RELATIVE LEFT FRONTAL HYPOACTIVATION IN ADOLESCENTS AT RISK FOR DEPRESSION

By

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Thesis

Submitted to the Faculty of the

Graduate School of Vanderbilt University

in partial fulfillment of the requirements

for the degree of

MASTER OF ARTS

in

Psychology

August, 2001

Nashville, Tennessee

Approved:

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ACKNOWLEDGEMENTS

This project was funded in part by NIMH grant MH49759 awarded to Andrew J. Tomarken, Ph.D. The support I received from Drs. Andrew J. Tomarken and Judy Garber, as well as graduate students and staff in their respective labs, were invaluable. I am particularly grateful for the support and guidance of Dr. Tomarken, without whom this project would not have been possible. Finally, I thank the families who participated in this study.

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CHAPTER I

INTRODUCTION

In this study we assessed whether adolescents who are at risk for depression differ in patterns of frontal cerebral activation asymmetry relative to low risk adolescents. We addressed this question because of evidence from a variety of sources indicating that frontal brain asymmetry (FBA) is linked to depression and may be a marker of vulnerability to depression. Specifically, this evidence indicates a linkage between unipolar depression and decreased activation of left relative to right hemisphere frontal brain regions (for reviews, see Davidson, 1995, 1998; Tomarken & Keener, 1998). For example, studies of the effects of unilateral lesions have indicated that left hemisphere lesions are associated with a "depressive-catastrophic" reaction, whereas right hemisphere lesions are associated with either positive affect or an "indifferent" profile. Robinson and his collaborators found that the severity of depressive symptomatology is correlated with the proximity of a left-hemisphere lesion to the frontal pole, whereas anterior right-hemisphere lesions produce emotional indifference (Robinson, Kubos, Starr, Rao, & Price, 1984; Robinson & Price, 1982; Robinson & Szetela, 1981). Other neurological. studies have provided results that are broadly consistent with the evidence indicating lateralized linkages to depression. (e.g., Mendez, Taylor, Doss, & Salguero, 1994; Morris, Robinson, Raphael, & Hopwood, 1996), although not all findings have been consistent in this area (e.g., Dam, Pedersen, & Ahlgren, 1989; House, Dennis, Warlow, Hawton, & Molyneux, 1990; MacHale, O'Rourke, Wardlaw, & Dennis, 1998).

Several studies that have assessed regional cerebral blood flow (rCBF) using positron emission tomography (PET) have shown that clinically depressed subjects demonstrate relative decreased left frontal activation when compared to nondepressed control subjects (e.g., Baxter et al., 1985; Baxter et al., 1989; Bench et al., 1992; Ebert, Feistel, & Barocka, 1991; Martinot et al., 1990). Consistent with these rCBF findings are the results of studies that have investigated resting EEG activity in depressed and nondepressed subjects. These studies have found that clinically depressed individuals or individuals characterized by elevated scores on the Beck Depression Inventory (Beck & Steer, 1987) demonstrate relative left frontal hypoactivation when

compared to controls (Allen, Iacono, Depue, & Arbisi, 1993; Davidson, Schaffer, & Saron, 1985; Schaffer, Davidson, & Saron, 1983).

Of prime relevance in the present context is evidence from EEG studies indicating that resting FBA may be a marker of risk indicating heightened vulnerability to depression. For example, two studies have found that currently euthymic individuals who have a history of depression demonstrate left frontal hypoactivation relative to control subjects (Allen et al., 1993; Henriques & Davidson, 1990). In addition, individual differences in resting FBA may be a biological marker of temperament that predicts affective reactivity to emotional elicitors and that may be a marker of differential risk for affective disorders. For example, several studies have shown that individuals characterized by a repressive-defensive coping style demonstrate relative left hyperactivation (e.g., Kline, Allen, & Schwartz, 1998; Tomarken & Davidson, 1994). These findings are consistent with the evidence that a repressive-defensive coping style is associated with decreased vulnerability to depression (Lane, Merikangas, Schwartz, Huang, & Prusoff, 1990).

However, these findings do not unequivocally suggest a link between left frontal hypoactivation (LFH) and heightened vulnerability to depression. The manifestation of LFH in individuals with remitted depression cannot distinguish whether LFH is a vulnerability factor for, or a consequence of, depression (Alloy, Abramson, Raniere, & Dyller, 1999). An assessment of at-risk populations who have not yet manifested depression represents a more direct test of whether LFH is a marker of vulnerability for depression. One such population is children of depressed parents. Children of depressed parents exhibit a range of negative outcomes and psychiatric diagnoses compared to children of parents without a psychiatric history (Downey & Coyne, 1990; Gelfand & Teti, 1990). In particular, children of depressed parents are at heightened risk of developing depression (Hammen, 1991; Warner, Weissman, Fendrich, Wickramaratne, & Moreau, 1992; Weissman, Fendrich, Warner, & Wickramaratne, 1992; Weissman, Warner, Wickramaratne, Moreau, & Olfson, 1997).

Several studies indicate that infants of depressed mothers exhibit LFH. Dawson, Frey, Panagiotides, Osterling, & Hessl (1997) found that 13- to 15-month-old infants of depressed mothers exhibited reduced left frontal EEG activity compared both to mothers with subthreshold depression and to mothers with no depression. Jones, Field, Fox, Lundy, & Davalos (1997) showed that these effects were generalizable to infants as young as one month old. Dawson and

her colleagues have also linked LFH in infants of depressed mothers to a variety of important correlates, including, 1) playful and distressing interactions with their mothers (Dawson, Klinger, Panagiotides, Hill, & Spieker, 1992); 2) playful interactions with both their mothers and with nondepressed adults (Dawson, Frey, Panagiotides et al., 1999), and 3) lower levels of affection toward their mothers (Dawson, Frey, Self et al., 1999).

To date, studies of FBA in children of depressed mothers have concentrated on infants. One goal of the present study was to investigate whether adolescent children of mothers with a history of depression demonstrated the same pattern of relative LFH that has been observed in previous studies with currently depressed adults, adults with a history of depression, and high-risk infants. Specifically, we compared patterns of resting frontal EEG asymmetry in young adolescent (12-14 years old) children of depressed and nondepressed mothers.

There were several reasons why we compared adolescent children in this age range. First, the presence of LFH in adolescent children of depressed mothers would indicate a continuity of risk beginning in infancy and extending into adolescence. Second, the peak age of onset of depression in children of depressed parents ranges from 14 to 20 years (Weissman et al., 1997). The presence of LFH in adolescent children of depressed mothers would indicate the presence of a marker of risk at a point in time that immediately antedates the dramatic increase in the incidence of depression. Third, the prevalence rate of depression in preadolescence is comparable in boys and girls, although by adulthood, nearly twice as many women are diagnosed with depression as men (Nolen-Hoeksema, McBride, & Larson, 1997). Thus, both increases in depressive symptoms and gender differences in such symptoms first emerge during adolescence. Although prior studies have not typically found gender differences in the linkages between FBA and depression, this is a largely unexplored area. We sought to examine the interrelations among gender, differential risk for depression, and FBA in adolescents at high and low risk for depression.

Fourth, we wished to address the issue of the generalizability versus context-specificity of the link between FBA and vulnerability to depression. In addition to assessing the role of gender, we also assessed whether other sociodemographic variables might moderate the relation between maternal history of depression and adolescent FBA. A number of epidemiological studies have indicated an inverse relation between social class and rates of rates of depression (Kaplan, Roberts, Camacho, & Coyne, 1987; Leventhal & Brooks-Gunn, 2000; Murphy et al.,

1991; Pearlin & Johnson, 1977; Weissman & Myers, 1978) and many other psychiatric illnesses (Hollingshead & Redlich, 1958; Rushing & Ortega, 1979; Dohrenwend, 2000; Goodman, 1999; Srole, 1962; Williams, 1990), although we should note that the strength of the linkage between depression and social class has varied somewhat across studies and there is debate concerning the directionality of this linkage (e.g., Fox, 1990; Rodgers & Mann, 1993). Additionally, some studies have failed to find that individuals of lower social class have higher rates of depression (e.g., Weissman, Bruce, Leaf, Florio, & Holzer III, 1991; Weissman & Myers, 1978). Despite these caveats, the available evidence suggests that social class is likely to be an important risk factor in the development of depression.

