

Quantitative Electroencephalographic Profiles for Children With Autistic Spectrum Disorder

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The present study examined quantitative electroencephalographic (QEEG) profile for children with autistic spectrum disorder (ASD). Five-minute QEEG data were obtained from 90 normal controls (NCs) and 66 children with ASD. Spectrum analyses revealed that ASD children showed significantly less relative alpha and more relative delta than NC. Specifically, 26% of ASD children and 2% of NCs showed 1.5 *SDs* of relative alpha below the normative mean. Children with this QEEG profile had 17 times the risk of having ASD than those without such a profile. Sensitivity and specificity of relative alpha were 91% and 73%, respectively. Split-half cross-validation yielded a sensitivity of 76%.

Keywords: autistic spectrum disorder, QEEG, screening, classification

Autistic spectrum disorder (ASD) is a neurodevelopmental disorder that is clinically characterized by impaired social interaction, language impairments, behavioral stereotypes, and some cognitive deficits. Given that an ASD-identifying laboratory test is not available, diagnoses are primarily based on detailed clinical interview and behavioral observation, such as the Autism Diagnostic Interview (Le Couteur et al., 1989), the Autism Diagnostic Observation Schedule (Lord et al., 1989), the Childhood Autism Rating Scale (CARS; Schopler, Reichler, & Renner, 1986), and the Checklist for Autism in Toddlers (Wong et al., 2004). Although behavioral observation remains the major diagnostic tool, it may be confounded by interrater bias (Waller, Armstrong, McGrath, & Sullivan, 1999). Thus, some efforts have been made to develop neurobiological measures including MRI measures (Akshoomoff et al., 2004; Courchesne, 2004; Courchesne et al., 2001) and genetic testing (Folstein & Rosen-Sheidley, 2001; Lord & Volkmar, 2002) that may provide more objective and sensitive diagnoses for ASD. However, reliable and affordable neurobiological measures have not been established.

Given that there is an increasing trend in the prevalence rate of ASD worldwide (Bertrand et al., 2001; Chakrabarti & Fombonne, 2001) and that early intervention is critical to remediate the symptoms, it is clinically significant to develop a biological screening test that is relatively easy and possible even for young children to perform. As previous research has suggested that as little as 1-min noise-free electroencephalographic (EEG) data would yield reli-

able and valid data (John, Prichep, Fridman, & Easton, 1988), it is possible to apply the EEG technique to children with special needs who may not be able to sit still for a long time or comply easily. Thus, the aim of the present study is to examine if quantitative EEG (QEEG) assessment is sensitive and yet simple enough to differentiate children with ASD from normal children.

QEEG is a type of electrophysiological assessment that applies computerized mathematical analysis to convert the raw waveform data into different frequency ranges including delta, theta, alpha, and beta. Each frequency range is averaged across a sample of data and quantified into mean amplitude (i.e., voltage in microvolts). The absolute power and relative power (i.e., percentage of total power) in each frequency band can be calculated. Given that the QEEG technique has the advantages of being less expensive, easier to perform, and noninvasive compared with some other neuroimaging techniques (e.g., positron emission tomography and computed tomography), it has been advocated as a potential clinical assessment for neurological and psychiatric disorders (Hughes & John, 1999).

Several groups of researchers have attempted to develop the QEEG technique as a screening assessment for neurodevelopmental disorders (Daoust, Limoges, Bolduc, Mottron, & Godbout, 2004; Dawson, Klinger, Panagiotides, Lewy, & Castelloe, 1995; Gasser, Rousson, & Gasser, 2003; Monastra, Lubar, & Linden, 2001; Monastra et al., 1999). Among the various disorders, attention-deficit/hyperactivity disorder (ADHD) seems to have been studied relatively more extensively (Barry, Clarke, & Johnstone, 2003; Bresnahan, Anderson, & Barry, 1999; Bresnahan & Barry, 2002; Chabot & Serfontein, 1996; Kuperman, Johnson, Arndt, Lindgren, & Wolraich, 1996; Monastra et al., 1999). In a recent study by Monastra et al. (2001), the QEEG profile of 469 individuals with ADHD was examined to develop a single-channel QEEG screening test for differentiating individuals with ADHD from normal subjects. They reported that the theta–beta ratio measured from the vertex (Cz) yielded a specificity of 94% and a sensitivity of 90%, and that the test–retest reliability was 0.96. So far, the empirical evidence on ADHD seems to support the notion that QEEG, even single channel, may have the potential to be developed into a sensitive measure for children with neurodevelopmental disorder.

