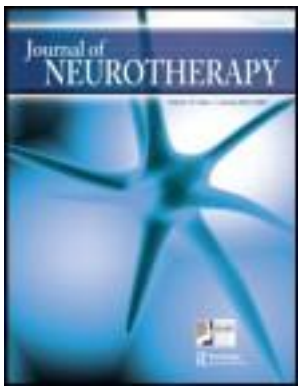

Journal of Neurotherapy: Investigations in Neuromodulation, Neurofeedback and Applied Neuroscience

A 9-Year-Old Boy with Multifocal Encephalomalacia: EEG Loreta and Lifespan Database, Magnetic Resonance Imaging and Neuropsychological Agreement

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RESEARCH ARTICLES

A 9-YEAR-OLD BOY WITH MULTIFOCAL ENCEPHALOMALACIA: EEG LORETA AND LIFESPAN DATABASE, MAGNETIC RESONANCE IMAGING AND NEUROPSYCHOLOGICAL AGREEMENT

Rex L. Cannon[1,2,3], Monica K. Crane[1], Paul D. Campbell[4], John H. Dougherty, Jr.[1], Debora R. Baldwin[2], Joel D. Effler[3], Lisa S. Phillips[2,3], Felicia Hare[1], Matthew Zachary[1], Kelli E. Cox[1,2,3], Dominic J. Di Loreto[2,3]

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The methods of quantitative electroencephalography (qEEG) and LORETA current source density comparisons to the Lifespan database with Neuroguide (Applied Neuroscience Laboratories) permit a comparison of the estimated intracerebral current density distribution with LORETA. This study sought to determine the agreement between EEG LORETA, Magnetic Resonance Imaging, and Neuropsychological data for a 9-year-old boy with possible cortical damage. EEG LORETA data were collected prior to magnetic resonance imaging (MRI). Historical and current testing indicated aphasic symptoms and central auditory processing disorder. Significant impairments in verbal fluency, visual-spatial, and attentional and working memory processes are indicated, as well as profound difficulties with mathematics. MRI data indicate multifocal Encephalomalacia in bilateral prefrontal cortex, parietal lobes more pronounced in the left hemisphere, and significant volume reduction in the corpus callosum. EEG LORETA shows current source density deficits in posterior cingulate, parietal, and frontal regions in nearly all frequencies in the left hemisphere, with frontal/temporal deficits in regions shown to be involved in language processes. EEG LORETA, MRI, and Neuropsychological data show agreement in the current case study. The EEG changes associated with functional reorganization still involve much uncertainty. However, comparisons to the Lifespan database may be a valid tool for evaluating patient symptoms and correlating them with neural processes. This is an area of interest to our laboratory, and we will continue to monitor this patient over time. Notable increases in current source density may be indicative of large-scale cerebral reorganization in this patient.

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We express sincere thanks to the patient and his parents for donating the MRI scans and for their courage, resilience, and contribution to science. We express a great amount of gratitude to Dr. Robert W. Thatcher for scholarship use of Neuroguide in our lab over the past 5 years. We also thank Deymed Diagnostics for their equipment and longstanding support of our lab. Although there were fees for MRI and initial diagnostic procedures, extensive Neuropsychological testing was provided without charge. We have no financial interest in any of the equipment/software used for this study. This study was conducted to answer one specific question for the parents: ''What, if anything, is wrong with our son?''

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INTRODUCTION

Low-resolution electromagnetic tomography (LORETA) is a collection of independent modules run in specific sequence to transform the raw electroencephalography (EEG) signal into LORETA images. It is one of the most widely used and tested inverse solutions for source localization of the EEG produced on the scalp. The EEG potentials on the scalp are measured in a linear fashion with respect to source amplitudes. In short, LORETA utilizes a fixed element method to solve the Poisson equation using geometric information known about the layers of the brain, skull, and scalp and their conductivities (Sanei, 2007). The methods of quantitative EEG (qEEG) and LORETA current source density (CSD) comparisons to the FDA-registered Lifespan Database (Thatcher, Biver, & North, 2003) with Neuroguide permits a comparison of the estimated intracerebral CSD distribution with LORETA (Thatcher, North, & Biver, 2005a, 2005b). This method allows for a comparison to a normative sample without the collection of a local control group. Thus EEG is the only neuroimaging technique that allows statistical comparison of individual recordings with age-matched or age regression lifespan normative databases (Hughes & John, 1999; John, Pricep, Fridman, & Easton, 1998; Thatcher et al., 2005a, 2005b). LORETA is employed to examine current source density in 1 Hz increments for the individual as compared to the normative sample. The current study sought to compare the structural magnetic resonance imaging (MRI) data from one subject with the LORETA current source density for baseline EEG as compared to the Lifespan database with the hypothesis that frequency specific deficits would be meaningful and accurate as contrasted with the MRI scans.

