Biofeedback
Volume 37, Issue 2, pp. 71–80

©Association for Applied Psychophysiology & Biofeedback
www.aapb.org

FEATURE ARTICLE

The Importance of Electroencephalogram Assessment for Autistic Disorders

Robert Coben, PhD

Neurorehabilitation & Neuropsychological Services, Massapequa Park, NY

Keywords: EEG, QEEG, autism, source localization, independent components analysis, connectivity

Autistic disorders are a set of complex syndromes that lead to challenges impacting communication, behavior repertoire, and social skills. The etiology of autism is unknown but is likely epigenetic in nature. It is likely associated with an inflammatory process leading to neuroinflammation in early childhood. Autistic disorders include seizures in approximately one-third of the cases and there are often regions of brain dysfunction associated with neural connectivity anomalies. The electroencephalogram (EEG) is presented as a premiere tool to assess these difficulties due to its' non-invasive nature, availability and utility in detailing these difficulties. Techniques for seizure detection, monitoring, and tracing their propagation are shown. Similar approaches can then be utilized for assessing EEG oscillations, which are at the heart of these neuronal regulation dysfunctions. Autistic disorders are clearly associated with regions of dysfunction and quantitative electroencephalogram strategies for assessing these impairments are shown. These include techniques for increasing the specificity and spatial resolution of the EEG such as source localization and independent components analysis. Lastly, advanced methods for assessing the neural connectivity problems that underlie the difficulties of these children are presented. EEG assessment, when processed and analyzed with the most advanced techniques, can be invaluable in the evaluation of autistic disorders.

Autism is a neurodevelopmental disorder characterized by deficits in social interaction, communication, and restricted repetitive behavior (Santangelo & Tsatsanis, 2005; Tidmarsh & Volkmar, 2003; Turner, Frost, Linsenbardt, McIlroy, & Muller, 2006). The heterogeneous range of pervasive developmental disorders (with onset by age 3 years) includes the following classifications: Autistic Disorder, Rett's Disorder, Childhood Disintegrative Disorder, Asperger's Disorder, and Pervasive Developmental Disorder-Not Otherwise Specified (American Psychological Association, 1994; *Diagnostic and Statistical Manual of Mental Disorders, fourth edition* [*DSM-IV*]).

DSM-IV Criteria for Autistic Disorder

In Autistic Disorder, social interaction is marked by a lack of appropriate eye gaze, facial expression, or gestures to regulate social interaction. There is often a failure to sustain developmentally appropriate peer relationships and an inability to initiate spontaneous shared activities. Delayed or lack of spoken language is frequently cited. Children with Autism often fail to initiate or sustain conversation. Communication is associated with stereotyped repetitive verbalizations or idiosyncratic language. Behavior may include an all encompassing preoccupation with one or more restricted areas of interest, inflexible adherence to routines or rituals, and repetitive motor patterns such as hand or finger flapping or twisting (American Psychological Association, 2000; *Diagnostic and Statistical Manual of Mental Disorders, fourth edition-text revision* [*DSM-IV-TR*]). Other pervasive developmental disorders (as listed above) share similar features, but often have varying severity levels. The notion of a spectrum of autistic disorders was coined to describe this spectrum of disorders and severity levels. Rett's and Child Disintegrative Disorder are associated with regressions from previous levels of functioning. In Asperger's Disorder, language dysfunction is absent.

The term Autistic Spectrum Disorder (ASD) represents a group of disorders which includes all five diagnostic subtypes above including Autism, Pervasive Developmental Disorder-Not Otherwise Specified, Rett's Disorder, Child Disintegrative Disorder, and Asperger's Disorder (Centers for Disease Control and Prevention [CDC], 2006).

Prevalence of ASD

The CDC (2006) reported the prevalence of ASD as two to six per 1000 children. The frequency of ASD can be summarized as ranging between one in 500 to one in 166 children in the United States. Over the past twenty years, approximately 500,000 individuals (infants to age 21) have been diagnosed with ASD. In fact, their most recent report (CDC, 2007) suggests a prevalence of one in 150.

Autism and Seizure Disorders

Autism may be viewed as a generalized inflammatory process impacting multiple body and metabolic systems (Becker, 2007; Herbert, 2005). The primary symptoms of autism should largely be considered a result of brain dysfunction, neuroinflammation, or oxidative stress (Chauhan & Chauhan, 2006). Multiple neuroimaging studies have demonstrated brain anomalies in autistics compared to healthy controls (Boddaert et al., 2002; McAlonan et al., 2004; Page et al., 2006). Consistent with this, seizures and epilepsy have been commonly observed in autistic samples. Recent analyses have estimated the prevalence of seizure disorders in autistic series at anywhere from 20% (Canitano, 2007) to 46% (Hughes & Melyn, 2005). Based on recent analyses, the average prevalence would be estimated near 36% (Danielsson, Gillberg, Billstedt, Gillberg, & Olsson, 2005; Hara,2007; Hughes & Melyn, 2005; Parmeggiani et al., 2007). Increasing cognitive/intellectual disability appears to be associated with seizure disorders in autism (Amiet et al., 2008; Danielsson et al., 2005; Hara, 2007). There also appears to be a greater risk for seizure disorders in autistic females (Amiet et al., 2008). Paroxysmal discharges occur in an even higher proportion of autistics, but the significance of these remain uncertain (Hughes & Melyn, 2005; Parmeggiani et al., 2007). Ray, Tao, Hawes-Ebersole, and Ebersole (2007) have suggested that the initial phase of cortical spikes may relate to underlying intracranial foci. Other work has suggested that EEG spikes may reflect underlying morphological brain abnormalities (Shelley, Trimble, & Boutros, 2008) and/or metabolic disturbances (Kobayashi, Bagshaw, Grova, Dubeau, & Gotman, 2006).

Recent estimates suggest that approximately one-third of all autistic children experience a regression in speech or behavior early in life (Canitano, 2007). Tuchman and Rapin (1997) were unable to relate early regression to seizure disorders, but suggested that the EEG is abnormal in a greater proportion of autistic children that regress than those that do not. Abnormal EEGs are also present in the majority of autistic children with seizure disorders (Hughes & Melyn, 2005). For these reasons, experts in the field have recommended the use of routine and sleep EEGs in the evaluation of autistic disorders, especially when there has been regression or there are signs of possible seizures (Kagan-Kushnir, Roberts, & Sneed, 2005).

Therefore, the first reason for the use of EEG assessment in cases of ASD is the detection of epileptiform and/or paroxysmal activity. The following exemplar is presented as a demonstration of the utility of such an assessment. This patient presented to our clinic in 2006 and was diagnosed by a pediatric neurologist with Pervasive Developmental Disorder-Not Otherwise Specified at the age of 3. He was delivered at 36 weeks gestation due to gestational diabetes and had high liver enzymes. There was no history of regression, but a developmental delay in speech/language abilities and a complete inability to identify letters or read words. At the time of his assessment he was taking no medication, was receiving speech, occupational, and physical therapies at school, and his intelligence was considered low average (Weschler Intelligence Scale for Children, Fourth Edition, Full Scale Intelligence Quotient = 80).