Published findings linking FBA and depression have failed to adequately examine whether socioeconomic status (SES) moderates or potentially mediates the FBA-depression link for a number of reasons. First, many investigators have not reported sociodemographic variables indicating SES (e.g., Allen et al., 1993; Dam et al, 1989; Dawson, Klinger, Panagiotides, Hill et al., 1992; Starkstein, Robinson, & Price, 1987). Second, among studies that have reported sociodemographic information, most have not examined linkages between SES and both the occurrence of mood disorders and patterns of FBA (e.g., Henriques & Davidson, 1990; Morris et al., 1996; Robinson et al., 1984; Robinson & Price, 1982; Robinson & Szetela, 1981; Starkstein et al., 1987). Third, researchers have tended to sample subjects from a single source and thereby produced groups that were both similar and restricted in range with respect to SES. For example, infant frontal EEG laterality studies typically have recruited mothers from inner-city hospitals, and thus depressed and nondepressed mothers in these studies were sampled from a population of low social class (e.g., Dawson, Klinger, Panagiotides, Hill et al., 1992; Dawson, Panagiotides, Klinger, & Hill, 1992; Field, Fox, Pickens, & Nawrocki, 1995; Jones, Field, Fox, Lundy, & Davalos, 1997). In other EEG studies, college students, a relatively homogenous group, have served as subjects (Davidson et al., 1985; Schaffer et al., 1983).

Among the infant frontal EEG laterality studies that have used more heterogeneous samples with respect to SES, depressed and nondepressed mothers have not differed with respect to SES, although the groups have differed with respect to other sociodemographic variables such as marital status and age (Dawson, Frey, Panagiotides et al., 1999; Dawson, Frey, Self et al., 1999). Finally, only one frontal EEG laterality study has examined the correlation between FBA and SES (Henriques & Davidson, 1991). Although this study failed to find a relation, no analysis

was reported that simultaneously included SES and depression status as predictors of FBA. The current study used a sample recruited from a metropolitan community, and thus subjects varied widely with respect to SES. We sought to examine the main and interactive effects of SES and risk status on FBA.

Our study reports EEG findings derived from three reference montages. Published EEG results derived from different reference montages have demonstrated inconsistencies (for reviews, see Davidson, 1998; Hagemann, Naumann, Becker, Maier, & Bartussek, 1998; Reid, Duke, & Allen, 1998). Illustratively, Reid, Duke, & Allen (1998) assessed FBA in depressed and nondepressed adults and found significant group differences only during the first two minutes of EEG recording using a linked mastoid reference; there were no group differences using average and Cz reference montages. In other contexts, questions have been raised about the consistency of findings linking depression in adults to EEG measures derived from various referencing strategies (Debener et al., 2000; Hagemann et al., 1998; Henriques & Davidson, 1991). Published findings concerning the relation between FBA and the risk for depression in infants have typically examined Cz-referenced data (e.g., (Dawson, Klinger, Panagiotides, Hill et al., 1992; Dawson, Panagiotides et al., 1992; Field et al., 1995), although others (e.g., (Dawson, Frey, Self et al., 1999) have employed a linked-mastoid reference strategy. Although our findings do not resolve these inconsistencies, we hope that our decision to report findings derived from various reference montages encourages other investigators to do the same.

In sum, this study addressed whether adolescents at high and low risk of developing depression differed with respect to resting FBA. In addition, we assessed the roles of gender and SES in predicting FBA and whether these two factors moderate the effect of risk status on FBA. We predicted that adolescent children of mothers with a history of depression would demonstrate relative LFH compared to adolescent children of non-depressed mothers. We did not have strong *a priori* hypotheses concerning the link between FBA and SES or gender. However, we expected that, if relations were found, LFH would be linked to female gender and to lower SES. To test these hypotheses, we used multiple EEG reference montages. There have been inconsistencies in the literature with respect to EEG results derived from different reference montages (for reviews, see Davidson, 1998; Hagemann et al., 1998; Reid et al., 1998). It is unfortunate that many EEG studies have reported findings from only one reference montage, and

we report our EEG findings as asymmetry values computed from three reference montages: referenced to the vertex, a computer averaged ears reference, and an average reference.

CHAPTER II

METHODS

Participants

Participants were drawn from a larger sample of 240 adolescent children and their mothers who were recruited for a study investigating the development of depression in adolescents. This sample was 54.2% female, 82% Caucasian, 14.7% African-American, and 3.3% other (Hispanic, Asian, Native American). The sample was predominantly lower-middle to middle class with a mean socioeconomic status SES (Hollingshead, 1975) of 41.84 (SD = 13.25).

Letters were sent to parents of children in the fifth grade in the Nashville metropolitan public schools. Parents were invited to participate and were asked to complete a brief health history questionnaire indicating whether they had ever had any of 24 medical conditions such as diabetes, cancer, heart disease, and depression, or if they had ever taken any of 34 medications. One thousand four hundred and ninety five parents indicated an interest in participating and were interviewed further by telephone. Based on this screening call, 349 mothers who reported a history of depression or no history of psychiatric problems were interviewed in person with the Structured Clinical Interview for DSM-III-R (SCID; (Spitzer, Williams, Gibbon, & Frist, 1990). Inter-rater reliability of the SCID interviews has been reported elsewhere (Garber & Robinson, 1997). Families were excluded if mothers indicated a history of solely nonaffective psychiatric disorders, a history of schizophrenia, or if a parent or child had serious medical problems. The final high risk (HR) sample included 185 mothers who indicated a history of mood disorders (i.e.., Major Depression, Dysthymia, Depression Not Otherwise Specified, Adjustment Disorder with Depressed Mood). The low risk group consisted of 55 mothers who were lifetime-free of psychiatric diagnoses.

Research staff, unaware of the mother's psychiatric history, administered a battery of questionnaires to the parents and their children. Only those assessment instruments relevant to the present study are described here. Families participated in yearly assessments after the initial interviews. Subjects were asked if they were interested in participating in future studies, and those indicating such an interest were contacted to participate in the current investigation.

Adolescents in the current study were recruited between the first and second yearly follow-up interviews.

Thirty-two HR and 15 LR subjects participated in resting EEG recording. Subjects were paid $30 for their participation. Two HR subjects and one LR subject were excluded from analyses because they were not right-handed, as assessed by the Edinburgh Inventory (Oldfield, 1971). Five HR subjects and one LR subject were excluded from analyses due to other issues that compromised the validity of the resting EEG recording for the present purposes (e.g., excessive sleeping, medication use). Thus, 25 HR (11 male) and 13 LR (7 male) subjects were included in the current analyses. The relatively greater number of HR than LR participants in the current study reflects the distribution of the larger subject pool from which these subjects were drawn. A primary goal of the larger ongoing study was to investigate the conditions under which at-risk youths develop depression. Additional aims of the current study included investigating the relation between FBA and other indicators of risk in children of depressed mothers (e.g., family history, stressful life event, etc.). Thus, a relatively greater number of HR than LR adolescents was selected to be in both the current and larger study.

High Risk adolescents included 24 Caucasians and one African American. Low Risk adolescents included 12 Caucasians and one Native American. The racial distributions of participants in the current study and in the larger sample from which subjects were drawn did not statistically differ, χ^2 (4, N = 283) = 5.08, $p > 0.25$.

Participants in the present study ranged in age from 12.2-14.0 years old at the time of their EEG recording, HR Mean = 13.1 (SD=0.3); LR Mean = 13.0 (SD=0.4). The two groups did not statistically differ with respect to age F(1, 37)=2.20, $p > .45$. The Low Risk group (Mean = 53.2 , SD = 6.9) had significantly higher SES than the HR group (Mean =37.3, SD = 13.3), F(1, 37)=16.38, $p<.0005$. Participants in the current study and in the larger cohort from which they were drawn did not differ with respect to SES, F(1, 216)= 0.01, $p>.90$, and there was no interaction of risk group status and whether subjects from the larger cohort were included in the current analyses on SES, F(1, 216)= 2.61, $p>.11$

Finally, we address the issue of selecting the appropriate EEG frequency band to test our hypotheses. The clear majority of published EEG FBA findings have investigated either adult or infant subjects. Investigators of the relation of FBA to depression in adults have defined alpha as 9-11 Hz (Schaffer et al., 1983), 9-12 Hz (Davidson et al., 1985), or 8-13 Hz (Henriques &

Davidson, 1990, 1991). The dominant EEG frequency band in infants, however, is far slower than in adults (Matousek & Petersen, 1973). Therefore, investigators of infant EEG alpha asymmetry have defined alpha as a relatively lower frequency band: 2-6 Hz (Jones et al., 1997), 3-12 Hz (Field et al., 1995), or 6-9 Hz (Dawson, Frey, Panagiotides, Osterling, & Hessl, 1997; Dawson, Frey, Panagiotides et al., 1999; Dawson, Frey, Self et al., 1999; Dawson, Klinger, Panagiotides, Hill et al., 1992; Dawson, Klinger, Panagiotides, Spieker, & Frey, 1992; Dawson, Panagiotides et al., 1992; Dawson, Panagiotides, Klinger, & Spieker, 1997). Subjects in the current study were neither adults nor infants, and thus the selection of the appropriate alpha band was not straightforward.