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The research was supported by Hong Kong Research Grant Council Grant CUHK 4648/05H. We thank the Parents' Association of Pre-School Handicapped Children in Hong Kong for their assistance in recruiting subjects.

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Fewer studies have been conducted to study the neuro-electro-physiological characteristics of children with ASD. Although the findings have been quite inconsistent, they have revealed some atypical EEG characteristics of ASD (Cantor, Thatcher, & Hrybyk, 1986; Daoust et al., 2004; Dawson et al., 1995; Harrison, Demaree, Shenal, & Everhart, 1998). That is, although some researchers reported reduced alpha activities (Cantor et al., 1986; Dawson et al., 1995), others reported lower beta and higher theta activities (Daoust et al., 2004). In a case study of a man with ASD, a heightened magnitude of delta at the left frontal regions was noted (Harrison et al., 1998). The inconsistent findings among the studies are possibly related to the small sample size and the heterogeneity of the samples (i.e., most previous studies recruited only about 10 autistic children). In addition, some studies recruited only high-functioning autistic children (Daoust et al., 2004), whereas others studied autistic children with a lower level of intelligence (Cantor et al., 1986; Dawson et al., 1995). Although the empirical data in regard to the nature of QEEG of autism remained inconclusive, these initial studies seemed to suggest that ASD is associated with atypical QEEG profiles. Thus, the present study recruited a larger sample, including both high-functioning and low-functioning children with ASD. The primary purpose is to explore if this technique may be applicable to differentiate children with ASD from normal children.

Method

Participants

A total of 156 children participated voluntarily in the present study. The normal control (NC) subjects were recruited from local primary schools by sending invitation letters to their parents. Parents were invited to complete and return the consent form to the research team if they agreed to have their children participate in the project. A total of 96 parents voluntarily signed up their children. Children who had a history of neurological problems or abnormal developmental milestones were excluded from the study, resulting in 90 children serving as NCs.

On the other hand, the children with ASD ($n = 66$) were either recruited from the Parents' Association of Pre-School Handicapped Children, which consists of over 1,000 members in Hong Kong, or from the subject database of our laboratory. Children with ASD were previously diagnosed by the pediatricians of the Child Assessment Centres in Hong Kong, which are government agencies providing clinical assessment service for children with special needs. In addition, the diagnosis of each child having ASD was confirmed or disconfirmed by clinical psychologists (who are coinvestigators of the present study) who conducted a standard clinical interview and administered the CARS (Schopler et al., 1986) with the child's parent as an informant during the parent interview. The CARS was chosen for interview primarily because the more commonly used diagnostic tools, including Autism Diagnostic Interview and Autism Diagnostic Observation Scale, have not yet been made available for the Chinese population (personal communication with a representative of C. Lord's lab, 2005). In addition, the diagnosis was made according to the Diagnostic and Statistical Manual of Mental Disorders (4th ed., text rev.; *DSM-IV-TR*; American Psychiatric Association, 2000), and the CARS was shown to be highly correlated with the *DSM-IV-TR* diagnostic criteria (Rellini, Tortolani, Trillo, Carbone, & Mantecchi, 2004). The general intelligence of each child was assessed by the Test of Nonverbal Intelligence, 3rd edition (Brown, Sherbenou, & Johnson, 1997). The demographic information of the NC and ASD groups is presented in Table 1. Both groups of subjects were matched in terms of age, $t(154) = -2.0$, $p = .05$, but not level of intelligence, $t(154) = 8.89$, $p < .001$.

Table 1

Demographic Characteristics of the Normal Controls (NC) and Children With Autistic Spectrum Disorder (ASD)

Variable	NC ($n = 90$)	ASD ($n = 66$)
Mean age (years)	8.82 (1.79)	9.65 (3.00)
Age range (years)	6–12	5–18
Gender (male/female)	48/42	60/6
TONI-III (deviation quotient)	111.42 (16.16)	83.36 (21.61)
CARS (total score)	—	33.95 (4.50)

Note. Standard deviations are in parentheses. Dashes indicate the CARS was not administered for normal controls. TONI-III = Test of Nonverbal Intelligence, 3rd edition; CARS = Childhood Autism Rating Scale.

