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Resting frontal brain activity: linkages to maternal depression and socio-economic status among adolescents

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Abstract

We tested the prediction that resting frontal brain asymmetry would be a marker of vulnerability for depression among adolescents. Baseline electroencephalographic (EEG) activity was recorded from 12 to14-year-old adolescents whose mothers had a history of depression (high risk group) and whose mothers were lifetime-free of axis I psychopathology (low risk group). High risk adolescents demonstrated the hypothesized pattern of relative left frontal hypo-activity on alpha-band measures. Such effects were specific to the mid-frontal region and generally consistent across reference montages. Socio-economic status (SES) also predicted alpha asymmetry. When the effects of SES and risk status were jointly assessed, SES contributed unique variance to the prediction of frontal brain asymmetry. The implications of the observed relations among maternal depression, SES, and frontal brain asymmetry are discussed.

Keywords: Frontal EEG asymmetry; Emotion; Risk for depression; Socio-economic status

1. Frontal brain asymmetry and depression

In this study, we assessed whether adolescents who are at-risk for depression differ in patterns of resting frontal brain activity when compared to low risk adolescents. We

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addressed this question because of evidence from a variety of sources indicating a linkage between unipolar depression and decreased activity of left relative to right hemisphere frontal brain regions (for reviews, see Davidson, 1995, 1998b; Davidson et al., 2002; Tomarken and Keener, 1998). Consistent with this conclusion are: (a) neurological studies indicating that the severity of depressive symptomatology is correlated with the proximity of a left-hemisphere lesion to the frontal pole (e.g., Morris et al., 1996; Pohjasvaara et al., 2002; Robinson and Downhill, 1995; Shimoda and Robinson, 1999); (b) regional cerebral blood flow (rCBF) studies showing that clinically depressed participants demonstrate relative decreases in left frontal activity when compared to non-depressed control participants (e.g., Baxter et al., 1989; Bench et al., 1992; Ebert et al., 1991; Martinot et al., 1990); (c) resting electroencephalographic (EEG) studies showing that clinically depressed individuals (Allen et al., 1993) or individuals characterized by elevated scores on the Beck Depression Inventory (Beck and Steer, 1987) demonstrate relative left frontal hypo-activity when compared to controls (Schaffer et al., 1983); and, (d) studies showing that transcranial magnetic stimulation of the left frontal cortex (which may well increase left frontal activity) produces clinical improvement in depressed individuals (e.g., George et al., 1997; Pascual-Leone et al., 1996). As a cautionary note, we should add that not all findings have been consistent in these areas (e.g., Dam et al., 1989; House et al., 1990; MacHale et al., 1998). In addition to these empirical linkages are theoretical perspectives proposing that left frontal dysfunction may be a neural substrate of core features of unipolar depression. For example, consistent with the approach-withdrawal model of frontal asymmetry (Davidson and Tomarken, 1989; Fox, 1991), several commentators have proposed that anhedonia reflects a deficit in a neural approach system, one component of which is the left frontal cortex (e.g., Davidson, 1998a).

2. Left frontal hypo-activity and vulnerability to depression: children of depressed mothers

Of prime importance in the present context are EEG studies indicating that resting frontal brain asymmetry may indicate heightened vulnerability to depression. For example, two studies have found that currently euthymic individuals who have a history of depression demonstrate left frontal hypo-activity relative to control participants (Allen et al., 1993; Henriques and Davidson, 1990). Unfortunately, studies of individuals with remitted depression cannot distinguish whether left frontal hypo-activity is a vulnerability factor for depression or a consequence of depression (Alloy et al., 1999). An assessment of at-risk populations who have not yet manifested depression represents a more direct test of whether left frontal hypo-activity indicates vulnerability. One such population is children of depressed parents. Such children exhibit a range of negative outcomes and psychiatric diagnoses compared to children of parents without a psychiatric history (Downey and Coyne, 1990; Gelfand and Teti, 1990) and appear to be at particularly heightened risk for developing depression (Hammen, 1991; Warner et al., 1992; Weissman et al., 1992, 1997).

Several studies have found that infants of depressed mothers do in fact exhibit left frontal hypo-activity (e.g., Dawson et al., 1997; see also Field et al., 1995; Jones et al., 1997).

Dawson and her colleagues also have linked left frontal hypo-activity in infants of depressed mothers to decreased positive affect and increased negative affect during interactions (Dawson et al., 1992a, 1999a,b). To date, studies of frontal brain asymmetry in children of depressed mothers have concentrated on infants. One goal of the present study was to investigate whether adolescent offspring of mothers with a history of depression demonstrated the same pattern of relative left frontal hypo-activity that has been observed in previous studies with currently depressed adults, adults with a history of depression, and high risk infants. To test this hypothesis, we compared patterns of resting frontal EEG asymmetry in young adolescent (12–14-year-old) offspring of depressed and non-depressed mothers.

There were several reasons why we assessed children in this age range. First, the presence of left frontal hypo-activity in adolescent offspring 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). Thus, left frontal hypo-activity in adolescent offspring of depressed mothers would indicate the presence of a potential indicator of risk at a point in time that immediately antedates the dramatic increase in the incidence of depression. Third, although the prevalence rate of depression in preadolescence is comparable in boys and girls, by adulthood nearly twice as many women are diagnosed with depression as men (Nolen-Hoeksema and Girgus, 1994). Thus, both increases in depressive symptoms and sex differences in such symptoms first emerge during adolescence. Although prior studies have not typically found sex differences in the linkages between frontal brain asymmetry and depression, this is a largely unexplored area. We sought to examine the interrelations among sex, differential risk for depression, and frontal brain asymmetry in adolescents at high and low risk for depression.

3. Relations with socio-economic status

We also assessed the relation between socio-economic status (SES) and frontal brain asymmetry. A number of epidemiological studies have indicated an inverse relation between social class and rates of unipolar depression (Kaplan et al., 1987; Leventhal and Brooks-Gunn, 2000; Murphy et al., 1991; Pearlin and Johnson, 1977; Weissman and Myers, 1978), as well as other psychiatric illnesses (Dohrenwend, 2000; Goodman, 1999; Hollingshead and Redlich, 1958; Rushing and Ortega, 1979; Srole, 1962; Williams, 1990). However, not all findings have been consistent (e.g., Weissman et al., 1991; Weissman and Myers, 1978), and, in other cases, there is debate concerning the causal direction of the linkage between social class and unipolar depression (e.g., Fox, 1990; Rodgers and Mann, 1993). Despite these caveats, the available evidence suggests that social class may often be implicated in the etiology of depression.

