ABSTRACT

Title of dissertation: BRAIN ELECTRICAL ACTIVITY IN INFANTS OF DEPRESSED AND ANXIOUS MOTHERS

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Numerous studies suggest that positive and negative emotions are associated with different patterns of cerebral hemisphere activation and that specific patterns of electroencephalographic (EEG) asymmetry may indicate risk for depression and anxiety. The extant developmental psychopathology literature has examined patterns of EEG asymmetry in the offspring of parents with affective disorders and such research has reported linkages between frontal EEG asymmetry and depression, suggesting that measures of EEG asymmetry may be important neurological markers of risk for affective disorders. Despite the greater prevalence of anxiety disorders than depressive disorders and the literature suggesting that resting EEG asymmetry may serve as an index of both depression and anxiety, no research has yet examined patterns of EEG asymmetry in the offspring of parents with anxiety disorders. The purpose of the present study was to examine early markers of risk for psychopathology in the biological domain (e.g., patterns of EEG asymmetry) in an attempt to elucidate some of the precursors of anxiety

and depression in children so that we might gain a better understanding of the development of these disorders.

The present investigation examined the relation between maternal history of depression and anxiety and patterns of EEG asymmetry in infant offspring. EEG measures of alpha power (4-6 Hz) in the right and left hemisphere were recorded in infants (four to eight months of age) of mothers with a documented history of major depressive disorder (n = 39), anxiety disorder (n = 22), and comparison subjects (n = 38) during a resting baseline task. Results suggest that maternal depression and maternal anxiety was statistically unrelated to patterns of infant asymmetry. The results suggested that fewer infants of mothers with specific phobia (with and without depression) had right mid-parietal asymmetry than infants of control mothers. Perceived social support was related to patterns of infant EEG asymmetry. These findings provide modest support for the hypothesis that maternal diagnostic history may be related to patterns of infant asymmetry in various regions of the brain during a resting state.

BRAIN ELECTRICAL ACTIVITY IN INFANTS OF DEPRESSED AND ANXIOUS MOTHERS

by

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Chapter I: Introduction

Theoretical Rationale

The past decade had shown an increase in developmental psychopathology research, which has lead to a greater understanding of depressive and anxiety disorders. This literature suggests that the offspring of depressed and anxious parents are at risk for numerous behavior problems and affective psychopathology. In addition, numerous studies suggest that positive and negative emotions are associated with different patterns of cerebral hemisphere activation and that specific patterns of electroencephalographic (EEG) asymmetry may indicate risk for depression and anxiety.

The theoretical foundation for investigations of anterior EEG asymmetry in both adults and children is the approach-withdrawal model of hemispheric lateralization (Davidson, 1984, 1992b, 1994; Fox, 1991; Tomarken & Keener, 1998). The approach-withdrawal model combines motivation-based theories (e.g., Gray, 1987; Schneirla, 1959) with lesion studies of neuropsychology accounts of anterior laterality effects of lesions on emotion (Robinson, Kubos, Starr, Rao, & Price, 1984) and suggests that emotions have motivational characteristics and that are either approach-related (e.g., joy), or withdrawal-related (e.g., fear) (Fox, 1991). This theory maintains that left frontal asymmetry (greater relative EEG activity in the left frontal sites) is associated with approach behavior. In contrast, right frontal asymmetry (greater relative EEG activity in right frontal sites) is predicted to be associated with withdrawal behavior. The literature examining EEG and emotion has also proposed several theories that implicate the parietal regions in the regulation of arousal (e.g., Heller & Nitschke, 1997).

The psychopathology literature has mapped the aforementioned approach-withdrawal models onto the study of adult affective disorders, providing increasing evidence that specific EEG patterns may indicate risk for depression and anxiety. For example, in a study of clinically depressed adults and matched controls, Henriques and Davidson (1991) found that depressed adults had less left-sided frontal EEG activation than controls. This work indicates a deficit in the approach mechanisms of clinically depressed participants. Other work by these researchers found similar patterns for participants with remitted depression compared to controls suggesting that such patterns may be state-independent. Work by Gotlib, Ranganath, and Rosenfeld (1998) supports these findings. Moreover, functional neuroimaging studies (e.g., positron emission tomography) of depression have reported evidence that is concordant with these models (see Dougherty & Rauch, 1997 for review). Despite the fact that anxiety disorders are more common than depressive disorders, less research has examined the relations among anxiety and EEG asymmetry. Those studies that have addressed these issues, however, reported differing patterns in both the frontal and parietal regions. To illustrate, recent research has reported increased right parietal brain activation in anxious adults during resting states (Bruder, Fong, Tenke, Leite, Towey, Stewart et al., 1997; Heller, Nitschke, Etienne, & Miller, 1997) while other studies have reported patterns of right frontal activation during anxious states (e.g., Davidson, Marshall, Tomarken, & Henriques, 2000).

Furthermore, the extant developmental psychopathology literature has examined patterns of EEG asymmetry in the offspring of parents with affective disorders. Such research has suggested linkages between frontal EEG asymmetry and depression. For

example, numerous studies have shown relative right frontal asymmetry under resting conditions in infants of depressed mothers and during mother-infant interactions (e.g., Dawson, Klinger, Panagiotides, Hill, & Spieker, 1992; Field, Fox, Pickens, & Nawrocki, 1995; Jones, Field, Fox, Lundy, & Davalos, 1997). Such findings are concordant with the adult literature and show that measures of EEG asymmetry may be important neurological markers of risk for affective disorders. Despite the greater prevalence of anxiety disorders than depressive disorders and the literature suggesting that resting EEG asymmetry may serve as an index of both depression and anxiety, no research has yet examined patterns of EEG asymmetry in the offspring of parents with anxiety disorders.

Overview of the Study

This dissertation reviews several areas of research including (1) history and symptoms of anxiety and depression; (2) risk for depression and anxiety in offspring; (3) the role of EEG in emotion; and (4) EEG asymmetry in both normative and clinical populations. A study was conducted to examine patterns in EEG asymmetry in the infant offspring of depressed mothers, anxious mothers, and mothers with no history of psychopathology. Resting EEG asymmetry was studied in 4- to 8-month-old infants in order to identify potential early markers of psychopathology as well as to examine neurobiological processes of this population. The present study included 99 mothers and their infant offspring who have been involved in a larger multidisciplinary program entitled “Early Developmental Pathways of Childhood Anxiety” examining risk factors for depression and anxiety. This larger project was conducted by Dr. Susan Warren at George Washington University.

EEG differences were expected in the offspring of both the depressed and anxious

groups relative to the control group. Specifically, it was hypothesized that infants of mothers with depression would show greater right frontal asymmetry than infants of matched controls with no history of psychopathology. In addition, it was hypothesized that infants of mothers with a history of anxiety would show an increase in right parietal asymmetry as compared to infants of mothers without psychopathology. Exploratory analyses were also conducted in order to examine the following variables as they related to EEG asymmetry: a) type of maternal anxiety (panic disorder, agoraphobia, social phobia, generalized anxiety disorder, posttraumatic stress disorder, and specific phobia); b) impact of psychiatric impairment, perceived stress and social support; and c) gender. The purpose of the present study was to examine early markers of risk for psychopathology in the biological domain (e.g., patterns of EEG asymmetry) in an attempt to elucidate some of the precursors of anxiety and depression in children so that we might gain a better understanding of the development of these disorders.

Definition of Key Terms

In the present study *depression* was operationally defined as a Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychiatric Association, 1994) based psychiatric diagnosis of depression (major depressive disorder). Mothers with a diagnosis of depression must have experienced a major depressive disorder (with or without anxiety)[1]. *Anxiety* was operationally defined as a DSM-IV based psychiatric diagnosis of an anxiety disorder (panic disorder, agoraphobia, social phobia,

[1] Previous studies of affect and EEG asymmetry have not excluded depressed participants on the basis of comorbid anxiety.

generalized anxiety disorder, posttraumatic stress disorder, and/or specific phobia). Mothers with anxiety must not have had a lifetime diagnosis of depression and may have had more than one anxiety disorder. To be enrolled as a control, the participants must have had a lifetime history free of major psychiatric disorder. However, control subjects were not excluded if they had a history of substance abuse prior to their pregnancy with the infant participating in the study. That is, control participants must not have had a history of drug dependence drug abuse/dependence during pregnancy or during the child's life. Diagnoses were obtained using the Structured Clinical Interview for DSM-IV Axis I Disorders, Non-patient Edition (SCID-I/NP, Version 2.0, First, Spitzer, Gibbon, & Williams, 1996).

The *electroencephalogram* (EEG) is a non-invasive means of examining patterns of brain electrical activity, that is, the tiny electrical impulses produced by the brain in order for cells to communicate. Electroencephalography involves the recording of the differences in electrical potential between various points on the surface of the scalp through the use of electrodes. The EEG is widely used and has been implemented as a tool to diagnose and manage seizure disorders such as epilepsy. It has also been used to diagnose brain damage, brain diseases (e.g., tumors, stroke), sleep disorders, degenerative diseases (e.g., Alzheimer's disease, Parkinson's disease), and some mental disorders such as schizophrenia and autism. *EEG asymmetry* is a measure of the differences in electrical activity in the two (right and left) cerebral hemispheres of the brain. Measures of EEG asymmetry that were used in the present study are derived from the extensive work of Davidson and colleagues who have found that individual differences in EEG asymmetry are stable over time, correlated with positron emission tomography (PET) measures of

regional glucose metabolism of the lateral prefrontal cortex, and are predictive of both psychological and biological measures of affect (Davidson, 1988; Davidson & Irwin, 1999). Outcome measures of the present study are measures of EEG asymmetry at mid-frontal, lateral frontal, and mid-parietal sites. For the analyses asymmetry metrics were computed as the natural logarithm of alpha power at the right recording site minus the left recording site (e.g., lnF4 – lnF3).

Purpose and Significance of the Present Study

The purpose of the present study was to examine patterns in neurological markers of risk for depressive and anxiety disorders in the offspring of clinically depressed and anxious mothers by addressing the following questions:

1. Do the infant offspring of mothers with a history of depression show different patterns of EEG asymmetry during a resting state than the infant offspring of control mothers?
2. Do the infant offspring of mothers with a history of anxiety show different patterns of EEG asymmetry during a resting state than the infant offspring of control mothers?
3. Do the infant offspring of mothers with specific types of anxiety (e.g., panic disorder, agoraphobia, social phobia, generalized anxiety disorder, posttraumatic stress disorder, and/or specific phobia) show different patterns of EEG asymmetry during a resting state than the infant offspring of control mothers?
4. Does maternal perceived stress, perceived social support, or their interaction relate to patterns of infant EEG asymmetry?

5. Are there gender differences in patterns in EEG asymmetry in infant offspring of mothers with psychopathology compared to offspring of control mothers?

The above compelling questions of the present study concern whether children at risk for depression and anxiety differ from children of control mothers in their underlying physiology. Although the extant literature suggests that relations exist between patterns of EEG asymmetry and depression, specifically to the at-risk infants of depressed mothers, less is known about such patterns in the infant offspring of anxious mothers. To date, no research has examined patterns of EEG asymmetry in the young offspring of anxious mothers nor has any research examined both of these groups within the same study. The present study focused upon underlying neural mechanisms of emotion in order to contribute to the understanding of markers of risk in both depression and anxiety by examining pattern and direction of frontal EEG asymmetry in 4- to 8-month-old infants.

CHAPTER II: Review of the Relevant Literature

The present study examined theoretical and empirical models of infant neurobiology with models of risk for psychopathology in infants of mothers with depression as well as infants of mothers with anxiety. The intent of the present review was to provide a framework in which to examine the role of using the electro-encephalogram (EEG) to study emotion in depressive and anxiety disorders. The review includes work from developmental and clinical psychology. Infants were grouped according to maternal diagnostic status (i.e., anxious, depressed, control) in order to examine patterns of EEG asymmetry during a resting state. The present investigation affords us with the unique opportunity to examine infants at risk for both depression and anxiety.

Depression and Anxiety

Description and Importance

The present investigation focused largely on depression and anxiety. These affective phenomena have a marked prevalence in the United States**,** and symptoms of each may fall anywhere on a continuum from mild to debilitating. While anxiety disorders have a greater prevalence than depressive disorders, both are more commonly occurring in women than men. (Issues of gender in affective disorder are discussed later in this review.) Depressive and/or anxious symptomatology and somatic complaints characterize internalizing behaviors. And, children who exhibit internalizing behaviors are often withdrawn, shy, and anxious. Importantly, these children are at risk for the development of later difficulties including depression, anxiety, and social isolation (Rubin & Mills, 1988). Externalizing behavior has received a fair amount of attention in

the research literature, perhaps because this behavior is disruptive and may be difficult to overlook. Internalizing behavior, however, has not received as much attention, conceivably because the symptoms are more subtle. Furthermore, children with internalizing problems are often not perceived as experiencing problems, as they are characteristically viewed as well behaved and easy to manage (Renken, Egeland, Marvinney, Mangelsdorf, & Sroufe, 1989). Investigations of children's internalizing problems have encountered difficulties both within determining reliable symptomatology and continuity across time, and in developing strong theoretical models as well. Perhaps in attempting to elucidate some of the precursors of anxiety and depression in children we can gain a better understanding of the development of these disorders.

Depression. Depression is one of the most prevalent psychiatric disorders. Depressive disorders are defined by dysphoric mood or melancholy (sadness, anhedonia, irritability). More specifically, depressive disorders are characterized by depressed mood, loss of interest or pleasure in activities, increased fatiguability, loss of confidence or self-esteem, unreasonable feelings of self-reproach, recurrent thoughts of death or suicide, diminished ability to think or concentrate, change in psychomotor activity, sleep disturbance, and/or change in appetite. Recent estimates suggest that nearly 20% of the U.S. population will experience a clinically significant episode of depression at some point during their lives and rates of recurrence indicate that over 75% of patients with depression experience more than one episode (Keller & Boland, 1998). Depression typically emerges in adolescence, is often chronic and recurrent (see Solomon, Keller, Leon, Mueller, Lavori, Shea et al., 2000).

The past decade has seen considerable increases in rates of depressive disorders. A recent United States epidemiological study found the prevalence for major depression to be 10.3% for the twelve months prior to the interview and 17.1% for lifetime major depression (Kessler, McGonagle, Zho, Nelson, Hughes, Eshleman et al., 1994). These rates of depression have led to an escalation in depression research examining the onset, course, and treatment of depressive disorders and an enhanced understanding of mood disorders.

In the last 20 years there has been an extension of depression research into the area of depressive disorders of childhood and adolescence. Depression was primarily considered an adult disorder and little attention was paid to its occurrence in childhood. In recent years, however, research has shown that initial episodes of depression often occur in adolescence (Angold & Costello, 1995). This research was inspired by both improvements in diagnoses of depression in children as well as the shift from examining only adult samples, to examining adolescents as well (e.g., Kovacs, Feinberg, Crouse-Novak, Paulauskas, & Finkelstein, 1984; Kovacs, Feinberg, Crouse-Novak, Paulauskas, Pollock, Finkelstein et al., 1984). Importantly, the literature suggests that there is considerable continuity of depression from childhood (or adolescence) through adulthood (e.g., Solomon et al., 2000). There is a growing literature suggesting that the offspring of parents with affective disorders are at-risk for developing psychopathology compared to the offspring of controls (see Goodman & Gotlib, 1999 for review).

Anxiety. Anxiety includes emotional, cognitive, and somatic features and according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychiatric Association, 1994) there are eleven classifications of anxiety

including generalized anxiety disorder, panic disorder, and specific phobias to name a few. The prevalence of anxiety disorder exceeds that of depression and has been recently reported as 17.2% for the twelve months prior to the interview and 24.9% for lifetime anxiety disorders (Kessler et al., 1994).

Anxiety disorders are a serious problem because they interfere with work/school, and social/family life. In addition, anxiety disorders are associated with both alcohol and substance abuse and symptoms of anxiety often manifest themselves physically, causing those affected to seek treatment from their physicians as well as in emergency rooms. Importantly, the past 20-25 years have seen an increase in attention to anxiety in childhood. Examining different clinical subtypes of anxiety may help us to understand the brain circuitry of anxiety. Anxiety disorders may be caused by both individual and social factors and often trigger physical, cognitive, emotional, or behavioral symptoms. Heritable factors (which in turn may be responsible for biochemical abnormalities) are also believed to play a role in the development of these disorders. In the present study anxiety was operationally defined as a DSM-IV based psychiatric diagnosis of an anxiety disorder (panic disorder, agoraphobia, social phobia, generalized anxiety disorder, posttraumatic stress disorder, and/or specific phobia). Each of these types of anxiety is described briefly below.

Panic Disorder. Panic disorder is characterized by sudden periods of intense fear or panic attacks. Symptoms of a panic attack include increased heart rate, chest pain, choking sensations, difficulty breathing, sweating, trembling, nausea, dizziness, or hot flashes. Panic attacks are often expected and may have an abrupt onset with symptoms typically lasting 10-15 minutes. This type of anxiety disorder is unique in the suddenness

and intensity of its symptoms as well as in its episodic nature. In addition, there also exist "limited symptom" forms of panic attacks in which the symptoms are less intense. This chronic disorder has a lifetime prevalence rate of approximately 3% (Kessler et al., 1994) and had been shown to be a familial disorder that has been distinguished from depressive disorders by family studies (Rush, Feldman-Koffler, Weissenburger, Giles, Roffwarg, & Orsulak, 1995).

Agoraphobia. Phobias are present when one experiences irrational fears of something that in truth is not dangerous yet cause the individual to avoid certain situations. For example, agoraphobia is characterized by a fear of places or situations where one might experience a panic attack and be unable to escape the situation or to find assistance. Agoraphobia may lead to the avoidance of such situations as being alone outside of the home, traveling in a car, bus, or airplane, or being in a crowded area (DSM-IV; American Psychiatric Association, 1994).

Social Phobia. Social phobia is characterized by a fear of being humiliated, judged, embarrassment, ridiculed, or scrutinized. Also known as social anxiety disorder, social phobia manifests itself as a persistent anxiety in social situations, including performances and public speaking. The fear experienced is considered excessive or unreasonable and causes the individual to avoid social situations. Common symptoms of social phobia include a fear of fainting, losing control of bodily functions, or that others may notice their anxious symptoms (e.g., sweating, trembling, blushing, etc.). This phobia is often linked to a great deal of anticipatory anxiety for periods of time before the social situation. The development of social phobia usually begins in childhood or adolescence and has been linked to shyness and inhibition (Kagan, Reznick, & Snidman,

1988). In addition, social phobia is also thought to have a familial component (see Bruch, 1989 for review).

Generalized Anxiety. Generalized anxiety disorder (GAD) is characterized by a period of excess worry and is the most commonly diagnosed anxiety disorder. According to DSM-IV diagnostic criteria, GAD is associated with a number of symptoms including muscle tension, easy fatiguability, poor concentration, insomnia, and irritability (DSM-IV; American Psychiatric Association, 1994). GAD is unlike social phobia and panic disorder in that the symptoms of anxiety are not caused by a fear of a specific situation, but rather, symptoms are caused by general worry about social relationships, finances, work, etc. Research had shown that rates of mood and anxiety disorders are greater among first-degree relatives of those with GAD (Kendler, Heath, Martin, & Eaves, 1987).

Posttraumatic Stress Disorder. Unlike other types of anxiety, posttraumatic stress disorder (PTSD) results from an identifiable traumatic event that must have occurred prior to the onset of symptoms. The experience or exposure to the initial trauma must have elicited intense fear or feelings of helplessness. Symptoms of this anxiety disorder are often classified into three types: re-experiencing of the trauma (e.g., flashbacks, dreams), avoidance of stimuli related to the trauma, and increased arousal (e.g., difficulty sleeping, irritability). According to the National Comorbidity Study (NCS, Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995) the prevalence of PTSD in women is 10.4%.

