A Meta-analysis of Quantitative EEG Power Associated With Attention-Deficit Hyperactivity Disorder

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Summary: A meta-analysis was performed on quantitative EEG (QEEG) studies that evaluated attention-deficit hyperactivity disorder (ADHD) using the criteria of the DSM-IV (*Diagnostic and Statistical Manual of Mental Disorders, 4th edition*). The nine eligible studies (N = 1498) observed QEEG traits of a theta power increase and a beta power decrease, summarized in the theta/beta ratio with a pooled effect size of 3.08 (95% confidence interval, 2.90, 3.26) for ADHD versus controls (normal children, adolescents, and adults). By statistical extrapolation, an effect size of 3.08 predicts a sensitivity and specificity of 94%, which is similar to previous results 86% to 90% sensitivity and 94% to 98% specificity. It is important to note that the controlled group studies were often with retrospectively set limits, and that in practice the sensitivity and specificity results would likely be more modest. The literature search also uncovered 32 pre–DSM-IV studies of ADHD and EEG power, and 29 of the 32 studies demonstrated results consistent with the meta-analysis. The meta-analytic results are also supported by the observation that the theta/beta ratio trait follows age-related changes in ADHD symptom presentation (Pearson correlation coefficient, 0.996, P = 0.004). In conclusion, this meta-analysis supports that a theta/beta ratio increase is a commonly observed trait in ADHD relative to normal controls. Because it is known that the theta/beta ratio trait may arise with other conditions, a prospective study covering differential diagnosis would be required to determine generalizability to clinical applications. Standardization of the QEEG technique is also needed, specifically with control of mental state, drowsiness, and medication.

Key Words: Attention deficit/hyperactivity disorder, Electroencephalography, Meta-analysis, Rating scales, Sensitivity.

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Attention-deficit hyperactivity disorder (ADHD) is the most prevalent neuropsychological disorder of childhood (Barkley, 1998; Olfson, 1992). ADHD has been conservatively estimated to affect 3%–5% of school-aged children (APA, 1994). Approximately 50% of visits by children to psychiatric clinics involve the diagnosis of this disorder (Cantwell, 1996). These figures indicate the importance of the accurate characterization of ADHD.

The general consensus of health care professionals addressing the diagnosis of ADHD supports the utilization of multiple assessment protocols (AMA, 1996; Barkley, 1998; Conners and Jett, 1999; Goldman et al., 1998; Kaplan and Sadock, 1998; NIH, 1998; Pary et al., 2002). A widely accepted set of guidelines provided by the American Academy of Pediatrics (AAP) recommends a clinician's evaluation using criteria of the *Diagnostic and Statistical Manual of Mental Disorders, 4th edition* (DSM-IV) (APA, 1994) with support from an array of assessment tests and evidence (e.g., behavior rating scales) (AAP, 2000).

A considerable body of EEG research over the last 30 years has explored brain electrical traits that might be present in ADHD but not in controls (normal children, adolescents, and adults). Previous reviews covering a limited sample of the pre–DSM-IV research have claimed that EEG traits associated with ADHD have been inconsistent among studies (AAP, 2000; Brown et al., 2001; Green et al., 1999; Nuwer, 1997). However, more recent medical and psychological reviews of ADHD have recognized promising EEG results (Bradley and Golden, 2001; Pary et al., 2002). The 2004 ADHD guide published by the American Academy of Pediatrics (AAP) predicted that ". . . new brain wave analysis techniques like quantitative electroencephalograms will help experts more clearly document the neurologic and behavioral nature of ADHD, paving the way for better understanding and treatment" (Reiff and Thomas, 2004).

In the last three decades, the diagnostic criteria for ADHD have undergone numerous iterations, as shown by changes in the definition of the disorder within different versions of the DSM. In fact, ADHD prevalence based on diagnoses performed according to DSM-III-R differs from that based on the most recent criteria of the DSM-IV (Baumgaertel et al., 1995; Wolraich et al., 1996). With the implications of the DSM changes in mind, the hypothesis of the current meta-analysis is that studies using the DSM-IV definition of ADHD have produced results supporting the presence of a quantitative EEG (QEEG) trait common to ADHD patients but not to normal children, adolescents, and adults. In addition, we have examined separately studies with previous DSM definitions of the disorder to determine whether past results were consistent with or contradictory to the DSM-IV meta-analytic results.