If lowered socio-economic status is a risk factor, it may moderate relations that have been observed between other risk variables (e.g., maternal history) and frontal brain asymmetry or between frontal brain asymmetry and depression. Alternatively, from a mediational perspective, SES could be a distal causal factor, the effects of which are mediated by other more proximal variables (e.g., maternal history). Unfortunately, prior findings linking

frontal brain asymmetry and depression have failed to adequately examine the potential role played by SES. First, many investigators have not reported the socio-demographic composition of their samples (e.g., Allen et al., 1993; Dam et al., 1989; Dawson et al., 1992a). Second, among studies that have reported socio-demographic information, most have not examined linkages between SES and both the occurrence of mood disorders and patterns of frontal brain asymmetry (e.g., Henriques and Davidson, 1990; Morris et al., 1996; Robinson et al., 1984; Robinson and Price, 1982; Robinson and Szetela, 1981; Starkstein et al., 1987). Third, some samples have been characterized by restricted range on SES measures. For example, in some EEG studies the clear majority of the participants were economically disadvantaged mothers and their infants (e.g., Dawson et al., 1992a,b; Field et al., 1995; Jones et al., 1997), whereas in other studies college students, a relatively homogenous group, have served as participants (Davidson et al., 1985; Schaffer et al., 1983). To our knowledge, only one frontal EEG study has examined the correlation between frontal brain asymmetry and SES (Henriques and Davidson, 1991). Although this study failed to find a significant relation, a more systematic investigation of this question is necessary. The current study used a sample recruited from a metropolitan community, and thus participants varied widely with respect to SES. We sought to examine the main and interactive effects of SES and risk status on frontal brain asymmetry.

4. Effects of reference montage

We assessed the relations among risk status, SES, and frontal asymmetry using three different EEG reference montages. There is evidence that the linkages between EEG asymmetry measures and measures of emotion or psychopathology are not always consistent across difference referencing schemes (for reviews, see Davidson, 1998b; Hagemann et al., 1998; Reid et al., 1998). Illustratively, Reid et al. (1998) assessed frontal brain asymmetry in depressed and non-depressed adults and found significant group differences only during the first 2 min of EEG recording using a linked-mastoid reference. There were no significant between-group differences using average and Cz reference montages. Published findings examining the relation between frontal brain asymmetry and risk for depression in infants have typically examined Cz-referenced data (e.g., Dawson et al., 1992a,b; Field et al., 1995), although others (e.g., Dawson et al., 1999b) have employed a linked-mastoid reference strategy. In the present study, to attend to the consistency issue, we included three reference montages (Cz, computer-averaged-ears, and average).

In sum, we addressed whether high and low risk adolescents differ in patterns of resting frontal brain asymmetry. In addition, we assessed the roles of sex and SES in predicting frontal brain asymmetry and whether these two factors moderated the effect of risk status on frontal brain asymmetry. We predicted that adolescent offspring of mothers with a history of depression would demonstrate relative left frontal hypo-activity compared to adolescent offspring of non-depressed mothers. We did not have strong a priori hypotheses concerning the link between frontal brain asymmetry and SES or sex. However, we expected that, if relations were found, left frontal hypo-activity would be linked to female sex and to lower SES. To test these hypotheses, we used multiple EEG reference montages.

5. Method

5.1. Participants

Participants were recruited from a larger sample of 240 adolescents and their mothers who were already participating in a study investigating the development of depression in adolescents. This larger sample was 54.2% female, 82% Caucasian, 14.7% African–American, and 3.3% other (Hispanic, Asian, Native American). The sample was pre-dominantly lower-middle class to middle class with a mean SES (Hollingshead, 1975) of 41.84 (S.D. = 13.25).

Participants for the larger study were recruited by letters 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 ever experienced any of 24 medical conditions such as diabetes, cancer, heart disease, and depression, or if they had ever taken any of 34 medications. Of the 1495 parents, who returned these questionnaires, telephone screening interviews were conducted with the 587 who had endorsed either a history of depression, use of antidepressants, or no history of psychopathology. Based on these screening calls, 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 (SCID, Spitzer et al., 1990). To assess inter-rater reliability of the SCID, a subset (20%) of audio-taped interviews was evaluated by a second interviewer blind to the ratings of the original interviewer. The kappa coefficient (Cohen, 1960) indicating chance–corrected agreement was 0.88 for SCID diagnoses of mood disorders.. Families were excluded if mothers indicated a history of solely non-affective psychiatric disorders, or if a parent or child had serious medical problems. The final high risk sample included 185 mothers who indicated a history of depressive disorders (i.e., major depression, dysthymia, depression not otherwise specified, and 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. Participants 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.

Of the 50 high risk and 20 low risk participants from the larger study who were contacted to participate in the current study, 32 high risk and 15 low risk participants agreed to participate in the resting EEG recording. Among those who participated, two high risk participants and one low risk participant were excluded from analyses because they were not right-handed, as assessed by the Edinburgh inventory (Oldfield, 1971). Five high risk participants and one low risk participant were excluded from analyses due to other issues that compromised the validity of the resting EEG recording for the present purposes (e.g., excessive fatigue during the session, medication use). Thus, 25 high risk (11 male) and 13 low risk (7 male) participants were included in the current analyses. Participants were

compensated US$ 30. The relatively greater number of high risk than low risk participants in the current study reflects the distribution of the larger participant pool from which these participants were drawn. A primary goal of the larger ongoing study was to investigate the conditions under which at-risk youths develop depression.

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 participants 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 to 14.0-year-old at the time of their EEG recording, high risk Mean = 13.1 (S.D. = 0.3); low risk Mean = 13.0 (S.D. = 0.4). The two groups did not significantly differ with respect to age, F(1,37) = 2.20, $P > 0.45$. Among participants in the current study, the SES of the low risk group (Mean = 53.2, S.D. = 6.9) was significantly higher than the high risk group (Mean = 37.3, S.D. = 13.3), F(1,37) = 16.38, $P < 0.001$. Participants in the current study and those from the larger cohort who did not participate in this study did not differ with respect to SES, F(1,216) = 0.01, $P > 0.90$. In addition, there was no significant interaction between risk group status and participant status (participated/did not participate) in SES, F(1,216) = 2.61, $P > 0.11$.

5.2. Measures

5.2.1. Psychopathology

Adolescent psychopathology (i.e., mood disorders, anxiety disorders, behavior disorders, and substance use 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 et al., 1982) and with the *Longitudinal Interval Follow-up Evaluation for Children* (K-LIFE, Keller and Neilsen, 1988) at each follow-up assessment. 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 0.81 for mood disorders, 0.72 for anxiety disorders, and 0.80 for behavior disorders.

5.2.1.1. 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 by 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 et al., 1984; Smucker et al., 1986). The internal consistency of the CDI in this sample was 0.81 at the initial assessment.

Additionally, weekly adolescent depressive symptomatology was ascertained based on the K-LIFE (Keller and 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 DSM criteria for major depressive disorder, whereas lower scores denoted that the adolescent had not met criteria for major depressive disorder.

5.2.2. Socio-economic status

Household SES was assessed with the four factor index of social status (Hollingshead, 1975), the most frequently used measure of SES (Cirino et al., 2002; Edwards-Hewitt and Gray, 1995). 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. Then, 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.

