, which reflects the attunement or association of cortisol levels between parent and child. Examination of adrenocortical concordance is particularly important given the links between HPA axis functioning and physical and mental health (Adam, 2005; Williams et al., 2013). Adrenocortical concordance may be a physiological process underlying interactions within the parent-child dyad and family functioning more broadly (Papp, Pendry, & Adam, 2009). Using a variety of cortisol indices, previous work has

demonstrated significant parent-child adrenocortical concordance both in response to stressors (Atkinson et al., 2013; Hibel, Blair, Granger, & Cox, 2009; Middlemiss, Granger, Goldberg, Nathans, 2012; Ruttle, Serbin, Stack, Schwartzman, Shirtcliff, 2011; Saxbe et al., 2014; Sethre-Hofstad, Stansbury, & Rice, 2002; van Bakel & Riksen-Walraven, 2008) and their diurnal patterns (Bright, Granger, & Frick, 2012; Hibel, Trumbell, & Mercado, 2014; LeMoult, Chen, Foland-Ross, Burley, & Gotlib, 2015; Papp, et al., 2009; Stenius, Theorell, Lilja, Scheynius, Alm, & Lindblad, 2007; Williams et al., 2013). In addition, there is evidence that concordance between parent and child cortisol is related to within-dyad characteristics. For example, greater adrenocortical concordance has been related to greater maternal sensitivity (Ruttle et al., 2011; Sethre-Hofstad et al., 2002) and increased time spent and activities shared between parent and child (Papp et al., 2009). These studies highlight important links between adrenocortical concordance and parent and child factors. While concordance has been demonstrated with cortisol, very little research has established its validity related to parent or child behavior or mental health outcomes. Consequently, we know little about the significance of concordant parent-child HPA axis functioning as a mechanism impacting the parent-child dyad. Given the HPA axis has been linked to critical mental and physical health outcomes (Chrousos & Gold, 1998; Gunnar & Vazquez, 2001; McEwen, 1998), it is important to elucidate the mechanisms or processes through which HPA axis functioning is related to these outcomes. Importantly, adrenocortical concordance between parent and child may be a specific biological process through which HPA axis functioning leads to child health outcomes.

Significance of the Cortisol Awakening Response (CAR)

One critical aspect of HPA-axis functioning is the cortisol awakening response or CAR (Hibel et al., 2014; LeMoult et al., 2015; Merwin et al., 2017; Williams et al., 2013). The CAR has received relatively little scientific inquiry in studies examining adrenocortical concordance, perhaps due to the methodological challenges in assessing the CAR accurately in parents and children, including the complex sampling protocols and adherence to these sampling methods (Smith & Dougherty, 2014). The CAR assesses the morning rise in cortisol across the waking period. The CAR is a unique aspect of the HPA axis, such that the awakening response is superimposed on the diurnal response. It is moderately heritable, but also sensitive to environmental factors including day-to-day social demands (Fries, Dettenborn, & Kirschbaum, 2009). Accurately assessing the CAR requires the assessment of several morning samples of parent and child cortisol across a short period of time (within 60 minutes post-waking) for at least two consecutive days to increase the reliability of measurement (Hellhammer et al., 2007). In addition, the samples must be yoked to both the parent and child's individual waking times. Despite these assessment challenges, methodological rigorous studies investigating the CAR have established its clinical and health significance more broadly. Specifically, the CAR has been linked with chronic stress, fatigue, and stress-related disorders (Chida & Steptoe, 2009). The CAR and morning cortisol levels have been linked to both internalizing (e.g., Dietrich et al., 2013; Saridjan et al., 2014) and externalizing (e.g., Shoal, Giancola, & Girillova, 2003) problems in young children. The CAR has also been consistently linked to internalizing problems throughout childhood and into adolescence and adulthood (e.g., Chida & Steptoe, et al., 2009; Dietrich et al., 2013; Saridjan et al., 2014). Moreover, abnormalities in the CAR have been observed in both currently and remitted depressed

patients (Bhagwagar et al., 2005; Vreeburg et al., 2009), and the high-risk offspring of depressed parents (Goodyer, Herbert, Tamplin, & Altham, 2000), suggesting that it may serve as a pre-existing vulnerability marker for depression. Importantly, the CAR has been found to predict both depressive and anxiety disorders in adolescents, even after controlling for other relevant risk factors (Adam et al., 2010; Adam et al., 2014). These findings suggest that the CAR may play an important role in the pathophysiology of depression and other stress-related illnesses.

Several studies have investigated parent-child concordance of the CAR (Hibel et al., 2014; LeMoult et al., 2015; Merwin et al., 2017; Williams et al., 2013). These studies focused on the concordance between parent and child CAR to characterize the relationship between family members' physiological responses across waking, which is consistent with a family systems perspective (Cox & Paley, 2003; Papp et al., 2009). In these studies, parent and child CAR showed significant positive associations in preschool-aged (2-5 years; Hibel et al., 2014; Merwin et al., 2017) and school-aged children (7-15 years; LeMoult et al., 2015; Williams et al., 2013). In the majority of these studies (Hibel et al., 2014; LeMoult et al., 2015; Williams et al., 2013), the CAR was quantified as the slope of change scores between cortisol levels at waking and 30 minutes post-waking. In a sample of 47 parents and their preschool-aged children (2-5 years), Hibel and colleagues (2014) reported significant concordance between mother and child CAR. Similarly, Williams and colleagues (2013) examined associations between mother and child CAR in a sample of 27 parents and their school-aged children (7-12 years) across two days. Calculation of the intra-class correlation (ICC) indicated that mothers and their children demonstrated high levels of concordance ($ICC = 0.99$). LeMoult and

colleagues (2015) assessed concordance of the CAR in a sample of 112 mothers with and without a history of depression and their daughters ages 9-15 years-old and found significant concordance in dyads; maternal history of depression did not moderate adrenocortical concordance.

One recent study (Merwin et al., 2017) examined parent-child adrenocortical concordance using a comprehensive analytic approach, which included an examination of the similarity in the curvature of parent and child CARs, and how parent and child individual samplings and average cortisol levels vary within the same dyad. In a sample of 136 dyads, parents' and preschool-aged children's CARs were assessed across two consecutive days and included collection of salivary cortisol samples at waking and 30 and 45 minutes post-waking. Merwin and colleagues (2017) observed several indicators of concordance between parent and child CAR. First, parents and children had similar cortisol responses across the morning, as indicated by the linear and quadratic effects of time on parent and child CAR. Second, parent average morning cortisol levels were also positively associated with children's average cortisol across the morning. Third, parent and child cortisol levels varied similarly with respect to their individual means at each sampling time, such that as a parent was above his/her individual mean at a particular time, the child was also above his/her mean at that time. These studies (Hibel et al., 2014; LeMoult et al., 2015; Merwin et al., 2017; Williams et al., 2013) suggest that parent-child concordance of the CAR emerges in early development and is present across childhood. Nevertheless, while parent-child concordance of the CAR has been established, no study has examined how this biological concordance may be related to parent and child outcomes.

To expand upon this literature, two recent studies have examined how parent-child concordance varies as a function of parent and child factors, but this emerging work has been somewhat mixed. Although LeMoult and colleagues (2015) did not find that maternal depression history moderated the concordance between mothers and daughters' (ages 9-15 years) CAR, Merwin and colleagues (2017) found that parental history of depression moderated associations between parents' and preschool-aged children's CAR. For only parents with a history of depression, parent's mean-centered cortisol was positively associated with the child's mean-centered cortisol, indicating that these high-risk dyads show similar changes in cortisol across the morning. High-risk offspring of depressed parents have demonstrated abnormal HPA axis functioning (Dougherty et al., 2013; Vreeburg et al., 2010). Thus, these findings suggest that parent-child concordance of the CAR may be a specific biological process underlying the parent-child relationship that plays a role in the transmission of risk from depressed parents to their children. Moreover, conflicting findings between studies by Merwin and colleagues and LeMoult and colleagues may suggest that parent and child factors affect concordance of the CAR differently depending on child development. These two studies also used different analytic approaches; LeMoult and colleagues (2015) examined the slope between cortisol levels at waking and 30 minutes post-waking to assess the CAR whereas Merwin and colleagues (2017) examined cortisol levels at three sampling times across the morning. These different approaches to assessing the CAR may also contribute to the conflicting results.

Merwin and colleagues also observed that early child temperamental emotionality moderated parent-child concordance of the CAR. Specifically, for children who

demonstrated high levels of NE only, parents' average morning cortisol was positively associated with children's average morning cortisol. In addition, for children who displayed high levels of PE only, parent's mean-centered cortisol was positively associated with the child's mean-centered cortisol, indicating that within these dyads parent and child cortisol levels varied similarly across the morning. The literature has documented how child temperamental emotionality plays a critical role in the parent-child relationship (Belsky, 1984) and importantly, these findings demonstrate how child factors impact biological processes underlying the dyad. These emerging findings suggest that the level of parent-child concordance varies as a function of both parent and child factors. These findings also highlight the need for more research on parent-child concordance of the CAR to determine whether specific aspects of adrenocortical concordance are associated with positive or negative outcomes and whether these developmental pathways vary with respect to child- and parent-level factors.

Adrenocortical Functioning and Hippocampal Structure

No study has yet examined parent-child adrenocortical concordance and associations with children's brain structure. This is particularly important given links between HPA axis activity and the developing brain (e.g., Carrion, Weems, & Reiss, 2007; Narita et al., 2012). Thus, it is likely that this biological process underlying the dyad plays a fundamental role in children's brain structure. Importantly, HPA axis activity has been linked to hippocampal structure in childhood and into adulthood (Belsky & de Haan, 2011; Carrion et al., 2007; Narita et al., 2012). Specifically, these studies have shown that stress early in life is linked to reductions in hippocampal volume via HPA axis activity. Carrion and colleagues (2007) found that increased levels of

cortisol were related to hippocampal volume reductions in children, whereas Narita and colleagues (2012) found that HPA axis hypoactivity was related to hippocampal volume reductions in adulthood. These studies indicate that developmental period critical to consider when examining the effects of HPA axis functioning on hippocampal structure. Importantly, the hippocampus has been shown to be particularly sensitive to environmental stressors, including the parenting context (Belsky & de Haan, 2011). The hippocampus is a brain structure that plays a critical role in the development of children's learning, memory, and emotional processing (Jacobson & Sapolsky, 1991). Moreover, it is highly sensitive to early life experiences, particularly the parenting environment. Functioning of the HPA axis has been linked to hippocampal structure and function, and animal studies have indicated that HPA axis functioning may mediate associations between life stress and brain development (Lupien et al., 2009). The rodent literature has established that the early environment and parenting context impacts hippocampal structure via dysregulation of the HPA axis (Liu et al., 1997). Specifically, the parenting environment impacts the development of the HPA axis, which in turn affects protein expression and synaptic development in the hippocampus (Liu et al., 1997; Liu et al., 2000). These effects occur through the process referred to as the "glucocorticoid cascade hypothesis", or the pathway through which chronic stress has lasting effects on the brain, such as damage to the hippocampus (Conrad, 2009; Frodl & O'Keane, 2013). Stressors trigger activation of the HPA axis, leading to production of glucocorticoids (i.e., cortisol) by the adrenal glands. Glucocorticoid receptors are present throughout the brain; thus, repeated activation of the HPA axis can have long-lasting effects on brain regions that regulate these hormones (Lupien et al., 2009). Receptors in the hippocampus have been

found to be highly sensitive to cortisol levels, and hyperactivity of the HPA axis has been linked to atrophy of dendrites leading to smaller hippocampal volume in rodents (Lupien et al., 2009; Watanabe, Gould, & McEwen, 1992). The hippocampus is central to the inhibition of HPA axis activity and excessive exposure to glucocorticoids in the hippocampus leads to reduction in neurogenesis and even cell death (Frodl & O'Keane, 2013). Consequently, this damage to the hippocampus reduces inhibition of the HPA axis through the hippocampus-mediated feedback, leading to further excessive cortisol secretion and further damage to the hippocampus (Goosens & Sapolsky, 2007).

Similar to the rat literature, in humans early childhood maltreatment and neglect have been linked to hippocampal volume reductions in adulthood (Belsky & de Haan, 2011). In a meta-analytic review, Woon and Hedges (2008) found hippocampal reductions in adults with a history of childhood maltreatment and posttraumatic stress disorder (PTSD). In addition, Rao and colleagues (2010b) found that exposure to early adversity such as physical neglect, physical or sexual abuse, or emotional abuse before age 11 predicted smaller hippocampal volumes in adolescents. While the majority of studies have examined effects of early adversity and extreme forms of negative parenting contexts on hippocampal volume, emerging literature has also examined the effects of normative levels of parenting behaviors on children's hippocampal structure. Rao and colleagues (2010a) found that greater maternal nurturance when children were four years of age was associated with smaller hippocampal volume in adolescence. Conversely, Luby and colleagues (2012) found that greater maternal support during the preschool years predicted larger hippocampal volume at school age, whereas other studies (Narita et al., 2012; Whittle et al., 2014) have found no association between early parenting and

later hippocampal volume in adolescence and adulthood. Although these findings are mixed, they generally support that the caregiving environment may impact hippocampal structure, particularly during early and middle childhood when the hippocampus is undergoing change (DeMaster, Pathman, Lee, & Ghetti, 2013; Sanchez, Ladd, & Plotsky, 2001; Tottenham & Sheridan, 2009),

While evidence has linked HPA axis functioning to hippocampal development, no research has examined the effects of parent-child adrenocortical concordance on hippocampal structure. The effect of early parent-child adrenocortical concordance on hippocampal structure is particularly important given that the hippocampus is sensitive to the early rearing environment and continues to undergo change across early and middle childhood. Moreover, previous literature has demonstrated associations between parenting and hippocampal structure (Luby et al., 2012; Rao et al., 2010a; Woon & Hedges, 2008) as well as cortisol levels and hippocampal structure (Belsky & de Haan, 2011; Carrion et al., 2007; Narita et al., 2012). The CAR in particular has also been linked to hippocampal volume (e.g., Buchanan, Kern, Allen, Tranel, & Kirschbaum, 2004; Clow, Hucklebridge, Stalder, Evans, & Thorn, 2010; Pruessner, Pruessner, Hellhammer, Pike, & Lupien, 2007) and associations have been found between larger hippocampal volume and greater CAR (Pruessner et al., 2007). Despite these links between the early rearing environment, HPA axis functioning, and hippocampal structure, no study has examined whether parent-child adrenocortical concordance, a biological process underlying the parent-child relationship, is related to children's hippocampal structure. Early parent-child adrenocortical concordance may be a more potent marker of hippocampal structure than behavioral indicators of the parenting

context. Moreover, it is possible that the effects of adrenocortical concordance on the hippocampus are present before behavior changes manifest in the child. Thus, alterations in hippocampal structure may mediate associations between concordance and child behavior, particularly as hippocampal structure has been linked to child outcomes, including vulnerability to increased stress response and risk for depression (e.g., Gilbertson et al., 2002; Rao et al., 2010b; Whittle et al., 2011).

In addition to examining whole hippocampal volume, recent work highlights the importance of examining the volumes of hippocampal subregions (i.e., head, body, tail). Recent findings have suggested that hippocampal subregions undergo distinct developmental trajectories (Gogtay et al., 2006; Lin et al., 2013) and may also demonstrate functional specialization (Poppenk, Evensmoen, Moscovitch, & Nadel, 2013). The hippocampus begins to develop in utero (Jacob et al., 2011) and continues to grow and change in early childhood and into adulthood (Gogtay et al., 2006). Interestingly, Gogtay and colleagues (2006) found that the anterior region showed a reduction in volume over time whereas the posterior region showed an increase in volume. These findings highlight developmental differences in hippocampal subregions; thus, these areas may be differentially impacted by HPA axis functioning and parent and child factors. In addition, in a sample of school-aged children (6-10 years) Lin and colleagues (2013) observed changes in shape over time in the anterior region of the hippocampus. Importantly, connectivity has been found between the anterior region of the hippocampus and the hypothalamus in humans (Bannerman et al., 2004; Gogtay et al., 2006; Poppenk et al., 2013), indicating potential region specificity in the impact of HPA axis activity on hippocampal structure. Further, results from recent rodent work

demonstrated that maternal care differentially impacted hippocampal subregion long term potentiation (LTP), an indicator of synaptic activity (Nguyen, Bagot, Diorio, Wong, & Meaney, 2015). Specifically, Nguyen and colleagues (2015) found that adult rat offspring that received low maternal care in early life demonstrated reduced LTP in the dorsal region of the hippocampus and increased LTP in the ventral region, suggesting potential regional specificity of the effects of early parenting. Thus, it is critical to examine associations between parent-child adrenocortical concordance and both whole hippocampal volume as well as subregion volumes. Investigating the effects of adrenocortical concordance on specific regions may provide critical information regarding the specificity of this biological process underlying the parent-child dyad and its impact on children's hippocampal structure.

