Regional electroencephalogram (EEG) spectral power and hemispheric coherence in young adults born at extremely low birth weight

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A B S T R A C T

Objectives: We examined the effects of extremely low birth weight (ELBW < 1000 g) on adult brain functioning.
Methods: We measured baseline regional EEG spectral power and hemispheric coherence in a cohort of 154 (M age = 23 years) non-impaired young adults who were born at ELBW (n = 71; M birth weight = 874 g, M gestation age = 27.5 weeks) and in a control group of full-term adults born at normal birth weight (NBW; n = 83).
Results: ELBW adults exhibited significantly more power in the low EEG frequency bands (delta and theta) and less in the high EEG frequency bands (alpha and beta) than the NBW adults. This relative difference in the amount of high to low-frequency power was especially salient in the frontal regions. ELBW adults also exhibited significantly more short-distance EEG coherence in the right hemisphere compared to the NBW adults.
Conclusions: Our results suggest that even among ELBW survivors without impairments, adverse events early in life may result in subtle neurological abnormalities.
Significance: This study provides a unique EEG profile of young adult survivors of ELBW showing that maturational delays of the brain may persist into late adolescence and emerging adulthood.

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1. Introduction

The development of the central nervous system (CNS) begins during the gestational period and proceeds post-natally as a series of genetically regulated cascades in which early occurring events exert causal influence over subsequent phases of neural ontogenesis (Feng et al., 2007; Nowakowski and Hayes, 1999). Brain maturation is exquisitely sensitive to environmental input and is compromised by adverse pre-, peri- and early post-natal experiences (Blair and Stanley, 1988; Cannon et al., 1993; Fraser et al., 2007; Kaufman et al., 2000; Meaney et al., 1991; Rees and Harding, 2004; Rees and Inder, 2005; Schore, 2001).

Adverse events early in life such as being born at extremely low birth weight and being born prematurely are examples of pre- and peri-natal trauma that are known to alter normal brain development. Non-human primate models of premature birth indicate that abrupt termination of the intrauterine environment is associated with white matter damage as well as subtle deficits in cerebral architecture and function (Dieni et al., 2004; Rees and Inder, 2005). Diffuse cerebral white matter lesions are one of the most common forms of neuropathology reported in premature human infants (Volpe, 2003). Magnetic resonance imaging (MRI) studies in human preterm populations indicate that other common forms of brain abnormality include enlargement of the lateral ventricles, decreased cortical surface area, decreased cortical complexity and regional reductions in cortical and sub-cortical gray matter volume (e.g., Ajayi-Obe et al., 2000; Maalouf et al., 1999; Nosarti et al., 2002; Peterson et al., 2000).

1.1. Development of EEG power and frequency

The electroencephalogram (EEG) represents another relatively non-invasive way to examine brain functioning and maturation in survivors of preterm birth (Thorpe, 1990). Background EEG patterns of preterm infants have been described by various researchers (e.g., Dreyfus-Brisac, 1962; Dreyfus-Brisac and Monod, 1987;
Lombroso, 1985), with the aim of establishing a set of standard criteria for the normative development of the premature infant's EEG. A primary emphasis of this work has been on the diagnostic and prognostic value of neonatal EEG (Tharp et al., 1981). Drastic changes in background EEG activity occur within the first few weeks and months of a premature infant's life, allowing experienced clinicians to estimate conceptional age within 1 week. Characteristic EEG patterns that typify the early preterm infant begin to disappear with increasing maturation (Biagioni et al., 1994; Hayakawa et al., 2001) as the preterm infant's EEG activity becomes morphologically similar to that of term-born infants. Changes in the cerebral electrical activity of preterm infants parallel changes in cortical structure (Biagioni et al., 2007).

Studies of EEG maturation in typically developing populations likewise show specific age-related changes (see Bell, 1998; Bell and Wolfe, 2008, for reviews). Landmark developmental studies by Lindsley (1939) and Smith (1938, 1941) relied on visual analysis techniques to identify the emergence of a 3- to 5-Hz occipital rhythm, which increased to 6–7 Hz by the beginning of the first year. This infant occipital rhythm is structurally and functionally analogous to the adult occipital alpha, which oscillates at a higher frequency range (8–13 Hz). In his longitudinal study, Smith (1941) noted that the adult-like 10 Hz occipital rhythm did not fully emerge until 16 years of age.