5.3. Procedure

Participants 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. Participants 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 accord with previous work (e.g., Tomarken et al., 1990, 1992), participants were not given highly specific instructions concerning the resting baselines.

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). Participants 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.

5.4. 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 and Anneveldt, 1982). The cap was positioned on the head using the 10–20 international system (American Electroencephalographic Society, 1994; Jasper, 1958). Fifteen standard scalp locations from the 10 to 20 system were used: F3, F4, F7, F8, T3, T4, T5, T6, P3, P4, C3, CZ, C4, Pz, and Fz. In addition, a forehead ground was used and tin drop electrodes from the cap were used to record from the left and right earlobes (A1–A2). Nine millimeter 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. Electrode impedances for EEG sites were under 5 kΩ, and impedances for homologous sites were within 1 kΩ of each other. Through pre- and post-recording checks we documented that impedances changed minimally during the course of the experiment.

Raw EEG and EOG signals were amplified and filtered using Grass Model 12 A5 AC pre-amplifiers (bandpass at half-voltage cut-off points 1 and 100 Hz for EEG and 1 and 30 Hz for EOG; 60 Hz notch filter in, filter rolloff = 6 dB per octave). The gain was set at 30,000 for EEG channels and 5,000 for EOG channels. Data were digitized at 1024 Hz using an Analogue Devices RTI-815A analogue to digital converter interfaced to the signal acquisition package Snapstream (HEM Inc.). Eight 1 min resting baselines, four with eyes-open and four with eyes-closed, were collected. All placements were referenced to the vertex (Cz) during the initial recording. A set of 50 μV sine waves at several different frequencies (e.g., 10 Hz) were used to calibrate the digitized EEG and to assess the technical integrity of the recording system. Calibration assessments 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 a computer-averaged-ears reference and an computer-averaged reference (see Henriques and Davidson, 1990). Averaged-ears EEG power at a given site is the difference between activity at that site and the averaged power recorded 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. At least one of the three referencing schemes used here (Cz, averaged-ears, or average) has been used in previous EEG studies on the correlates of frontal asymmetry.

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 were 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 participant 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.

Consistent with the general procedures used in prior research on resting frontal asymmetry (e.g., Tomarken et al., 1992), a natural log transformation was used to normalize the distribution of power density values of a given baseline trial. We then computed weighted means separately for the eyes-open and eyes-closed baselines for each participant. We weighted by the number of chunks within each baseline. In the next step, we computed the average of the eyes-open and eyes-closed baselines to generate a composite measure of EEG power density. Such composite values were computed for each combination of site, band, and reference montage. Finally, asymmetry scores were computed for each combination of region, band, and reference montage by subtracting power density in the left-hemisphere

site from power density in the homologous right hemisphere site (i.e., log right minus log left). The high risk and low risk groups did not differ in the total number of artifact-free chunks per participant used in computations of the composite power and asymmetry measures (high risk Mean = 176.08, S.D. = 81.61; low risk Mean = 208.23, S.D. = 93.47, $t(36) = 1.10$, $P > 0.25$).

To test hypotheses, we 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 activity in that region (Davidson, 1988; Miller and Tomarken, 2001; Pfurtscheller, 1986; Pfurtscheller and Klimesch, 1991) higher values on the asymmetry metric denote greater relative left frontal activity. The selection of the 8.5–12.5 Hz band as the focus of hypotheses merits comment given the small number of prior asymmetry studies that have assessed adolescents. The clear majority of prior studies indicating linkages between frontal EEG asymmetry and emotion or psychopathology have used either adults or infants. Investigations of the relation between frontal brain asymmetry and 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 and Davidson, 1990, 1991). Whereas the dominant EEG frequency band in very young children is clearly lower (Marshall et al., 2002), the relative proportion of slow wave activity in children decreases with age (Benninger et al., 1984; Colon et al., 1979; Matousek and Petersen, 1973), until about 10 years of age (Benninger et al., 1984; Gasser et al., 1988; Matousek and Petersen, 1973). Concomitant with the decrease in slow wave power during childhood are increases in faster frequency activity (e.g., alpha 2 band activity, Gasser et al., 1988; John et al., 1980; Matousek and Petersen, 1973).

Participants in the current study ranged in age from 12.2 to 14.0-year-old. Prior results would indicate that the majority of the transition from lower to higher frequency activity has been completed by this age (Gasser et al., 1988). For this reason, our primary focus of analyses was the adult alpha-band of 8.5–12.5 Hz. Our decision was consistent with the approach used by Kentgen et al. (2000), who assessed frontal EEG asymmetry among adolescents using an alpha-band equivalent of 7.8–12.5 Hz. We also report the results of exploratory analyses of other bands, with a particular interest in the theta band (4–7 Hz) containing frequencies immediately below the alpha range.

6. Results

6.1. Depressive symptoms

We examined CDI scores from four of the yearly assessments to examine whether high and low risk participants differed on symptoms of depression prior to or after the EEG recording. Across the two yearly assessments preceding and the two yearly assessments following the EEG session, the mean low risk CDI was 3.9 (S.D. = 3.7) and the mean high risk CDI was 4.5 (S.D. = 3.4). Thus, both groups clearly scored in the non-depressed range. Separate *t*-tests on risk status conducted at each of the four time points revealed the absence of any differences with respect to CDI scores, all t's < 0.50, all P's > 0.25. Consistent with these results, an omnibus risk status X time ANOVA failed to yield any significant main effects or interactions, all P's > 0.17.

During the eight weeks prior to the EEG session, the week of the EEG session, and the eight weeks following the EEG session, all participants averaged less than 2 (i.e., possible mild depressive symptoms) on the retrospective measure of weekly depressive symptoms (potential range = 1–6). All low risk participants received scores of one (no depressive symptoms) on this scale for every week during this time period. With the exception of four adolescents, all high risk participants received scores of two or below during this time period (i.e., mild symptoms of major depressive disorder). The remaining four received scores of three or four on this measure (indicating some symptoms of major depressive disorder and impairment, but falling short of the criteria for major depressive disorder). Thus, no low risk and high risk participants met criteria for major depressive disorder during the two-months prior to and the two months after the EEG recording. When the analyses reported below were redone with those four individuals who demonstrated symptoms of major depressive disorder removed, the results and conclusions were unchanged.

6.2. Lifetime criteria for mood disorders

Based on the K-SADS-E administered at baseline and K-LIFE administered at the first yearly follow-up interview, no low risk participant met lifetime criteria for any mood disorder. One high risk participant met lifetime criteria for dysthymia. When the analyses reported below were redone with this individual removed, the results and conclusions were unchanged.