Gaps in the Literature

Recent literature has established links between parent-child behavioral synchrony and biological processes (Feldman, 2012; Feldman et al., 2010; Feldman et al., 2011; Gordon et al., 2010; Moore & Calkins, 2004). Moreover, emerging work has established parent-child adrenocortical concordance of the CAR across childhood (Hibel et al., 2011; LeMoult et al., 2015; Merwin et al., 2017; Williams et al., 2013), which may serve as an important mechanism impacting child outcomes. However, despite these advances, there are still important gaps in our understanding of the significance of adrenocortical concordance, which were discussed above and are summarized here.

First, no study, to our knowledge, has examined the concurrent or longitudinal associations of adrenocortical concordance of any HPA axis index on children's development. Parent-child behavioral synchrony has been established as an important

precursor to children's social and emotional development in childhood and even into adolescence (Barber et al., 2001; Feldman & Greenbaum, 1997; Feldman, 2007a,b, 2012; Feldman et al., 1999; Harrist & Waugh, 2002). Examining associations between parent-child biological concordance and child outcomes is a critical next step. Moreover, examining adrenocortical concordance of the CAR is particularly important given the CAR has been consistently linked to physical and mental health and has even been shown to prospectively predict psychopathology in youth (Adam et al., 2010; Adam et al., 2014). Indeed, abnormalities in the CAR have been hypothesized as a marker of risk explaining how the early environment and parenting context may be a predictor of psychopathology. Elucidating the longitudinal impact of parent-child adrenocortical concordance, specifically the CAR, could help identify the underlying biological mechanisms leading to children's negative psychological outcomes.

Second, no work has yet examined links between biological concordance and children's hippocampal volume. The hippocampus undergoes change from birth through childhood and into adulthood (DeMaster et al., 2013; Sanchez et al., 2001; Tottenham & Sheridan, 2009; Uematsu et al., 2012). Moreover, factors associated with parenting and the parent-child dyad have been shown to impact hippocampal volume (Belsky & de Haan, 2011; Luby et al., 2012; Rao et al., 2010a; Woon & Hedges, 2008). Importantly, HPA axis functioning has been linked to hippocampal structure (Lupien, McEwen, Gunnar, & Heim, 2009; Carrion et al., 2007; Narita et al., 2012). Thus, it is likely that biological processes underlying the parent-child dyad, specifically adrenocortical concordance, would similarly impact children's hippocampal structure. Moreover, recent literature has demonstrated hippocampal subregion differences both in rodents (Nguyen

et al., 2015) and humans (Gogtay et al., 2006; Lin et al., 2013), highlighting the importance of examining not only the whole hippocampus but also its subregions. Specifically, the anterior and posterior hippocampal subregions continue to develop during childhood, and recent work has found that the anterior region of the hippocampus, in particular, may be linked to the hypothalamus (Bannerman et al., 20014; Gogtay et al., 2006; Poppenk et al., 2013). These findings highlight the importance of examining the impact of adrenocortical concordance on hippocampal subregions during this developmental period. As adrenocortical concordance between parent and child may have lasting effects on children's brain structure, impacting a number of important developmental processes including learning, memory, and regulatory processes (Jacobsen & Sapolsky, 1991), a critical next step is to examine associations between adrenocortical concordance and children's hippocampal structure.

Current Study

The current study aimed to address these gaps in the literature by examining the concurrent and longitudinal impact of parent-child adrenocortical concordance of the CAR on child outcomes in a sample of 142 parents and their preschool-aged children. Specifically, we examined concurrent associations between parent-child concordance of the CAR assessed during the preschool years and the parenting context, children's internalizing and externalizing symptoms, and children's functional impairment. Further, we examined longitudinal associations between parent-child concordance of the CAR and the later parenting context, children's internalizing and externalizing symptoms, and children's functional impairment three years later. Finally, we examined associations

between parent-child concordance of the CAR assessed during the preschool years and children's hippocampal structure three years later.

The current study included a methodologically rigorous assessment of parent and child CAR, including multiple morning cortisol samples across two days. Furthermore, parent-child concordance of the CAR was quantified using advanced statistical analyses by calculating the dyad-level random slope using multi-level regression modeling. Given previous literature has demonstrated that both high and low CAR have been related to outcomes (Chida & Steptoe, 2009; Fries et al., 2009), we also explored whether level of parent or child cortisol responses moderates associations between parent-child concordance and child outcomes. In addition, parenting was assessed using an observational assessment, and child psychological and psychosocial functioning was assessed using a parent-reported clinical interview. Lastly, to examine children's hippocampal structure, whole hippocampal volumes as well as subregion volumes were calculated to assess specificity of associations with parent-child adrenocortical concordance. In sum, the study will examine three specific aims:

Aim 1: Examine concurrent associations between parent-child concordance of the CAR assessed during the preschool years and observed parenting behavior and children's concurrent psychiatric symptoms and psychosocial functioning.

Hypothesis: Parent-child behavioral synchrony has been related to increased attachment security and mutual affiliation within the parent-child relationship (Feldman, 2012; Harrist & Waugh, 2002), and a number of positive child outcomes (Feldman, 2007; 2012). In addition, previous work has demonstrated that adrenocortical concordance in response to stressors and has been associated with increased maternal sensitivity (Ruttle

et al., 2011; Sethre-Hofstad et al., 2002; van Bakel & Riksen-Walraven, 2008) and concordance of diurnal patterns has been associated with increased time spent and activities shared between the parent and child (Papp et al., 2009). Thus, we hypothesized that stronger parent-child adrenocortical concordance of the CAR would be associated with less concurrent negative parenting, fewer internalizing and externalizing symptoms, and better psychosocial functioning.

Aim 2: Examine longitudinal associations between parent-child concordance of the CAR assessed during the preschool years and observed parenting behavior and children's psychiatric symptoms and psychosocial functioning three years later.

Hypothesis: Given previous literature demonstrating associations between indices of parent-child adrenocortical synchrony and maternal sensitivity and time spent together (e.g., Sethre-Hofstad et al., 2002; Papp et al., 2009) as well as associations between parent-child behavioral synchrony and positive child outcomes such as increased self-regulation and fewer behavior problems (Feldman, 2007; 2012), we hypothesized that stronger early parent-child concordant CAR would be associated with less negative parenting, fewer internalizing and externalizing symptoms, and better psychosocial functioning three years later. Moreover, we hypothesized that these associations would persist after controlling for the corresponding scale at Wave 1 to demonstrate that parent-child concordance uniquely predicts changes in parenting and child outcomes from Wave 1 to Wave 2.

Aim 3a: Examine the longitudinal association between parent-child concordance of the CAR assessed during the preschool years and children's total hippocampal volume three years later.

Hypothesis: Evidence has shown that HPA axis activity is linked to hippocampal structure and volume (Carrion et al., 2007; Narita et al., 2012). Moreover, previous literature has demonstrated that negative parenting and adversity in early childhood predicts smaller hippocampal volume (Belsky & de Haan, 2011; Rao et al., 2010b). In addition, although the literature has been conflicting, some work has demonstrated that positive parenting (e.g., maternal support) has been linked to larger hippocampal volumes in young children (Luby et al., 2012, cf. Rao et al., 2010a). Taken together, it is likely that adrenocortical concordance is related to hippocampal volume. Given the majority of studies examining early parenting, HPA axis activity, and the hippocampus have examined whole hippocampal volume and given no study has examined the effects of concordance on any aspect of hippocampal structure, a critical first step is to investigate these associations with children's total hippocampal volume. We hypothesized that greater parent-child adrenocortical concordance at Wave 1 would predict larger whole hippocampal volume three years later.

Aim 3b: Explore hippocampal region specificity by examining the associations between early parent-child concordance of the CAR assessed during the preschool years and children's hippocampal subregion volumes (i.e., head, body, tail) three years later.

Hypothesis: There is a significant lack of research examining HPA axis functioning and volume of specific subregions in children this age. However, recent work in the animal literature has demonstrated links between maternal care and differential hippocampal subregion functioning highlighting potential regional specificity (Nguyen et al., 2015). Moreover, given connections between the HPA axis and the anterior region of the hippocampus (Bannerman et al., 2004; Gogtay et al., 2006; Poppenk et al., 2013) and

observed changes in the anterior region across development (Gogtay et al., 2006; Lin et al., 2013), we tentatively hypothesized that greater adrenocortical concordance would predict larger volume of the anterior region (i.e., head).

Exploratory Aim: Explore the moderating role of parent- and child- level factors between adrenocortical concordance and child psychological and neural outcomes. Specifically, we examined the moderating role of early parenting behavior, parental history of depression, and child sex.

First, our sample included a subset of parents with a lifetime history of depression (see Method below). Disruptions in parenting, including less warmth and more hostility, have been observed in depression (Lovejoy et al., 2000). Given characteristics associated with parental depression, such as negative parenting behaviors and parent negative affect, are associated with greater concordance between parent and child diurnal cortisol levels (Papp et al., 2009) and cortisol reactivity (Hibel et al., 2009) and given the additional links between parental depression, parenting behavior, and parent and child stress system functioning (e.g., Dougherty et al., 2009; Martorell & Bugental, 2006; Murray et al., 2010; Vreeburg et al., 2009), we explored whether the associations between parent-child adrenocortical concordance and child psychological and neural outcomes differ as a function of early parenting behaviors or parental history of depression. Second, sex differences have been observed for the CAR such that females tend to demonstrate smaller decreases in cortisol after peak morning cortisol, resulting in larger total cortisol output for the CAR (Wüst et al., 2000). Sex differences have also been observed in rates of children's emotional and behavioral problems (Mash & Barkley, 2009; Rutter, Caspi, & Moffitt, 2003). Throughout early childhood and into early adolescence, boys display

higher rates of externalizing problems (Mash & Barkley, 2009). However, while boys and girls display similar rates of internalizing problems in early and middle childhood, girls exhibit a sharp increase in internalizing problems by adolescence, which persists into adulthood (Mash & Barkley, Rutter et al., 2003). Thus, we explored the moderating role of child sex on associations between parent-child adrenocortical concordance and child outcomes.

Hypothesis: Given the limited research on associations between parent-child adrenocortical concordance of the CAR and child outcomes, our moderation analyses were merely exploratory; thus, we held no a priori hypotheses on the moderating role of early parenting, parental history of depression, or child sex on associations between early parent-child adrenocortical concordance and children's psychological and neural outcomes.

Chapter 2: Method

Study Implementation

At Wave 1, parents and their children came to the laboratory and completed an observational parent-child interaction task to assess the early parenting context.

Additionally, parents received instructions and materials to complete a home salivary cortisol assessment to assess their respective CARs. Parents were instructed to obtain cortisol samples for themselves and their child at waking, and 30 and 45 minutes post-waking across two days to assess the CAR (6 cortisol samples each for both the parent and child). Parents also completed a parent-report clinical interview regarding their child's emotional and behavioral functioning. Finally, parents completed a self-report questionnaire on child and family demographics.

Wave 2 was conducted approximately three years later ($M = 2.86$, $SD = .52$, Range = 1.86-4.21) when children were 5-9 years old. Parents and their children returned for a behavioral assessment and again completed a laboratory-based observational parent-child interaction task to assess parenting behavior. Additionally, parents completed a parent-report interview regarding their child's emotional and behavioral functioning. At the end of the visit, parents were invited to have their child participate in a second visit involving an MRI scan. A subsample of 64 families agreed to participate in the MRI scan. At the neuroimaging visit, parents first completed a safety screening to ensure that there was no metal in/on the child's body and to assess for any other MRI contraindications (e.g., cardiac pacemaker, breathing problem or motion disorder, claustrophobia). Next, the child participated in an MRI training session to acclimate the child to the MRI environment. Finally, the child completed the anatomical MRI session.

Participants

Participants included 175 preschool-aged children and their biological parent (Dougherty et al., 2013). Participants for the study were recruited from the Washington, DC metropolitan area using print advertisements (73.1%) and a commercial mailing list (26.9%). The study targeted a subsample of parents with a history of depression, which was assessed using the Structured Clinical Interview for DSM-IV, Non-Patient version (SCID-NP; First, Spitzer, Gibbon, & Williams, 1996). Based on audiotapes of 16 SCID interviews, the kappa for inter-rater reliability was 1.00 for a lifetime depressive disorder. Families who met eligibility requirements at Wave 1 had to have a child between 3-5 years, who had no significant medical condition or developmental disability, with no parental history of bipolar or psychotic disorder, and who lived with at least one English-speaking biological parent. The study was approved by the University of Maryland's human subjects review board, and informed consent was obtained from parents.

Of the 175 participating families, 156 parent-child dyads provided home cortisol samples at Wave 1. Cortisol samples from seven children and three parents were excluded due to extreme cortisol values ($>3 SD$ above the mean Gunnar & White, 2001); five children were excluded for taking corticosteroid medications ($n = 4$) or being sick with fever ($n = 1$); and five parents were excluded for taking corticosteroid medications. Thus, at Wave 1 valid cortisol samples were provided by 142 parent-child dyads (81.1%) and only these dyads are included in the current study.

Children's mean at Wave 1 age was 49.80 months ($SD = 9.64$; Range = 36.00-71.00) and 52.1% were female. Parents' mean age at Wave 1 was 34.90 years ($SD = 6.52$; Range = 21.00-57.00), and primary caregivers participating in the study were

typically mothers (93.0%). Participating families identified themselves as White ($n = 68$; 48.2%), Black/African-American ($n = 49$; 34.8%), Asian ($n = 2$; 1.4%), multiracial ($n = 10$; 7.1%), or other race ($n = 12$; 8.5%); 23 (16.4%) families were of Hispanic/Latino descent. More than half of parents ($n = 85$; 60.2%) at Wave 1 reported having at least a 4-year college degree. Families reported a range of family incomes at Wave 1: less than \$20,000 (7.2%), \$20,000-\$40,000 (10.9%), \$40,001-\$70,000 (19.6%), \$70,001-\$100,000 (27.5%), and greater than \$100,000 (34.8%). The majority of participating parents ($n = 104$; 73.2%) at Wave 1 were married or cohabitating. Of parents who provided cortisol at Wave 1, 49.6% (65 mothers, 4 fathers) had a lifetime history of depressive disorder. See Table 1 for complete demographic characteristics of the sample from Wave 1.

At Wave 2, 115 (65.7%) of the initial 175 families participated. Of these 115 families, 98 dyads (85.2%) provided valid cortisol data at Wave 1. Of those that provided cortisol data at Wave 1, 87 (88.8%) completed the parent-child interaction task at Wave 2, and 96 (98.0%) completed the semi-structured parent report interview. At the Wave 2 behavioral assessment, children were 5-9 years old ($M = 81.80$ months, $SD = 11.86$, Range = 60.00-108.00), and 49.0% were female. Parents' mean age at Wave 2 was 38.88 years ($SD = 5.89$, Range = 24.00-51.00) and the majority (94.3%) of participating parents was mothers. Of parents who provided cortisol at Wave 1 and returned for the Wave 2 behavioral assessment, 54.6% (51 mothers, 2 fathers) had a lifetime history of depressive disorder. Families who provided valid cortisol data at Wave 1 and returned for the behavioral assessment at Wave 2 ($n = 98$) were compared to those who only provided Wave 1 data ($n = 77$) on all study variables. There was one significant difference: parents who provided data at both Wave 1 and Wave 2 were more likely to have at least a 4-year

college degree, $\chi^2(2, N = 172) = 5.34, p = .021$. See Table 1 for complete demographic characteristics of the sample from the Wave 2 behavioral assessment.

All families who attended the behavioral assessment at Wave 2 were invited to participate in the MRI assessment; a subsample of 64 families agreed. The MRI assessment included a structural and resting state scan, a functional MRI reward task, and diffusion tensor imaging (DTI), but only structural data are included in the current study. Of the 64 families, 63 completed the scan (one child did not complete the scan due to claustrophobia) and 51 provided valid cortisol data at Wave 1. Of the 51 families who provided cortisol data at Wave 1 and who participated in the anatomical MRI screening at Wave 2, children's mean age was 79.53 months ($SD = 10.99$, Range = 60.00-108.00) and 49.0% were females. Parents' mean age was 38.20 years ($SD = 6.16$, Range = 24.00-51.00), and 94.0% of parents were mothers. Of parents who provided cortisol at Wave 1 and returned for the Wave 2 neuroimaging assessment, 54.0% (25 mothers, 2 fathers) had a lifetime history of depressive disorder. Families who completed the neuroimaging assessment at Wave 2 and who had valid cortisol data at Wave 1 ($n = 51$) were compared to the Wave 1 sample who did not complete the neuroimaging assessment at Wave 2 ($n = 124$) on all Wave 1 study variables. There were no significant differences between families who completed the cortisol assessment at Wave 1 and the neuroimaging assessment at Wave 2 and the families who completed the Wave 1 assessment only. Families who completed the neuroimaging assessment ($n = 51$) were also compared to families that completed only the Wave 2 behavioral assessment ($n = 47$) on all study variables. There were two significant differences: children who completed the neuroimaging assessment were younger, $t(96) = 2.00, p = .048$, and parents of the

children who completed the neuroimaging assessment were less likely to have a 4-year college degree, $\chi^2(2, N = 97) = 6.18, p = .013$. See Table 1 for complete demographic characteristics of the sample from the Wave 2 neuroimaging assessment.

