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Emotion Regulation in Infants of Depressed Mothers: A Multi-Systems Approach

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Emotion Regulation in Infants of Depressed Mothers: A Multi-Systems Approach

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An abstract of
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Abstract

Emotion Regulation in Infants of Depressed Mothers: A Multi-Systems Approach
By Cara M. Lusby

The goal of the current study was to examine associations between multiple behavioral and biological systems of emotion regulation over the course of infancy and the role of maternal depressive symptoms in predicting these associations. Participants were women with a history of depression and/or anxiety and their infants (n = 242). Women were recruited during pregnancy and their depressive symptoms were measured repeatedly throughout pregnancy and the postpartum. Infant behavioral (temperament, observed affect) and biological (EEG, RSA, cortisol) measures were collected at 3-, 6-, and 12-months of age, and mothers' concurrent depressive symptoms were also measured. Infant baseline RSA and resting cortisol did not significantly interact to predict infant observed negative affect concurrently or prospectively; however, there was a significant main effect for cortisol at 6 months predicting observed negative affect at 12 months. In addition, infants clustered into different emotion regulation profiles based on biology and behavior at 3-, 6-, and 12-months of age, and maternal perinatal depressive symptoms differentially predicted membership in these profiles. Findings highlight the importance of exploring how biological and behavioral domains of emotion regulation relate over the course of infancy and may be associated with depressive symptomatology in mothers. Future research should consider indices of biological responsivity to stressors in addition to baseline or resting measures, as well as how these multiple indices together may predict the development of psychopathology.

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Emotion Regulation in Infants of Depressed Mothers: A Multi-Systems Approach

Emotion regulation is a concept that has been defined in many different ways as a search for one standard definition continues. One commonly accepted definition, as evidenced by multiple citations, is that of Thompson (1994), who describes emotion regulation as involving internal and external processes that work to modify the intensity and duration of emotional reactions in order to accomplish goals. Children's problems with emotion regulation are at the core of many disorders, including depression (Cole, Michel, & Teti, 1994), and may represent one pathway to mental disorder. Individual differences in emotion regulation begin to emerge as early as infancy (Stifter, 2002), and poorer regulation during infancy is associated with higher levels of psychopathology in childhood and adolescence (Degangi, Breinbauer, Doussard-Roosevelt, Porges, & Greenspan, 2000; Fendrich, Warner, & Weissman, 1990; Stifter & Jain, 1998). Thus emotion regulation difficulties may be a marker of vulnerability to the later development of psychopathology, and therefore, a better understanding of early indicators of emotion regulation holds great promise in furthering understanding of the etiology of psychopathology.

As is true for the Thompson (1994) definition of emotion regulation, most emotion regulation definitions include the notion of multivariate domains (Calkins, Dedmon, Gill, Lomax, & Johnson, 2002; Keenan, 2000; Stifter, 2002). Such domains include the stress response system (including the autonomic nervous system and the neuroendocrine system), cortical activity, and behavioral systems (Davidson et al, 1998; Gotlib et al, 1998). Nonetheless, most published studies of emotion regulation in infants operationally define it as a single one of these domains. Given this approach, the

associations within and between these domains has been largely unexplored, with theoretical disagreement in the literature about how highly interrelated these domains may be. While some argue that systems are closely linked (Calkins et al., 2002), others suggest instead that strong relations among the domains are not expected (Gunnar, Brodersen, Krueger, & Rigatuso, 1996; Keenan, 2000), but that despite their distinction, all domains represent critical emotion regulation processes (Mauss & Robinson, 2009). In general, studies of behavioral measures of emotion regulation, such as temperament, rarely examine biological variables (Calkins et al., 2002). In a seminal paper on domains of emotion regulation, Bauer, Quas, and Boyce (2002) called for investigation of how multiple systems relate to each other, albeit with a specific focus on biological systems, as being promising in enhancing prediction of later psychopathology.

Examining emotion regulation in more than one domain would allow for the study of the "coupling" of emotion regulation processes (Monk, 2001). Coupling is defined as the response of one system that immediately precedes or immediately follows that of another system (DiPietro, Hodgson, Costigan, Hilton, & Johnson, 1996). In support of the argument that systems are closely linked (Calkins et al., 2002), coupling of fetal heart rate and movement has been suggested to index well-being (DiPietro et al., 1996). Coupling of domains of emotion regulation in infants may similarly be suggestive of more adaptive regulation. Further, Nigg (2006) suggested that if behavioral, physiological, and temperamental domains do not co-regulate, there is increased risk for the development of psychopathology.

The extent to which emotion regulation systems are linked likely varies over the course of development. For example, there is theoretical support for developmental

changes in the correlation between behavioral and biological measures of emotion regulation (Beauchaine, 2001); in other words, as normative behavioral changes take place across development, the relation between biology and behavior will also change. Further, it has been suggested that behavioral traits and neural systems associated with emotion regulation may change at differing rates across development (Kagan & Snidman, 2004). As such, systems of emotion regulation may continually adapt, reorganize, and differentiate from one another over time (Nigg, 2006). Yet, there is little knowledge of how systems may relate to each other differently at different points over the course of infancy.

Given the understanding that multiple systems are involved in emotion regulation, and based on the idea that the relation between multiple systems may enhance prediction of later psychopathology (Bauer et al., 2002), three particularly significant unanswered questions with regard to multiple systems of emotion regulation in infants are: (1) to what extent are the biological systems of emotion regulation coordinated, (2) is this coordination of biological systems related to behavioral indices of emotion regulation, and (3) how do the associations between systems change over the course of infancy. Examining the associations between biological and behavioral systems over the course of infancy may elucidate the role that biological systems play in regulating behavior and help reveal whether systems may become reorganized over the course of development (Bauer et al., 2002; Shiner et al., 2012). In turn, understanding the relation between multiple biological and behavioral systems would allow for identification of "response profiles" in individuals that may represent vulnerability to later psychopathology (Bauer et al., 2002; Keenan, 2000).

Behavioral Systems of Emotion Regulation

Temperament and behavioral approach and withdrawal processes (indexed by observed affect) are the two behavioral systems widely accepted as indexing emotion regulation processes, beginning in infancy. As defined by Rothbart (Rothbart & Derryberry, 1981; Rothbart & Sheese, 2007), temperament in infants is a measure of individual differences in reactivity and self-regulation of emotion, and is comprised of Negative Affectivity, Surgency/Extraversion, and Orienting/Regulation (Rothbart & Derryberry, 1981). Behavioral approach and withdrawal processes have likewise been suggested to index emotion regulation (Calkins et al., 2002; Stifter, 2002), with a particular emphasis in the literature on negative affect constructs (Crockenberg, Leerkes, & Lekka, 2007; Leerkes & Crockenberg, 2003). Though understood to be related, temperament and approach and withdrawal processes are distinct constructs, with behavioral approach and withdrawal processes representing context-specific responses and temperament reflecting a more generalized, trait-like response tendency across situations (Calkins et al., 2002). The temperament construct of negative affectivity (NA) has been a particular focus of study of emotion regulation given that it can be reliably identified as early as three months of age (Gartstein & Rothbart, 2003), has been found to be stable over time, even as early as infancy (Lee & Bates, 1985; Putnam, Rothbart, & Gartstein, 2008; Roberts & DelVecchio, 2000) and has been found to be prospectively associated with the later development of psychopathology (Gartstein, Putnam, & Rothbart, 2012; Putnam & Stifter, 2005; Rothbart, Derryberry, & Hershey, 2000)

Biological Systems of Emotion Regulation

There is strong theoretical and empirical support for four biological systems being important components of emotion regulation: cortical activity (indexed by frontal electroencephalogram [EEG] activation), the neuroendocrine system (indexed by hypothalamic-pituitary-adrenal [HPA] axis activity, specifically cortisol), and within the autonomic nervous system, both the sympathetic nervous system (SNS; indexed by sympathetic-adrenal-medullary [SAM] axis activity, specifically alpha-amylase), and the parasympathetic nervous system (PNS; indexed by vagal tone). The SAM axis, indexed by alpha-amylase concentrations, has been studied in relation to emotion regulation; however, since both the SNS and the PNS are considered to reflect physiological responses of the ANS to stress, we chose to focus on vagal tone given its longer history of study in infants and strong evidence of reliability and stability beginning as early as the newborn period (Fracasso et al, 1994).

EEG

EEG patterns have been theorized to be indicative of emotion regulation at the physiological level based on the association between left hemisphere activation and approach systems and the right hemisphere with withdrawal systems (Fox, 1991). Fox and colleagues (1991) proposed a model that includes separate behavioral approach and withdrawal systems that are present at birth, with approach including joy, interest, and anger, and withdrawal including distress, disgust, and fear. Activation of these two systems has been theorized to be involved in the regulation of an individual's emotional response, either approach or withdrawal, to arousing stimuli (Davidson, 1993; Fox, 1994). As these behavioral systems are thought to be associated with different frontal hemispheres of the brain, measures of EEG activation in each hemisphere, and

specifically asymmetries between the two measures, have been studied for their association with these behavioral systems. Studies of infants and older populations find greater relative left frontal activation associated with approach behavior/positive affect and greater relative right frontal activation associated with withdrawal behavior/negative affect (Davidson & Fox, 1982; Fox & Davidson, 1988; Tomarken, Davidson, & Henriques, 1990; Wheeler, Davidson, & Tomarken, 1993). Thus, EEG patterns appear to reflect individual differences in emotion regulation as early as infancy (Fox, 1991, 1994); specifically, measures of baseline frontal activity are thought to reflect trait-like tendency and style of processing affective information (Quaedflieg, Meyer, Smulders, & Smeets, 2015). Importantly, infant EEG shows predictive validity, such that infants with relative right frontal EEG asymmetry displayed more stable observed behavioral inhibition over the first 4 years of life (Fox, Henderson, Rubin, Calkins, & Schmidt, 2001). Month-to-month correlations of EEG asymmetry scores from 7 to 12 months of age are moderate, and are consistently associated with infant affect (Bell & Fox, 1994). In addition, 7 out of 8 infants who showed right frontal asymmetry at 3 to 6 months showed the same patterns at 3 years of age (Jones, Field, Davalos, & Pickens, 1997), suggesting that across infancy, EEG asymmetry scores are moderately stable and predictive of later behavior. Baseline EEG asymmetry scores in particular have been most frequently studied in infants, as beginning within the first month of life, these values are found to be at least moderately stable over time (Bell & Fox, 1994; Diego, Field, Jones, & Hernandez-Reif, 2006; Jones, Field, Fox, Lundy, & Davalos, 1997).

Vagal Tone

Cardiac vagal tone, quantified as the amplitude of respiratory sinus arrhythmia (RSA), has been theorized to be associated with emotion regulation and arousal beginning in infancy (Porges, Doussard-Roosevelt, & Maita, 1994). Porges et al. (1996) put forth two roles of vagal tone: 1) to maintain homeostasis (indexed by baseline vagal tone) and 2) to act as a break, which regulates cardiac output in response to environmental challenge (indexed by vagal suppression, or a decrease in vagal tone, in response to challenge, relative to baseline). Greater baseline vagal tone and vagal suppression, both of which are considered to be adaptive, are associated with more capacity for self-regulation and greater emotional regulation of a stressor, respectively (Porges, Doussard-Roosevelt, & Maita, 1994; Porges et al., 1996). Baseline vagal tone in particular has been a construct of interest in infants, as it is measurable as early as 1 week of age (Jones et al., 1998), and has predictive validity. However, findings on the direction of the association are somewhat contradictory. Whereas results of one study suggested that newborns who displayed higher baseline vagal tone during active sleep exhibiting higher maternal-rated frustration and fear at 5 months of age (Stifter & Fox, 1990), results of another study indicated that higher baseline vagal tone in 9-month-old infants is associated with lower levels of maternal-rated difficult temperament at 3 years of age when controlling for 9-month temperament (Porges, Doussard-Roosevelt, Portales, & Suess, 1994). Thus, even early infancy measures of baseline RSA are predictive of later behavior, although the expected direction of association is unclear.

Cortisol

The HPA axis is well-established as an index of emotion regulation beginning in infancy. The HPA circadian rhythm emerges at approximately 3 months of age (Gunnar

et al., 1996; Price, Close, & Fielding, 1983) and, by this time, human infants have adult-equivalent levels of cortisol and are capable of responding to stress (Arborelius, Owens, Plotsky, & Nemeroff, 1999). In response to a stressor, the central nervous system (CNS) is activated and cortisol subsequently released (cortisol response), which provides feedback to the CNS in order to organize and sustain emotional and behavioral stress responses (Erickson, Drevets, & Schulkin, 2003; Stansbury & Gunnar, 1994). Following a stressor, cortisol is down-regulated by the HPA axis (cortisol recovery) to promote physical and emotional recovery. Baseline cortisol may follow an inverted u-shaped curve in which a moderate-range of cortisol is most adaptive (Erickson et al., 2003). Patterns of high intra-individual variability has been found in basal cortisol in infants between 5- and 8-months of age (De Weerth & van Geert, 2002), whereas cortisol changes in response to stress have been found to be moderately associated within infants from 4- to 6-months of age (Gunnar et al., 1996). Overall, the HPA axis becomes increasingly less responsive to stressors over the first year of life (Gunnar & Quevedo, 2007). Baseline cortisol has been studied as early as the newborn period (Diego et al., 2004; Field, Diego, et al., 2004; Keenan, Gunthorpe, & Grace, 2007; Lundy et al., 1999) as a measure of infants' resting cortisol scores separate from their cortisol response to a stressor. Further, understanding baseline cortisol is essential to better understanding of cortisol response, especially given the law of initial value, which suggests that infants with high initial cortisol levels are less likely to show an increase in cortisol in response to a stressor (Lacey & Lacey, 1962; Wilder, 1957). Of note, although the term "baseline" is commonly used in the literature, the term "resting" may be more accurate to describe cortisol levels prior to a stressor, given that many other factors that may contribute to this

initial cortisol level and it therefore may not represent a true "baseline."