6.3. Electroencephalographic data

6.3.1. Effects of risk status on mid-frontal alpha asymmetry

As noted above, the primary focus of analyses was the alpha (8.5–12.5 Hz) frequency band. Because the majority of prior studies linking frontal brain asymmetry to depression have focused on the mid-frontal (F3/F4) recording sites, we focused on measures of alpha asymmetry in this region. We predicted that high risk participants would demonstrate greater relative left frontal hypo-activity (greater relative left versus right alpha-band power) than low risk participants.

Table 1 shows mean log-transformed alpha power density (in μV) values for the mid-frontal sites (F4 and F3) and mean asymmetry scores [ln(F4) − ln(F3)] derived from the three reference montages for males and females. Recall that more positive asymmetry scores indicate greater relative left frontal activity. Because of how the asymmetry metric is computed, a main effect of risk status on asymmetry values is equivalent to an interaction between risk status and hemisphere on log power density values. Analyses used to test hypotheses in the current study focused on asymmetry values rather than on log power density. When analyses were done on log power values from each of the three reference montages with hemisphere as a factor, no main effects of risk status were observed that would indicate between-group differences on overall power averaged across the two frontal sites (all P's > 0.90). In addition, no between-group differences were yielded by separate analyses of F3 and F4 log power density (all P's > 0.60). These results reflect the likelihood that a high proportion of the between-subject variability in power is due to skull thickness and other factors that are not of substantive interest. For these reasons, to simplify the

Table 1
Mid-frontal (F3/F4) alpha-band log power density (in μV) and asymmetry for and low risk adolescents

	High Risk			Low risk		
	F3 power	F4 power	F3/F4 asymmetry	F3 power	F4 power	F3/F4 asymmetry
Averaged-ears						
Male	1.200 (0.579)	1.208 (0.572)	0.009 (0.049)	1.448 (0.353)	1.496 (0.372)	0.047 (0.041)
Female	1.634 (0.540)	1.629 (0.536)	−0.004 (0.067)	1.320 (0.572)	1.366 (0.551)	0.046 (0.057)
All	1.442 (0.588)	1.444 (0.581)	0.001 (0.059)	1.380 (0.451)	1.450 (0.448)	0.047 (0.047)
Average						
Male	0.388 (0.589)	0.379 (0.563)	−0.009 (0.094)	0.760 (0.558)	0.796 (0.579)	0.039 (0.126)
Female	0.825 (0.576)	0.824 (0.574)	−0.001 (0.120)	0.509 (0.604)	0.600 (0.612)	0.091 (0.086)
All	0.633 (0.611)	0.629 (0.601)	−0.004 (0.107)	0.644 (0.570)	0.706 (0.578)	0.061 (0.114)
Vertex (Cz)						
Male	0.932 (0.637)	0.953 (0.598)	0.021 (0.092)	1.200 (0.553)	1.172 (0.543)	−0.027 (0.082)
Female	1.059 (0.576)	1.054 (0.580)	−0.005 (0.056)	0.739 (0.721)	0.844 (0.709)	0.105 (0.035)
All	1.002 (0.594)	1.010 (0.578)	0.007 (0.073)	0.987 (0.653)	0.621 (0.172)	0.034 (0.093)

Note: High risk male $N = 11$. High risk female $N = 14$. Low risk male $N = 7$. Low risk female $N = 6$. Standard deviations are indicated in parentheses.

presentation of results, we report below only the results of analyses performed on asymmetry values.

Fig. 1 shows the mean log-transformed mid-frontal alpha asymmetry values, derived from three reference montages, for low risk and high risk adolescents. This figure indicates that across all three montages, there was greater relative left frontal activity in the low risk group compared to the high risk group. The results of risk status (low risk/high risk) X sex (male/female) ANOVAs performed on computer-averaged-ears referenced and average referenced mid-frontal EEG asymmetry values were consistent with these observations. The analysis of computer-averaged-ears referenced data revealed a significant main effect of risk status, $F(1,37) = 5.49$, $P < 0.05$, but no significant effects of sex, $F(1,37) = 0.23$, $P > 0.50$, or the risk status X sex interaction, $F(1,37) = 0.09$, $P > 0.50$. Similarly, the analysis of

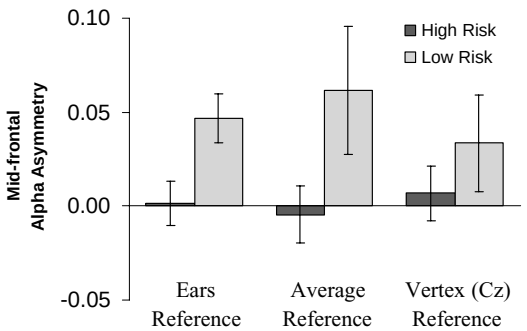

Fig. 1. Mid-frontal (F3/F4) alpha asymmetry [ln(left) − ln(right)] across three reference montages for high risk ($N = 25$) and low risk ($N = 13$) adolescents. Error bars indicate one standard error of the mean.

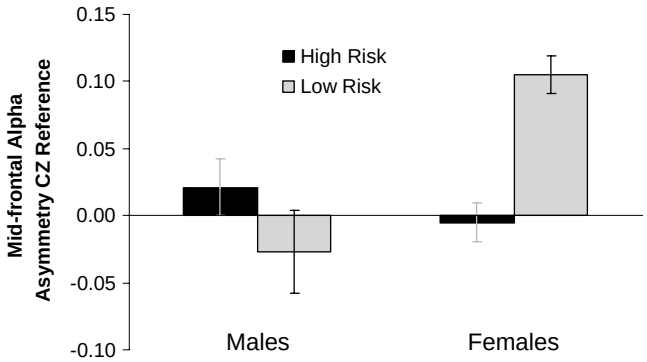

Fig. 2. Mid-frontal (F3/F4) vertex (Cz)-referenced alpha asymmetry [ln(left) − ln(right)] for male and female high and low risk adolescents. Error bars indicate one standard error of the mean.

average referenced mid-frontal asymmetry revealed a significant main effect of risk status, $F(1,37) = 5.37$, $P < 0.05$, but no significant main effect of sex, $F(1,37) = 0.50$, $P > 0.40$, and no significant interaction between risk status and sex, $F(1,37) = 1.44$, $P > 0.20$.

Although the marginal means for vertex (Cz) referenced asymmetry values shown in Fig. 1 indicates greater relative left frontal activity in the low risk group, Fig. 2 indicates more complex, interactive relations with sex. As this figure indicates, high risk females, but not high risk males, demonstrated relative left frontal hypo-activity when compared to their low risk counterparts. The analysis of Cz asymmetry in the mid-frontal region revealed no main effect of risk status, $F(1,37) = 1.21$, $P > 0.20$, no main effect of sex, $F(1,37) = 1.49$, $P > 0.20$, but a significant risk status X sex interaction, $F(1,37) = 10.49$, $P < 0.01$. Subsequent simple effects analyses indicated that, among females, high risk adolescents demonstrated significantly greater left frontal hypo-activity when compared to low risk participants, $F(1,19) = 19.43$, $P < 0.01$. No significant effects were yielded by the simple effects analysis performed on males' asymmetry values, $F(1,17) = 1.20$, $P > 0.25$.