Measures

Wave 1

Parent and child salivary cortisol assessment. Parents were instructed to obtain a total of 12 salivary cortisol samples (six parent, six child) across two consecutive days. For each day, they were instructed to take three samples immediately after waking, and 30 and 45 minutes post-waking to assess the CAR. Samples were collected across two days, and on weekdays only as the type of day has been associated with cortisol levels (Kunz-Ebrecht, Kirschbaum, Marmot, & Steptoe, 2004). For the collection of cortisol, parents and children were instructed to chew on a cotton dental roll. After the cotton roll was saturated, parents were instructed to use a needleless syringe to expel their and their child's saliva into separate vials for each sample. Parents were instructed to label and refrigerate the samples until returning to the laboratory for a second visit. At that time, the samples were then stored at -20° Celsius until assayed. Samples were assayed in duplicate at the University of Trier, Germany. Samples were assayed with a time-resolved immunoassay with fluorometric end point detection (DELFI). Inter- and intra-assay coefficients of variation ranged between 7.1%-9.0% and 4.0%-6.7%, respectively.

Previous work has indicated that compliance with sampling procedures impacts morning cortisol levels (Kudielka et al., 2007; Smith & Dougherty, 2014). To assess adherence to sampling protocols, parents completed a daily diary measure to record their time of waking and sampling times. Based on previous work (e.g., Broderick et al.,

2004), samples that compose the CAR will be considered compliant if the sample was collected within a time window of ± 10 minutes of the specified sampling time. Parents also completed a daily diary recording their child's time of waking and sampling times to assess compliance of child cortisol samples. In addition, for a random subsample of children ($n = 78$; 54.9%), parental adherence to their child's instructed sampling times was assessed using electronic monitoring. Electronic monitoring data was obtained when parents removed the cotton dental roll from bottles with a pressure-activated micro-circuitry cap that recorded the date and time of each bottle opening (MEMS Track Cap; Aardex Ltd., Zug, Switzerland). Compliance data for child cortisol samples was based on electronic monitoring if available or parent-reported compliance if electronic monitoring was not collected. Of the 670 parent cortisol samples, 152 (22.7%) were non-compliant; of the 790 child cortisol samples, 119 (15.1%) were non-compliant. Parent and child compliance at the sample level was dummy coded as compliant or non-compliant (0 = compliant, 1 = non-compliant), and both parent and child dummy-coded compliance variables will be included as covariates when extracting parent-child concordance in hierarchical linear modeling (HLM) analyses (described below).

Parent-Child Concordance of the CAR. Parent-child adrenocortical concordance will be defined as the within-dyad concordance between parent and child cortisol levels at each time point, relative to the individual's grand mean cortisol levels (i.e., total average cortisol across sample times and days). Due to the nested nature of the parent and child cortisol levels, we will use the Hierarchical Linear Modeling (HLM) program, version 6 to examine parent-child adrenocortical concordance (Raudenbush et al., 2004). In HLM, all child cortisol values will be included as the dependent variable (DV) and all

parent mean-centered cortisol values will be included as the independent variable (IV). Specifically, parents' cortisol will serve as a predictor and will be centered on each parent's mean score; thus, this variable reflects only within-dyad variation (see Enders & Tofghi, 2007). This effect would reflect parents and children changing in the same way and at a similar rate across the waking period (i.e., concordance). Next, the slope will be estimated between the parent and child CAR for each dyad. Slopes will be modeled as random effects and therefore will vary across dyads (Mohr et al., 2013). Models will also include the following covariates: parent and child time of waking, dummy-coded compliance for children's samplings, and dummy-coded compliance for parents' samplings (0=noncompliant, 1=compliant). The dyad-level slope will be extracted from the HLM residuals file (Raudenbush & Bryk, 2002) and then merged with Wave 1 and Wave 2 data in SPSS. A positive slope would indicate that as the parent's cortisol is above their average at a particular time, the child's cortisol is also above their respective average at that time; thus, a positive slope would indicate concordance between parent and child CAR. A negative slope would indicate that as the parent's cortisol is above their average at a particular time, the child's cortisol is below their respective average; thus, a negative slope would indicate discordance between parent and child CAR.

Parental hostility. Primary caregivers ($n = 142$; 132 mothers, 10 fathers) and children participated in a parent-child interaction task, which was a modified version of the Teaching Tasks battery (Egeland et al., 1995). The battery included five standardized tasks including book reading, a guessing game, a maze, story sequencing, and a puzzle. The tasks were designed to elicit the parent's involvement with his or her child. Each task was videotaped and coded for parental hostility. Parental hostility was defined as the

parent's expression of anger, frustration, and criticism toward the child. For each task, parental hostility was rated on a 5-point scale and then averaged across the five episodes for an aggregate measure ($M = 1.15$, $SD = .30$, Range = 1.00-2.60). Internal consistency (α) and the intraclass correlation coefficient (ICC) for inter-rater reliability were good for the parental hostility scale ($\alpha = .76$, $ICC = .89$).

Child psychiatric symptoms. To assess children's current psychiatric symptoms, parents ($n = 140$; 127 mothers, 8 fathers, 5 both parents) were administered the Preschool-Age Psychiatric Assessment (PAPA Version 1.4; Egger & Angold, 2004). The PAPA is a parent-reported structured clinical interview that assesses emotional and behavioral problems in preschool aged-children (2-6 years) during the past three months. The PAPA includes a broad set of diagnostic criteria adapted from the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR; American Psychiatric Association, 2000). Internalizing disorders included depressive (i.e., major depressive disorder, dysthymic disorder, or depression not otherwise specified) and anxiety (i.e., specific phobia, separation anxiety disorder, social phobia, generalized anxiety disorder, agoraphobia, and/or selective mutism) disorders. Externalizing disorders included attention-deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD). Symptom scales for depression ($M = 3.54$, $SD = 2.59$, Range = 0-14.00), anxiety ($M = 12.74$, $SD = 8.11$, Range = 0-55.00) ADHD ($M = 2.50$, $SD = 3.66$, Range = 0-17.00), and ODD ($M = 4.41$, $SD = 2.83$, Range = 0-14.00) were created by summing items in each diagnostic category. Based on 15 audio-recordings of PAPA interviews, internal consistency and inter-rater reliability were good

for the depression ($\alpha = .94$; $ICC = .89$), anxiety ($\alpha = .81$; $ICC = .97$), ADHD ($\alpha = .84$; $ICC = .94$), and ODD ($\alpha = .71$; $ICC = .87$) diagnostic disorder symptom scales.

Child psychosocial functioning. To assess children's ($n = 140$) current psychosocial functioning the interviewer also completed the Children's Global Assessment Scale (CGAS; Shaffer, Gould, & Brasic, 1983) and functional impairment ratings after completion of the PAPA. The CGAS provides a global measurement of children's level of functioning. Scores range from 0=worst functioning to 100=superior functioning ($M = 72.46$, $SD = 13.88$, Range = 43-100). Based on 15 audio-recordings, the CGAS scale demonstrated good inter-rater reliability ($ICC = .88$). Functional impairment was also rated across several domains (parent, sibling, peer relationships, school, activities) on a 5-point impairment scale. For a total impairment rating, scores were averaged across domains ($M = .99$, $SD = 0.52$, Range = 0-2.80). The total impairment scale demonstrated good inter-rater reliability ($ICC = .88$).

Wave 2 Behavioral Assessment

Parental hostility. At Wave 2, 87 parent-child dyads participated in a parent-child interaction task (Egeland et al., 1995). The battery at Wave 2 included four standardized tasks including a guessing game, a traffic game, a maze, and blocks. These tasks were different from the tasks at Wave 1 so that they would be novel and developmental appropriate for the age group, but were similar in that they were designed for the child and parent to work together and require some parental instruction and guidance. Similar to Wave 1, each task was videotaped and coded for parental hostility averaged across tasks (see coding description under Wave 1 Measures). The Wave 2 Parental Hostility scale ($M = 1.14$, $SD = .38$, Range = 1.00-3.25) demonstrated adequate internal

consistency ($\alpha = .84$), and based on video-recordings of 28 dyads, the ICC for inter-rater reliability was .96.

Child psychiatric symptoms. At Wave 2, 96 parents were interviewed regarding their children's emotional and behavioral functioning. To maintain comparability, the PAPA was again administered to parents (see Wave 1 Measures above) to assess for children's psychiatric symptoms at Wave 2. There are no standardized clinical interviews for children 8 years of age and younger and although the PAPA was created for use in 2-6 year-olds, it has also been used in children up to 8 years of age (Luby et al., 2013). Similar to Wave 1, depression ($M = 5.04$, $SD = 3.37$, Range = 0-16.00), anxiety ($M = 12.50$, $SD = 8.24$, Range = 0-43.00), ADHD ($M = 4.76$, $SD = 6.32$, Range = 0-33.00), and ODD ($M = 4.17$, $SD = 2.83$, Range = 0-14.00) symptoms scales were assessed. Based on 12 audio-recordings of PAPA interviews, internal consistency and inter-rater reliability were good for the depression ($\alpha = .99$; $ICC = .71$), anxiety ($\alpha = .98$; $ICC = .83$), ADHD ($\alpha = .98$; $ICC = .91$), and ODD ($\alpha = .97$; $ICC = .73$) symptom scales.

Child psychosocial functioning. Similar to Wave 1, children's ($n = 96$) psychosocial functioning was assessed after completion of the PAPA at Wave 2. The CGAS provided an assessment of children's global functioning on a scale from 0 = worst functioning to 100 = superior functioning ($M = 71.35$, $SD = 11.82$, Range = 41-98). Children's functional impairment at Wave 2 was also assessed across domains (parent, sibling, peers, school, activities). Impairment was rated on a 5-point scale for each domain and scores were averaged for a total functional impairment score ($M = .86$, $SD = .48$, Range = 0-2.14). Based on 12 audio-recordings of PAPA interviews, inter-rater reliability for the CGAS and total impairment scores were good ($ICC = .82$ and $.90$, respectively)

Wave 2 Neuroimaging Assessment

Hippocampal structure. Of the 115 families who returned for the Wave 2 behavioral assessment, 63 families completed an anatomical MRI scan that lasted approximately 5 minutes. Of these 63 families, 51 provided valid cortisol data at Wave 1. Prior to the MRI scan, parents completed a safety screening to ensure that there was no metal in/on the child's body and to assess for any MRI contraindications. Next, the child participated in an MRI training session. The child-friendly mock scanner simulates the MRI environment and while in the mock scanner, the child practiced being still and acclimated to the sounds that he/she would hear while in the scanner. This training acclimated the child to the MRI environment and the experimenter provided the child with feedback if any movement was noticed. Next, the child completed the anatomical MRI session. Children were asked to relax and stay still and watched an age-appropriate movie during the scan.

MRI data was collected on a Siemens Trio 3-Tesla scanner (MAGNETOM Trio Tim System, Siemens Medical Solutions) using a 12-channel coil. High resolution structural scans were obtained with a T1-weighted magnetization-prepared rapid gradient-echo (MPRAGE) sequence with standard parameters (176 contiguous sagittal slices, 1×1×1mm voxel size; 1900 ms repetition time, 2.52ms echo time, 900ms inversion time; 9° flip angle, 256x256 pixel matrix). Structural images were analyzed using FreeSurfer Version 5.1.0, an automatic volumetric segmentation program (surfer.nmr.mgh.harvard.edu). This program has been used in previous work (Fischl, 2012) and has been validated in children as young as four years of age (Ghosh et al., 2010). As recommended by FreeSurfer's guidelines, manual quality control checks were

performed throughout the procedure. Hippocampal volumes were manually segmented into three subregions: head, body, and tail (See Table 2 for hippocampal volumes). To account for variation in hippocampal volumes due to brain size differences related to age, hippocampal volumes were adjusted using intracranial volume (ICV). As described in Raz et al. (2005), adjusted volumes were created based on the analysis of covariance approach. Adjustments were performed on each subregion in each brain hemisphere. The formula for adjusted volumes is $\text{raw volume} - b \times (\text{ICV} - \text{mean ICV})$; b is the regression slope of a subregion volume on the ICV (Raz et al., 2005). Adjusted volumes are presented in all tables and figures and used as the dependent variable in analyses. Dependent variables will include whole hippocampal volume, right and left whole hemisphere volume, and subregion (head, body, and tail) volumes.

Design Considerations

There are several important design considerations for the current study. First, we chose the CAR specifically as a measure of children's HPA axis functioning. The CAR is of particular importance as it is a unique marker of HPA axis activity that is moderately heritable but also sensitive to environmental factors (Fries et al., 2009). Moreover, the CAR specifically has been associated with parenting and parent and child health outcomes including chronic stress, fatigue, and depression (Chida & Steptoe, 2009) and has been shown to prospectively predict the onset of emotional disorders in adolescence (Adam et al., 2010; Adam et al., 2014).

Second, we chose to examine concordance of the CAR rather than assessing temporal sequencing. The CAR is yoked to the individual's wake time; thus, as the parent

and child may not awaken at the same time, concordance of the CAR could not be assessed temporally.

Third, we chose to examine how level of parent and child cortisol response (high vs. low) moderates associations between parent-child adrenocortical concordance and child outcomes. Previous literature has been conflicting, demonstrating that both high and low levels of the CAR are related to outcomes (Chida & Steptoe, 2009; Fries et al., 2009). This conflicting evidence highlights the importance of continued examination of the CAR and how specific CAR responses may be differentially associated with child outcomes. When examining parent-child concordance, we did not control for parent or child average cortisol levels thus allowing us to assess the unique effects of high and low cortisol response on associations between concordance and child outcomes.

Fourth, we considered developmental timing when examining the impact of adrenocortical concordance on children's concurrent and longitudinal psychological and neural outcomes. The parenting context and parent-child relationship has been shown to impact children's stress system functioning in early childhood (e.g., Dougherty et al., 2009; Gunnar et al., 2001). Moreover, parent-child concordance of the CAR has been observed in preschool-aged children (Hibel et al., 2015; Merwin et al., 2017), demonstrating the early emergence of biological processes underlying the dyad. Moreover, early experiences have lasting effects on children's development and we wanted to capture the concurrent and longitudinal impact on children's development. In addition, psychopathology and behavior problems have been shown to emerge during the preschool years and persist into childhood putting children at greater risk for later psychopathology, highlighting the importance of assessing psychological outcomes at

this age (Bufferd, Dougherty, Carlson, Rose, & Klein, 2012; Caspi & Moffitt, 1996; Zahn-Waxler, Shirtcliff, & Marceau, 2008). Furthermore, previous work has shown that the hippocampus displays a large increase in growth in the first several years of life and this growth peaks at ages 9-11 (Uematsu et al., 2012). This highlights early childhood and school age as a critical time for brain development, during which the hippocampus may be particularly susceptible to environmental factors. Indeed, early childhood has been noted as a critical time when exposure to stressors and experiences can have lasting effects on both HPA axis functioning and hippocampal development (Tottenham & Sheridan, 2009). Thus, a developmental perspective must be taken to understand how early adrenocortical concordance will predict outcomes later in childhood and throughout the lifespan.

Finally, we chose to examine hippocampal total volume as well as volumes of specific hippocampal subregions (head, body, tail). While hippocampal structure is often evaluated as a whole, recent literature has shown that hippocampal subregions demonstrate developmental differences (DeMaster et al., 2013; Riggins, Blankenship, Mulligan, Rice, & Redcay, 2015) and heterogeneous functions (Poppenk et al., 2013). Examining the volume of specific subregions will provide unique and critical information regarding the impact of HPA axis functioning on hippocampal structure, which can inform the understanding of subregion functional specialization. Moreover, examining these associations will shed light on the mechanisms underlying children's outcomes and developmental trajectories.

Data Analytic Plan

We will conduct regression analyses where the dyad-level random slope between the parent and child CAR will serve as the independent variable in all models (see Parent-Child Concordance of the CAR above). In models examining concurrent associations, dependent variables will include Wave 1 parental hostility, child internalizing and externalizing symptom scales (i.e., depression, anxiety, ADHD, ODD), child CGAS scores, and child global impairment in separate models. In models examining longitudinal associations, dependent variables will include Wave 2 parental hostility, child internalizing and externalizing symptom scales (i.e., depression, anxiety, ADHD, ODD), child CGAS scores, child global impairment, and whole hippocampal and hippocampal subregion volumes in separate models. We will also examine several covariates to see if they are associated with our dependent variables. Specifically, we will examine child baseline and current age, child sex, parental education, and race/ethnicity as potential covariates. Any covariates significantly associated with outcome variables will be included in the model with that outcome.