BACKGROUND ON QEEG

Electrical activity recorded at the scalp best represents radially-oriented currents from neurons in proximity to the surface of the brain (Arciniegas and Beresford, 2001; Binnie and Prior, 1994; Kaplan and Sadock, 1998). When a disorder is associated with a change in the collective firing pattern of large assemblies of surface neurons, then this pattern is potentially a quantifiable marker for the disorder (Arciniegas and Beresford, 2001; Duffy et al., 1994; Hughes and John, 1999; Wallace et al., 2001).

Developments in digitization and analytical techniques of QEEG technology have greatly facilitated the use of brain electrical activity data in clinical and research settings. Relative to traditional methods of visual inspection of EEG, modern QEEG techniques have been shown to provide greater access to the information inherent in the brain electrical activity data (Johannesson et al., 1979). By utilizing QEEG techniques including computerized acquisition, refined signal processing, mathematical transformations, advanced data analysis, and large database comparisons, brain electrical activity patterns can be explored and precise measurements can be made. (Arciniegas and Beresford, 2001; Duffy et al., 1994; Hughes and John, 1999; Wallace et al., 2001).

Quantitative EEG techniques include the mathematical transformation of brain electrical activity data from the time domain into the frequency domain. Traditional EEG methods support the separation of the frequency data into four main frequency bands: delta (1–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), and beta (13–30 Hz) (Kaplan and Sadock, 1998). Application of an optimization algorithm has suggested a similar separation (0–2.0 Hz, 2.0–3.75 Hz, 3.75–7.5 Hz, 7.5–15 Hz, 15–30 Hz) (Stassen et al., 1988).

MATERIALS AND METHODS

The criteria for the studies to qualify for inclusion in the meta-analysis are listed in detail in Table 1. Five stages of search and inclusion/exclusion criteria were applied to the literature in an ordered manner. First, a literature search was conducted on MEDLINE (1966 through July 2002) for articles examining EEG associated with different versions of ADHD based on terminology and definitions that have evolved as marked by each successive edition of the DSM. The search terminology for this purpose was entered into PubMed as follows: *"attention deficit" OR hyperact* OR hyperkin* OR "brain dysfunction' OR 'cerebral dysfunction" OR methylphenidate OR stimulant AND EEG.* Eligible studies had been published in peer-reviewed journals by researchers independent of the authors of this meta-analysis. Of the 1229 articles uncovered by this search, 960 met the further requirement of English language.

Abstracts and titles were reviewed from the search list to determine whether the studies covered ADHD (current or previous terms) and any methods of EEG. Studies that focused on disorders other than ADHD and did not involve EEG were excluded. Animal or mechanism studies, infant studies, and case studies were excluded as well. Of the 960 articles, 176 remained. Then, full articles and abstracts were reviewed specifically for the reporting of EEG power variables and the analysis of data in terms of ADHD versus controls

TABLE 1. Inclusion Criteria for the Studies Reviewed in the Meta-analysis

Stages of Inclusion Criteria	Studies Included After the Stage
I. Literature search MEDLINE (1966 to July 2002). Search terminology: "attention deficit" OR hyperact* OR hyperkin* OR "brain dysfunction" OR "cerebral dysfunction" OR methylphenidate OR stimulant AND EEG. Peer-reviewed, published studies by researchers independent of the authors of this meta-analysis	1229
II. Language English	960
III. Review of abstracts and titles EEG (any version) and ADHD (current or previous related definitions). No animal or mechanism studies. No infants. No case studies	176
IV. Review of articles and abstracts EEG power variables (no epilepsy/seizures/spikes, no ERP, no neurofeedback, no sleep). Analysis of data in terms of ADHD vs. controls (must have controls for relative comparison, grouped by ADHD vs. controls and not by some other factor such as IQ, EEG results of ADHD not combined with those of subjects with other disorders not ADHD, no comorbidities, no aging studies without comparison between groups of ADHD vs. controls, no studies of medication effects). No reviews or letters without independent data	41
V. Quality of data Modern definition of ADHD (DSM-IV). Sufficient diagnosis of ADHD per standard guidelines conducted in clinical setting with complete description in article. Diagnosis considered insufficient if depended solely on layperson opinion, or standardized observation, or rating scales, or checklists. EEG data must include eyes closed or eyes open baseline. If data used in multiple studies, included the study with most complete set and excluded others	Included: 9 (Table 3) Excluded: 32 (Table 4)