Parent Interview

A detailed interview with the parent of each child was conducted by a clinical psychologist. During the interview, parents of all participants were interviewed with a standard questionnaire on the developmental and medical history of the children. Specifically, the parents were asked about their children's previous history of possible prenatal, perinatal, and physical problems, as well as their children's current and past medical conditions, including any possible physical and psychiatric treatment being received and possible history of head injury. The children's school type (e.g., special education) and academic performance were also obtained. Parents of children who served as NCs reported any negative previous history of neurological problems or abnormal developmental milestones. For the ASD group, participants were excluded from the analysis if their parents reported any developmental (e.g., epilepsy, ADHD) or psychiatric (e.g., depression) diagnosis (other than ASD) by pediatricians, if they were currently receiving psychiatric treatment or special education for developmental problems other than ASD, or if they met any diagnostic criteria in the *DSM-IV-TR* other than for ASD.

EEG Recording

Each child was tested individually in a sound- and light-attenuated room. Before the EEG assessment, the child and/or the parent were given a brief verbal explanation on the procedure along with a written description and a series of photos showing the hookup procedure. Informed consents were obtained from the parents of all subjects, and the experimental procedure was preapproved by the Clinical Research Ethics Committee of The Chinese University of Hong Kong.

After the parents had indicated that they understood the procedure, an electrode cap with 24 electrodes, based on the International 10–20 System (Jasper, 1958) referenced to linked ears, was positioned on the head of the child. To keep the children engaged and awake, we asked them to focus on a computer screen, which displayed some swimming fish of different colors. We recorded 5 min of continuous EEG signals in the eyes-open condition twice. One of the research assistants was responsible for recording the data, and the other observed the behavior of the child and recorded the time of all behavior that might affect the data, such as stereotypical behavior, excess motor movement, and eye blinking. These data were used to guide subsequent data selection in obtaining at least 1-min artifact-free data. The EEG signal was digitized at 256 samples per second per channel, with a high-frequency limit pass band of 30 Hz.

Data Analysis

The raw data were analyzed by another research assistant who was blind to the rationale of the study and the subject's classification (i.e., NC vs. ASD). According to the criteria suggested to produce a reliable

measure, only data that had at least 1-min artifact-free EEG data were selected (see Evans & Abarbanel, 1999; John et al., 1988, for general discussion of QEEG method). The raw data were processed with the fast Fourier transformation to determine the magnitude of each frequency band in microvolts. The frequency bands were classified into delta (1.0–3.5 Hz), theta (4.0–7.5 Hz), alpha (8.0–12.0 Hz), low beta (12.0–15.0 Hz), and high beta (15.0–17.5 Hz). Data from 17 electrode sites including F3, F4, F7, F8, Fz, T3, T4, T5, T6, C3, C4, Cz, P3, P4, Pz, O1, and O2 were selected for further analysis. The absolute power (the amount of energy in μV^2) and the relative power (the percentage of total power within each frequency band) were calculated for each frequency band in each electrode site. The interrater reliabilities of the data at five frequency bands averaged across the 17 channels were tested with 10 randomly selected subjects (5 NC and 5 ASD children), which ranged from 0.96 to 0.99 ($p < .05$). The data were analyzed with multivariate analyses of variance (MANOVAs) or analyses of variance with repeated measures followed by multiple t tests if the main effect of group difference was significant. To control for inflated Type I errors due to post hoc multiple comparisons, we adopted the Bonferroni correction for the alpha level of .003. Both analyses using the means and standard deviations as cutoffs and discriminant function analyses (DFAs) were used to evaluate the sensitivity of the QEEG measures for screening children with ASD.

Results

Mean Absolute and Relative Power of Normal Children and Children with ASD

The absolute and relative power of each frequency band among the 17 channels for the NC and ASD groups were averaged and compared using MANOVA. The topographic maps demonstrating the mean absolute and relative powers of delta, theta, alpha, low beta, and high beta between the two groups are presented in Figure 1. Significant multivariate group differences were found for both absolute, $F(5, 150) = 6.52, p < .001$, and relative power, $F(5, 150) = 8.4, p < .001$. Univariate results revealed that the ASD group demonstrated significantly higher absolute delta (ASD: $M = 17.22, SD = 7.50$; NC: $M = 13.29, SD = 6.03$), $F(1, 154) = 13.2, p < .001$, relative delta (ASD: $M = 39.63, SD = 7.19$; NC: $M = 35.22, SD = 7.26$), $F(1, 154) = 14.18, p < .001$, and lower relative alpha (ASD: $M = 17.76, SD = 6.68$; NC: $M = 23.21, SD = 7.12$), $F(1, 154) = 23.5, p < .001$, than the NC group. The delta–alpha ratio was significantly different between the two groups, $t(154) = -4.04, p < .001$, in which the NC group ($M = 2.05, SD = 1.01$) showed a significantly lower ratio than the ASD group ($M = 2.98, SD = 1.66$). However, absolute and relative power of theta, high beta, low beta, and absolute alpha were not significantly different between two groups (range of F values = 0.01–3.03, $ps > .05$). MANOVA results suggested that there was no significant difference in the EEG pattern for boys and girls in the NC group: absolute power across five frequency bands, $F(5, 84) = 1.47, p > .05$; relative power across five frequency bands, $F(5, 84) = 1.11, p > .05$. Thus, these results were unlikely because of unequal distribution of gender between NC and ASD.