Associations between Biological Systems

Given the theoretical and empirical support for these three biological systems being essential components of emotion regulation, it is important to consider the potential associations over time between biological systems. Porges and colleagues (2011; 1994) posit that the vagal system does not function independently of other neurophysiological and neuroendocrine systems, but rather works with brain function and peripheral autonomic nervous system (ANS) to regulate emotion, suggesting an association with both EEG and HPA axis activity. One brain structure that is believed to play a critical role in emotion regulation processes is the anterior cingulate cortex, as it is connected to limbic structures and is involved in the regulation of autonomic (vagal tone), endocrine (HPA), and visceromotor systems (Bush, Luu, & Posner, 2000). The peptides that regulate cortisol (e.g., vasopressin and corticotrophin-releasing hormone) also influence areas in the brainstem responsible for regulating vagal activity (Porges, Doussard-Roosevelt, & Maita, 1994). In these and other ways, the biological systems involved in emotion regulation are inherently interrelated. Despite the strong theory and understanding of underlying biology suggesting interrelations among biological systems of emotion regulation, few researchers report tests of such associations. In one study, 6-month old infants' relative right frontal EEG asymmetry was found to be related to their cortisol levels. However, it was relative right frontal EEG asymmetry during baseline, specifically, that was found to be associated with higher stress cortisol levels (Buss et al., 2003). Conversely, relative right frontal EEG asymmetry during a withdrawal task was associated with higher baseline cortisol in these infants (Buss et al., 2003).

Other researchers have explored the question of whether the degree of association between biological systems of emotion regulation is associated with the later development of psychopathology. Specifically, there have been two approaches taken to examining these associations. One group has focused on the association between an index of the SNS, salivary alpha-amylase, and cortisol and found that similar levels of activity (either high or low) in both systems predicted higher symptom levels (El-Sheikh, Erath, Buckhalt, Granger, & Mize, 2008; Gordis, Granger, Susman, & Trickett, 2006). In contrast, another study focused on the associations between the PNS, indexed by RSA, and cortisol in predicting internalizing symptoms (El-Sheikh, Arsiwalla, Hinnant, & Erath, 2011). In this study, baseline RSA moderated the relationship between baseline cortisol levels and symptom levels, such that 8- and 9-year old children with higher baseline cortisol levels and higher baseline RSA displayed the lowest concurrent level of internalizing symptoms. Given that both RSA and cortisol have been found to be independently associated with behavioral indices of emotion regulation as early as infancy (Keenan, 2000; Porges, Doussard-Roosevelt, Portales, et al., 1994), we chose to focus on the coordination between these systems, specifically whether they may best predict behavioral indices of emotion regulation in an additive or interactive model (Bauer et al., 2002). An additive model suggests that biological systems are associated with lower behavioral risk when there is an overall medium level of activity in both systems, or when there is high activity in one system and low activity in the other. An interactive model suggests that biological systems are associated with lower behavioral risk when system activity is balanced (either both low or both high).

Associations across Behavioral and Biological Domains of Emotion Regulation

Given that most definitions of emotion regulation include the notion of multivariate domains, including both biology and behavior (Calkins et al., 2002; Keenan, 2000; Stifter, 2002), which have been found to be individually associated with emotion regulation, another essential question is the potential degree of association between individual differences in behavioral and biological indices of emotion regulation (Shiner et al., 2012). Some studies have demonstrated associations between biological and behavioral (particularly temperament) systems of emotion regulation as early as infancy. For example, relative right frontal EEG asymmetry during baseline has been found to be associated with higher maternal-ratings of fear in 9-month-old infants (Schmidt, 2008) and greater distress in response to maternal separation in 10-month-olds (Davidson & Fox, 1989). Similarly, relative right frontal EEG asymmetry during a withdrawal task was associated with more observed sadness and fear during a stranger approach task in 6-month-olds (Buss et al., 2003). In addition, in 9-month-old infants, greater maternal-rated distress in response to limitations was associated with greater cortisol response during a separation from the mother (Gunnar, Larson, Hertsgaard, Harris, & Brodersen, 1992). Vagal tone has also been found to be associated with behavior, although in the opposite direction as would be expected. Specifically, 5-month-old infants with higher baseline vagal tone displayed greater negative reactivity during emotion (anger)-eliciting tasks and less maternal-rated smiling/laughing than those with lower vagal tone (Stifter & Fox, 1990). In addition, higher baseline vagal tone in 9-month-old infants was associated with greater maternal-reported difficult temperament (Porges, Doussard-Roosevelt, Portales, et al., 1994). Finally, 3-month-old infants who demonstrated vagal suppression

in response to a laboratory temperament task were reported by mothers to be easier to soothe and to have longer attention spans (Huffman et al., 1998).

These studies support associations between behavioral systems, temperament and observed withdrawal behavior, and indices of three biological systems of emotion regulation, cortisol, EEG, and RSA. However, they fall short of addressing associations between behavioral systems and the *coordination* of biological systems. In addition to the need to examine *multiple* biological and behavioral systems together, exploration of how these systems may relate differently over the course of infancy is critical as this would aid in our understanding of how the coordination across emotion regulation systems unfold over the course of infancy.

The Role of Maternal Depression in the Transmission of Risk for Problems with Emotion Regulation

These questions regarding how biological systems of emotion regulation relate to one another and associations between domains are perhaps best addressed among infants already at risk for the development of psychopathology, such as those with perinatally-depressed mothers. Perinatal depression is a significant risk factor for the development of psychopathology in offspring (Goodman et al., 2011) and may influence infants' emotion regulation in two key ways: 1) both pre- and post-natal depression are associated with the fetal and infant development of neuroregulatory systems (heart rate, brain electrical activity), with resulting behavioral traits and cognitions (Calkins, 1994), and 2) postnatal depression is associated with mothers showing less of the sensitive responsiveness that infants need for their developing emotion regulation (Calkins, 1994; Kopp, 1989). Thus, maternal influences during the pre- *and* post-natal periods are

implicated. Maternal depression may also moderate the association between infants' emotion regulation problems and later psychopathology. Silk and colleagues found support for this in preschool-aged children in that problems with emotion regulation were only associated with internalizing problems among children of mothers with childhood-onset depression who also had high concurrent depressive symptomology (Silk, Shaw, Forbes, Lane, & Kovacs, 2006). These mechanisms by which maternal depression may influence infant emotion regulation, as well as support for maternal depression as a moderator in the relation between infants' emotion regulation and later psychopathology, suggests the particular importance of examining emotion regulation strategies in the at-risk population of infants of depressed mothers. Also, according to theory, biological and behavioral systems may be more strongly associated in at-risk populations and behavioral indices may be more stable across development than in low-risk populations (Keenan, 2000).

Prenatal depression. The association between prenatal depression (elevated symptom levels or diagnosed major depressive disorder) and infant behavioral and biological indices of emotion regulation has been well documented as early as the newborn period. Prenatal depression is associated with infant temperament as indexed by higher ratings of difficult temperament in 4- and 6-month-olds (Austin, Hadzi-Pavlovic, Leader, Saint, & Parker, 2005), greater observed negative reactivity in 2- and 4-month-olds (Davis et al., 2007; Davis et al., 2004), and greater negative affect in 3- (Rouse & Goodman, 2014) and 6-month-olds (Huot, Brennan, Stowe, Plotsky, & Walker, 2004). Prenatal depression is also associated with observed approach/withdrawal behaviors in that infants of depressed mothers, compared to controls, displayed less positive affect and

greater fussiness both when interacting with the mother as well as with a non-depressed adult (Field, Diego, & Hernandez-Reif, 2006). In terms of biological indices of emotion regulation, newborns and 14-month- olds of mothers with higher prenatal depressive symptoms have been found to display greater relative right frontal EEG activation (Diego et al., 2004; Field, Diego, Hernandez-Reif, Schanberg, & Kuhn, 2002; Field, Diego, Hernandez-Reif, et al., 2004). Newborns of mothers with higher prenatal depressive symptoms have also been found to display lower baseline RSA (Field et al., 2003; Jones et al., 1998) and higher baseline cortisol levels (Field, Diego, et al., 2004; Keenan et al., 2007; Lundy et al., 1999) as compared to newborns of mothers with lower prenatal depressive symptoms (Dawson et al., 2003).

Postpartum depression. In addition to these predictive associations between prenatal depression and infant emotion regulation, there is support for concurrent associations between maternal postpartum depressive symptoms and both behavioral and biological constructs of emotion regulation. In the behavioral domain, these include greater infant difficulty at 3 months of age (Cutrona & Troutman, 1986), less positive affect at 3 months of age, and greater fussiness both when interacting with the mother as well as with a non-depressed adult (Field, 1984; Field et al., 1988). In the biological domain, postpartum depression was associated with greater relative right frontal EEG activation during a neutral condition among newborns, 1-month-olds, 3- to 6- month-olds, and 13- to 15-month-olds (Dawson et al., 2001; Diego et al., 2006; Field, Fox, Pickens, & Nawrocki, 1995; Jones, Field, Davalos, et al., 1997; Jones, Field, Fox, et al., 1997). In addition, 13- to 15-month-old infants of mothers who were concurrently depressed displayed higher heart rates than infants of non-depressed mothers (Dawson et

al., 2001). It is important to note that these studies have typically relied exclusively on a concurrent measure of maternal depressive symptoms, rather than a measure that reflects the infants' overall exposure to the mother's depressive symptoms throughout the postpartum.

Additive or interactive effects. A few studies have also examined the effects of both pre- and postnatal depression, with results of one study indicating that higher levels of both were associated with higher cortisol levels and greater relative right frontal EEG asymmetry in newborns, as compared to newborns of nondepressed mothers (Diego et al., 2004). In other studies, when both prenatal and postpartum depression symptoms were considered as predictors of 3-month old infants' negative affectivity (NA), only prenatal depression symptoms significantly predicted infant NA (Rouse & Goodman, 2014). In still other studies, an interactive relation was supported. Specifically, low prenatal and high postnatal depressive symptoms predicted the greatest infant cortisol reactivity, suggesting that discontinuity of symptoms between pre- and postnatal environments may predict worse outcomes in infants (Laurent, Ablow, & Measelle, 2011). By contrast, higher levels of prenatal depressive symptoms have been found to be associated with greater relative right frontal EEG asymmetry scores specifically among infants whose mothers had higher levels of depressive symptoms postnatally at both 3 and 6 months of age (Lusby, Goodman, Bell, & Newport, 2014). Further study of the potential effects of both pre- and postnatal depression is critical for several reasons, including that prenatal depression is one of the strongest predictors of postpartum depression (O'Hara & Swain, 1996); thus many infants are dually exposed and studies limited to examining prenatal *or* postnatal depression may not capture this double

exposure. In addition, findings suggesting that prenatal depression is as important as postnatal in predicting infant emotion regulation would provide empirical support for intervention during pregnancy, rather than waiting until the postpartum period to intervene.

Current Study

In the context of strong theoretical and empirical support for both biological and behavioral systems of emotion regulation in infants and the importance of further understanding emotion regulation in infants of women with perinatal depression, this study addressed three questions among infants of women at risk for perinatal depression: (1) how are biological indices of emotion regulation coordinated, (2) how do behavioral and biological indices of emotion regulation relate to each other over the course of infancy, and (3) what role does maternal perinatal depression play in predicting these associations. The study tested the following aims and hypotheses, taking both a variable-oriented and a person-centered approach, as individuals may cluster into profiles of emotion regulation based on particular biological and behavioral response patterns (Shiner et al., 2012; Stifter, 2002).

Our first aim was to explore the associations between systems in the biological domain of emotion regulation. Specifically, we extended Bauer's (2002) model from having tested associations between SAM activity and HPA activity in a general population sample to evaluating models of additive or interactive associations between two biological systems of emotion regulation, cortisol and vagal tone, in infants of depressed mothers, which represents a sample at risk for the development of psychopathology. We hypothesized (Hypothesis 1) that cortisol and vagal tone would

predict infant behavior in an interactive model at both 6 and 12 months of age, such that their interaction would be associated with infants' higher observed negative affect both concurrently and prospectively. Observed negative affect as early as 6 months of age is associated with later internalizing and externalizing symptoms (Moore, Cohn, & Campbell, 2001; O'Connor, 2001); thus, this construct itself may represent an early marker of vulnerability to later psychopathology.