More recent developmental studies have relied on computerized techniques of power spectral analysis in order to derive EEG band power density within pre-specified frequency ranges. A general trend in EEG development is towards decreased power in the low-frequency bands (delta and theta; 1–7 Hz) and greater power in the high-frequency ranges (alpha and beta; 8–20 Hz) across multiple scalp locations (e.g., Clarke et al., 2001; Gibbs and Knot, 1949; Hagne, 1968, 1972; John et al., 1980; Matousek and Petersen, 1973; Mizuno et al., 1970; Somsen et al., 1997). Age-related changes in EEG band power distribution proceed along a posterior-to-anterior dimension (Gasser et al., 1988). High amplitude delta and theta activity in older children can be indicative of neurological and cognitive dysfunction (Gasser et al., 2003). Developmental changes in EEG power spectra reflect the maturation of neurophysiological systems, including the excitability of neuronal groups and the establishment of cortical connections (Nunez, 1981).

Relatively few studies have examined EEG power spectra in children who were born pre-term. Bell et al. (1991) recorded EEG during active sleep from healthy term and preterm neonates at 3 days of age. Preterm neonates exhibited greater absolute power in the delta range, with delta I (<1 Hz) and delta II (2–3 Hz) power being inversely related to gestational age. These findings concur with other research that has reported greater delta amplitude in preterm compared to term neonates (Havlícek et al., 1975; Koterazawa et al., 1990). In contrast, the relation between power in the beta band (i.e., >14 Hz) and gestational age appears to obey a quadratic function (Bell et al., 1991). More recently, Rozhkova (2008) recorded EEG during quiet wakefulness in a group of premature and term-born schoolchildren with educational problems. Compared to their term counterparts, premature schoolchildren showed greater power in the theta I (3.6–5 Hz) and high-frequency beta (20.1–30 Hz) and gamma (30.1–40.2 Hz) bands. The observed increase in gamma power may reflect a compensatory mechanism in schoolchildren who were born prematurely similar to the increase in gamma synchrony that has been reported to be associated with age-related cognitive decline (Paul et al., 2005). The EEG spectral characteristics of prematurely born children may be attributed to dysregulated processes in neural ontogeny resulting from the initial developmental insult. Specifically, disturbance of thalamocortical regulatory structures has been hypothesized to underlie the EEG differences between premature and term-born children (Rozhkova, 2008).

1.2. Development of EEG coherence

In addition to EEG spectral power, measures of EEG coherence have also been related to brain development and functioning. EEG coherence yields a cross-correlation value in the frequency domain between two spatially distinct electrode sites. Functionally, coherence has been suggested to reflect the number and strength of corticocortical synaptic connections, with greater coherence values indicating increased neural coupling between brain regions and decreased coherence values indicating more cortical differentiation (Nunez, 1981; Thatcher, 1992). According to the two-compartment model, EEG coherence reflects the activity of short and long axon fiber systems (Thatcher et al., 1986). The ratio of short-to-long axon fibers in this model determines the rate of change in EEG coherence with inter-electrode distance. Hemispheric differences in the short-to-long ratio have been reported, with the left hemisphere exhibiting more short distance axonal connections and greater cortical differentiation than the right hemisphere (Thatcher et al., 1986; Tucker et al., 1986). A right hemisphere bias toward more long distance axonal connections is consistent with findings indicating a higher white to gray matter ratio in the right, compared to the left, cerebral hemisphere (Gur et al., 1980). Neurophysiological mechanisms such as axonal sprouting, synaptogenesis, synaptic pruning and myelination likely drive increases in EEG coherence (Thatcher, 1992). It is important to note that high EEG coherence values are not directly related to greater maturation. For example, decreased coherence has been associated with higher intelligence scores, increased speed and efficiency of cognitive processing, and mastery of key developmental milestones (Bell and Fox, 1996; Thatcher et al., 1983, 2005).