Given that the NC and ASD groups were different in their levels of general intelligence, the analyses on absolute and relative power were repeated with IQ scores as the covariate. Although the ASD group showed consistently higher relative delta, $F(1, 153) = 9.17, p < .005$, and lower relative alpha, $F(1, 153) = 9.85, p < .005$, the group difference in absolute delta became nonsignificant, $F(1, 153) = 5.23, p = .024$, with the adjusted alpha level at .01. When

the ASD group was further divided into those with IQ scores below 70 and those at or above 70, the statistics again revealed no significant difference between the two groups on both absolute, $F(5, 60) = 1.84, p > .05$, and relative power, $F(5, 60) = 1.56, p > .05$. Thus, the level of general intelligence did not seem to be a significant factor affecting the QEEG profile of ASD children.

To examine whether there may be left–right hemispheric variation, we divided the channels into the left hemisphere (F3, F7, T3, T5, C3, P3, O1) and right hemisphere (F4, F8, T4, T6, C4, P4, O2). Patterns of relative power and the delta–alpha ratio consistent with that of the 17-channel average were revealed (delta and alpha of each hemisphere: range of F values = 10.11–23.62, $ps < .005$; delta–alpha ratio of each hemisphere: t values = -3.94 and -4.17 , respectively, $ps < .001$; theta and high and low beta of each hemisphere: range of F values = 0.00–3.51, $ps > .05$). Given the consistent pattern of relative power in delta and alpha bands and its advantage of eliminating the individual variations by calculating the proportion of each frequency band relative to the others, relative powers were therefore selected for subsequent in-depth analyses.

Relative Delta and Relative Alpha on All Channels

Separate 2×17 (Groups \times Channels) analyses of variance with repeated measures were performed on the relative power of delta and alpha bands. A significant Group \times Channel interaction was found for the delta, $F(16, 133) = 1.74, p < .05$, and alpha bands, $F(16, 133) = 1.89, p < .05$. The delta and alpha profiles of the two groups across channels are presented separately in Figure 2. Subsequent t tests were performed to explore the simple effect of group at each channel with the adjusted alpha level of .003 to control for inflated Type I error as a result of multiple comparisons. Although the ASD group demonstrated significantly higher relative delta at C3, C4, Cz, P3, P4, Pz, and T6 (range of t values = -3.10 to $-5.14, ps < .003$) than the NC group, both groups yielded comparable delta levels at the remaining channels (range of t values = -0.79 to $-2.98, ps > .003$). For relative alpha, the ASD group demonstrated significantly lower power at 15 out of 17 channels (range of t values = 3.47–5.66, $ps < .002$), with the exception of C3 and C4 (t values = 2.49 and 2.46, respectively, $ps > .01$). The same set of between-group comparisons on delta–alpha ratio was performed again, and a significant Group \times Channel interaction effect was found, $F(16, 133) = 2.01, p < .05$. The ASD group showed a significantly higher ratio than the NC group (range of t values = -3.21 to -4.99) at 11 channels (F3, F4, F7, Fz, Cz, P3, P4, Pz, T3, T6, O1; $ps < .003$), but both groups yielded comparable ratios at the remaining channels (range of t values = -0.87 to $-3.09, ps > .003$).