Our second aim was to determine the association between three systems of biological (EEG, RSA, and cortisol) and two systems of behavioral (temperament and observed negative affect) domains of emotion regulation. Specifically, we attempted to identify infants with different emotion regulation profiles based on biological and behavioral data and to examine maternal depression as a predictor of profiles. We hypothesized (Hypothesis 2) that infants would divide into clusters based on emotion regulation strategies as measured by both biology and behavior. In addition, we hypothesized (Hypothesis 3) that maternal pre- and post-natal depressive symptoms would separately and interactively predict infant membership in a cluster marked by poorer emotion regulation.

We tested these aims and hypotheses in 3-, 6-, and 12-month-old infants of women who had been depressed and/or anxious prior to their pregnancy in order to enhance the likelihood that infants would have been exposed to maternal depressive symptoms either during the prenatal period, during the postpartum period, or both. History of depression has been found to be one of the strongest predictors of postpartum depression (O'Hara & Swain, 1996) and depression and anxiety are highly inter-correlated, even during pregnancy (Goodman & Tully, 2009). In addition, rates of

depression during the peripartum period in general population samples are comparable to each other as well as to general rates for adult women at any point of life (Evans et al., 2001). In perinatal women with histories of major depressive episodes prior to pregnancy, rates of depression are doubled (Goodman & Tully, 2009), which, in conjunction with the multiple negative infant outcomes that have been linked to maternal depression (Goodman et al., 2011), provide compelling arguments for studying emotion regulation in infants born to women at risk for perinatal depression.

Method

Participants

This study takes advantage of a prospective, longitudinal investigation of a unique sample of women at high risk for perinatal depression and their infants as part of a larger study, Perinatal Stress and Gene Influences: Pathways to Infant Vulnerability. Specifically, we focused on the subset of participants (n = 234) who completed at least one infant laboratory visit at 3-, 6-, or 12-months of age. There were 8 sets of twins in the sample, yielding a sample size of 242 total infants. Women were recruited during pregnancy through a women's mental health program in a psychiatry department, and all met DSM-IV criteria for lifetime Major Depressive Disorder or Depressive Disorder Not Otherwise Specified (82%) or for an anxiety disorder (Panic Disorder, Obsessive Compulsive Disorder, Generalized Anxiety Disorder, or Social Anxiety Disorder) (18%). Further inclusion criteria were: less than 16 weeks pregnant measured from last menstrual period at intake and between ages 18 and 45. Exclusion criteria were: active suicidality or homicidality, psychotic symptoms, bipolar disorder, schizophrenia, or currently active eating disorder, active substance use disorder within six months prior to last menstrual

period or positive urine drug screen, illness requiring treatment that can influence infant outcomes (epilepsy, asthma, autoimmune disorders), and abnormal thyroid stimulating hormone or anemia.

Participating mothers ranged from 20.7 to 44.5 years of age at delivery (*M* = 33.84 years, *SD* = 4.49). Most (88%) were married. On average, mothers had completed 16.51 years (*SD* = 2.01) of education. Around half (43%) were primiparous. Total Hollingshead scores for women and their partners were on average 50.71 (*SD* = 8.98), indicating middle to upper-middle class. The majority of the mothers were European-American (89%), with the remaining 9% being African American, 1% Asian, and < 1% each Native American and multi-racial. Of the infants, 48% were female and 52% were male. Similar to findings with other samples of pregnant women with histories of major depressive episodes (Goodman & Tully, 2009), 82 (34%) of the mothers had at least one major depressive episode during the prenatal period, and 55 (23%) had at least one episode during the postpartum year.

Procedure

All women participated in an informed consent procedure and all procedures were approved by the Emory University Institutional Review Board. Data including depression symptom levels were collected from the women at multiple time points throughout pregnancy and the first 12 months postpartum. During pregnancy, women completed an average of 5.48 Beck Depression Inventory scales (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961), with a range from 1 to 13 times (*SD* = 1.69). During the postpartum year, women completed an average of 5.74 BDI scales, with a range of 1 to 18 times (*SD* = 2.60). Mothers and infants participated in lab visits at infant

ages 3-, 6-, and 12-months. During these visits, mothers and their infants were video-recorded during face-to-face interactions and infants' EEG and RSA were collected during a 3-minute baseline, 5-minute feeding, and 5-minute play segment, following Dawson et al. (1997). At 12 months, three additional segments were included: 2-minute peek-a-boo, 5-minute distract, and 1-minute unavailable. Women also completed the Beck Depression Inventory – Second Edition (BDI-II; Beck, Steer, & Brown, 1997) at all three time points to assess depressive symptoms concurrent with the infant measures. In addition, they completed the Infant Behavior Questionnaire - Revised (IBQ-R) as a measure of infant temperament at each of the three infant ages.

At the 3- and 6-month visits, prior to the baseline segment, an EEG cap was secured to the infant's head while a research assistant manipulated toys in order to distract the infant. Three electrodes were placed on the infant's chest and a respiration belt around the infant's stomach in order to collect RSA data. The baseline segment was designed to keep the infant quiet and alert and minimize eye movements and gross motor movements. Infants sat on their mothers' laps and a research assistant blew bubbles for the infants to watch (Dawson, Frey, Panagiotides, & Osterling, 1997). Mothers were instructed not to talk to their infant during this segment of the EEG recording. Following Lehtonen et al. (2002), during the feeding segment, the mother breast- or bottle-fed her infant. Finally, consistent with Morasch and Bell (2011), during the play segment, the mother was provided with toys and instructed to play with her child in any way she would like.

At the 12-month visit, upon arrival to the lab, a baseline infant saliva sample was collected using a Salimetrics children's swab. All saliva samples were immediately

frozen until thawed for assay. Next, mothers, infants, and a lab volunteer completed the Strange Situation procedure (Ainsworth, Blehar, Waters, & Wall, 1978), consisting of a series of separations and reunions, which is designed to be at least mildly distressing. The Strange Situation mimics developmentally relevant stressors, namely separation from mothers, being left alone, and interacting with a stranger. It consists of eight 3-minute segments during which the infant is alone, with his/her mother, a female stranger, or with both the mother and stranger in an unfamiliar setting. The infant is separated from his or her mother a total of two times during the procedure. Segments are shortened if the infant is extremely distressed for at least 20 seconds. Previous studies have documented individual differences among infants' cortisol response to the Strange Situation (Hertsgaard, Gunnar, Erickson, & Nachmias, 1995; Nachmias, Gunnar, Mangelsdorf, Parritz, & Buss, 1996; Spangler, 1998; Spangler & Grossmann, 1993). A second saliva sample (post-stressor) was taken 30 minutes following the first separation episode in order to capture peak cortisol response. Infants were consoled as necessary before completing the rest of the laboratory visit protocol. A third and final cortisol sample was taken 60 minutes following the first separation episode in order to capture cortisol recovery from the stressor.

Following the Strange Situation, mothers and their infants were video-recorded and infants' EEG and RSA was collected during 3-minute baseline, 2-minute peek-a-boo, 1-minute unavailable, 5-minute feeding, 5-minute free play, and 5-minute distract segments. For all segments except baseline, infants were seated in a high chair with mothers seated directly in front of them. Procedures for the baseline, feeding, and free play segment followed those put forth at the 3- and 6-month visits. During the peek-a-

boo segment, mothers were given a washcloth and toy and invited to play their version of peek-a-boo with their infants. The unavailable segment consisted of mothers turning around in their chairs and ignoring their infant. Finally, during the distract segment, mothers were asked to fill out paperwork and pay little attention to their infants. Infant affect was coded from video recordings of all segments at all three ages.

In addition, a research assistant met with mother and infant at the infant's routine 6-month pediatrician visit, when inoculations are recommended, following the procedures of Lewis and Ramsay to measure response to the stressor of the well-baby exam and the inoculations (Lewis & Ramsay, 1995; Ramsay & Lewis, 1994, 2003). Salivary cortisol levels were collected using a Salimetrics children's swab. The research assistant collected three salivary samples (baseline, post-exam, and post-inoculation), which were later assayed for cortisol levels. The baseline saliva sample was taken in the waiting room of the pediatrician's office. The post-exam sample was collected within the first five minutes following the inoculation in order to measure the infant's peak response to the well-baby exam, which occurred prior to inoculations. The post-inoculation saliva sample measured the level of stress experienced due to inoculations and was collected twenty minutes after the inoculations, again, to measure the optimal peak in cortisol level. In addition, observed distress was rated to both the exam and inoculations.

Measures

Maternal depression. Depression symptom levels were measured with both the Beck Depression Inventory (BDI) and Beck Depression Inventory-Second Edition (BDI-II). Data were collected as part of a larger, long-standing clinical research protocol that relied on the BDI. When the women and their infants were in the lab for infant data

collection, there was the opportunity to add measures and the BDI-II was selected as the measure of concurrent depressive symptoms for its advantages of being more parallel to the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV) relative to its predecessor.

Beck Depression Inventory (Beck et al., 1961). The BDI is a 21-item self-report measure of depression symptom severity in the past week, with each item rated on a 4-point scale, ranging from 0 to 3. The score is a sum across items, with higher scores indicating greater severity of depressive symptoms. Scores of 0-9 indicate no depression, 10-18 indicates mild-moderate depression, 19-29 indicates moderate-severe depression, and 30-63 indicates severe depression (Beck et al., 1961). The BDI has been found to be both a valid and reliable measure of depression severity, with an especially high degree of content validity and internal consistency reliability (Beck et al., 1961; Ji et al., 2011). For pregnancy, we calculated area under the curve (AUC) scores for each woman to represent the overall depression severity level across the pregnancy, standardized to a 40-week pregnancy. Although analyses were conducted using total AUC scores, both AUC scores and mean BDI scores during pregnancy are shown in Table 1 for ease of interpretation. For the postpartum, separate AUC scores were calculated for each woman to represent the overall depression severity level during the first three months postpartum, the first six months postpartum, and the first twelve months postpartum. Again, all analyses were conducted using total AUC scores. However, for descriptive purposes, these AUC scores were divided by number of weeks (13, 26, or 52, respectively) in order to determine the average weekly BDI score. Descriptive statistics for the total AUC scores and the weekly AUC scores are shown in Table 1.

Beck Depression Inventory-Second Edition (Beck, Steer, & Brown, 1997). The BDI-II is a 21-item self-report measure of depressive symptom severity. As answers are based on the past two weeks, the BDI-II parallels the DSM-IV duration criterion for a major depressive episode. Items are rated on a 4-point scale, ranging from 0 to 3 and summed, with higher total scores indicating greater severity of depressive symptoms. Depression scores ranging from 0 to 13 indicate no or minimal depression; 14-19 indicates mild depression; 20-28 indicates moderate depression; and 29-63 suggests a severely depressed individual. Based on these empirically established cut scores, a score of 14 or higher is considered to indicate depression (Beck, Steer, & Brown, 1997). The BDI-II is a valid and reliable measure of depression severity, with an especially high degree of content validity, construct validity, and internal consistency (Beck et al., 1997). The BDI-II has good concurrent validity with measures of both antenatal and postpartum depression (Boyd, Le, & Somberg, 2005; Steer, Scholl, & Beck, 1990). Scores on the BDI-II were used as measures of depressive symptoms concurrent with the infant measures. At infant age 3 months, 41 women (20%) reported at least mild depression (score of 14 or higher), 42 women (21%) reported at least mild depression at infant age 6 months, and 30 women (19%) reported at least mild depression at infant age 12 months. Descriptive statistics for these scores are in Table 1.

Infant behavior.

Temperament. Mothers completed the 191-item scale of infant temperament, the Infant Behavior Questionnaire - Revised (IBQ-R; Gartstein & Rothbart, 2003), which is factor-analytically based on Rothbart and Derryberry's definition of temperament (1981). Mothers rate the items regarding the infant's behavior during the past week in a variety of

domains on a seven-point scale, from one (Never) to seven (Always). The questionnaire yields 14 scales, with 10 to 18 items per scale and scale scores being the mean of items on that scale. Scales cluster into three overarching factor scores: Orienting/Regulatory Capacity, Surgency/Extraversion, and Negative Affectivity (NA). NA, the variable of interest in this study, is calculated as the mean of four scales: Falling Reactivity, Fear, Frustration/Distress to Limitations, and Sadness, with a possible range of one to seven. Higher scores indicate higher levels of NA, which is conceptualized as poorer emotion regulation.

The IBQ-R is a reliable and valid index of infant temperament (Gartstein & Rothbart, 2003) and has been proven to be resistant to the potentially biasing influence of parental depression (Gartstein & Marmion, 2008). For the current sample, the alpha coefficient(s) for NA at 3 months was .71 and for the scales were as follows: Falling Reactivity (.83), Fear (.89), Frustration/Distress to Limitations (.71), and Sadness (.86). Internal consistency at 6 months for NA was .76 and for the scales was as follows: Falling Reactivity (.88), Fear (.88), Frustration/Distress to Limitations (.82), and Sadness (.82). Finally, the alpha coefficient(s) for NA at 12 months was .87 and for the scales were as follows: Falling Reactivity (.84), Fear (.89), Frustration/Distress to Limitations (.82), and Sadness (.84). Descriptive statistics for the infant temperament (NA) scores can be found in Table 2. Of note, there was a restricted range of NA scores in this sample, with most infants falling at a moderate level of NA. This pattern is consistent not only with the sample on which the IBQ-R was developed (Gartstein & Rothbart, 2003), but also with similar population samples (Rouse & Goodman, 2014).