Since EEG coherence provides an index of cortical network dynamics, it is a useful tool for examining brain connectivity in survivors of extreme prematurity. Als et al. (2004) found that a Newborn Individualized Developmental Care Program instituted shortly after birth increased EEG coherence at 2 weeks of age between left frontal and occipital leads and decreased coherence between midline central and occipital leads in a group of low risk premature infants. More recently, it was reported that one effect of early foster care placement among previously institutionalized children in Romania was a reduction in right hemisphere short-distance EEG coherence (Marshall et al., 2008). A new study has also reported atypical electrocortical synchrony in infants born at extremely low birth weight, using measures of intra- and interhemispheric EEG coherence (Grieve et al., 2008). To our knowledge, no studies have examined the long-term impact of adverse early life events such as extremely low birth weight on patterns of brain development or functional brain connectivity as indexed by EEG spectral and coherence characteristics.

1.3. The present study

The purpose of the present study was to assess the influence of early insult (extremely low birth weight) on brain development and functioning in young adulthood by investigating EEG spectral power and coherence differences between adult survivors of extremely low birth weight (ELBW) and normal birth weight controls. We chose to examine ELBW survivors because infants born at ELBW (i.e., <1000 g) are the smallest and most-at risk babies. With major advances in neonatal intensive care over the last few decades, it is now possible to study survivors of extreme prematurity into adulthood.

We collected measures of resting regional EEG spectral power and coherence during a baseline condition in a cohort of young
adults born at ELBW and in normal birth weight (NBW) term controls. By design, we selected homogenous groups from the ELBW and NBW cohorts in that all participants were free from neurosensory or psychiatric impairment, and all were right-handed. The two groups did not significantly differ on parent social class or education. The ELBW cohort has been followed longitudinally since birth and assessed at key developmental stages (see Saigal et al., 1990, 1991, 1996, 2003, 2006a; Szatmari et al., 1990, 1993).

If early adversity negatively impacts brain development, then these effects may persist into adulthood even in non-impaired survivors. Accordingly, we predicted that adults born at ELBW would exhibit relatively greater spectral power in the low-frequency bands (<7 Hz) and decreased spectral power in the high-frequency bands (>8 Hz) than their matched NBW counterparts, indicating a potential maturation lag. We further hypothesized that differences in EEG spectral characteristics would be particularly salient for the frontal brain regions, given the anatomical, neurochemical and electrophysiological evidence that the frontal lobes continue to develop into late adolescence and young adulthood (Benes, 2001; Caviness et al., 1996; Gasser et al., 1988; Giedd et al., 1999; Huttenlocher, 1999; Huttenlocher and Dabholkar, 1997a,b; Segalowitz and Davies, 2004). We also predicted that extremely low birth weight would be associated with changes in cortical connectivity and that this would be reflected in EEG coherence differences between the ELBW and NBW participants. In particular, we examined group differences in the ratio of short-to-long distance coherence in the left and right cerebral hemispheres.

2. Methods

2.1. Participants and study overview

2.1.1. ELBW cohort

The extremely low birth weight (ELBW) cohort comprised 397 predominantly Caucasian infants (birth weight 501–1000 g) born between 1977 and 1982 to residents of a geographically defined region in central-west Ontario, Canada, and recruited at birth. Of these 397 infants, 179 (45%) survived to hospital discharge from the Neonatal Intensive Care Unit. There were 13 late deaths, therefore 166 survived to young adulthood. ELBW survivors were followed longitudinally from birth and neurosensory impairments (cerebral palsy, blindness, deafness, mental retardation, and microcephaly) were diagnosed by a neonatologist and a developmental pediatrician. By design, we chose to constitute a fairly homogenous group of participants and therefore excluded individuals with neurosensory impairments (n = 46), psychiatric problems (n = 2), and those who were non-right handed (n = 25). We selected only right-handed individuals (Oldfield, 1971) because participants in the present study were part of a larger study examining regional EEG asymmetry correlates of emotion processing, and left-handers are known to differ in the lateralization of emotion (Heller and Levy, 1981). Of the 93 ELBW adult survivors eligible to participate, 7 were lost to follow-up, 4 refused the entire young adulthood study, and 11 either refused or were unable to be recalled to the laboratory. A total of 71/93 (76%) eligible ELBW adult survivors participated in the present study.