Specific Phobia. Specific phobia, formerly known as simple phobia, is characterized by persistent fear that is excessive or unreasonable, prompted by the existence or anticipation of a specific object or situation. When a person is exposed to

the phobic object or situation, it often causes an immediate anxiety response. Adults with specific phobias recognize that their fear is excessive or unreasonable. Persons with a specific phobia will either avoid the stimulus or situation, or when exposed, will experience intense distress. This avoidance or intense distress when encountering the stimulus or situation interferes with one's everyday functioning (i.e., maintaining a normal routine, work or school functioning, social functioning).

Risk Factors for Offspring of Depressed Parents

Children of parents with psychopathology, specifically depression and anxiety, were chosen as the focus of the present study because they are a high-risk population. These infants are at an increased risk due to increased genetic influences as well as exposure to clinical symptoms of depression and/or anxiety by their primary caregiver. Parental depression is an important risk factor for psychopathology in children including behavior problems, socio-emotional maladjustment, and affective disorders (Bland, Newman, & Orn, 1986; Downey & Coyne, 1990; Kupfer, Frank, Carpenter, & Neiswanger, 1989; Mendlewicz & Baron, 1981; Moldin, Reich, & Rice, 1991; Price, Kidd, & Weissman, 1987; Weissman, Gammon, John, Merikangas, Warner, Prusoff et al., 1987).

Risk for Affective Disorder. The extant literature has reported socioemotional difficulties in children of depressed mothers (Cohn & Campbell, 1992; Downey & Coyne, 1990; Field, 1992; Zahn-Waxler, Cummings, Iannotti, & Radke-Yarrow, 1984; Zahn-Waxler, Cummings, McKnew, & Radke-Yarrow, 1984). Offspring of a parent with an affective disorder were more than five times more likely to develop an affective disorder than offspring of non-depressed parents (Todd, Reich, Petti, Joshi, DePaulo,

Nurnberger et al., 1996). In a study of familial depression, Weissman and colleagues (Weissman et al., 1987) found that parental depression was related to depression in their offspring compared to non-depressed parents. Murray and colleagues suggest relations between exposure to maternal depression in childhood and later difficulties in psychological adjustment (Murray, Sinclair, Cooper, Ducournau, & Turner, 1999). Subtypes of depression have also been linked to risk for offspring of depressed mothers. For example, Hammen, Burge, Burney, and Adrian (1990) found that the offspring of both unipolar and bipolar depressed women were at an increased risk of developing psychiatric disorder relative to controls. These studies are part of a growing body of evidence indicating the increased risk of an affective disorder in the offspring (both child and adolescent) of parents with an affective disorder. (See Lapalme, Hodgins, and LaRoche [1997] for a recent meta-analysis of children of parents with bipolar disorder).

Risk for Behavior Problems. Previous research has found a number of risk factors associated with internalizing problems in children and adolescents. Depressed mothers tend to have children that are withdrawn and less active than children of non-depressed mothers (Field, 1992; Field, Healy, Goldstein, & Guthertz, 1990; Field, Sandberg, Garcia, Vega-Lahr, Goldstein, & Guy, 1985). Similarly, Kochanska (1991) found that children of depressed mothers were more likely to be behaviorally inhibited than children of non-depressed mothers. These findings are believed to be due in part to the patterns of interaction between depressed mothers and their offspring and thus have an environmental component. Research has also indicated that parental depression may be a risk factor for the difficulty in the development of children's peer relationships and such influences may have a biological and/or environmental basis as well (Zahn-Waxler,

Denham, Iannotti, & Cummings, 1992). Externalizing behaviors in children has also been related to maternal depression. A recent meta-analysis by Beck (1999) showed that children of depressed mothers were more likely than children of non-depressed mothers to display conduct problems. The influence of child exposure to maternal depression and its relation with later difficulties in child psychological adjustment has also been discussed by Murray and colleagues (Murray et al., 1999).

EEG Patterns in Offspring of Depressed Mothers. A number of studies have suggested that offspring of depressed parents exhibit unique patterns of EEG asymmetry. For example, work by Field and colleagues (Field et al., 1995) has shown that young infants (ages three- to six-months) of depressed mothers have relative right frontal asymmetry (reduced left frontal activation), indicating a possible predisposition for these infants to express or experience negative affect. Infants of depressed mothers who are at increased risk for developing mental disorders (e.g., Murray & Cooper, 1997) have exhibited reduced left frontal activation when interacting with their depressed mothers (Dawson, Frey, Panagiotides, Yamada, Hessl, & Osterling, 1999; Dawson et al., 1992; Field et al., 1995; Jones, Field, Fox et al., 1997).

Risk Factors for Offspring of Anxious Parents

Family history data, twin studies, and empirical research have provided increasing evidence of poor outcome in the offspring of adults with anxiety disorders. An increasing literature has attempted to uncover the origins of anxiety through the study of offspring of parents with anxiety disorders given that these offspring are at risk for anxiety disorders (Hettema, Neale, & Kendler, 2001). For example, Turner, Beidel, Costello (1987) reported that compared to the offspring of parents without

psychopathology and normal school children, children of anxiety disordered parents were found to be more anxious and fearful, evidence more school difficulties, report more worries about both family members and themselves, have more somatic complaints, and spend more time engaged in solitary activities.

It has been well documented that maternal history of anxiety is an antecedent of child internalizing problems. Behavioral inhibition in children has been linked to maternal diagnosis of anxiety disorder (Manassis, Bradley, Goldberg, Hood, & Swinson, 1995). This research suggests a link between familial and developmental factors where family history of psychopathology is related to withdrawal in offspring. Similar findings have been reported for various types of anxiety. For example, Rosenbaum, Biederman, Gersten, Hirshfeld-Becker, Meninger, Herman et al. (1988) reported that children of parents with panic disorder were more likely than children of controls to display signs of behavioral inhibition. Other studies have reported that children of parents with panic disorder are at increased risk for multiple anxiety disorders (Biederman, Faraone, Hirshfeld-Becker, Friedman, Robin, & Rosenbaum, 2001; Biederman, Rosenbaum, Bolduc, Faraone, & Hirshfeld, 1991).

Research on childhood anxiety and children at risk for anxiety has also examined physiological process in this population. For example, Warren, Schmitz, & Emde (1999) reported heritable influences on both physiologic and social anxiety symptoms in seven-year-old children. Baving, Laucht, & Schmidt (2002) reported that anxious school-aged girls showed greater left than right frontal brain activation which is consistent with previous studies examining EEG patterns in internalizing preschoolers. Recently, Warren and colleagues (Warren, Gunnar, Kagan, Anders, Simmens, Rones et al., 2003) reported

that infants of mothers diagnosed with panic disorder had higher cortisol levels than infants of matched controls. This finding of neurophysiological patterns in the offspring of panic disordered mothers suggests that these infants may experience heightened levels of arousability. To date, no research had examined the EEG patterns in offspring of anxious parents. Such research would elucidate the relations between underlying neurobiological markers of anxiety and aid researchers in identifying children at risk for psychopathology.

A comorbidity study found that the offspring ages 4-20 years of parents with panic disorder and agoraphobia or with panic disorder, agoraphobia and major depression, were more than twice as likely as offspring of control parents to have an anxiety disorder (Biederman et al., 1991). This study also found that the offspring of parents with concurrent major depression had a prevalence of anxiety disorder four times that of the offspring of controls, suggesting the shared etiological influences on anxiety and depression. Weissman and colleagues (Weissman, Leckman, Merikangas, Gammon, & Prusoff, 1984; Weissman, Warner, Wickramaratne, Moreau, & Olfson, 1997) have found familiality of anxiety disorders, cross-generational familiality of anxiety disorders, and familiality of the relations between depressive and anxious disorders. While the question of whether the familial influence of depression and anxiety is biological, environmental, or some combination of the two has yet to be determined, such broad questions cannot be answered in the present study.

Developmental Psychopathology

In order to conduct research on the offspring of parents with a history of psychopathology it is important to consider, both theoretically and empirically, the

processes that influence the impact of maternal psychopathology on infant outcomes. Developmental psychopathology is a field that takes a developmental perspective in order to understand the origins, pathways, and treatment of affective disorders. Major theories of developmental psychopathology include genetic, temperament, biological factors, and family-based processes. While a comprehensive examination into the complex factors leading to the development of child psychopathology was beyond the scope of the present study, the aim of this investigation was to integrate the diverse fields of psychiatry, neurophysiology, and development in order to elucidate underlying neurophysiological markers of risk for psychopathology.

Current research on prevalence rates reveal how risk for psychopathology changes over the course of the lifespan and helps to illuminate the factors that may influence the development of psychopathology. What we know less about however, are the pathways by which anxiety and depression develop in children. Many studies of maternal psychopathology and child outcomes examine one single developmental time period. Yet, integrating our understanding of the risk factors in the population as well as the parent-child transactions that take place over these time periods will aid research in uncovering the pathways by which this transmission takes place.

Depression models. A growing literature has put forth a number of causal models of parental depression (Gelfand & Teti, 1990) implicating genetics, observational learning, and impaired parenting (Downey & Coyne, 1990). It is not known whether these traits in young children are genetically or environmentally transmitted. Research has also indicated that parental depression may be a risk factor for difficulty in the development of children's peer relationships and such biological influences are most

suitably understood as interacting with environmental factors that influence a child's development (Cicchetti & Toth, 1998; Zahn-Waxler et al., 1992). Such outcomes are considered to be the result, in part, of patterns of interaction between depressed mothers and their offspring, suggesting an environmental component. They may also reflect an underlying biological disposition (e.g., temperament) of the offspring of depressed women. Most likely, the behavior of the offspring of depressed women is a result of both biological and interactional factors. However, these associations between maternal depression and child behavior problems may not be directly causal. For example, infant characteristics such as negative reactivity may either initiate or exacerbate the development of maternal depression. Furthermore, behavior problems in offspring of depressed mothers may be associated with deficits in parenting common to depressed women. For example, clinically depressed mothers have been described as uninvolved, ineffective, insensitive, disengaged, and intrusive when interacting with their children (Cummings & Davies, 1994; Gelfand & Teti, 1990). A number of mother-child observational studies have found that depressed mothers, when compared to controls, are less likely to interact in an adaptive way with their children, and tend to display less positive and more negative affect towards them (Cohn, Campbell, Matias, & Hopkins, 1990; Cohn, Matias, Tronick, Connell, & Lyons-Ruth, 1986; Cohn & Tronick, 1989; Field et al., 1990; Field et al., 1995; Field, Healy, Goldstein, Perry, Bendall, Schanberg et al., 1988). This research suggests that maternal depression is related to increased levels of insensitivity and withdrawal in mother-child interactions (Teti, O'Connell, & Reiner, 1996). Lovejoy, Graczyk, O'Hare, & Neuman (2000) reported in a recent meta-analysis

that maternal depression was related to lower levels of maternal engagement with offspring.

Murray and colleagues have also discussed the influence of child exposure to maternal depression and its relation with later difficulties in child psychological adjustment. They suggest that maternal sensitivity may play a key role in mediating the relation between maternal depression and child social functioning (Murray & Cooper, 1996). Murray argues that children's later functioning may not be directly related to their experience of maternal depression necessarily, but rather, that child outcomes may be a result of a pattern of interaction between the mother and child within the context of depression. Thus, maternal depression may influence parenting behaviors such as poor maternal communication, which may be a determining factor in the development of psychopathology. In summary, research has indicated that parental depression is associated with psychopathology in their offspring including difficulties in the areas of socio-emotional functioning, behavior problems, and affective disorders. Such influences may have a biological and/or environmental basis, the latter of which may be the result of a parent being unable to appropriately respond to their offspring's emotional responses.

Anxiety models. Not unlike depressive disorders, anxiety disorders are believed to be the result of both genetic and environmental factors and furthermore, may be the result of the interaction of these factors that take place over the course of development. Despite the fact that over the past 20 years there has been an increased interest in the research on anxiety in children, there is much more that needs to be understood about the pathways by which anxiety disorders develop in children. Those researchers who align themselves with a developmental psychopathology perspective would agree that anxiety disorders in

children are most likely reached through multiple pathways. For example, researchers have reported differing pathways to the development of general social phobia and specific phobia in children (Stemberger, Turner, Beidel, & Calhoun, 1995). This study found that among the offspring of parents with social phobia, those with a generalized form of the disorder were more likely to be shy, neurotic, and introverted than offspring with specific social phobia, who were more likely to disclose specific traumatic events. These results suggest that generalized social phobia may result from shyness (temperament) while specific social phobia may result from respondent conditioning. Furthermore, parenting behaviors described as inconsistent or restrictive have been reported to be associated with childhood anxiety (e.g., Kohlmann, Schumacher, & Streit, 1988; Krohne & Hock, 1991), as have other environmental factors such as poor housing or poverty (Goodyer, 1990). Despite these findings there may be additional pathways to the development of these disorders in children.

A developmental psychopathology perspective also considers that both risk and protective factors may be short-lived or long-term. Furthermore, these influences may shift along the continuum of a child's development. To illustrate, research has shown that children predisposed to anxiety may be more likely to develop PTSD following a traumatic event than children who did not experience anxiety prior to the event (e.g., La Greca, Silverman, & Wasserstein, 1998). This is one example of risk factors outweighing protective factors. Yet another viewpoint of the developmental psychopathology perspective is that the disorders researchers are investigating take place within a developing individual. Thus, if we are interested in studying anxiety disorders from this perspective, we must consider examining differences in age with respect to both

onset of the disorder as well as prevalence of the disorder. Another example of this notion has been put forth by Cicchetti and Cohen (1995) who suggest that stressors a child experiences may result in different behavioral outcomes depending upon the developmental time frame during which they occur.

In summary, the developmental psychopathology literature offers both important theoretical and empirical foundations for the effect of maternal psychopathology on infant outcomes. While factors that influence outcome are believed to be both familial as well as heritable, in many circumstances they are the result of interactions among both of these factors. The present study attempts to integrate the fields of psychiatry and neurophysiology from a developmental perspective in order to elucidate associations between maternal psychopathology (e.g., depression and anxiety) and differences in patterns of infant brain electrical activity.

Theoretical Approaches to Emotion

Research on emotion has used various theoretical approaches including dimensional approaches, which emphasizes the characteristics that emotions have in common. Dimensional approaches describe emotions using only one or two dimensions. Two-dimensional circumplex models often propose a valence dimension (e.g., positive vs. negative affect) and an arousal dimension (see Larsen & Diener, 1992). Thus, for example, emotions of sadness and fearfulness would be located in the negative or unpleasant area of the circumplex and would be characterized by varying (increasing) levels of arousal.

In addition to the two-dimensional circumplex model, it has been proposed that emotions may be organized simply based on their approach or withdrawal tendencies

(Davidson, 1992b). Using this approach, emotions of fear and sadness may be classified as emotions often distinguished by withdrawal tendencies. Gray (1994) proposed that there is both a Behavioral Inhibition System (BIS) related to approach behaviors and a Behavioral Activation System (BAS) related to withdrawal behaviors. The former serves to inhibit behavior and is associated with anxiety while the latter serves to increase behavior and is associated with impulsivity (Derryberry & Rothbart, 1984). Within this theoretical perspective Gray suggested that the BIS is affiliated with functioning of the hippocampus, while the BAS is affiliated with the "fight or flight" (Cannon, 1927) mechanism in the amygdala. Investigations in the field of cognitive neuroscience have evidenced support for this theory (Gray, 1994). Dimensional approaches to emotion have a number of limitations, however (see Larson & Diener, 1992 for review and critique of the circumplex model). For example, emotions that are close to each other in the circumplex (e.g., fear and anger) may have important differences; yet, the circumplex model may not adequately recognize these differences. The role of approach–withdrawal theories, particularly those of Davidson, rely primarily on research that has examined patterns of frontal brain activation. While Davidson's neuropsychological model focuses primarily on anterior brain regions, a similar model has been put forth by Heller, who suggests that there is a system located in the frontal lobes that may regulate the valence of emotion as well as a system located in the parietotemporal region that may be involved in the emotion-related arousal. This theory is discussed in greater detail later in this review. To date, few studies of brain laterality and emotion have examined EEG regions anterior to F3 and F4 sites (dorsolateral prefrontal positions). Relations between emotions and EEG asymmetry are discussed later in this review.

EEG Asymmetry

History of Frontal EEG Asymmetry

Research on frontal EEG asymmetry and emotion has a brief history. In the late 1970s a paper was presented at the Society for Psychophysiological Research (SPR) that was the first to suggest a potential relation between patterns of frontal brain electrical activity and the experience of both positive and negative affect. This paper was the first published work to examine emotional experience using frontal electroencephalogram (EEG) asymmetry (Davidson, Schwartz, Saron, Bennett, & Goleman, 1979). The decade that followed found a scarcity of this type of work; however, there has been an increased interest in using frontal EEG asymmetry to study emotion and psychopathology over the past fifteen years. The extant literature reveals that frontal EEG asymmetry has been used as both state and trait markers of depressive and anxious symptoms and has been effective in identifying individuals at risk for later psychopathology. And, variations in the patterning of EEG asymmetry have been found when emotions are manipulated. Furthermore, the role of frontal EEG asymmetry and affective style has been examined in studies with both clinical and non-clinical adult populations, as well as developmental studies with children.

The extant literature suggests that the neural circuitry in the brain responsible for emotion in humans may be open to both genetic and environmental influences (see Davidson, Putnam, & Larson, 2000). This neural circuit includes a number of brain regions, including the prefrontal cortex, the amygdala, hippocampus, and hypothalamus (see Davidson & Irwin, 1999 for review). The regulation of emotion involves an individual increasing, decreasing, or maintaining an emotion. When this process is

interrupted, dysregulation occurs. Researchers have put forth neuroanatomical models of depression that argue for a system of extensively interconnected central nervous system (CNS) structures that mediate emotion and affect. For example, Byrum, Ahearn, & Krishnan (1999) believe that the numerous areas of the brain involved in the relations between emotion and depression are so interconnected that any one dysfunctional component of the system may propel the entire system into a depressed state.

Henriques and Davidson (1991) review the extant literature on lesions related to asymmetry. For example, lesions in the left frontal region of the adult brain have been found to be associated with depression, anxiety, and (pathological) crying while lesions in the right frontal region have been associated with (pathological) laughing and joking. Due to the fact that brain lesions disrupt the functioning of the brain (in some capacity), lesion studies suggest that the left frontal region may be related to positive affect while the right frontal region may be related to negative affect.

The pattern of brain electrical activity, in particular, the balance of left and right electroencephalogram (EEG) activity, is a physiological characteristic believed to play an important role in emotion (Davidson, 1984, 1992b, 1994; Fox, 1991; Tomarken & Keener, 1998). Asymmetry, as this pattern is termed in the present study, has been investigated as an index of both stable individual differences and universal emotional states (Coan & Allen, 2003). Many EEG studies reported asymmetry findings (e.g., right hemisphere activation minus left hemisphere activation). These scores may indicate a decrease in activation of either the right or left hemisphere, an increase in activation of a homologous region, or a combination of the two (Tomarken & Keener, 1998).