Aim 1: We will examine associations between parent-child concordance of the CAR and concurrent parenting, and children's concurrent psychological and psychosocial functioning. We will use regression analyses using the dyad-level slope as described above as a measure of adrenocortical concordance. In regression models, parent-child adrenocortical concordance will be the IV, and the DV will include Wave 1 parental hostility, internalizing symptom scales (i.e., depression, anxiety), externalizing symptom scales (i.e., ADHD, ODD), CGAS scores, and global impairment ratings in separate models. We hypothesize that parent-child synchronous CAR will be negatively associated with concurrent negative parenting, children's internalizing and externalizing

symptom scales, and global impairment, and positively associated with children's CGAS ratings. In addition, given cortisol levels, albeit conflicting (both high and low), have been linked to child outcomes (Chida & Steptoe, 2009; Fries et al., 2009), we will explore whether parents' or children's mean level of morning cortisol response, measured by average cortisol (i.e., average cortisol across all sample times and days) moderates associations between concordance and child outcomes. Parents' and children's average cortisol and the interaction terms between the dyad-level slope (i.e., concordance) and parents' average cortisol and between the dyad-level slope and children's average cortisol will be included as additional predictors in a single model. Significant interactions will be probed using simple slopes analyses, as described by Aiken and West (1991). Specifically, we will examine the effects of parent and child average cortisol at 1 SD above and below their respective mean to assess whether associations are specific to high (+1 SD) or low (-1 SD) cortisol responses.

Aim 2: We will examine longitudinal associations between parent-child adrenocortical concordance of the CAR and parenting behavior, children's psychiatric symptoms, and children's psychosocial functioning three years later (Wave 2). In these models, we will first examine bivariate associations in which parent-child adrenocortical concordance at Wave 1 will be the IV and the DV will include Wave 2 parental hostility, internalizing symptom scales (i.e., depression, anxiety), externalizing symptom scales (i.e., ADHD, ODD), CGAS scores, and global impairment ratings in separate models. Next, we will further control for the corresponding scale at Wave 1 to examine whether parent-child adrenocortical concordance predicts change from Wave 1 to Wave 2 in any of these outcome measures. We hypothesize that adrenocortical concordance at Wave 1

will be negatively associated with negative parenting, children's internalizing and externalizing symptom scales, and global impairment, and positively associated with children's CGAS ratings three years later (Wave 2). In addition, we hypothesize that concordance at Wave 1 will similarly predict parenting and child psychological and psychosocial outcomes three years later (Wave 2), over and above the corresponding scale at Wave 1. We will also include the early parenting context as an additional covariate in analyses to examine whether parent-child concordance predicts child psychiatric outcomes over and above early parenting. As described in Aim 1, we will also explore whether parent's or children's mean level of morning cortisol responses, measured by average cortisol, moderates associations between concordance (slope) and child longitudinal outcomes. Parents' and children's average cortisol and the interaction terms between the dyad-level slope (i.e., concordance) and average cortisol will be included as additional predictors in separate models. Significant interactions will be probed using simple slopes analyses (± 1 SD; Aiken & West, 1991).

Aim 3: We will assess associations between early parent-child concordance and children's later hippocampal volume. As described above, FreeSurfer was used to analyze structural images and hippocampal volumes were manually segmented into three subregions (i.e., head, body, tail). All hippocampal volumes were adjusted for ICV and adjusted values will be used in all analyses. Using the model described above, whole hippocampal volume, left and right hippocampal hemisphere volumes, and subregion (head, body, tail) volumes will serve as the dependent variable in separate models. We hypothesize that greater adrenocortical concordance at Wave 1 will predict larger whole hippocampal volume and larger volume of the anterior region (e.g., head) at Wave 2. In

addition, we will again explore whether parent's or children's mean level of morning cortisol responses (i.e., average cortisol) moderates associations between adrenocortical concordance and child hippocampal volumes. Parents' and children's average cortisol and the dyad-level slope x average cortisol interaction term will be included as additional predictors in separate models. Simple slopes analyses (± 1 SD; Aiken & West, 1991) will be used to probe significant interactions.

Exploratory Aim: We will explore whether parent- and child- level factors (i.e., early parenting, parental history of depression, child sex) moderate associations between parent-child concordance at Wave 1 and concurrent and longitudinal child outcomes three years later (Wave 2). To conduct the moderation analyses, we will use Hayes' (2012) PROCESS macro in SPSS. Adrenocortical concordance (i.e., dyad-level random slope) and the exploratory moderator (i.e., early parenting, parental depression, child sex) will be centered and the centered variables and their respective cross-product will be entered as predictors in the regression model. In separate models, dependent variables will include Wave 1 and Wave 2 parental hostility, child internalizing symptoms, externalizing symptoms, CGAS scores, global impairment ratings, and Wave 2 whole hippocampal volume, left and right hippocampal hemisphere volumes, and hippocampal subregion volumes. Significant interactions will be probed using simple slopes analyses (± 1 SD; Aiken & West, 1991).

Sample Size Considerations

We have conducted a power analysis based on the sample sizes for each aim and effect sizes in the literature. The sample size at Wave 1 is 142 dyads and the sample size at Wave 2 is 98 dyads, examining concurrent and prospective associations between

parent-child adrenocortical concordance and parenting, child psychiatric symptoms, and psychosocial functioning. To address Aims 1 and 2, we estimated our effect size based on prior studies examining the effect of behavioral synchrony on children's later internalizing and externalizing problems (Feldman et al., 1999; Feldman & Eidelman, 2004). Effect sizes for these studies range from medium ($r = .32$; Feldman et al., 1999) to large ($r = .62$; Feldman & Eidelman, 2004). Given these estimates, in order to achieve 80% power ($\alpha = .05$) with a medium effect size for a correlation, a sample size of 85 is required (Cohen, 1992). Thus, our sample sizes for Aims 1 and 2 will be sufficient.

The sample size for Aim 3 is 51 and examines associations between early parent-child adrenocortical concordance and children's neural outcomes. Previous studies using standard MRI and fMRI methodologies have suggested a sample size of 20 per group provides adequate power (e.g., Thirion et al., 2007). However, the current project relies on individual differences, which usually yield smaller effects. To our knowledge, no previous study has examined the longitudinal effects of adrenocortical concordance on children's brain structure. However, research examining associations between cortisol levels and hippocampal structure in children with a history of maltreatment and post-traumatic stress have yielded large effect sizes ($r = .48$ to $r = .50$; Carrion et al., 2007). Using these estimates, a sample size of 28 is required to achieve 80% power ($\alpha = .05$) with a large effect size (Cohen, 1992). All 51 participants provided usable structural data and thus will provide us with sufficient power to detect significant effects.

Our sample size is limited for the models examining whether parent- and child-level factors moderate associations between parent-child concordance and child outcomes. However, given the state of the literature and limited work on associations

between parent-child adrenocortical concordance and children's concurrent and longitudinal outcomes, this aim is exploratory and these analyses will be used to inform future hypotheses.

Chapter 3: Results

Preliminary analyses

Parent-child concordance

Given the nested nature of parent and child cortisol, a two-level hierarchical linear model was created using HLM version 6 (Raudenbush et al., 2004) to estimate concordance between parent and child morning cortisol. HLM allows for the assessment of repeated measures within an individual and/or dyad. Importantly, multiple observations within individual and dyad provide increased power to detect effects. In the current study, 12 data points per dyad were included in analyses (6 parent, 6 child). Parent and child cortisol were treated as nested data within sampling time (waking, and 30 and 45 minutes post-waking) and dyad. In addition, parents and children collected cortisol on two separate days. Dyad-level slopes were created for each parent-child pair on each sampling day. These two slopes were then averaged across the two days to create one slope representing parent-child concordance, which served as the independent variable in the primary analyses.

To estimate parent-child concordance, the following model was estimated. Children's individual cortisol levels were entered as the dependent variable at Level-1, and parents' group-centered cortisol was entered as a level-1 predictor. Concordance between parent and child cortisol was indicated if parent cortisol significantly predicted child cortisol. Additional level-1 predictors included the linear and quadratic effects of sampling time (calculated as the sample time since waking) for parent and child, and dummy-coded compliance (0=noncompliant, 1=compliant) for parent and child cortisol samplings. Level-2 variables included parent and child time of waking in hours. Results

indicated that parent cortisol was a significant predictor of child cortisol ($B = 0.27$, $SE = 0.07$, $t = 4.01$, $p < .001$), demonstrating significant concordance. In addition, there was significant variability across dyads, $\chi^2(259) = 317.68$, $p = .01$, indicating that there were between-dyad differences in concordance.

Next, the model residuals were extracted to yield the dyad-level slope between parent and child cortisol on each day. The dyad-level slopes across both days were then averaged to create a final dyad-level random slope, representing concordance between parent and child morning cortisol ($M = 0.27$, $SD = 0.11$, Range = $-.04-.72$).

Potential covariates

We examined associations between the dependent variables and several potential covariates, including child race/ethnicity (0 = non-Hispanic White, 1 = non-White or Hispanic), parental education (0 = no parent with a four year college degree, 1 = at least one parent with a four year college degree), child age, and child sex (0 = male, 1 = female). Non-Hispanic White children had fewer ADHD symptoms at Wave 1, $t(135) = -2.32$, $p = .02$, fewer anxiety symptoms at Wave 1, $t(103) = -2.93$, $p = .004$, and their parents demonstrated lower levels of parental hostility at Wave 1, $t(126) = -4.14$, $p < .001$, and Wave 2, $t(44) = 2.69$, $p = .01$, compared to non-White or Hispanic children. Parents with a four year college degree or more demonstrated lower levels of parental hostility at Wave 1, $t(139) = 3.62$, $p < .001$, than parents with less than a four year college degree. Males had more ADHD symptoms at Wave 1, $t(138) = 2.90$, $p = .004$, and Wave 2, $t(94) = 2.21$, $p = .03$, and had greater average impairment at Wave 1, $t(120) = 2.77$, $p = .01$, than females. In addition, males had larger volume of the left hippocampal head than females, $t(49) = 2.43$, $p = .02$. Finally, child age at Wave 2 was significantly positively

associated with volume of the right hippocampal body, $r = .38$, $p = .006$. Thus, race/ethnicity was included as a covariate in subsequent analyses when ADHD symptoms (Wave 1), anxiety symptoms (Wave 1), or parental hostility (Wave 1 and 2) served as the dependent variable. Parental education was also included as a covariate in analyses with parental hostility as the dependent variable. Child sex was included as a covariate in analyses when ADHD symptoms (Wave 1 and 2), average impairment (Wave 1), and left hippocampal head volume (Wave 2) served as dependent variables. Child age at Wave 2 was included as a covariate in analyses when right hippocampal body volume served as the dependent variable.

Concurrent associations between adrenocortical concordance and parenting and children's psychiatric symptoms and psychosocial functioning at Wave 1

We examined bivariate correlations between parent-child adrenocortical concordance at Wave 1 and observed parental hostility, children's psychiatric symptoms (i.e., ADHD, ODD, depression, anxiety), and children's psychosocial functioning (i.e., CGAS, global impairment) at Wave 1. As seen in Table 3, bivariate correlations indicated that greater parent-child adrenocortical concordance at Wave 1 was significantly associated with higher levels of children's concurrent ADHD symptoms and functional impairment, and lower levels of children's CGAS scores at Wave 1. Next, we ran regression models controlling for significant demographic covariates as noted above. After controlling for significant demographic covariates, greater parent-child adrenocortical concordance at Wave 1 was significantly associated with lower levels of children's CGAS scores ($b = -2.87$, $SE = 1.18$, $t = -2.43$, $p = .016$) at Wave 1; greater adrenocortical concordance at Wave 1 was also associated with higher levels of

children's ADHD symptoms ($b = .05$, $SE = .03$, $t = 1.71$, $p = .089$) and average impairment ratings ($b = .09$, $SE = .05$, $t = 1.88$, $p = .062$) at Wave 1 at a trend level.

Parent-child adrenocortical concordance at Wave 1 was not significantly correlated with observed parental hostility or children's ODD, anxiety, or depression symptom scales at Wave 1.

Longitudinal associations between parent-child adrenocortical concordance at Wave 1 and observed parenting and children's psychiatric symptoms and psychosocial functioning at Wave 2

We first examined bivariate correlations between parent-child adrenocortical concordance at Wave 1 and observed parental hostility, children's psychiatric symptoms (i.e., ADHD, ODD, depression, anxiety), and children's psychosocial functioning (i.e., CGAS, global impairment) at Wave 2. As seen in Table 3, greater parent-child adrenocortical concordance at Wave 1 was significantly associated with higher levels of parental hostility, children's ADHD and depressive symptoms, and lower levels of children's CGAS scores three years later at Wave 2.

Next, we ran a regression model with observed parental hostility at Wave 2 as the dependent variable and controlled for significant demographic covariates and observed parental hostility at Wave 1. As seen in Table 6, after controlling for significant demographic covariates and parental hostility at Wave 1, greater parent-child adrenocortical concordance at Wave 1 predicted increases in observed parental hostility from Wave 1 to Wave 2 ($b = .04$, $SE = .01$, $t = 3.96$, $p < .001$).

We then ran regression models with children's psychiatric symptoms at Wave 2 as the dependent variable and controlled for significant demographic covariates and the

corresponding symptom scale at Wave 1. As seen in Table 6, after controlling for significant demographic covariates and the corresponding scale at Wave 1, greater parent-child concordance at Wave 1 predicted increases in children's depressive symptoms from Wave 1 to Wave 2 ($b = .70, SE = .31, t = 2.24, p = .028$) and was marginally significantly associated with increases in children's ADHD symptoms from Wave 1 to Wave 2 ($b = .08, SE = .04, t = 1.96, p = .053$).

As seen in Table 7, after controlling for significant demographic covariates, greater parent-child adrenocortical concordance at Wave 1 predicted children's lower CGAS scores at Wave 2 ($b = -2.64, SE = 1.19, t = -2.23, p = .028$). In addition, we ran an additional model controlling for children's psychiatric symptoms (i.e., ADHD, ODD, depression, anxiety) at Wave 1, and greater parent-child adrenocortical concordance was marginally significantly associated with lower CGAS scores ($b = -2.12, SE = 1.10, t = -1.93, p = .057$).

Longitudinal associations between parent-child adrenocortical concordance at Wave 1 and children's hippocampal volumes at Wave 2

As seen in Table 8 and Table 9, parent-child adrenocortical concordance at Wave 1 was not significantly associated with children's hippocampal volume at Wave 2 (i.e., hippocampal head, body, tail, left and right hemispheres, total hippocampal volume).

Moderation analyses

We examined whether several factors (i.e., parental hostility at Wave 1, parental history of depression, child sex, and parent and child average cortisol levels) moderated associations between parent-child adrenocortical concordance and parent and child concurrent and longitudinal outcomes. Specifically, we examined the interactive effects

of parent-child adrenocortical concordance at Wave 1 and parental hostility at Wave 1, parental history of depression, child sex, and parent and child average cortisol levels on parent and child outcomes at Wave 1 and 2.

Parent-child adrenocortical concordance x parental hostility

We examined whether parental hostility at Wave 1 moderated associations between parent-child adrenocortical concordance at Wave 1 and parent and child outcomes at Wave 1 and Wave 2. As seen in Table 10 and Figure 1, we observed a significant interactive effect between adrenocortical concordance and parental hostility at Wave 1 on observed parental hostility at Wave 2 after controlling for significant demographic covariates ($b = .03, SE = .01, t = 3.78, p < .001$). For parents who demonstrated high levels of parental hostility at Wave 1, greater adrenocortical concordance at Wave 1 predicted increases in parental hostility from Wave 1 to Wave 2 ($b = .07, SE = .01, t = 5.64, p < .001$), whereas for parents who demonstrated low levels of parental hostility at Wave 1, adrenocortical concordance at Wave 1 was not associated with changes in parental hostility at Wave 2 ($b = .002, SE = .01, t = .19, p = .849$). Regions of significance testing indicated that this moderated effect was specific to dyads with levels of parental hostility greater than $-.54$ (standardized z-score). Reversing the moderator, this effect was also specific to dyads with levels of adrenocortical concordance greater than $-.57$ (standardized z-score).

Parent-child adrenocortical concordance x parental lifetime depression

We examined whether parental history of depression moderated associations between parent-child adrenocortical concordance at Wave 1 and parent and child outcomes at Wave 1 and Wave 2. As seen in Table 11 and Figure 2, we found a

significant interaction between parent-child adrenocortical concordance at Wave 1 and parental history of depression on observed parental hostility at Wave 2 after controlling for significant demographic covariates and parental hostility at Wave 1 ($b = -.05$, $SE = .02$, $t = -3.08$, $p = .003$). For parents with a history of depression, greater adrenocortical concordance at Wave 1 predicted increases in parental hostility from Wave 1 to Wave 2 ($b = .06$, $SE = .01$, $t = 5.07$, $p < .001$), whereas for parents without a history of depression, adrenocortical concordance at Wave 1 was not associated with changes in parental hostility ($b = .004$, $SE = .01$, $t = .34$, $p = .738$). Reversing the moderator, regions of significance testing indicated that this moderated effect was specific to dyads with levels of adrenocortical concordance less than -1.07 and greater than $.30$ (standardized z-score).