6.3.2. Effects of risk status on mid-frontal EEG Asymmetry in other bands

We computed two-way risk status X sex ANOVAs on mid-frontal (F3/F4) EEG asymmetry in each of the six EEG bands extracted: delta (1.5–3.5 Hz), theta (4.0–7.0 Hz), alpha 1 (i.e., low alpha; 8.5–10.5), alpha 2 (i.e., high alpha; 11.0–12.5), beta 1 (13.5–19.5 Hz), and beta 2 (20.5–29.5 Hz). We assessed effects in alpha 1 and alpha 2 separately because: (1) in some previous studies, differential effects have been observed in these bands (e.g., Davidson et al., 2000); and, (2) the fact that our participants were young adolescents suggested that such effects might be particularly likely to occur (see the discussion of band selection in Section 5). Such analyses were computed for each of the three references. Because the number of ANOVAs was large, we used a step-down Bonferroni procedure to control for multiple significance tests (e.g., Westfall et al., 1999; Westfall and Young, 1992). Three sets of corrections were used (i.e., one per reference montage).

After step-down Bonferroni correction, there were highly significant main effects for risk status in the theta band on both computer-averaged-ears referenced [corrected $P < 0.001$,

low risk M (S.D.) = 0.071 (0.077); high risk (M) = −0.032 (0.060)] and average referenced [corrected $P < 0.001$, low risk M (S.D.) = 0.120 (0.117); high risk (M) =−0.037 (0.090)] mid-frontal asymmetry. We also found a significant main effect of risk status on average referenced delta band asymmetry [corrected $P < 0.025$, low risk (M) S.D. = 0.110 (0.136); high risk $M = -0.017$ (0.121)] and on Cz-referenced asymmetry in the low alpha-band (corrected $P < 0.02$). These significant effects all indicated that high risk participants showed greater relative power in the left relative to right frontal region for the target band. Thus, the direction of these effects parallels that of the alpha-band (8.5–12.5 Hz) effects reported above. No other significant effects were observed.

6.3.3. Effects of risk status on EEG alpha asymmetry in other regions

For each of the three references, we computed two-way risk status X sex ANOVAs on EEG asymmetry in each of five regions: lateral frontal (F7/F8), parietal (P3/P4), anterior temporal (T3/T4), posterior temporal (T5/T6), and central (C3/C4). Because the clear focus of our predictions was alpha asymmetry in the mid-frontal sites and because the number of ANOVAs was large, we once again used a step-down Bonferroni procedure to control for multiple significance tests. Across all three references, the only significant effects that emerged were main effects of region (all P's < 0.01). These effects reflected topographic differences in the patterning of asymmetry. Most importantly, there were no significant main effects or interactions involving risk status (all P's > 0.05).

Table 2 conveys the overall direction and strength of the relation between risk status and alpha-band asymmetry across regions. Presented are point biserial correlations between the dichotomous variable risk status (coded 0 for low risk and 1 for high risk) and measures of brain asymmetry [ln(right − ln(left)] in a given band. Consistent with the main effects of risk status on mid-frontal asymmetry presented above, the correlations between risk status and ears-referenced ($r = -0.37$) and average-referenced ($r = -0.36$) mid-frontal asymmetry are both significantly greater than 0. Although the correlation involving Cz-referenced frontal asymmetry is not significant, recall that the ANOVAs revealed a more complex risk status X sex interaction on this measure. Although the correlations involving lateral

Table 2
Correlations between risk status and alpha-band asymmetry across regions

Region	Reference montage		
	Averaged-ears	Average	Vertex (Cz)
Mid-frontal (F3–F4)	−0.37**	−0.36**	−0.16
Lateral frontal (F7–F8)	−0.24	−0.25	−0.09
Central (C3–C4)	0.15	0.16	0.08
Anterior temporal (T3–T4)	0.25	0.06	0.08
Posterior temporal (T5–T6)	−0.15	−0.19	−0.14
Parietal (P3–P4)	−0.17	−0.19	−0.35*

Note: $N = 38$. Point-biserial correlations are shown. Risk status coding: 0 = low risk, 1 = high risk. Mid-frontal correlations were evaluated at a per-correlation alpha level = 0.05. Within each reference montage, step-down Bonferroni corrections were applied to correlations involving the five other sites.

* Uncorrected $P < 0.05$, but step-down Bonferroni corrected $P > 0.15$.

** $P < 0.05$.

frontal asymmetry (F7/F8) are in the predicted direction, their magnitude is lower than that of the mid-frontal correlations and is not statistically significant. Overall, other than the aforementioned mid-frontal correlations, only one of the correlations shown in Table 3 was statistically significant when considered in isolation (Cz-referenced P3/P4; $P = 0.03$). Moreover, even this value was not statistically significant when step-down Bonferroni corrections were used to account for the total number of correlations computed among the five regions that were not of the focus of our initial hypotheses ($P = 0.15$).

6.3.4. Effects of socio-economic status

6.3.4.1. Zero-order correlations. One subsidiary goal was to assess the relation between SES and frontal asymmetry. This question is particularly salient in the present context because the high risk and low risk groups differed on SES. When participants in both risk status groups were pooled into one sample, we observed a significant overall correlation between SES and alpha-band mid-frontal asymmetry for two of the three reference montages, computer-averaged-ears reference $r = 0.57$, $P < 0.001$, average reference $r = 0.50$, $P < 0.001$, Cz reference $r = 0.16$, $P > 0.30$. These correlations indicate that higher SES predicted greater relative left frontal activity. Fig. 3 shows scatter plots depicting the relation between frontal brain asymmetry (derived from three reference montages) and SES, with risk status symbolically indicated. Although this figure makes evident the small number of low SES participants in the low risk group, it also clearly illustrates the relation between relative left frontal activity and SES.

To investigate further the relation between alpha asymmetry in the mid-frontal region and social class, correlations were computed separately for each risk group. Within the high risk group, frontal asymmetry measures derived using the computer-averaged-ears and average references both correlated significantly with SES, computer-averaged-ears reference $r = 0.56$, $P < 0.004$, average reference $r = 0.50$, $P < 0.01$, Cz reference $r = 0.14$, $P > 0.50$. Within the low risk group, there were no significant correlations between SES and frontal brain asymmetry, computer-averaged-ears reference $r = 0.04$, average reference $r = 0.05$, Cz reference $r = -0.03$, all P's > 0.80. Clearly, however, caution is necessary here because: (1) differences between relevant pairs of correlations (e.g., high risk computer-averaged-ears versus low risk computer-averaged-ears) were not statistically significant (all P's > 0.10); (2) there was a restricted range of SES in the low risk group that could significantly influence the magnitude of the observed correlation (low risk $M = 53.2$, S.D. $= 6.8$; high risk $M = 37.3$, S.D. $= 13.3$) and, (3) due to the differences in variability, comparisons of unstandardized beta weights are likely more appropriate than comparisons of correlations (e.g., Tukey, 1954). Such comparisons constituted the SES X risk status interaction effects tested in the multiple regression analyses reported below.