(normal children, adolescents, and adults). Studies were excluded if brain electrical activity data were only provided in the form of evoked response potential (ERP) or seizure activity analysis. Reviews or letters without independent data were excluded. After applying these criteria, 41 articles remained from the previous 176.

The final stage of the inclusion criteria covered quality of data. Only those studies whose reference standard (ADHD diagnostic protocol) approximated the recommendations of modern ADHD assessment guidelines were included. The studies that were included utilized a comprehensive evaluation of

ADHD performed by a qualified clinician using DSM-IV criteria, complemented by commonly used ADHD screening tests, occurring in a clinical setting. Studies were excluded if the ADHD assessment protocol was not described in the article precluding further review, or if the assessment was not sufficient per standard guidelines. Diagnostic protocols were considered insufficient if the outcome depended solely on measures not intended as stand-alone diagnostics, such as rating scales or checklists. Classification based solely on the opinions of laypeople or observations in standard settings were also not considered sufficient for inclusion.

To maintain independence between included data sets, information was sought in the articles and through personal communication with the authors to determine whether the same data had been used in multiple studies. If the data sets overlapped among studies, the study with the most complete set was included while excluding the others.

After the final stage of application of inclusion criteria, 32 articles were excluded and 9 articles remained for the meta-analysis. For the 32 articles excluded at this final stage, descriptions of the study findings and the specific reasons for exclusion of each study are provided for reference in Table 4.

In the meta-analysis of the nine included studies, standardized mean effect sizes were calculated for QEEG power variables for ADHD versus controls (normal children, adolescents, and adults). QEEG variables of relative power were used when available; absolute power was substituted when necessary. When the published data were sufficient or when the data were supplied by the original authors, Glass' delta was directly calculated (Glass et al., 1981). Otherwise, F-statistics or P values were converted using standard methods (Glass et al., 1981). Effect sizes of relevant variables were reported and pooled for all included studies using sample-weighted mean combinations of effect sizes. Estimates of 95% confidence intervals (CI) were determined using standard methods (Hasselblad and Hedges, 1995). Differences among the included studies were examined by analysis of heterogeneity using the Q-statistic as well as subgroup analysis (Hardy and Thompson, 1998; Sutton et al., 2000).

RESULTS

Effect Size Results of the QEEG Pattern

In the literature search of MEDLINE (1966 through July 2002), 1229 articles were uncovered by the search terminology (see Table 1). Forty-one of these articles provided a comparison of EEG power variables between controls (normal children, adolescents, and adults) and ADHD subjects. Of these 41 articles, 9 studies (N = 1498) were identified which met the full inclusion criteria of the meta-analysis, requiring ADHD diagnosis per standard guidelines based on the DSM-IV.

Five independent research groups were responsible for these nine included studies. Independence of the subjects among studies was determined in review of the articles or in personal communication with the authors. Differences among the included studies are summarized in Table 2, with heterogeneity analysis reported in a later section.