Observed affect. Video-recorded observations of infants in face-to-face interactions with their mother were coded for infant's approach and withdrawal affect, based on infant facial expressions, vocalizations, and body movements. The free play context was chosen in order to examine infants' emotion regulation in a positive interpersonal context as opposed to a neutral context or a stressor (Dawson, Frey, Panagiotides, et al., 1999). Observers coded continuously by taking note of the rating that characterized the infant's state as the observation began, then rewinding and toggling in slow motion until the second at which the observer determined that an affective change had occurred; this procedure continued for the duration of each segment. At 3 months, infant affective behavior was coded as Approach, Withdrawal, or Neutral, as modified from Field et al. (1998) (see Appendix A). To capture the broader range of affect displayed by 6-month-olds relative to 3-month-olds, Approach was divided into High and Low Approach and Withdrawal divided into High and Low Withdrawal (see Appendix B). For 12-month-olds, we followed the coding scheme of Dawson et al. (Dawson, Frey, Self, et al., 1999), which was modified from Osofsky's system (Osofsky, 1987), and expands on the scheme used with 6-month-olds to include three categories each of Approach and Withdrawal in order to reflect the even broader range of affect displayed by 12-month-olds (see Appendix C). At all ages, additional codes accounted for uninformative data, such as if the infant was out of the view of the camera, a researcher entered the room, or the infant fell asleep. All raters were unaware of other data on the mothers and infants. Inter-rater reliability was tested on a randomly selected approximately 20% of the recordings and was found to be high (Cronbach's α = 0.92-0.98). Consistent with the literature on observed behavioral indices of emotion regulation

(Calkins et al., 2002; Stifter, 2002), observed negative affect was operationally defined as the relative duration, or the total percentage of time, the infant spent in negative states during the free play segment at each age. The advantage of using relative duration is that it is a statistic that controls for segments of time that were uncodeable due to various error data. This method of looking at percentage of time spent in a negative affective state (relative to positive or neutral) has been extensively employed in the literature (e.g., Crockenberg, Leerkes, & Lekka, 2007; Leerkes & Crockenberg, 2003). The range of this variable was from 0 to 1, with higher scores indicating greater relative duration of time spent in negative, which is conceptualized as poorer emotion regulation. Descriptive statistics on the infant affect scores can be found in Table 2. At all three ages, the observed negative affect variable was significantly skewed (K-S tests between .18-.27, p's < .001), given that many infants spent little time in negative affect; therefore, robust statistical techniques were utilized that could accommodate skewed data.

Infant biology.

EEG. The baseline EEG recordings were made from 16 left and right scalp sites: frontal pole (Fp1, Fp2), medial frontal (F3, F4), lateral frontal (F7, F8), central (C3, C4), anterior temporal (T3, T4), posterior temporal (T7, T8), parietal (P3, P4), and occipital (O1, O2), referenced to Cz. EEG was recorded using a stretch cap (Electro-Cap, Inc., Eaton, OH) with electrodes in the 10/20 system pattern and recommended procedures regarding EEG data collection with infants and young children were followed (Pivik et al., 1993). After the cap was placed on the infant's head, a small amount of abrasive gel was placed into each recording site and the scalp gently rubbed. Following this, conductive gel was placed in each site. Electrode impedances were measured and

accepted if they were below 5K ohms. The electrical activity from each lead was amplified using separate SA Instrumentation Bioamps (San Diego, CA) and band passed from 1 to 100 Hz. Activity for each lead was displayed on the monitor of the acquisition computer. The EEG signal was digitized on-line at 512 samples per second for each channel so that the data were not affected by aliasing. The acquisition software was Snapshot-Snapstream (HEM Data Corp., Southfield, MI) and the raw data were stored for later analysis.

Infant EEG data were examined and analyzed using EEG Analysis System software developed by James Long Company (Caroga Lake, NY). First, the data were re-referenced via software to an average reference configuration. Average referencing, in effect, weighted all the electrode sites equally and eliminated the need for a noncephalic reference. Active (F3, F4, etc.) to reference (Cz) electrode distances vary across the scalp. Without the re-referencing, power values at each active site may reflect interelectrode distance as much as they reflect electrical potential. The average reference configuration requires that a sufficient number of electrodes be sampled and that these electrodes be evenly distributed across the scalp. Currently, there is no agreement concerning the appropriate number of electrodes (Davidson, Jackson, & Larson, 2000; Hagemann, Naumann, & Thayer, 2001; Luck, 2005), although the 10/20 configuration that we used does satisfy the requirement of even scalp distribution.

The average reference EEG data were artifact scored for eye blinks using Fp1 and Fp2 (Myslobodsky et al., 1989), with a peak-to-peak criterion of 100 uV or greater. Artifact associated with gross motor movements over 200 uV peak-to-peak was also scored. These artifact-scored epochs were eliminated from all subsequent analyses. The

data then were analyzed with a discrete Fourier transform (DFT) using a Hanning window of one-second width and 50% overlap. Power was computed for the 6 to 9 Hz frequency band. Infants and young children have a dominant frequency between 6 to 9 Hz (Bell & Fox, 1994; Marshall, Bar-Haim, & Fox, 2002), and this particular frequency band has been correlated with patterns of emotion reactivity and emotion regulation during infancy (Bell & Fox, 1994; Buss et al., 2003; Dawson, 1994) and early childhood (Fox et al., 2001). The power was expressed as mean square microvolts and the data transformed using the natural log (Tottenham et al.) to normalize the distribution.

Frontal EEG asymmetry values were computed by subtracting ln power at left frontal (F3) from ln power at right frontal (F4). In infants and young children, power in the 6-9 Hz band has been shown to be inversely related to cortical activation during emotion reactivity and regulation (Bell & Fox, 1994). Thus, a negative asymmetry score reflects greater relative right frontal activation (conceptualized as poorer emotion regulation), whereas a positive asymmetry score reflects greater relative left frontal activation. Given that baseline EEG asymmetry has been found to be stable in infants (Diego et al., 2006; Jones, Field, Fox, et al., 1997) and also appears to reflect a trait-like ability to process affective information, relative to the more state-like response to a context (Quaedflieg et al., 2015), only baseline EEG scores were used for this study. Descriptive statistics on the infant EEG scores can be found in Table 3.

RSA. Infant EKGs were recorded from disposable electrodes. Event markers were used to separate the resulting file into the different conditions of the visit. The infant EKG recordings were edited by trained research assistants, who were considered to be certified in the editing process after successfully completing a number of practice files

and obtaining values within the specification. CardioEdit (Brain-Body Center, 2006-2007) software was used in order to extract 3- to 5-minutes of fully analyzable EKG. Following procedures developed by Porges (1985), a cardiac vagal tone index was computed for each segment using CardioBatch (Brain-Body Center, 2006-2007) software. This technique uses time-domain filters to extract the RSA and calculate the amplitude (variance) of the pattern (Porges, Doussard-Roosevelt, & Maita, 1994). Although both baseline vagal tone and vagal suppression are thought to index emotion regulation, baseline scores only were chosen for this study given that they have been found to be measurable early in infancy (Jones et al., 1998), and also in order to address questions regarding capacity for emotion regulation rather than response to a stressor (Porges, Doussard-Roosevelt, & Maita, 1994; Porges et al., 1996). In addition, individual differences in baseline RSA scores have been found to be reliable from early in infancy (Fracasso, Porges, Lamb, & Rosenberg, 1994). Higher baseline RSA scores indicate higher vagal tone, which is conceptualized as more adaptive emotion regulation despite the sometimes contradictory findings (Porges, Doussard-Roosevelt, Portales, et al., 1994; Stifter & Fox, 1990). Descriptive statistics on the infant RSA scores can be found in Table 3.

Cortisol. Skilled lab technicians conducted the analysis of salivary cortisol. Swabs used to collect saliva samples were first centrifuged in order to obtain the fluid. Using a syringe, the fluids were collected and frozen within a protective tube. Before analysis began, the oral fluids were thawed and centrifuged once again to ensure the removal of any protein debris. Salivary cortisol was measured by means of a series of laboratory tests, using a modification of the competitive binding immunoenzymatic

assay. Cortisol in the specimen being analyzed competed with a cortisol-alkaline phosphate conjugate for binding sites on a rabbit anti-cortisol antibody. Paramagnetic particles coated with goat anti-rabbit capture antibody were then added. The captured antigen-antibody complexes were separated in a magnetic field and washed to remove any unbound substances. A chemiluminescent phosphatase substrate was added to the salivary substance, producing a light that was measured with a luminometer. This light was inversely proportional to the concentration of cortisol. In some cases, the quantity of saliva was insufficient to be able to measure cortisol and thus was coded as "quantity not sufficient," reducing the sample size for analyses with these variables.

Baseline, or as we will call them, "resting," cortisol levels were used, following Ramsay and Lewis (Lewis & Ramsay, 1995; Ramsay & Lewis, 1994, 2003), in order to reflect infants' resting cortisol separate from their cortisol response to a stressor. Higher cortisol scores reflect higher resting cortisol, which is conceptualized as poorer emotion regulation. Importantly, the HPA circadian rhythm emerges at approximately 3 months of age (Gunnar et al., 1996; Price et al., 1983). Resting cortisol measures have been found to be reliable in infants (Gunnar et al., 1996; Gunnar & Quevedo, 2007). For infant cortisol variables, we followed the procedures set forth by Granger (2012) in taking three steps : 1) values greater than 4.0 ug/dl were considered to be problematic and recoded to missing, 2) the Kolmogorov-Smirnov test for normality was run and was significant for both baseline values (at 6 months, K-S = .25, and at 12 months, K-S = .29; p's < .001) indicating violation of the assumption of normality; however, robust statistical techniques were utilized that accommodate skewed data, and 3) values > 3 *SD*

from the mean were identified as outliers. Descriptive statistics on the infant raw cortisol scores can be found in Table 3.

Data Analytic Strategy

Preliminary analyses. Data were checked for outliers and descriptive statistics were run using IMB SPSS Statistics 22. We also determined whether data were missing at random.

Specific aim 1. This aim explored the associations between systems in the biological domain of emotion regulation. **1a.** In order to test whether infant vagal tone and cortisol best predicted observed negative affect in an additive or interactive model, multiple regression analyses were conducted separately for infant ages 6 and 12 months in order to examine both concurrent and prospective associations with infant observed negative affect. We used a bootstrap of 10,000 samples and bootstrap standard errors and confidence intervals to determine statistical significance (Good, 2001). Given this robust technique, the raw values of resting cortisol scores were used. The predictor variables were infant baseline RSA and resting cortisol scores and the interaction term of these two variables. The outcome variable was relative duration of time observed to be in a negative state during the free play segment. For the regression equations, the predictor variables were centered and a statistical interaction term created following the widely accepted approach to testing for interaction effects using multiple regression (Cohen, Cohen, West, & Aiken, 2003). This interaction term was entered in the second step of each regression, following the baseline RSA and cortisol scores, which were entered in the first step. Predictor variables were entered as predicting both concurrent outcomes (e.g., 6 month biology predicting 6 month negative affect, 12 month biology predicting

12 month affect) and prospective outcomes (e.g., 6 month biology predicting 12 month negative affect). Analyses were conducted using IMB SPSS Statistics 22.

Specific aim 2. This aim examined the associations between biological and behavioral systems of emotion regulation over time and the role of maternal depression in predicting these associations. **2a.** In order to address whether infants could be grouped into "response profiles," MPlus software was used to conduct latent class analysis (Muthen & Muthen, 2007). Bootstrapping and maximum likelihood estimation were used. Infant variables included were biological: RSA, cortisol (raw values), and EEG (all baseline/resting scores); and behavioral: temperament scores (Negative Affectivity) and observed affect (relative duration of negative affect during free play with mother). Clusters were determined separately at each of the three infant ages. **2b.** Logistic regression models were run to determine the role of maternal prenatal and postpartum depressive symptoms, both separately and interactively, on the likelihood that infants would belong to a cluster marked by poorer emotion regulation at each age. At infant age 3 months, a multinomial logistic regression was used, with maternal prenatal depressive symptoms, maternal postpartum depressive symptoms, and the interaction term entered within the same step of the model. At infant ages 6 and 12 months, binomial logistic regressions were used. The interaction term was entered in the third step of the regression, following maternal prenatal depressive symptoms in the first step, and postpartum depressive symptoms in the second step. In addition, one-way ANOVAs and independent samples t-tests were run in order to examine differences in maternal prenatal, postpartum, and concurrent depressive symptoms based on infant class membership at each age.