Specificity and Sensitivity of Relative Alpha and Delta and Their Ratio in Differentiating Normal Children and Children with ASD

As the results showed that the ASD group demonstrated significantly lower relative alpha and higher relative delta and delta–alpha ratio, further analyses were conducted to examine the specificity and sensitivity of the two frequency bands and their ratio in discriminating between the groups. The data were first analyzed

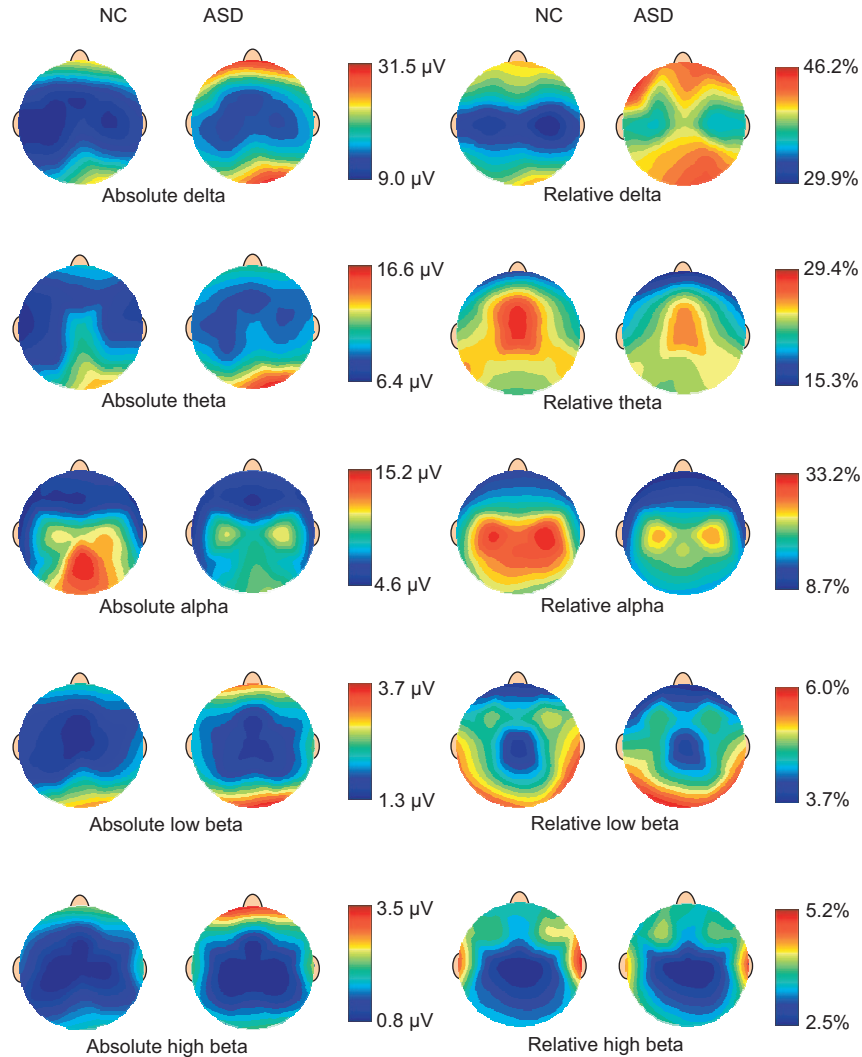


Figure 1. Topographic comparisons of normal controls (NC) and children with autistic spectrum disorder (ASD) for absolute and relative power of delta, theta, alpha, low beta, and high beta.

using means and standard deviations as cutoff points, which is common in clinical assessments. Also, the DFA, a more advanced statistical technique, was performed to evaluate the model.

The means and standard deviations of relative alpha ($M = 24.2$, $SD = 7.57$), delta ($M = 34.32$, $SD = 7.37$), and delta–alpha ratio ($M = 1.95$, $SD = 1.03$) based on half of the NCs ($n = 45$) were calculated, whereas data from the other half were used for cross-validation of the model. The cutoff values were set at 1.0, 1.5, and 2.0 SD s below mean relative alpha and above mean relative delta and delta–alpha ratio. Results of the cross-validated sample were comparable with that of the original model. The percentage of the NC and ASD children demonstrating various degrees of deviation from the mean data is presented in Table 2. The odds ratios were calculated to compare the likelihood of having ASD at different degrees of variation for the two frequency bands and their power ratio. The odds ratios showed that the cutoff points based on the relative alpha were more sensitive than that of the relative delta and delta–alpha ratio. Specifically, although almost half of the

children with ASD showed relative alpha falling below 1.0 SD , only 20% of the normal children showed the same degree of deviation from the mean value. At the 1.5 SD cutoff point, the percentage of ASD children (26%) falling below the cutoff was 13 times higher than that of normal children (2%). The odds ratio of relative alpha at 1.5 SD was 17, which means children showing relative alpha of more than 1.5 SD s below mean were 17 times more likely to have ASD. When the cutoff point was set at 2.0 SD s below the mean, the odds ratio even reached infinity as none of the normal children demonstrated such significantly low relative alpha.