The EEG of young children contains mostly slow waves (i.e., theta band activity) and the proportion of slow waves decreases with age (Benninger, Matthis, & Scheffner, 1984; Colon, de Weerd, Notermans, & de Graaf, 1979; Matousek & Petersen, 1973). The decline in relative slow wave activity is greatest in early childhood and then stops at around 10 years of age (Benninger et al., 1984; Gasser, Verleger, Bacher, & Sroka, 1988; Matousek & Petersen, 1973). Concomitant with the decrease in theta power during childhood are increases in faster frequency activity (e.g., alpha 2 band activity; (Gasser et al., 1988). Over the course of childhood development, the dominant frequency becomes more rapid (John et al., 1980; Matousek & Petersen, 1973), and there is evidence of a substitution of fast-wave for slow-wave activity during this time. For example, Matousek & Petersen (1973) found that correlations between age and absolute and proportional theta (3.5-7.5 Hz) power were -.61 and -.42, respectively, up to age 15. Between the ages of 16- and 21-years old, however, the correlations were .13 and -.20, respectively.

Most relevant to the current investigation is Gasser et al.'s (1988) finding that the age at which the maximum decrease of theta band (3.5-7.5 Hz) activity occurred was 11.7- and 11.8-years old for the right and left midfrontal sites, respectively. The age at which the maximum increase of alpha 2 band (9.5-12.5) activity occurred was 12.0- and 11.9- years old for the right and left midfrontal sites, respectively. Subjects in the current study ranged in age from 12.2-14.0 years old. It is likely that the majority of the transition from slower to faster frequency activity has occurred by this age, and thus we defined the alpha band in our subjects as it is typically defined for adults, 8.5-12.5 Hz. While *a priori* hypotheses will be restricted to asymmetry in this

band, exploratory analyses will investigate midfrontal asymmetry group differences in other bands as well.

Measures

Psychopathology

Adolescent psychopathology (i.e., mood disorders, anxiety disorders, impulsivity disorders, and substance-related disorders) was assessed at the first evaluation with *The Schedule for Affective Disorders and Schizophrenia for School-Age Children Epidemiological Version* (K-SADS-E; (Orvaschel, Puig-Antich, Chambers, Tabrizi, & Johnson, 1982) and with *The Longitudinal Interval Follow-up Evaluation for Children* (K-LIFE; (Keller & Neilsen, 1988) at each follow-up interview. All interviews were audiotaped. A second interviewer who was unaware of the first interviewer's ratings reviewed a randomly-selected 25% of the interviews. Kappas were .81 for mood disorders, .72 for anxiety disorders, and .80 for externalizing disorders.

Depressive Symptoms

Two measures assessed adolescent depressive symptomatology. At the initial interview and at each annual follow-up interview, children's depressive symptoms were assessed with the Children's Depression Inventory (CDI), a widely used self-report measure of depressive symptoms in children (Kovacs, 1981). The CDI has adequate internal consistency, test-retest reliability, and convergent validity with other self-report measures of depressive symptoms (Saylor, Finch, Spirito, & Bennett, 1984; Smucker, Craighead, Craighead, & Green, 1986); the internal consistency of the CDI in this sample was .81 at the initial assessment.

Additionally, weekly adolescent depressive symptomatology was ascertained based on the yearly K-LIFE (Keller & Neilsen, 1988). Symptoms were dated and given a severity score that ranged from one (no symptoms of depression) to six (severe symptoms of depression). A score of five or six on this scale denoted that the adolescent met criteria for DSM-III-R major depressive disorder (MDD), whereas lower scores denoted that the adolescent had not met criteria for DSM-III-R MDD.

Socioeconomic Status

Household SES was assessed with the Four Factor Index of Social Status (Hollingshead, 1975). Possible scores on this index range from 8 (lowest SES) to 66 (highest SES). To calculate the SES score of a household, scale values for occupation (which range from one to nine) and for education (which range from one to seven) were multiplied by factor weights of five and three, respectively. These two products were then summed. To calculate the SES score of a household, adjustments were made for marital status and related factors (e.g., receipt of child-support or alimony payments from an absent spouse) as outlined in Hollingshead, 1975. Adolescents were assigned the household SES score.

Procedure

Subjects were accompanied to the EEG session by a parent, and all subjects were run individually. Subjects were told that the purpose of the study was to look at brain wave activity in adolescents. After informed consent was obtained from both the adolescent and parent, electrodes were applied for the measurement of EEG. Subjects were then informed that: 1) there would be eight 1-min resting baselines; 2) four baselines would be conducted with eyes-open and four would be conducted with eyes-closed; and 3) during the resting baselines, they should try to minimize eye blinks and movements, but should not be so concerned about doing so that they were distracted. In accordance with previous work in our laboratory (e.g., (Tomarken, Davidson, & Henriques, 1990; Tomarken, Davidson, Wheeler, & Doss, 1992), subjects were not given highly specific instructions concerning the resting baselines. They were simply told to be as "restful" as possible.

Two randomly assigned, counterbalanced orders were used for the eyes-open and eyes-closed trials of the resting baselines (O-C-C-O-C-O-O-C and C-O-O-C-O-C-C-O). Subjects heard one tone denoting the beginning of each 60-s baseline and two tones denoting the end of each baseline. There was a 3-min interval between the fourth and fifth baselines. A 45-s interval occurred between all other baselines. Following the eighth and final resting baseline, electrodes were removed.

Electroencephalographic Recording and Quantification

EEG recording followed standard guidelines (see Pivik et al., 1993). 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 using the 10-20 International System (American Electroencephalographic Society, 1994; Jasper, 1958). EEG's were recorded from 14 standard scalp locations selected from the 10-20 system: F3, F4, F7, F8, T3, T4, T5, T6, P3, P4, C3, C4, Pz, and Fz., and a forehead ground was used. In addition, tin drop electrodes from the cap were used to record from the left and right earlobes (A1-A2). Nine-mm tin cup electrodes were placed above and below the eyes to record blinks and vertical eye movements and on the outer canthi to record horizontal eye movements. The electrooculogram (EOG) was recorded using a bipolar reference, and EOG electrode impedances were under 15 kΩ. All other electrode impedances were under 5 kΩ, and impedances for homologous sites were within 1 kΩ of each other. Impedances were documented to change minimally during the course of the experiment. EEG and EOG data were amplified and filtered with a bioamplifier from the James Long Company, set for bandpass filtering with half power cutoff frequencies of 1 and 120 Hz (12 dB/octave roll-off) and with the 60 Hz notch filter in. The gain was 30,000 for EEG channels and 5,000 for EOG channels. Data were digitized at 1024 Hz using the signal acquisition package Snapstream. Eight 1-minute resting baselines, 4 with eyes open and 4 with eyes closed, were collected. All placements were referenced to the vertex (Cz) during the initial recording. Zero Hz, 5 Hz, 10 Hz, 20 Hz, 40 Hz, and 100 Hz 10-μV sine waves were digitized on each channel to calibrate the digitized EEG and to assess the technical integrity of the recording system. These trials were run both immediately before and immediately after each experimental session.

Manual post-session artifact scoring with EEGEDIT software (James Long Company) was performed to edit the EEG signals. This procedure eliminated epochs that were confounded by artifacts such as movement, extensive muscle tension, and saccades. Following the artifact-reduction procedures, data were re-referenced offline using James Long Company EEG Analysis System software. In particular, we performed linear transformations of the digitized EEG to derive an computer-averaged ears reference (AE) and an computer-averaged reference (AR) (see Davidson, 1988; Senulis & Davidson, 1989). Averaged ears EEG power at a given site is the difference between activity at that site and the averaged power across the two ears. Averaged

reference EEG power at a given site is the difference between power at that site and the averaged power across all active sites. These referencing schemes are consistent with the analytic approach often adopted in the literature (e.g., (Henriques & Davidson, 1990, 1991; Tomarken et al., 1990; Tomarken, Davidson, Wheeler, & Kinney, 1992).