LORETA and the standardized version (sLORETA) are reliable inverse solutions for estimating cortical electrical current density originating from scalp electrodes utilizing optimal smoothing to estimate a direct 3D solution for the electrical activity distribution. This method computes distributed electrical activity within the cerebral volume, which is discretized and mapped onto a dense grid array containing sources of electrical activity at each point in the 3D grid with a low error solution for source generators. In addition LORETA generates statistical maps modeling distribution currents of brain activity (Holmes, Brown, & Tucker, 2004; Lehmann et al., 2001; Lehmann et al., 2005; Lehmann, Faber, Gianotti, Kochi, & Pascual-Marqui, 2006; Pascual-Marqui, Esslen, Kochi, & Lehmann, 2002; Pascual-Marqui et al., 1999) utilizing realistic electrode coordinates (Towle et al., 1993) for a three-concentric-shell spherical head model coregistered on a standardized MRI atlas (Talairach, 1988). The procedures provide accurate approximation of anatomical labeling within the neocortical volume, including the anterior cingulate, hippocampus, and amygdaloid complex (Cannon et al. 2005; Coutin-Churchman & Moreno, 2008; Esslen, Pascual-Marqui, Hell, Kochi, & Lehmann, 2004; Lancaster et al., 2000). LORETA operates under the assumption that the spatial gradient of voltage will change gradually and as such selects the distribution of source magnitudes that is maximally smooth. The physiological justification underlying this constraint is that activity in neurons in neighboring patches of cortex is correlated. Of importance, LORETA has been demonstrated to provide better temporal resolution than can be achieved with either PET or fMRI (Kim et al., 2009), whereas PET and MRI offer superior spatial resolution. Ultimately, combining these methods may prove important to integrating the ''what and where'' of the brain in normal cognitive processes and psychopathology (Cannon, Congedo, Lubar, & Hutchens, 2009).

LORETA has undergone extensive validation by independent laboratories, including mathematical proofs (Sekihara, Sahani, & Nagarajan, 2005; Wagner, Fuchs, & Kastner, 2004). This method finds a particular solution to the nonunique EEG inverse problem by assuming similar activation of neighboring neuronal sources, followed by an appropriate standardization of the current density, producing images of electric neuronal activity without

localization bias (Greenblatt, Gan, Harmatz, & Shader, 2005; Pascual-Marqui, 2002; Sekihara et al., 2005). LORETA (Pascual-Marqui, Michel, & Lehmann, 1994) has received considerable validation from studies combining it with more established localization methods, including fMRI (Mulert et al., 2004; Vitacco, Brandeis, Pascual-Marqui, & Martin, 2002), structural MRI (Worrell et al., 2000), PET (Oakes et al., 2004; Zumsteg, Wennberg, Treyer, Buck, & Wieser, 2005), and invasive implanted electrode recordings (Zumsteg, Andrade, & Wennberg, 2006). The results from these studies and others serve as validation for the LORETA method. It has also been demonstrated that deep structures such as the anterior cingulate cortex (Pizzagalli, Oakes, & Davidson, 2003) and mesial temporal lobes (Zumsteg et al., 2006) can be correctly localized with LORETA.

This clinical case report is for a 9-year-old, left-handed Caucasian boy presenting for neurofeedback for attentional and educational difficulties. His medical history includes diffuse perinatal subarachnoid hemorrhage over left temporo-parieto-occipital regions with associated seizures. Seizures were adequately addressed with anticonvulsants. Parents report patient suffered paresis on the right side of his body that was present at time of discharge from hospital. However, with recommendations for physical therapy his prognosis for recovery was good at 13 months, as EEG and CT findings did not indicate any focal abnormalities. No EEG or neuroimaging data have been collected since this time. Physical therapy was employed to train him to use the left side of his body, and he presents as left-handed with weakness still evident on the left side. Of particular interest, he will describe his right hand as not useful, nor does he use it for many things: ''It is just there;'' however, during this description his right hand/arm is moving in synchrony with the conversation. His standing diagnoses at time of evaluation were Central Auditory Processing Disorder (CAPD) and Abnormal Auditory Processing, Unspecified. His individualized education program was adapted to these diagnoses. Parents have expressed disappointment with results and report the patient has increasing difficulties with memory, attention, distractibility, and task completion and failure to learn and maintain age-appropriate reading and arithmetic skills. Language testing by the school system did not detect any anomalies in language processes.

The prevalence of CAPD in children is estimated to be between 2% and 3% (Chermak, Hall, & Musiek, 1999; Chermak, Somers, & Seikel, 1998; Riccio, Hynd, Cohen, Hall, & Molt, 1994), with it being twice as prevalent in boys. It often coexists with other disabilities, such as speech and language disorders or delays, learning disabilities or dyslexia, attention deficit disorders with or without hyperactivity, and social and/or emotional problems. This patient has been evaluated for auditory processing on two occasions, and all obtained scores were in the severely impaired range. Speech pathology, on the other hand, indicated that receptive and expressive language functions were within normal limits, except for tasks requiring auditory memory. No language disorder was detected by the Clinical Evaluation of Language Fundamentals–Fourth Edition. Auditory and reading assessments produced scores below his current grade level and were consistent with the diagnosis of CAPD. Further auditory results revealed no abnormalities in Otoscopic, pure tone audiometry, middle ear tympanograms, or stapedial reflexes.