Details summarizing the ADHD assessment protocols, study details, and the effect size results of the nine included studies are presented in Table 3. The effect size results demonstrated a consistent increase in theta power, ranging for the studies from 0.55 to 1.95, with a pooled value of 1.31 (95% confidence interval [CI], 1.14, 1.48). As a reference point, studies that specifically reported values of relative EEG power observed a mean excess of theta power of 32% in ADHD relative to normal controls (Clarke et al., 2001c, 2002a, b). There was also a consistent decrease in beta power, with an effect size range of −0.94 to −0.02, and a pooled value of −0.51 (95% CI, −0.65 to −0.35). For reference, associated studies reported a mean decrease of beta power of −6% in ADHD relative to normal controls (Clarke et al., 2001c, 2002a, b). With this consistent increase in theta and decrease in beta, it was to be expected that there was a consistent increase in the theta/beta ratio, which ranged from 0.87 to 4.33, with a pooled value of 3.08 (95% CI, 2.90 to 3.26).

An effect size represents the standardized difference in mean scores between two populations. The larger the effect size, the more likely the two populations can be considered distinct with minimal overlap. Typically an effect size of 3, which represents three standard deviations between the populations, is interpreted as demonstrating that two populations are relatively distinct (Glass et al., 1981). The effect size for QEEG found in this meta-analysis supports that the theta/beta ratio trait is commonly observed in ADHD patients relative to normal children, adolescents, and adults. By statistical extrapolation, an effect size of 3.08 predicts a sensitivity and specificity of approximately 94% (Green et al., 1999). It is important to note that because these meta-analytic results are derived from controlled group studies often with retrospectively set limits, in practice a more modest outcome would be expected. Because this QEEG trait is known to arise with other conditions (Coutin–Churchman et al., 2003; Hughes and John, 1999), the clinical applications of these results remain unknown.

Excluded Studies of EEG and ADHD

Of the 41 studies which examined EEG power variable changes in ADHD relative to normal controls, the 32 excluded from the meta-analysis are accounted for in Table 4. The findings of these studies and the reasons for exclusion have been listed for reference. Most of the excluded studies did not use the DSM-IV. Of the five that did, four incorporated data sets that overlapped with other studies included in the meta-analysis, and were excluded so that the included studies would represent independent samples. The one further DSM-IV study was not included due to use of rating scales as the sole diagnostic for ADHD.

A total of 6 of the 32 excluded studies produced results contradictory to the findings of the meta-analysis. Of these 6 contradictory studies, 3 observed mixed results with some ADHD subjects consistent with the meta-analysis showing an increase in theta activity, and other subjects instead showing an increase in alpha activity. Given that increased alpha results were not observed in the other 29 excluded studies or in the 9 included in the meta-analysis, it may be important to

TABLE 2. Differences Between the Included Studies

Studies	Conditions	Artifact Removal	Electrodes	Spectral Analysis (Hz)	Medication	Drowsiness
Clarke et al., 2001b, 2002a,b	EC, resting state	EOG rejection at 50 μV Visual appraisal	Fp1, Fp2, Fz, F3, F4, F7, F8, Cz, C3, C4, T3, T4, T5, T6, Pz, P3, P4, O1, O2	Linked earDelta (1.5–3.5), theta (3.5–7.5), alpha (7.5–12.5), beta (12.5–25)	No history of medication use for ADHD	Not addressed
El-Sayed, et al., 2002	EO, fixed gaze, resting state. (also vigilance task)	Rejection at ±132 μV for eye and muscle Visual appraisal	F3, F4, F7, F8, P3, P4, T3, T4, T5, T6	ChinTheta (4–7.5), alpha (8–12.5), beta (beta-1, 13–16.5; beta-2, 17–30)	Not taking medication	Rejection of drowsy epochs
Monastra et al., 1999	EO, fixed gaze, resting state; (also reading, listening, and drawing)	Rejection with eye rolls, blinks, overall EMG >15 μV	Cz	Linked earTheta (4–8), beta (13–21)	Not taking medication or at least 12 hours off	Evaluations between 9 am and 3 pm
Monastra et al., 2001	EO, fixed gaze, resting state; (also reading, listening, and drawing)	Rejection with eye rolls, blinks, overall EMG >15 μV	Cz	Linked earTheta (4–8), beta (13–21).	No history of medication use for ADHD	Evaluations between 9 am and 3 pm
Bresnahan et al., 1999	EO, fixed gaze, resting state	Rejection of epochs with EOG activity ±100 μV	Fz, Cz, Pz	Linked earDelta (2–4), theta (4–8), alpha (8–13), beta (13–30)	Not addressed	Not addressed
Lazzaro et al., 1998, 1999	EO, fixed gaze, resting state	EOG correction using regression analysis	Fp1, Fp2, Fz, F3, F4, F7, F8, Cz, C3, C4, T3, T4, T5, T6, Pz, P3, P4, O1, O2	Linked earDelta (1–3), theta (4–7), alpha (8–13), beta (14–30)	No medication history or at least 2 weeks off	Not addressed