All artifact-free chunks that were 2.00 s in duration were extracted through a Hanning window, used to prevent spurious estimates of spectral power. Chunks overlapped by 50% to counteract the differential weighting of data points attributable to the use of a Hanning window. The EEG Analysis System software was then used to execute discrete Fourier transforms of the digitized EEG. This process derived estimates of spectral power (in μV^2) in different half-hertz frequency bins. These power values were then averaged across each of the artifact-free chunks of a given resting baseline trial. When a subject had fewer than eight artifact-free chunks for a given baseline, that baseline was not included in the computation; that is, it received a weight of zero. Power values were converted to power density (μV^2/Hz) in each of seven bands: delta (1.3-3.5 Hz), theta (4.0-7.0), alpha 1 (8.5-10.5 Hz), alpha 2 (11.0-12.5), alpha (8.5-12.5), beta 1 (13.5-19.5 Hz), and beta 2 (20.5-29.5 Hz). Power density was computed by summing power values across all the half-hertz bins within a band and then dividing by the number of summed bins.

All power density values were transformed to natural logarithms to normalize the distribution of scores. Prior research has indicated that a weighted average of eyes-open and eyes-closed data produces more stable estimates of EEG asymmetry than either baseline type alone (Tomarken, Davidson, Wheeler, & Kinney, 1992). Thus, to generate measures of EEG power and EEG asymmetry for a given experimental session, we computed composite variables of the mean of the eyes-open and eyes-closed trials by using the number of artifact-free chunks within each baseline as a weighting factor. These composite variables were used in all subsequent analyses. The asymmetry metrics were computed by subtracting left-sided alpha power density from right-sided alpha power density (log right minus log left).

In this article, analyses used to test hypotheses focused on measures of log power density in the alpha frequency band. Because decreased alpha power in a given region has been linked to increased cortical activation in that region (Davidson, 1988; Pfurtscheller, 1986; Pfurtscheller & Klimesch, 1991) higher values on these asymmetry metrics denote greater relative left frontal activation (equivalent to less relative left frontal hypoactivation).

CHAPTER III

RESULTS

Depressive Symptoms

We examined CDI scores from four of the yearly assessments to examine whether HR and LR subjects in the current study differed with respect to symptoms of depression prior to or after the EEG recording. The two groups did not differ in terms of CDI scores at the two yearly assessments preceding and the two yearly assessments following the EEG session. The mean CDI of the LR group across these four assessments was 3.9 (SD=3.7) and of the HR group was 4.5 (SD=3.4) (all F's (1,37) < .17, all *p*'s > 0.63). Subjects in both risk groups did not differ with respect to CDI scores across assessment periods ($F(3,30)=1.79$, $p>.16$), and the group x assessment period interaction was not significant ($F(3,30) = .053$, $p = .98$).

For the eight weeks prior to, the week of, and the eight weeks after the EEG recording, all subjects averaged less than 2 (i.e., possible mild depressive symptoms) on the retrospective measure of weekly depressive symptom. All LR subjects received scores of one on this scale for every week during this time period (i.e., LR subjects were essentially free of symptoms of MDD). All HR subjects except four received scores of two or below during this time period (i.e., mild symptoms of MDD), while the remaining four received scores of four or below on this measure (i.e., symptoms of MDD and impairment, but did not meet criteria for MDD). Thus, LR and HR subjects did not meet criteria for MDD during the two-months prior to and the two months after the EEG recording. Furthermore, the majority of subjects demonstrated no symptoms of MDD.

Psychopathology Data

We assessed the presence of psychopathology during the two years prior to and the two years following EEG recording. There were no symptoms of any mood disorders, conduct disorder, or substance-related disorders present in LR subjects during these four assessment periods. One LR subject demonstrated symptoms of overanxious disorder and met criteria for simple phobia, another demonstrated symptoms of simple phobia, while a third met criteria for separation anxiety disorder.

Five HR subjects demonstrated symptoms of one or more mood disorders. Symptoms of bipolar disorder and MDD were displayed by one HR subject each, while three HR subjects showed symptoms of adjustment disorder. Four HR subjects met criteria for adjustment disorder.

Eight HR subjects demonstrated symptoms of one or more anxiety disorders. These included social phobia (one HR subject), simple phobia (five HR subjects), generalized anxiety disorder (one HR subject), overanxious disorder (one HR subject), and separation anxiety disorder (five HR subjects). Four HR subjects met criteria for one or more anxiety disorders. These included panic disorder (one HR subject), simple phobia (one HR subject), overanxious disorder (two HR subjects), and separation anxiety disorder (one HR subject).

Four HR subjects demonstrated symptoms of an impulsivity disorders. These included oppositional-defiant disorder (one HR subject) and attention deficit disorder with hyperactivity (three HR subjects). Three HR subjects met criteria for one or more impulsivity disorders. These included oppositional-defiant disorder (three HR subject) and conduct disorder (one HR subject).

Finally, one HR subject demonstrated symptoms of nicotine dependence while another met criteria for nicotine dependence.

Electroencephalographic Data

Midfrontal Alpha Asymmetry

Because prior research indicating a link between FBA and depression has examined group differences in alpha power, we had specific hypotheses about activity in this frequency band. We predicted that HR and LR adolescents would differ in alpha band asymmetry in the midfrontal (F3 and F4) regions. Specifically, we predicted that HR subjects would demonstrate greater relative LFH (that is, less relative left versus right alpha band power) than LR subjects. These analyses are presented first.

Table 1. Mean log-transformed alpha power density and asymmetry values (in μV) for the frontal regions (F3 and F4) derived from three reference montages for high and low risk adolescents, subdivided by gender. Parenthetical values indicate standard deviations for power density values and standard errors of the mean for asymmetry values.

		Ears Reference	Average Reference	Cz Reference
High Risk Males *(n=11)*	F3 Power	1.200 (0.579)	0.388 (0.589)	0.932 (0.637)
	F4 Power	1.208 (0.572)	0.379 (0.563)	0.953 (0.598)
	F3/F4 Asymmetry	0.009 (0.015)	-0.009 (0.025)	0.021 (0.027)
High Risk Females *(n=14)*	F3 Power	1.634 (0.54)	0.825 (0.576)	1.059 (0.576)
	F4 Power	1.629 (0.536)	0.824 (0.574)	1.054 (0.58)
	F3/F 4 Asymmetry	-0.004 (0.018)	-0.001 (0.019)	-0.005 (0.015)
Low Risk Males *(n=7)*	F3 Power	1.448 (0.353)	0.760 (0.558)	1.200 (0.553)
	F4 Power	1.496 (0.372)	0.796 (0.579)	1.172 (0.543)
	F3/F 4 Asymmetry	0.047 (0.015)	0.036 (0.056)	-0.027 (0.031)
Low Risk Females *(n=6)*	F3 Power	1.320 (0.572)	0.509 (0.604)	0.739 (0.721)
	F4 Power	1.366 (0.551)	0.600 (0.612)	0.844 (0.709)
	F3/F 4 Asymmetry	0.046 (0.023)	0.091 (0.037)	0.105 (0.014)

Table 1 indicates mean log-transformed alpha power density and asymmetry values (in μV) for the midfrontal regions (F4 and F3) and mean asymmetry scores (ln(F4)-ln(F3)) derived from three reference montages for adolescent males and females. Higher absolute alpha power density values are associated with relatively less cortical activation, while more negative asymmetry values indicate greater relative left frontal hypoactivation (LFH).

Because of how the asymmetry metric is computed, a main effect of risk status on asymmetry values is equivalent to an interaction involving hemisphere on absolute power density values. Analyses used to test hypotheses in the current study will focus on asymmetry rather than on absolute power.

Figure 1 shows the mean log-transformed midfrontal alpha asymmetry values, derived from three reference montages, for LR and HR adolescents. This figure indicates that for AE and AR EEG, there was greater relative left frontal activation (equivalent to less relative LFH) in the LR group. The results of Risk Status (low risk / high risk) X Gender (male / female) ANOVAs performed on AE and AR mid-frontal EEG asymmetry values were consistent with these observations. The analysis of AE asymmetry in the midfrontal region revealed a main effect of risk status, $F(1, 37) = 5.49$, $p<.05$, no main effect of gender, $F(1,37) = 0.23$, $p>0.50$, and

no significant interaction between risk status and gender, F(1,37) = 0.09, p>0.50. Similarly, the analysis of AR asymmetry in the midfrontal region revealed a main effect of risk status, F(1, 37) = 5.37, p<.05, no main effect of gender, F(1,37) = 0.50, p>0.40, and no significant interaction between risk status and gender, F(1,37) = 1.44, p>0.20.