We observed two additional interaction effects between parent-child adrenocortical concordance and parental depression predicting changes in children's ADHD symptoms from Wave 1 to Wave 2 and changes in children's CGAS scores from Wave 1 to Wave 2. However, when we probed these interactions, regions of significance testing indicated that the significant effects were driven by very few participants. Therefore, these additional results are included in Appendix A only.

Parent-child adrenocortical concordance x child sex

We examined whether child sex moderated associations between parent-child adrenocortical concordance at Wave 1 and parent and child outcomes at Wave 1 and Wave 2. First, we examined whether child sex moderated the concurrent or longitudinal associations between parent-child concordance at Wave 1 and parental hostility at Wave 1 and Wave 2. As seen in Table 12 and Figure 3, we found a significant interaction between parent-child adrenocortical concordance at Wave 1 and child sex on observed

parental hostility at Wave 2 after controlling for significant demographic covariates and parental hostility at Wave 1 ($b = .05, SE = .02, t = 2.97, p = .004$). For females, greater parent-child adrenocortical concordance at Wave 1 was associated with increases in parental hostility from Wave 1 to Wave 2 ($b = .06, SE = .01, t = 5.02, p < .001$). For males, parent-child adrenocortical concordance at Wave 1 and observed parental hostility at Wave 2 were not significantly related ($b = .01, SE = .01, t = .82, p = .413$). Reversing the moderator, regions of significance tests also demonstrated that this moderated effect was specific to dyads with levels of adrenocortical concordance less than -0.38 and greater than 1.81 (standardized z-score).

Next, we examined whether the interaction between parent-child adrenocortical concordance and child sex was associated with children's psychiatric symptoms after controlling for significant demographic covariates. As seen in Table 13 and Figure 4 and Figure 5, there was a significant interaction between adrenocortical concordance at Wave 1 and child sex on children's depression symptoms at Wave 1 ($b = .98, SE = .42, t = 2.33, p = .021$) and Wave 2 ($b = 1.33, SE = .65, t = 2.07, p = .042$). For females, greater parent-child adrenocortical concordance at Wave 1 was associated with higher levels of girls' depressive symptoms at Wave 1 ($b = .69, SE = .30, t = 2.34, p = .021$) and Wave 2 ($b = 1.46, SE = .46, t = 3.19, p = .002$), whereas for males, adrenocortical concordance at Wave 1 and depressive symptoms were not significantly associated at Wave 1 or Wave 2 ($b = -.29, SE = .30, t = -.97, p = .334$ and $b = .12, SE = .65, t = .26, p = .797$, respectively). Reversing the moderator, regions of significance tests demonstrated that this moderated effect was specific to dyads with levels of adrenocortical concordance less than -2.68 and greater than .82 (standardized z-score) at Wave 1 and less than -0.27

(standardized z-score) at Wave 2. When we further controlled for Wave 1 depressive symptoms in the longitudinal model, the interaction did not predict changes in depressive symptoms from Wave 1 to Wave 2 ($b = .91$, $SE = .62$, $t = 1.47$, $p = .145$).

Parent-child adrenocortical concordance x average parent cortisol x average child cortisol models

Lastly, we examined interactions between adrenocortical concordance and parent and child average cortisol levels on children's concurrent and longitudinal outcomes. Neither parent nor child levels of cortisol responses moderated associations between adrenocortical concordance and child outcomes.

Chapter 4: Discussion

The present study examined early parent-child adrenocortical concordance of the CAR and its concurrent associations with parenting, children's psychopathology and psychosocial functioning, as well as its longitudinal associations with parenting, children's psychopathology and psychosocial functioning, and children's hippocampal structure in middle childhood. We found that stronger parent-child concordance of the CAR predicted increases in parental hostility from early to middle childhood (Wave 1 to Wave 2). Moreover, this association was moderated by several factors including higher levels of parental hostility in early childhood (Wave 1), parental history of depression, and child female sex. In addition, we found that concordance was associated with children's ADHD and depressive symptoms in early (Wave 1) and middle (Wave 2) childhood, and the associations with children's depressive symptoms were moderated by child female sex. Finally, stronger parent-child concordance of the CAR was associated with children's poorer concurrent psychosocial functioning at Wave 1 and predicted poorer psychosocial functioning in middle childhood (Wave 2). No significant findings emerged between early parent-child concordance and children's total hippocampal volume or hippocampal subregion volumes in middle childhood. To our knowledge, this is the first study to examine the concurrent and longitudinal associations of parent-child adrenocortical concordance of the CAR with children's outcomes.

Contrary to our hypotheses, our findings demonstrated that stronger parent-child concordance was associated with negative outcomes. The extant literature has demonstrated that stronger parent-child *behavioral synchrony* has been linked to positive outcomes in children such as increased self-regulation, fewer behavior problems, and

emotional adjustment (Barber et al., 2001; Feldman, 2007b; Feldman & Greenbaum, 1997). In contrast, studies examining associations between biological concordance and child outcomes are limited, and the findings have been mixed. For example, stronger parent-child adrenocortical concordance has been associated with greater maternal sensitivity (e.g., Hibel, Granger, Blair, & Finegood, 2015; Ruttle et al., 2011) as well as greater child or mother negative affect during mother-adolescent interactions (Papp et al., 2009), and greater restrictive and punitive parenting (Hibel et al., 2009). In a study examining a separate index of physiological synchrony, Suveg and colleagues (Suveg, Shaffer, & Davis, 2016) found that child self-regulation was lowest under high family risk (i.e., single parent status, GED/high school diploma or less, economic disadvantage, maternal psychopathology symptoms) and higher synchrony of parent-child interbeat intervals (IBI; time between heartbeats) during a parent-child interaction task; at high levels of family risk, lower physiological synchrony of parent and child IBI was related to greater child self-regulation. These findings suggest that high levels of synchrony in the context of high risk may be related to poorer outcomes. Similarly, in our sample, adrenocortical concordance of the CAR may have been related to poorer outcomes because we oversampled offspring with parents with a lifetime history of depression. It will be important to assess whether these associations are present in large community-based unselected samples.

Parent-Child Adrenocortical Concordance of the CAR and Parenting

Parent-child adrenocortical concordance of the CAR was not associated with concurrent parenting. However, greater parent-child concordance in early childhood predicted increases in parental hostility from early to middle childhood. Moreover, this

association was moderated by several risk factors, namely parental hostility at Wave 1 and parental history of depression. For parents who displayed higher levels of hostility at Wave 1, and/or for parents with a lifetime history of depression, parent-child concordance of the CAR was associated with increases in parental hostility three years later. Conversely, for parents who displayed low levels of hostility at Wave 1 and/or did not have a lifetime history of depression, we observed no significant association between concordance and parental hostility in middle childhood.

Although the literature has been mixed (e.g., Hibel et al., 2015; Ruttle et al., 2011; Sethre-Hofstad et al., 2002), our findings are consistent with a study demonstrating associations between negative parenting styles and greater adrenocortical concordance of cortisol in response to an acute stressor (Hibel et al., 2009), and we extended these findings to other indices of adrenocortical concordance. In addition, we previously demonstrated in this sample that dyads with a parental history of depression displayed greater parent-child concordance of the CAR (Merwin et al., 2017). Importantly, both high levels of parental hostility and parental history of depression emerged as moderators to the association between concordance and later parenting, which is particularly interesting given the close links between parenting and depression. Indeed, depression has been consistently linked to disruptions in parenting, including more hostile and less warm parenting behaviors (Lovejoy et al., 2000). Parents with a history of depression and/or parents who display high levels of hostility toward their child represent dyads at increased risk for poor outcomes, and it is possible that in combination with these well-established risk factors, parent-child adrenocortical concordance plays a role in the risk for maladaptive outcomes. Given previous evidence linking depression (e.g., LeMoult et

al., 2015; Nelemans et al., 2014; Vreeburg et al., 2009) and parenting (e.g., Murray et al., 2010; Sturge-Apple et al., 2009) with dysregulated stress system functioning in adults and youth, these high-risk dyads may demonstrate concordance of a dysregulated stress response system. Thus, the specific combination of these risk factors (i.e., familial liability for depression, high levels of parental hostility) and concordance of dysregulated CAR may contribute to a trajectory of persistent negative parenting behaviors and problematic parent-child interactions often observed in parents with a history of depression.

The association between early parent-child adrenocortical concordance and increases in parental hostility was also moderated by child sex. For females only, greater concordance was associated with increases in parental hostility from early to middle childhood. Our findings suggest that females' stress physiology may be particularly sensitive to interactions with their parents and their parents' stress system functioning. Interestingly, Booth and colleagues (2008) found that for females in particular, quality of social relationships and morning cortisol levels were associated: for adolescent girls only, lower morning cortisol was associated with poorer quality of social relationships with parents, siblings, and peers. Moreover, while males have been shown to engage in risk and dominance behavior when facing stressors (Moffitt, Caspi, Rutter, & Silva, 2001), females may be more likely to engage interpersonally when facing challenges (Booth et al., 2008). If females are more likely to engage interpersonally with their parent, perhaps they are more likely to be attuned physiologically. Indeed, this is consistent with findings that increased time spent between parents and children was associated with stronger diurnal concordance (Papp et al., 2009). In addition, given our sample includes a

subsample of parents with a history of depression, these dyads may be more prone to negative interactions and increased engagement by females may contribute to continued negative interaction. Interestingly, given the majority of our parents were mothers, it is possible that concordance within mother-daughter dyads in particular is associated with the persistence of negative interactions and increasing parental hostility due to the close relation between females' stress system functioning and social relationships. It will be important for future research to examine father-daughter and father-son dyads to assess whether similar findings will emerge for fathers and their children. In addition, based on the bio-behavioral model of synchrony (Feldman, 2012), it is likely that parent and child physiology and behavior are mutually influential over time. To further understand the associations between early parent-child concordance and parenting, it will be important to examine concordance at multiple time points and investigate whether stronger concordance in middle childhood would be observed in addition to increases in parental hostility.

We did not observe associations between early parent-child concordance and concurrent parenting. These findings are inconsistent with the current literature demonstrating links between adrenocortical concordance and concurrent parenting (e.g., Hibel et al., 2009; Ruttle et al., 2011; Sethre-Hofstad et al., 2002). However, concordance was associated with parenting in middle childhood and these associations were moderated by risk factors within the dyad. It is possible that in the context of risk, the effects of concordance of the CAR emerge over time. Indeed, if concordance of the CAR for high-risk dyads represents a dysregulated stress response system, it may take time for the behavioral effects to manifest, highlighting concordance of the CAR as a potential

early indicator of risk prior to observable outcomes. This is merely speculative at this time and further research is needed to investigate whether physiological concordance is associated with a specific dysregulated cortisol profile shared between the parent and child, and whether it is concordance or the dysregulated adrenocortical profile or both that uniquely predict negative outcomes for children.

Parent-Child Adrenocortical Concordance of the CAR and Child Clinical and Functional Outcomes

Depressive symptoms. Bivariate correlations revealed a significant positive association between parent-child concordance of the CAR and children's depressive symptoms at Wave 2. Moreover, the association between concordance and children's depressive symptoms at Wave 1 and Wave 2 was moderated by child sex. Both concurrently and longitudinally, parent-child concordance of the CAR was positively associated with depressive symptoms for girls only. Further examination of regions of significance testing indicated that stronger parent-child adrenocortical concordance in early childhood was associated with higher levels of depressive symptoms for girls. In addition, weaker parent-child concordance in both early and middle childhood was associated with fewer depressive symptoms for girls.

Depression in particular has been consistently linked to the CAR. Specifically, abnormalities in the CAR have been observed in both currently and remitted depressed patients (Bhagwagar et al., 2005; Vreeburg et al., 2009) and the high-risk offspring of depressed parents (Goodyer, Herbert, Tamplin, & Altham, 2000), and prospectively predicts depression in adolescents (Adam et al., 2010). Indeed, the extant literature suggests that dysfunctional CAR may serve as a pre-existing vulnerability marker for

depression. As noted above, we had a high-risk sample comprised of approximately half of parents with a history of depression. Thus, it is possible that parents and children are demonstrating concordance of dysregulated CAR. This is only speculative at this time because our study focused on the level of concordance and its associations with child outcomes rather than the specific characteristics of the CAR in these high-risk dyads. Nevertheless, daughters of parents with a history of depression are at particular risk for developing depression themselves (Gotlib & Colich, 2014). Moreover, while rates of depression are similar for males and females in early childhood, females diverge from males in adolescence, displaying increased depressive symptomatology (Angold, Costello, & Worthman, 1998; Castelao & Kroner-Herwig, 2013). Our findings may be particularly noteworthy because we identified a female specific association between adrenocortical concordance and depressive symptoms prior to when the emergence of differentiation between male and female depressive symptomatology typically occurs in adolescence. Previous evidence consistently demonstrates the implication of the CAR in the pathophysiology of depression, and it is possible that parent-child concordance of the CAR more specifically serves as a mechanism contributing to sex differentiation in depression risk. Importantly, the association between social relationships and stress system functioning is particularly relevant for females (Boothe et al., 2008), which is salient to our findings given parent-child concordance of the CAR reflects the intersection between the parent-child relationship and stress physiology.

We also found that for girls only, weaker parent-child concordance (or discordance) of the CAR was associated with fewer depressive symptoms in early and middle childhood, which suggests that weaker adrenocortical discordance may be

protective. These findings are consistent with work by Suveg and colleagues (2016) whose findings demonstrated that low parent-child physiological synchrony or discordance in the context of high contextual risk factors was associated with children's better self-regulation. To further elucidate the role of parent-child adrenocortical concordance in the development of depression, future research is needed to examine whether low parent-child adrenocortical concordance of the CAR reduces the incidence of depression in the high-risk female offspring of depressed parents. Finally, it will be important to assess whether adrenocortical concordance emerges as a mechanism related to depressive symptomatology for males later in development or whether it remains a specific marker of risk for girls only.

ADHD symptoms. Bivariate correlations also revealed that stronger parent-child concordance of the CAR was associated with children's greater ADHD symptoms both concurrently and longitudinally. In regression models controlling for significant demographic covariates, the association between parent-child concordance and children's concurrent ADHD symptoms at Wave 1 reduced to trend level but remained significant for children's ADHD symptoms at Wave 2. When further controlling for children's ADHD symptoms at Wave 1, there was a marginally significant association between stronger parent-child concordance and increases in ADHD symptoms at Wave 2. Alterations in morning cortisol levels (Blomqvist et al., 2007; Ma et al., 2011) and cortisol levels in response to a stressor (Maldonado et al., 2009) have been linked to ADHD in children. Moreover, parenting a child with ADHD is particularly stressful for parents and adversely impacts parenting quality (Johnston & Mash, 2001; Thomas et al., 2016). Thus, parents of children with ADHD may experience disrupted stress responses

as well, and greater adrenocortical concordance in these dyads may be particularly problematic. Nevertheless, our findings should be interpreted with caution given associations reduced to trend levels once we controlled for additional covariates.

Psychosocial functioning. In addition to our findings demonstrating that parent-child adrenocortical concordance was associated with children's psychiatric symptoms (as described above), we extended those findings to demonstrate that adrenocortical concordance is also associated with impairments across multiple domains of functioning, including family and peer relationships, recreation, and academics. We observed significant bivariate associations between stronger parent-child concordance and children's poorer psychosocial functioning and greater global impairment ratings at Wave 1 and poorer psychosocial functioning at Wave 2. When controlling for significant covariates, only the association between stronger adrenocortical concordance and poorer psychosocial functioning at Wave 1 remained significant. Our findings provide further support for the validity of adrenocortical concordance as a clinically informative measure. It is particularly important to examine functional impairment in addition to psychiatric symptoms as poorer psychosocial functioning has been associated with negative outcomes in early adulthood (Lundh et al., 2016) highlighting its clinical significance and predictive validity.

There are several possible explanations for the association between parent-child concordance and children's symptoms and psychosocial functioning. First, it is possible that risk moderates associations between early concordance and children's later outcomes and stronger concordance is associated with poorer psychosocial functioning due to the observed increased psychiatric symptoms as described above. Second, it is possible that

adrenocortical concordance mediates associations between early parenting behavior and child outcomes. Persistent negative interactions and high levels of hostile parenting may lead to abnormal stress system functioning in both the parent and child and subsequent concordance. In turn, concordance of dysregulated stress physiology may lead to adverse outcomes for the parent and child due to abnormal stress response. Moreover, while we examined risk factors including parental history of depression and parental hostility, concordance may interact with other risk factors within the environment and parent-child dyad, including lack of peer support or high negative emotionality in the child. These processes are likely complex with different risk factors contributing to concordance and later outcomes, influencing trajectories of risk and resilience. Third, concordance within high-risk dyads may be predictive of negative outcomes because of shared genetic and environmental factors specific to the dyad. That is, shared genetic, biological, and environmental factors may contribute to concordance in high risk dyads and serve as an additional liability for maladjustment. At this time, the mechanisms through which concordance is related to child outcomes is unknown and these possible explanations are merely speculative. Future research is needed to identify these mechanisms and understand how parent-child adrenocortical concordance is related to child risk and resilience.