Prior psychoeducational testing administered in 2009 included the Woodcock–Johnson Tests of Cognitive Ability, Third Edition. The patient produced a total standard score of 76, which is classified in the borderline to low range. Both long-term and short-term recall abilities were shown to be significantly lower than would be expected. Similar results were obtained for the Listening Comprehension subtest of the Wechsler Individual Achievement Test–II. He obtained a standard score of 76, which places him in the lower 5th percentile. The patient produced lower scores on tests of phonological awareness with a standard score of 84, which places him in the 14th percentile. Parents and teachers showed

significant agreement for attentional deficits on rating scales (BASC-2). Identification of deficits in functional communication were endorsed by one parent. Composite scores indicating mastery of educational materials were also endorsed by the teacher. Of interest, the Universal Nonverbal Intelligence Test was administered with the psychoeducational procedures, and the patient produced a result of 96, which indicates an average range of cognitive ability (Hooper & Bell, 2006).

The cumulative results of prior testing to date concluded that primary deficits in neurocognitive functions were attributable to CAPD or other Auditory Processing Disorder. The summaries and disagreement between several test results may be the consequence of nonspecific neuropsychological testing. In short, educational assessment may not be sensitive to specific neurocognitive dysfunctions and the important correlative structure between cognitive domains. Therefore, to ascertain a more specific range of functionality, a brief neuropsychological screening using portions of the Reitan Battery for the Neuropsychological Evaluation of Children was employed. In addition, simple tests of working memory, visual-spatial, language functions including category naming (verbal fluency), auditory and visual attention, and arithmetic were also performed. During all procedures the patient was compliant and effortful in his attempts to complete the tasks. He was able to maintain concentration during those tasks that required less time to complete. The longer the task, the more distracted he became. The patient was given several working memory tasks, including recall of numbers, letters, and words. When asked to recall the presented items, on average he was able to retain one of the three presented items, regardless of format. He was given six arithmetic problems with simple addition and subtraction using symbols, numbers, and word problems. He was able to complete the number problems rapidly and correctly. Symbols and word problems presented the most difficulty and errors. He was given clock drawing and complex figure-copying tasks. The clock was drawn semicircular with numbers irregularly spaced, and the clock hands were not drawn and placed at the correct time (3:45). Notably, he did point at the clock identifying the correct location of where the numbers should have been placed. Specific parts of the complex figure were crude (diamond and triangle) but correctly drawn; however, integrating the gestalt was not achieved.

Verbal fluency was assessed with category (animal) naming. The patient was asked to name as many animals as he could in a 1-min period. The patient could name only eight in the allotted time. Reading was assessed on several occasions with a predominant pattern of slow, deliberate attempts to comply with the task. This pattern of reading was also present in a book he practices with at home and has read on numerous occasions with his father. He was able to write out his name and the alphabet. He could recall and write out the 12 months of the year using only abbreviations. He was oriented to the month and date but did not know the year. He was able to recall his birthday and age. His scores on the integrative visual and auditory continuous performance tasks (IVA + Plus) indicated extreme deficits in both auditory and visual attention as well as sustained attention. He produced scores within normal limits in persistence in both auditory and visual domains, with a high degree of random responding. In sum, the child is extremely cooperative and effortful in attempts to comply with instructions. Parents did not report any current or history of odd or aggressive behaviors. Thus, although the patient presented for evaluation of potential benefits from neurofeedback training, given the aforementioned and somewhat conflicting testing results in combination with the EEG and LORETA findings the patient was referred for further Neuropsychological testing (pro-bono) and MRI scans (clinical procedure).

The patient underwent several neurocognitive testing procedures to obtain more specific information. He completed the Stanford Binet Intelligence Scales–Fifth Edition. To accommodate possible auditory and language processing disorders the testing procedure was conducted such that the patient could attend to

examiner's face during word and subtest presentation. The authors concluded that the testing results were a valid measure of the patient's overall neurocognitive functioning. As noted in prior assessments he was compliant and effortful in his attempts to complete all tasks given to him. He exhibited maintenance of attention only when attending directly to the examiner; otherwise, if not in a directed gaze his retention level was diminished. He obtained a verbal intelligence quotient (VIQ) scaled score of 100, which places in the 50th percentile. His nonverbal intelligence quotient (NVIQ) scaled score was 77, which places in the 6th percentile. His full-scale intelligence quotient was 88, which falls in the 21st percentile. Upon examination of the scaled scores for the subtests given, he produced significantly lower scores in the nonverbal domain in quantitative reasoning, visual spatial, and working memory subtests. Similar findings for quantitative reasoning were also produced in the verbal domain. Of interest, the other domains appear at or near the mean for normative data in the verbal domain subtests. He exhibited difficulty in the picture assembly portion of the visual spatial task. He was not able to integrate two pieces of a circle and expressed that ''he must have knocked a piece of the puzzle (the circle) onto the floor.'' He searched until he was advised that no pieces were missing and asked to try his best to complete it. He was not able to complete the visual spatial processing subtest at his starting level; however, the lower basal level was completed without difficulty. He appeared to have extreme difficulty organizing and constructing the images. Likewise, he had difficulty with working memory processes specific to single digits as contrasted with repeating the last word in a sentence or groups of sentences. He voiced being frustrated by the puzzles and trying to remember letters or numbers. The quantitative nonverbal reasoning subtest produced low scores. He tended to get the first block touched but could not keep up as the length of digits increased. In the standardized sample 1.9% showed a difference of 23 points between the NVIQ and VIQ. This is a significant and meaningful difference in this patient's case, given the associated cortical data available.