An increasing literature has demonstrated that psychophysiological measures such as EEG asymmetry are related to emotion in both adults and children. However, important questions remain regarding patterns of physiology in populations diagnosed with depression and anxiety as well as their young offspring at high-risk for developing these disorders. Several previous studies of normally developing children have found that frontal asymmetry is associated with withdrawal behavior but not approach behavior (Calkins, Fox, & Marshall, 1996; Fox, Schmidt, Calkins, Rubin, & Coplan, 1996; Henderson, Fox, & Rubin, 2001). For example, behavioral inhibition, described as restraint and caution in response to unfamiliar people and events (Kagan et al., 1988), has been linked to patterns of greater right frontal EEG activity. Furthermore, one study found that infants who exhibited high motor activity and high negative affect (believed to be related to inhibition) at four months of age had greater relative right frontal EEG asymmetry at nine months, whereas infants who exhibited high motor activity and high positive affect did not exhibit left frontal asymmetry (Calkins et al., 1996). Research has also shown that infants who display patterns of stable right frontal activity across infancy have a greater likelihood of showing signs of inhibited behavior at 14 and 24 months than are infants who display left frontal activity (Fox, Calkins, & Bell, 1994). And it has been reported that children who maintain a classification of inhibited behavior through the fourth year of life also display patterns of right frontal asymmetry (Fox, Henderson, Rubin, Calkins, & Schmidt, 2001).

The Role of Frontal EEG Asymmetry in Emotion

The expression, experience, and regulation of emotion are linked to a number of underlying neural mechanisms; yet, these complex elements do not have a specific region

of cortex or sub-cortex that is dedicated to their integration. However, the frontal region is unusual in that it has inputs from all cortical and sub-cortical areas believed to be associated with the expression of emotion (Fuster, 1980; LeDoux, 1993). One factor that has been correlated with emotion is the patterning of cortical activation, particularly as measured via the EEG over the prefrontal areas. A number of researchers have speculated that differential activity of the left or right prefrontal regions is related to biases to approach or withdraw from novelty (Fox, 1991, 1994; Davidson, 1992b). Further, these biases may influence the valence around which contexts and stimuli are processed. For example, Davidson and colleagues reported that adult subjects displaying right frontal EEG asymmetry were more likely to view affective stimuli in a negative manner compared to adults displaying left frontal EEG asymmetry. Adults who self rated themselves as high on a scale of behavioral approach were more likely to display left frontal EEG asymmetry, while adults self rated as low on approach were more likely to display right frontal EEG asymmetry. Several investigations have examined changes in EEG activity in healthy children during emotion-eliciting paradigms. For example, Fox and Davidson (1988) recorded EEG in 10-month-old infants. Infant facial expressions of emotion were elicited during a stranger approach, mother approach, and maternal separation. Results from this study show that expressions of sadness (including crying) were characterized by more right frontal activation compared to sadness expressions without crying. Furthermore, Fox, Bell, and Jones (1992) reported that infants who display greater relative right frontal EEG asymmetry are more likely to exhibit crying behavior in response to maternal separation. In addition, Fox and colleagues (Fox, Rubin, Calkins, Marshall, Coplan, Porges et al., 1995) found that children who are

socially withdrawn at four years of age are more likely to exhibit greater relative right frontal EEG asymmetry than their less withdrawn peers.

These differences in bias have also been extended to clinical populations. Henriques and Davidson (1991), for example, reported that depressed adults displayed resting right frontal EEG asymmetry and that previously depressed individuals, now in remission, had less left-sided anterior and less right-sided posterior activation (i.e., more alpha activity) than did never depressed controls (Henriques & Davidson, 1990). Recent research findings on depression and frontal asymmetry (Miller, Fox, Cohn, Forbes, Sherrill, & Kovacs, 2002) have provided further support for this assertion in adults with a history of depression. Building on the initial model, Tomarken and Keener (1998) proposed an extension of the approach-withdrawal hypothesis (e.g., Davidson, 1992b; Fox, 1991), suggesting that frontal brain asymmetry may be linked to self-regulatory processes that promote the temporal continuity and shifting of motivational or emotional priorities and the suppression of interference by competing sources of motivation or emotion.

Affect that is associated with withdrawal (e.g., sadness, disgust, distress, and fear) elicits immediate enervation of the sympathetic nervous system and motor activity which may require right hemisphere activation, while affect associated with approach (e.g., joy, anger) is linked to more sequential motor activity and analytic skills and thus may require activation of specific areas of the left hemisphere. Alternatively, circumplex models (Watson & Tellegen, 1985) are consistent with Heller's (1993a) proposal that the fundamental dimension is that of emotional valence (e.g., pleasant vs. unpleasant) rather than approach/withdrawal. However, because positive emotions are often related to

approach and negative emotions to withdrawal, these theories are difficult to disentangle from one another. (One exception is anger-induced avoidance, which would be associated with withdrawal as opposed to approach.)

The extant literature suggests that the anterior regions of the brain are implicated in the expression, experience, and regulation of affect. Overall, the data suggest that the left and right frontal regions are differentially specialized for approach and withdrawal behaviors. For example, Sobotka, Davidson, and Senulis (1992) found that normal college students exhibited greater right frontal activation during a punishment condition compared to a reward condition on a computer task. Silberman and Weingartner (1986) have shown with lesion studies and WADA testing in adults that the left anterior region is associated with both the expression and experience of negative affect while the right anterior region is associated with both the expression and experience of positive affect. Furthermore, Borod (1992) has shown that the frontal region is closely involved in both the expression of emotion as well as the type of emotion experienced. In addition, the right parietotemporal region is involved in the intensity of emotion (Heller, 1993a) and/or the perception of emotion (Gur, Skolnick, & Gur, 1994). Research from both the adult and developmental literature has found empirical evidence to support the significance of the frontal region in the expression of affect. To illustrate, Davidson and colleagues (Davidson, Ekman, Saron, Senulis, & Friesen, 1990) found that frontal EEG activation in adults was a function of the type of facial affect expressed (elicited using film clips) such that facial expressions of disgust were associated with greater relative right frontal EEG and positive affect facial expressions were associated with greater relative left frontal EEG activity. Furthermore, this study reported that Duchenne smiles (defined as smiles

exhibited in response to felt happiness or enjoyment) were related to significantly more left-sided activation (as compared to other types of smiles) in the anterior and parietal regions. Similarly, Fox and Davidson (1987) found relations between frontal EEG patterns and facial expression of positive and negative affect in normal infants.

In terms of individual differences, there are individuals whose response style to a mild stressor is one of approach and experience of positive emotions while other individuals display a style of withdrawal and negative emotions. These differences in an individual's tendency to express either patterns of approach or withdrawal in response to novelty are thought to be fundamental to an individual's personality and motivation. The differences involve various brain systems where the propensity to express negative emotions and withdrawal is thought to be systematized within the right hemisphere and the propensity to express positive emotions and approach in the left hemisphere.

In sum, there is a marked prevalence of anxiety disorders and depressive disorders as well as a literature suggesting that offspring of parents with affective disorders may be at risk for psychopathology. Furthermore, there is growing research implicating resting EEG asymmetry as an index of both depression and anxiety. Despite this, there is a paucity of literature examining the patterns of EEG asymmetry in the at-risk offspring of mothers diagnosed with depression and anxiety. While there is an extant literature that has examined EEG asymmetry patterns in the infant offspring of depressed mothers, less is known about the at-risk infants of anxious mothers. To date, no research has examined patterns of EEG asymmetry in the young offspring of anxious mothers nor has any research examined both of these groups within the same study.

Resting Frontal Asymmetry and Trait vs. State Emotion

Frontal brain asymmetry is believed to be a trait marker related to psychopathology as well as a state marker associated with acute emotional response. Next, this review differentiates between the use of frontal EEG asymmetry in studies of both state and trait emotion and discusses the approach used in the present study.

Investigations of frontal asymmetry as a trait marker assume that it reflects dispositional differences in tendencies to experience and express approach and withdrawal emotions (Fox, 1991, 1994). Studies of anterior EEG asymmetry as a trait marker have shown that asymmetrical activity is related to depression. However, such research has shown conflicting results. Right frontal asymmetry appears to be consistently related to negative affect and to the expression of withdrawal-related emotion. However, left frontal asymmetry is not as consistently related to positive affect. For example, in adults, one study found that greater right frontal activity during a resting state was related to higher self-report of negative affect, yet there was not the equivalent relation with positive affect for those with greater left frontal activity (Tomarken, Davidson, & Henriques, 1990). And, in a child study, resting asymmetry scores were related to children's social wariness but not to sociability (Henderson et al., 2001).

Research on frontal EEG asymmetry has also explored task-related asymmetry and state emotion. These investigations have investigated frontal EEG asymmetry during emotion-eliciting tasks such as viewing films. Both the adult and developmental literature has reported that frontal EEG asymmetry is associated with emotions of approach and withdrawal. Studies of frontal asymmetry during tasks designed to elicit emotions have evidenced that emotional states of approach and withdrawal are related to

patterns of EEG asymmetry. For example, 10-month-old infants exposed to videotapes of a female adult displaying facial expressions of happiness show left frontal asymmetry (Davidson & Fox, 1982), and during maternal separation infants' left frontal activity increases (Fox & Davidson, 1987). Furthermore, during a social presentation task, shy school-age children have shown greater relative task-related increases in right frontal activity than control children (Schmidt, Fox, Schulkin, & Gold, 1999). The adult literature has found that individuals participating in computer tasks with both reward and punishment conditions show greater relative left activity during reward trials (Miller & Tomarken, 2001; Sobotka et al., 1992) as well as greater relative right activity during punishment trials (Sobotka et al., 1992). Using emotion-inducing tasks with personal content, Waldstein and colleagues (Waldstein, Kop, Schmidt, Haufler, Krantz, & Fox, 2000) found that adults have greater relative left frontal EEG activity during tasks intended to induce happiness.

Coan and Allen (2003) have suggested that resting asymmetry is a measure of trait-like, stable individual differences in one's emotional response while task-related asymmetry is a measure of universals in emotional state. To illustrate, it has been hypothesized that resting left frontal asymmetry is reflective of a stable predisposition to respond to events with approach-related behaviors. Several studies from the adult literature have reported stability of resting frontal asymmetry over time (Sutton & Davidson, 1997; Tomarken, Davidson, Wheeler, & Doss, 1992; Tomarken, Davidson, Wheeler, & Kinney, 1992; Wheeler, Davidson, & Tomarken, 1993), which provides support to assertions that frontal asymmetry is indicative of qualities that are trait-like. The developmental literature has also examined the stability of resting EEG asymmetry

over time and shown similar results (see Bell, 1998; Schmidt & Fox, 1998 for reviews). For example, Jones, Field, Davalos, & Pickens (1997) examined EEG stability in infants and children of depressed mothers from infancy to early childhood. This study examined resting EEG during a three-minute period. The results from this study showed stability of EEG asymmetry from three months to three years of age. Specifically, offspring who showed patterns of right frontal EEG asymmetry in infancy also showed right frontal EEG asymmetry at age three. The results of this study are consistent with previous findings that have reported stability of EEG from six to twelve months (Fox et al., 1992). The present investigation examined resting asymmetry in young infants as a trait-like marker of risk for affective disorder.

Studies of emotion have also examined frontal asymmetry during emotion-eliciting tasks such as viewing film clips. These investigations with adults and children have reported frontal asymmetry to be associated with approach and withdrawal emotions. As previously discussed, there is a literature suggesting variation in activation of the anterior brain regions during the experience or expression of both positive and negative emotions such that greater relative left anterior activation is associated with positive emotions and greater relative right anterior activation is associated with negative emotions. For example, the adult literature has reported greater relative left frontal resting EEG activity in adults who self-report greater positive affect in response to pleasant films (Wheeler et al., 1993) as well as greater change in positive affect from pleasant to unpleasant films (Tomarken et al., 1990). Furthermore, Tomarken and colleagues (Tomarken et al., 1990) reported that adults who exhibit right frontal EEG

asymmetry are more likely to rate video clips with various affective content in a negative manner as compared to adults who show stable left frontal EEG asymmetry.

EEG as a Marker for Affective Disorders

The extant adult literature suggests that right frontal EEG asymmetry is a marker for affective disorders (e.g., Henriques & Davidson, 1990; 1991; Miller et al., 2002; Tomarken & Keener, 1998) and research from the developmental literature suggests that this holds true for the offspring of mothers with psychopathology (e.g., Dawson, Frey, Panagiotides et al., 1999; Dawson, Frey, Self et al., 1999; Dawson et al., 1992; Field et al., 1995; Jones, Field, Davalos et al., 1997). The next section examines findings from both the adult and developmental literature of the relations between patterns of EEG asymmetry and affective disorders.

Depression. Clark and Watson (1991) assert that depression is associated with lower levels of positive affect while anxiety is associated with higher levels of negative affect. Thus, this notion is consistent with an approach/withdrawal model whereby there is a deficit in the region associated with approach. Tomarken and Keener (1998) reviewed the literature on frontal brain asymmetry and depression and proposed an extension of the approach-withdrawal hypothesis (e.g., Davidson, 1995; Fox, 1991). They suggest that this relationship may be explained by self-regulatory processes that promote the temporal continuity and shifting of motivational or emotional priorities and the suppression of interference by competing sources of motivation or emotion that reflect core functions of the prefrontal cortex.

The extant adult literature on depression posits that right frontal EEG asymmetry is a trait marker for affective disorders (Tomarken & Keener, 1998). This assertion is

based on literature suggesting that in depression there is an increase in negative affect (i.e., higher withdrawal behavior) and a reduction in engagement in activities associated with reward (i.e., lower approach) (Clark & Watson, 1991; Depue & Iacono, 1989; Fowles, 1988). For the most part, examinations of the relations between depression and frontal EEG asymmetry confirm this assertion in adults with both current and remitted depression (Henriques & Davidson, 1990, 1991; Miller et al., 2002).

In the adult literature for example, Henriques and Davidson (1991) reported that depressed adults displayed resting right frontal EEG asymmetry and that previously depressed individuals, now in remission, had less left-sided anterior and less right-sided posterior activation (i.e., more alpha activity) than did never depressed controls (Henriques & Davidson, 1990). Recent findings on depression and frontal asymmetry have provided further support for this assertion in adults with a history of depression (Miller et al., 2002). And Henriques and Davidson (1991) reported that depressed adults display resting right frontal EEG asymmetry. In addition, previously depressed individuals had less left-sided anterior and less right-sided posterior activation (i.e., more alpha activity) than did never depressed controls (Henriques & Davidson, 1990). The locus of the asymmetry in these aforementioned studies appears to be in the left frontal region. Thus, right frontal asymmetry in depressed adults and previously depressed adults is due to left frontal hypoactivation (less left frontal activity). This pattern of left frontal activation corresponds to the theory that depression is an effect of the lack of motivation for positive affect or approach behaviors as opposed to increased negative affect.

Adult studies of lateralized brain activity in depression have also examined the posterior regions although this work has been limited. Findings from the posterior region suggest that there is less right activity in the parietotemporal area in depressed mood states (e.g., Heller, Etienne, & Miller, 1995). Heller's (1993a) proposed model states that the arousal axis is hypothesized to relate to the right posterior region, where decreased activation (increased power) of the right parietotemporal cortex is related to depression. Henriques & Davidson (1990) reported that previously depressed individuals had less right-sided posterior activation (i.e., more alpha activity) than did never depressed controls and several investigations have reported right posterior dysfunction in depressed individuals (see Heller, 1993a, 1993b; Heller et al., 1995).

The first infant study of the relations between frontal EEG asymmetry and affect was conducted by Davidson and Fox (1982). In this study, 10-month-old infants observed a videotape of a woman exhibiting both happy and sad facial expressions. The infants showed less left frontal EEG activation when observing the sad facial expressions compared to observing the happy facial expressions. These findings were interpreted (Fox and Davidson, 1988) as reflective of differences in the activation of the approach and withdrawal systems, where greater left frontal EEG is associated with happy (i.e., approach) emotions and less left frontal EEG is associated with sad (i.e., withdrawal) emotions. Since that time, the developmental literature has begun to map EEG measures of the approach and withdrawal systems onto psychopathology, particularly depression.

Evidence linking depression and frontal asymmetry in adults has also been found in the children of depressed mothers (Tomarken, Simien, & Garber, 1994), and infants of mothers with depressive symptoms (e.g., Dawson, Frey, Panagiotides, Osterling, &

Hessl, 1997; Dawson, Frey, Panagiotides et al., 1999; Dawson et al., 1992; Field et al., 1995; Jones, Field, Davalos et al., 1997). For example, Dawson and colleagues (Dawson et al., 1997) reported that 13- to 15-month-old infants of depressed mothers had less left frontal activity than those of non-depressed mothers. In addition, a decrease in left frontal activity discriminated the infants of mothers diagnosed with major depression from the infants of mothers with sub-threshold depressive symptoms. This same laboratory has also found that infants of depressed mothers show less affection and relatively less left frontal activity during resting states as well as during interaction with their mothers and while interacting with familiar strangers (Dawson, Frey, Panagiotides et al., 1999). Earlier work from this laboratory (Dawson et al., 1992) examined EEG patterns in 11- to 17-month-old infants of depressed and non-depressed mothers during a baseline task as well as during a task designed to elicit positive affect (a game of peek-a-boo with their mothers). The results of this study showed that infants of depressed mothers displayed reduced left frontal activity during both the baseline task and during the task designed to elicit positive affect than did infants of non-depressed mothers.

Numerous findings from another laboratory have shown similar results. To illustrate, Field and colleagues (Field et al., 1995) found that 3- to 6-month-old infants of mothers with a diagnosis of depression displayed right frontal EEG asymmetry during a resting state compared to the infants of non-depressed mothers. These results are consistent with previous research suggesting that patterns of anterior brain electrical activity may indicate a disposition to express negative affect. In a recent study of EEG patterns in three month-old infants of depressed mothers, Diego and colleagues (Diego, Field, Hart, Hernandez-Reif, Jones, Cullen et al., 2002) found that infants of withdrawn

vs. intrusive (two predominant interaction styles) depressed mothers showed differences in the physiological responses to interactions with their mothers as well as with strangers. And infants of withdrawn depressed mothers showed greater relative right frontal EEG asymmetry than infants of intrusive depressed mothers during a baseline task. These results are consistent with previous findings of greater relative right frontal asymmetry in the infant offspring of withdrawn depressed mothers (Jones, Field, Davalos et al., 1997).

Furthermore, there have been investigations that have shown right frontal EEG asymmetry in infants of depressed mothers from very early ages. For example, Jones and colleagues (Jones, Field, Fox et al., 1997) reported greater relative right frontal EEG asymmetry (due to reduced left frontal activation) in one month-old infant of depressed mothers. Additionally, this pattern of EEG asymmetry was related to patterns of EEG asymmetry in these same infants at three months of age. In a study of the three month-old infants of depressed mothers, Field and colleagues (Field, Pickens, Fox, Gonzalez, & Nawrocki, 1998) examined the EEG responses to both happy and sad faces and voices. Infants of non-depressed mothers showed less left frontal EEG activation during the observation of the sad face/voice than during the happy face/voice. These infants also showed less left frontal EEG activation during the sad face/voice than infants of depressed mothers. These results may be explained as an expected or "normal" response because left frontal EEG activation is related to sad stimuli (i.e., withdrawal).

In reviewing this literature we must also consider that the stability of EEG asymmetry has not been fully established and that we do not know whether these patterns of frontal asymmetry precede the onset of depression or whether they are an effect of the current or previous depressive state. Furthermore, depression may be comorbid with

anxiety (see Enns, Swenson, McIntyre, Swinson, Kennedy, & CANMAT Depression Work Group, 2001 for review), and it is unclear whether sensitivity to these disorders is evidenced through frontal EEG asymmetry. We do know, however, that the existing literature suggests that this pattern of brain electrical activity may reflect a trait marker for the disposition to express negative or dysphoric affects (those associated with withdrawal), which lead to the prediction that left frontal hypoactivation would be found in offspring at risk for depression.

In sum, previous research has consistently shown that both infants and children of depressed mothers have greater relative right frontal EEG asymmetry (Field et al., 1995; Jones, Field, Davalos et al., 1997; Jones, Field, Fox et al., 1997). Based on previous adult and developmental studies of frontal asymmetry and depression (e.g., Field et al., 1995; Henriques & Davidson, 1990) the present study predicted that the offspring of mothers with a history of clinical depression would differ from the offspring of control mothers on measures of EEG asymmetry.