A clinical EEG (resting) conducted in our clinic at intake resulted in the following: Resting eyes closed and open data was acquired with the Deymed 32-True Scan acquisition system (Deymed Diagnostic USA, Payette, ID) (Deymed Diagnostic, 2004) and viewed/analyzed with the Persyst/Reveal–spike and seizure detection system (Persyst Development Corporation, Prescott, AZ) (Persyst, 2004). This included 19 cephalic, ground, and reference channels. Figure 1a shows 4 epochs (seconds) of data during which the patient clearly evidenced paroxysmal activity consistent with a focal spike and wave pattern (Fisch, 1999; Goldensohn, Legatt, Koszer, & Wolf, 1999). On the right side of this figure is a voltage topographic map suggestive of a left occipital-parietal-temporal localization.

Figure 1b is the spike review of all detected events through the reveal analysis. There was a significant 160 events detected over the 20 minute recording time. Analysis of individual components of such activity showed four separate patterns with similar areas of morphological disturbance. These all involve the left posterior region likely including regions near the left occipital and left temporo-parietal junction.

Figure 1c is a spike review propagation map. It shows the propagation of averaged activity over all 160 spike review events in 15 millisecond time blocks preceding and subsequent to the spike event itself. This shows how the

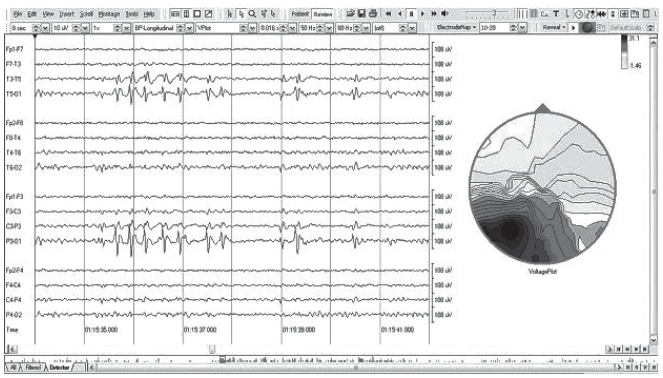

Figure 1a. Spike and wave pattern detected by the Persyst/reveal–spike and seizure detection system (longitudinal montage) with voltage mapping.

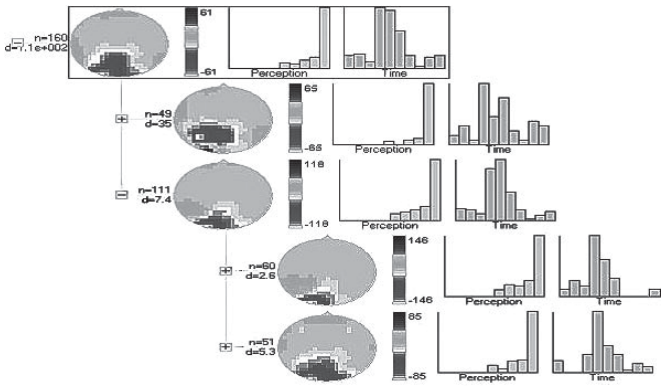

Figure 1b. Summary of spike reveal/reveal with component mapping, time, and perception.

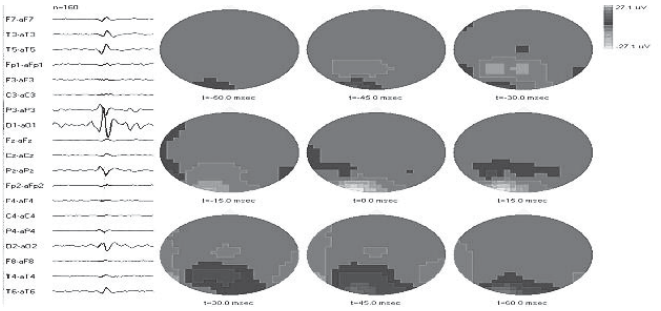

Figure 1c. Spike review propogation mapping.

voltage increased over the occipital region and decreased over the parietal area prior to the spike event. This pattern then reverses near the event itself and is then followed by an increased voltage pattern over these regions and a decrease in voltage over bilateral temporal regions. This allows one to understand the process of events that occur related to these transient events. Interestingly, these regions of the brain are viewed as crucial for recognition of letters, graphemes and reading (Rosen, 2006) and this patient was completely alexic upon his initial presentation. Interestingly, intervention that reduced these paroxysmal events led to significant reductions in autistic symptoms and improvements in his letter recognition and beginning reading skills.

Seizure and paroxysmal activity that is or resembles epileptiform activity is just one type of EEG oscillation that can be seen in the electroencephalogram. EEG oscillations are viewed as a marker of neural integration and are thought to be generated by the summation of excitatory and inhibitory post-synaptic potentials (Speckman, Elger, & Altrup, 1993). These oscillations appear to be related to the integrity of neural circuits in cortical and thalamocortical pathways (Cacioppo, Tassinary, & Berntson, 2007). The significance of EEG oscillations across multiple frequencies has been demonstrated (Hermann & Demiralp, 2005; Knyazev, 2007). It is these oscillations in various EEG waveforms that are the basis of the EEG phenotype approach (Gunkelman, 2006; Johnstone, Gunkelman, & Lunt, 2005). This approach seeks to classify individuals with neuropsychiatric disturbances by their EEG profiles (waveform oscillations) and not by *DSM* standards (Gunkelman, 2006). Use of EEG oscillatory anomalies has been shown helpful in the prediction of medication response in both attention (Arns, Gunkelman, Breteler, & Sponk, 2008) and depressive disorders (Suffin & Emory, 1995; Suffin, Emory, Schiller, & Kling, 2007). When observable, these patterns in the EEG are considered important and likely are the underlying reason for the success of quantitative EEG methods (Chabot, di Michele, & Prichep, 2005; Monastra, Lubar, & Linden, 2001; Prichep, 2007).

Figure 2a shows an oscillatory pattern localized over C3 and C4 (see Chatrian, Lettich, & Nelson, 1985, for clarification of standardized EEG electrode positioning). This pattern is within the alpha band, has a wicket-like appearance, and is referred to as a mu rhythm (Fisch, 1999). Oberman et al. (2005) showed that poor mu rhythm suppression was present in some autistic children and that this related to the concept of mirror neuron dysfunction (diPellegrino, Fadiga, Fogassi, Gallese, & Rizzolatti, 1992) which leads to deficits in their observation-execution system.

Figure 2b is another example of an oscillatory pattern often seen in autistic children. In this resting eyes open EEG recording there is apparent slow (delta and theta) activity over the right posterior regions of the cortex, including occipital, parietal, and posterior temporal areas. Recent research has suggested that these are common regions of dysfunction in the brains of autistic children (Coben, Clarke, Hudspeth, & Barry, 2008; Stroganova et al., 2007). In fact, Pelphrey, Morris, McCarthy, and Labar (2007) have shown that neural systems underlying these regions (fusiform gyrus, superior temporal sulcus, amygdala) are critical to the processing of human facial emotions and deficits in these may underlie social skill impairments in such children.