The Reiten Aphasia Screening was administered to the patient following the SB-V. He was able to perform all the tasks adequately except for four items. He was presented 7 SIX 2 and was not able to pronounce it as 762 (instead he read it as ''7-S-I-X-2''), he could not repeat ''Episcopal,'' and finally he could not complete the arithmetic problems correctly. Similarly, aphasia tasks were administered from Eisenson (1954). Auditory verbal comprehension appears intact. Naming of objects is maintained. Of interest, as contrasted with memory assessment with letters, numbers, and words he was 100% accurate in recalling five everyday items he was shown on three separate trials. He was able to identify and name numbers and letters and complete basic, simple mathematical problems. However, integrative functions appeared to be impaired, such that when set shifting was required, that is, switching between numbers and letters or utilizing a combination of the two processes, a notable dysfunction was present. Similarly, if attention was not maintained, then memory for the set and procedures was also hindered significantly. He was able to name all colors provided in the screening. He completed the Rey Complex Figure Test and Recognition Trial. The time to complete the Rey trial was 600 s. He became extremely frustrated during this task. He was observed blinking as if to clear vision and turned the copy figure in numerous directions to ''see it better.'' The total score for the copy task was 7, which is shown in less than 1% of the normative sample. He could not perform the immediate or delayed recall tasks, which is representative of the sample of brain damaged patients provided in the test. Of interest, he did complete the recognition portion with a score of 8, which places in the 16th percentile.

METHODS

Prior to the EEG recording the head was measured and marked for frontal electrode

placement using a measure of the circumference of the head and the distance between the nasion and inion. Ears and forehead were cleaned with a mild abrasive gel (Nuprep; Weaver and Company, Aurora, CO) to remove any oil and dirt from the skin surface. The patient was introduced to the EEG interface and facial, mouth, and eye movements that produce artifacts. He was encouraged to remain as still as possible during the EEG recordings. Four-minute eyes-closed baseline (ECB) and eyes-opened resting baseline (EOB) recordings were obtained with the Deymed Truscan EEG acquisition system, with 19-leads (10/20 system) and linked-ear reference. The EEG was artifacted using Neuroguide, and the selected segments for analysis showed test–retest coefficient of greater than .90 between all segments. The total time for the analyzed EEG for EOB and ECB recordings was more than 1.30 min. The EOB and ECB samples were compared with age-matched individuals ($n = 43$) from the lifespan qEEG normative database. The database shows sensitivity of .98 and undefined specificity, although it is commonly used in evaluation of traumatic brain injury with classification rates greater than .95. Binomial probability distributions are calculated for individual patients using nonparametric statistics to obtain the alpha level for control of Type I and Type II errors (Thatcher, Walker, Biver, North, & Curtin, 2003). The LORETA images were obtained and analyzed nearly 45 days prior to the MRI scans. The study was therefore analyzed from archival data donated by the parents with permission for scientific use by the authors.

The MRI Brain & Stem without contrast scans were conducted with a Siemens 1.5 T Avanto scanner (Siemens Medical Solutions, Erlangen, Germany) located at the Department of Radiology at the University of Tennessee Medical Center. Head restraint with headphones and cushions were used to immobilize the subject to minimize movement artifacts and attenuate echo noise. Axial T2-weighted images were obtained with the following parameters Spin Echo (Se): 10/11, Repetition Time (TR): 3400.0, Echo Time (TE): 99.9, Dynamic Field of View (DFOV): 20.0×20.0 cm. Coronal T2-weighted images were obtained with Se: 11/11, TR: 3516.7, TE: 88.1, DFOV: 18.0×18.0 cm and saggital T1-weighted images were obtained with SE: 8/11, TE: 0, TR: 650.0, TE: 14.0, DFOV: 22.0×22.0 cm. The images were degraded due to motion artifacts. The MRI scans were evaluated clinically by a board-certified neuroradiologist and a board-certified neurologist.

RESULTS

The results for the MRI/LORETA procedures are shown in the figures. In the left side of each figure is the MRI image and to the right is the LORETA image in a specific 1 Hz frequency interval. Figure 1 shows an axial T2-weighted image showing multifocal Encephalomalacia with surrounding gliosis most pronounced in the frontal lobes near the anterior and middle cerebral artery watershed distributions. The basal ganglia and brain stem are intact except for a minimal disturbance on the anterior portion of the left caudate. The encephalomalacic changes are also seen in parietal regions with more pronounced effects in the left hemisphere extending to the perisylvian region. The left hemisphere is shown in the right of the MRI image. The corresponding LORETA image is for the alpha frequency (10 Hz). The red in the image indicate z scores with significant increased current source density, whereas blue indicate z scores with significant decreased current source density as compared to the database. The maximum region of decreased current source density in the mid-alpha range of 10 Hz as compared to the database is shown at posterior cingulate/precuneus ($x = -10$, $y = -53$, $z = 29$) with a z score of -2.08. Similar z scores were shown for the inferior parietal lobes (BA 40), with higher z scores in the left hemisphere. This pattern is similar for all frequencies with the exception of mid-beta in the right hemisphere. Higher deficits in the beta frequency domain extend to the left insula and auditory processing regions.