Anxiety. Although fear and anxious responses may be adaptive from an evolutionary perspective, anxiety may become maladaptive when it interferes with one's functioning. It has been posited that a certain amount of arousal may increase motivation while too much arousal may hamper motivation (Yerkes & Dodson, 1908). For example, increased feelings of arousal while taking an exam may allow for increased concentration or better performance, however, if these feelings become too overwhelming they may interfere with one's ability to perform well. Thus, too much arousal or anxiety may have a negative impact on one's ability to function. The prevalence of anxiety disorders in both adults and children has lead to increased research on their underlying neural

mechanisms. And, because of the relative ease with which anxiety/conditioned fear may be evoked in animals (i.e., the use of an aversive stimulus such as shock) much of this work has been conducted with animals (e.g., Davis, 1992; Mineka, 1985). Although this work has uncovered much about the underlying neural mechanisms of anxiety in animals, less is known about the cortical brain regions in humans and their relations to anxiety. There is a literature that has examined the electrophysiological response to induced anxiety (e.g., anticipating giving a public speech) as well as with anxious adult populations and several investigations have reported patterns of right frontal activation during anxious states (e.g., Davidson et al., 2000).

In a study of anxiety-disordered patients, Rauch and colleagues (Rauch, Savage, Alpert, Dougherty, Kendrick, Curran et al., 1997) found an increase in right frontal activation when symptoms of anxiety were provoked. Similarly, a recent study of social phobia by Davidson and colleagues (Davidson et al., 2000) found that phobics showed an increase in right-sided activation in the anterior temporal and lateral prefrontal regions when anticipating public speaking as compared to controls. These findings are consistent with Tillfors and colleagues (Tillfors, Furmark, Marteinsdottir, Fischer, Pissiota, Langstrom et al., 2001; Tillfors, Furmark, Marteinsdottir, & Fredrikson, 2002) who found enhanced cerebral blood flow in the right dorsolateral prefrontal cortex in social phobic adults anticipating giving a public speech.

Relating Gray's neurophysiological theories (Gray, 1987, 1992) to investigations of state anxiety and public speaking we might expect that this social experience would influence the BIS, causing inhibitory responses in physiological correlates. And, using an approach-withdrawal model, Wiedemann and colleagues (Wiedemann, Pauli, Dengler,

Lutzenberger, Birbaumer, & Buchkremer, 1999) reported that patients with panic disorder exhibited greater right frontal activation both during a resting phase and when challenged with anxiety-relevant stimuli. Findings from the aforementioned studies suggest that anxiety patients may be characterized by greater activation of the right frontal withdrawal system in situations of negative valence. These observations indicate that there are differences in the patterning of hemispheric activation that may correspond to various affective disorders. Overall, these differences may be indicative of variations in emotion regulation strategies, which may influence an individual's vulnerability to affective disorders.

Less research, however, has examined patterns of EEG asymmetry and fear and/or anxiety in children. Importantly, to date, no research has examined patterns of EEG asymmetry in infants of anxious mothers. The extant developmental literature has found evidence of patterns of right frontal EEG asymmetry in infants and young children who exhibit behaviors related to fearfulness or anxiety. As previously discussed, Calkins (Calkins et al., 1996) studied EEG patterns in nine month-old infants who exhibited behaviors related to inhibition at four months of age. These infants displayed right frontal asymmetry compared to infants who did not exhibit these behaviors at four months of age. Similarly, infants who were found to have stable right frontal asymmetry from nine months to 24 months of age were more likely to show signs of fearfulness and inhibition during several experimental tasks (Fox, Calkins, & Bell, 1994). In addition, Fox and colleagues (Fox et al., 1995) found that children who are socially withdrawn at four years of age are more likely to exhibit greater relative right frontal EEG asymmetry than their less withdrawn peers. It may be concluded from these studies that right frontal

EGG asymmetry may be reflective of fearfulness or inhibition in normally developing infants and children.

Given the discrepant findings of EEG patterns in the anxiety literature, Heller put forth a theory to explain these differences. Heller posited that the valence dimension of the circumplex model of emotion is linked with activity in the anterior regions of the brain (see Davidson, 1984; 1992a) and the arousal dimension is linked with activity in the posterior regions of the brain. In other words, Heller suggested that there is a system located in the frontal lobes that may regulate the valence of emotion as well as a system located in the parietotemporal region that may be involved in the emotion-related arousal. Heller postulates that greater activation in the right frontal cortex is related to negative emotion, while high activation of the right parietotemporal cortex is expected to be associated with high arousal. Recent research has reported increased right parietal brain activation in anxious adults during resting states (Bruder et al., 1997; Heller et al., 1997), supporting Heller's model stating that anxious arousal is associated with enhanced right parietal activation.

The findings from the aforementioned literature shape many of the questions that were addressed in the present study concerning whether children at risk for anxiety differ from children of control mothers in their underlying physiology. Although the extant literature suggests that relations exist between patterns of EEG asymmetry and anxiety, to date, no research has examined patterns of EEG asymmetry in the infant offspring of anxious mothers. Moreover, no study has yet to examine the infant offspring of both clinically depressed and anxious mothers within the same study.

Panic Disorder. Findings from the panic disorder literature have revealed similar patterns. For example, Wiedemann and colleagues (Wiedemann et al., 1999) reported frontal brain asymmetry (reduced right alpha power/increased right frontal activation) in panic disordered patients during a resting state (perhaps reflecting an overactive avoidance-withdrawal system). This same pattern emerged when panic disordered patients were exposed to anxiety inducing stimuli. Wiedemann and colleagues (Wiedemann et al., 1999) reported that patients with panic disorder exhibited greater right frontal activation both during a resting condition and when challenged with anxiety-relevant stimuli. Furthermore, using near-infrared reflection spectroscopy (NIRS; a measure of tissue oxygenation) Akiyoshi, Hieda, Aoki, & Nagayama (2003) found hypoactivity of the left frontal cortex in panic disordered patients. A study of resting EEG asymmetry in (spider) phobic patients showed a relation between greater relative right parietal hyperactivation (overactivation) and more severe phobic symptoms (Merckelbach, Muris, Pool, & De Jong, 1998). These results are consistent with the notion that the right frontal areas serve to mediate avoidance behavior (e.g., Tomarken et al., 1990) while the right parietal areas may be involved in fear and arousal (e.g., Heller et al., 1995). In sum, these studies from the adult literature suggest that among anxious participants, differences in emotional responses are reflected in the patterns of asymmetric EEG activation, specifically, right frontal activation.

Panic attacks are believed to be the result of difficulties in brain pathways that control the acquisition of conditioned fear (e.g., the amygdala, the brain stem, the hippocampus, and parts of the pre-frontal cortex) (Sinha, Papp, & Gorman, 2000).

Research has shown that panic disordered patients exhibit higher blood flow in the right parahippocampal gyrus (a region proximal to the temporal lobe) during periods of non-panic attacks, and increased blood flow in the left right temporal poles during induced panic attacks (Reiman, Raichle, Robins, Mintun, Fusselman, Fox et al., 1989).

Issues of Comorbidity. Depression has been found to have high rates of comorbidity with other psychiatric disorders, the most prevalent of which are anxiety. These high rates of comorbidity between these two disorders may be biological in nature, as genetic studies suggest a biologic link between depression and anxiety (Leckman, Weissman, Merikangas, Pauls, & Prusoff, 1983). The extant literature has also suggested that depression and anxiety may have opposing patterns of asymmetry, particularly within the right parietotemporal region (see Heller, 1990, 1993a, 1993b), whereby depressives show a relative decrease in right posterior activity and anxious participants show a relative increase in right posterior activity (Keller, Nitschke, Bhargava, Deldin, Gergen, Miller et al., 2000). Similarly, in a study of regional brain asymmetries in major depressive disorder (MDD) with and without anxiety disorder Bruder et al. (1997) reported that non-anxious depressed patients exhibited less activation over the right than left posterior sites, while anxious-depressed patients exhibited greater activation over right than left anterior and posterior sites. In a child study, Kentgen and colleagues (Kentgen, Tenke, Pine, Fong, Klein, & Bruder, 2000) reported that adolescents with MDD (without anxiety) showed alpha asymmetry suggestive of less activation over right than over left posterior sites. Within adolescents with MDD, those with comorbid anxiety disorders had reduced posterior alpha asymmetry. These results remind us of the

importance of considering the comorbidity of depression and anxiety in future investigations.

Heller (1993a) proposed a model of cerebral activation during emotional processing. This circumplex model partitions the brain into four quadrants, differentiated by valence (pleasant vs. unpleasant) and arousal (high vs. low). Under this model, the arousal axis is hypothesized to relate to the right posterior region where decreased activation (increased power) of the right parietotemporal cortex is related to depression. Heller's work has emphasized the importance of considering different subtypes of depression and anxiety, as well as their comorbidity in studying regional brain activity (Heller & Nitschke, 1998). They argue that various subcomponents of the symptomatology of depression and anxiety disorders are related to discrete regions of the brain and the extent to which comorbidity exists among them makes the identification of their underlying neural mechanisms all the more complex. In addition, may studies fail to create clear distinctions between depression and anxiety, for example, often using measures of depression and anxiety that are highly correlated. Thus, specificity in symptomatology may aid researchers in discerning inconsistencies in the literature. The present study used DSM-IV criteria to measure depressive and anxiety disorders. All probands in the depressed group met DSM–IV diagnostic criteria for major depressive disorder (with or without anxiety). All probands in the anxious group met DSM–IV diagnostic criteria for an anxiety disorder including panic disorder, agoraphobia, social phobia, generalized anxiety disorder, posttraumatic stress disorder, and/or specific phobia. Mothers with anxiety must not have a lifetime diagnosis of depression and may have had more than one type of anxiety disorder.

Utility of EEG Measures

Today, the study of emotion and psychopathology often bring to mind some of the numerous studies that utilize functional neuroimaging (e.g., positron emission tomography [PET], functional magnetic resonance imaging [fMRI]). Given such increases in technology one might wonder why some researchers continue to use EEG as a means of examining psychopathology; however, there are a number of advantages to its employment. For example, on a practical level, EEG is relatively inexpensive, non-invasive, and accessible. Importantly, measurements of frontal EEG asymmetry have been established in the substantial research literature, purporting both its construct validity as a measure of underlying approach or withdrawal tendencies or motivational style (Davidson, Jackson, & Kalin, 2000; Harmon-Jones, 2004) as well as its usefulness as a marker of risk for psychopathology such as depression and anxiety (see Coan and Allen, 2004).

As previously mentioned, in the last decade an increasing amount of attention has been paid to the neuropsychological correlates of emotion and psychophysiological correlates of depression in adults (see Borod, 1993; Marshall & Fox, 2000 for reviews)**.** For example, research has examined patterns of regional brain electrical activity, autonomic functioning, and patterns of facial muscle movement (EMG) in individuals with depressive disorders. However, to date, less research has examined the pathophysiology of infants at risk for psychopathology.

Gender

Depression and Anxiety

Depression is a common psychiatric disorder that occurs more frequently in women than men (Nolen-Hoeksema, 1987, 1990). The majority of sizeable epidemiological studies in the United States report that approximately two times as many women as men meet the criteria for major depressive or dysthymic disorder (Eaton, Anthony, Gallo, Cai, Tien, Romanoski et al., 1997; Keller & Shapiro, 1981; Kessler, McGonagle, Swartz, Blazer, & Nelson, 1993). To illustrate, the National Comorbidity Study found a lifetime prevalence of major depressive disorders and anxiety disorders among women to be 21.3% and 30.5% respectively and 12.7% and 19.2% among men respectively (Kessler et al., 1993). Women also are inclined to score higher than men on measures of sub-clinical depressive symptoms (Nolen-Hoeksema, 1987, 1990). Like depression, anxiety is more commonly occurring in females than males. Approximately 13.3 % of the United States' population has an anxiety disorder and women are more likely than men to have such a disorder. More specifically, women are twice as likely as men to have panic disorder, generalized anxiety disorder, agoraphobia, and specific phobia. In social phobia, however, males and females have an equal chance of being affected (Robins & Regier, 1991).

EEG Patterns

An important question of the present investigation concerns the potential for gender differences in infant EEG asymmetry patterns, especially with respect to their mothers' history of psychopathology. Research has found gender difference in electrophysiological measures of regional brain activity in both normative and depressive

populations. For example, the literature on EEG asymmetry has shown inconsistent findings and researchers have suggested that gender may play a central role in such discrepancies (Davidson, Schwartz, Pugash, & Bromfield, 1976). Recent work found gender differences in regional patterns of brain activity among depressive probands (adults previously diagnosed with childhood onset depression) and matched controls during a baseline procedure (Miller et al., 2002). Specifically, women previously diagnosed with childhood-onset depression showed greater right mid-frontal alpha suppression and men with childhood depression showed higher left mid-frontal alpha suppression relative to matched controls. In addition, across diagnostic groups, women had greater alpha power than men. These results provide support for the notion that gender differences may exist in regional brain activity and suggest that these differences may be due to gender differences in the biological propensity for emotion regulation.

The importance of gender differences in EEG studies of depression is not fully known because depression has commonly been examined in female populations (Reid, Duke, & Allen, 1998; Kentgen et al., 2000). It is important to note that although much of the literature on EEG asymmetry in children has included both males and females, few studies have explicitly examined gender differences. Work by Baving and colleagues has found gender differences in school-aged children with and without attention deficit hyperactivity disorder (Baving, Laucht, & Schmidt, 1999) as well as differences in frontal brain activation between anxious girls and control girls.

The effect of gender on EEG asymmetry warrants further study and the present investigation examined these potential relations via exploratory analyses. Work by Bruder and colleagues (Bruder, Stewart, Tenke, McGrath, Leite, Bhattacharya et al.,

2001) found that extreme relative right alpha asymmetry predicts non-response to the antidepressant fluoxetine only in depressed adult females. These studies are concordant with previous findings in the non-clinical literature that suggest differences in EEG asymmetry among men and women. For example, Davidson and colleagues (Davidson et al., 1976) reported gender differences in EEG asymmetry during self-generated cognitive and affective tasks, where females showed greater bilateral flexibility than males. In a study of motivation, Miller and Tomarken (2001) reported finding gender differences in frontal brain asymmetry during tasks designed to elicit approach and withdrawal. Specifically, this study showed that males and females evidenced opposing linear changes in mid-frontal asymmetry. These studies underscore the importance of gender differences in EEG studies of depression. While the specific focus on gender in relation to mood disorders is too large for the scope of the present study, exploratory analyses were conducted in order to examine the potential relations between gender and EEG patterns. Potential gender differences in the present study may reflect regulatory tendencies in infants characterized by approach or withdrawal.

Rationale for the Developmental Period to be Investigated

There are a number of reasons for investigating infants between the ages of four months and six months. First, children as young as one and two years old have been identified with anxiety disorders and a wealth of literature has been linked to risk for psychopathology in the offspring of depression mothers. By examining children at risk for such disorders prior to their onset the present study was able to identify early markers of children at risk for depression and anxiety. Second, the extant literature suggests that not only does the brain develop over the course of one's life, but that during the first two

years of life the brain is particularly sensitive to the experiences in the environment. Animal studies have shown that there are "sensitive periods" for which the developing brain is more highly impacted by stressors in the environment as well as behaviors of a parent than other periods in the animal's development (see Andersen, 2003 for review).

Furthermore, since the first documented study of EEG in infants and children (Berger, 1932) there has been an abundance of work utilizing measures of EEG in this population. For example, numerous investigations have examined the development of the EEG during infancy and into childhood (see Bell, 1998; Schmidt & Fox, 1998 for reviews). The alpha band, which is the most prominent EEG rhythm, has typically been used in the adult literature. Alpha power varies inversely with cortical activation, that is, higher power values represent less activation, while lower power values represent higher activation at a target location. By comparing the relative amounts of alpha power between the two hemispheres of the brain we can determine the direction of asymmetrical activation. This same approach to the measurement of EEG has been taken with infants and children with one important difference. Research has shown that from infancy to young adulthood, changes take place in the frequency of the alpha rhythm. Specifically, the frequency band that corresponds to alpha in adults (typically 8-12 Hz) is slower in infants. Therefore, the frequency band that is used as a measure of EEG varies with age. Importantly, the majority of previous frontal EEG and emotion findings in both the adult and child literature pertain to the alpha band (see Davidson & Tomarken, 1989). For infants of the age of those in the present study (four to six months), the alpha range is typically defined as 4-6 Hz (see Marshall, Bar-Haim, & Fox, 2002).

Measures of EEG asymmetry that were used in the present study are derived from the extensive work of Davidson and colleagues who have found that individual differences in EEG asymmetry are stable over time. The developmental literature has also examined the stability of resting EEG asymmetry over time and shown similar results in infants of depressed mothers (Jones, Field, Davalos et al., 1997). By examining at-risk infants at this young age the present study revealed an early snapshot of underlying neurobiological markers before the development of psychopathology.

Overview of the Present Study

The purpose of the present study is to examine the relationship between maternal psychopathology and infant physiological reactivity in a sample of 99 families. The present study included infants of mothers who were involved in a larger multidisciplinary study entitled "Early Developmental Pathways of Childhood Anxiety," examining risk factors for depression and anxiety. This larger project was conducted by Dr. Susan Warren at George Washington University. The present study focused on three groups, identified by maternal diagnosis. One group included mothers with anxiety disorders, another group included mothers with depression and the third included mothers without a history of psychopathology. In order to assess the infants' physiological reactivity, brain electrical activity was recorded during a resting state.

The overall hypothesis of the present study was that differences in patterns of EEG asymmetry would be found among the offspring of both the depressed and anxious mothers relative to the control group. Based on the extant literature it was specifically hypothesized that right frontal EEG asymmetry would be associated with infants of depressed mothers (relative to infants of control mothers) and right posterior asymmetry

was predicted to be associated with infants of anxious mothers (relative to infants of control mothers). Exploratory analyses were also conducted in order to examine the following variables as they relate to EEG asymmetry: a) type of maternal anxiety (panic disorder, agoraphobia, social phobia, generalized anxiety disorder, posttraumatic stress disorder, and specific phobia); b) impact of psychiatric impairment, perceived stress, and social support; and c) gender. The purpose of the present study was to examine early precursors in the biological (e.g., patterning of frontal EEG asymmetry) domain as markers of risk for psychopathology.

CHAPTER III: Methodology

Participants

The present study included infants of 39 mothers who were diagnosed with depression, 22 mothers who were diagnosed with anxiety, and 38 mothers with no history of major psychopathology. Mothers with young infants (four to eight months of age) were recruited through mass mailings and newspaper media advertisements. All probands in the depressed group met DSM–IV diagnostic criteria for major depressive disorder (with or without anxiety). All probands in the anxious group met DSM–IV diagnostic criteria for an anxiety disorder (described in more detail below). Mothers with anxiety must not have a lifetime diagnosis of depression and may have had more than one anxiety disorder. Potential control subjects were excluded if they had a lifetime history of a major psychiatric illness. However, control subjects were not excluded if they had a history of substance abuse prior to their pregnancy with the infant participating in the study. That is, control participants must not have had a history of drug dependence drug abuse/dependence during pregnancy or during the child's life. Inclusion in the present study was based on a lifetime history of psychopathology, not current symptoms. In addition, families were excluded if the infant had experienced major medical illness, or if the child had a history of abuse or trauma.