2.1.2. NBW cohort

The normal birth weight (NBW) control group comprised 145 individuals who were selected from a random sample of children born at term and obtained from class lists of 8-year-old children from several local public school boards, and of similar race, sex, and socioeconomic status distribution as the ELBW cohort (Szatmari et al., 1993). The controls were not followed prospectively from birth. Of the 145 NBW controls originally enrolled, we excluded those with neurosensory impairment (n = 3), non-right handed individuals (n = 27), and those who had epilepsy and multiple sclerosis at young adulthood (n = 2). Of the 113 eligible NBW control participants, 4 were lost to follow-up, 7 refused the entire young adulthood study, and 19 either refused or were unable to be recalled to the laboratory. A total of 83/113 (74%) NBW adults participated in the present study.

The 154 (ELBW, n = 71; NBW, n = 83) participants in the present study were part of a larger study examining transition to young adulthood (Saigal et al., 2006a), health status (Saigal et al., 2007), and quality of life (Saigal et al., 2006b) of individuals born at ELBW. The analyses below focus on the EEG spectral power and coherence measures collected at baseline during their young adulthood visit to our laboratory.

2.2. Procedures

Upon arrival to the laboratory, the procedures were explained to the participants and written informed consent was obtained. Participants then had their EEG collected continuously during two minutes of resting baseline (1 min eyes-open [EO], 1 min eyes-closed [EC]). All procedures were conducted under the supervision of trained research staff and approved by the McMaster University Health Sciences Research Ethics Board. The study was conducted from 2001 to 2004.

2.3. Electroencephalogram (EEG) data collection

2.3.1. EEG recording

Regional EEG was collected using a lycra stretch cap. The cap electrodes are positioned according to the 10/20 system of the International Federation (Jasper, 1958). The experimenter used the blunt end of a Q-tip in combination with an abrasive gel (Omm-prep) and gently abraded each electrode surface. Each electrode site was then filled with a small amount of electrolyte gel which served as a conductor. Electrode impedances below 10 kΩ per site and within 500 Ω between homologous sites were considered acceptable.

EEG was recorded from the left and right anterior, mid-line and posterior regions of the scalp (i.e., mid-frontal: F3, F4; central: C3, C4; parietal: P3, P3; occipital: O1, O2). All active EEG sites were referenced to Cz during acquisition.

A calibration signal (10 Hz/47 V rms sine wave) was input through each amplifier prior to each data collection. The output of this signal was 50 μV, with a gain of 10,000. The nine EEG channels were amplified by individual SA Instrumentation Bioamplifiers, with filter settings for all channels set at 1 Hz (high pass) and 100 Hz (low pass). The data from all nine EEG channels were digitized on-line at a sampling rate of 512 Hz.

2.3.2. EEG data reduction and quantification

The EEG data were re-referenced to an average reference in software and visually scanned for artifact due to movement (e.g., eye blinks and body movements) and edited out using software developed by James Long Company (EEG Analysis Program, Caroga Lake, NY). The electrode array used in the present study was extended by individual SA Instrumentation Bioamplifiers, with filter settings for all channels set at 1 Hz (high pass) and 100 Hz (low pass). The data from all nine EEG channels were digitized on-line at a sampling rate of 512 Hz.

A natural log (ln) transformation was performed on the
EEG power values in order to reduce skewness. Data were excluded from individual channels if the ln transformed power values for a given frequency band exceeded 3SD.

We computed high-to-low frequency power ratio scores. High-frequency power was computed separately for each electrode site as the total amount of ln transformed power density for the alpha and beta bands (7.5–20.5 Hz). Low-frequency power was computed separately for each electrode site as the total amount of ln transformed power density for the delta and theta bands (0.5–7.5 Hz). The ratio was calculated as high-frequency power/low-frequency power such that a high ratio reflects greater high-frequency power relative to low-frequency. Power ratio scores of this sort have been previously used as indicators of metabolic and blood flow changes following cerebral ischemia (Gotman et al., 1986; Nagata, 1988; Sotaniemi et al., 1980).