Parent-Child Adrenocortical Concordance of the CAR and Associations with Parent and Child Average Cortisol Levels

Previous research has demonstrated that level of cortisol response is related to child and parent outcomes, but the literature has been mixed with both high and low CAR or morning cortisol linked to children's physical and mental health outcomes (Chida &

Steptoe, 2009; Fries et al., 2009). Thus, we explored whether parent or child average morning cortisol moderated associations between adrenocortical concordance of the CAR and child outcomes described above. Results revealed that neither parent nor child average morning cortisol levels moderated associations between concordance and child outcomes. These findings suggest that our measure of parent-child concordance adds unique information that is separate from the level of the parent or child's morning cortisol response. Nevertheless, our study did not examine the concordance of the change in cortisol across the waking period or whether the magnitude of the change in cortisol levels moderated associations between concordance and child outcomes. This may be an avenue for future research given that change in morning cortisol levels has been specifically linked to depression and anxiety in adolescents (Adam et al., 2010; Adam et al., 2014; Vrshek-Schallhorn et al., 2013). Further investigation of the associations between different indices of adrenocortical concordance (e.g., average morning cortisol, amount of change in cortisol across the morning) and child outcomes will be important in further delineating how these biological processes are related to outcomes in children.

Parent-Child Adrenocortical Concordance of the CAR and Children's Hippocampal Volumes

Parent-child concordance of the CAR was not associated with children's hippocampal total volume or subregion volumes (i.e., head, body, tail) in middle childhood. There are several possible reasons for our null findings.

First, it is possible that our analyses were underpowered for our neuroimaging analyses. The current study relied on examining individual differences, which typically

yields smaller effect sizes. We detected small to medium effect sizes and it is possible that with a larger sample size we would have observed significant associations.

Second, there are a number of other factors that have been linked to children's hippocampal volume that must be considered, including level of children's cortisol response and parenting. For example, in the rodent literature, excess glucocorticoids have been linked to alterations in hippocampal structure, an effect that can be referred to as glucocorticoid toxicity (Woolley et al., 1990). Similarly, studies in humans examining links between HPA axis functioning and hippocampal volume have also examined amount of cortisol or changes in cortisol and found that increased levels of cortisol have been linked to smaller hippocampal volumes in children (Carrion et al., 2007), whereas decreased cortisol levels have been linked to smaller hippocampal volumes in adulthood (Narita et al., 2012). In addition, while the literature has been mixed (e.g., Rao et al., 2010a; Luby et al., 2012) evidence has demonstrated that the hippocampus is sensitive to the caregiving environment (e.g., Belsky & de Haan, 2011; Luby et al., 2012; Rao et al., 2010a,b). For example, one study observed associations between early childhood abuse and neglect and smaller hippocampal volumes in adolescence (Rao et al., 2010b), whereas another study found that maternal support during preschool years predicted larger hippocampal volumes in adolescence (Luby et al., 2012; cf. Rao et al., 2010a). Thus, it is possible that total cortisol volume and parenting may be related to hippocampal volume whereas concordance is not. It is also possible that associations between parent-child adrenocortical concordance and hippocampal structure may be dependent on both level of children's cortisol response and the parenting context. This highlights the need for future longitudinal investigations of adrenocortical concordance

and children's hippocampal volumes with close consideration of different indices of cortisol, such as total cortisol output, as well as the parenting context.

Third, our findings may be explained by the developmental timing of our measurements. The hippocampus continues to grow and change in childhood with hippocampal subregions undergoing distinct developmental trajectories (Gogtay et al., 2006; Lin et al., 2013), highlighting possible age effects on hippocampal structure. Indeed, while we may not see the effects of concordance on the hippocampus in middle childhood, differences may emerge in adolescence or even in adulthood. For example, evidence has consistently documented links between early childhood trauma and alterations in hippocampal volume in adults, but these associations are not present in childhood (e.g., Frodl & O'Keane, 2013). Future work would benefit from continued assessment of the associations between adrenocortical concordance and children's hippocampal volume over time.

Finally, given our other findings linking concordance of the CAR to risk factors for depression, it is possible that concordance may be associated with other brain regions linked to depression, such as the amygdala (e.g., Rosso et al., 2005; Thomas et al., 2001) and the ventral striatum (e.g., Epstein et al., 2006; Forbes & Dahl, 2012; Hanson, Hariri, & Williamson, 2015). For example, one study documented altered amygdala volumes in adolescent pediatric patients with depression compared to healthy controls but no changes in hippocampal volumes (Rosso et al., 2005). Furthermore, the amygdala plays an important role in HPA axis functioning (Herman, Ostrander, Mueller, & Figueiredo, 2005; Lupien et al., 2009), and previous work has also demonstrated that parenting behaviors, specifically negative parenting, has been related to larger amygdala volumes

in adolescent males (Whittle et al., 2009). Given concordance reflects the intersection between HPA axis functioning and the parent-child relationship, these studies further highlight the importance of examining associations between parent-child adrenocortical concordance and this brain region. In addition, functional neuroimaging studies may be another important area for future research. One study demonstrated that high levels of stress were associated with lower levels of positive affect in young adults with low ventral striatum reactivity to reward (Nikolova, Bogdan, Brigidi, & Hariri, 2012). Furthermore, decreased reward-related activity in the ventral striatum has been linked to depression (Epstein et al., 2006; Forbes & Dahl, 2012; Hanson et al., 2015; Sharp et al., 2014), and these brain systems involved in response to reward also have an important overlap with parenting (Barrett & Fleming, 2011). Evidence has shown that securely attached (Strathearn et al., 2009) and non-depressed mothers (Lorberbaum et al., 2002; Morgan et al., 2015) show increased activity in the ventral striatum in response to their own infants, whereas intrusive parenting has been linked to decreased ventral striatal activity (Rilling, 2013). Furthermore, brain regions do not function in isolation, but are connected by numerous systems, emphasizing the need to take a network perspective in future research. For example, increased release of dopamine in the ventral striatum has been related to cortisol release in response to a psychosocial stressor (Pruessner, Champagne, Meaney, & Dagher, 2004), highlighting links between regions associated with reward and stress response systems. Furthermore, functional MRI studies have demonstrated significant differences in functional connectivity between brain regions in adolescents with depression. For example, greater depressive symptoms in adolescents have been associated with decreased amygdala-hippocampal connectivity (Cullen et al.,

2014) and increased connectivity between the subgenual anterior cingulate cortex and amygdala (Ho et al., 2014). These studies highlight the complexity of the connections between these brain regions and the need to take a comprehensive network approach. If parent-child concordance of the CAR is a biological process linked to depression risk as our findings suggest, associations between parent-child adrenocortical concordance and the structure and function of other brain regions such as the amygdala and ventral striatum as well as their larger connectivity networks may be of particular interest to further understanding these pathways of risk.

Study Strengths and Limitations

The present study had several strengths. First, this is the first study to examine associations between parent-child adrenocortical concordance of the CAR and children's concurrent and longitudinal outcomes. Parent-child behavioral synchrony has been identified as an important factor impacting children's social and emotional development (e.g., Feldman & Greenbaum, 1997; Feldman, 2007a,b,2012), yet no prior study has examined how adrenocortical concordance is related to children's outcomes. Our findings are a critical next step to identifying how parent-child concordance may serve as a mechanism of risk. Second, we used a longitudinal assessment that allowed for the examination of children's outcomes over time. Importantly, children were first assessed during the preschool age and were followed-up three years later, which allowed us to assess the prediction of changes in children's outcomes, including changes in psychiatric symptoms and psychosocial functioning.

Third, our study included a rigorous assessment of parent and child CAR that included multiple cortisol samplings across the morning on two consecutive days.

Moreover, while previous work has quantified concordance of the CAR by examining concordance of parent and child slope of change scores between cortisol at waking and 30 minutes post-waking, we used advanced statistical analyses to include all 12 morning cortisol samplings (six parent, six child) in multilevel modeling and extracted the dyad-level random slope to represent concordance between parent and child cortisol levels across the morning. Our models also controlled for sampling related covariates, including parent and child waking time and compliance to sampling time. Fourth, this study had several methodological strengths through the incorporation of multiple methods. Specifically, our methods included semi-structured clinical interviews of parent psychopathology and child psychiatric symptoms and psychosocial functioning, an observational laboratory assessment of parenting behavior, rigorous assessment of the CAR, and neuroimaging methodologies, which included assessment of total hippocampal and subregion volumes.

This study also had limitations. First, we did not include temporal sequencing in our definition of adrenocortical concordance. However, the CAR is yoked to the individual's waking time, which is likely different between parent and child, preventing us from assessing concordance of the CAR temporally.

Second, we did not assess for parent-child adrenocortical concordance in middle childhood (Wave 2). Previous studies have investigated variability and stability of HPA axis functioning over time including examination of indices such as cortisol reactivity (e.g., Hankin, Badanes, Smolen, & Young, 2015; Leppert, Kushner, Smith, Lemay, & Dougherty, 2016) and the CAR (e.g., Platje et al., 2013; Ross, Murphy, Adam, Chen, & Miller, 2014), and future work would benefit from similar examination of adrenocortical

concordance. In addition, examination of concordance at multiple time points will provide important information on how associations between concordance and child outcomes may change across development. For example, one study found that parental history of depression was not associated with adrenocortical concordance for parents and adolescent females (LeMoult et al., 2015), whereas we previously observed stronger concordance in dyads with a parent with history of depression in a sample of parents and their preschool aged children (Merwin et al., 2017). Given the limited research at this time, further examination of concordance during different developmental periods is needed to fully understand these associations.

Third, we did not have a neuroimaging assessment in early childhood (Wave 1). Thus, we could not control for early hippocampal volumes or examine changes in children's total hippocampal or subregion volumes. The hippocampus has been found to undergo change in early childhood, including specific developmental trajectories for distinct subregions (DeMaster et al., 2013; Gogtay et al., 2006; Lin et al., 2013); thus, further examination of associations between concordance and the hippocampus over time will be particularly important for future investigation to identify whether adrenocortical concordance plays a role in hippocampal growth or change during other developmental time periods.

Fourth, our study included a limited number of fathers. Evidence has demonstrated sex differences for morning cortisol levels (Wüst et al., 2000) as well as differences in parenting behavior between mothers and fathers (e.g., Gable, Belsky, & Crnic, 1992). Given parent-child adrenocortical concordance represents a measure capturing the intersection between the parent-child relationship and HPA axis

functioning, future research would benefit from recruiting a larger number of fathers to examine how parent-child concordance differs for mothers and fathers and how concordance between fathers and children may be differentially related to children's outcomes.

Finally, approximately half of the parents included in our study had a lifetime history of depression. Interestingly, our findings suggest that in the context of risk, such as parental history of depression or increased negative parenting, parent-child concordance is related to children's poorer outcomes over time. However, our findings cannot be generalized to community or clinical samples and it will be important for future work to examine if stronger concordance may be related to positive outcomes for other dyads.

Conclusion

The extant literature has demonstrated that stronger behavioral synchrony between the parent and child provides an important perspective into the parent-child relationship and serves as a marker for positive outcomes for children. In an effort to understand the biological mechanisms underlying the parent-child relationship, biological synchrony or concordance has emerged as another critical process that may be relevant to children's outcomes. Indeed, our findings identified parent-child adrenocortical concordance of the CAR as an important process related to children's concurrent and longitudinal outcomes. Interestingly, we found that stronger parent-child adrenocortical concordance in the context of parent- and child-level risk factors was related to poorer outcomes for children. Our findings are consistent with recent work by Suveg and colleagues (2016), who found that children displayed low self-regulation in dyads with

high family risk and strong parent-child IBI synchrony. Stronger concordance observed in these high-risk dyads may represent concordance of a dysregulated stress response, leading to adverse outcomes for the dyad. Importantly, there are other factors likely impacting parent-child adrenocortical concordance and models explaining associations between concordance and child outcomes, including genetics and epigenetic factors, child temperament, and shared environmental factors such as shared sleep patterns, and exposure to chronic and/or social stressors (Fries et al., 2009). The processes involved are likely complex and incorporation of these variables will be important to further understanding the mechanisms through which parent-child adrenocortical concordance is related to children's outcomes.

Nevertheless, our findings hold important clinical implications for future prevention and intervention. For example, our findings further emphasize the importance of intervening at the level of the dyad and highlight the need to develop interventions that target the intersection between the parent-child relationship and underlying physiological functioning. To achieve this goal, research must further investigate how behavioral interventions promoting responsive parenting and positive parent-child interactions are related to parent-child adrenocortical concordance. Recent work has demonstrated that interventions promoting nurturing, responsive, and supportive parenting facilitates more typical cortisol production in young maltreated children (Bernard, Dozier, Bick, & Gordon, 2015; Cicchetti, Rogosch, Toth, & Sturge-Apple, 2011) and children removed from neglecting environments also show more normative cortisol rhythms across the day (Gunnar & Donzella, 2002). Similarly, emerging work has demonstrated that interventions targeted at enhancing the parent-child relationship within high-risk families

also promote adaptive parent stress system functioning (Toth, Sturge-Apple, Rogosch, & Cicchetti, 2015). If behavioral interventions have the ability to impact parents' and children's stress physiology, it is likely that parent-child adrenocortical concordance is also impacted. Investigation into these questions and how children's outcomes are subsequently influenced will shed light on the mechanisms through which the parent-child dyad and underlying biological processes have a profound impact on children's trajectories toward risk or resilience.

Table 1. *Parent and child demographic characteristics and salivary cortisol indicators*

	Wave 1 (<i>N</i> =142)	Wave 2 Behavioral Assessment (<i>n</i> =98)	Wave 2 MRI Assessment (<i>n</i> =51)
Child sex (female), <i>N</i> (%)	74 (52.1)	48 (49.0)	25 (49.0)
Parent sex (female), <i>N</i> (%)	127 (93.4)	90 (94.0)	47 (94.0)
Child age (months), <i>M</i> (<i>SD</i>); <i>range</i>	49.80 (9.64); 36.00-71.00	81.80 (11.86) 60.00-108.00	79.53 (10.99); 60.00-108.00
Parent age (years), <i>M</i> (<i>SD</i>); <i>range</i>	34.90 (6.52); 21.00-57.00	38.88 (5.89); 24.00-51.00	38.20 (6.16); 24.00-51.00
Parent marital status, <i>N</i> (%)			
Married or cohabitating	104 (69.7)	70 (71.4)	36 (70.5)
Divorced, separated	11 (7.7)	14 (14.3)	14 (11.9)
Never married	27 (19.0)	14 (14.2)	9 (17.6)
Parent education, <i>N</i> (%)			
Some high school	1 (.7)	0 (0)	0 (0)
High school graduate (or GED)	6 (4.3)	3 (3.1)	3 (6.0)
Some college (or 2 year degree)	49 (34.8)	25 (26.0)	18 (36.0)
4 year college degree or more	85 (60.2)	68 (70.9)	29 (58.0)
Child race/ethnicity, <i>N</i> (%)			
White	68 (48.2)	46 (47.4)	24 (47.1)
Black/African-American	49 (34.8)	28 (28.9)	16 (31.4)
Asian	2 (1.4)	0 (0)	0 (0)
Multi-racial	10 (7.1)	20 (20.6)	10 (19.6)
Other	12 (8.5)	3 (3.1)	1 (2.0)

Hispanic	23 (16.4)	15 (16.1)	8 (17.0)
Income, % (N)			
<\$20,000	10 (7.2)	7 (7.1)	5 (9.8)
\$20,001-\$40,000	15 (10.9)	5 (5.1)	3 (5.9)
\$40,001-\$70,000	27 (19.6)	20 (20.4)	10 (19.6)
\$70,001-\$100,000	38 (27.5)	22 (22.4)	11 (21.6)
>\$100,000	48 (34.8)	44 (44.9)	22 (43.1)
Parental lifetime depressive disorder, % (N)	69 (49.6)	53 (54.6)	27 (54.0)
<i>Child salivary cortisol indicators, M (SD); range</i>			
Time of waking (h), Day 1	7:22 (0:54); 4:28-10:15	7:20 (0:55); 4:28-10:15	7:31 (0:56); 5:29-10:15
Time of waking (h), Day 2	7:22 (1:02); 4:46-11:00	7:16 (0:57); 4:46-11:00	7:23 (1:00); 5:27-11:00
Cortisol waking values (nmol/L), Day 1	7.57 (5.07); .12-31.57	7.28 (4.24); .12-20.32	7.68 (3.90); .12-18.91
Cortisol waking values (nmol/L), Day 2	7.83 (5.15); .22-28.26	8.02 (5.40); 1.10-28.26	7.89 (4.88); 1.34-22.77
Cortisol waking + 30 min values (nmol/L), Day 1	9.91 (5.91); .52-31.02	9.88 (5.98); .52-31.02	9.93 (5.96); 1.95-31.02
Cortisol waking + 30 min values (nmol/L), Day 2	9.74 (5.07); .46-25.72	9.98 (4.99); .64-25.72	10.18 (4.85); 1.18-24.29
Cortisol waking + 45 min values (nmol/L), Day 1	7.94 (5.21); .15-32.36	7.77 (4.97); .15-32.36	7.71 (4.92); .15-32.36
Cortisol waking + 45 min values (nmol/L), Day 2	7.74 (4.85); .38-32.90	7.84 (4.60); .38-32.90	7.48 (3.32); .97-15.49
<i>Parental salivary cortisol indicators, M (SD); range</i>			
Time of waking (h), Day 1	6:58 (1:02); 3:00-9:55	6:54 (0:56); 3:48-9:55	6:53 (0:50); 4:58-9:20
Time of waking (h), Day 2	6:56 (1:06); 4:00-11:05	6:48 (1:00); 4:00-11:05	6:50 (1:03); 4:00-11:05
Cortisol waking values (nmol/L), Day 1	9.20 (5.22); .44-26.51	9.25 (4.97); .44-26.51	9.17 (5.35); .91-26.51
Cortisol waking values (nmol/L), Day 2	9.06 (4.38); .25-23.38	9.17 (4.45); .25-23.38	9.02 (4.48); 1.50-22.10

Cortisol waking + 30 min values (nmol/L), Day 1	11.75 (6.51); .53-31.16	11.85 (6.48); .53-30.85	11.90 (6.13); 1.84-27.84
Cortisol waking + 30 min values (nmol/L), Day 2	11.27 (5.13); .56-29.87	11.74 (5.31); .56-29.87	11.25 (4.58); 1.69-21.15
Cortisol waking + 45 min values (nmol/L), Day 1	10.01 (5.43); .52-33.31	10.11 (5.37); .52-33.31	10.01 (4.70); 1.36-23.28
Cortisol waking + 45 min values (nmol/L), Day 2	9.44 (4.49); .77-25.06	9.78 (4.68); .78-25.06	9.56 (3.94); 2.12-19.12

Note. Categorical variables are presented as frequency and percentage; continuous variables are presented as mean and standard deviation. Cortisol values reflect raw values and are presented in nmol/L.