Only biological mothers who are primary caregivers were included in the sample for the purpose of maintaining consistency among groups and only one child per family was assessed. Both male and female infants were included. Families were primarily recruited from Fairfax County and Arlington County in Virginia. Based on 2000 Census Data (duplicated count), it was expected that the racial/ethnic backgrounds of the families

to whom recruitment materials were sent was as follows: within Fairfax County: 8.6% Black or African American, 0.3% American Indian and Alaskan Native, 13.0% Asian, 0.1% Native Hawaiian and other Pacific Islanders, 4.5% Other, 3.7% persons reporting two or more races, 11% Hispanic or Latino, and 64.4% Caucasian not of Hispanic/Latino origin and within Arlington County: 9.3% Black or African American, 0.3% American Indian and Alaskan Native, 8.6% Asian, 0.1% Native Hawaiian and other Pacific Islanders, 8.3% Other, 4.3% persons reporting two or more races, 18.6% Hispanic or Latino, and 60.4% Caucasian not of Hispanic/Latino origin. The median family income for Arlington County and Fairfax County for the 2000 Census was $63,001 and $81,050 respectively. All interested families were contacted and every attempt was made to match the demographics of the families who visit the laboratory to the Census data, however, with this type of research there may be an over-representation of one or more ethnic groups and families of a particular socio-economic status in the status in the sample.

The demographic characteristics of the sample are presented in Table 1. The infants of depressed mothers, infants of anxious mothers, and infants of comparison participants were balanced on basic demographic characteristics. The infants of depressed mothers included 20 males and 19 females, and their mean age was 6.43 months (*SD* = 1.91). The group was 0% American Indian or Alaska Native, 5.13% Asian, 12.82% African American, 0% Native Hawaiian or Pacific Islander, 79.49% Caucasian, and 2.56% declined to identify a category. 17.95% of mothers reported their infants to be of Hispanic or Latino ethnicity. The infants of anxious mothers included 16 males and 6 females, and their mean age was 6.28 months (*SD* = 2.03). The group was

0% American Indian or Alaska Native, 4.55% Asian, 13.64% African American, 0% Native Hawaiian or Pacific Islander, and 81.82% Caucasian. 13.64% of mothers reported their infants to be of Hispanic or Latino ethnicity. The infants of control mothers included 21 males and 17 females, and their mean age was 5.51 months (*SD* = 1.55). The group was 0% American Indian or Alaska Native, 10.53% Asian, 21.05% African American, 0% Native Hawaiian or Pacific Islander, and 68.42% Caucasian. 10.53% of mothers reported their infants to be of Hispanic or Latino ethnicity. Last, 8.08% of the mothers reported taking psychotropic medication at the time of the interview.

Table 1

Demographic Characteristics of the Sample

	Offspring of Depressed	Offspring of Anxious	Offspring of Control
Variable	Mean (SD) or Percentage		
Age in months	6.43 (1.9)	6.28 (2.03)	5.51 (1.55)
Gender			
Male	20	16	21
Female	19	6	17
Race			
American Indian/Alaska Native	0% (n = 0)	0% (n = 0)	0% (n = 0)
Asian	5.13% (n = 2)	4.55% (n = 1)	10.53% (n = 4)
African American	12.82% (n = 5)	13.64% (n = 3)	21.05% (n = 8)

Native Hawaiian/Pacific Islander	0% (n = 0)	0% (n = 0)	0% (n = 0)
Caucasian	79.49% (n = 31)	81.82% (n = 18)	68.42% (n = 26)
Missing or refused	2.56% (n = 1)	0% (n = 0)	0% (n = 0)
Ethnicity			
Hispanic	17.95% (n = 7)	13.64% (n = 3)	10.53% (n = 4)
Maternal Education Level			
High school diploma	10.53% (n = 4)	0% (n = 0)	7.89% (n = 3)
Attended college	5.26% (n = 2)	9.09% (n = 2)	18.42% (n = 7)
Associate's degree	0% (n = 0)	9.09% (n = 2)	2.63% (n = 1)
Bachelor's degree	47.37% (n = 18)	63.64% (n = 14)	44.74% (n = 17)
Master's degree	34.21% (n = 13)	13.64% (n = 3)	15.79% (n = 6)
Ph.D., M.D. or JD	2.63% (n = 1)	4.55% (n = 1)	10.53% (n = 4)
Missing or refused	2.63% (n = 1)	0% (n = 0)	0% (n = 0)
Paternal Education Level			
High school diploma	8.33% (n = 3)	9.09% (n = 2)	8.33% (n = 3)
Attended college	11.11% (n = 4)	13.64% (n = 3)	13.89% (n = 5)
Associate's degree	0% (n = 0)	0% (n = 0)	2.78% (n = 1)
Bachelor's degree	44.44% (n = 16)	50.00% (n = 11)	52.78% (n = 19)
Master's degree	22.22% (n = 8)	27.27% (n = 6)	16.67% (n = 6)
Ph.D. or M.D.	13.89% (n = 5)	0% (n = 0)	5.56% (n = 2)
Missing or refused	8.33% (n = 3)	0% (n = 0)	5.56% (n = 2)
Family Income Level			
<25,000	3.03% (n = 1)	0% (n = 0)	10.34% (n = 3)

25, 000 – 50,000	6.06% (n = 2)	5.88% (n = 1)	13.79% (n = 4)
50,000 – 100,000	57.58% (n = 19)	47.06% (n = 8)	62.08% (n = 18)
>100,000	33.33% (n = 11)	47.06% (n = 8)	13.79% (n = 4)
Missing or refused	15.38% (n = 6)	22.73% (n = 5)	23.68% (n = 9)

Note. $N = 99$. Data on infant age, infant gender, infant race/ethnicity, and parent education levels were obtained through maternal-report demographic questionnaires. Maternal history of psychopathology was determined using the Structured Clinical Interview for DSM-IV Axis I Disorders, Non-patient Edition (SCID-I/NP, Version 2.0, First, Spitzer, Gibbon, & Williams, 1996).

Procedure

Ascertainment and Assessment of Cases and Controls. Participants were enrolled in the study if they had a history of depression or anxiety, or had no history of psychiatric illness (normal controls). Depression was operationally defined as a DSM-IV based psychiatric diagnosis of depression (major depressive disorder with or without anxiety disorder). Mothers with major depressive disorder were not excluded if they had comorbid anxiety. Anxiety was operationally defined as a DSM-IV based psychiatric diagnosis of an anxiety disorder (panic disorder, agoraphobia, social phobia, generalized anxiety disorder, posttraumatic stress disorder, and/or specific phobia). To be enrolled as a control, the participants must have had a lifetime history free of major psychiatric disorder. However, control subjects were not excluded if they had a history of substance abuse prior to their pregnancy with the infant participating in the study. That is, control participants must not have had a history of drug dependence drug abuse/dependence during pregnancy or during the child's life.

Two strategies were used to recruit mothers with psychopathology and control participants. Advertisements were placed in local parent newspapers and with the Anxiety Disorders Association of America. In addition, a pool of participants was recruited through commercially available mailing lists. The company used provided names and address labels by date of the child's birth and family zip code. Families were mailed a cover letter describing the study (See Appendix A for Recruitment Letter). Families that were interested in the study were asked to reply with their contact information using a postage-paid business reply envelope. There were no racial, ethnic, religious, social, or economic qualifications.

Mothers who responded by returning the information card were contacted via telephone by a research assistant and given the details about the study and procedures and informed consent was obtained. Mothers took part in a pre-screening procedure (See Appendix B for SCID-I Screener) over the telephone that was used to rule out individuals unlikely to qualify. In addition, mothers were asked whether they had experienced a major psychotic illness, whether the infant had experienced major medical illness, or the infant had a history of abuse or trauma. If the family was not excluded for any of these reasons and the mother was willing to participate, she was then scheduled to have a diagnostic interview conducted in her home by a trained research assistant. These assessments were conducted using the Structured Clinical Interview for DSM-IV Axis I Disorders, Non-patient Edition (SCID-I/NP, Version 2.0, First et al., 1996).

Overview of Laboratory Visit. Infants in the present study were accompanied to the session by their mothers. Upon arrival to the laboratory, the mother was given general descriptions of the tasks and the purpose of the research visit. Mothers were told

that their participation and that of their infants was voluntary and they may choose to stop at any time. Mothers remained in the testing room while the procedures took place. During the assessment, the infant sat on the mother's lap while the physiological sensors were placed. After the physiological sensors were placed, infants sometimes remained in their mother's lap and completed the baseline task. This task was followed by other tasks examining temperament and physiology in infants at risk for depression and anxiety as part of the larger multidisciplinary program. The present investigation examined the baseline task only. At the end of the visit, the mothers were given a $10 gift card to Toys-R-Us for participating in the study. Two infants would not tolerate the placement of the EEG cap and eight had unusable data due to artifact for a total of 10 infants with missing EEG data.

Measures

Resting Baseline. At the laboratory visit brain electrical activity (EEG) was continuously collected during a resting condition. In order to minimize the chance that the infant would become fussy and to minimize movement, infants were sometimes held in their mother's lap during the baseline procedure. While the infant was in a quiet, alert state, a plastic bingo wheel was held in front of the infant. The experimenter placed varying numbers of colored balls (0, 1, 2, 3, 4, or 6) in the wheel and spun the wheel for 20 seconds each. Trials were separated by 10-second intervals for a total of three minutes. These procedures were videotaped and EEG was recorded during the duration of the three-minute task.

Maternal Report of Current Symptoms. During the visit in the home, interviewers conducted an assessment of maternal history of psychopathology and administered a number of scales assessing current symptoms.

Structured Clinical Interview for DSM-IV Axis I Disorders, Non-patient Edition (SCID-I/NP, Version 2.0, First et al., 1996). Interviewers used the SCID to conduct an assessment of maternal history of psychopathology. The SCID, developed by Biometrics Research, New York State Psychiatric Institute, NY, is semi-structured and conducted face-to-face by trained interviewers in order to acquire DSM-IV diagnoses. Over the past 20 years the SCID has been revised several times and has been adapted for various patient groups. The original SCID-I has an inter-rater reliability of $k > 0.60$ for the majority of categories (Spitzer, Williams, Gibbon, & First, 1992; Williams, Gibbon, First, Spitzer, Davies, Borus et al., 1992). The Non-patient Edition was used in the present study because the mothers in the study were members of the community as opposed to psychiatric patients. SCID interviewers were trained in diagnostic assessments by a board certified and licensed psychiatrist. To establish overall reliability rates as well as to control for interviewer drift, inter-rater reliability was obtained during the course of the present study for approximately 39% of the sample (kappas ranged from .71 to 1.0). In the present study, all probands in the depressed group met DSM–IV diagnostic criteria for major depressive disorder (with or without anxiety) ($n = 39$). All probands in the anxious group met DSM–IV diagnostic criteria for anxiety disorder including panic disorder ($n = 3$), agoraphobia ($n = 2$), social phobia ($n = 7$), generalized anxiety disorder ($n = 2$), posttraumatic stress disorder ($n = 4$), and specific phobia ($n = 11$). Mothers with anxiety must not have had a lifetime diagnosis of depression and may have had more than

one anxiety disorder. Of the 22 mothers who met criteria for anxiety disorder, 16 had one anxiety disorder, five had two anxiety disorders, and one had three anxiety disorders. Potential control subjects were excluded if they had a lifetime history of a major psychiatric illness. However, control subjects were not excluded if they had a history of substance abuse prior to their pregnancy with the infant participating in the study. That is, control participants must not have had a history of drug dependence drug abuse/dependence during pregnancy or during the child's life. Inclusion in the present study was based on a lifetime history of psychopathology, not current symptoms.

Sheehan Disability Scales and Stress and Social Support Scales (SDS, Leon, Olfson, Portera, Farber, & Sheehan, 1997). The Sheehan Disability Scales, made available in 1994 as the first disability scales, examine three main areas of life (work, social, and family) and two domains (self-perceived stress and social support). The three-item measure allows for the assessment of psychiatric impairment. Items are worded, "To what extent have emotional symptoms disrupted your (work, family life/home responsibilities, social) life in the last month?" Responses for each item range from 0 to 10, where 0 = not at all, 1-3 = mildly, 4-6 = moderately, 7-9 = markedly, and 10 = extremely. Total scores range from 0 to 30. The SDS has a high internal consistency (coefficient alpha = 0.89) and construct validity ranging from 0.67 for work impairment to 0.77 for family impairment and 0.81 for social impairment. The scale for self-perceived stress asks, "In the past month, how much were you set back by stressful events or personal problems, such as work, home, social, health, or financial problems?" and is rated on the aforementioned scale. The scale for perceived social support asks, "In the past month, how much support have you received from friends, relatives, co-workers,

etc, as a percentage of the amount you needed to cope?" and ranges from 0% to 100%. The present study used an average of scores across the three main areas of life (work, social, and family) in order to rate overall disability due to psychiatric impairment (total functional disability) as well as the two domains of perceived stress and social support. (See Appendix C for Sheehan Disability Scales and Stress and Social Support Scales).

Demographic information. Data on participant demographic characteristics (e.g., age, ethnicity, [parent] education level, and family income) was also collected from mothers. This information was used for descriptive purposes only. In addition, maternal data were collected regarding use of psychotropic medication.

Behavioral Coding

Behavioral data were coded during the baseline task to determine whether the infants were in a quiet and alert state as required for the task to begin. The coding system examined both motor scores and affect (both positive and negative) and three categories were computed: motor scores, positive affect, and negative affect. Overall motor scores were coded as sum of the frequency of leg kicks (leg movements greater than 45 degrees from the resting position), leg kick bursts (three or more continuous leg kicks) x 2, arm waves (arm movements greater than 45 degrees from the resting position), arm wave bursts (three or more continuous arm waves) x 2, arching (arching of the back x 2), and hyperextension of the arms or legs. Overall positive affect was coded as the sum of the frequency of smiles and neutral or positive vocalizations while overall negative affect was coded as the sum of the frequency of fussing and crying. Proportions were computed for the three behavioral composites of positive affect, negative affect, and motor scores in order to standardized the amount of time that was coded. Inter-rater reliability was

obtained for 20% of the sample. Spearman correlations ranged from r = .84 to r = .99. This coding system has been used by previous researchers (e.g., Calkins et al., 1996; Kagan & Snidman, 1991).

EEG Data Acquisition

Prior to collecting EEG data from each participant, a 50 uV sine wave calibration signal was input into each of the channels. This calibration signal was recorded for each participant. Recording of physiological signals followed standard guidelines (see Pivik, Broughton, Coppola, Davidson, Fox, & Nuwer, 1993) and was conducted in a sound proof and electrically shielded testing room. EEG recordings were made from tin scalp electrodes sewn into a Lycra stretchable cap from Electro-Cap International, Inc. (see Blom & Anneveldt, 1982). The cap was positioned on the head according to the expanded 10-20 International System (American Electroencephalographic Society, 1994). Cap size was chosen according to the measurement of the circumference of the participant's skull. In order to anchor the cap and to minimize movement the cap was snapped to a chest harness. A minimal amount of Electro-gel (from Electro-Cap International) was inserted into the 18 sites of interest to ensure contact between the scalp and the electrode. Sites were gently abraded using the blunt end of a Q-tip. Impedances were checked after cap placement, and sites were further abraded as needed to obtain impedances below 5 kΩ (kOhms). Impedances for homologous sites were generally within 0.5 kΩ of each other.

Sites included: mid-frontal (F3, F4), lateral frontal (F7, F8), frontal midline/zero (Fz), mid-central (C3, C4), central midline/zero (Cz), mid-parietal (P3, P4), frontal pole (FP1, FP2), occipital (O1, O2), mastoids (A1, A2), parietal midline (Pz), and anterior

frontal midline/zero (AFz). These sites were chosen to replicate previous EEG studies. In addition, they allow for the possibility of examining long and short distance coherence in the anterior to posterior direction in both hemispheres. All sites were referenced to vertex (Cz) and an average mastoid reference was derived off-line using left (A1) and right (A2) mastoid data. The vertex (Cz) was used as the reference location because it has been used almost exclusively in the infant EEG literature (see Field, Diego, Hernandez-Reif, Schanberg, & Kuhn, 2002; Fox et al., 1992; Jones, Field, & Fox, 1998). The frontal midline site (AFz) was used as the isolated common ground. One channel of electrooculogram (EOG) was recorded. Tin cup electrodes (6 mm) were placed below the left eye in line with the pupil and on the outer canthus of the left eye to record blinks and eye movements. The electrooculogram (EOG) was recorded using a bipolar reference. EOG data were used to identify eye movement artifact.

EEG and EOG data were amplified and filtered with a bioamplifer from the James Long Company set for bandpass filtering with half-power cutoff frequencies of 0.01 Hz (high-pass) and 100 Hz (low-pass) (12 dB/octave rolloff). The gain was 5000 for the EEG channels and 1000 for the EOG channels. The output of the amplifiers was processed by a 12-bit Analog-to-Digital (A-D) Converter Board with a range set to 5 V (i.e., 1 mV full scale input sensitivity for EEG channels and 2 mV full scale input sensitivity for the vertical EOG channel). The A-D board ran from a Pentium laboratory computer. The physiology signals were digitized at 512 Hz (512 samples per second), using the signal acquisition package Snapshot Snapstream (HEM Data Corp., Southfield, MI). The physiology record was synchronized with task events using the James Long Company STIM Stimulus Presentation System.

EEG Data Reduction

Although the data for the present study had previously been collected, the processing of the physiological files had not been conducted. A large undertaking of the present study was to process and reduce the EEG data into a useable format. Initial data processing for the present study minimized the effects of artifacts in the EEG signals. First, a set of automated programs was used to remove the effects of blinks from the EEG data (see Miller & Tomarken, 2001). Using a temporary data file that includes blink exemplars, the vertical EOG signals were regressed on each unique EEG site in order to estimate the propagation factors (i.e., beta weights) that characterize the linear relation between the vertical EOG site and the blink artifact at each EEG site. Using the entire original data, the blink correction was then implemented by using the propagation factors as coefficients in linear transformations to residualize the EEG from the blink-contaminated signal by computing (EEG-βEOG) for each EEG sample. In addition, given that the automated correction procedure addressed only blink artifacts and EEG data containing signals +/- 250 uV, manual post-session reviews of the EEG signals with James Long Company EEGEDIT software was performed. This procedure identified periods that might have been confounded by artifacts such as movement, extensive muscle tension, and large saccades. These periods were excluded from analyses.

Following the artifact-reduction procedures, data were re-referenced offline using James Long Company EEG Analysis System software. In particular, linear transformations of the digitized EEG were performed to derive an average mastoid reference. Discrete Fourier transforms of the digitized EEG during the baseline task were performed. The software uses a Hanning window to identify 1-second periods of artifact-

free data within the task. The windows overlapped by 50 percent. The resulting estimates of spectral power from 1-hertz bins were clustered together into broad bands. The clear majority of previous frontal EEG and emotion findings pertain to the alpha band (see Davidson & Tomarken, 1989). For infants of this age, the alpha range is typically defined as 4-6 Hz (see Marshall et al., 2002). For the present study, spectral power in the 4-6 Hz frequency band was computed for each site used in the analyses by summing the single hertz bins in these three frequencies across the resting baseline condition.

The average power scores (in pico-watt-ohms or μV^2) were transformed to natural logarithms to normalize the distribution of scores that were used in statistical analyses (Gasser, Bacher, & Mocks, 1982). The natural logarithm of alpha power and asymmetry scores were reported in the analyses. Given that alpha power varies inversely with cortical activation, higher power values represent less activation, while lower power values represent higher activation at a target location. Asymmetry metrics were computed as the natural logarithm of alpha power at the right recording site minus the left recording site (e.g., lnF4 – lnF3). For all infants, those with fewer than 20-30 dft windows (approximately 20 seconds of data) were excluded from the analyses across the pairs of sites examined in the analyses.

Hypotheses and Plan for Analysis

The primary hypotheses of the present study state that the infant offspring of mothers with a documented history of psychopathology would exhibit different patterns and direction of mid-frontal, lateral frontal, and mid-parietal brain electrical activity during a resting state relative to the infant offspring of controls. An alpha level of .05

was used for all statistical tests. Type I error was minimized by limiting the number of tests to that required for hypothesis testing.