Intra-hemispheric (frontal-central and frontal-occipital) EEG coherence was also computed for the delta, theta, alpha and beta frequency bands using the algorithm developed by Salzberg et al. (1986). Frontal-central coherence was computed since we were particularly interested in short-distance EEG coherence within the anterior portion of the scalp and frontal-occipital coherence was computed as an index of long-distance EEG coherence between the most anterior and posterior sites, respectively. Although average referencing may lead to inflated EEG coherence values due to common reference effects (Nunez et al., 1997), it remains a frequently used reference configuration for estimating coherence (Bell and Fox, 1996; Bell and Wolfe, 2007) and is regarded as the optimal configuration by some (Fein et al., 1988).

2.4. Statistical analyses

The two groups differed in head circumference at the young adulthood visit, t(149) = −3.98, p = .001, with the ELBW group showing a smaller mean head circumference, 55.33 cm (SD = 2) than the NBW group, 56.66 cm (SD = 2.08). Because power values are sensitive to confounds of volume conduction owing to differences in inter-electrode distance and the two groups differed on head circumference, head circumference at the young adulthood visit was included as a covariate in all EEG analyses.

To examine group differences in regional EEG spectral power, we performed separate repeated measures analysis of covariance (ANCOVAs) using Group (ELBW and NBW) as the between-subjects factor and Region (frontal and occipital) and Hemisphere (left and right) as the within-subjects factors. The dependent measures were absolute power in the delta, theta, alpha, and beta frequency bands and the high-to-low frequency ratio score.

To examine group differences in EEG hemispheric coherence, we performed a separate repeated measures ANCOVA with Group (ELBW and NBW) as the between-subjects factor and Hemispheric region (frontal and occipital) and Hemisphere (left and right) as the within-subjects factors. The dependent measures were EEG coherence values for each of the frequency bands: delta, theta, alpha, beta.

For the repeated measures ANCOVAs, Box’s M test was used to measure the homogeneity of variance/covariance matrices across groups. Where the Box’s M test indicated unequal covariance, a Greenhouse–Geisser correction was applied.

3. Results

3.1. Socio-demographic data

Table 1 presents the socio-demographic data for the ELBW and NBW groups. The mean birth weight of the ELBW cohort was 874g (SD = 11) and 3395g (SD = 470) for the NBW cohort. The gestational ages for the two groups were 27.5 (2.2) weeks and term, respectively. There were no significant group differences in gender, parental social class, educational status, or age at assessment (ps > .05).

3.2. Regional EEG spectral power and hemispheric coherence data

3.2.1. Prediction No. 1a: spectral density in low and high EEG frequency bands

There was a significant Group × Hemisphere × Region interaction on absolute delta power, F(1,136) = 5.90, p = .02. In order to decompose the Group × Hemisphere × Region interaction, we performed Group × Hemisphere ANCOVAs separately for each region on absolute delta power. There was a significant main effect of Group for the frontal region only, F(1,140) = 4.43, p = .04. As predicted, the ELBW group exhibited significantly greater absolute delta power compared to the NBW group (see Fig. 1A).

There was also a significant main effect of Group on absolute beta power, F(1,138) = 4.40, p = .04, with the ELBW group showing significantly less beta power than the NBW group across the scalp.

3.2.2. Prediction No. 1b: ratio of high-to-low frequency band EEG spectral power

The analyses revealed a significant main effect of Group on the ratio of high-to-low power, F(1,132) = 4.49, p = .04. As predicted, the ELBW group exhibited a significantly lower ratio compared to the NBW group across the scalp sites. That is, the ELBW group exhibited relatively greater EEG spectral power for the low-frequency bands than for the high-frequency bands compared to the NBW group across region and hemisphere.