6.3.4.2. Multiple regression results. To investigate further the relations among SES, frontal brain asymmetry, and risk status, we conducted multiple regression analyses in which risk status, sex, and SES were specified as predictors of mid-frontal asymmetry in the alpha-band. These analyses were designed to test the unique effects of each of the three predictors on frontal asymmetry and to test for moderator effects. For example, a significant risk status X SES two-way interaction would suggest that the magnitude of the relation between SES and

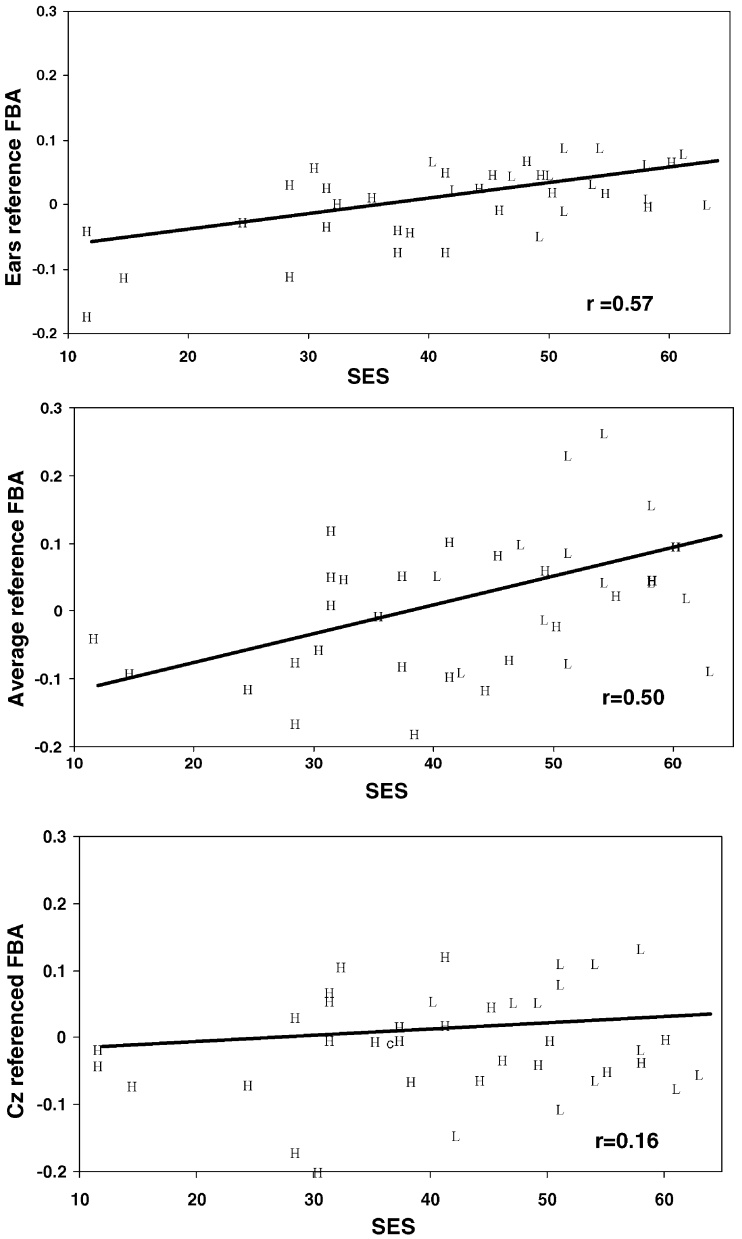

Fig. 3. Scatter plots of the relation between SES and mid-frontal (F3/F4) alpha asymmetry for each of three reference montages. Top panel: averaged-ears reference; middle panel: average reference; bottom panel: vertex (Cz) reference; H: high risk adolescents; L: low risk adolescents.

Table 3
Multiple regression analyses predicting mid-frontal alpha asymmetry

Predictors	Mid-frontal asymmetry measure		
	Ears reference	Average reference	Vertex (Cz)
First-order			
Risk status			
β	−0.067	−0.128	−0.122
Sr^2	0.003	0.011	0.010
Sex			
β	0.094	−0.096	−0.175
Sr^2	0.009	0.009	0.030
SES			
β	0.529**	0.432*	0.096
Sr^2	0.191	0.128	0.006
$R^2_{Increment}$ (set)	0.336**	0.270*	0.064
Two-way interactions			
Risk status × sex			
β	0.005	0.136	0.631**
Sr^2	0.000	0.011	0.226
Risk status × SES			
β	0.211	−0.069	−0.249
Sr^2	0.011	0.001	0.016
Sex × SES			
β	−0.170	−0.243	0.120
Sr^2	0.016	0.032	0.008
$R^2_{Increment}$ (set)	0.054	0.102	0.277*
Three-way interaction			
Risk status × sex × SES			
β	−0.344	0.004	0.091
Sr^2	0.028	0.000	0.002
$R^2_{Increment}$ (set)	0.028	0.000	0.002

A hierarchical structure was used in which first-order terms were entered in an initial step, followed by two-interaction terms, and the three-way interaction in subsequent steps. For first-order terms, the β's are standardized coefficients. For second-order terms, the β's are the unstandardized coefficients for terms that are the product of standardized variables but are not standardized themselves. This procedure was followed in order to yield test statistics and probability values that are invariant with respect to the unstandardized analyses of the raw data values. Sr^2: squared semi-partial correlation. $R^2_{Increment}$ (set): the increment in proportion of variance accounted for by the set of predictors entered in a given step.

* $P < 0.025$.

** $P < 0.005$.

frontal asymmetry is conditional on risk status and, conversely, that the relation between risk status and frontal asymmetry is conditional on level of SES.

A hierarchical structure (Cohen and Cohen, 1983) was used for the three analyses (one per reference). In the first step, the three predictors were entered simultaneously (risk status, sex, and SES). This step was used to test for the main effects of each predictor on frontal

asymmetry removing shared variance with the other predictors. In the second step, the three two-way interaction terms (risk status X SES, risk status X sex, sex X SES) were entered as a set. In the third step, we entered the risk status X sex X SES three-way interaction term. At each step, we tested the statistical significance of each of the individual regression coefficients in the set just entered and the significance of the incremental variance attributable to the set. To facilitate the interpretation of coefficients, we centered SES (i.e., expressed it as deviations from its mean, thus resulting in a transformed mean of 0, e.g., Aiken and West, 1991). We used dummy codes for the categorical variables of risk status (0 = low risk, 1 = high risk) and sex (0 = females, 1 = males). It is important to note that identical results and conclusions were yielded when alternative model-testing strategies were used (e.g., for descriptions of alternative approaches, see, e.g., Aiken and West, 1991).