Demographic and Descriptive Data. The first step in the present analyses was to examine the demographic and descriptive data obtained. Distributions of all data were examined in order to determine normality of the data as well as to identify potential outliers. Gender, race, ethnicity, parental education level, and family income were computed for infants by maternal diagnostic group. Means and standard deviations for infant age were also computed for each diagnostic group. Means and standard deviations for measures of asymmetry and behavior (proportions) were also computed.

Testing Primary Hypotheses. The second step in the present data analysis was to test the primary hypotheses of the study.

The first primary hypothesis states that infants of depressed mothers would exhibit right frontal asymmetry relative to infants of control mothers. The second primary hypothesis states that infants of anxious mothers would exhibit right parietal asymmetry relative to infants of control mothers. In order to test these hypotheses, one-way analyses of variance (ANOVAs) with planned contrasts were conducted to determine whether the independent variable of maternal diagnostic group (depressed, anxious, control) was different for each of the following dependent measures of asymmetry (e.g., ln right hemisphere – ln left hemisphere): mid-frontal (F3, F4) asymmetry and lateral frontal (F7, F8). Multivariate analyses of variance (MANOVAs) with planned contrasts were also conducted to determine whether the independent variable of maternal diagnostic group (depressed, anxious, control) was different for the dependent measure of mid-parietal (P3, P4) asymmetry. Contrasts compared the

depressed group to the control group for each of the three dependent measures of asymmetry as well as the anxious group to the control group for each of the three dependent measures of asymmetry. (Note: Given that alpha power varies inversely with cortical activation, higher power values represent less activation, while lower power values represent higher activation at a target location. Asymmetry metrics were computed as the natural logarithm of alpha power at the right recording site minus the left recording site [e.g., lnF4 – lnF3]. Thus, a negative score indicated right asymmetry while a positive score indicated left asymmetry). In order to support the hypothesis that infants of depressed mothers would display greater right frontal asymmetry relative to infants of control mothers, a main effect would be significant for the mid-frontal and/or lateral frontal sites, while a main effect would be non-significant for the mid-parietal sites suggesting that the effect is specific to the frontal region. In order to support the hypothesis that infants of anxious mothers would display greater right mid-parietal asymmetry relative to infants of control mothers, a main effect would be significant for the mid-parietal sites, while a main effect would be non-significant for the mid-frontal and lateral frontal sites which would suggest that the effect is specific to the mid-parietal region. All dependent variables included alpha activity in the 4-6 Hz range.

In the present study, power analyses were conducted and assuming alpha equal = .05, power = .90, and a large effect size (.40), the sample size required for each group would have been n = 28.

Exploratory Analyses. The third step in the data analysis was to conduct exploratory analyses.

a) Anxiety Types

Six different types of anxiety included diagnoses of panic disorder, agoraphobia, social phobia, generalized anxiety disorder, posttraumatic stress disorder, and specific phobia. Distributions were examined to determine the number of anxiety types in each group. These exploratory analyses were conducted if the number of subjects (based upon both anxiety type and useable EEG data) for each group allowed for the examination of group differences. Power analyses were conducted and assuming alpha equal = .10, power = .90, and a large effect size (.40) the sample size required for each group was n = 16. This type of exploratory analysis allowed for the present study to examine potential trends in EEG asymmetry between these types of anxiety. Any group with fewer than n = 16 participants was excluded from the analysis. In order to explore the potential differences between these various types of anxiety and the patterning of brain electrical activity, one-way analyses of variance (ANOVAs) with planned contrasts were conducted to determine whether the independent variable of type of maternal anxiety (panic disorder, agoraphobia, social phobia, generalized anxiety disorder, posttraumatic stress disorder, and specific phobia) differs for each of the following dependent measures of asymmetry (e.g., ln right hemisphere – ln left hemisphere): mid-frontal (F3, F4) asymmetry, lateral frontal (F7, F8) and mid-parietal (P3, P4) asymmetry. Contrasts compared each type of anxiety group to the control group for each of the three dependent measures of asymmetry. No specific hypotheses were made a priori.

b) Psychiatric Impairment and Perceived Stress and Social Support (SDS)

It is possible that the effects of depression and anxiety are due to general disability, stress levels, and /or social support. In order to assess the potential differences between the extent to which the emotional symptoms of depression and anxiety may

impact psychiatric impairment as well as the perceived stress and social support and patterns of mid-frontal EEG asymmetry in infant offspring, regression analyses were conducted. Regression analyses were conducted with the following predictors: (1) psychiatric impairment, (2) perceived stress, (3) perceived social support, (4) perceived stress x perceived social support. The dependent variables included each of the following measures of asymmetry (e.g., ln right hemisphere – ln left hemisphere): mid-frontal (F3, F4) asymmetry, lateral frontal (F7, F8), and mid-parietal (P3, P4) asymmetry. No specific hypotheses were made a priori.

c) Gender

Univariate analyses of variance (ANOVAs) were conducted to determine whether patterns of brain electrical activity during a resting state were different for various offspring groups and gender. Analyses included group (depressed, anxious, control) and gender (male, female) as the between-subjects factors. The dependent variables were three measures of asymmetry (e.g., ln right hemisphere – ln left hemisphere): mid-frontal (F3, F4) asymmetry, lateral frontal (F7, F8), and mid-parietal (P3, P4) asymmetry. In order to examine significant effects from the ANOVAs, post hoc Tukey's HSD tests were conducted. No specific hypotheses were made a priori.

d). Cluster Analysis.

In order to examine whether the asymmetry data formed natural groups, hierarchical cluster analyses were conducted. This was followed by a k-Means cluster analysis, which involves choosing a specific number of clusters a priori by which to divide participants into meaningful groups (Hair, Anderson, Tatham, & Black, 1998). The three physiological variables of mid-frontal, lateral frontal, and mid-parietal

asymmetry were entered into the analysis and three clusters were modeled to correspond to the natural clusters that resulted from the original analysis. No specific hypotheses were made a priori.

e). Asymmetry Groups and Maternal Diagnosis.

Chi-square analyses were conducted to determine whether the infants showed the pattern of asymmetry that was predicted for their maternal diagnostic group. Using asymmetry scores, dichotomous variables were computed such that infants were classified as having either left or right asymmetry at each set of sites. Infants were divided into two groups (right vs. left asymmetry) such that an infant who had an asymmetry score less than zero was considered to have right asymmetry, while an infant who had an asymmetry score that was greater than zero was considered to have left asymmetry. Chi square analyses were also conducted with maternal anxiety type (for those that have a minimum of n = 16) and asymmetry group.

f). Asymmetry Groups and Behavior.

Univariate analyses of variance (ANOVAs) were conducted with between-subjects factors of asymmetry group (right vs. left) and three dependent variables of infant behavior (proportions of positive affect, negative affect, and motor scores) to explore whether there were differences in behavior for infants who showed specific patterns of asymmetry.

CHAPTER IV: Results

Preliminary Analyses

Asymmetry and Behavioral Variables. Descriptive statistics for all asymmetry and behavioral variables are found in Table 2. Visual inspection of the data for each of these variables showed that they were normally distributed. Measures of asymmetry were computed as the natural log of EEG power (μv) the right hemisphere minus the natural log of EEG power (μv) in the left hemisphere. Asymmetry was calculated for the mid-frontal (F3, F4), lateral frontal (F7, F8), and mid-parietal (P3, P4) electrode sites.

Table 2

Mean (SD) of Asymmetry and Behavioral Variables

Variable	Mean (SD)	Range
Mid-Frontal Asymmetry	.01 (.21)	-.77 – 1.08
Lateral Frontal Asymmetry	.06 (.26)	-1.08 – 1.02
Mid-Parietal Asymmetry	-.03 (.28)	-0.78 – 0.82
Composite Variables		
Positive Affect	.02 (.03)	0 – .19
Negative Affect	.06 (.11)	0 – .67
Motor Scores	.04 (.04)	0 – .19

Note. n = 95 for behavioral variables, n = 88 for mid-frontal asymmetry, and n = 89 for both lateral frontal asymmetry and mid-parietal asymmetry variables.

Analyses of the asymmetry variables showed that mid-frontal and lateral frontal sites were not correlated (r = .03, p = .76) and neither the mid-frontal nor lateral frontal variables were related to mid-parietal asymmetry (r = .14, p = .17 and r = -.02, p = .84, respectively). Analyses of the behavioral composites (proportions) showed that negative affect was not related to positive affect (r = -.14, p = .18). Motor scores were related to negative affect (r = .34, p < .001) and there was a trend for motor scores to be related to positive affect (r = .17, p = .09). Table 3 lists the content of the three composite variables of Positive Affect, Negative Affect, and Motor Scores.

Table 3

Composite Behavioral Variables

Composite Variable	Constituent Variables
Positive Affect	Smiles + Vocalizations
Negative Affect	Fussing + Crying
Motor Scores	Arm Waves + (Arm Wave Bursts x 2) + Leg Kicks + (Leg Kick Bursts x 2) + (Arching x 2) + Hyper-extensions

Note: Crying behavior was not observed in the sample.

In order to determine whether the infants' behavior on the three composite measures (proportions) of behavior differed by diagnostic group, one-way analyses of variance (ANOVAs) were conducted with between-subjects factors of group (depressed, anxious, control) and within-subjects factors of behavior (positive affect, negative affect,

and motor scores). These results showed that positive affect, negative affect, and motor scores did not differ among the groups ($F(2, 92) = .54$ $p = .58$; $F(2, 92) = 1.38$ $p = .25$; and $F(2, 92) = 1.79$, $p = .17$, respectively). Means and standard deviations for the three behavioral composites (proportions) by group can be found in Table 4.

Table 4

Means and Standard Deviations for Behavioral Variables by Diagnostic Group

	Offspring of Depressed (n = 37)	Offspring of Anxious (n = 21)	Offspring of Control (n = 37)
Variable (proportions)		Mean (SD)	
Positive Affect	.02 (.03)	.03 (.04)	.02 (.03)
Negative Affect	.07 (.14)	.02 (.04)	.06 (.11)
Motor Scores	.04 (.04)	.05 (.06)	.03 (.03)

Note. $N = 95$. Behavioral data were missing for 4 infants: 1 from the control group, 1 from the anxious group, and 2 from the depressed group.

Primary Analyses

The primary data analyses of the present study focused on maternal psychopathology and patterns of mid-frontal, lateral frontal and mid-parietal brain electrical activity in infant offspring during a resting baseline task. The results are organized by hypothesis.

Hypothesis 1: Infants of depressed mothers will exhibit *right frontal* asymmetry relative to infants of control mothers.

Contrary to the hypotheses, planned contrasts indicated that maternal depression was statistically unrelated to measures of both mid-frontal ($F(1, 87) = .09$, $p = .76$) and lateral frontal ($F(1,87) = .21$, $p = .64$) asymmetry during the resting baseline task. Means and standard deviations of asymmetry variables by maternal diagnostic group can be found in Table 5.

Hypothesis 2: Infants of anxious mothers will exhibit *right parietal* asymmetry relative to infants of control mothers.

Maternal anxiety was statistically unrelated to parietal asymmetry ($F(1,88) = .33$, $p = .56$). Means and standard deviations of asymmetry variables by maternal diagnostic group can be found in Table 5.

Table 5

Means and Standard Deviations of Asymmetry Variables by Maternal Diagnostic Group

	Offspring of Depressed	Offspring of Anxious	Offspring of Control
Variable		Mean (SD)	
Mid-Frontal Asymmetry	.02 (.14)	-.02 (.17)	.03 (.27)
Lateral Frontal Asymmetry	.08 (.25)	.04 (.16)	.05 (.32)
Mid-Parietal Asymmetry	-.02 (.31)	-.06 (.25)	-.02 (.26)

Exploratory Analyses

Exploratory analyses were conducted to examine anxiety types, psychiatric impairment, perceived stress and social support, and gender on the dependent measures of EEG asymmetry.

Anxiety types. Distributions were examined to determine the number of anxiety types in each group. Exploratory analyses were conducted on anxiety type in order to examine potential trends in EEG asymmetry between the various type of maternal anxiety. The breakdown for other anxiety groups was as follows: panic disorder (n = 3), agoraphobia (n = 2), social phobia (n = 7), generalized anxiety disorder (n = 2), posttraumatic stress disorder (n = 4), and specific phobia (n = 11). The aforementioned power analysis for maternal anxiety type determined that the sample size required for each group was n = 16. Therefore, the none of these anxiety categories allowed for these analyses. Because specific phobia (n = 11) was the anxiety type with the largest number of participants, it was decided to include all participants with specific phobia (n = 22). Therefore, this group included mothers with and without depression.

One way analyses of variance (ANOVAs) with maternal anxiety (specific phobia, control) as the independent variable showed that history of specific phobia was statistically unrelated to mid-parietal asymmetry ($F(1,53) = .29$, $p = .59$). Multivariate analyses of variance (MANOVA) with maternal anxiety (specific phobia, control) as the independent variable showed that history of specific phobia was statistically unrelated to measures of mid-frontal ($F(1,53) = .48$, $p = .49$) and lateral frontal asymmetry ($F(1,53) = .03$, $p = .86$).

Psychiatric Impairment and Perceived Stress and Social Support. Regression analyses were conducted to explore the potential differences in the extent to which the emotional symptoms of depression and anxiety may impact psychiatric impairment, degree of perceived stress and social support, and patterns of EEG asymmetry in infant offspring. In the model the predictors entered into the regression analysis were: (1) psychiatric impairment, (2) perceived stress, (3) perceived social support, (4) perceived stress x perceived social support. The dependent variables included each of the following measures of asymmetry: mid-frontal, lateral frontal and mid-parietal. Correlations among the variables used in the regression model are found in Table 6.

Table 6

Correlations Among Psychiatric Impairment, Stress, Social Support, and Asymmetry Variables

Variable	1	2	3	4	5	6
1. Mid-Frontal	--	.03	.14	-.05	.02	-.07
2. Lateral Frontal		--	-.02	-.07	.13	-.36****
3. Mid-Parietal			--	.01	.12	.05
4. Impairment				--	.29***	-.19**
5. Stress					--	-.20*
6. Support						--

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

For mid-frontal asymmetry, the overall prediction of the regression model was non-significant ($F(4, 80) = .28$, $p = .89$), as were the main effects of impairment, stress, and social support ($t(80) = -.72$, $p = .47$; $t(80) = .64$, $p = .52$; $t(80) = .10$, $p = .92$, respectively). The interaction of stress and social support were also non-significant ($t(80) = -.62$, $p = .54$).

The full model accounted for a significant amount of variance (16%) in lateral frontal asymmetry ($F(4, 81) = 3.89$, $p < .01$). The main effects and interaction effect were all non-significant ($t(81) = -1.54$, $p = .13$; $t(81) = .87$, $p = .39$; $t(81) = -1.63$, $p = .11$, $t(81) = -.57$, $p = .57$, respectively). A significant negative correlation was found between perceived social support and lateral frontal asymmetry ($r = -.36$) suggesting that as perceived social support increases, lateral frontal asymmetry decreases. Parietal asymmetry was not predicted by the variables in the full regression model ($F(4, 81) = .50$, $p > .10$). Main effects and interaction effects were also non-significant ($t(81) = .01$, $p = .99$; $t(81) = -.23$, $p = .82$; $t(81) = -.11$, $p = .92$, $t(81) = .64$, $p = .53$, respectively) indicating that the effect for asymmetry was specific to the lateral frontal region. Table 7 shows the regression model for each set of asymmetry variables.

Table 7

Regression Model Predicting Infant Asymmetry Using Maternal Psychiatric Impairment, Perceived Stress, Perceived Social Support, and the Interaction of Stress and Support

Predictors	β	*t*	*p*
Mid-Frontal Asymmetry			
Impairment	-0.09	-0.72	0.47

Perceived Stress	0.23	0.64	0.52
Perceived Support	0.10	0.10	0.92
Stress X Support	-0.22	-0.62	0.54
Lateral Frontal Asymmetry			
Impairment	-0.17	-1.54	0.13
Perceived Stress	0.29	0.87	0.39
Perceived Support	-0.28	-1.63	0.11
Stress X Support	-0.19	-0.57	0.57
Mid –Parietal Asymmetry			
Impairment	0.00	0.01	0.99
Perceived Stress	-0.08	-0.23	0.82
Perceived Support	-0.02	-0.11	0.92
Stress X Support	0.23	0.64	0.52

Note: Standardized β are presented.

*p<0.10, **p<0.05***p<0.01

Because the interaction term in the regression model was non-significant for mid-frontal, lateral-frontal, and mid-parietal asymmetry, the regression model was re-run without the interaction term. For mid-frontal asymmetry the new regression model was non-significant for the overall model ($F(3, 81) = .25$, $p = .86$), as well as the main effects of impairment, stress, and social support ($t(1, 81) = -.63$, $p = .53$; $t(1, 81) = .18$, $p = .85$; $t(1, 81) = -.65$, $p = .52$, respectively). Similarly, for mid-parietal asymmetry, the new regression model was non-significant for the overall model ($F(3, 82) = .53$, $p = .66$), as well as the main effects of impairment, stress and social support ($t(1, 82) = -.11$, $p = .92$; $t(1, 82) = 1.15$, $p = .26$; $t(1, 82) = .68$, $p = .50$, respectively). However, the new full

model accounted for a significant amount of variance (16%) in lateral-frontal asymmetry ($F(3, 82) = 5.12$, $p < .01$). The main effect of support was also significant ($t(1, 82) = -3.49$, $p < .001$), again suggesting that as perceived social support increases, lateral frontal asymmetry decreases ($r = -.36$). The main effects of impairment and stress were non-significant ($t(1, 81) = -1.47$, $p = .14$ and $t(1, 81) = 1.04$, $p = .30$, respectively). Table 8 shows the regression model for each set of asymmetry variables.

Table 8

Regression Model Predicting Infant Asymmetry Using Maternal Psychiatric Impairment, Perceived Stress, and Perceived Social Support

Predictor	β	*t*	*p*
Mid-Frontal Asymmetry			
Impairment	-0.07	-0.63	0.53
Perceived Stress	0.02	-0.18	0.85
Perceived Support	0.07	-0.65	0.52
Lateral Frontal Asymmetry			
Impairment	-0.16	-1.47	0.14
Perceived Stress	0.11	1.04	0.30
Perceived Support	-0.36	-3.49	0.00**
Mid –Parietal Asymmetry			
Impairment	-0.01	-0.11	0.92
Perceived Stress	0.13	1.15	0.26
Perceived Support	0.08	0.68	0.50

Note: Standardized β are presented.

*p<0.10, **p<0.05***p<0.01

Gender. Multivariate analyses of variance (MANOVA) were conducted with between-subjects factors of group (depressed, anxious, control) and gender (male, female) to determine whether patterns of brain electrical activity at frontal sites during a resting state were different for the various offspring groups as a function of gender. The overall MANOVA for mid-frontal and lateral frontal asymmetry were non-significant ($F(3, 84) = 1.09$, $p = .36$ and $F(3, 84) = .14$, $p = .94$, respectively). Results showed that mid-frontal asymmetry was neither related to the main effects of maternal diagnostic group nor infant gender ($F(2, 84) = .42$, $p = .67$ and $F(1, 84) = 2.45$, $p = .12$, respectively). Likewise, lateral frontal asymmetry was neither related to maternal diagnostic group nor infant gender ($F(2, 84) = .17$,$p = .84$ and $F(1, 84) = .08$, $p = .78$, respectively). For mid-parietal asymmetry, univariate analyses of variance (ANOVAs) were conducted with between-subjects factors of group (depressed, anxious, control) and gender (male, female). The overall ANOVA model was non-significant ($F(3, 85) = .64$, $p = .59$) as were the main effects of maternal diagnostic group ($F(2, 85) = .21$, $p = .81$) and infant gender ($F(1, 85) = 1.50$, $p = .22$).