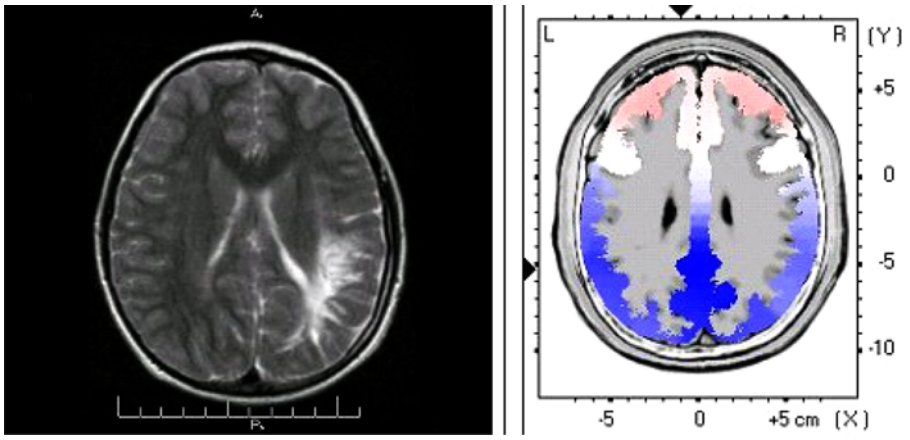

FIGURE 1. The left shows a T2-weighted axial image of 9-year-old boy showing multifocal areas of Encephalomalacia (EPm). EPm changes with surrounding gliosis are most pronounced in the frontal lobes near the ACA/MAC watershed distributions, and also present in both parietal lobes with left (in the right of the image) showing more pronounced infarcts near the perisylvian region. There is also disproportionate volume loss in the posterior corpus callosum. The right image shows the LORETA image for the 10 Hz frequency domain in the eyes-opened condition as compared to the Life-span database. The regions of significant deficit compared to the normative sample are Brodmann Area (BA) 40 at inferior parietal lobe, BA 7 precuneus and superior parietal lobe and BA 30/31 posterior cingulate. The total regions of decrease may reflect functionally related connections involved in numerous integrative processes, with an emphasis on language. The deficits shown in alpha extend to other frequencies with increased activity shown in the right hemisphere for nearly all frequency domains.

Figure 2 shows a saggital T1-weighted image of the brain. The volume of the posterior corpus callosum is significantly disproportionate than would be expected. The LORETA image is for the theta frequency (5 Hz). The maximum deficit is shown at ($x=-3$, $y=-39$, $z=22$) anterior cingulate gyrus with a $z=-7.74$. Deficits are also shown in the left insula. Theta power is increased in the bilateral prefrontal cortices, with higher increases shown in the right hemisphere. Figure 3 shows a coronal T2-weighted image with emphasis on the temporal lobes. Atrophy to Encephalomalacia is evident in left temporal and bilateral frontal regions. The LORETA image is for low-beta (15 Hz) in a coronal view. The region of maximum decreased current source density is shown at left BA 40 in the inferior parietal lobe ($x=-52$, $y=-32$, $z=43$) with $z=-8.74$.

Figures 4 (ECB) and 5 (EOB) show 6 s of the raw EEG data collected from the patient. The

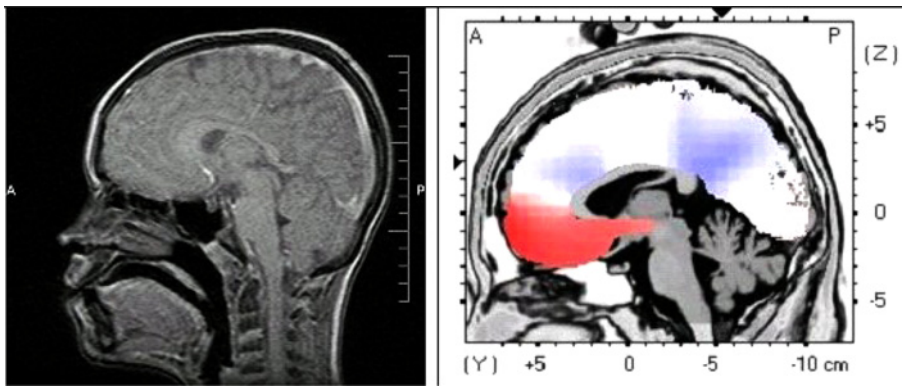

FIGURE 2. The left shows a T1-weighted saggital image of the brain. Notice the volume in the posterior corpus callosum. The right image is a saggital view of LORETA current source density. Significant deficits in theta activity are shown in anterior (BA 24/32) and posterior cingulate (BA 31/7) cortices. Interestingly, increased alpha activity is shown in subgenual cingulate and medial/orbital prefrontal cortex.