Results

Preliminary Analyses

Tests of normality and outliers. Data were determined to be missing completely at random, χ^2 (951) = 944.90, p = .55, suggesting no significant group differences between those with data and those who were missing certain data points (Little, 1988).

A total of 220 women and their infants (91% of the total sample) completed the lab visit at infant age 3 months, and 22 (9%) missed the visit. At infant age 6 months, 209 women and their infants (86%) participated in the lab visit, 22 (9%) missed the visit, and 11 (5%) were dropped from the study prior to the visit. A total of 206 women and their infants (85%) participated in the pediatrician visit, 29 (12%) missed the visit, and 7 (3%) were dropped from the study prior to the visit. Finally, at infant age 12 months, 166 women and their infants (69%) completed the visit, 44 (18%) missed the visit, and 32 (13%) were dropped from the study prior to their visit. A total of 137 women and their infants (57%) completed all four visits.

Of the 220 infants and their mothers who participated in the 3 month lab visit, 160 (73%) had usable baseline RSA data, data for 40 (18%) were unable to be edited due to too much artifact, 12 infants (5%) had no RSA data collected, and data for 8 infants (4%) were excluded as outliers (± 2 standard deviations from the mean). For infant baseline EEG data, 200 infants (91%) had usable data, data for 9 infants (4%) were unable to be edited due to too much artifact, data for 7 infants (3%) were excluded for an insufficient quantity (less than 10 seconds) of good data, data for 2 infants (1%) were excluded as outliers (+/- 3 standard deviations from the mean), data for 1 infant (<1%) was unusable due to technical problems, and 1 infant (<1%) had no EEG data collected. For infant observed affect, 203 infants (92%) had usable affect data, data for 10 infants (5%) were

unusable due to technical problems, and data for 7 infants (3%) were not collected. Finally, in terms of infant temperament data, 215 infants (98%) had IBQ data, and for 5 infants (2%), the IBQ was not collected. A total of 140 infants (64%) had usable data for all the variables at 3 months.

Of the 209 infants and their mothers who participated in the 6 month lab visit, 160 infants (77%) had usable baseline RSA data, data for 35 (17%) were unable to be edited due to too much artifact, 7 infants (3%) had no RSA data collected, and data for 7 infants (3%) were excluded as outliers (± 2 standard deviations from the mean). In terms of infant baseline EEG data, 194 infants (93%) had usable data, data for 7 infants (3%) were unable to be edited due to too much artifact, data for 3 infants (1%) were excluded for an insufficient quantity (less than 10 seconds) of good data, data for 1 infant (<1%) was excluded as an outliers (+/- 3 standard deviations from the mean), data for 2 infants (1%) was unusable due to technical problems, and 2 infants (1%) had no data collected. In terms of observed affect, 201 had usable affect data at 6 months (96%), data for 6 infants (3%) were unusable due to technical problems, and 2 infants (1%) had no free play segment. Finally, in terms of infant temperament data, 200 infants (96%) had IBQ data, and for 9 infants (4%), the IBQ was not collected. Of the 206 infants and their mothers who participated in a pediatrician visit, 189 (92%) had usable resting cortisol data, data for 10 infants (5%) were recoded to missing (values <4 ug/dL), data for 1 infant (<1%) had an insufficient quantity, and 6 infants (3%) had no sample collected. All together, a total of 117 infants had usable data for all the variables at 6 months.

Finally, of the 166 infants and their mothers who participated in the 12 month lab visit, 120 infants (72%) had usable baseline RSA data, data for 34 infants (21%) were

unable to be edited due to too much artifact, 5 infants (3%) had no RSA data collected, and data for 7 infants (4%) were excluded as outliers (± 2 standard deviations from the mean). In terms of infant baseline EEG data, 145 infants (87%) had usable data, data for 7 infants (4%) were unable to be edited due to too much artifact, data for 4 infants (2%) were excluded for an insufficient quantity (less than 10 seconds) of good data, data for 2 infants (1%) were excluded as outliers (+/- 3 standard deviations from the mean), data for 2 infants (1%) were unusable due to technical problems, and 6 infants (4%) had no data collected. In terms of observed affect, 158 had usable affect data at 12 months (95%), data for 2 infants (1%) were unusable due to technical problems, and 6 infants (4%) had no free play segment. In terms of infant temperament data, 162 infants (98%) had IBQ data, and for 4 infants (2%), the IBQ was not collected. In terms of infant resting cortisol data, 140 infants (84%) had usable data, data for 8 infants (5%) were recoded to missing (values <4 ug/dL), data for 6 infants (4%) had an insufficient quantity, and 12 infants (7%) had no sample collected. All together, a total of 88 infants (53%) had usable data for all the variables at 12 months.

Identification of potential control variables. In order to test for possible confounding variables, we first tested associations between demographic variables (maternal age, infant's gestational age at birth, infant gender, and antidepressant usage during pregnancy or the first year postpartum) and the five infant variables (observed affect, temperament NA, EEG, RSA, and cortisol) at each infant age. Maternal age was only associated with infant's NA at 6 months of age at a trend level, $r(198) = -.14$, $p = .05$; all other associations between maternal age and infant variables at 3, 6, and 12 months of age were not significant (r's < 0.10, p's > .19). Infant's gestational age at birth

was only significantly associated with baseline RSA at 3 months of age, $r(158) = -.17$ $p = .04$, and baseline RSA at 6 months of age, $r(158) = -.18$ $p = .02$; all other associations between infant gestational age and infant variables at 3, 6, and 12 months of age were not significant (r's < 0.13, p's > .10). The only group differences by gender in infant variables were in infant EEG at 6 months, $t(192) = 2.10$ $p = .04$, in which case, female infants had greater relative right frontal EEG asymmetry than male infants. All other group differences by gender in infant variables were not significant (t's < 2.10, p's > .05) The number of prenatal weeks that infants were exposed to maternal antidepressant use was not significantly associated with any infant variables at any age (r's < .11 , p's > .19), nor was the number of postpartum weeks that mothers were taking antidepressants (r's < .15, p's > .06). Given this pattern of findings, only infant gestational age at birth was controlled for in first set of analyses involving RSA, although not in the second set of analyses given the lack of significant associations between infant gestational age at birth and all other infant variables. No other control variables were included in analyses.

Finally, we examined possible effects of time of day and other potential confounds on infant cortisol scores by running correlations between the infant resting cortisol values at both ages and time since awakening at cortisol collection, time since last feeding at cortisol collection, duration of naps since first awakening, and duration of trip to the visit. These associations were not significant at 6 months of age (r's < .13, p's > .10) or at 12 months of age (r's < .10, p's > .20); therefore, we did not control for these variables in analyses.

Descriptive analyses. Results of Pearson product moment correlations revealed no significant associations between any infant variables at 3 months of age (see Table 4).

At infant age 6 months, baseline RSA was significantly negatively associated with resting cortisol, $r(132) = -.24$ $p = .01$, such that higher baseline RSA was associated with lower resting cortisol. There were no other significant associations between infant variables at 6 months (see Table 5). Finally, at 12 months of age, baseline EEG was significantly negatively associated with baseline cortisol, $r(122) = -.20$ $p = .03$, such that greater relative right frontal EEG asymmetry was associated with higher resting cortisol. No other significant associations between infant variables were significant at 12 months (see Table 6).

Prospective associations between variables were also examined (see Tables 7-9). In addition to stability of some of the infant variables over time, albeit not all, there were also several significant prospective associations between different infant variables. Specifically, infant negative affectivity at 3 months of age was significantly positively correlated with baseline RSA at 6 months and resting cortisol at 12 months, such that greater negative affectivity at 3 months was associated with higher baseline RSA at 6 months and higher resting cortisol at 12 months. Further, observed negative affect at 3 months was significantly positively correlated with infant negative affectivity at 12 months, such that greater relative duration of time spent in negative at 3 months was associated with greater infant negative affectivity at 12 months. In addition, negative affectivity at 6 months was significantly positively correlated with resting cortisol at 12 months, such that greater negative affectivity at 6 months was associated with higher resting cortisol at 12 months. Finally, resting cortisol at 6 months was significantly correlated with observed negative affect at 12 months, such that higher resting cortisol at

6 months was associated with greater relative duration of time spent in negative at 12 months.

Hypothesis Testing

Associations between systems in the biological domain of emotion regulation. The first hypothesis of the study was that cortisol and vagal tone would predict infant behavior in an interactive model at 6- and 12-months of age, such that their interaction would be associated with infants' observed negative affect (specifically, greater relative duration of time spent in negative) both concurrently and prospectively. Contrary to this hypothesis, regression analyses revealed that the interaction of infant cortisol and RSA did not significantly predict observed negative affect concurrently at either 6- or 12-months of age (see Table 10).

Prospectively, regression analyses revealed that the interactive effect of infant cortisol and RSA also did not significantly predict observed negative affect, again, failing to support the hypothesis (see Table 11). However, there was a significant main effect: 6 month infant resting cortisol significantly predicted 12 month observed negative affect, such that higher resting cortisol at 6 months predicted greater relative duration of time spent in negative at 12 months, $t(93) = 2.97$, $p = .004$. Results of these analyses did not significantly change when controlling for infant's gestational age at birth in the first step of the regressions.

Associations between biological and behavioral systems of emotion regulation. The second hypothesis of the study was that infants would divide into clusters based on emotion regulation strategies as measured by both biology and behavior. Consistent with this hypothesis, results of latent class analysis at infant age 3

months revealed that a 4 class model was the best fit for the data (BIC = 646.16, LRT Test = 36.38, $p = .04$). There were significant differences between classes for infant negative affectivity scores, $F(3, 211) = 6.33$, $p < .001$, with a medium effect size ($\eta^2 = 0.08$), and observed negative affect, $X^2(3) = 170.30$, $p < .001$, with a medium effect size ($\eta^2 = 0.10$) (see Figure 1). Specifically, infants in class 1 (n=123) had significantly lower relative duration of time spent in negative than infants in any other class. Infants in class 2 (n=24) had significantly greater relative duration of time spent in negative than infants in the other classes, and descriptively (albeit not significantly), they were the only class with relative right frontal EEG asymmetry. Class 3 infants (n=44) spent significantly greater relative duration of time in negative than class 1 infants. Finally, infants in class 4 (n=29) had significantly higher negative affectivity than infants in the other classes, and also spent half of their time in negative affect.

Again consistent with our hypothesis, at infant age 6 months, a 2 class model was determined to be the best fit for the data (BIC = 682.00, LRT Test = 157.83, $p = .02$). Descriptive statistics of infant variables in each class are displayed in Table 12. There were significant differences between classes for infant EEG, $t(192) = 2.16$, $p = .03$, with a small effect size ($d = 0.44$), and observed negative affect, $t(20.83) = 13.46$, $p < .001$, with a large effect size ($d = 3.87$). Compared to class 2 infants (n=204), class 1 infants (n=21) had significantly higher relative duration of time spent in negative, but significantly lower relative right frontal EEG asymmetry, and descriptively had greater negative affectivity, lower baseline RSA, and higher resting cortisol.

Finally, at infant age 12 months, a 2 class model was again determined to be the best fit for the data (BIC = 569.46, LRT Test = 107.83, $p = .08$), which was consistent

with our hypothesis. Although the LRT Test was only significant at a trend level, analyses revealed statistically significant differences in infant variables between the classes, and therefore a 2-class model was chosen over a 1-class model in order to take into account these meaningful differences. Descriptive statistics of infant variables in each class are displayed in Table 13. There were significant differences between classes for infant EEG, $t(143) = -2.33$, $p = .02$, with a moderate effect size ($d = -0.57$), and cortisol, $t(17.65) = 11.18$, $p < .001$, with a large effect size ($d = 3.54$). In addition, the difference between classes in infant negative affectivity was at a trend level, $t(160) = -1.89$, $p = .06$, with a small effect size ($d = -0.44$). Relative to class 2 infants (n=148), class 1 infants (n=19) had significantly greater relative right frontal EEG asymmetry and higher resting cortisol, a trend toward lower negative affectivity, and descriptively had lower baseline RSA, and lower relative duration of time spent in negative.

The third hypothesis was that maternal prenatal and postpartum depressive symptoms, both separately and interactively, would predict infant membership in a cluster marked by poorer emotion regulation. Results of the multinomial regression at infant age 3 months indicated that the full model containing all predictors was statistically significant, $\chi^2(9) = 21.19$, $p = .01$, indicating that full model predicts significantly better than the null model. Contrary to hypothesis, the interaction of maternal pre- and post-natal depressive symptoms did not make a unique statistically significant contribution to the model (see Table 14). However, consistent with our hypothesis, maternal prenatal depressive symptoms independently did, such that a one unit increase in maternal prenatal depressive symptoms was associated with a .003 increase in the relative log odds of being in class 2 versus class 1, while controlling for

the influence of the other predictors. In addition and also consistent with our hypothesis, a one unit increase in maternal prenatal depressive symptoms was also associated with a .003 increase in the relative log odds of being in class 3 versus class 1, while controlling for the influence of the other predictors. Finally, a one unit increase in postpartum depressive symptoms was associated with a .011 decrease in the relative log odds of being in class 3 versus class 1, while controlling for the influence of the other predictors, although the direction of this association was opposite of what was predicted. However, neither of these predictors had an effect on the odds ratio of class 2 versus class 1 membership or class 3 versus class 1 membership.