DFA has been advocated as a sensitive diagnostic method; thus, the data were evaluated again with this alternative analysis. Three stepwise DFAs were performed separately for relative alpha, delta, and delta–alpha ratio to select the specific channel(s) out of 17 that can significantly discriminate between the NC and ASD groups. The models were again cross-validated with the split-half method (i.e., 45 NC and 33 ASD). Although four channels for relative

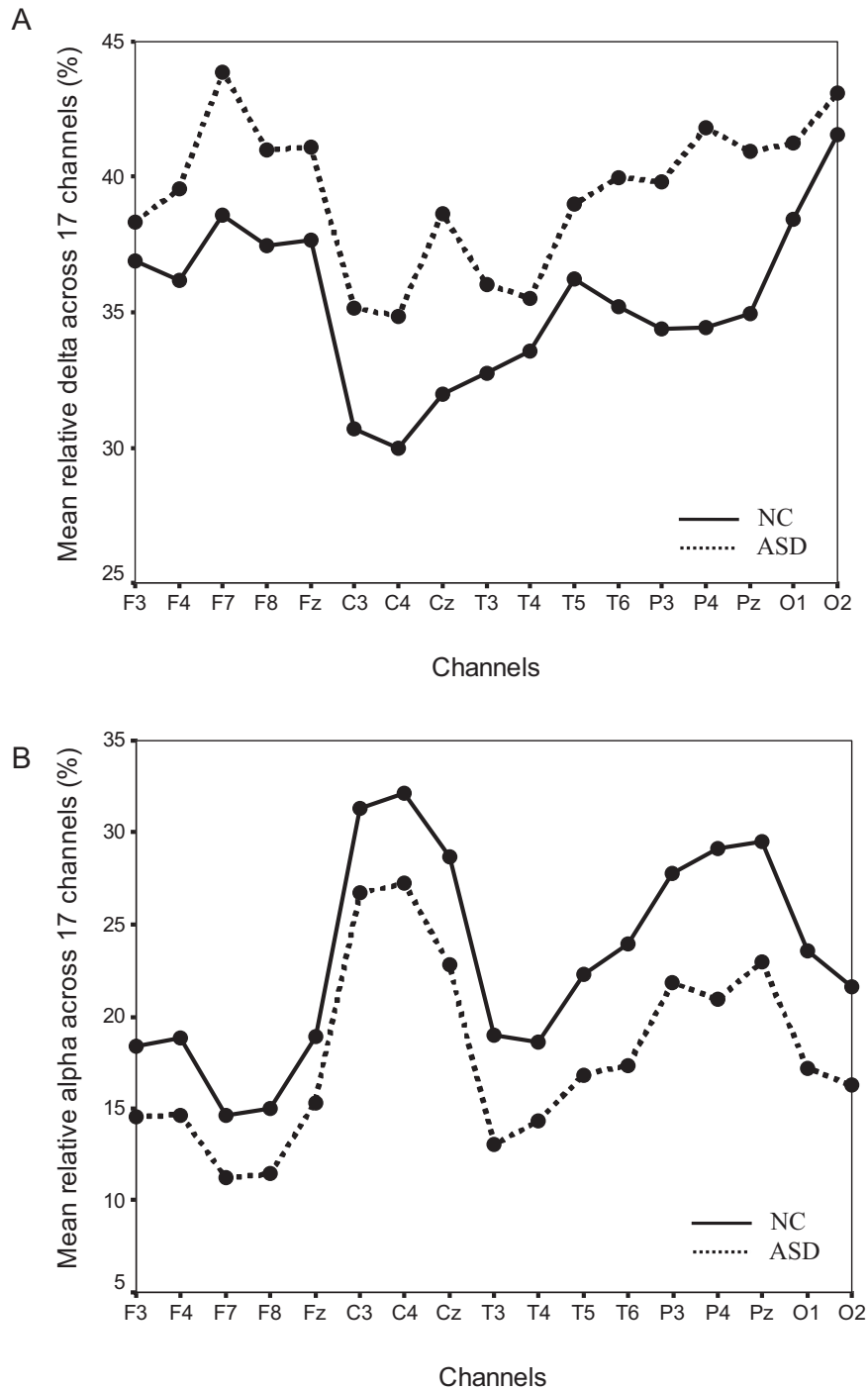


Figure 2. Magnitude of relative delta (A) and alpha (B) across 17 channels of normal controls (NC) and children with autistic spectrum disorder (ASD).