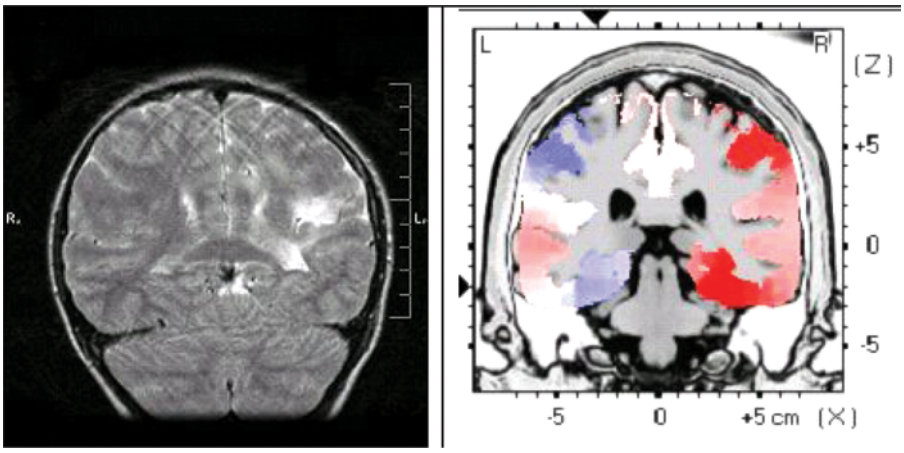

FIGURE 3. The left shows a coronal T2-weighted image of the brain highlighting Encephalomalacia in fronto-temporal regions (perisylvian regions). The left hemisphere is shown on the right side of the MRI image. The right image shows LORETA current source density deficits in mid beta activity in temporal areas including BA 6, 7, 13, 20, 37, 30, 23 and hippocampus in the left hemisphere.

EEG shows high amplitude theta activity at numerous locations over central and parietal locations. A notable asymmetry in the occipito-parietal areas is present, with faster activity shown in the right hemisphere. Increased alpha activity is shown in frontal leads with deficient alpha shown posteriorly. Increased amplitude activity is shown in the right hemisphere for all frequency domains with asymmetry seen across channels.

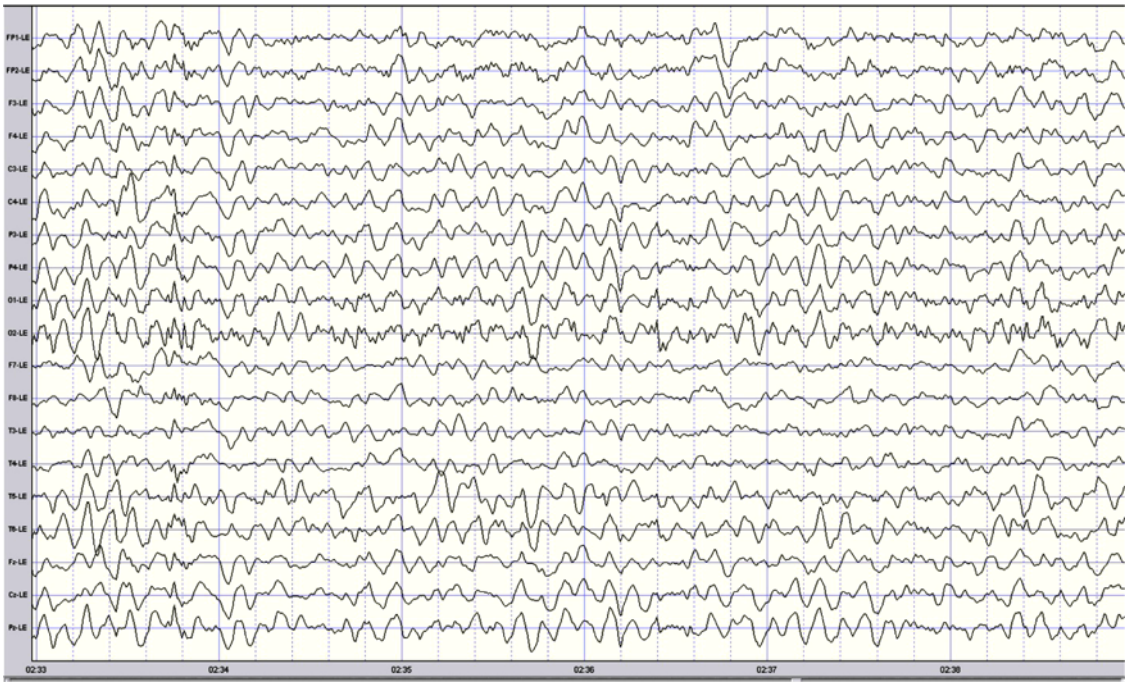

FIGURE 4. Six s of raw EEG tracings in the eyes-closed resting. This record is scaled at 80 mV. The 19-channels are shown in the left of the image. Excess beta is shown in posterior leads, especially concerning the right parietal region. The mean peak posterior dominant frequency is 8.80 mV with asymmetry present. High amplitude theta is shown throughout the record with higher levels appearing in the left hemisphere.