Logistic regression was performed to assess the impact of maternal perinatal depression variables on the likelihood that infants would belong to class 1 (n = 21), relative to class 2 (n = 204), at infant age 6 months. The full model containing all predictors was not statistically significant, χ^2 (3) = 1.46, p = .69. Further, the model as a whole only explained between .70% (Cox and Snell R square) and 1.50% (Nagelkerke R square) of the variance in class membership. Maternal pre- and post-natal depressive symptom variables did not separately or interactively predict likelihood of infant membership in class 1 relative to class 2, failing to support our hypothesis (see Table 15).

At infant age 12 months, the full model containing all predictors was statistically significant, χ^2 (3) = 11.65, p = .01, indicating that the model was able to distinguish between infants who were in class 1 (n = 19) versus class 2 (n = 148). The model as a whole explained between 7.2% (Cox and Snell R square) and 13.8% (Nagelkerke R square) of the variance in class membership. Contrary to hypothesis, the interaction of maternal pre- and post-natal depressive symptoms did not make a unique statistically

significant contribution to the model (see Table 16). However, consistent with our hypothesis, maternal postpartum depressive symptoms independently did, such that an increase in maternal postpartum depressive symptoms resulted in increased probability of class 1 membership for infants, although this predictor did not have an effect on the odds ratio of class 1 versus class 2 membership.

Results of one-way ANOVA's revealed that there were no significant differences between classes at infant age 3 months in terms of maternal prenatal depressive symptoms AUC, $F(3, 209) = 1.68$, $p = .17$, postpartum depressive symptoms AUC, $F(3, 199) = .89$, $p = .45$, or concurrent depressive symptoms, $F(3, 205) = 1.47$, $p = .22$, all with small effect sizes (η^2 range .01-.02). These findings failed to support our hypothesis. At infant age 6 months, also contrary to our hypothesis, results of independent samples t-tests revealed no significant class differences in maternal prenatal depressive symptoms AUC, $t(215) = -1.02$, $p = .31$, or postpartum depressive symptoms AUC, $t(209) = -.65$, $p = .52$. In both cases, the effect size was small ($d = -.25$ and $d = -.16$, respectively). However, maternal concurrent depressive symptoms differed between the two classes at a trend level, $t(30.05) = -1.73$, $p = .09$. Specifically, mothers of infants in class 2 had slightly higher concurrent depressive symptoms that mothers of infants in class 1, with a small effect size ($d = -.35$) (see Table 17). Finally, at infant age 12 months, results of independent samples t-tests revealed no significant class differences in maternal prenatal depressive symptoms AUC, $t(159) = .31$, $p = .76$, or postpartum depressive symptoms AUC, $t(19.67) = 1.34$, $p = .20$, both with a small effect size ($d = .06$ and $d = .38$, respectively). Maternal concurrent depressive symptoms also did not differ significantly between the two classes, $t(19.16) = 1.67$, $p = .11$, although the effect size was medium (d

= .50). These findings at infant age 12 months again failed to support our hypothesis. Maternal concurrent depressive symptoms by class are presented in Table 17.

Discussion

In this prospective, longitudinal study, we investigated the associations between biological and behavioral indices of emotion regulation over the course of infancy and the role of maternal perinatal depression in predicting these associations. The first aim was to explore associations between biological systems of emotion regulation by extending Bauer's (2002) model from a general population sample to a sample of infants at risk for the development of psychopathology given their mothers' history of depression. Our hypothesis that infant baseline vagal tone and resting cortisol would interact to predict infant observed affect both concurrently and prospectively was not supported. In addition, the main effects of cortisol and vagal tone were not significant predictors of infant observed affect concurrently; however, higher 6 month resting cortisol significantly predicted greater relative duration of time spent in negative at 12 months.

There are several possible explanations for the lack of significance in our findings of the interaction of RSA and cortisol in predicting observed negative affect. Although researchers have found support for cortisol and RSA each separately predicting of infant behavior (Gunnar, Larson, Hertsgaard, Harris, & Brodersen, 1992; Porges, Doussard-Roosevelt, Portales, et al., 1994; Stifter & Fox, 1990), studies of the coordination between biological systems of emotion regulation have focused largely on the SNS and cortisol (El-Sheikh et al., 2008; Gordis et al., 2006), with associations between RSA and cortisol in predicting behavior limited to populations of school-aged children (El-Sheikh

et al., 2011). Therefore, little is known about these associations in infancy, although given that vagal tone increases with maturation over the course of development (Porges, Doussard-Roosevelt, & Maita, 1994), and that resting cortisol has high intra-individual variability during infancy (De Weerth & van Geert, 2002), it is expected that the association between these two variables likely changes over the course of infancy. By contrast, and although not a hypothesis of this study, the significant main effect of 6 month resting cortisol significantly predicting 12 month observed negative affect is consistent with findings of the association between infant cortisol and behavior (Gunnar et al., 1992). This finding yields further support for associations between systems of emotion regulation over the course of infancy.

The second aim of the study was to explore the associations between biological and behavioral domains of emotion regulation at multiple time points during infancy and maternal depression as a predictor of these associations. Although previous studies have supported associations between one behavioral and one biological system of emotion regulation (Buss et al., 2003; Davidson & Fox, 1989; Gunnar et al., 1992; Huffman et al., 1998; Porges, Doussard-Roosevelt, Portales, et al., 1994; Schmidt, 2008; Stifter & Fox, 1990), this was, to our knowledge, the first attempt to examine the coordination of multiple biological and behavioral systems together in infants. Consistent with theory (Shiner et al., 2012; Stifter, 2002), we found support for our hypothesis that infants would divide into clusters based on emotion regulation strategies, with at least one cluster at each age marked by poorer emotion regulation, as measured by both biology and behavior. At infant age 3 months, infants divided into four classes. The first was a large resilient class of infants (n=123), with scores reflecting good emotion regulation in all

systems, and who spent significantly less relative duration of time in observed negative affect than infants in other classes. In addition, there was a moderately resilient class of infants (n=44) who spent significantly greater relative duration of time in observed negative affect than the highly resilient class, but otherwise had no significant indices of poor emotion regulation in any system. Finally, there were two classes of infants who appeared to be at-risk behaviorally: a class of infants (n=24) who had significantly higher relative duration of time spent in observed negative affect than any other infants, and descriptively the only class with greater relative right frontal EEG asymmetry, as well as a class of infants (n=29) that were significantly higher in temperament negative affectivity than infants in the other classes, and who also spent half of the time in observed negative affect. As significant differences in these classes were related only to behavioral measures, these findings suggest that early behavioral regulation strategies are very important for differentiating infants at risk.

At infant age 6 months, there was a larger resilient class of infants (n=204), who descriptively had lower negative affectivity, higher baseline RSA, and lower resting cortisol, and who spent significantly lower relative duration of time in observed negative affect, although they also had significantly greater relative right frontal EEG asymmetry. In addition, there was a smaller class of infants (n=21) who spent significantly greater relative duration of time in observed negative affect, and who descriptively had greater negative affectivity, lower baseline RSA, and higher resting cortisol, although they also had significantly lower relative right frontal EEG asymmetry. As compared to the 3 month classes, by 6 months of age, infants appear to divide into regulation classes based not only on behavioral systems, with all systems seemingly in synchrony (e.g., infants

with poorer emotion regulation in one domain also have poorer emotion regulation in another domain). The exception to this is infant EEG, which significantly differed between classes, such that infants with higher behavioral risk also had lower biological risk as measured by EEG. This finding may reflect the result of a different trajectory of brain development, relative to other systems, over the course of infancy (Fox, 1994). Further, the decrease in class size from 3 to 6 months of age suggests an increase in consolidation of biological and behavioral systems of emotion regulation (i.e., systems are becoming more coordinated) during this developmental period.

Finally, at infant age 12 months, there was a larger class of infants (n=148) characterized by less biological risk (significantly lower relative right frontal EEG asymmetry, significantly lower resting cortisol, and descriptively higher baseline RSA) but who appeared descriptively to be more at-risk behaviorally (higher negative affectivity, greater relative duration of time spent in observed negative affect). This is in contrast to a biologically at-risk class of infants (n=19), who had significantly greater relative right frontal EEG asymmetry, significantly higher resting cortisol, and descriptively lower baseline RSA, although these infants appeared to be less at-risk behaviorally (descriptively lower negative affectivity, less relative duration of time spent in observed negative affect). These findings suggest that, in addition to the consolidation of emotion regulation systems that is taking place over the course of infant development, biological and behavioral systems of emotion regulation also begin to differentiate later in infancy. Overall, these findings across all three ages are consistent with the idea that systems of emotion regulation continually reorganize over the course of development (Bauer et al., 2002; Shiner et al., 2012).

Our third hypothesis was that maternal prenatal and postpartum depressive symptoms, both separately and interactively, would predict infant membership in a cluster marked by poorer emotion regulation. At infant age 3 months, our findings supported this hypothesis. Specifically, higher prenatal depressive symptoms predicted an increase in likelihood of membership in a behaviorally at-risk class (those who spent greater relative duration of time spent in negative and also had relative right frontal EEG asymmetry) versus membership in the larger, resilient class of infants. Findings were similar for another class as well, such that higher prenatal depressive symptoms predicted an increase in likelihood of membership in the class with higher relative duration of time spent in observed negative affect (the moderately resilient class), versus membership in the larger, resilient class of infants. This pattern was in the opposite direction for postpartum depressive symptoms, such that higher postpartum depressive symptoms predicted a decrease in the likelihood of membership in the class with higher relative duration of time spent in negative (the moderately resilient class), versus membership in the larger, resilient class of infants. Overall, group differences between classes in maternal prenatal AUC, postpartum AUC, and concurrent depressive symptom levels were not significant, and the effect sizes were small. Given these contradictory patterns of association, as well as the fact that the interaction for pre- and post-partum depressive symptoms was at a trend level of significance, it is possible that both prenatal and postpartum depressive symptoms are important in predicting class membership at infant age 3 months. Overall these findings highlight the importance of taking both prenatal and postnatal maternal depressive symptoms into account as predictors of infant emotion regulation profiles.

Of note, the effects of maternal depression on the likelihood of class membership differed based on infant age. In particular, at infant age 6 months, maternal prenatal and postpartum depressive did not separately or interactively predict increased likelihood of membership in the class with poorer emotion regulation versus the resilient class. However, there was a trend for infants in the class with poorer emotion regulation to have mothers with lower concurrent depressive symptoms, albeit with a small effect size, which is contradictory to results of previous studies which suggest that higher postpartum maternal depressive symptoms are associated with poorer (more at-risk) emotion regulation strategies (e.g., Cutrona & Troutman, 1986; Dawson et al., 2001; Diego et al., 2006). By contrast, at infant age 12 months, greater maternal postpartum depressive symptoms from birth through 12 months significantly predicted increased likelihood of membership in a biologically at-risk class relative to the larger, resilient class. In addition, although the classes did not significantly differ in terms of their prenatal AUC, postpartum AUC, or concurrent depressive symptom levels, there was a medium effect size for the group differences in concurrent depressive symptoms, with mothers of infants in the biologically at-risk class displaying higher depressive symptoms. These findings are consistent with those of previous studies suggesting that higher postpartum depression is associated with more biological risk in infants (Dawson et al., 2001; Diego et al., 2006; Field et al., 1995; Jones, Field, Davalos, et al., 1997; Jones, Field, Fox, et al., 1997). Overall, findings suggest that associations between systems of emotion regulation in infants differ based on developmental time period, and that these associations also are influenced by maternal depressive symptoms to varying degrees over the course of development.

Strengths and Limitations

The study had several notable strengths, the first of which was the prospective, longitudinal study design, during which data were collected beginning in pregnancy and through 12 months postpartum. Depressive symptoms were measured at multiple time points throughout and infant measures were collected at three ages and in multiple contexts at each age. The sampling strategy was effective in yielding larger percentages of women with clinically significant levels of depression than are found in general population samples. Further, the sample consisted of predominately middle class, Caucasian women and their infants, which allowed for the examination of the association between maternal depressive symptoms and infant variables among women with histories of depression, without potential confounds associated with stressors such as poverty, maternal age, SES, etc. In conjunction, however, is the limitation that findings from this sample may not be generalizable to non-clinical or more ethnically and socio-demographically diverse samples.

Notably, there was a restricted range in our sample of infant negative affectivity, such that infants on average had a middle-range of temperament negative affectivity with a very small standard deviation. This was also true for infant observed negative affect, such that many infants displayed very little negative affect. For negative affectivity, this is consistent with findings in other samples (Gartstein & Rothbart, 2003; Rouse & Goodman, 2014), and for observed negative affect, this is not unexpected given that it was measured during a generally positive context (free play with mother). However, such restricted ranges make it difficult to detect statistically significant effects in terms of associations between variables.