Regions of Brain Dysfunction in Autistic Disorders

In addition to paroxysmal disturbances, there is significant evidence of morphological and functional disturbances in brain functioning in individuals on the autistic spectrum. Neuroimaging findings have shown dysfunction in various regions in the brains of autistic individuals. The findings of a voxel-based magnetic resonance imaging (MRI) study indicated that children with Autism had a significant reduction in total grey matter volume as well as fronto-striatal and parietal networks. In addition, white matter was reduced in the cerebellum, left internal capsule, and fornices (McAlonan

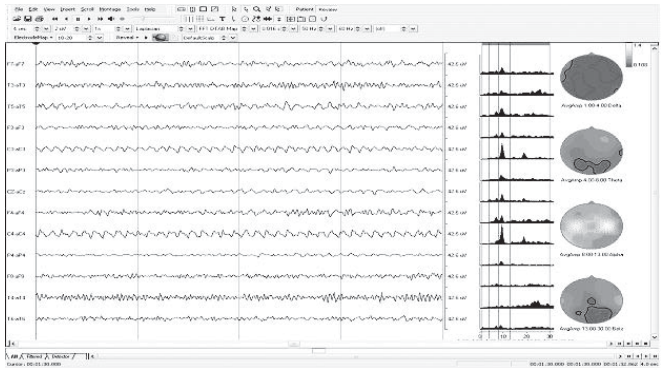

Figure 2a. Mu oscillation with EEG, spectral display, and topographical mapping (laplacian montage).

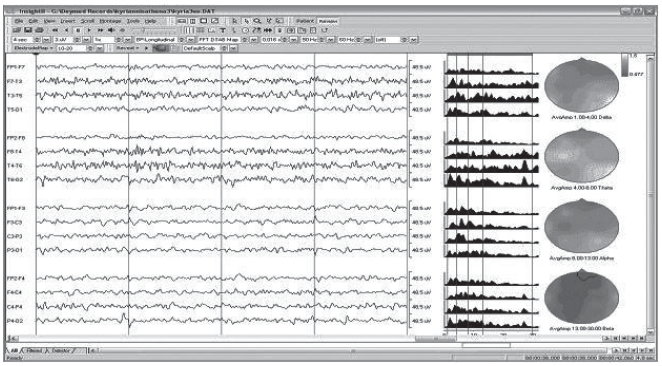

Figure 2b. Right posterior slow activity with EEG, spectral display, and topographical mapping (longitudinal montage).

et al., 2004). Anomalies in brain metabolites have also been reported in the amygdala-hippocampal regions in ASD (Page et al., 2006). Boddaert et al. (2002) utilized positron emission tomography (PET) to assess localized brain dysfunction in Autism. Findings indicated significant bilateral temporal hypoperfusion in the superior temporal gyrus and sulcus. In the study, temporal hypoperfusion was noted in 77% of the children with Autism. Other research utilizing functional neuroimaging has linked social cognition dysfunction and language deficits in Autism to neural substrates (Just, Cherkassky, Keller, & Minshew, 2004; McAlonan et al., 2004; Pelphrey, Adolphs, & Morris, 2004; Welchew et al., 2005). For example, the functional integrity of occipital-temporal brain regions (amygdala, the superior temporal sulcus, and fusiform gyrus) have been implicated in facial processing and social skills (Pelphrey et al., 2004).

Assessment of regional brain dysfunction requires functional brain imaging techniques as static measures tend to find few abnormalities in autistic disorders. This would include techniques such as functional MRI, PET, single photon emission computed tomography, EEG, or magnoencephalography (MEG). Some of these techniques require sedation or injection of radioactive material so as to make participation difficult for a typical autistic child. EEG appears to be the most clinically available and least invasive of these techniques. There is emerging evidence that EEG data can be used to assess regions of neural dysfunction in autistic children (Chan, Sze, & Cheung, 2007; Coben, Clarke et al. 2008). Recently, Coben, Chabot, and Hirshberg (2008) have demonstrated that autistic children can be distinguished from typically developing children by their EEGs alone at a rate in excess of 88%. They were also able to show that unique patterns of regional dysfunction could be discerned through the quantitative analysis of the EEG.

The following two examples are provided to demonstrate how spectral and quantitative analysis of the resting EEG can assess regions of brain functioning in individuals on the autistic spectrum. Case one presented at the age of 19 after he withdrew from his first year of college. His diagnoses included Asperger's Disorder and Nonverbal Learning Disability. Presenting symptoms included difficulties with motivation, organization, lying, stealing, and social anxiety. He preferred to be alone and had no significant relationships outside of his family. He also struggled academically in math and science classes. His return home from college occurred after he withdrew academically and socially and would not leave his room.

Cross-spectral analysis of EEG data involves multiple steps of artifacting, data conversion, and topographical mapping (John, 1977). The cases presented display findings from resting eyes open EEG data. These data were artifacted so that muscle, eye, and other artifacts (see Sethi, Sethi, Torgovnick, & Arsura, 2007, for a discussion of such artifacts) are removed from the data set. Once this data is relatively artifact-free a conversion of the data is performed with digital filtering/complex demodulation (Schroeder & Barr, 2000; Walter & Adey, 1965) or a fast fourier transform function (Bendat & Piersol, 1971; Cooley & Tukey, 1965), following which frequency analyses may be performed. Specific analyses may then be performed and converted into topographical maps for visual display purposes with interpolation of data between electrode sites used to fill in missing data points. Spherical spline interpolation may be one of the most effective forms of this technique (Shaw & Koles, 1993).

Figure 3a displays the results of topographical mapping of EEG magnitude with a weighted average reference (Lemos & Fisch, 1991) for case one as described above. Figure 2a above displayed his mu oscillatory pattern seen over 4 epochs (1 second of data). Figure 3a now shows mapping of averaged data over a 2-minute, artifact free recording period. From this, it now becomes apparent that the greatest magnitude for his mu rhythm activity is between 9 and 11 Hz which is common for such a presentation (Fisch, 1999). There is

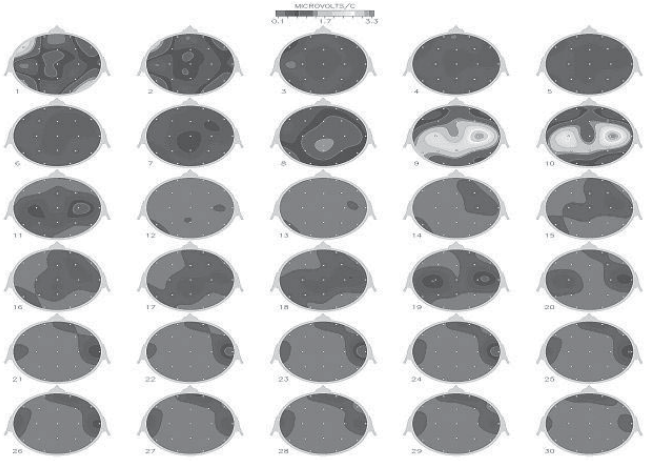

Figure 3a. Topographical mapping of EEG magnitude data in single Hz bins (weighted average montage). Mu seen maximally at 9–11 Hz.

also a second reverberation of this rhythm seen at 19–20 Hz attesting to its prominence. Such a prominent rhythm is often seen in individuals with mirror neuron dysfunction. This has been shown to exist in children on the autistic spectrum and likely impairs their observation-execution system involved in activity, imitation, and socialization (Bernier et al., 2007; Williams et al., 2006).