alpha (T3, T6, C3, and F4; $\Lambda = .582, p < .001$) were selected, there was only one channel selected for delta (P4; $\Lambda = .766, p < .001$) and delta–alpha ratio (T6; $\Lambda = .782, p < .001$) that could significantly differentiate normal children from children with ASD. The discriminative power of relative alpha was much more significant than that of relative delta and delta–alpha ratio (see

Table 3). The model using relative alpha from the four channels yielded a sensitivity of 91% and specificity of 73%. The overall classification rate (i.e., the total correct classification) was 81%. This model was used to classify the remaining half of the sample for cross-validation. It resulted in a correct classification rate of 76% for ASD children and 53% for normal children.

Table 2
Odds Ratios for Autistic Spectrum Disorder Associated With Various Cutoff Levels of Relative Alpha, Relative Delta, and Delta–Alpha Ratio

Cutoff value	NC (%) ^a	ASD (%) ^b	OR (95% CI)
Relative alpha			
<16.63 (1.0 SD below mean)	20	49	3.8 (1.57–9.04)
<12.85 (1.5 SD below mean)	2	26	17.0 (3.96–74.85)
<9.06 (2.0 SD below mean)	0	3	Infinite
Relative delta			
>41.69 (1.0 SD above mean)	11	35	4.0 (2.06–9.22)
>45.38 (1.5 SD above mean)	9	18	2.0 (0.94–5.21)
>49.06 (2.0 SD above mean)	2	8	4.0 (0.88–20.59)
Delta–alpha ratio			
>2.98 (1.0 SD above mean)	13	42	5.0 (2.39–9.81)
>3.50 (1.5 SD above mean)	9	27	4.0 (1.66–8.45)
>4.01 (2.0 SD above mean)	9	17	2.0 (0.88–4.90)

Note. NC = normal controls; ASD = children with autistic spectrum disorder; OR = odds ratio; CI = confidence interval.

^a Percentage of NC ($n = 45$) that were below the cutoff of relative alpha and above the cutoff of relative delta and delta–alpha ratio. ^b Percentage of children with ASD ($n = 66$) that were below the cutoff of relative alpha and above the cutoff of relative delta and delta–alpha ratio.

As relative delta, alpha, and delta–alpha ratio were analyzed separately, it would be interesting to explore whether correct classification can be further enhanced by combining the relative alpha, delta and delta–alpha ratio at their selected channels for discriminating between the normal and ASD children. Results of the DFA revealed that discrimination using a combination of predictors yielded comparable sensitivity (91%) and specificity (76%) to the results yielded by using relative alpha only. Given that significant enhancement of discriminative power was not noted when additional measures (delta and delta–alpha ratio) were included, relative alpha seemed to be the prominent QEEG marker for children with ASD.

Discussion

The findings of the present study revealed that children with ASD demonstrated significantly higher relative delta and lower relative alpha compared with their age-matched normal counter-

parts; their relative theta and high and low beta frequency ranges were not significantly different from normal children. Specifically, although there was a 5-point difference between the NC and ASD children in both the relative delta and alpha, the difference between the other frequency bands is less than or about 1 point. In addition, the level of intelligence did not seem to be a significant factor affecting the QEEG profile of children with ASD, given that consistent results were obtained when the data were analyzed using the level of intelligence as a covariate.

The clinical value of this QEEG profile of ASD was evaluated with normative data comparison and DFAs. Twenty-six percent of ASD children and 2% of the normal children fell under the cutoff point (1.5 SDs from the normative mean relative alpha [12.85]). The results of the odds-ratio measure suggested that children who demonstrated relative alpha of below 12.85 would have 17 times higher risk of having ASD than children without that QEEG profile. To further evaluate the sensitivity of the relative alpha in

Table 3
Sensitivity, Specificity, and Total Classification Rate of Relative Alpha, Delta, and Delta–Alpha Ratio in Differentiating between Normal Controls and Children With Autistic Spectrum Disorder Using Discriminant Function Analyses

Target discriminator(s)	Sensitivity (%) ^a	Specificity (%) ^b	Total (%) ^c
Relative alpha			
T3 + T6 + C3 + F4 ^d	91	73	81
Relative delta			
P4 ^d	76	78	77
Delta–alpha ratio			
T6 ^d	58	80	71
Combination ^e			
Relative alpha (T3 + T6 + C3 + F4) + relative delta (P4) + delta–alpha ratio (T6)	91	76	82