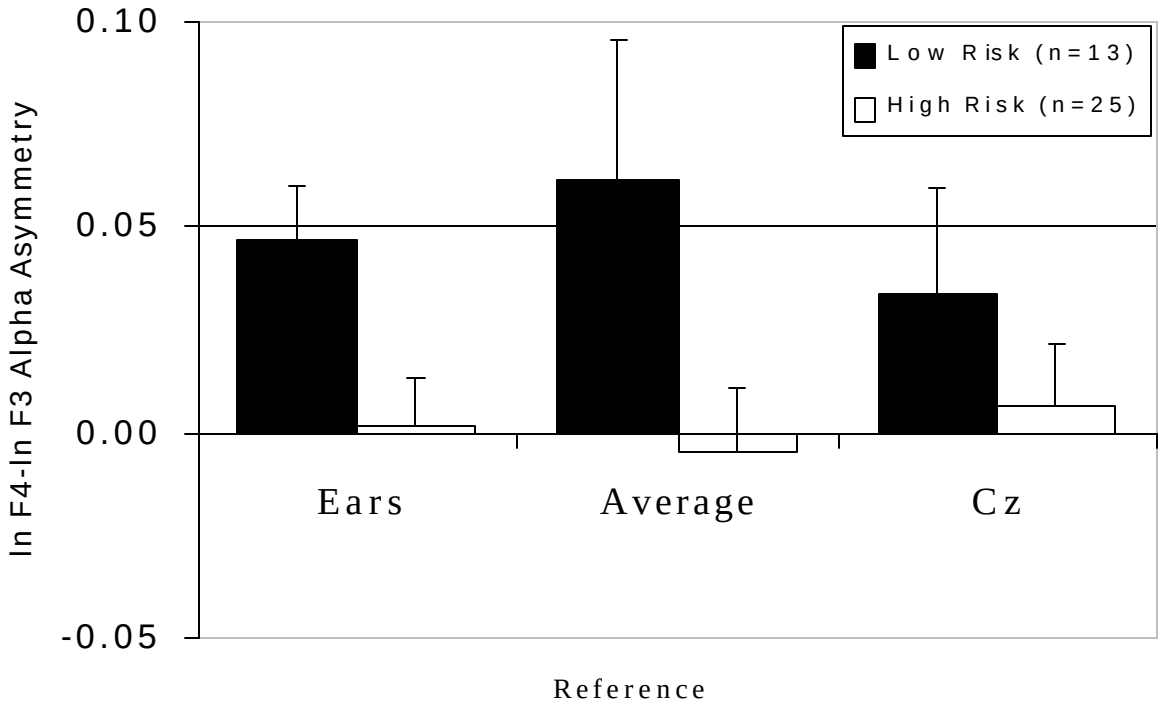


Figure 1. Mean log-transformed alpha power (in μV) asymmetry (left-right) for the midfrontal regions (F3 and F4), derived from three reference montages, for LR (n=13) and HR (n=25) adolescents. Error bars are standard errors of the mean.

Figure 2 illustrates mean log-transformed midfrontal alpha power values, derived from three reference montages, for LR and HR adolescents males and females. This figure suggests that HR females, but not HR males, demonstrated relative LFH with respect to Cz-referenced FBA. The analysis of Cz asymmetry in the midfrontal region revealed no main effect of risk status, F(1, 37) = 1.21, p>.0.20, no main effect of gender, F(1,37) = 1.49, p>0.20, but a significant interaction between risk status and gender, F(1,37) = 10.49, p<.003. Specifically, there was a main effect of risk status for females, F(1,19) = 19.43, p<.0003, but not for males, F (1,17) = 1.20, p>.25. Analyses of ER and AR asymmetry in the midfrontal region revealed no significant interaction between risk status and gender, F(1,37) < 1.45, p>.23.

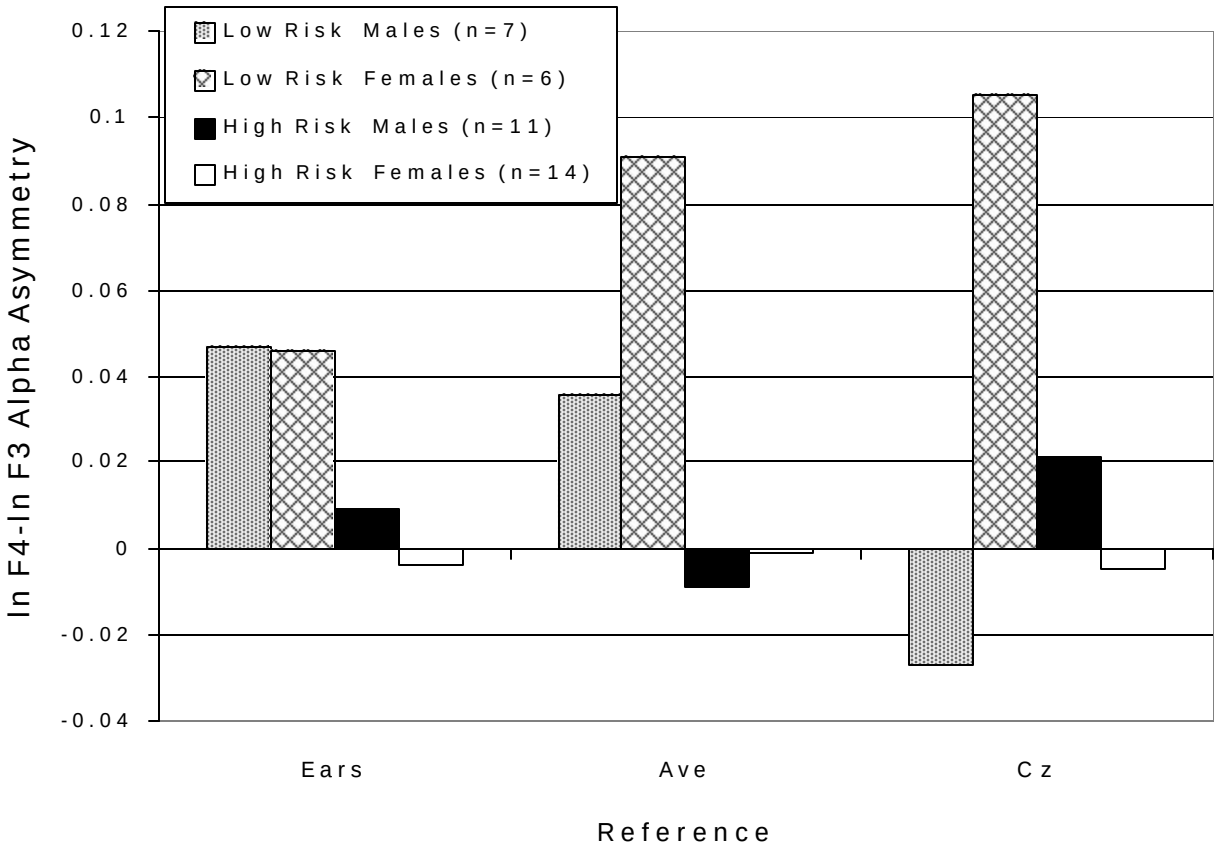


Figure 2. Mean log-transformed alpha power (in μV) asymmetry (left-right) for the midfrontal regions (F3 and F4) derived from three reference montages for male and female LR and HR adolescents. More negative numbers indicate greater relative left frontal hypoactivation.

EEG Asymmetry in Other Regions

Because we had no specific hypotheses about activity in other regions, we computed three-way MANOVAs for each other region (i.e., lateral frontal (F7/F8), parietal (P3/P4), anterior temporal (T3/T4), posterior temporal (T5/T6), and central (C3/C4)) with risk status as a between-groups variable and gender and region as within-groups variables.

Ears Reference There were no significant main effects for risk status for F7/F8, P3/P4, T3/T4, T5/T6, or C3/C4 AE asymmetry. There was a significant effect of region, $F(4, 31)=5.54$, $p<.002$, and a significant interaction of region and risk status, $F(4,31)=2.72$, $p<.05$. When these effects were examined, it was found that none of the univariate group differences for individual regions was significant (p's>.15).

Average Reference There were no significant main effects for risk status or interactions with risk status for F7/F8, P3/P4, T3/T4, T5/T6, or C3/C4 AR asymmetry. There was a significant effect of region , F(4, 31)=6.09, *p*=.001. When this effect was examined, it was found that none of the univariate group differences for individual regions was significant (*p*'s>.18).

Cz Reference There were no significant main effects for risk status or interactions with risk status for F7/F8, T3/T4, T5/T6, or C3/C4 Cz asymmetry. There was a significant main effect for risk status on P3/P4 Cz asymmetry, F(1,34)=5.52, *p*<.05, reflecting the fact that HR adolescents showed greater relative left parietal activation than LR adolescents. There was a significant main effect of region, F(4, 31)=5.45, *p*<.002, and no significant interactions with risk status for asymmetry in any region.