Figure 3b displays the results of a standardized low resolution brain electromagnetic tomography (sLoreta) analysis. This is an advanced inverse mathematical solution that localizes the sources of the EEG signal of interest (Pascual-Marqui, 2002; Pascual-Marqui, Esslen, Kochi, & Lehmann, 2002). The interested reader should consult Pascual-Marqui (1999) for a discussion of these formulae and solution. Standardized low resolution brain electromagnetic tomography (an improvement upon the original Loreta solution) is considered an accurate solution. Based on the eyes open resting relative power data from case one,

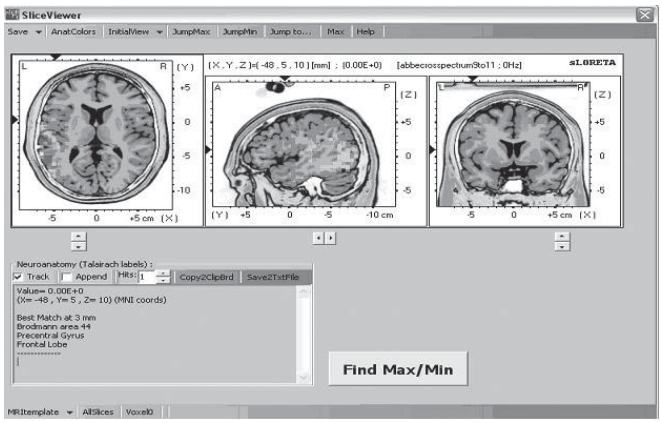

Figure 3b. Source localization of mu pattern performed and displayed with sLoreta slice viewer. Maximal localization shown in white, red, yellow, and green. A color version of this figure will be posted, along with this article, at http://www.aapb.org/magazine.html.

Figure 3b shows regions of significant source localization. Relative power is defined as amplitude squared (absolute power) within a frequency divided by the total absolute power (Evans & Abarbanel, 1999). These data suggest source localization of his significant mu rhythm to the frontal pars opercularis (Brodmann 44), precentral gyrus, middle and superior temporal gyri, fusiform gyrus, and insula. Interestingly, Dapretto et al. (2006) have shown that high functioning autistic children showed diminished activity in the pars opercularis while imitating and observing emotional expressions and this was significantly correlated with their ratings of social skill impairments.

Figure 3c displays findings from an independent components analysis (ICA) performed with the runica function (Makeig et al., 1997) of EEGLAB (Delorme & Makeig, 2004; Onton & Makeig, 2006; Onton, Westerfield, Townsend, & Makeig, 2006). ICA blindly decomposes multi-channel EEG data into maximally independent component processes (Hyvarinen, Karhunen, & Oja, 2001) that express brain generated EEG activities once artifacts are removed (Onton & Makeig, 2006). ICA reduces redundancy and reveals unique EEG components. This was performed on the logged power of the EEG data of case one for the eyes open condition, focusing on 10 Hz activity which was the peak frequency of his mu rhythm. These multiple components suggest bilateral and distributed dysfunction including frontal, temporal, and central neural systems. The sLoreta data reviewed above also confirms the notion that mirror neuron dysfunction is a distributed problem across a complicated neuronal system as Coben, Hudspeth, and colleagues (2008) have suggested.

Case two presented at the age of six with a diagnosis of ASD. Presenting symptoms included problems with attention, distractibility, social skills, eye contact, motor planning, math, and comprehension. She was withdrawn from most people other than her parents and her conversations were

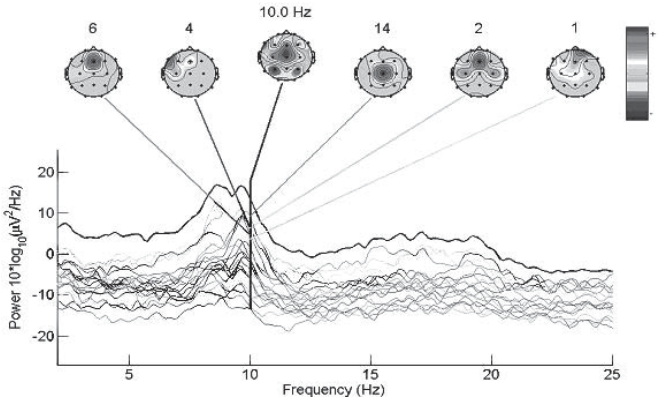

Figure 3c. Independent component analysis (ICA) (runica function of EEGLAB) of 10 Hz mu activity showing ICA. Maximal activity is shown in darker colors.

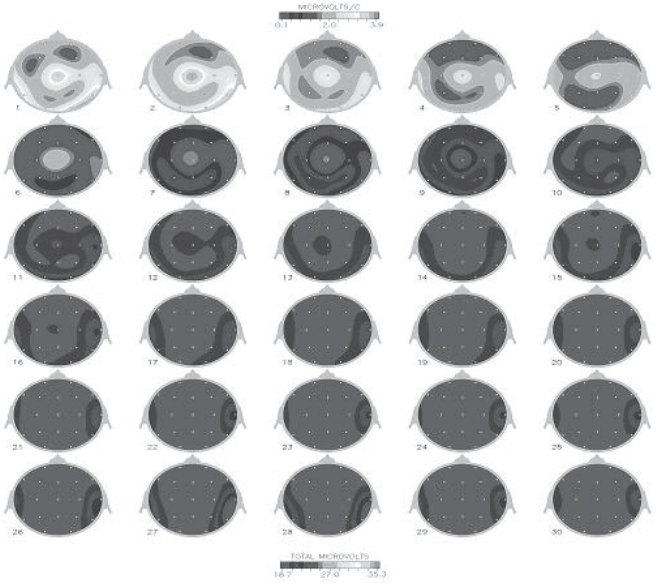

Figure 4a. Topographical mapping of EEG magnitude data in single Hz bins (weighted average montage). Maximal right posterior slow activity shown in white–gray from 1–4 Hz.

largely self-directed and not reciprocal. Figure 4a displays the results of topographical mapping of EEG magnitude with a weighted average reference for case two. Figure 2b above displayed her slow wave oscillatory pattern seen over 4 epochs (1 second of data). Figure 4a now shows mapping of averaged data over a 2-minute, artifact free recording period. Again, these eyes open data show apparent slow (delta and theta) activity over the posterior regions of the cortex, which appear to be of greatest amplitude on the right side. While there are excesses from 1 to 5 Hz, this is maximal in the delta range from 1 to 3 Hz. These cortical regions overly regions of the brain that are substrates of social cognitive dysfunction in autistics, including the amygdala, superior temporal gyrus and fusiform gyrus (Pelphrey et al., 2004; Pelphrey et al., 2007). Van Kooten et al. (2008) have recently shown that autistics showed reductions in neuron densities and number in the fusiform gyrus compared to controls. Due to the inability to fully activate the fusiform gyrus, autistics appear to recruit different, less effective, neural networks and rely on different strategies when processing facial emotions (Hubl et al., 2003; Wang, Dapretto, Hariri, Sigman, & Bookheimer, 2004).