Table 2. *Hippocampal subregion volumes (n=51)*

	<i>M (SD)</i>	Min	Max
Total hippocampal volume	8450.17 (534.15)	7037.70	9644.07
Right hippocampal total volume	4267.34 (303.35)	3523.88	4862.83
Right hippocampal head	2148.33 (282.32)	1597.65	2772.06
Right hippocampal body	1421.41 (157.95)	1056.06	1812.16
Right hippocampal tail	697.19 (119.38)	377.54	981.02
Left hippocampal total volume	4182.83 (292.71)	3513.82	4854.97
Left hippocampal head	1992.39 (299.83)	1431.75	2843.41
Left hippocampal body	1536.82 (201.60)	1002.41	1972.95
Left hippocampal tail	654.56 (111.68)	297.89	924.21

Note. Volumes are presented in mm³. Volumes adjusted to control for total intracranial volume (Raz et al., 2005).

Table 3.

Bivariate correlations among major study variables

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	
1. Parent-child concordance	-																					
Wave 1 outcomes																						
2. ADHD symptoms	.18*	-																				
3. ODD symptoms	.02	.27**	-																			
4. Depression symptoms	.09	.41***	.55***	-																		
5. Anxiety symptoms	.11	.31***	.13	.41***	-																	
6. CGAS score	-.21*	-.46***	-.63***	-.65***	-.44***	-																
7. Global impairment	.18*	.33***	.51***	.52***	.30***	-.76***	-															
8. Observed parental hostility	.15	.08	-.03	.02	-.09	.08	.99***	-														
Wave 2 outcomes																						
9. ADHD symptoms	.21*	.49***	.20*	.27**	.13	-.37***	.29**	.02	-													
10. ODD symptoms	-.06	.32**	.40***	.49***	.10	-.38***	.39***	-.04	.39***	-												
11. Depression symptoms	.24*	.28**	.23*	.47***	.26*	-.50***	.39***	-.03	.30**	.50***	-											
12. Anxiety symptoms	.16	.25*	.19	.38***	.46***	-.48***	.31**	-.03	.34**	.32**	.60***	-										
13. CGAS score	-.23*	-.37***	-.33**	-.50***	-.26*	.57***	-.47***	.002	-.61***	-.62***	-.70***	-.60***	-									
14. Global impairment	.16	.23*	.20	.36***	.15	-.47***	.44***	-.09	.33**	.59***	.74***	.51***	-.78***	-								
15. Observed parental hostility	.40***	.14	-.04	.15	.09	-.09	-.002	.48***	.11	-.08	.09	-.02	.10	.98***	-							
Covariates																						
16. Child sex	-.10	-.24**	-.13	.04	.14	.16	-.22**	-.08	-.22*	-.05	-.15	-.02	.15	-.14	-.13	-						
17. Child age Wave 1	-.05	-.03	-.01	.09	-.07	.002	-.04	-.11	.12	.11	.07	.04	-.08	.22*	.02	-.04	-					
18. Child age Wave 2	.08	-.11	-.07	-.08	-.15	.16	.21*	-.13	.11	.01	.03	.02	.01	.04	.12	.10	.04	-				
19. Child race/ethnicity	.06	.19*	-.05	.13	.25**	-.04	.05	.30***	.08	-.004	.10	-.003	.01	-.07	.33**	-.01	-.02	.04	-			
20. Parent education status Wave 1	-.09	-.12	-.11	.002	.02	-.02	-.09	-.32***	.10	<.001	-.02	.13	-.03	.11	-.09	-.03	.09	.10	-.22*	-		
21. Parent education status Wave 2	-.05	-.18	-.19	-.13	.04	.12	-.19	-.26*	.06	-.02	-.02	.13	.03	.08	-.07	-.02	.08	.13	-.11	.94***	-	
22. Parental depression history	.13	.13	.18*	.22*	.20*	-.24**	.22*	.04	.12	.11	.20	.17	-.20	.17	.09	-.11	-.04	-.29**	.05	-.06	-.04	

Note. Wave 1 $N = 142$ dyads. Wave 2 $n = 98$ dyads. ADHD symptoms, anxiety symptoms, and parental hostility scales were \log_{10}

transformed. Parent and child average cortisol represents the average of raw cortisol levels in nmol/L. * $p < .05$, ** $p < .01$, *** $p < .001$.

Table 4.

Concurrent associations between parent-child adrenocortical concordance at Wave 1 and children's psychiatric symptoms and observed parenting at Wave 1

	Wave 1 parental hostility		Wave 1 ADHD symptoms		Wave 1 ODD symptoms		Wave 1 depressive symptoms		Wave 1 anxiety symptoms	
	<i>b</i> (<i>SE</i>)	<i>B</i>	<i>b</i> (<i>SE</i>)	<i>B</i>	<i>b</i> (<i>SE</i>)	<i>B</i>	<i>b</i> (<i>SE</i>)	<i>B</i>	<i>b</i> (<i>SE</i>)	<i>B</i>
Child age	--	--	--	--	--	--	--	--	--	--
Child sex	--	--	-.17 (.06)	-.23**	--	--	--	--	--	--
Child race/ethnicity	.05 (.02)	.24**	.15 (.06)	.20*	--	--	--	--	.16 (.05)	.29**
Parent education status	-.04 (.02)	-.21*	--	--	--	--	--	--	--	--
Wave 1 parent-child adrenocortical concordance	.01 (.01)	.12	.05 (.03)	.14 [†]	.03 (.25)	.01	.19 (.21)	.08	.02 (.02)	.09

Note. Parental hostility, ADHD symptoms, and anxiety symptoms scales were log₁₀ transformed. [†]*p* < .10, **p* < .05, ***p* < .01, ****p* < .001.

Table 5.

Concurrent associations between parent-child adrenocortical concordance at Wave 1 and children's psychosocial functioning at Wave 1

	Wave 1 CGAS score		Wave 1 Average Impairment	
	<i>b(SE)</i>	<i>B</i>	<i>b(SE)</i>	<i>B</i>
Child age	--	--	--	--
Child sex	--	--	-.22 (.09)	-.21*
Child race/ethnicity	--	--	--	--
Parent education status: at least a 4-year college degree	--	--	--	--
Wave 1 parent-child adrenocortical concordance	-2.87 (1.18)	-.21*	.09 (.05)	.16 [†]

Note. [†] $p < .10$, * $p < .05$, ** $p < .01$, *** $p < .001$.

Table 6.

Longitudinal associations between parent-child adrenocortical concordance and children's psychiatric symptoms and observed parenting at Wave 2

	Adrenocortical Concordance at Wave 1			
	Adjusted for significant demographic covariates		Adjusted for significant demographic covariates and corresponding scale at Wave 1	
	<i>b(SE)</i>	<i>B</i>	<i>b(SE)</i>	<i>B</i>
Wave 2 parental hostility	.04 (.01)	.37***	.03 (.01)	.35***
Wave 2 ADHD symptoms	.87 (.41)	.21*	.73 (.37)	.18†
Wave 2 ODD symptoms	-.16 (.28)	-.06	-.12 (.26)	-.04
Wave 2 depressive symptoms	.79 (.33)	.24*	.70 (.31)	.21*
Wave 2 anxiety symptoms	.04 (.03)	.16	.02 (.03)	.08

Note. ADHD symptoms, anxiety symptoms, and parental hostility scales were \log_{10} transformed. † $p < .10$, * $p < .05$, ** $p < .01$,

*** $p < .001$.

Table 7.

Longitudinal associations between parent-child adrenocortical concordance at Wave 1 and children's psychosocial functioning at Wave 2

	Adrenocortical Concordance at Wave 1			
	Wave 2 CGAS score		Wave 2 Average Impairment	
	<i>b(SE)</i>	<i>B</i>	<i>b(SE)</i>	<i>B</i>
Not adjusted	-2.64 (1.19)	-.23*	.08 (.05)	.16
Adjusted for Wave 1 psychiatric symptoms	-2.12 (1.01)	-.18 [†]	.06 (.05)	.12
Adjusted for Wave 2 psychiatric symptoms	-.55 (.78)	-.05	-.002 (.03)	-.004

Note. [†] $p < .10$, * $p < .05$, ** $p < .01$, *** $p < .001$.

Table 8.

Bivariate correlations among adrenocortical concordance at Wave 1, total hippocampal and subregion volumes at Wave 2, and study covariates

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1. Parent-child concordance at Wave 1	-														
Hippocampal volumes at Wave 2															
2. Total volume	.21	-													
3. Right hemisphere	.16	.90***	-												
4. Right head	.11	.75***	.79***	-											
5. Right body	.11	.04	.04	-.48***	-										
6. Right tail	.02	.46**	.59***	.23	-.03	-									
7. Left hemisphere	.22	.89***	.61***	.56***	.03	.23	-								
8. Left head	.23	.68***	.52***	.74***	-.44**	.12	.70***	-							
9. Left body	-.03	.08	.24	.57***	-.13	.13	.13	-.49***	-						
10. Left tail	-.05	.34*	.03	.05	.49***	.37**	.37**	.1	-.26	-					
Covariates															
11. Child sex	-.10	-.18	-.20	-.25	.19	-.08	-.12	-.33*	.25	-.11	-				
12. Child age at Wave 2	.04	-.001	.03	-.18	.38**	-.04	-.03	-.03	.09	.08	.10	-			
13. Child race/ethnicity	-.10	-.08	.04	-.12	.19	.20	-.18	.19	-.12	.10	-.10	.04	-		
14. Parent education status Wave 2	-.11	.13	.19	.14	-.004	.10	.04	.03	.06	.05	.17	.18	-.19	-	
15. Parental depression history	.17	.07	.03	.11	-.09	-.07	.09	.20	-.14	.04	-.20	-.19	.07	-.17	-

Note. Wave 2 MRI visit $n = 51$. Hippocampal volumes were adjusted to control for total intracranial volume (Raz et al., 2005). † $p <$

.10, * $p < .05$, ** $p < .01$, *** $p < .001$.

Table 9.

Longitudinal associations between adrenocortical concordance at Wave 1 and children's hippocampal volumes at Wave 2

	Left hippocampal volumes								
	Left head		Left body		Left tail		Total left hemisphere		
	<i>b</i> (<i>SE</i>)	<i>B</i>	<i>b</i> (<i>SE</i>)	<i>B</i>	<i>b</i> (<i>SE</i>)	<i>B</i>	<i>b</i> (<i>SE</i>)	<i>B</i>	
Child sex	-176.37 (82.21)	-.30*	--	--	--	--	--	--	--
Child age at Wave 2	--	--	--	--	--	--	--	--	--
Child race/ethnicity	--	--	--	--	--	--	--	--	--
Parent education status Wave 2	--	--	--	--	--	--	--	--	--
Parent-child adrenocortical concordance	63.80 (43.76)	.20	-5.50 (31.39)	-.03	-5.74 (17.52)	-.05	67.20 (43.55)	.22	

	Right hippocampal volumes								Total	
	Right head		Right body		Right tail		Total right hemisphere		Total volume	
	<i>b</i> (<i>SE</i>)	<i>B</i>	<i>b</i> (<i>SE</i>)	<i>B</i>	<i>b</i> (<i>SE</i>)	<i>B</i>	<i>b</i> (<i>SE</i>)	<i>B</i>	<i>b</i> (<i>SE</i>)	<i>B</i>
Child sex	--	--	--	--	--	--	--	--	--	--
Child age at Wave 2	--	--	5.44 (1.96)	.38**	--	--	--	--	--	--
Child race/ethnicity	--	--	--	--	--	--	--	--	--	--
Parent education status Wave 2	--	--	--	--	--	--	--	--	--	--
Parent-child adrenocortical concordance	32.60 (42.82)	.11	15.84 (22.61)	.10	2.24 (18.44)	.02	51.52 (46.22)	.16	118.71 (80.19)	.21

Note. Hippocampal volumes were adjusted to control for total intracranial volume (Raz et al., 2005). † $p < .10$, * $p < .05$, ** $p < .01$, *** $p < .001$.

Table 10.

The interactive effect between parent-child adrenocortical concordance at Wave 1 and parental hostility at Wave 1 predicts changes in observed parental hostility from Wave 1 to Wave 2

	Wave 2 observed parental hostility		
	<i>b</i>	<i>SE</i>	<i>t</i>
Child age	--	--	--
Child sex	--	--	--
Child race/ethnicity	.03	.02	1.72 [†]
Parent education status	.01	.02	.33
Wave 1 observed parental hostility	.04	.01	4.37***
Wave 1 Parent-child adrenocortical concordance	.04	.01	4.42***
Parent-child adrenocortical concordance x Wave 1 observed parental hostility	.03	.01	3.77**

Note. [†] $p < .10$, * $p < .05$, ** $p < .01$, *** $p < .001$.

Table 11.

The interactive effect between parent-child adrenocortical concordance at Wave 1 and parental history of depression predicts changes in observed parental hostility from Wave 1 to Wave 2

	Wave 2 observed parental hostility		
	<i>b</i>	<i>SE</i>	<i>t</i>
Child age	--	--	--
Child sex	--	--	--
Child race/ethnicity	.04	.02	1.99*
Parent education status	.02	.02	1.06
Wave 1 observed parental hostility	.11	.03	3.77***
Wave 1 Parent-child adrenocortical concordance	.06	.01	5.07***
Parental history of depression	-.01	.02	-.78
Parent-child adrenocortical concordance x Parental history of depression	-.05	.02	-3.08**

Note. 0 = No parental history of depression, 1 = Parental history of depression. † $p < .10$,

* $p < .05$, ** $p < .01$, *** $p < .001$.

Table 12.

The interactive effect between parent-child adrenocortical concordance at Wave 1 and child sex on observed parental hostility at Wave 1 and Wave 2

	Wave 1 observed parental hostility			Wave 2 observed parental hostility		
	<i>b</i>	<i>SE</i>	<i>t</i>	<i>b</i>	<i>SE</i>	<i>t</i>
Child age	--	--	--	--	--	--
Child race/ethnicity	.05	.02	3.37**	.03	.02	1.48
Parent education status	-.03	.02	-1.96 [†]	.01	.02	.58
Wave 1 parental hostility	--	--	--	.14	.03	4.81***
Child sex	-.01	.02	-.41	-.02	.02	-1.11
Wave 1 parent-child adrenocortical concordance	.01	.01	1.23	.01	.01	.82
Wave 1 parent-child adrenocortical concordance x Child sex	-.06	.02	-.42	.05	.02	2.97**

Note. Child sex 0 = male, 1 = female. [†] $p < .10$, * $p < .05$, ** $p < .01$, *** $p < .001$.

Table 13.

The interactive effect between parent-child adrenocortical concordance at Wave 1 and child sex on children's depressive symptoms at Wave 1 and Wave 2

	Wave 1 depressive symptoms			Wave 2 depressive symptoms		
	<i>b</i>	<i>SE</i>	<i>t</i>	<i>b</i>	<i>SE</i>	<i>t</i>
Child age	--	--	--	--	--	--
Child race/ethnicity	--	--	--	--	--	--
Parent education status	--	--	--	--	--	--
Child sex	.26	.42	.62	-.95	.64	-1.49
Wave 1 parent-child adrenocortical concordance	-.29	.30	-.97	.12	.46	.26
Wave 1 parent-child adrenocortical concordance x Child sex	.98	.42	2.33*	1.34	.65	2.07*

Note: Child sex 0 = male, 1 = female. † $p < .10$, * $p < .05$, ** $p < .01$, *** $p < .001$.