In order to localize the scalp regions accounting for the significant group difference, we performed Group × Hemisphere ANCOVAs separately for the frontal and occipital regions. Analyses focused on the frontal and occipital regions, in order to index the most anterior and posterior poles of the scalp, respectively. There was a trend toward a significant main effect of Group, F(1,137) = 3.42, p = .06, for the frontal region only. As predicted,

Table 1

| Socio-demographic and individual variables for the ELBW and NBW groups. |
|-----------------|-----------------|
| Variable                          | Group           |
|                                | ELBW (n=71) | NBW (n=83) |
| Birth weight (g)                  | Mean 874       | 3395        |
| SD                               | 11             | 470         |
| Gestational age (weeks)           | Maximum 34     | Term        |
| Minimum 23                       | Mean 27.59     | SD 2.18     |
| Sex (F/M)                        | 41/30          | 48/35       |
| Current highest education (%)     | 1.23            | 1.11        |
| <High school                      | 7               | 5            |
| Completed high school             | 36              | 39           |
| Partial postsecondary college     | 23              | 22           |
| Completed university/college      | 5               | 16           |
| Age at assessment (years)         | Mean 23.3      | 23.6         |
| SD                               | 1.4            | 1.1          |

* Based on Hollingshead classification. Data were missing for 3 ELBW participants and 2 NBW participants.
* Data were missing for 1 NBW participant.

V. Miskovic et al. / Clinical Neurophysiology 120 (2009) 231–238
the ELBW group displayed a lower ratio in the frontal scalp sites compared with the NBW group (see Fig. 1B). There were no significant main or interaction effects for the occipital region ($p > .09$).

3.2.3. Prediction No. 2: short-to-long distance EEG hemispheric coherence

The ANCOVA revealed a separate significant Group $\times$ Hemisphere $\times$ Distance interaction on EEG coherence in the theta, $F(1,142) = 9.93$, Greenhouse–Geisser-corrected $p = .002$, alpha, $F(1,142) = 7.76$, Greenhouse–Geisser-corrected $p = .01$, and beta, $F(1,142) = 6.32$, Greenhouse–Geisser-corrected $p = .01$, frequency bands. In order to decompose these separate interactions, we performed Group $\times$ Distance ANCOVAs separately for each hemisphere on each frequency band. There were separate significant Group $\times$ Distance interactions for right hemisphere EEG coherence in the theta, $F(1,142) = 8.11$, $p = .01$, alpha, $F(1,142) = 9.95$, $p = .002$, and beta, $F(1,142) = 6.43$, $p = .01$, frequency bands.

We next computed short-to-long distance EEG coherence ratio scores in order to decompose the Group $\times$ Distance interactions separately for each frequency band. Coherence ratio scores were computed for the right hemisphere as the amount of frontal-central coherence/frontal-occipital coherence in order to reflect the ratio of short-to-long distance coherence (see Mundy et al., 2000). A high ratio score indicates relatively more short-distance coherence.

We found that the ELBW group exhibited a significantly higher coherence ratio scores in the theta, $t(146) = 2.73$, $p = .01$, alpha, $t(146) = 2.81$, $p = .01$ and beta, $t(146) = 2.7$, $p = .01$ frequency bands than the NBW group (see Fig. 2). Overall, the ELBW group had relatively more short-distance coherence in the right hemisphere compared to the NBW group.

4. Discussion

The goal of the present study was to examine the impact of adverse events early in life on brain development and functioning in non-impaired adult survivors. To this end, we compared regional EEG spectral power and coherence characteristics of young adults born at ELBW and full-term NBW. As predicted, we found that young adults born at ELBW exhibited significantly more power in the low (i.e., delta and theta) EEG frequency bands relative to power in the high (i.e., alpha and beta) EEG frequency bands than their NBW peers. This between-group difference was most salient in the frontal regions. This pattern of increased EEG spectral power in lower frequency bands has been reported in studies of premature infants (Bell et al., 1991; Havlicek et al., 1975; Koterazawa et al., 1990) and, to some extent, in premature school age children (Rozhkova, 2008).

We also assessed cortical connectivity using measures of EEG coherence. We found that the ELBW group did not manifest the typical pattern of greater long-distance coherence in the right hemisphere (Thatcher et al., 1986), possibly indicating a state of neurophysiological “disconnection” in this cohort (Leuchter et al., 1994).