^a Percentage of correct classification of children with ASD ($n = 33$). ^b Percentage of correct classification of normal children ($n = 45$). ^c Percentage of total correct classification rate. ^d Channels selected by stepwise discriminant function analysis yielding significant discriminant functions ($p < .001$). ^e A combination of all significant channels selected by the stepwise method as predictors in discriminant function analyses.

differentiating ASD children from normal children, we used a split-half cross-validation statistical method. The original model yielded a sensitivity of 91% and specificity of 73%, suggesting that it correctly differentiated 91% of the children with ASD and 73% normal children. Reliability of the established model was tested by a new group of subjects, and it was able to correctly classify 76% of ASD children. Thus, the results seem to support the notion that the QEEG measure is a sensitive measure for differentiating children with ASD from NCs.

The present results also revealed some electrophysiological findings that are consistent with the general understanding of the neuropathological involvement of autism. As revealed by the profile in Figure 2, the high-delta and low-alpha QEEG characteristics do not seem to be regionally specific; rather, they are observed across the cortex of children with ASD. It seems that such abnormality in relative alpha among ASD children is not restricted only to a single and specific location of the brain but instead appears in a widespread pattern across the brain. The widespread pattern could possibly reflect the neurophysiological abnormality associated with ASD. That is, numerous neuroimaging studies reported widespread structural (Brambilla et al., 2003; Carper, Moses, Tigue, & Courchesne, 2002; Courchesne, 2004; Courchesne et al., 2001) and functional (Belmonte & Yurgelun-Todd, 2003; Hubl et al., 2003) abnormalities in neural network involving the fronto-temporo-parietal cortex, limbic system, cerebellum, and ventricular volume.

In contrast to the EEG profile of ADHD, characterized by increased relative theta and theta-beta ratio as well as decreased relative beta (Barry et al., 2003; Bresnahan & Barry, 2002; Clarke, Barry, McCarthy, & Selikowitz, 2001; Clarke, Barry, McCarthy, Selikowitz, & Brown, 2002; Clarke et al., 2003; Monastra et al., 2001, 1999), children with ASD in the present study demonstrated abnormal delta-alpha activity, but their theta-beta activity was comparable with the NC. Specifically, theta-beta activity at Cz and certain frontal locations (F3, F4) was reported to be a sensitive QEEG marker for ADHD (Lubar, 1995; Lubar, Swartwood, Swartwood, & Timmermann, 1996), whereas widespread abnormal alpha activity was found to be more sensitive to ASD. This dissociation might be suggestive of unique EEG characteristics of different neuropathology associated with different neurodevelopmental disorders. That is, children with ADHD have been consistently found to be associated with frontal dysfunction, but neuropathology among children with ASD was relatively more extensive, resulting in more global functional deficiency. On the other hand, alpha rhythm has been associated with various cognitive processing such as memory (Jensen, Gelfand, Kounios, & Lisman, 2002) and arousal states (Cantero, Atienza, Gomez, & Salas, 1999). Because the present study examined the EEG pattern of the resting state, it is unclear if the relatively lower alpha is related to the overall cognitive arousal level of the ASD children or if it reflects some specific cognitive dysfunction. Further studies on the event-related EEG alpha have been conducted in our laboratory to shed some light on this issue.

Although the present finding is encouraging, more studies are needed to test the reliability and validity of the results before the technique can be applied clinically. Specifically, further studies should compare the profile of a larger sample of subjects with various developmental problems, including Asperger syndrome, specific learning disorders, epilepsy, and developmental language

delay. Although the present results remain consistent after controlling for general intelligence in the ASD groups, further studies will be needed to compare children with a similar level of general intelligence to examine the specificity of this method to ASD. In addition, given that past neuroimaging studies on ASD have revealed neuroanatomical abnormality after birth up to age 4 (Carper et al., 2002; Courchesne, Carper, & Akshoomoff, 2003; Courchesne et al., 2001), it is not known if the unique QEEG profile found in the present study, in which only children aged 5 or above were recruited, would be applicable to children at a younger age. Besides, all the subjects were Chinese, and it will be important to examine if the results can be applicable to different ethnic groups such as Caucasians. Therefore, further studies are needed to explore the clinical value of EEG assessment for the screening of ASD.

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Received August 16, 2005

Revision received July 14, 2006

Accepted July 20, 2006 ■