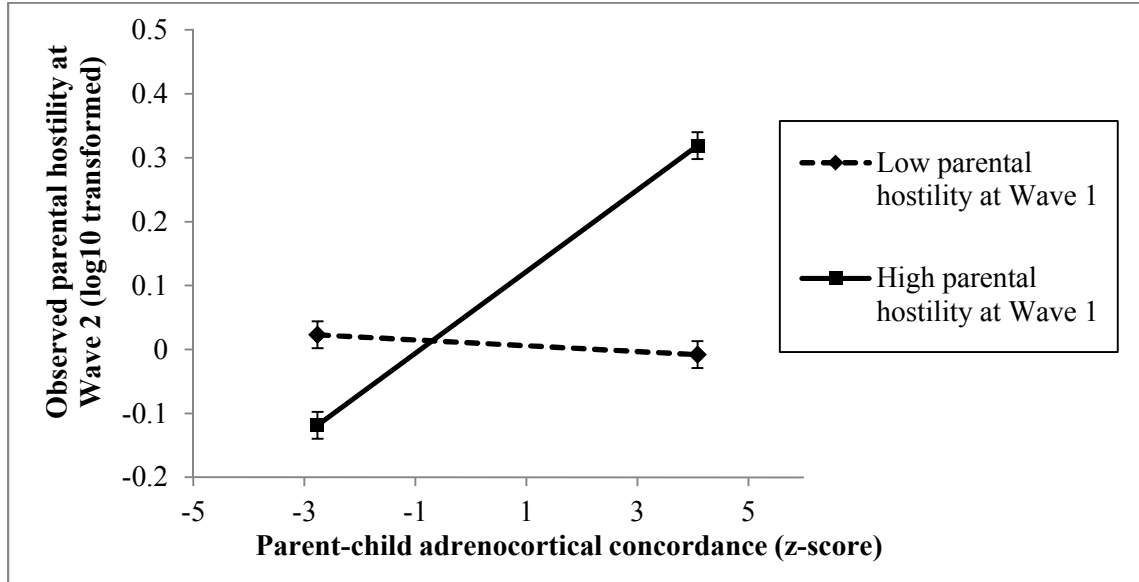


Figure 1. Changes in observed parental hostility from Wave 1 to Wave 2 as a function of Wave 1 parental hostility and parent-child adrenocortical concordance. Observed parental hostility at Wave 2 was log₁₀ transformed.

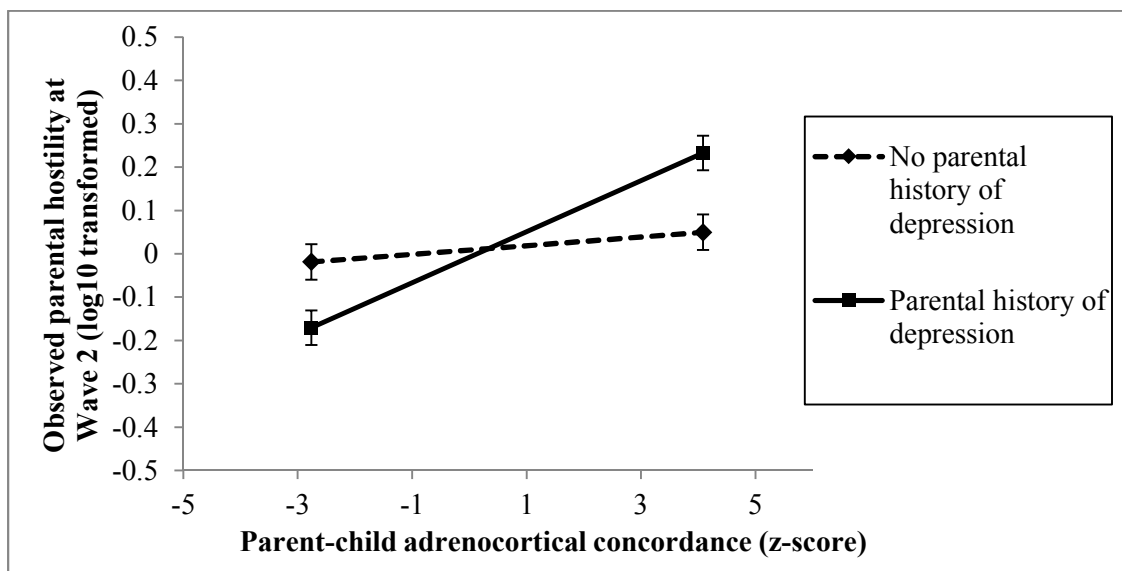


Figure 2. Changes in observed parental hostility from Wave 1 to Wave 2 as a function of parental history of depression and parent-child adrenocortical concordance. Observed parental hostility was log₁₀ transformed

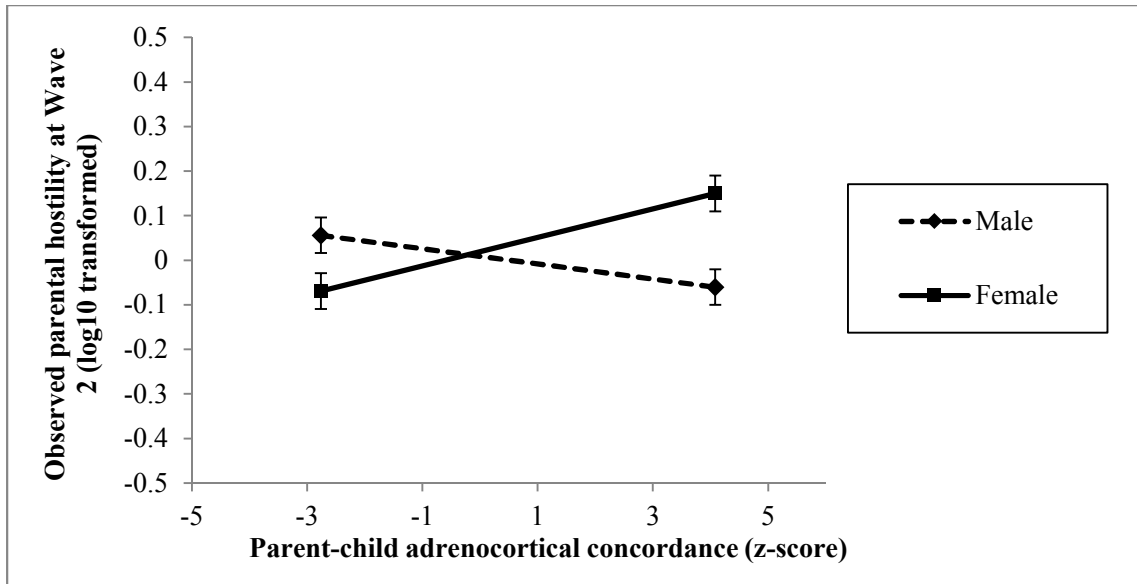


Figure 3. Changes in observed parental hostility from Wave 1 to Wave 2 as a function of child sex and parent-child adrenocortical concordance. Observed parental hostility was \log_{10} transformed.

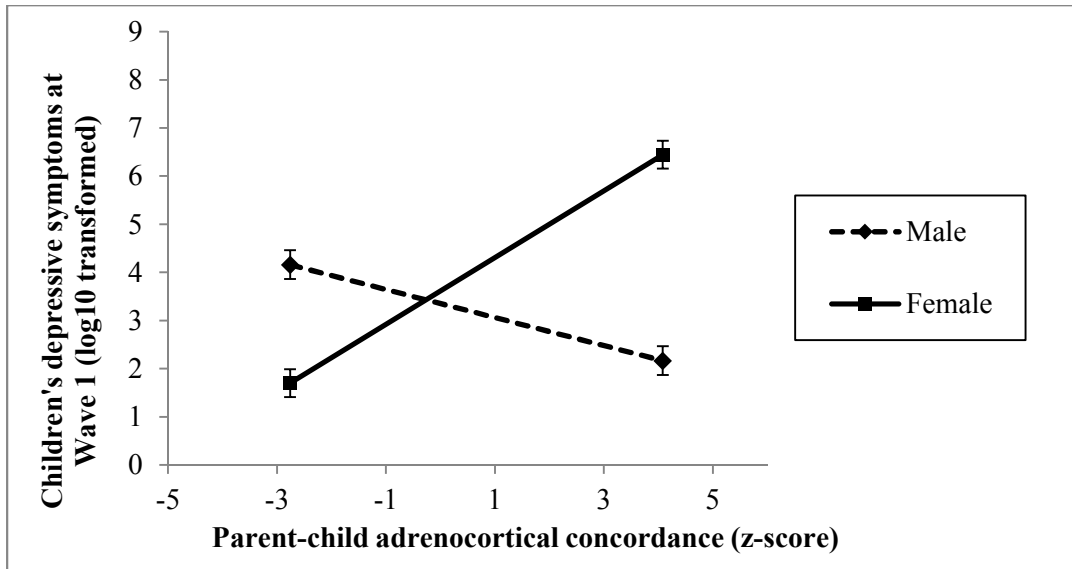


Figure 4. Children's depressive symptoms at Wave 1 as a function of child sex and parent-child adrenocortical concordance.

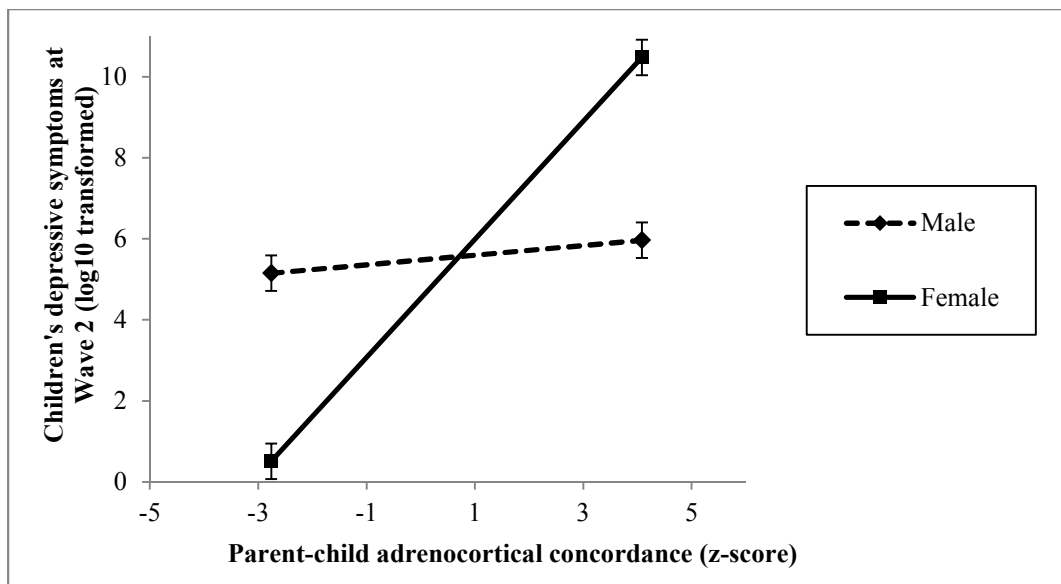


Figure 5. Children's depressive symptoms at Wave 2 as a function of child sex and parent-child adrenocortical concordance.

Appendix A. Supplemental Analyses

Parent-child adrenocortical concordance x parental lifetime depression

We examined the interaction between parent-child adrenocortical concordance at Wave 1 and parental history of depression with children's psychiatric symptoms at Wave 1 and Wave 2 as the dependent variable in separate models. When controlling for significant demographic covariates and the corresponding symptom scale at Wave 1, there was a marginally significant interaction between parent-child adrenocortical concordance at Wave 1 and parental history of depression on children's ADHD symptoms at Wave 2 ($b = .16$, $SE = .09$, $t = 1.93$, $p = .057$). For parents without a history of depression, lower parent-child adrenocortical concordance at Wave 1 predicted decreases in children's ADHD symptoms from Wave 1 to Wave 2 ($b = .17$, $SE = .06$, $t = 2.72$, $p = .008$), whereas for parents with a history of depression, parent-child adrenocortical concordance at Wave 1 was not significantly associated with changes in children's ADHD symptoms from Wave 1 to Wave 2 ($b = .01$, $SE = .05$, $t = .18$, $p = .857$). Reversing the moderator, regions of significance tests also demonstrated that this moderated effect was specific to dyads with levels of adrenocortical concordance less than -2.58 (standardized z -score). However, at this level of adrenocortical concordance, the findings only apply to two parent-child dyads.

Next, we examined the interaction between adrenocortical concordance at Wave 1 and parental history of depression on children's psychosocial functioning at Wave 1 and Wave 2. As seen in Table 1A and Figure 1A, when controlling for children's CGAS scores at Wave 1, we observed a significant interaction between adrenocortical concordance at Wave 1 and parental history of depression on children's CGAS scores at

Wave 2 ($b = -4.15$, $SE = 2.04$, $t = -2.03$, $p = .046$). For parents without a history of depression, lower adrenocortical concordance at Wave 1 was associated with increases in children's CGAS scores from Wave 1 to Wave 2 ($b = -3.97$, $SE = 1.57$, $t = -2.54$, $p = .013$), whereas for parents with a history of depression, adrenocortical concordance at Wave 1 was not associated with changes in children's Wave 2 CGAS scores ($b = .18$, $SE = 1.31$, $t = .14$, $p = .893$). Reversing the moderator, regions of significance tests demonstrated that this moderated effect was specific to levels of adrenocortical concordance less than -1.33 (standardized z-score). This interaction effect persisted after controlling for all psychiatric symptom scales at Wave 2 in addition to significant covariates ($b = -4.53$, $SE = 2.24$, $t = 2.02$, $p = .046$). However, at this level of adrenocortical concordance, the findings only apply to six parent-child dyads.

Table 1A.

The interactive effect between parent-child adrenocortical concordance at Wave 1 and parental history of depression predicts changes in children's CGAS scores from Wave 1 to Wave 2

	Wave 2 CGAS score		
	<i>b</i>	<i>SE</i>	<i>t</i>
Child age	--	--	--
Child gender	--	--	--
Child race/ethnicity	--	--	--
Parent education status	--	--	--
Wave 1 CGAS scores	.43	.07	5.98***
Wave 1 parent-child adrenocortical concordance	.18	1.31	.14
Parental history of depression	1.03	2.04	.50
Wave 1 parent-child adrenocortical concordance x parental history of depression	-4.15	2.04	-2.03*

Note. 0 = no parental history of depression, 1 = parental history of depression. † $p < .10$, * $p < .05$, ** $p < .01$, *** $p < .001$.

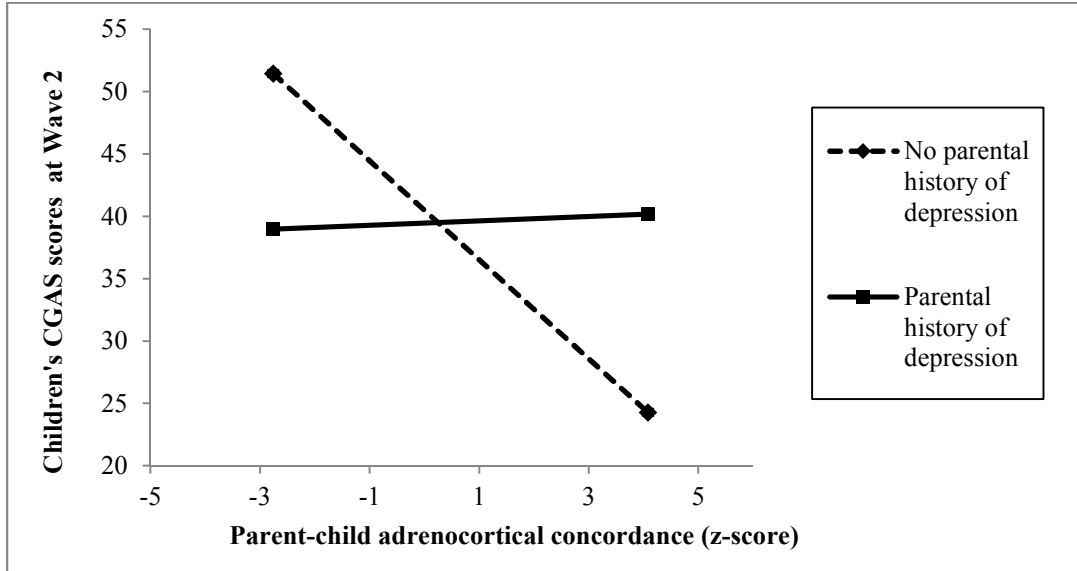


Figure 1A. Changes in children's CGAS scores from Wave 1 to Wave 2 as a function of parental history of depression and parent-child adrenocortical concordance.

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