What do differences in EEG power and coherence among adult survivors of ELBW reflect? Brain development is governed by epigenetic processes in which genetic regulatory cascades interact with, and are modulated by, environmental input (Edelman, 1987; Feng et al., 2007). Early traumatic experiences can be conceptualized as introducing an element of turbulence that perturbs typical developmental trajectories. There is increasing evidence from human studies that early adversity, in the form of deprivation or abuse, can produce subtle neurological abnormalities. For example, survivors of severe physical or sexual abuse in childhood exhibit deficits in cortical network dynamics, involving decreased...
cortical differentiation as reflected in EEG coherence left-right asymmetries with a bias toward more coherence in the left hemisphere (Ito et al., 1998). More recently, an EEG study by Marshall and Fox (2004) showed that in comparison with age-matched children who were never institutionalized, institutionalized Romanian children exhibited a pattern of increased spectral power in the low-frequency region of the EEG spectrum and decreased high-frequency power. Two models were advanced to account for these results: a maturational lag model that interprets an excess of low-frequency power as indicative of delayed CNS development and the cortical hypoarousal model that interprets a deficit in high-frequency power as indicative of chronically low levels of cerebral activation. Other studies have reported similar patterns of excessive low-frequency EEG band power among children growing up in psychosocially disadvantaged environments when they were assessed at multiple age points (Harmony et al., 1988; Harmony et al., 1990; Otero et al., 2003).

In addition to the impact of negative experiences occurring in the early post-natal period, sub-optimal pre- and peri-natal factors also influence brain development (Kapellou et al., 2006; Rees and Harding, 2004). Previous research has indicated that prematurity is associated with a range of structural abnormalities (Ajayi-Obe et al., 2000; Maalouf et al., 1999; Nosarti et al., 2002; Peterson et al., 2000; Volpe, 2003). Survivors of prematurity also exhibit atypical EEG activity, largely involving greater power density in the low-frequency bands (delta and theta) compared with their matched term peers (Bell et al., 1991; Havlicek et al., 1975; Koterazawa et al., 1990; Rozhkova, 2008). The present study extends earlier work by examining the impact of being born at extremely low birth weight on brain development and functioning beyond childhood to emerging adulthood.

The pattern of increased spectral power in the low-frequency EEG bands (delta and theta) and decreased power in the high-frequency bands (alpha and beta) in the ELBW group suggest a maturational delay of the underlying neural generator sources. A maturational delay is inferred because studies of typically developing infants, children and adolescents have shown a clear trend in a re-distribution of power from the low to the high-frequency regions of the EEG spectrum with increasing age (e.g., Clarke et al., 2001; Gibbs and Knott, 1949; Hagne, 1968, 1972; John et al., 1980; Matousek and Petersen, 1973; Mizuno et al., 1970; Somsen et al., 1997).

The present findings do not provide definitive support for either the maturational lag or the cortical hypoarousal model, since between-group differences in the relative amounts of high- and low-frequency power reflect a mixture of excessive delta power and deficient beta power in the ELBW group. Relatively greater low-frequency power may reflect a non-specific form of CNS pathology, resulting from adverse experiences occurring either pre- and peri- (Bell et al., 1991; Havlicek et al., 1975; Koterazawa et al., 1990; Rozhkova, 2008) or post-natally (Harmony et al., 1988; Harmony et al., 1990; Marshall and Fox, 2004).

We found that differences in EEG spectral characteristics between the ELBW and NBW groups were specific to the frontal region. This finding is consistent with evidence showing that EEG maturation proceeds in the anterior–posterior dimension, with development of the power spectrum progressing from the posterior to the anterior derivations (Gasser et al., 1988). Since the anterior regions are the latest to develop (Clarke et al., 2001; Gasser et al., 1988; Matousek and Petersen, 1973), they should also be the most likely to display maturational lags at the young adult assessment. By contrast, maturation in the posterior regions may have been delayed but nevertheless completed by the time of testing in the present study, explaining why we did not find significant group differences in the high-to-low frequency power ratio for the occipital leads. Similar maturational delays have been reported in studies of the premature infant’s background EEG, with abnormal transients disappearing during the first few weeks and months of birth as the cerebral electrical activity became increasingly similar in morphology to that of term infants (Thorpe, 1990).