F34, Other Bands

Because we had no specific hypotheses about activity in other bands, we computed three-way MANOVAs on midfrontal (F3/F4) asymmetry for delta (1.5 – 3.5 Hz), theta (4.0 – 7.0 Hz), alpha 1 (8.5-10.5), alpha 2 (11.0-12.5), beta 1 (13.5 – 19.5 Hz), and beta 2 (20.5 – 29.5 Hz) bands with risk status as a between-groups variable and gender as a within-groups variable.

Ears Reference There was a main effect of frequency band, F(5,30) = 5.46, *p*<.002. There was a main effect of risk status on ER F3/F4 asymmetry for the delta band, F(1,37)=5.26, p<.05, the theta band, F(1,37)=19.86, p<.0001, and the alpha 1 band, F(1,37)=4.85, p<.05 such that, for these three bands, HR subjects showed greater relative ER midfrontal LFH. There was no main effect of risk status in the alpha 2, beta 1, or beta 2 bands. There was no main effect of gender or interaction of gender with risk status for ER F3/F4 asymmetry for any band.

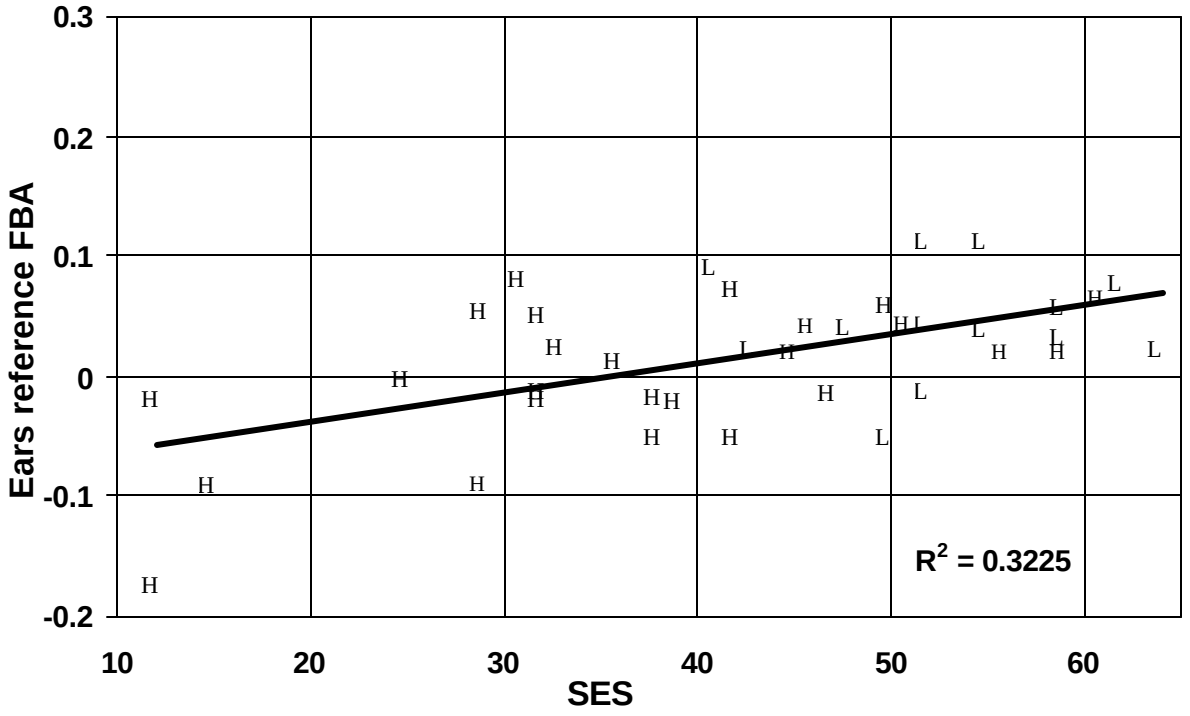
Average Reference There was a main effect of frequency band, F(5,30) = 4.45, *p*<.01. There was a main effect of risk status on AR F3/F4 asymmetry for the delta band, F(1,37)=8.35, p<.01, the theta band, F(1,37)=20.57, p<.0001, and the alpha 1 band, F(1,37)=4.79, p<.05 such that, for these three bands, HR subjects showed greater relative AR midfrontal LFH. There was no main effect of risk status in the alpha 2, beta 1, or beta 2 bands. There was no main effect of gender or interaction of gender with risk status for ER F3/F4 asymmetry for any band.

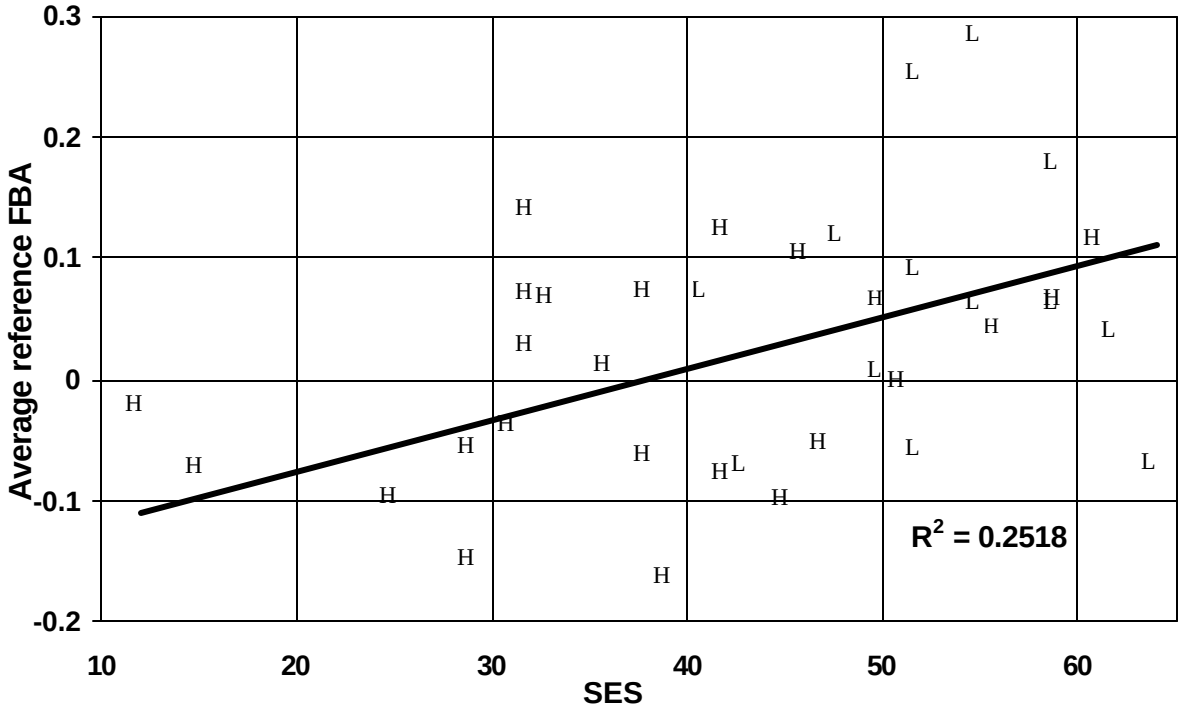
Cz Reference There was a main effect of frequency band, $F(5,30) = 5.63$, $p<.001$. There were no significant main effects for risk status or gender for Cz F3/F4 asymmetry in any of the six bands analyzed. There were significant interactions of risk status with gender for the beta 1 band, $F(1,37) = 4.25$, $p<.05$, and the alpha 1 band, $F(1,37) = 10.16$, $p<.005$. When these interactions were examined, it was found that there was a main effect of risk status on Cz F3/F4 asymmetry for females both in the beta 1 band, $F(1,19) = 4.89$, $p<.05$, and the alpha 1 band, $F(1,19) = 17.09$, $p<.001$, but not for males in either band, p's>.30.

Socioeconomic Status

Because the HR and LR groups differed with respect to SES, we sought to investigate if the observed group differences on midfrontal alpha asymmetry were a function of this difference in social class. There was a significant correlation between SES and FBA across both risk groups for two of the three reference montages, ER r(p) = .57 (.0002), AR r(p) = .50 (.001), Cz r(p) = .16 (.33). Specifically, lower household SES was correlated with ER and AR LFH. To investigate further the relation between alpha asymmetry in the midfrontal region and social class, correlations were computed separately for each risk group. Within the HR group, ER and AR FBA correlated significantly with SES, ER r(p) = .56 (.0035), AR r(p) = .50 (.01), Cz r(p) = .14 (.52). Within the LR group, there were no significant correlations between SES and FBA, AE r(p) = .04 (.89), AR r(p) = .05 (.88), Cz r(p) = -.03 (.92).