EC, eyes closed; EO, eyes, open; EOG, electro-oculogram; EMG, electromyography.

note that all 3 of the alpha increase studies relied on the same normative database (Neurometric; John et al., 1988). In addition, 2 of the alpha increase studies used the same data set and used rating scales as a stand-alone diagnostic for ADHD. In fact, of the 6 studies contradictory to the meta-analysis, 4 utilized rating scales or teacher opinion as stand-alone diagnostics, and the remaining 2 studies did not fully explain their diagnostic protocols. None of the 6 studies used DSM-IV criteria.

Counting the 3 mixed result studies, a total of 29 of the 32 excluded studies presented results that were consistent with the findings of the meta-analysis. These 29 excluded studies observed increases in theta, decreases in beta, or in other words a "slowing" of brain activity in ADHD-related subjects. Combining these excluded studies with those included in the meta-analysis yields a total of 38 studies from over the last 30-plus years which support that the QEEG trait of slowing is commonly observed in ADHD relative to normal controls. Although beyond the date range of our literature search, it is interesting to note that this trait was first observed about 75 years ago by Herbert Jasper, who observed increased frontal theta power in responders to stimulant medications (Cutts and Jasper, 1939; Jasper et al., 1938).

Inclusion Criteria Applied to the Studies of Previous Reviews

Meta-analysis of 9 DSM-IV studies supports the presence of a QEEG trait in ADHD relative to normal controls that is further supported by 29 pre–DSM-IV studies. In contrast, previous reviews of pre–DSM-IV studies have claimed that EEG-ADHD results were inconsistent. To investigate why our meta-analysis results are at odds with previous reviews, we examined the studies covered in those previous reviews per the inclusion criteria of the meta-analysis (Table 1). The results of this examination are listed in Table 5 showing the exclusion criteria that would have been applied to these studies and the findings of EEG power associated with ADHD when reported. We found that very few of the studies included in the previous reviews examined EEG power for ADHD versus normal controls with diagnoses per standard guidelines.

American Academy of Neurology and American Clinical Neurophysiology Society

Of the 22 attention-related studies reviewed by the AAN and ACNS (Nuwer, 1997), 18 did not examine any version of ADHD but rather other disorders such as dyslexia. Of the remaining 4 studies, 1 did not report EEG power, and 1 was a

TABLE 3. Meta-Analysis for EEG Power Associated With ADHD Diagnosed per Standard Guidelines Based on the DSM-IV