A putative physiological mechanism that affects power distribution within the EEG spectrum involves neuromodulatory influences from the midbrain (Nunez, 2000). Aberrations in the EEG spectral profile of prematurely born children have been attributed to alterations in thalamo-cortical functioning, since these distributed anatomical structures regulate the EEG rhythm (Rozhkova, 2008). Excessive low frequency amplitude may result from the hyperpolarizing action of γ-amino butyric acid (GABA) release from the thalamic nucleus reticularis and/or the action of oscillator cells located within the thalamus or deep layers of the cortex (Hughes and John, 1999). There is presently insufficient data to clarify which of these neurological mechanisms specifically determines the nature of EEG spectrum abnormalities in our ELBW cohort.

The NBW group exhibited a pattern of relatively more long than short-distance coherence in the right hemisphere. This finding is consistent with previous research indicating that the right hemisphere has a more diffuse organization, characterized by an abundance of long-distance corticocortical association fibers linking distant cortical regions, and that the left hemisphere is more differentiated, with greater amounts of short-distance connections (Thatcher et al., 1986; Tucker et al., 1986). Similarly, other research has found a greater ratio of white to gray matter in the right hemisphere (Gur et al., 1980), indicating the presence of more long axonal fibers. By comparison, the ELBW group had significantly more short-distance coherence in the right hemisphere. This pattern of atypical right hemisphere connectivity may have a neuroanatomical basis in white matter deficits. White matter lesions are among the most common forms of neuropathology in survivors of premature birth (Volpe, 2003). Decreases in EEG coherence between distant brain regions have been associated with cortical fiber damage in Alzheimer’s disease, suggesting that coherence is sensitive to neurophysiological “disconnection” (Leuchter et al., 1994). Neurophysiological “disconnection” can reflect the degeneration of neuronal bodies or demyelination of association fibers. Our findings suggest that early trauma, such as being born at ELBW, may be associated with some degree of subtle “disconnection” in the right hemisphere. Interestingly, Marshall et al. (2008) have recently reported that early placement in foster care, among previously institutionalized Romanian children was associated with decreases in short-distance EEG coherence within the right hemisphere. Together, these findings may indicate that the right hemisphere is particularly sensitive to the effects of early occurring adverse, as well as positive, experiences.

4.1. Limitations

There were several limitations in the present study. First, the EEG reflects the activity of large-scale neuronal populations and has a poor spatial resolution. Brain electrical activity recorded at the frontal leads may actually reflect activity from more posterior generators given the properties of passive current spread in a volume conductor. As a result, some level of caution is warranted in interpreting the finding of a maturational delay within the frontal brain regions. Moreover, we used measures of scalp EEG coherence in order to make inferences about functional connectivity. However, scalp coherence can be confounded by the effects of volume conduction and as a result produce artificial estimates of cortical connectivity. Future studies should use dense-array electrode montages that allow for the use of source modeling and the computation of source coherence estimates thereby providing more accurate measures of corticocortical coupling (Hoechstetter et al., 2004). Moreover, future studies should also include measures of...
‘frontal lobe’ tasks (e.g., working memory, response inhibition, set shifting tasks), in order to examine whether the EEG spectral aberrations have functional significance.

A second limitation of the study was that there could have been other confounding variables, intervening between birth and altered brain development and functioning at the young adult visit. However, we adequately controlled for the contributions of socio-economic status and selected a relatively homogenous, non-impaired ELBW sample. Our results suggest that even among ELBW survivors without major impairments, the early trauma results in subtle neurological abnormalities as reflected in measures of EEG spectral power and coherence.

A final limitation was that, since ELBW could be the outcome of multiple adverse intra-uterine influences (Shiono and Behrman, 1995), our study does not clarify what aspects are specifically related to altered brain development. Moreover, although all of our ELBW adults were born at <1000 g, and the majority born prematurely, some were born at term. Accordingly, we need to caution the use of the word premature. Future EEG work needs to be conducted on survivors of prematurity in which prematurity has arisen from multiple reasons.

5. Conclusions

The present study suggests that early traumatic experience in the form of extremely low birth weight was related to atypical patterns of CNS development and functioning. In particular, being born at ELBW was a risk factor for maturational delays of the brain that persist into late adolescence and emerging adulthood.

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