Figure 4b displays the results of a sLoreta analysis of this EEG data stream. Based on the eyes open resting relative power data from case two, Figure 4b shows regions of significant source localization. These data suggest source localization of her significant slow wave oscillations over posterior cortices to the fusiform gyrus, inferior occipital gyrus, inferior and middle temporal gyri, parahippocampal gyrus, and lingual gyrus.

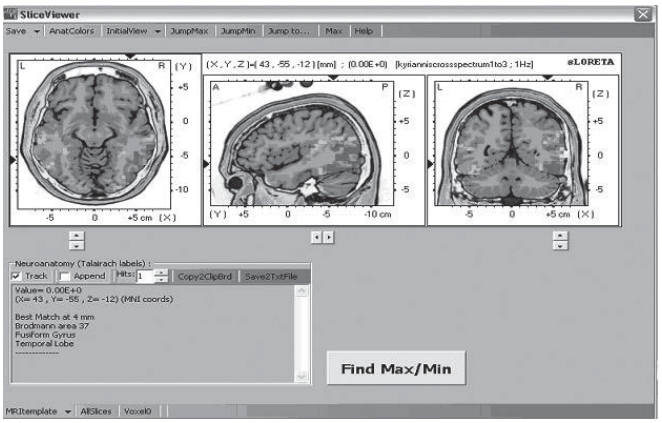

Figure 4b. Source localization of right posterior slow activity pattern performed and displayed with sLoreta slice viewer. Maximal localization shown in white, purple, red, yellow, and green. A color version of this figure will be posted, along with this article, at http://www.aapb.org/magazine.html.

Figure 4c are findings from an ICA performed with the runica function of EEGLAB. This was performed on the logged power of the EEG data of case two for the eyes open condition, focusing on 2 Hz activity. These multiple components (especially components 1, 6, 8, and 9) suggest dysfunction along a system composed of occipital, posterior temporal, and anterior temporal regions. This concurs with the sLoreta analysis suggesting a distributed network involved in these processes. As a result, the notion of neural connectivity between such regions becomes critical in understanding autistic symptoms and neural disturbances.

Autism as a Disorder of Neural Connectivity

"Connectivity" is defined as any number of means of measuring the communication between two or more neural

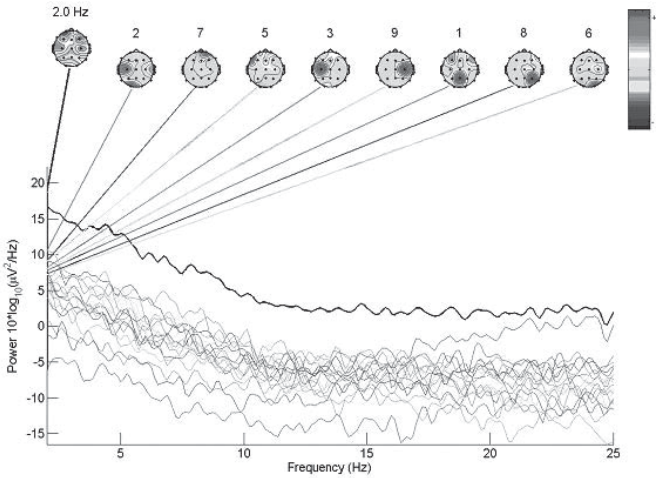

Figure 4c. ICA (runica function of EEGLAB) of 2 Hz activity showing independent components of activity. Maximal activity is shown in darker colors with special emphasis on components 1, 6, 8, and 9.

locations. Multiple research studies have now shown that neural connectivity is disordered in autistic individuals. There is evidence for both a pattern of hypoconnectivity (Cherkassky, Kana, Keller, & Just, 2006; Coben, Clarke et al., 2008; Hughes, 2007) and regions of hyperconnectivity (Mizuno, Villalobos, Davies, Dahl, & Muller, 2006; Turner et al., 2006) as well.

Rippon, Brock, Brown, and Boucher (2007) proposed a model of Autism associated with information integration deficits resulting from reduced connectivity between specialized local neural networks and overconnectivity within individual neural assemblies. A fascinating theory has been put forth by Courchesne and Pierce (2005). They theorized that early developmental neuroinflammatory reactions may cause malfunction of frontal minicolumn microcircuitry. This includes brain overgrowth that interferes with connectivity between units of cerebral information processing. Buxhoeveden, Semendeferi, Schenker, and Courchesne (2004) have shown that by the age of three these regions have expanded and neuropil space is reduced. This, then, would lead to excessive connectivity within the frontal lobes and limited connectivity between frontal cortex and other systems. This is of significant concern given their crucial role in developing linguistic, cognitive, and emotional control, and social processes.

The theory that autistic brains have both regions of excessive connectivity and other areas that are too loosely connected appears to have been recently confirmed by at least two separate EEG studies (Coben, Hudspeth, Clarke, & Barry, 2006; Murias, Webb, Greenson, & Dawson, 2007). Coben and Myers (in press) have discussed this "connectivity theory of autism" and suggest that EEG multivariate connectivity measures may be used for assessment and treatment planning.

Figure 5a now shows a multivariate connectivity analysis (Hudspeth, in press) for the eyes open EEG from case one reviewed above based on coherence data. These analyses are based on principal components analysis which reduces redundancy and displays unique data. The analysis of the alpha band only is shown as this is the frequency band of interest for this case. Stretched lines indicate underconnectivity and electrode sites near or on top of each other suggest overconnectivity. There is clear evidence in this example of underconnectivity between temporal/central and frontal sites which is more prominent on the left side. This is consistent with the source localization (sLoreta) analysis shown in Figure 3b and the ICA component number 4 shown in Figure 3c. This completes the picture of a neural system connectivity disturbance underlying the mu rhythm/mirror neuron dysfunction.

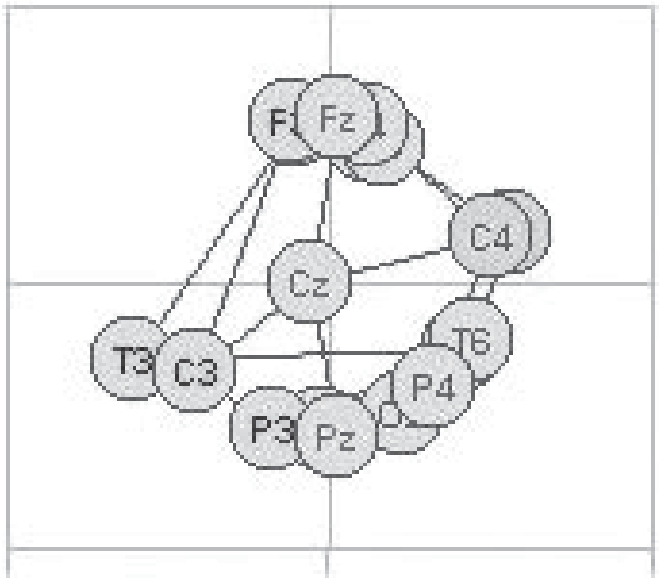

Figure 5a. Multivariate connectivity analysis (Hudspeth, 2008) in the horizontal view showing findings in the alpha band for mu activity.