Study	Clinical Assessment/Referral	Clinical Site	Evaluative Tests and Evidence	Comparison	M/F	Age (y)	N	Theta	Beta	Theta/Beta
		Assessment of ADHD		Study Details				Effect Sizes (95% CI)		
1. Clarke et al., 2002a	Agreement of pediatrician and psychologist	Private pediatric practice	DSM-IV, medical history, physical examination, behavioral observations, neurologic assessment, school reports, reports from other professionals, structured interview with parent, WISC-III, Neale-Reading, WRAT-Spelling	ADHD (combined) vs. normal controls	M/F	8–12	114	1.95 (1.37, 2.52)	−0.51 (−0.89, −0.12)	2.60 (2.10, 3.10)
2. Clarke et al., 2002b	Agreement of pediatrician and psychologist	Private pediatric practice	Same as Clarke et al. 2002a (above)	ADHD (inattentive) vs. normal controls	M	8–13	140	1.53 (1.03, 2.03)	−0.02 (−0.38, 0.35)	*
3. El-Sayed et al., 2002	Neuropsychiatric assessment, pediatric neurologist, hospital teacher	Children's hospital, psychiatric	DSM-IV, ICD-10, neuropsychiatric and neurologic assessment, YCI, WISC-III, speech and language evaluation, GDS	ADHD vs. normal controls	M/F	6–16	99	0.56†§ (0.13, 0.98)	−0.73† (−1.16, −0.30)	*
4. Monastra et al., 2001	Physician, mental health professionals, school	Private outpatient psychological clinic	DSM-IV, physician's evaluation, ADDES, Barkley's ADHD Clinical Parent Interview, TOVA	ADHD vs. normal controls	M/F	6–20	129	*	*	4.33 (3.67, 4.99)
5. Clarke et al., 2001c	Agreement of pediatrician and psychologist	Private pediatric practice	Same as *Clarke et al. 2002a* (above), and CPRS-48	ADHD (combined) vs. Normal Controls	M/F	8–12	224	1.91 (1.37, 2.46)	−0.58 (0.85, −0.30)	2.43 (2.02, 2.84)
6. Bresnahan et al., 1999	Pediatrician and psychologist, confirmed by an independent psychiatrist	Private pediatric practice	DSM-IV, CBCL, CPRS, CTRS, Barkley's Semi Structured Interview for Adult ADHD, WURS, childhood history	ADHD vs. Normal Controls	MF	6–42	150	0.99‡ (0.64, 1.33)	−0.38‡ (−0.71, −0.05)	0.87‡ (0.53, 1.21)
7. Lazzaro et al., 1999	Pediatrician, psychiatrist, clinical psychologist	Hospital, cognitive neuroscience	DSM-IV, semi-structured interview, history, clinical records, CBCL, CPRS, CTRS, K-BIT, WIAT	ADHD vs. normal controls	M	11–17	108	0.55† (0.17, 0.94)	−0.70‡ (−1.09, −0.31)	*
8. Monastra et al., 1999	Physician, mental health professionals, school	Private outpatient psychological clinic	DSM-IV, ADDES, ADD-H: Comprehensive Teacher's Rating Scale, Barkley's ADHD Clinical Parent Interview, Conners' CPT, TOVA, GDS	ADHD vs. normal controls	M/F	6–30	482	*	*	3.84 (3.50, 4.17)

TABLE 3. *Continued*

Study	Assessment of ADHD			Study Details				Effect Sizes (95% CI)		
	Clinical Assessment/Referral	Clinical Site	Evaluative Tests and Evidence	Comparison	M/F	Age (y)	N	Theta	Beta	Theta/Beta
9. Lazzaro et al., 1998	Pediatrician	Hospital, cognitive neuroscience	DSM-IV, neurologic examination, structured interview, history, clinical records, CPRS, CTRS, K-BIT, WIAT	ADHD vs. normal controls	M	11–17	52	0.60†§ (0.04, 1.15)	−0.94‡ (−1.51, −0.36)	*
				Pooled results:			N 1498	Theta 1.31 (1.14, 1.48)	Beta −0.51 (−0.65, −0.35)	Theta/Beta 3.08 (2.90, 3.26)

*Variable not examined in original study.
†Original data not available for meta-analysis; effect size estimated using *P* value conversion; tendency for underestimation of effect size.
‡Original data not available for meta-analysis; effect size estimated using F value conversion; tendency for underestimation of effect size.
§Reported absolute instead of relative power.
WISC-III, Wechsler Intelligence Scale for Children; WRAT, Wide Range Achievement Test; ICD-10, The International Statistical Classification of Diseases and Related Health Problems; ADDES, Attention Deficit Disorders Evaluation Scale; YCI, Yale Children's Inventory; GDS, Gordon Diagnostic System; TOVA, Test of Variables of Attention; CPT, Continuous Performance Test; CPRS, Conners' Parent Rating Scale; CTRS, Conners' Teacher Rating Scale; CBCL, Child Behavior Checklist; WURS, Wender Utah Rating Scale; K-BIT, Kaufman Brief Intelligence Test; WIAT, Wechsler Individual Achievement Test.

review without original data. Therefore, only 2 of the 22 studies of the review of the AAN and ACNS examined ADHD versus normal controls using QEEG power variables. Of these 2 studies, 1 used rating scales as the diagnostic and the other did not provide a full description of the diagnosis and used a normative database (John et al., 1988) associated with mixed results in other studies (Chabot et al., 1999; Chabot and Serfontein, 1996).