Future Directions

As the first aim of the current study was to extend Bauer's (2002) model to examine interactions between RSA and cortisol, a further extension of this will be to test additive and interactive associations between difference combinations of two of our three biological systems (RSA, cortisol, and EEG). Further, given our findings that the associations between biological and behavioral systems of emotion regulation differ at different infant ages, thereby suggesting that systems of emotion regulation may reorganize and differentiate over the course of infant development, planned analyses with these data will examine how these associations unfold over the course of infancy. Such analyses will address unanswered questions regarding how emotion regulation strategies develop (Planalp & Braungart-Rieker, 2014). This is especially important given findings suggesting that not only may early emotion regulation strategies lay the groundwork for later emotion regulation problems, but also early life stress itself may also have a long-term impact on the development of system coupling (Hastings et al., 2011; Ruttle, Shirtcliff, Armstrong, Klein, & Essex, 2013).

Further, the development of emotion regulation has been conceptualized as a dynamic interplay that unfolds over time, given continuing influence of environmental factors (e.g., maternal depression) (Laurent, 2014). These findings, combined with our results suggesting that maternal pre- and post-natal depressive symptoms differentially influence class membership based on infant age, suggest that another important consideration is how changing maternal depression over time may influence infants' changing emotion regulation. This question will also be addressed with future multi-level modeling analyses. Overall, identification of the emergence of vulnerability

patterns as early as infancy yields greater understanding of the etiology of psychopathology and provides essential information for the design of preventive and early interventions (Keenan, 2000).

Additional planned analyses will move beyond the focus on resting or baseline infant biological indices of emotion regulation to also consider indices of biological responsivity to stressors. Although in this study, we conceptualized emotion regulation as baseline or resting indices measured in a neutral context, examining multiple indices of systems is important given that the associations between biological systems have been found to differ based on context (baseline versus a stressor) (Buss et al., 2003; Quaedflieg et al., 2015). In addition, infants' hyper- or hypo-responsivity to stressors has been suggested to be another early vulnerability marker to the later development of psychopathology (Degangi et al., 2000; Fendrich et al., 1990; Jansen, Beijers, Riksen-Walraven, & de Weerth, 2010; Stifter & Jain, 1998). In support for hypo-responsivity to stressors also representing a maladaptive pattern of emotion regulation, researchers have suggested that vigorous responses in terms of cortisol and behavior to mild stressors during early infancy signal more optimal functioning in later infancy (DiPietro & Porges, 1991), and that infants who do not express a negative reaction to a mild stressor in early infancy are at risk for continued poor development of emotion regulation and a long-term vulnerability to psychopathology (Chaplin & Cole, 2005). Findings have supported these theories, such that infants who demonstrated low cortisol reactivity in response to a mild stressor in early infancy also displayed a more negative temperament later in the first year of life, presumably due to a lower level of overall neurobiological organization (Gunnar et al., 1995). Therefore, researchers should begin to consider how indices of biological

responsivity to a stressor may also be important in the development of emotion regulation, which in turn is associated with later psychopathology.

The idea of considering multiple indices of a biological system (i.e., the index of responsivity to a stressor in addition to a resting or baseline index), is also important as researchers are increasingly recognizing that any single index (e.g., baseline RSA versus RSA suppression) of a biological system may not adequately capture individual differences, despite possible associations between these indices (Hinnant & El-Sheikh, 2009; Rottenberg, Clift, Bolden, & Salomon, 2007; Yaroslavsky, Rottenberg, & Kovacs, in press). Support for such an approach of measuring multiple indices includes the finding that only in the context of high RSA suppression was low baseline RSA predictive of high internalizing symptoms, demonstrating that both indices were necessary in order to predict later symptomatology (Hinnant & El-Sheikh, 2009). Therefore, future research should aim to include not only multiple *domains* and *systems* of emotion regulation, but also multiple *indices* within those systems. In conjunction with this, although the focus of the current study was on the temperament factor Negative Affectivity, it is unclear whether our findings were specific to Negative Affectivity versus other temperament factor scores; therefore, future studies should also consider other factors within temperament including Orienting/Regulatory Capacity and Surgency/Extraversion.

Conclusion

In this study, we incorporated measures of multiple domains of emotion regulation at multiple time points over the course of infancy in order to begin to explore how these domains relate to one another. In addition to finding significant associations

between domains, the different number and pattern of emotion regulation classes at different infant ages, as well as the differential impact of maternal depressive symptoms in predicting class membership, suggest that how these domains of emotion regulation are associated likely changes with development. Further analyses of these data are needed, taking a more fine-grained approach, in order to investigate to what extent associations between domains change with development (i.e., how co-regulation of systems changes over time), as well as how changing maternal depressive symptoms may be associated with these changes in associations/co-regulation. In addition, indices of biological stress reactivity should be considered, given their individual association with later psychopathology as well as support for associations between multiple indices within systems enhancing prediction of psychopathology. Such examination of how emotion regulation unfolds over the course of development yields great prospect for understanding early vulnerability, and thus how psychopathology develops over time.

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Table 1

Descriptive Statistics of Maternal Depressive Symptom Levels

Variables	*M*	*SD*	Minimum	Maximum	N
Prenatal					
AUC	381.96	275.04	0	1493.88	234
Mean	9.01	6.41	0	36.67	234
Postpartum					
AUC through 3 months	116.83	87.73	0	519.00	222
Average weekly AUC through 3 months	8.99	6.75	0	39.92	222
AUC through 6 months	224.51	168.79	0	926.80	222
Average weekly AUC through 6 months	8.64	6.49	0	35.65	222
AUC through 12 months	451.50	352.19	0	1830.85	222
Average weekly AUC through 12 months	8.68	6.77	0	35.21	222
BDI-II at 3 months	8.58	7.72	0	44	210
BDI-II at 6 months	8.50	8.01	0	43	197
BDI-II at 12 months	7.78	8.01	0	42	160

Note. AUC stands for Area under the Curve. Depression symptoms were measured with the Beck Depression Inventory (BDI) except when otherwise noted.

Table 2

Descriptive Statistics of Infant Behavior Variables

Variables	*M*	*SD*	Minimum	Maximum	N
Negative Affectivity[a]					
3 months	3.38	.45	2.38	5.22	215
6 months	3.49	.44	2.52	4.69	200
12 months	3.81	.44	2.34	5.26	162
Observed Negative Affect[b]					
3 months	.26	.29	0	1.00	203
6 months	.08	.12	0	.64	201
12 months	.12	.16	0	.86	158

[a]Negative Affectivity measured by the IBQ-R. [b]Observed Negative Affect quantified as the relative duration of time an infant spent in negative during free play with mother.

Table 3

Descriptive Statistics of Infant Biological Variables

Variables	*M*	*SD*	Minimum	Maximum	N
Baseline EEG					
3 months	.004	.24	-.97	1.02	200
6 months	.11	.31	-.76	1.23	194
12 months	.06	.26	-.77	.94	145
Baseline RSA					
3 months	3.00	.80	1.24	4.76	160
6 months	3.44	.79	1.64	5.11	160
12 months	3.48	.70	1.95	5.07	120
Resting Cortisol					
6 months	.41	.57	.03	3.40	189
12 months	.45	.63	.01	3.23	140

Note. EEG = Electroencephalogram; RSA = Respiratory Sinus Arrhythmia (vagal tone).

Table 4

Concurrent Associations among Infant Variables at 3 Months of Age

	1	2	3	4
1. Negative Affectivity[a]	__	.03	.10	.07
2. Observed Negative Affect[b]		__	-.07	.10
3. EEG			__	.03
4. RSA				__

Note. EEG = Electroencephalogram, measured during baseline. RSA=Respiratory Sinus Arrhythmia (vagal tone), measured during baseline.
[a]Negative Affectivity measured by the IBQ-R. [b]Observed Negative Affect quantified as the relative duration of time an infant spent in negative during free play with mother.
* $p < .05$. ** $p < .01$.

Table 5

Concurrent Associations among Infant Variables at 6 Months of Age

	1	2	3	4	5
1. Negative Affectivity[a]	__	.11	-.02	.05	.04
2. Observed Negative Affect[b]		__	.06	-.01	-.02
3. EEG			__	.06	.05
4. RSA				__	-.24**
5. Cortisol					__

Note. EEG = Electroencephalogram. RSA=Respiratory Sinus Arrhythmia (vagal tone). EEG, RSA, and Cortisol all measured during the baseline/resting context.
[a]Negative Affectivity measured by the IBQ-R. [b]Observed Negative Affect quantified as the relative duration of time an infant spent in negative during free play with mother.
* $p < .05$. ** $p < .01$.

Table 6

Concurrent Associations among Infant Variables at 12 Months of Age

		1	2	3	4	5
1.	Negative Affectivity[a]	__	-.04	.06	.06	.02
2.	Observed Negative Affect[b]		__	.03	-.03	-.01
3.	EEG			__	.12	-.20*
4.	RSA				__	-.14
5.	Cortisol					__

Note. EEG = Electroencephalogram. RSA=Respiratory Sinus Arrhythmia (vagal tone). EEG, RSA, and Cortisol all measured during the baseline/resting context.
[a]Negative Affectivity measured by the IBQ-R. [b]Observed Negative Affect quantified as the relative duration of time an infant spent in negative during free play with mother.
* $p < .05$. ** $p < .01$.

Table 7

Prospective Associations of Infant Variables from 3 to 6 Months of Age

	6 Months				
	Negative Affectivity[a]	Observed Negative Affect[b]	EEG	RSA	Cortisol
3 Months					
Negative Affectivity[a]	.53**	-.03	.09	.20*	.02
Observed Negative Affect[b]	.07	.18*	.11	.02	-.03
EEG	-.06	-.05	.14	.07	.09
RSA	-.03	-.05	.08	.55**	-.02

Note. EEG = Electroencephalogram. RSA=Respiratory Sinus Arrhythmia (vagal tone). EEG, RSA, and Cortisol all measured during the baseline/resting context.
[a]Negative Affectivity measured by the IBQ-R. [b]Observed Negative Affect quantified as the relative duration of time an infant spent in negative during free play with mother.
* $p < .05$. ** $p < .01$.

Table 8

Prospective Associations of Infant Variables from 3 to 12 Months of Age

	12 Months				
	Negative Affectivity[a]	Observed Negative Affect[b]	EEG	RSA	Cortisol
3 Months					
Negative Affectivity[a]	.49**	-.11	-.09	.14	.22*
Observed Negative Affect[b]	.20*	-.04	-.05	.08	-.08
EEG	-.06	.08	.11	.03	.09
RSA	-.04	.02	-.01	.34**	-.07

Note. EEG = Electroencephalogram. RSA=Respiratory Sinus Arrhythmia (vagal tone). EEG, RSA, and Cortisol all measured during the baseline/resting context.
[a]Negative Affectivity measured by the IBQ-R. [b]Observed Negative Affect quantified as the relative duration of time an infant spent in negative during free play with mother.
* $p < .05$. ** $p < .01$.

Table 9

Prospective Associations of Infant Variables from 6 to 12 Months of Age

	12 Months				
	Negative Affectivity[a]	Observed Negative Affect[b]	EEG	RSA	Cortisol
6 Months					
Negative Affectivity[a]	.58**	-.03	-.07	.19	.22*
Observed Negative Affect[b]	.05	-.06	.06	-.05	-.15
EEG	-.03	-.07	.25**	.11	-.12
RSA	.08	-.02	-.05	.33**	-.19
Cortisol	-.02	.20*	.06	-.15	.28**

Note. EEG = Electroencephalogram. RSA=Respiratory Sinus Arrhythmia (vagal tone). EEG, RSA, and Cortisol all measured during the baseline/resting context.
[a]Negative Affectivity measured by the IBQ-R. [b]Observed Negative Affect quantified as the relative duration of time an infant spent in negative during free play with mother.
* $p < .05$. ** $p < .01$.

Table 10

Summary of Hierarchical Regression Analyses for Infant RSA and Cortisol Predicting Concurrent Observed Negative Affect at 6 and 12 Months of Age

	Observed Negative Affect			
	6 months		12 months	
Predictor	ΔR^2	β	ΔR^2	β
Step 1	.002		.008	
Resting cortisol		.015		-.039
Baseline RSA		-.035		.077
Step 2	.002		.003	
Interaction term		-.050		-.059
Total R^2	.003		.011	
n	130		101	

Note: Results of the regressions represent concurrent effects, such that 6 month cortisol and RSA are predicting 6 month observed negative affect, and 12 month cortisol and RSA are predicting 12 month observed negative affect. RSA = Respiratory Sinus Arrhythmia (vagal tone).
* $p < .05$. ** $p < .01$.

Table 11

Summary of Hierarchical Regression Analyses for Infant RSA and Cortisol Predicting Prospective Observed Negative Affect from 6 to 12 Months of Age

	Observed Negative Affect	
Predictor	ΔR^2	β
Step 1	.088*	
Resting cortisol		.299**
Baseline RSA		.022
Step 2	.010	
Interaction term		-.118
Total R^2	.098	
n	95	

Note: Results of the regressions represent prospective effects, such that 6 month cortisol and RSA are predicting 12 month observed negative affect. RSA = Respiratory Sinus Arrhythmia (vagal tone).
* $p < .05$. ** $p < .01$.