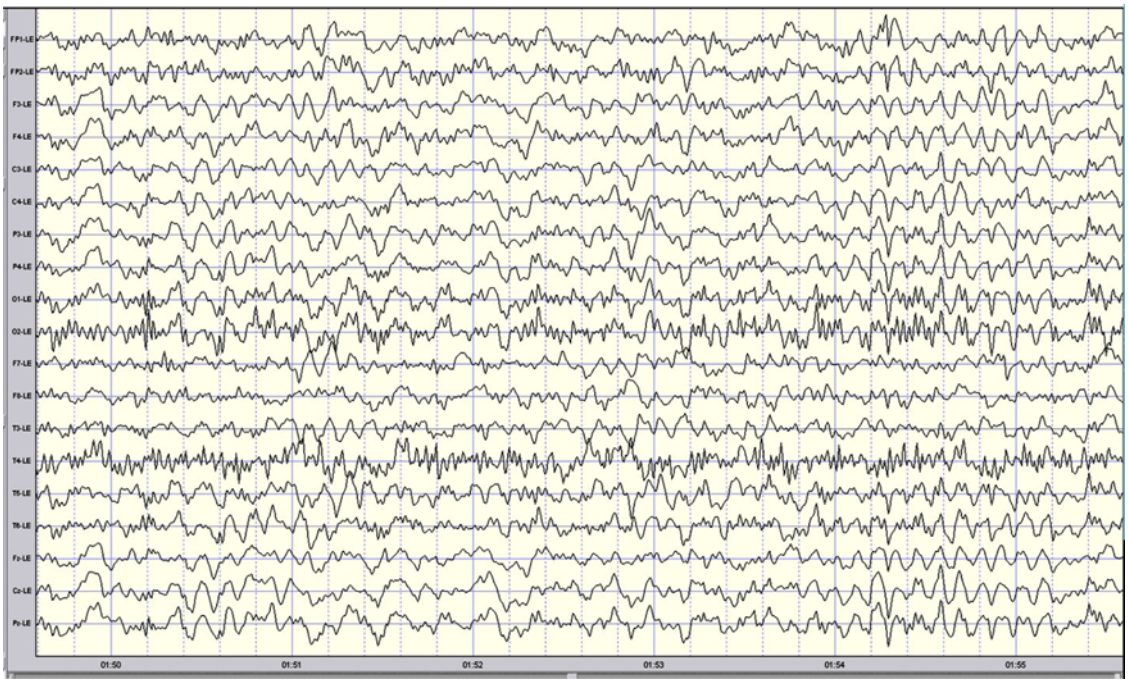

FIGURE 5. Six s of raw EEG tracings for the eyes-opened recording. The record is scaled at 60 mV. The EEG channels are shown in the left of the image. Increases in higher amplitude theta more pronounced over the left hemisphere are noted in addition to increased beta activity (faster activity over right temporal and occipital leads. Eye-movements are present in frontal leads in addition to slight EMG artifacts being present in the T4 tracing.

DISCUSSION

This is the first study of its kind to examine EEG current source density distributions in a pediatric case as compared to the Lifespan database with MRI validation. The neurocognitive sequelae associated with the MRI and EEG data include significant deficits in attention and self-regulation, working memory (and in fact all variants of memory), mathematics, visual-spatial organization and construction, orientation, verbal acuity and production, and language processing in general. It is important to note that both animal and human studies of developmental brain plasticity have indicated that the degree of sparing or recovery of functions following damage to the central nervous system is dependent upon the age of the individual when the lesion is acquired. Another important factor is lesion size, which shows a general relationship between lesion size and recovery, such that small neocortical lesions are associated with compensation mediated by brain regions ipsilateral to the side of injury, whereas larger lesions trigger compensatory changes in the contralateral hemisphere (Chugani, Muller, & Chugani, 1996). Functional reorganization or compensatory shifts may be evident with the increased EEG CSD activity in nearly all frequency domains in the right hemisphere. Similar increases in CSD are shown in the left hemisphere in nonaffected regions.

Recent data examining the network structural core of the human cortex indicate that posterior medial regions including the posterior cingulate, precuneus, isthmus of cingulate and paracentral lobules, extending to parietal and temporal lobes especially in the left hemisphere maintain the highest degree of influence in network core rankings (Hagmann et al., 2008). In this patient nearly all regions associated with the default network of the brain have been damaged, which may elucidate its role in numerous executive processes including attention (Cannon et al., 2009;

Raichle & Gusnard, 2005; Raichle et al., 2001; Raichle & Snyder, 2007). The deficits in retaining proper names of individuals has been associated with damage to regions in the left hemisphere, specifically left temporal, parieto-occipital, fronto-temporal, and thalamic regions (Reinkemeier, Markowitsch, Rauch, & Kessler, 1997). Prefrontal and anterior cingulate regions, interacting with parietal areas, have been routinely demonstrated to represent core components of the circuitry executing top-down control of attentional processing (Gehring & Knight, 2002). The corpus callosum and posterior cingulate are important regions involved in functional integration processes (Bush et al., 1999; Bush, Luu, & Posner, 2000; Whalen et al., 1998) including verbal/language functions, as well as learning and memory in association with the hippocampus and medial temporal lobes (Zhou et al., 2008).