Given the lack of significant effects of maternal diagnostic group and infant gender on patterns of brain electrical activity at both frontal and parietal sites, the potential interaction effects of gender and maternal diagnosis on asymmetry scores were also examined. Results for mid-frontal, lateral frontal, and mid-parietal asymmetry were non-significant ($F(2, 82) = 1.14$, $p = .33$; $F(2, 83) = .38$, $p = .69$; and $F(2, 83) = 2.01$, $p = .14$, respectively).

Cluster Analysis. In order to examine whether the infant EEG asymmetry data may group together in a meaningful way, a hierarchical cluster analysis was conducted.

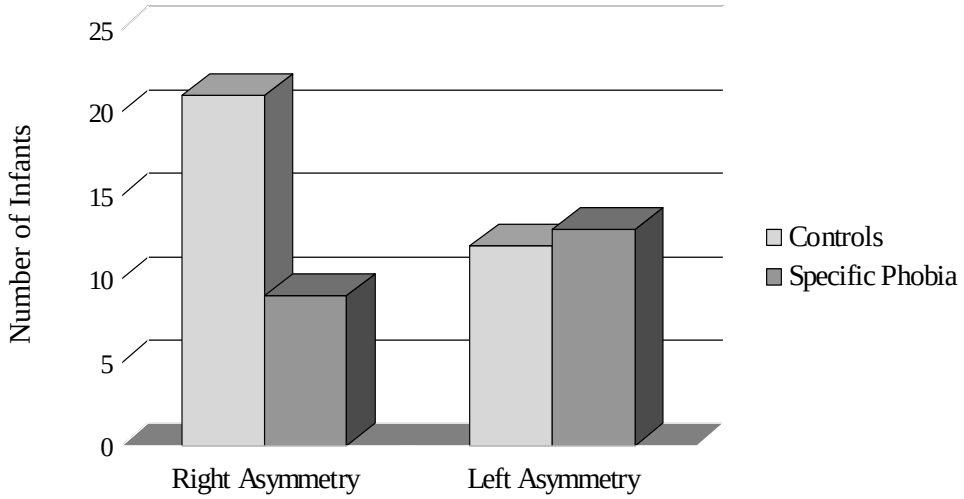
Three stopping rules were used including cubic clustering criteria (local maximum), pseudo-F criteria (local maximum), and pseudo-t criteria (t-square), in order to determine if there were distinct natural structures in the asymmetry data. The results of this analysis did not reveal a clear cut-off for distinct clusters, however the general pattern pointed to three clusters. Next, a k-Means cluster analysis was conducted. This method of non-hierarchical clustering involves choosing a specific number of clusters a priori by which to divide participants into meaningful groups (Hair et al., 1998). The three physiological variables of mid-frontal, lateral frontal, and mid-parietal asymmetry were entered into the analysis and three clusters were modeled to correspond to the three clusters of the original analysis. Results of this analysis yielded three clusters with n = 1 in the first cluster, n = 2 in the second cluster, and n = 86 in the third cluster. The results were non-significant when compared to the three maternal diagnostic groups ($\chi^2(4, N = 89) = 2.41$, $p = .66$). Further analyses were not conducted with the results of the cluster analysis.

Asymmetry Groups and Maternal Diagnosis. Chi-square analyses were conducted to determine whether the infants showed the predicted pattern of asymmetry based on their maternal diagnostic group. Using asymmetry scores, dichotomous variables were computed such that infants were classified as having either left or right asymmetry at each set of sites. Infants were divided into two groups (right vs. left asymmetry) such that an infant who had an asymmetry score less than zero was considered to have right asymmetry, while an infant who had an asymmetry score that was greater than zero was considered to have left asymmetry. Chi square analyses indicated that diagnostic group was statistically unrelated to mid-frontal asymmetry group ($\chi^2(2, N = 88) = 1.11$, $p = .57$), lateral frontal asymmetry group ($\chi^2(2, N = 89) = .12$, $p = .94$), and mid-parietal

asymmetry group ($\chi^2(2, N = 89) = 2.57, p = .28$). Of the 33 infants of depressed mothers with mid-frontal asymmetry data, 13 (40%) showed the expected pattern of right mid-frontal asymmetry while of the 34 infants of depressed mothers with lateral frontal asymmetry data, 13 (38%) showed the expected pattern of right lateral frontal asymmetry. Of the 22 infants of anxious mothers with mid-parietal asymmetry data, 12 (55%) showed the expected pattern of right mid-parietal asymmetry.

Chi square analyses were also conducted with maternal anxiety type (specific phobia with and without depression, control) and asymmetry group. There was a trend for maternal diagnostic group to be related to parietal asymmetry group ($\chi^2(1, N = 55) = 2.75, p = .09$), such that fewer infants of mothers with specific phobia had right parietal asymmetry than infants of control mothers. Neither mid-frontal asymmetry group nor lateral frontal asymmetry group were related to specific phobia ($\chi^2(1, N = 55) = .01, p = .91$) and ($\chi^2(1, N = 55) = .00, p = 1.00$, respectively), indicating that this pattern of asymmetry associated with specific phobia is specific to the parietal region. Figure 1 illustrates the number of infants in each mid-parietal asymmetry group for infants of mothers with social phobia and infants of controls.

Figure 1: Mid-Parietal Asymmetry for Specific Phobia and Controls



Asymmetry Groups and Behavior. Univariate analyses of variance (ANOVAs) were conducted with between-subjects factors of asymmetry group (right vs. left) to determine whether patterns in infant behavior (proportions of positive affect, negative affect, and motor scores) were different for infants who showed specific patterns of asymmetry. Results indicated that there was no relation between asymmetry group and infant behavior (*F*-values ranged from .07 to 1.89, *ps* >.10).

CHAPTER V: Discussion

There is a growing body of literature examining the relations between emotion and its underlying neurobiological markers. Numerous studies suggest that positive and negative emotions are associated with different patterns of cerebral hemisphere activation and that specific patterns of electroencephalographic (EEG) asymmetry may indicate risk for depression and anxiety. The extant developmental psychopathology literature has examined patterns of EEG asymmetry in the offspring of parents with affective disorders and such research has reported linkages between frontal EEG asymmetry and depression, suggesting that measures of EEG asymmetry may be important neurological markers of risk for affective disorders. Despite the greater prevalence of anxiety disorders than depressive disorders and the literature suggesting that resting EEG asymmetry may serve as an index of both depression and anxiety, no research has yet examined patterns of EEG asymmetry in the offspring of parents with anxiety disorders.

The purpose of the present study was to examine early markers of risk for psychopathology in the biological domain (e.g., patterns of EEG asymmetry) in an attempt to elucidate some of the precursors of anxiety and depression in children so that we might gain a better understanding of the development of these disorders. The present study examined the resting physiological patterns in the infant offspring of mothers with a history of depression and mothers with a history of anxiety, relative to infants of control mothers. Measures of EEG asymmetry and infant behavioral reactivity during a resting baseline task were collected. The data from this study provided modest support for the hypothesis that maternal diagnostic history may be related to patterns of infant asymmetry in various regions of the brain during a resting state.

Primary analyses. One goal of the present study was to replicate the current literature that has reported patterns of right frontal EEG asymmetry in the infant offspring of depressed mothers. Primary analyses were conducted to examine the potential influence of maternal diagnostic history on the three dependent measures of asymmetry. The current study did not find support for the expected pattern of asymmetry. It was predicted that infants of mothers with a history of depression would exhibit right mid-frontal and/or lateral frontal asymmetry compared to infants of controls, however, the data did not show any direct effects of diagnostic history on frontal asymmetry during the task. Given the extant literature that has shown relative right frontal asymmetry under resting conditions in infants of depressed mothers (e.g., Dawson et al., 1992; Field et al., 1995; Jones et al., 1997) the negative results of the present study are surprising. However, the infants in the present study were slightly older than the infants in some of these earlier studies who were 3- to 6-months of age (e.g., Field et al., 1995; Jones et al., 1997) and younger than the infants in other studies who were 11- to 17-months of age (e.g., Dawson et al., 1992). Perhaps these differences in the age of the infants in these studies are different enough that the results of the present study are not showing this expected pattern of right frontal asymmetry.

Another possible explanation for this might be the characteristics of the sample of mothers that participated in the current study. Perhaps if the mothers in the study were a clinical sample (as opposed to a community sample) the results may have been in line with the extant literature and the infants of depressed mothers would have exhibited right frontal asymmetry relative to the infants of control mothers. In addition, the eligibility criterion for the present study was a lifetime history of depression as opposed to current

symptomatology; therefore, mothers who were currently asymptomatic (n = 26) were included in this study. The mothers in these aforementioned studies (e.g., Jones et al., 1997; Dawson et al., 1992) met criteria for depression during the child's lifetime with the exception of one, where mothers in the depressed group had experienced elevated scores on the Beck Depression Inventory (BDI) at either the neonatal period or within the child's lifetime (Field et al., 1995). Thus, the infants in the present study may never have experienced their mothers' depression and as a result, it might be less likely that they would have EEG asymmetry patterns consistent with previous studies. The differences in patterns of brain activity that were expected may have to do with the infant's experience with their mother who has been diagnosed with depression or anxiety.

The developmental psychopathology literature reviewed previously implicates that it is (at least in part) the processes that are manifested in this relationship between the mother and child that might lead to the expected asymmetry differences. For example, clinically depressed mothers have been described as uninvolved, ineffective, insensitive, disengaged, and intrusive when interacting with their children (Cummings & Davies, 1994; Gelfand & Teti, 1990) and a number of mother-child observational studies have found that depressed mothers, when compared to controls, are less likely to interact in an adaptive way with their children, and tend to display less positive and more negative affect towards them (Cohn et al., 1990; Cohn et al., 1986; Cohn & Tronick, 1989; Field et al., 1990; Field et al., 1995; Field, Healy, Goldstein, Perry, Bendall, Schanberg et al., 1988). This research suggests that maternal depression is related to increased levels of insensitivity and withdrawal in mother-child interactions (Teti, O'Connell, & Reiner, 1996). Therefore, if the infant has not interacted with the mother during her depressive

experience, then it might be less likely that their patterns of EEG asymmetry would be in line with infants whose mothers have experienced depression in their lifetime. However, not unlike infants who have experienced their mother's depression, infants whose mothers have not experienced depression in their lifetime have still been born with a genetic vulnerability to depression, as have infants whose mothers experienced depression in their lifetime. That is, both infants whose mothers experienced depression prior to their birth, as well as infants whose mothers experienced depression after their birth share genetic vulnerability to psychopathology. By including mothers in the present study who were asymptomatic during the infant's lifetime, we may begin to understand the impact of biological risk versus environmental risk on infant asymmetry patterns.

While the past 20 years have brought increased research on psychopathology in children, including depression and anxiety, most of this research has focused on individual factors without considering the role of development. In addition to the studies that have emerged, research needs to elucidate the pathways by which anxiety and depression develop in children. Recently, developmental psychopathology theories have been put forth, calling attention to the need to examine the influences on the development of these disorders in children, as well as how these disorders change across development (e.g., Cicchetti & Cohen, 1995; Kazdin & Kagan, 1994). For example, the child anxiety literature has revealed an emerging framework for examining the complex interactions involved in the development of psychopathology (e.g., Chorpita & Barlow, 1998; Stemberger et al., 1995) suggesting multiple factors (e.g., attachment, parenting, biology, resilience) may play a role in its development. Similarly, a stress-diathesis model that explains the potential relation among genes, the environment, and risk for disorder has

emerged from the childhood depression literature, suggesting that for any given individual there is a diathesis between their genetic influences and their environmental influences and that the diathesis will only be expressed if the stressors in the environment exceed a specific threshold (e.g., Monroe & Simons, 1991). The present investigation was aimed at elucidating risk for the development of psychopathology and considered that there may be multiple causal mechanisms. While factors that influence outcomes in the infants of the present study are believed to be familial as well as heritable, in many circumstances they are the result of interactions among both of these factors. Perhaps for some of the infants in the present study, genetic vulnerability alone was not enough to influence patterns of EEG asymmetry at this early age. This may have been particularly true for infants in the present study whose mothers were asymptomatic after their birth.

Alternatively, another possible explanation for why the current study did not find the expected pattern of asymmetry in the offspring of depressed mothers may have to do with issues of comorbidity. Given the high rate of comorbidity of depression and anxiety, the sample was examined to determine rates of comorbidity with anxiety among participants in the depressed group. It was found that a greater number of mothers in the depressed group had comorbid anxiety (n = 22) than mothers with major depressive disorder alone (n = 17). The present study examined these potential differences post hoc and did not find significant differences among mothers with anxiety, depression and anxiety, and depression only, relative to control mothers. However, previous studies of affect and EEG asymmetry have generally not excluded depressed participants on the basis of comorbid anxiety. For example, Henriques and Davidson (1991) reported that depressed adults displayed resting right frontal EEG asymmetry and that previously

depressed individuals, now in remission, had less left-sided anterior and less right-sided posterior activation (i.e., more alpha activity) than did never depressed controls (Henriques & Davidson, 1990). In each of these studies, participants met criteria for major depressive disorder, yet were not excluded if they also met criteria for an anxiety disorder. The null findings of the exploratory analyses in the present study suggest that further study may be warranted to distinguish patters of infant asymmetry in the offspring of depressed mothers and the offspring of depressed and anxious mothers. Perhaps if infants of mothers with major depressive disorder only (without anxiety) were examined the present study may have yielded different results.

Much of the literature on resting EEG asymmetry in the infant offspring of depressed mothers has not examined the potential impact of anxiety, despite the high rates of comorbidity among these disorders. For example, many studies using clinical interviews or measures of depressive symptoms did not measure maternal anxiety (e.g., Dawson et al., 1992; Field et al., 1995; Jones et al., 1997). Similarly, in a study of EEG asymmetry in the preschoolers of depressed mothers, anxiety was also not taken into account (Jones, Field, & Davalos, 2000). One laboratory has examined symptoms of anxiety in relation to maternal depression and infant EEG patterns using a maternal self-report questionnaire (Dawson et al., 1997). While infant frontal EEG activity was not related to maternal symptoms of anxiety, the study did not examine patterns of parietal activity in these infants during a baseline task. Similarly, Dawson and colleagues (Dawson, Frey, Panagiotides et al., 1999) used the same self-report measure to control for symptoms of anxiety and found that it did not account for patterns of infant EEG activity. While the aforementioned studies did take into account maternal self-ratings of anxiety

symptoms, firm conclusions cannot be drawn, given the high rate of comorbidity of depressive disorders and anxiety disorders. More research looking at the separate and combined effects of these disorders is needed. And, while the present study did not draw the same conclusions as the extant literature with respect to maternal depression and infant EEG asymmetry, the previous literature has not clearly researched the impact of anxiety disorders in their samples. Future investigations should measure clinical levels of both depressive and anxiety disorders in relation to neurobiological markers of risk in infant offspring.

A second goal of the present study was to be the first to examine the patterns of EEG asymmetry in the infant offspring of anxious mothers. Based on the extant literature on EEG patterns in anxious adult populations, it was hypothesized that infants of anxious mothers would exhibit right parietal asymmetry relative to infants of control mothers. While the results of this analysis were statistically non-significant, when the mean parietal asymmetry scores for these two groups were examined, it could be seen that the infants of anxious mothers exhibited greater right parietal asymmetry than the infants of control mothers. This suggests that the results were in the hypothesized direction, but because the relations were not significant firm conclusions cannot be drawn. However, the results are in line with theories and research that implicate the parietal regions in the regulation of arousal (e.g., Heller & Nitschke, 1997) and would be in accordance with Heller's (1993a) proposed model in which the arousal axis is hypothesized to relate to the right posterior region. The extant literature has also suggested that anxious participants show a relative increase in right posterior activity using measures of perceptual asymmetry (Keller et al., 2000). Similarly, in a study of

regional brain asymmetries in major depressive disorder (MDD) with and without anxiety disorder, Bruder et al. (1997) reported that anxious-depressed patients exhibited greater activation over right than left anterior and posterior sites. Given that the sample size in the present research was small (n = 22) and that the results were not statistically significant these patterns of infant asymmetry need to be interpreted with caution. The anxious sample fell short of the required sample size for each group to detect large effect sizes (n = 28) (see aforementioned power analysis). Increasing the number of participants in this group might have brought the findings to a statistical level of significance.

There may be additional reasons why the analyses of maternal anxiety did not reach significance. Perhaps one reason might be that the anxiety types that composed the anxious group were too diverse. While all probands in the anxious group met DSM–IV diagnostic criteria for anxiety disorder, there were multiple types of anxiety that a mother may have experienced. The anxiety types endorsed by the mothers in the present study included six distinct types: panic disorder, agoraphobia, social phobia, generalized anxiety disorder, specific phobia, and posttraumatic stress disorder. Perhaps the impact of having a mother with a history of generalized anxiety disorder, for example, differs from the impact of having a mother with posttraumatic stress disorder. For example, it may be that mothers with anxiety disorders such as generalized anxiety disorder or social phobia may interact with their infants differently than mothers with specific phobia or posttraumatic stress disorder. There simply is too little known about these associations to draw definitive conclusions. However, the present study also aimed to examine the

relations between various types of anxiety and infant brain activity as will be discussed shortly.

In addition to the diversity of anxiety types there was also variability in the numbers of participants in each of these anxiety groups. Two mothers had a history of agoraphobia, seven had a history of social phobia, two had a history of generalized anxiety disorder, three had a history of panic disorder, four had a history of posttraumatic stress disorder, and 11 had a history of specific phobia. While the present study included mothers with a number of different types of anxiety, the limited literature that has investigated the relations between anxiety and EEG asymmetry has also examined diverse populations. For example, patterns of EEG asymmetry have been examined in adults diagnosed with social phobia (Davidson et al., 2000), adults with panic disorder (Wiedemann et al., 1999), and non-clinical undergraduate populations using self-report anxiety questionnaires (Heller et al., 1995). The various subcomponents of the symptomatology of anxiety disorders are believed to be related to discrete regions of the brain making the identification of their underlying neural mechanisms all the more complex (Heller & Nitschke, 1998). Furthermore, the examination of offspring of mothers with affective disorders (as opposed to examining other maternal factors) adds another layer of complexity to the equation. Thus, future research should be aimed at increasing specificity in symptomatology when examining relations between anxiety and asymmetry for a given participant, as well as maternal anxiety and infant asymmetry.

While many of the aforementioned studies of EEG asymmetry and anxiety were conducted during resting states (e.g., Bruder et al., 1997; Heller et al., 1997) some utilized an emotion-eliciting task such as induced anxiety (e.g., Davidson et al., 2000;

Fox & Davidson, 1988; Rauch et al., 1997; Tillfors et al., 2001; Tillfors et al., 2002). Perhaps if the present study had examined infants during an emotion-eliciting task the infants may have exhibited different patterns of asymmetry. For example, offspring of depressed mothers may exhibit patterns of greater relative right frontal asymmetry during tasks designed to elicit negative emotion. This may be an important direction for future research. Furthermore, it may well be that the infants of anxious mothers in the present study have not reached an age at which these expected differences in asymmetries manifest themselves. Given that the present study is the first of its kind to examine the relations between EEG asymmetry and maternal anxiety, this cannot be ruled out as a possible explanation. Future research is needed to determine whether these patterns of asymmetry in the infant offspring of mothers with anxiety disorders may vary with infant age as well.