Figure 5b shows a similar multivariate connectivity analysis but only for the delta band for case two which showed excessive slow activity focused in this frequency band. Here, there is clear evidence for right sided underconnectivity between temporal-parietal-occipital and more anterior temporal regions. This is the same pathway that has been shown to be involved in facial affect processing in autistics and is impaired in this child with severe social problems. It is also consistent with the source localization and ICA analyses shown above in Figures 4b and c. These examples illustrate the power of EEG data to assess and conceptualize

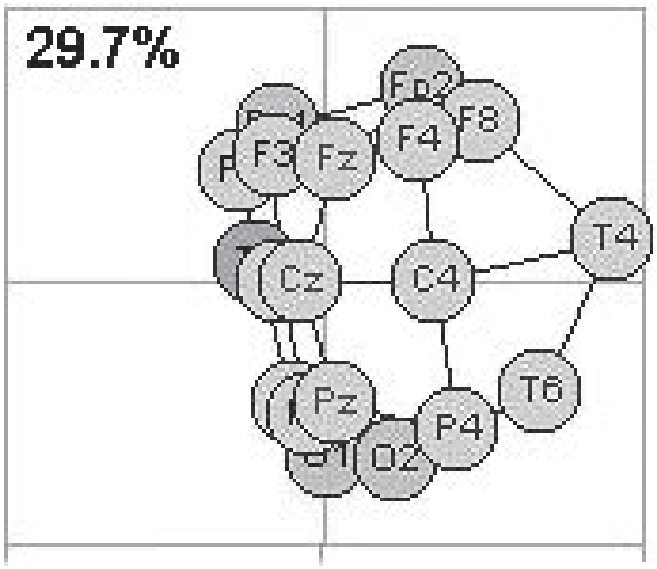

Figure 5b. Multivariate connectivity analysis (Hudspeth, 2008) in the horizontal view showing findings in the delta band for slow activity over the right posterior regions.

the neurophysiological impairments of autistic children in a way that few other types of assessments can.

Summary

Children with ASD have neurophysiological dysfunctions that underlie their symptomatology. This article has presented information to support the idea that these difficulties can be assessed accurately and specifically with EEG data. Such an assessment is possible with the vast majority of autistic children and is not invasive. The temporal resolution of EEG is superior to other techniques and source localization and other techniques illustrated above can enhance its spatial resolution. EEG data may be beneficial in the assessment and diagnosis of autistic disorders, screening for possible seizures, and assessing the neurophysiological challenges of these children. Such data may then be used for treatment planning and to evaluate the effects of intervention as well.

References

American Psychological Association (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.

American Psychological Association (2000). *Diagnostic and statistical manual of mental disorders-text revision.* (4th ed.). Washington, DC: Author.

Amiet, C., Gourfinkel-An, I., Bouzamondo, A., Tordjman, S., Baulac, M., Lechat, P., et al. (2008). Epilepsy in autism is associated with intellectual disability and gender: Evidence from a meta-analysis. *Biological Psychiatry, 64*, 577–582.

Arns, M., Gunkelman, J., Breteler, M., & Sponk, D. (2008). EEG phenotypes predict treatment outcome to stimulants in children with ADHD. *Journal of Integrative Neuroscience, 7*(3), 1–18.

Becker, K. G. (2007). Autism, asthma, inflammation, and the hygiene hypothesis. *Medical Hypotheses, 69*, 731–740.

Bendat, J. S., & Piersol, A. G. (1971). *Random data: Analysis and procedures.* New York: Wiley.

Bernier, R., Dawson, G., Webb, S., & Murias, M. (2007). EEG mu rhythm and imitation impairments in individuals with autism spectrum disorder. *Brain and Cognition, 64*, 228–237.

Boddaert, N., Chabane, N., Barthelemy, C., Bourgeois, M., Poline, J. B., Brunelle, F., et al. (2002). Bitemporal lobe dysfunction in infantile autism: Positron emission tomography study. *Journal of Radiology, 83*, 1829–1833.

Buxhoeveden, D., Semendeferi, K., Schenker, N., & Courchesne, E. (2004). Decreased cell column spacing in autism. *Social Neuroscience, 582*, 6.

Cacioppo, J. T., Tassinary, L. G., & Berntson, G. (2007). *Handbook of psychophysiology.* New York: Cambridge University Press.

Canitano, R. (2007). Epilepsy in autism spectrum disorders. *European Child and Adolescent Psychiatry, 16*, 61–66.

Cantor, D. S., Thatcher, R. W., Hrybyk, M., & Kaye, H. (1986). Computerized EEG analyses of autistic children. *Journal of Autism and Developmental Disorders, 16*,169–187.

Centers for Disease Control and Prevention (2006). How common are autistic spectrum disorders (ASD)? Retrieved December 1, 2006, from http://www.cdc.gov/ncbddd/autism/asd_common.htm

Centers for Disease Control and Prevention (2007). Prevalence of the autism spectrum disorders (ASDs in multiple areas of the United States, 2000 and 2002). *MMWR, 56 (SS 1–2)* 12–28.

Chabot, R. J., di Michele, F., & Prichep, L. (2005). The role of quantitative electroencephalography in child and adolescent psychiatric disorders. *Child and Adolescent Psychiatric Clinics of North America, 14*, 21–53.

Chan, A. S., Sze, S. L., & Cheung, M. C. (2007). Quantitative electroencephalographic profiles for children with autistic spectrum disorder. *Neuropsychology, 21*, 74–81.

Chatrian, G. E., Lettich, E., & Nelson, P. L. (1985). Ten percent electrode system for topographic studies of spontaneous and evoked EEG activity. *American Journal of EEG Technology, 25*, 83–92.

Chauhan, A., & Chauhan, V. (2006). Oxidative stress in autism. *Pathophysiology, 13*, 171–181.

Cherkassky, V. L., Kana, R. K., Keller, T. A., & Just, M. A. (2006). Functional connectivity in a baseline resting-state network in autism. *NeuroReport, 17*, 1687–1690.

Coben, R., Chabot, R., & Hirshberg, L. (2008). *Neurophysiology of autistic spectrum disorder.* Presented at the 39th Annual Meeting of the American Association of Psychophysiology and Biofeedback, Daytona Beach, Florida.

Coben, R., Clarke, A. R., Hudspeth, W. J., & Barry, R. J. (2008). EEG power and coherence in autistic spectrum disorder. *Clinical Neurophysiology, 119*, 1002–1009.

Coben, R., Hudspeth, W. J., Clarke, A., & Barry, R. (2006). *QEEG in autistic disorders: Power and connectivity analyses*. Presented at the 14th Annual Conference of the International Society for Neuronal Regulation, Atlanta, Georgia.

Coben, R., Hudspeth, W. J., Sherlin, L., & Myers, T. (2008). Mu/mirror neuron dysfunction in autistic spectrum disorder: Source localization and connectivity analyses. Manuscript submitted for publication.