Table 3 shows the results of the regressions on alpha-band asymmetry for each of the three references. To provide an interpretable metric, this table displays standardized regression coefficients β's for each first-order (i.e., main effect) term (risk status, sex, SES). The test statistics and P values for such first-order coefficients are identical to those for the unstandardized coefficients that were yielded by an analysis of the raw data values in their original metric. In the case of two- and three-way interactions, the coefficients shown in Table 3 are actually the unstandardized coefficients yielded by an analysis of interaction terms that were the product of standardized first-order terms. Such interaction terms were not, however, themselves standardized. By this means, we were able to present interaction coefficients that had both a reasonably interpretable metric and test statistics and significance levels identical to those yielded by analyses of the raw data values in their original metric (Aiken and West, 1991; Friedrich, 1982). Also shown in Table 3 are squared semi-partial correlations denoting the proportion of the total variance in asymmetry scores uniquely attributable to each predictor (see, e.g., Cohen and Cohen, 1983) and R^2 values indicating the increment in variance accounted for by each set of predictors.

As indicated by Table 3, the results of the regressions of mid-frontal asymmetry on the first-order terms (risk status, SES, and sex) were consistent across the ears referenced and average referenced montages. In each case, SES, but not risk status or sex, contributed significant unique variance to the prediction of alpha-band asymmetry (ears referenced $P < 0.005$, average referenced $P < 0.025$). The squared semi-partial correlation coefficients shown in Table 3 indicate that SES accounted for a notably higher proportion of the variance in ears referenced and average referenced frontal asymmetry scores than the other two predictors (see Table 3). We should emphasize that the effects shown for each of the three predictors in Table 3 are adjusted for the effects of the other two predictors in the equation (i.e., the three predictors were entered simultaneously as a set). When Cz-referenced mid-frontal asymmetry was the outcome variable, no effects for first-order terms were significant.

In subsequent steps testing for moderation, we entered the two-way and three-way interaction terms in the regression equations. As shown in Table 2, the only significant effect across all three dependent measures was the risk status X sex interaction on Cz-referenced mid-frontal asymmetry ($P < 0.005$). This effect was also yielded by the risk status X sex ANOVA reported above and reflects greater differences between the high and low risk groups among females relative to males. There were no significant two- or three-way interactions involving SES (all P's > 0.20).

6.3.4.3. Components of SES. We also examined the relations between the components of SES and alpha-band asymmetry. Our measure of SES (Hollingshead, 1975) is derived primarily from parental occupation, education, and marital status. We first calculated zero-order correlations between risk status and these three components of SES. To orient readers to the scaling and direction of relations, 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), and marital status was coded as either 0 (unmarried) or (1) married. The high and low risk groups differed on these components of SES in a manner that paralleled the differences on the composite SES index reported above (occupation $P < 0.001$; education $P < 0.005$; marital Status $P < 0.02$). Parents of low risk participants were more likely to have attained higher occupation and educational levels and were more likely to be married.

When participants in both risk status groups were pooled into one sample, we observed a significant overall correlation between occupation and alpha-band mid-frontal asymmetry for two of the three reference montages, ears reference $r = 0.50$, $P < 0.002$, average reference $r = 0.45$, $P < 0.01$, Cz reference $r = 0.06$, $P > 0.50$. We also observed a significant overall correlation between education and alpha-band mid-frontal asymmetry for two of the three reference montages, ears reference $r = 0.33$, $P < 0.05$, average reference $r = 0.38$, $P < 0.05$, Cz reference $r = 0.19$, $P > 0.20$. Finally, we observed a significant overall correlation between marital status and alpha-band mid-frontal asymmetry for one of the three reference montages, ears reference $r = 0.42$, $P < 0.0.01$, average reference $r = 0.20$, $P > 0.20$, Cz reference $r = 0.12$, $P > 0.40$. Thus, higher occupation, more years of education, and being married generally predicted greater relative left frontal activity.

7. Discussion

7.1. Primary hypotheses

The primary goal of the present study was to assess whether children of mothers with a history of depression demonstrated relative left frontal hypo-activity when compared to low risk children. Across the three reference montages assessed, analyses supported predictions. The risk status X sex ANOVAs performed on ears referenced and average referenced mid-frontal asymmetry values indicated that high risk participants demonstrated relative left frontal hypo-activity when compared to low risk participants.[1] The pattern of effects on the Cz-referenced mid-frontal asymmetry measures was more complex. The two risk status groups differed in frontal asymmetry among females but not among males. These latter findings are intriguing and may link up meaningfully with the evidence for sex differences in depression that emerge during early adolescence (e.g., Heller, 1993; Hankin et al., 1998; Nolen-Hoeksema and Girgus, 1994).

[1] As indicated by Fig. 1, the low risk group on average demonstrated relative left frontal hyper-activity (i.e., greater alpha suppression in the left relative to right hemisphere) whereas the high risk group demonstrated a more symmetrical pattern. In this regard, it is relevant to note that unselected adult participants typically demonstrate relative left frontal activity on these measures (Reid et al., 1998; Tomarken et al., 1992). Thus, although the high risk group did not demonstrate left frontal hypo-activity in an absolute sense, their pattern does appear to deviate from the norm.

From a broad perspective, each of the three references provided support for the notion that resting frontal asymmetry may indicate heightened vulnerability to depression. This is an important observation because, as noted above, questions have been raised about the degree to which mid-frontal EEG asymmetry findings are consistent across references (e.g., Hagemann et al., 1998; Reid et al., 1998). The degree of convergence that we found suggests that we may have tapped into a robust phenomenon.

The present results were also generalizable across several different EEG bands. For example, we found particularly notable effects of risk status on theta band measures of ears referenced and averaged referenced asymmetry and additional effects on delta band measures of average referenced asymmetry. This convergence across the lower-frequency EEG components may be related to the fact that participants were young adolescents. Our lower-band asymmetry effects merit replication and extension. Our alpha asymmetry effects were, however, not generalizable across EEG sites. The only significant effects that emerged were for the mid-frontal region.

7.2. Implications of risk status findings

Our results significantly extend previous findings indicating that relative left frontal hypo-activity may indicate vulnerability to depression. Prior studies using adult participants have compared non-depressed samples to either currently depressed (e.g., Schaffer et al., 1983) or remitted samples (Henriques and Davidson, 1990). As noted above, both comparisons do not allow unambiguous inference concerning whether resting frontal asymmetry indicates vulnerability. More compelling evidence has been provided by studies comparing infants of depressed and non-depressed mothers (e.g., Dawson et al., 1997; Jones et al., 1997). Our findings link up with these latter results and suggest that there may be continuity of risk that extends beyond infancy. If frontal brain asymmetry is an indicator of risk that demonstrates such continuity, it should be stable over time. Prior evidence suggests that resting asymmetry is moderately stable in both adults (Tomarken et al., 1992) and in infants and young children (e.g., Jones et al., 1997). Our findings mandate an examination of the stability of resting frontal asymmetry among adolescents.