Agency for Health Care Policy and Research

Of the eight studies reviewed by the AHCPR (of the US Department of Health and Human Services; Green et al., 1999), six did not examine EEG power. Most of these studies covered a range of EEG-related techniques, from evoked response potentials to brainstem auditory evoked potentials, which do not provide direct insight into EEG power results. Of the remaining two studies, one reported results contradictory to the meta-analysis, but had used rating scales as a stand-alone diagnostic for ADHD. The other reported results consistent with the meta-analysis, yet had used referrals with no further description of the diagnosis.

American Academy of Pediatrics

The AAP reviews (2000; Brown et al., 2001) relied exclusively on the aforementioned AHCPR review.

Although the previous reviews claimed that the results of pre-DSM-IV ADHD and EEG studies are inconsistent, these reviews did not provide comprehensive coverage of the literature. These reviews included only 4 of the 41 studies of EEG and ADHD uncovered by the current meta-analysis. In addition, 26 of the 30 studies in the previous reviews covered disorders other than ADHD and/or compared the unrelated EEG methods of evoked potential to spectral power analysis. Although these reviews may have demonstrated that a conglomeration of studies using a variety of EEG techniques examining numerous disorders yields different results, they did not include a sufficient sample of the existing literature to draw reasonable conclusions on the consistency of EEG power results with ADHD versus normal controls.

Sensitivity and Specificity for ADHD Versus Normal Controls

The meta-analysis yielded an effect size of 3.08 for the theta/beta ratio trait in ADHD versus controls. By statistical extrapolation, the sensitivity and specificity for an effect size of this magnitude is predicted to be approximately 94% (Green et al., 1999), which is similar to results of previous studies predicting 86% to 90% sensitivity and 94% to 98% specificity by comparisons between groups of ADHD and control subjects ages 6 to 30 years using the Cz electrode with eyes-open, fixed-gaze EEG data (Monastra et al., 2001; Monastra et al., 1999). It is important to note that the studies of controlled groups were often with retrospectively set limits, and that in practice the results would likely be more modest. Rating scales, which are widely used to determine the presence of ADHD behavioral traits, have been typically evaluated in a similar manner by retrospective studies examining ADHD and control groups. To provide a comparison of the presence of the QEEG trait versus the presence of behavioral traits observed with rating scales, a literature search was

TABLE 4. Studies of EEG Power and ADHD Not Meeting the Inclusion Criteria of the Meta-analysis