To explore the relation of risk status and FBA in adolescents of varying SES, we plotted FBA, derived from three reference montages, against SES. Figure 3 illustrates that there were no individuals of relatively low SES in the LR group (i.e., the minimum SES in the LR group was 41), and thus a restriction of range likely attenuated our ability to detect a relation between SES and FBA in the LR group. Nevertheless, Figure 3 suggests that, within the HR group, relative LFH, derived from EA and AR montages, was greatest for the subjects of lower SES, and was least for the subjects of higher SES. This inverse SES-FBA linear relation suggested that SES may mediate or moderate the observed relations between FBA and risk status.


Ears reference FBA
SES
0.3
0.2
0.1
0
-0.1
-0.2
10
20
30
40
50
60
R^2 = 0.3225


Average reference FBA
SES
0.3
0.2
0.1
0
-0.1
-0.2
10
20
30
40
50
60
R^2 = 0.2518

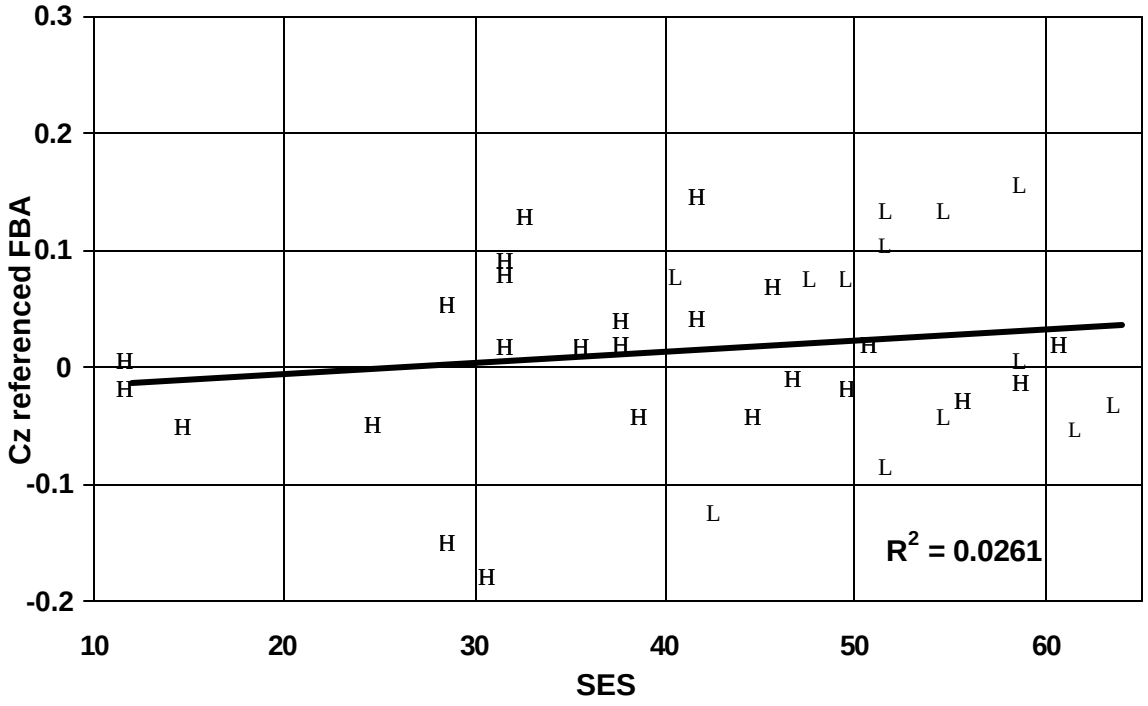


Figure 3. Scatterplots (with linear trendlines) in which FBA is plotted against SES. FBA represents mean log-transformed alpha power (in μV; right- left) for the midfrontal regions (F3 and F4). L=low risk adolescents; H=high risk adolescents. Top: ears reference; middle: average reference; bottom: Cz reference.

To investigate further the relations among SES, FBA, and risk status, we conducted hierarchical multiple regressions in which risk status, gender, and SES predicted FBA. This plan of analysis was bases on three observations: 1) the significant correlations between risk status and SES; 2) the significant correlations between FBA and SES within the HR group; and 3) the significant interaction of gender and risk status on Cz FBA. As shown in Table 2, the regression equations containing risk status, gender, and SES as predictors were significant for both AE (R^2 = .34, $p < .003$) and AR (R^2 = .27, $p < .02$) alpha FBA, but not for Cz alpha FBA (R2 = .06, $p > .5$). Because of the main effect of risk status that was observed in the alpha 1, delta, and theta bands, we performed hierarchical multiple regressions with the same predictors (i.e., risk status, gender, and SES) on FBA in these bands. As shown in Table 2, the regression equations were significant for AR FBA in all the bands analyzed, for ER FBA in the alpha 1 and theta bands, and for Cz FBA in the delta band.

Surprisingly, as shown in table 2, only SES contributed significant unique variance to the prediction of ER and AR alpha FBA. The standardized beta weights and significance of the

three predictors of FBA in the delta, theta, and alpha 1 bands are also presented in Table 2. When predicting alpha 1 ER and AR FBA, only SES contributed significant unique variance. Similarly, in regressions predicting delta AR and Cz FBA, only SES contributed significant unique variance. In the theta band, however, risk status continued to predict significant unique ER and AR FBA variance when SES was included as a predictor.

Table 2. R-square values and standardized regression coefficients (β) derived from hierarchical multiple regressions in which risk status, gender, and SES predicted alpha (8.5-12.5 Hz), alpha 1 (8.5-10.5 Hz), theta (4.0-7.0 Hz), and delta (1.5-3.5 Hz) ER, AR, and Cz FBA.

	Alpha			Alpha 1			Theta			Delta		
	ER	AR	Cz	ER	AR	Cz	ER	AR	Cz	ER	AR	Cz
R-square	0.34**	0.27*	0.06	0.34**	0.23*	0.05	0.37**	0.39***	0.13	0.15	0.32**	0.29**
Risk Status β	-0.07	-0.13	-0.12	-0.057	-0.14	-0.14	-0.61***	-0.59***	-.27	-0.29	-0.20	-0.002
Gender β	-0.09	0.1	0.18	-0.19	-0.03	0.10	-0.08	-0.08	-0.15	-0.08	-0.15	-0.08
SES β	0.53**	0.43*	0.10	0.52**	0.38*	0.11	-.03	0.03	0.07	0.12	0.40*	0.53**

*p<.05; ** p<.01; ** p<.005

We next sought to investigate which components of SES were most strongly related to FBA. Our measure of SES, The Four Factor Index of Social Status (Hollingshead, 1975) is computed from the occupation, education, and marital status of the heads of a household (the fourth factor used to calculate the Hollingshead Index, gender, does not directly effect the computation of SES). We first calculated bivariate correlations between risk status and the components of SES. Occupation and education were coded as outlined in Hollingshead (1975): occupation ranged from 0 (unemployed) to 9 (higher professional); education ranged from 1 (less that 6 years of schooling) to 7 (more than 18 years of schooling). Because the marital status variable as outlined in Hollingshead (1975) is less amenable to ordering than occupational status and education level, we coded marital status as either 0 (unmarried) or 1 (married).

Occupation level, education, and marital status were each significantly inversely correlated with risk status, occupation r(p)=-0.52(.0007), education r(p)= -0.48(.002), and marital status r(p)=-.40 (.01). Parents of LR subjects were more likely to have attained a more advanced occupation level, higher educational level, and were more likely to be married. To explore which of these three components of SES predicted FBA, we conducted additional hierarchical multiple regressions in which risk status, gender, and the components of household

SES (parental occupation, parental education, or parental marital status) predicted FBA derived from three reference montages. We conducted this analysis for FBA in our primary band of interest, alpha, as well as the three other bands that showed a main effect of risk status.

As can be seen from the Tables 3-5, parental occupation accounted for a greater proportion of AE and AR alpha FBA variance ($\underline{R^2}$ = .28 and .23, respectively) than education ($\underline{R^2}$ = .15 and .20, respectively) or marital status ($\underline{R^2}$ = ..23 and .15 respectively). Significant unique alpha ER FBA variance was predicted by parental occupation, but not by parental education or marital status, ($\underline{\beta}$ = .44, .11, and .32, respectively). Alpha AR and Cz FBA was not significantly predicted by parental occupation, education or marital status. Hierarchical multiple regressions predicting FBA in the alpha 1, theta, and delta bands from the components of FBA do not suggest the importance of any one component of SES in predicting FBA.