Coben, R., & Myers, T. (2008). Connectivity theory of autism: Use of connectivity measures in assessing and treating autistic disorders. *Journal of Neurotherapy, 12*, 161–179.

Cooley, J. W., & Tukey, J. W. (1965). An algorithm for the machine calculation of complex Fourier series. *Mathematics and Computation, 19*, 297–301.

Courchesne, E., & Pierce, K. (2005). Why the frontal cortex in autism might be talking only to itself: Local over-connectivity but long-distance disconnection. *Current Opinion in Neurobiology, 15*, 225–230.

Danielsson, S., Gillberg, I.C., Billstedt, E., Gillberg, C., & Olsson, I. (2005). Epilepsy in young adults with autism: A prospective population-based follow-up study of 120 individuals diagnosed in childhood. *Epilepsia, 46*, 918–923.

Dapretto, M., Davies, M. S., Pfeifer, J. H., Scott, A. A., Sigman, M., Bookheimer, S. Y., et al. (2006). Understanding emotions in others: Mirror neuron dysfunction in children with autism spectrum disorders. *Nature Neuroscience, 9*, 28–30.

Dawson, G., Warrenburg, S., & Fuller, P. (1982). Cerebral lateralization in individuals diagnosed as Autistic in early childhood. *Brain and Language, 15*, 353–368.

Delorme, A., & Makeig, S. (2004). EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent components analysis. *Journal of Neuroscience Methods, 134,* 9–21.

Deymed Diagnostic (2004). TruScan 32 Specifications. Retrieved March 24, 2006, from http://www.deymed.com/truscan32.asp

diPellegrino, G., Fadiga, L., Fogassi, L., Gallese, V., & Rizzolatti, G. (1992). Understanding motor events: A neurophysiological study. *Experimental Brain Research, 91,* 176–180.

Evans, J. R., & Abarbanel, A. (1999). *Introduction to quantitative EEG and neurofeedback.* San Diego, CA: Academic Press.

Fisch, B. J. (1999). *Fisch and Spehlmann's EEG Primer: Basic principles of digital and analog EEG* (3rd ed.). New York: Elsevier.

Goldensohn, E. S., Legatt, A. D., Koszer, S., & Wolf, S. M. (1999). *Goldensohn's EEG Interpretation: Problems of overreading and underreading.* Armonk, NY: Futura Publishing.

Gunkelman, J. (2006). Transcend the DSM using phenotypes. *Biofeedback, 34,* 95–98.

Hara, H. (2007). Autism and epilepsy: A retrospective follow-up study. *Brain Development, 29,* 486–490.

Herbert, M. R. (2005). Large brains in autism: The challenge of pervasive abnormality *The Neuroscientist, 11,* 417–440.

Herrmann, C. S., & Demiralp, T. (2005). Human EEG gamma oscillations in neuropsychiatric disorders. *Clinical Neurophysiology, 116,* 2719–2733.

Hubl, H., Bölte, S., Feineis–Matthews, S., Lanfermann, H., Federspiel, A., Strik, W., et al. (2003). Functional imbalance of visual pathways indicates alternative face processing strategies in autism. *Neurology, 61,* 1232–1237.

Hudspeth, W. J. (in press). Multivariate connectivity within a spherical space. *Journal of Neurotherapy.*

Hughes, J. R. (2007). Autism: the first firm finding = underconnectivity? *Epilepsy and Behavior, 11,* 20–24.

Hughes, J. R., & Melyn, M. (2005). EEG and seizures in autistic children and adolescents: Further findings with therapeutic implications. *Clinical EEG and Neuroscience, 36,* 15–20.

Hyvarinen, A., Karhunen, J., & Oja, E. (2001). *Independent components analysis.* New York: John Wiley and Sons.

John, E. R. (1977). *Neurometrics: Clinical applications of quantitative electrophysiology.* Hillsdale, NJ: Lawrence Erlbaum.

Johnstone, J., Gunkelman, J., & Lunt, J. (2005). Clinical database development: Characterization of EEG phenotypes. *Clinical EEG & Neuroscience, 36,* 99–107.

Just, M. A., Cherkassky, V. L., Keller, T. A., & Minshew, N. J. (2004). Cortical activation and synchronization during sentence comprehension in high-functioning autism: Evidence of underconnectivity. *Brain, 127,* 1811–1821.

Kagan-Kushnir, T., Roberts, S. W., & Sneed, O. C. 3rd (2005). Screening electroencephalograms in autism spectrum disorders: Evidence-based guidelines. *Journal of Child Neurology, 20,* 197–206.

Knyazev, G. G. (2007). Motivation, emotion, and their inhibitory control mirrored in brain oscillations. *Neuroscience and Biobehavioral Review, 31,* 377–395.

Kobayashi, E., Bagshaw, A. P., Grova, C., Dubeau, F., & Gotman, J. (2006). Negative BOLD responses to epileptic spikes. *Human Brain Mapping, 27,* 488–497.

Lemos, M. S., & Fisch, B. J. (1991). The weighted average montage. *Electroencephalgraphy and Clinical Neurophysiology, 79,* 361–370.

Makeig, S. et al. (1997). Matlab toolbox for analyses of electrophysiological data. http://www.cnl.salk.edu/-scott/ica.html

McAlonan, G. M., Cheung, V., Cheung, C., Suckling, J., Lam, G. Y., Tai, K. S, et al. (2004). Mapping the brain in autism: A voxel-based MRI study of volumetric differences and intercorrelations in autism. *Brain, 128,* 268–276.

Mizuno, A., Villalobos, M. E., Davies, M. M., Dahl, B. C., & Muller, R. A. (2006). Partially enhanced thalamocortical functional connectivity in autism. *Brain Research, 1104,* 160–174.

Monastra, V. J., Lubar, J. F., & Linden, M. (2001). The development of a quantitative electroencephalographic scanning process for attention deficit-hyperactivity disorder: Reliability and validity studies. *Neuropsychology, 15,* 136–144.

Murias, M., Webb, S. J., Greenson, J., & Dawson, G. (2007). Resting state cortical connectivity reflected in EEG coherence in individuals with autism. *Biological Psychiatry, 62,* 270–273.

Oberman, L. M., Hubbard, E. M., McCleery, J. P., Altschuler, E. L., Ramachandran, V. S., Pineda, J. A. (2005). EEG evidence of mirror neuron dysfunction in autism spectrum disorders. *Brain Research and Cognitive Brain Research, 24,* 190–198.

Ogawa, T., Sugiyama, A., Ishiwa, S., Suzuki, M, Ishihara, T, & Sato, K. (1982). Ontogenic development of EEG-Assymetry in early Infantile Autism. *Brain and Development, 4,* 439–449.

Onton, J., & Makeig, S. (2006). Information-based modeling of event-related brain dynamics. *Progress in Brain Research, 159,* 99–120.

Onton, J., Westerfield, M., Townsend, J., & Makeig, S. (2006). Imaging human EEG dynamics using independent components analysis. *Neuroscience and Biobehavioral Review, 30,* 808–822.