Encephalomalacic damage to numerous regions associated with language is present with the maximal deficits in all EEG frequency domains being the posterior parietal lobes including left BA 40, posterior cingulate, and the precuneus (BA 31, 7, 23, 29, 30, 39, and 40). This identification may be directly associated with the deficits in the volume of the corpus callosum, such that research shows white matter activation of the isthmus is associated with gray matter activation in parietal lobes. This has important implications for multifunctional integration processes (Gawryluk, D'Arcy, Mazerolle, Brewer, & Beyea, 2010; Mazerolle et al., 2010). Significant deficits in nearly all frequency domains are shown in left parieto-temporal regions including auditory cortex and association areas (Heschl's gyrus, transverse/superior temporal gyrus BA 41/42, BA 21/22) in the left hemisphere. Bilateral prefrontal regions are also compromised with EEG deficits identified in bilateral middle and medial prefrontal regions including BA 6, 8, 9 10/47, and 11. BA 40, 39, and 2 show decrements in both hemispheres with higher levels in the left. The anterior cingulate gyrus shows deficits in both hemispheres with higher levels in the right hemisphere (BA 24/32). Nearly all of the affected regions in this patient are shown to be increased in blood oxygenation level dependent activity in control subjects during reading and word generation tasks (Liegeois et al., 2004). Of importance, concerning working memory and integrative functions associated with learning and encoding novel information, regions in the left dorsolateral prefrontal cortex involved in auditory and verbal working memory also show significant deficits in activity (Grasby et al., 1993; Paulesu, Frith, & Frackowiak, 1993). Changes in the EEG alpha rhythm may represent a variety of important cognitive functions, including encoding and retrieval, and information processing (Doppelmayr, Klimesch, Hodlmoser, Sauseng, & Gruber, 2005; Doppelmayr et al., 2005; Gruber, Klimesch, Sauseng, & Doppelmayr, 2005; Sauseng, Klimesch, Doppelmayr, et al., 2005; Sauseng, Klimesch, Schabus & Doppelmayr, 2005; Sauseng, Klimesch, Stadler, et al., 2005). Moreover, selective bands within the alpha frequency are also proposed to play a particular role in attention and working memory, with the lower alpha band (8–10 Hz) being associated with attention and the higher alpha band (10–12 Hz) being associated with working memory processes (Sauseng, Klimesch, Stadler, et al., 2005). Alpha band power was also detected as having frontal (anterior cingulate) and limbic variants that are not susceptible to suppression by anxiolytics like posterior alpha rhythms (Connemann et al., 2005). Of interest, the hallmark signature of EEG changes due to dementia of the Alzheimer's type is a general slowing and decrease of alpha activity, which also shows an increase in theta activity. Cognitive decline is shown to be associated with changes in higher frequency domains in occipital and temporal regions and such changes are shown to correlate with disease severity (Jeong, 2004). Posterial commissural fibers within the corpus callosum have shown the strongest correlation with the alpha frequency, such that the Isthmus and Tapetum in the superior occipital cortex show the highest positive association with the alpha frequency. Data suggest that the period of cortico-thalamocortical cycles may modulate

the alpha frequency domain, and white matter architecture is more associated with the alpha frequency domain than neocortical region or grey matter (Valdes-Hernandez et al., 2010).

EEG LORETA, MRI, and neuropsychological data show agreement in the current case study. Although the specific network integrity and correlative relationships with cognitive test scores was not analyzed, it can be surmised that localized functional integrity can be dependent on functional network assemblies (Cannon et al., 2009; Hagmann et al., 2008). Therefore, comparisons to the Lifespan database may be a valid tool for evaluating patient symptoms and correlating them with neural processes. In addition, this type of analyses is important to differential diagnosis, measuring treatment efficacy and developing multidisciplinary treatment models. The LORETA analyses for this patient as compared to the Lifespan database identify multifocal deficits in regions also identified by MRI. Although the specific functions of the EEG, and reasons for specific deficits in specific frequencies as a result of damage remain uncertain, we know them to be involved in cognitive and attentive processes and disruptions in specific regions and associated EEG frequency domains are associated with psychiatric syndromes (Coutin-Churchman et al., 2003; Hughes, 1995, 1996). Of interest, social and activities of daily functioning are minimally impaired in this patient. He interacts appropriately with siblings and peers, although difficulty with memory for names presents significant challenges. Comparison to a control group is often a challenge in the clinical setting, and the Lifespan database offers a potential method to facilitate more comprehensive clinical data to better serve the patient. Two important limitations to the current data are that we cannot discern if the Encephalomalacia is an end-point or progressive in nature and we are not certain of hemispheric language dominance at birth. We will continue to monitor this patient over time. The cumulative data show agreement between MRI, EEG LORETA, and neuropsychological data, and further multidisciplinary studies of this type are needed to further our understanding of neurocognitive mechanisms in pediatric populations.

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