Table 3. R-square values and standardized regression coefficients (β) derived from hierarchical multiple regressions in which risk status, gender, and three components of SES (top: occupation; middle: education; bottom: marital status) predicted alpha (8.5-12.5 Hz), alpha 1 (8.5-10.5), theta (4.0-7.0), and delta (1.5-3.5) FBA.

	Alpha			Alpha 1			Theta			Delta		
	ER	AR	Cz	ER	AR	Cz	ER	AR	Cz	ER	AR	Cz
R-square	.28**	.23*	.06	.33***	.18	.05	.37***	.40***	.16	.14	.25*	.17
Risk Status β	-.13	-.19	-.21	-.09	-.20	-.25	-.63***	-.68***	-.41	-.34	-.30	-.12
Gender β	-.13	.07	.18	-.23	-.04	.11	-.07	-.07	-.13	-.08	.-17	-.10
Occupation β	.44*	.34	-.07	.49**	.28	-.09	-.06	-.13	-.20	.04	.23	.32

*p<.05; ** p<.01; ** p<.005

	Alpha			Alpha 1			Theta			Delta		
	ER	AR	Cz	ER	AR	Cz	ER	AR	Cz	ER	AR	Cz
R-square	.15	.20	.17	.16	.12	.11	.37***	.39***	.17	.14	.25*	.27*
Risk Status β	-.31	-.25	-.09	-.32	-.26	-.06	-.58***	-.58***	-.26	-.38*	-.33	-.07
Gender β	-.07	.13	.20	-.17	.008	.13	-.07	-.08	-.14	-.08	-.12	-.01
Education β	.11	.26	.17	.04	.19	.30	.02	.07	.10	-.05	.21	.48**

*p<.05; ** p<.01; ** p<.005

	Alpha			Alpha 1			Theta			Delta		
	ER	AR	Cz	ER	AR	Cz	ER	AR	Cz	ER	AR	Cz
R-square	.23*	.15	.06	.32***	.14	.05	.39***	.41***	.15	.16	.26*	.19
Risk Status β	-.24	-.23	-.14	-.17	-.29	-.20	-.66***	-.67***	-.37	-.30	-.34*	-.17
Gender β	-.04	.12	.19	-.12	.01	.11	-.10	-.10	-.17	-.06	-.11	-.02
Marital Status β	.32	-.08	-.09	-.44**	-.15	-.01	.17	.15	.16	-.15	-.22	-.33

*p<.05; ** p<.01; ** p<.005

CHAPTER IV

DISCUSSION

In the current study, we sought to examine the boundary conditions and generalizability of the links between FBA and depression. Specifically, we sought to explore the relations between FBA, the risk for depression, gender, and SES in adolescent children of depressed parents. This is a largely unexplored area in the infant EEG literature. Consistent with predictions, we found that HR and LR adolescents differed with respect to AE and AR alpha band FBA. Interestingly, we found an interaction between risk status and gender on Cz FBA such that HR females, but not HR males, followed the predicted pattern of LFH. One goal of the current study was to examine the relation between FBA and risk at a point in development when gender differences in depressive symptoms first emerge, and our data indicate potentially greater vulnerability to depression in adolescent girls than adolescent boys. Similar results were observed in the mid-frontal region in other EEG frequency bands, but group differences were not present in other sites. These results are consonant with prior findings indicating that infants of mothers with a history of depression demonstrate greater relative left frontal hypoactivation than infants whose mothers are lifetime-free of significant psychopathology. Our results extend such findings to include older children.

In addition, we found that when SES and risk status were included in the same regression equation, the former but not the latter contributed significant unique variance to predicting alpha and alpha 1 band FBA. Previous studies of the link between FBA and the risk of depression have typically neglected to examine the relative contribution of SES. Our results imply that SES is an important correlate of the risk for depression and should be examined in future studies of markers of risk for depression. One unexpected result was the robust relation between risk status, SES, and theta band ER and AR FBA. High risk adolescents demonstrated greater relative left frontal hypoactivation in the theta band. Moreover, risk status continued to predict unique theta band ER and AR FBA variance in regression equations containing SES and the component of SES as predictors.

The Four Factor Index of Social Status (Hollingshead, 1975) is computed from occupation, education, marital status, and gender, and we found that parental occupation was the

only component of SES that significantly predicted alpha band FBA among HR and LR adolescents. It is likely, however, that other factors that are not reflected by the Four Factor Index of Social Status but that are linked with SES (such as income or economic hardship) relate to FBA and the risk for depression. In order to elucidate the complex relation between SES, FBA, and vulnerability to depression, further research should attempt to identify those correlates or components of SES that predict FBA, and only a longitudinal assessment would allow for an evaluation of mediational hypotheses.

The links between SES and vulnerability to depression may stem from the association between low SES and differential exposure to chronic stressors. Many authors have proposed that LFH is linked to a heightened predisposition for depression (i.e., LFH functions as a diathesis that predisposes an individual to develop depression in the presence of appropriate elicitors) rather than to depression per se. In the absence of stressors, differences in depressive symptomatology among individuals with different patterns of FBA would not be expected, and, thus, stressors likely play a critical role in the link between FBA and the risk for depression.

It is well established that stress plays a crucial role in the onset and maintenance of depression (Billings, Cronkite, & Moos, 1983; Brown & Harris, 1989; Hammen, 1992; Kendler et al., 1995; Kessler, 1997; Lloyd, 1980a, 1980b). Depressed individuals tend to experience relatively more stressful events just prior to the onset of depression than do control subjects (Lloyd, 1980b). Moreover, stress incrementally adds to the prediction of impaired child functioning beyond the degree accounted for by having a depressed parent (Billings et al., 1983). Although there are findings of a strong link between major stressors and depressive symptoms, there is relatively little data that addresses the impact of minor and chronic events on child outcomes in families with a depressed parent. A few such studies have indicated that childhood depression is associated with chronic stress (Depue & Monroe, 1986; Rudolph et al., 2000). Furthermore, self-reported child emotional and behavioral problems are predicted by reports of daily hassles in 10- to 15-year-olds (Compas, Howell, Phares, Williams, & Giunta, 1989). However, to date no studies have examined the links between chronic stressors and vulnerability to depression. Although we have reported a linkage between FBA and SES, rather than stress per se, SES is an indicator of differential exposure to chronic stress: lower SES is associated with increased incidence of depression (Murphy et al., 1991) and there is evidence that the inverse

relation between SES and depression is mediated by exposure to stressful life events (Turner & Lloyd, 1999), although research on the causal link between SES and depression is scarce.

It is important to address the fact that subjects in the current study varied with respect to SES to a greater degree than in previously published findings. This likely stems from the sampling method used in the current study. Subjects were recruited from public schools, rather than from treatment centers, and thus subjects of a wide range of social classes were sampled. The standardized difference between the means of the two risk groups (Cohen's *d*) in our sample was 1.38, a relatively large value compared to previously reported findings, which have ranged from 0.15 (Dawson, Klinger, Panagiotides, Hill et al., 1992) to 1.59 (Henriques & Davidson, 1991). The large SES differences between risk groups in the current study may have contributed to our ability to detect a link between SES and FBA.

Another potential source of bias in the current study should be noted. LR subjects were selected to be lifetime-free any Axis I psychopathology. As outlined earlier, low SES is linked to a wide range of psychopathology. For example, an inverse relation has been observed between SES and psychosis (Hollingshead & Redlich, 1958), anxiety disorders (Murphy et al., 1991), alcohol abuse (Helzer, Burnam, & McEvoy, 1991) and schizophrenic disorders (Keith, Regier, & Rae, 1991) (although it should be noted that some disorders have higher prevalence rates among those of higher social class, e.g., bipolar disorder (Welner et al., 1979). Because of the inverse relation between SES and a wide range of psychopathology, LR subjects in the current study may have been preselected to be higher in SES. This sampling scheme may have created a larger SES difference between risk groups than would have been present if parents of LR subjects had been lifetime-free of depression only. Such preselection may have biased our results towards finding a link between SES and FBA.

These potential sources of bias imply that future studies examining the links between SES and FBA in groups that are more similar with respect to SES are needed to corroborate the results of the current study. Despite such caveats, however, the present study represents an important addition to the growing body of literature linking FBA to depression. Our results imply that researchers should derive measures of EEG FBA from a variety of reference montages, and should assess the roles of sociodemographic variables such as gender and SES in examining link between FBA and the risk for depression.

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