While its been noted that there were six different types of anxiety that composed the anxious group in the present study, it is also important to note that many of these mothers experienced more than one type of anxiety in their lifetime. For example, of the 11 mothers diagnosed with specific phobia (without depression) that were included in the analyses of anxiety type, six of them also had a history of another anxiety disorder. Perhaps experiencing multiple types of anxiety has a unique influence on infant offspring as well. While the statistical power in the present study did not allow for the examination of this specific question, future research might benefit from addressing such issues. Furthermore, some anxiety disorders such as social phobia and generalized anxiety disorder have been found to be comorbid (Brown, Campbell, Lehman, Grisham, & Mancill, 2001). These anxiety disorders are context specific and have general triggers.

In contrast, an anxiety disorder such as specific phobia doesn't generalize across contexts, but rather, has specific stimulus triggers (e.g., crossing a bridge, seeing a snake) and an idiosyncratic etiology. Therefore, anxiety disorders that are closely related theoretically such as GAD and social phobia may have different underlying neurological mechanisms than anxiety disorders such as specific phobia. For this reason, future investigations may benefit from combining anxiety disorders such as GAD and social phobia and comparing them to anxiety disorders such as specific phobia when examining patterns of EEG asymmetry in the infants of mothers with these disorders. Unfortunately, the sample size of the present study did not allow for such analyses.

While the findings of this analysis were non-significant, the present study is important in that it begins to shed light on the associations between maternal anxiety and patterns of infant brain electrical activity in the early months of life. The present study has taken a small step toward gaining a better understanding of the development of anxiety disorders.

Exploratory analyses. The present study also aimed to examine the potential relations between types of maternal anxiety and patterns of infant brain electrical activity. After power analyses were conducted and group distributions were examined, it was determined that mothers with specific phobia (with and without depression) had an adequate number of participants for analyses to be conducted (n = 22). Unfortunately, there was insufficient statistical power to examine any of the other types of anxiety that mothers in the sample had experienced. The present study did not find differences in the EEG patterns of infants of mothers with specific phobia relative to infants of control mothers when exploring continuous measures of asymmetry. However, when the same

two diagnostic groups were compared on a dichotomous measure of EEG asymmetry (relative right vs. relative left) trends for differences did emerge in the pattern of mid-parietal asymmetry with respect to maternal anxiety type. Fewer infants of mothers with specific phobia (with and without depression) had right mid-parietal asymmetry than infants of control mothers. No specific hypotheses were made a priori regarding the patterns of infant asymmetry due to the paucity of literature on the offspring of mothers with anxiety, as well as the inconsistencies in the adult literature that have examined relations between anxiety and EEG patterns. However, these results would be inconsistent with the overall hypothesis that the infant offspring of mothers with anxiety disorders would show right parietal asymmetry relative to infants of control mothers, as well as with a previous study of regional brain asymmetries in major depressive disorder (MDD) with and without anxiety disorder, that reported that anxious-depressed patients exhibited greater activation over right than left anterior and posterior sites (Bruder et al., 1997). Nonetheless, these findings lend support to the notion that specificity in anxiety type is an important area for future research.

It may be that infant asymmetries vary with different types of maternal anxiety, or perhaps these results are due to the fact that one-half of these mothers with specific phobia also had a history of major depressive disorder. Perhaps the comorbidity of these disorders influences infant EEG asymmetry. Given that the present study is the first of its kind to examine patterns of asymmetry in the offspring of anxious mothers, further research is needed in order to elucidate some of the underlying neurobiological markers in at-risk infants. These results are unique in that they are the first to show distinct patterns of brain activity in the offspring of mothers with specific phobia. Importantly,

these findings suggest a need for greater specificity in anxiety studies that examine underlying neurobiological markers in at-risk infants.

While the larger questions of whether lifetime diagnostic history of maternal depression and anxiety are related to asymmetry in at-risk offspring were central to the present study, a further goal was to examine whether maternal self report of impairment, perceived stress, and perceived social support might be related to infant asymmetry. It is possible that the effects of depression and anxiety are due to general disability (i.e., psychiatric impairment), stress levels, and/or social support. The assessment of the potential differences between the extent to which the emotional symptoms of depression and anxiety may impact psychiatric impairment as well as the perceived stress, social support, and patterns of mid frontal EEG asymmetry in infant offspring, yielded surprising results. Unexpectedly, while maternal impairment and perceived stress were statistically unrelated to patterns of infant asymmetry, the present study found that higher levels of social support were associated with lower levels of lateral frontal asymmetry. These findings are in the unexpected direction in that lower levels of social support would be expected to correspond with lower levels of lateral frontal asymmetry. A potential explanation for these results might be that the Sheehan Disability Scales and Stress and Social Support Scales (Leon et al., 1997) used in this study might not be adequate to uncover the influences that the present study aimed to investigate. The measure of impairment reflected the mothers' rating of the degree to which her symptoms of depression/anxiety disrupted her work, social life, and family while the measures of social support and stress were also limited in that they each consisted of just one question. Instead, a more detailed measure of current symptoms of depression and

anxiety levels might have been a better assessment of current impairment and may have yielded different results.

Another explanation for why these findings are in the unexpected direction has to do with how a mother may perceive the need for support. Mothers were asked, "In the past month, how much support have you received from friends, relatives, co-workers, etc., as a percentage of the amount of time you needed to cope?" Perhaps the mothers who reported higher levels of support were also the mothers who were experiencing depression or anxiety. That is, mothers who felt the need for greater support were also the mothers who reported receiving greater support. If a mother was not feeling the need for support from friends and family in order to cope, then perhaps she reported lower levels of support (because it was not needed). In addition, questions regarding social support may have been subject to issues of social desirability in that mothers who participated may not have wanted to report lower levels of social support. Last, it is possible that the mothers who reported lower levels of support (and consequently had infants with higher lateral frontal asymmetry scores) are participating in less of the parenting of these infants. While the mothers in the present study were the primary caregivers of the infants, including a measure of parenting would have revealed a bit more about this complex issue.

An additional objective of the present study was to explore whether patterns of brain electrical activity during a resting state were different for various offspring groups and gender. There is a small literature that has begun to explore gender differences in EEG studies of depression while there is a paucity of literature that has examined gender differences in EEG studies of anxiety. For example, a recent study by Miller and

colleagues (Miller et al., 2002) found gender differences in regional patterns of brain activity among depressive probands (adults previously diagnosed with childhood onset depression) and matched controls during a baseline procedure providing support for the notion that gender differences may exist in regional brain activity. However, the importance of gender differences in EEG studies of depression is not fully known because depression has commonly been examined in female populations (Reid et al., 1998; Kentgen et al., 2000). Adult EEG studies that have examined gender and depression are limited and although much of the literature on EEG asymmetry in children has included males and females, few studies have explicitly examined these potential gender differences in children. Those that have however, did not conducted gender specific analyses in EEG asymmetry, rather they have examined gender in relation to other factors in their investigations. For example, Baving and colleagues have reported gender differences in frontal asymmetry in school-aged children with and without attention deficit hyperactivity disorder (Baving, Laucht, & Schmidt, 1999) as well as varying patterns in frontal activation among boys and girls with externalizing behavioral problems (Baving, Laucht, & Schmidt, 2003). In addition, in a study of infant temperament, researchers reported that behavior in infancy was predictive of later social wariness for male infants with specific types of EEG asymmetry and not for girls (Henderson et al., 2001). Thus, the lack of gender differences in the present study should be interpreted cautiously and the effect of gender on EEG asymmetry warrants further study. In addition, there was an imbalance of infant gender in the maternal anxiety group (n = 6 females, n = 16 males) that may have influenced these null results. Similarly, the

present study also explored whether the infant asymmetry data formed natural groups, however, the results of this exploratory analysis were inconclusive.

Additional analyses explored whether infants showed the patterns of asymmetry that were predicted for their maternal diagnostic group. While the findings were not statistically significant, the strongest relations were between maternal history of anxiety and patterns of right mid-parietal asymmetry and were in line with the primary hypotheses of the study (as previously discussed). Furthermore, the present study also investigated whether patterns of infant behavior were different for infants who showed specific patterns of asymmetry. It could be argued that infants who were higher on motor scores and negative affect might exhibit patterns of right frontal asymmetry while infants who were high on motor scores and positive affect might exhibit left frontal asymmetry. While such findings have been reported in the normative developmental literature (e.g., Calkins et al., 1996), the fact that many of the infants in the present sample were the offspring of mothers with a history of psychopathology may explain why these results were negative in the present study. Perhaps infants of mothers with a history of psychopathology are less likely to exhibit patterns of behavior that are related to patterns of EEG asymmetry than infants that have been examined in the normative literature because of factors that were beyond the scope of the present study. For example, Jones and colleagues (Jones, McFall, & Diego, 2004) reported that although infants of depressed mothers have shown patterns of reduced left frontal activity and temperaments that are more reactive relative to infants of control mothers, these patterns were not found in one-month-old infants who had a stable pattern of breastfeeding.

In summary, the results of the present study provide modest support for the hypothesis that infants of mothers with psychopathology may differ from infants of comparison subjects in their underlying neurobiological markers of anxiety and depression. This examination of early precursors of risk for psychopathology was the first of its kind to do so with the infant offspring of mothers with anxiety disorders.

Limitations

There are several limitations to the present study. First, as previously mentioned, power analyses were conducted suggesting that the sample size required for each of the three maternal diagnostic groups would have been n = 28. While two of the groups (infants of depressed mothers and infants of control mothers) exceeded this requirement, one group, (infants of anxious mothers) did not. The findings of the study related to the group of infants of anxious mothers should be interpreted somewhat cautiously given the small number of participants in this group. The present study would have benefited from an increased number of participants in this group. In the same vein, a greater number of participants would have aided in the exploratory analyses, particularly those of specific types of anxiety. While six discrete types of anxiety were included in the anxious group, only one (specific phobia) had enough participants to provide the needed statistical power to allow for the exploration of the relation between this type of maternal psychopathology and infant EEG patterns.

Another limitation of the present study is that the screener that was used over the telephone to identify potential participants asked a number of sensitive questions (e.g., "Have you used street drugs?"). While mothers were asked these same questions again in person during the interview process, issues of social desirability may have influenced the

sample. In addition, participants in the present study were required to travel to the laboratory and given little reimbursement. These factors may have influenced the final sample as well. And, the use of mass mailings and advertisements may not have provided a reasonably diverse sample racially and ethnically.

As previously mentioned, the eligibility criterion for the present study was a lifetime history of psychopathology as opposed to current symptomatology; therefore, mothers who were currently asymptomatic were included in this study. Thus, not all of the infants in the present sample may have experienced their mothers' psychopathology. However, including mothers with a history of psychopathology tell us something about biological risk that studies of mothers with current depressive or anxious symptoms does not and extents the extant literature to an area of psychopathology that has not been as well studied with respect to infant EEG asymmetry patterns. Furthermore, while the present study did examine current levels of impairment it did not examine explicit measures of current depression and anxiety levels. It would be useful in the future to examine current levels of depression and anxiety relative to patterns of infant asymmetry.

Another limitation of the present study may be that the mothers in the control group had a more diverse background demographically than the depressed or anxious groups. It is possible that this group, while serving a control group, may themselves be at risk for environmental stressors and psychopathology. In addition, mothers in the control group were not excluded if they had a history of substance abuse prior to their pregnancy with the infant participating in the study. It was believed that because the two mothers who fit these criteria had experimented with drugs and alcohol many years before they gave birth to the infants in the present study, this history might not have affected their

ability to be considered members of a control group. However, it is possible that these two mothers may have used drugs and alcohol as a means of self-medicating depression or an anxiety disorder and thus would not be appropriate members of the control group.

The present study was not designed in such a way that allowed for the partitioning of specific genetic influences from environmental influences. To accomplish this, the study would have needed to incorporate a twin or adoptive study design, which, given the need for a high-risk sample was not feasible. In addition, the present study would have benefited from a longitudinal design in which these infants could have been followed to an age at which they may self-report symptoms of anxiety and depression. Last, while the developmental psychopathology literature lends support to the investigation of processes that moderate the impact of maternal psychopathology on infant functioning, the inclusion of a measure of parenting processes, and/or mother-infant interaction, was beyond the scope of the current study and could not be incorporated into the methodology. For example, parenting processes and parent-infant interaction may be more salient to infant outcome than the experience of maternal psychopathology. Researchers have asserted that a secure attachment may buffer physiological stress reactivity in young offspring (e.g., Nachmias, Gunnar, Mangelsdorf, Hornick-Parritz, & Buss, 1996). This design limitation could be remedied in future studies by the addition of measures that examine the impact of parenting or mother-infant interaction (e.g., maternal sensitivity and intrusiveness).

Conclusions

The present study extends research on the underlying neurobiological markers of risk for affective disorders. The study is distinctive in that it examines EEG asymmetry

in infants of both mothers with a history of depression as well as infants of mothers with a history of anxiety. Although many of the hypothesized relations between maternal psychopathology and infant EEG asymmetry were not significant, the results suggest that patterns of infant brain electrical activity during a resting state may be related to maternal history of psychopathology.

The study is similar to extant studies of emotion and affective disorders yet there are important differences. Unlike previous studies of the relations between infant EEG patterns and maternal affective disorder, the present study included infants of mothers with a history of anxiety as well as infants of mothers with a history of depression. While the patterns of asymmetry in the offspring of depressed mothers did not differ from the offspring of control mothers, there were differences in the offspring of anxious mothers with respect to infant asymmetry. The results of this study suggest that there may be a number of valuable paths for further research into underlying neurobiological markers in infants at risk for affective disorder. By examining types of maternal anxiety we may gain a better understanding of the brain electrical activity in at-risk infants. The ability to increase our knowledge of these patterns would enhance our understanding of the development of psychopathology.

Another avenue for future research would be to examine offspring of anxious mothers in emotion–eliciting contexts so that we might understand how these offspring respond physiologically to states of approach and withdrawal. While the theoretical basis for investigation of EEG asymmetry in both adults as well as children is the approach-withdrawal model of hemispheric lateralization (Davidson, 1984, 1992b, 1994; Fox, 1991; Tomarken & Keener, 1998), recent research has also indicated that the ability to

regulate emotion may be less flexible with depression (e.g., Rottenberg, Kasch, Gross, & Gotlib, 2002). Perhaps the hypothesized differences in patterns of infant EEG asymmetry might be more apparent during an emotional challenge and a suggested approach for future work examining these relations would be to consider the utilization of such a task. By examining the psychophysiological correlates of emotion regulation such as the electrical activity of the central nervous system in the offspring of mothers with depression and anxiety during an emotion regulation task, we can gain insight into the affective responses of children at risk for affective disorder.

Another avenue for future research may be to examine patterns of EEG asymmetry in both mothers with depression and anxiety as well as their infant offspring. Perhaps infants of mothers who themselves show the expected patterns of asymmetry reflective of their respective disorders may be more likely to show similar patterns of asymmetry. In addition, the present study examined mean differences in infant EEG asymmetry among maternal diagnostic groups, which may have washed out the effects of interest. Perhaps by examining infants who score on the extremes of EEG asymmetry the expected patterns of EEG asymmetry may become evident. Last, while investigations of emotion and EEG asymmetry such as the present study are important in elucidating markers of vulnerability for psychopathology, future research should attempt to understand the mechanisms by which these asymmetries occur in the at-risk offspring of mothers with depression and anxiety.

In summary, the present study integrated the fields of psychiatry and neurophysiology from a developmental perspective in order to elucidate associations between maternal psychopathology (e.g., depression and anxiety) and differences in

patterns of infant brain electrical activity. This examination of early precursors of risk for psychopathology was the first of its kind to do so with the infant offspring of mothers with anxiety disorders. Two compelling questions that have been brought forth by the present study are whether these patterns of EEG asymmetry in infants of anxious mothers might hold with a larger sample size as well as how such patterns might emerge when examining additional types of anxiety. The answers to these questions would enhance our knowledge of the development of psychopathology in infants at risk for anxiety disorders. The findings of the present study underscore the need for greater specificity in examining maternal psychopathology and early precursors of risk for psychopathology in infant offspring, so that we might gain a better understanding of the development of these disorders.

APPENDICES

Appendix A: Recruitment Letter

Susan L. Warren, M.D.
Center for Family Research
Department of Psychiatry and Behavioral Science
2300 Eye St., N.W., 550 Ross Hall
Washington, DC 20037

202.994.0033(fax) 2192

Dear Parent:

New research is showing that infants are more intellectually and emotionally advanced than originally expected. Research is also providing answers about the best ways to help young children grow and develop to reach their full potential. I am writing to tell you about an exciting opportunity for you to participate in similar research at The George Washington University Medical Center.

I am currently recruiting participants for a new study that is exploring early emotional development and the brain. The long term aim of this research is to understand the associations between emotions and brain function so that we will be able to use this information to help families and young children.

If you decide to participate in the study, it will be at no cost to you and you will be compensated for participation. Your privacy is of the utmost importance; therefore, all information you provide will be kept confidential and will only be made available to my research team.

If you are interested in learning more about this study, please let me know by completing and returning the enclosed information card. Someone from my office will then contact you.

If you have any further questions, before or after you are contacted, please feel free to call me at 202-994-3475 and ask to speak with someone regarding The Parent-Child Health Project.

Thank you for your time and consideration. I think this will be an enjoyable experience for you. I look forward to speaking with you soon.

Sincerely,

Susan L. Warren, MD
Principal Investigator
The Parent-Child Health Project
The George Washington University Medical Center

Appendix B: SCID-I Screener

SCID SCREENING MODULE

Now I want to ask you some more specific questions about issues you may have experienced.

1. Has there been a period of time when you were feeling depressed or down most of the day nearly every day?	1	2	3
2. Have you lost interest or pleasure in things you usually enjoyed?	1	2	3
3. Has there been a period of time when you've had five or more drinks (beer, wine, or liquor) on one occasion?	1	2	3
4. Have you used street drugs?	1	2	3
5. Have you gotten hooked on a prescribed medicine or taken more of it than you were supposed to?	1	2	3
6. Have you had a panic attack, when you suddenly felt nervous or anxious or suddenly developed a lot of physical symptoms?	1	2	3
7. Have you been afraid of going out of the house alone, being in crowds, standing in a line, or traveling on buses or trains?	1	2	3
8. Has there been anything you've been afraid to do or felt uncomfortable doing in front of other people, like speaking, eating or writing?	1	2	3
9. Are there any other things that you have been especially afraid of, like flying, seeing blood, getting a shot, heights, closed places, or certain kinds of animals or insects?	1	2	3
10. Have you been bothered by thoughts that didn't make any sense and kept coming back to you even when you tried not to have them?	1	2	3

11. Has there been anything that you have had to do over and over again and couldn't resist doing, like washing your hands again and again, counting to a certain number, or checking something several times to make sure you'd done it right?	1	2	3
12. Have you been particularly nervous or anxious?	1	2	3
13. Have you weighed much less than other people thought you ought to weigh?	1	2	3
14. Have you often had times when your eating was out of control?	1	2	3

Appendix C: Sheehan Disability Scales and Stress and Social Support Scales

DISABILITY SCALES

The following three scales are scored from 0-10 where 0 = not at all, 1-3 = mildly, 4-6 = moderately, 7-9 = markedly, and 10 = extremely

Work
The symptoms have disrupted your work: _____

Social Life
The symptoms have disrupted your social life: _____

Family Life/Home Responsibilities
The symptoms have disrupted your family life/home responsibilities: _____

STRESS AND SOCIAL SUPPORT SCALES

The following scale is scored from 0-10 where 0 = not at all, 1-3 = mildly, 4-6 = moderately, 7-9 = markedly, and 10 = very severely

Perceived Stress Scale

In the past month, how much were you set back by stressful events or personal problems, such as work, home, health, or financial problems? ____

The following scale is scored from 0%-100% where 0% = no support at all, 10-30% = a little, 40-60% = moderate, 70-90% = considerable, and 100% = ideal support

Perceived Social Support Scale

In the past month, how much support have you received from friends, relatives, co-workers, etc., as a percentage of the amount of time you needed to cope? ____

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