Table 12

Mean Estimates and Standard Errors of the Estimate of Latent Classes at 6 Months of Age

	Classes	
	1 M (SE)	2 M (SE)
Negative Affectivity[a]	3.60 (.08)	3.47 (.03)
Observed Negative Affect[b]	.39 (.03)	.04 (.004)
EEG	.25 (.09)	.10 (.02)
RSA	3.31 (.23)	3.46 (.06)
Cortisol	.43 (.17)	.41 (.04)
Sample Size	21	204

Note. EEG = Electroencephalogram. RSA=Respiratory Sinus Arrhythmia (vagal tone). EEG, RSA, and Cortisol all measured during the baseline/resting context.
[a]Negative Affectivity measured by the IBQ-R. [b]Observed Negative Affect quantified as the relative duration of time an infant spent in negative during free play with mother.

Table 13

Mean Estimates and Standard Errors of the Estimate of Latent Classes at 12 Months of Age

	Classes	
	1 M (SE)	2 M (SE)
Negative Affectivity[a]	3.62 (.11)	3.84 (.04)
Observed Negative Affect[b]	.09 (.03)	.13 (.01)
EEG	-.06 (.07)	.07 (.02)
RSA	3.24 (.15)	3.52 (.07)
Cortisol	1.90 (.19)	.25 (.02)
Sample Size	19	148

Note. EEG = Electroencephalogram. RSA=Respiratory Sinus Arrhythmia (vagal tone). EEG, RSA, and Cortisol all measured during the baseline/resting context.
[a]Negative Affectivity measured by the IBQ-R. [b]Observed Negative Affect quantified as the relative duration of time an infant spent in negative during free play with mother.

Table 14

Multinomial Logistic Regression Predicting Likelihood of Risk Class Membership at 3 Months of Age

Predictor	*B*	*S.E.*	95% CI for Odds Ratio		
			Lower	e^B	*Upper*
Class 2[a]					
Prenatal	.003*	.001	1.00	1.00	1.01
Postpartum	.001	.005	.99	1.00	1.01
Interaction Term	.00	.00	1.00	1.00	1.00
Class 3[a]					
Prenatal	.003*	.001	1.00	1.00	1.01
Postpartum	-.011*	.004	.98	.99	1.00
Interaction Term	.00[†]	.00	1.00	1.00	1.00
Class 4[a]					
Prenatal	.00	.001	1.00	1.00	1.00
Postpartum	-.002	.004	.99	1.00	1.01
Interaction Term	.00[†]	.00	1.00	1.00	1.00
χ^2		21.19*			
df		9			

Note. Depression symptoms were measured with the Beck Depression Inventory (BDI) and quantified as the Area under the Curve score.
[a]The reference category is Class 1.
* $p < .05$.

Table 15

Logistic Regression Predicting Likelihood of Risk Class Membership at 6 Months of Age

Predictor	*B*	*S.E.*	95% CI for Odds Ratio		
			Lower	e^B	*Upper*
Depression Variables					
Prenatal	-.001	.001	1.00	1.00	1.00
Postpartum	.001	.002	1.00	1.00	1.01
Interaction Term	.000	.000	1.00	1.00	1.00
Constant	-2.18***	.23		.11	
χ^2		1.46			
df		3			

Note. Depression symptoms were measured with the Beck Depression Inventory (BDI) and quantified as the Area under the Curve score.
* $p < .05$. ** $p < .01$. *** $p < .001$.

Table 16

Logistic Regression Predicting Likelihood of Risk Class Membership at 12 Months of Age

Predictor	*B*	*S.E.*	95% CI for Odds Ratio		
			Lower	e^B	*Upper*
Depression Variables					
Prenatal	.000	.001	1.00	1.00	1.00
Postpartum	.003*	.001	1.00	1.00	1.00
Interaction Term	.000	.000	1.00	1.00	1.00
Constant	-1.98***	.25		.14	
χ^2		11.65*			
df		3			

Note. Depression symptoms were measured with the Beck Depression Inventory (BDI) and quantified as the Area under the Curve score.
* $p < .05$. ** $p < .01$. *** $p < .001$.

Table 17

Maternal Depressive Symptom Levels Concurrent with Infant Variables

Variables	*M*	*SD*	N
3 Months			
Class 1	7.71	7.18	116
Class 2	11.04	7.07	23
Class 3	9.26	8.67	43
Class 4	9.30	8.74	27
6 Months			
Class 1	6.29	5.91	21
Class 2	8.76	8.19	176
12 Months			
Class 1	12.53	13.80	19
Class 2	7.14	6.71	141

Note. Depression symptoms were measured with the BDI-II score.

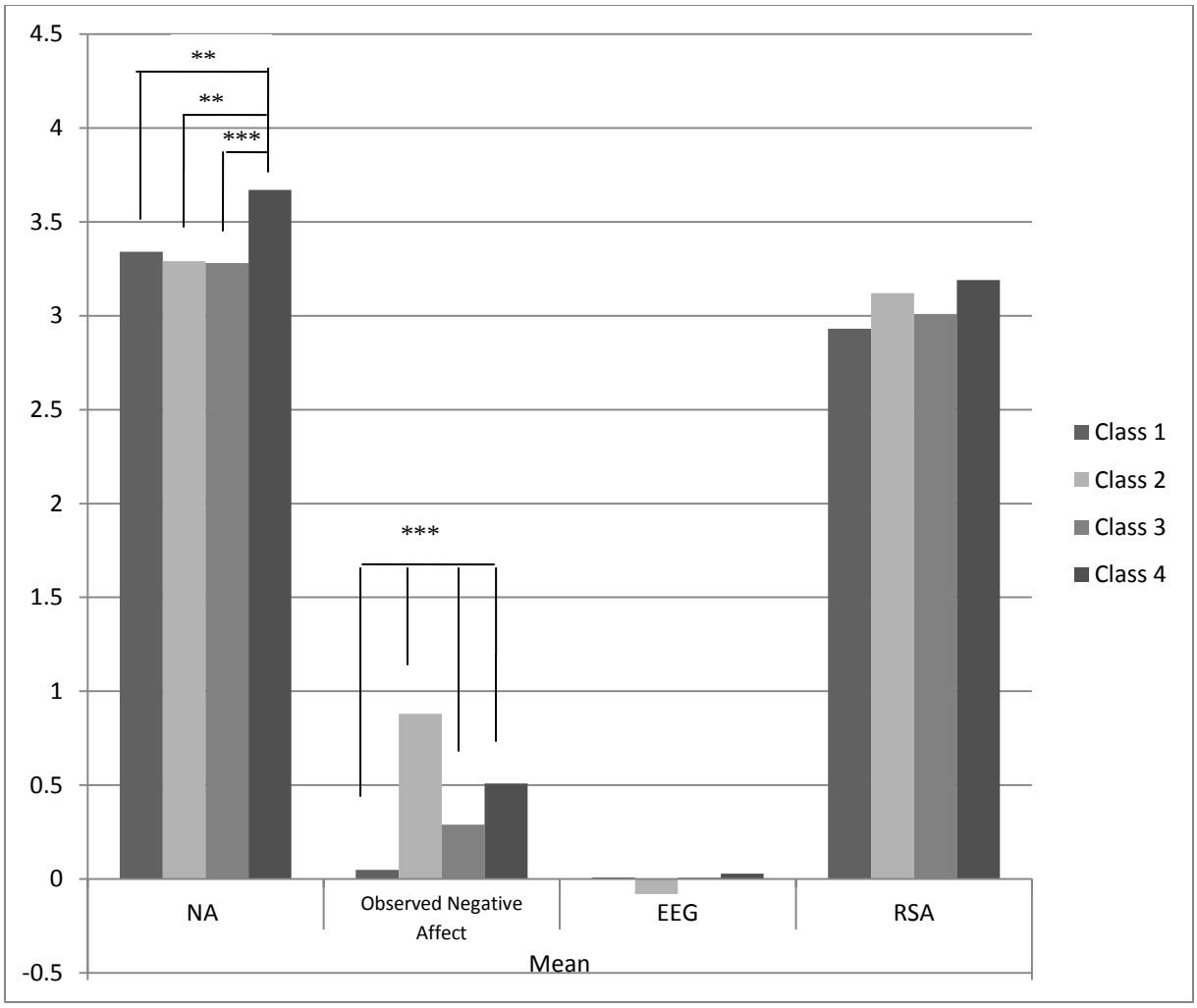

Figure 1. Mean estimates of scores for each index of emotion regulation within each latent class at infant age 3 months. EEG = Electroencephalogram. RSA=Respiratory Sinus Arrhythmia (vagal tone). EEG and RSA measured during the baseline context. Negative Affectivity (NA) measured by the IBQ-R. Observed Negative Affect quantified as the relative duration of time an infant spent in negative during free play with mother. For NA, class 4 significantly differed from Class 1, 2, and 3, and for observed negative affect, all classes significantly differed from one another. ** $p < .01$. *** $p < .001$.

Appendix A

Infant 3 Month Coding

	Positive or *Approach* **A**	Negative/Sad or *Withdrawal* **W**	*Neutral* **N**
Specific emotion expressions	Happy/joy Surprise Interest	Sadness Distress	Quiet alert
Facial markers	Smiles, cheeks raised	Grimace, squinting eyes, quivering mouth, furrowed brow	Eyes open, alert, focused (on mother or object)
Vocal cues	Giggle Coos?	Fuss, whimper, protest or cry or pre-cry	Coo with no indication of positive
Body cues	Limb movement (in the context of coos, giggles)?	Thrashing, head side to side, looking away/gaze aversion, arching back, stiffness	Still, calm, focused gaze, body at rest or slow, rhythmic movements

Appendix B

Infant 6 Month Coding

High level approach: Vocalizations: Excitement/ Smile/ Laughter/ Squeal	+3	-Laughter -Smiles -Clearly high pleasurable vocalizations (i.e., happy gurgling, pleasure screeches -Excited body movements or leaning forward in addition to positive facial or vocal cues
Low level approach: Positive interest/ Active engagement	+2	-Any large body movements showing positive interest and attentiveness (to people or toys) without additional facial or vocal cues -Visual tracking -Attentive stillness
Neutral	1	-None of the above or below (no clearly positive or negative affect) -May have blunt affect -No raised eyebrows or large body movements which show interest -Eyes wandering (“staring into space”) -Indicating lack of engagement
Low level withdrawal: Negative Interest/ Frown/ Furrowed brow	-2	-Negative concentration -Facial expressions may include wrinkled or furrowed brow in concentration (distress) -Smile with furrowed brow also included, as well as withdrawal movements -Pouting, pre-cry face, disgust, or clearly distinguishable distress frown
High level withdrawal: Vocalizations:	-3	-Negative vocalizations (i.e., grunt, protest, or frustration sounds – these tend to be in single bursts with a strident tone or vocal tensions)

Protest Fuss/Whimper Marked distress/cry		-Whimpering, fussing w/ frown -Negative vocal w/ strident tones -Crying distress, but no continuous cry -Marked distress if face and voice. Cry accompanied by appropriate facial expressions (i.e., screwing up face, closed eyes, maybe tears -High intensity, high-pitched distress sounds simultaneous frown face (mouth turned downward; brow and forehead may be wrinkled), temporary cessation of breathing, kicking, flailing of body

Appendix C

Infant 12 Month Coding: The Dawson ratings of Infant Positive – Negative Hedonic Tone

Laughter/ Squeal	+ 4	High intensity, high-pitched positive sounds with simultaneous smiling. Vigorous smiles with either: 1. Laughter 2. Smiles with excited body movement, or 3. Clearly high pleasurable vocalizations (i.e. happy gurgling, pleasure screeches, or laughter)
Excitement or Smile	+ 3	-Fleeting smiles w/ or w/o eye involvement or vocalization -Excitement in body movements or vocalizations
Positive Interest	+2	-Any large body movements showing positive interest and attentiveness (to people or toys) -Smiles with raised eyebrows, or leaning forward (i.e. facial expression not blunt). -Visual tracking -Slight smile with interest
None	1	-None of the above or below (no clearly positive or negative affect). --May have blunt affect. -No raised eye-brows or large body movements which show interest.
Negative Interest	-2	-Negative concentration. -Facial expressions may include wrinkled or furrowed brow in concentration (distress). -Smile with furrowed brow also included, as well as withdrawal movements. -Mild negative vocal

Frown/Protest Fuss/Whimper	-3	-Pouting, pre-cry face, disgust, or clearly distinguishable distress frown -Negative vocalizations (i.e. grunt, protest or frustration sounds – these tend to be in single bursts with a strident tone or vocal tensions). -Whimpering, fussing w/ frown - Negative vocal w/ strident tones -Crying distress, but no continuous cry
Marked Distress/Cry	- 4	-Marked distress in face and voice. Cry accompanied by appropriate facial expressions (i.e. screwing up face, closed eyes, maybe tears) - High intensity, high-pitched distress sounds simultaneous frown face (mouth turned downward; brow and forehead may be wrinkled), temporary cessation of breathing, kicking, flailing of body.