Page, L. A., Daly, E., Schmitz, N., Simmons, A., Toal, F., Deeley, Q., et al. (2006). In vivo H-magnetic resonance spectroscopy study of amygdala-hippocampal and parietal regions in autism. *American Journal of Psychiatry, 163,* 2189–2192.

Parmeggiani, A., Posar, A., Antolini, C., Scaduto, M. C., Santucci, M., & Giovanardi-Rossi, P. (2007). Epilepsy in patients with pervasive developmental disorder not otherwise specified. *Journal of Child Neurology, 22,* 1198–1203.

Pascual-Marqui, R. D. (1999). Review of methods for solving the EEG inverse problem. *International Journal of Bioelectromagnetism, 1,* 75–86.

Pascual-Marqui, R. D. (2002). Standardized low resolution brain electromagnetic tomography (sLoreta): Technical details. *Methods and Findings in Experimental and Clinical Pharmacology, 24D,* 5–12.

Pascual-Marqui, R. D., Esslen, M., Kochi, K., & Lehmann, D. (2002). Functional imaging with low resolution brain electromagnetic tomography (LORETA): A review. *Methods and Findings in Experimental and Clinical Pharmacology, 24C,* 91–95.

Pelphrey, K., Adolphs, R., & Morris, J. P. (2004). Neuroanatomical substrates of social cognition dysfunction in autism. *Mental Retardation Developmental Disabilities Research Review, 10,* 259–271.

Pelphrey, K. A., Morris, J. P., McCarthy, G., & Labar, K. S. (2007). Perception of dynamic changes in facial affect and identity in autism. *Social Cognition and Affective Neuroscience, 2,* 140–149.

Persyst. (2004). Spike and Seizure Detection System Online User's Guide. Retrieved January 4, 2006, from http://www.eeg-persyst.com/web/OnlineUsersGuide.html

Prichep, L. S. (2007). Quantitative EEG and electromagnetic brain imaging in aging and the evolution of dementia. *Annals of the NY Academy of Science, 1097*, 156–167.

Ray, A., Tao, J. X., Hawes-Ebersole, S. M., & Ebersole, J. S. (2007). Localizing value of scalp EEG spikes: A simultaneous scalp and intracranial study. *Clinical Neurophysiology, 118*, 69–79.

Rippon, G., Brock, J., Brown, C., & Boucher, J. (2007). Disordered connectivity in the autistic brain: Challenges for the "new psychophysiology." *International Journal of Psychophysiology, 63*, 164–172.

Rosen, G. D. (2006). *The dyslexic brain*. Mahwah, NJ: Lawrence Erlbaum Associates.

Santangelo, S. L. & Tsatsanis, K. (2005). What is known about autism: Genes, brain, and behavior. *American Journal of Pharmacogenomics*, *5*, 71–92.

Schroeder, M. J., & Barr, R. E. (2000). An alpha modulation index for electroencephalographic studies using complex demodulation. *Medical and Biological Engineering and Computing, 38*, 306–310.

Sethi, N. K., Sethi, J., Torgovnick, E., & Arsura, E. (2007). Physiological and non-physiological EEG artifacts. *The Internet Journal of Neuromonitoring,* 5(1). Retrieved October 13, 2008, from http://www.ispub.com/journal/the_internet_journal_of_neuromonitoring/volume_5_number_2_35/article/physiological_and_non_physiological_eeg_artifacts.html

Shaw, G. R., & Koles, Z. J. (1993). On the optimality of spherical spline interpolation for EEG topographical mapping. *Engineering in Medicine and Biology Society, 1993. Proceedings of the 15th Annual International Conference of the IEEE*, 338–339.

Shelley, B. P., Trimble, M. R., & Boutros, N. N. (2008). Electroencephalographic cerebral dysrhythmic abnormalities in the trinity of nonepileptic general population, neuropsychiatric, and neurobehavioral disorders. *Journal of Neuropsychiatry and Clinical Neuroscience, 20*, 7–22.

Speckman, E., Elger, C. E., & Altrup, U. (1993). Neurophysiologic basis of the EEG. In E. Wyllie (Ed.), *The treatment of epilepsies: Principles and practices* (pp. 185–201). Philadelphia: Lea & Febiger.

Stroganova, T. A., Nygren, G., Tsetlin, M. M., Posikera, I. N., Gillberg, C., Elam, M., et al. (2007). Abnormal EEG lateralization in boys with autism. *Clinical Neurophysiology, 118*, 1842–1854.

Suffin, S. C., & Emory, W. H. (1995). Neurometric subgroups in attentional and affective disorders and their association with pharmacotherapeutic outcome. *Clinical Electroencephalography, 26*, 76–83.

Suffin, S. C., Emory, W. H., Schiller, M. J., Kling, A. (2007). A QEEG database method for predicting pharmacotherapeutic outcome in refractory major depressive disorders. *Journal of American Physicians and Surgeons, 12*, 104–108.

Tidmarsh, L. & Volkmar, F. R. (2003). Diagnosis and epidemiology of autism spectrum disorders. *Canadian Journal of Psychiatry, 48*, 517–525.

Tuchman, R. F., & Rapin, I. (1997). Regression in pervasive developmental disorders: Seizures and epileptiform electroencephalogram correlates. *Pediatrics, 99*, 560–566.

Turner, K. C., Frost, L., Linsenbardt, D., McIlroy, J. R., & Muller, R. A. (2006). Atypically diffuse functional connectivity between caudate nuclei and cerebral cortex in autism. *Behavioral and Brain Functions, 2*, 34. Retrieved December 1, 2006, from http://www.behavioralandbrainfunctions.com/content/2/1/34

van Kooten, I. A. J., Palmen, S. J. M. C., von Cappeln, P., Steinbusch, H. W. M., Korr, H., Heinsen, H., et al. (2008). Neurons in the fusiform gyrus are fewer and smaller in autism. *Brain, 131*, 987–999.

Walter, D. O., & Adey, W. R. (1965). Analysis of brain-wave generators as multiple statistical time series. *IEEE Transactions on Biomedical Engineering, 12*, 8–13.

Wang, A. T., Dapretto, M., Hariri, A. R., Sigman, M., & Bookheimer, S. Y. (2004). Neural correlates of facial affect processing in children and adolescents with autism spectrum disorder. *Journal of American Academy of Child and Adolescent Psychiatry, 43*, 481–490.

Welchew, D. E., Ashwin, C., Berkouk, K., Salvador, R., Suckling, J., Baron-Cohen, S., et al. (2005). Functional disconnectivity of the medial temporal lobe in Asperger's Syndrome. *Biological Psychiatry, 57*, 991–998.

Williams, J. H. G., Waiter, G. D., Gilchrist, A., Perrett, D. I., Murray, A. D., Whiten, A. (2006). Neural mechanisms of imitation and "mirror neuron" functioning in autistic spectrum disorder. *Neuropsychologia, 44*, 610–621.

Robert Coben

Correspondence: Robert Coben, PhD, Director, Neurorehabilitation & Neuropsychological Services, 1035 Park Blvd., Suite 2B, Massapequa Park, NY 11762, email: robcoben@optonline.net.