Of course, if frontal brain asymmetry indicates differential risk for depression, it should predict the long-term onset and/or maintenance of depressive symptoms. In this regard, the 12–14 year age range that we have studied is ideal because this is the point in development immediately prior to the increased onset of depressive symptoms that occurs in mid-adolescence (e.g., Hankin et al., 1998; Nolen-Hoeksema and Girgus, 1994). There is a need for longitudinal studies that address whether those adolescents characterized by relative left frontal hypo-activity are most likely to demonstrate an increase in depressive symptoms and a higher proportion of diagnosable episodes over time. We believe that such effects are most likely to be observed in interaction with other factors (e.g., stressful events).

7.3. Effects of socio-economic status

We assessed the effects of SES because it has been largely neglected in prior studies of anterior brain asymmetry and because there is strong evidence for inverse relations between SES and rates of unipolar depression (e.g., Leventhal and Brooks-Gunn, 2000; Murphy

et al., 1991). Consistent with the latter results, in the present study high and low risk groups differed notably in mean household SES on the Hollingshead index. Our correlational results indicated reasonably strong relations between SES and mid-frontal alpha asymmetry for two of the three reference montages assessed. That is, higher SES predicted relative left frontal activity. We also found a significant relation between SES and mid-frontal asymmetry among high risk participants alone.

It is unclear precisely, why SES is correlated with mid-frontal asymmetry. The major theories concerning the linkage between SES and psychopathology are one basis for speculation (Johnson et al., 1999). According to social causation theory, the chronic stress and other adversities linked to low SES contribute to the onset of psychopathology. According to social selection theory, biological, and environmental factors contribute to the onset of psychopathology, which, in turn, induces downward social drift toward lower socio-economic classes. Although current research favors the social causation hypothesis in application to unipolar depression, there are findings that support both views (for a review, see Johnson et al., 1999).

Extensions of both these hypotheses might provide a basis for speculation about the nature of the relation between SES and frontal asymmetry. For example, a variant of the social causation hypothesis would be the proposal that the chronic stress and other adversities associated with low SES produce long-term changes in brain asymmetry. Although no human studies have addressed this issue, there is infrahuman evidence that stress can induce changes in lateralization of neurotransmitter functions that appears correlated with anxiety-related behaviors (e.g., Fride and Weinstock, 1988). In addition, there are a variety of factors other than chronic stress per se that are correlated with SES and could conceivably produce effects on brain asymmetry. Such factors include maternal warmth, peer group instability, social support, and cognitive stimulation (for a review, see, e.g., Dodge et al., 1994).

7.4. Joint effects of maternal history of depression and socio-economic status

Our multiple regression analyses addressed the unique and interactive effects of maternal history (denoted risk status), sex, and SES on measures of mid-frontal brain asymmetry derived from the alpha-band. Somewhat surprisingly, SES but not risk status significantly predicted asymmetry measures derived from the averaged-ears and average references. No other main effects or interactions were significant. In contrast, we observed a significant risk status X sex interaction on Cz-referenced frontal asymmetry values.

From a causal modeling perspective (e.g., Baron and Kenny, 1986; Bollen, 1989), the overall pattern of correlational and multiple regression results that we observed on ears referenced and averaged referenced frontal asymmetry might be taken to indicate that SES has a direct causal effect on frontal brain asymmetry but that maternal history of depression has only a weak direct effect at best. One possible model consistent with the data would specify that SES largely mediates the effects of maternal history of depression on brain asymmetry among children. This model would stipulate that: (1) maternal episodes of depression or related vulnerability factors induce a downward drift in SES; and, (2) lowered SES, in turn, is a proximal cause of changes in brain asymmetry among the children of such mothers. This model has features of both the social causation and social selection perspectives on the relation between SES and psychopathology.

Although such an interpretation might initially appear plausible, there are a host of reasons why it is premature. First, this conclusion is based on data that if, not cross-sectional in a strict sense, embody many of the features and limitations of cross-sectional data. Clearly, a more systematic evaluation of the causal relations among these variables would require a longitudinal design involving repeated assessments over time and across generations (see, e.g., Johnson et al., 1999). Estimates of causal parameters can be seriously misleading when cross-sectional designs are used to model effects that, by their very nature, occur over time (e.g., Cole and Maxwell, 2003).

A second issue that complicates interpretation of our regression analyses is the problem of omitted variables (e.g., Berk, 2004; Tomarken and Waller, 2003). Undoubtedly, there are a number of relevant variables that are correlated with risk status, SES, and/or frontal brain asymmetry and may be implicated in a complex, multi-factorial causal nexus. For example, we did not assess chronic stress or frontal brain asymmetry in the parents of adolescents. Both factors could well have causal linkages to the variables assessed in the present study (e.g., Field et al., 1995; Kessler, 1997). It is well known that the omission of important predictors from regression analyses can strongly bias estimates of coefficients and result in highly misleading causal inferences (e.g., Gollob, 1991; Reichardt and Gollob, 1986).

There are additional factors limit that limit conclusions. Via effects on univariate and joint distributions, the general absence of low SES participants from the low risk group and the overall approach used to sample participants might have significantly affected the results of the multiple regression analyses (e.g., McClelland and Judd, 1993; Sher and Trull, 1996). For example, these factors might have significantly lowered the power of tests for moderation. In addition, risk status was treated as a dichotomous variable. A continuous measure of maternal history might have yielded more robust effects. Finally, some prior findings in this area may be inconsistent with a model stipulating that maternal depression has only indirect effects on brain asymmetry that are mediated by SES. For example, this model cannot easily accommodate evidence that infants of depressed and non-depressed mothers can differ on frontal EEG asymmetry even when the two groups fail to differ on measures of SES (e.g., Field et al., 1995).

In sum, although the results of our regression analyses are intriguing, they should be viewed with caution and certainly require replication and extension in the context of a longitudinal design that includes additional variables. We should also note that the ultimate goal of such a research program is not simply to clarify the effects of maternal history of depression and SES on frontal brain asymmetry. Rather, it is to examine the joint effects of all three variables on the onset and maintenance of depression.

8. Summary and conclusions

In accord with predictions, we found that adolescent offspring of mothers with a history of depression demonstrated relative left frontal hypo-activity relative to low risk adolescents. At least some support for this hypothesis was found across all three reference montages assessed. Such effects were specific to the mid-frontal region. We also found that lower SES predicted greater relative left frontal hypo-activity. This linkage remained significant even when we controlled for maternal history of depression. Further longitudinal studies

that include a broader array of variables are necessary to clarify the precise causal linkages among these variables.

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