Study	Findings Consistent With Meta-analysis	Contradictory Findings	Reasons for Exclusion
1. Clarke et al., 2001d	Increased theta and decreased beta		Data set overlapped with data set of other study
2. Clarke et al., 2001e	Increased theta and decreased beta		Data set overlapped with data set of other study
3. Clarke et al., 2001b	Increased theta and decreased beta		Data set overlapped with data set of other study
4. Gustafsson et al., 2000	Some had increased slow activity		DSM-III-R. Insufficient diagnosis (checklist). Subjects also in medication study
5. Chabot et al., 1999	Some had increased theta activity	Some had increased alpha rather than increased theta	DSM-III. Insufficient diagnosis (rating scales). Included subjects as "ADHD" who tested negative. Controls from Neurometric database (John et al., 1988). *Note: same data set as study listed below (Chabot and Serfontein, 1996)*
6. Clarke et al., 1998	Increased theta and decreased beta		Data set overlapped with data set of other study
7. Chabot and Serfontein, 1996	Some had increased theta activity	Some had increased alpha rather than increased theta	DSM-III. Insufficient diagnosis (rating scales). Included subjects as "ADHD" who tested negative. Controls from Neurometric database (John et al., 1988)
8. DeFrance et al., 1996	Increased theta activity		Insufficient diagnosis of ADHD (rating scales).
9. Kuperman et al., 1996		Increased beta activity	DSM-III-R. Insufficient diagnosis (rating scales). Screened entire schools
10. Ucles and Lorente, 1996	Increased theta/alpha ratio		DSM-III-R. Diagnosis not fully described
11. Janzen et al., 1995	Increased theta activity		DSM-III-R. Diagnosis not described
12. Suffin and Emory, 1995	Increased theta activity	Some had increased alpha rather than increased theta	DSM-III-R. Diagnosis not described. Controls from neurometric database (John et al., 1988)
13. Matsuura et al., 1993	Increased slow wave activity		*Classification by referral with no further explanation of diagnosis
14. Mann et al., 1992	Increased slow activity. Decreased beta activity. Prediction of ADHD		*Insufficient diagnosis (rating scales)
15. Lubar, 1991	Increased theta/beta ratio (with drawing)		*Data set used in other study. No EEG without task
16. Halperin et al., 1986		No association between EEG and response to stimulants	*Insufficient diagnosis (subjects classified as hyperactive by teacher opinion)
17. Lubar et al., 1985	Excess theta. Prediction of attention deficit		*Insufficient diagnosis (minimal brain dysfunction equated with learning disability)
18. Callaway et al., 1983	Decreased beta activity		*Insufficient diagnosis (rating scales)
19. Dykman et al., 1982	Decreased fast wave activity		*Diagnosis of hyperactivity analyses together with learning disability group
20. Nahas and Krynicki, 1978	Excess slow wave most common abnormality		*Diagnosis of minimal brain dysfunction
21. Shouse and Lubar, 1978	Reduced sensorimotor activity (12–14 Hz)		*Diagnosis of hyperkinesis. EEG only in terms of sensorimotor activity
22. Small et al., 1978		No association between EEG and response to stimulants	*Diagnosis of hyperkinesis. Diagnosis not fully described
23. Grunewald-Zuberbier et al., 1975	Decreased beta activity		*Diagnosis of hyperactivity by observation in standard situations
24. Murdoch, 1974	Excess slow wave most common abnormality		*Diagnosis of minimal cerebral dysfunction

TABLE 4. *Continued*

Study	Findings Consistent With Meta-analysis	Contradictory Findings	Reasons for Exclusion
25. Satterfield et al., 1974	Excess slow wave most common abnormality. Best stimulant responders had excess slow		*Diagnosis of hyperactive child syndrome
26. Satterfield et al., 1973b	Excess slow wave most common abnormality. Best stimulant responders had excess slow		*Diagnosis of minimal brain dysfunction
27. Satterfield, 1973	Excess slow wave most common abnormality. Best stimulant responders had excess slow		*Diagnosis of hyperactive child syndrome
28. Satterfield et al., 1973a	Excess slow wave most common abnormality		*Diagnosis of hyperactive child syndrome
29. Satterfield et al., 1972	Increased slow wave activity. Best stimulant responders had even higher theta activity		*Diagnosis of hyperkinetic child syndrome
30. Satterfield, 1971	Best stimulant responders had excess slow		*Diagnosis of hyperkinesis
31. Wikler et al., 1970	Increased theta activity		*Referrals (scholastic and/or behavior problems). Hyperactivity (checklist)
32. Capute et al., 1968	Excess slow wave most common abnormality		*Diagnosis of minimal cerebral dysfunction

*Study prior to development of DSM-IV.

conducted for studies reporting sensitivity and specificity of ADHD behavior rating scales. The findings are reported in Table 6.

Rating scale studies were excluded from the comparison if it appeared that the experimental designs and statistical methods would have spuriously raised the sensitivity and specificity predictions (Snyder, 2004; Snyder et al., 2004). Exclusion criteria for the rating scales studies were as follows:

1. Did not evaluate an ADHD sample: Yale Children's Inventory (Shaywitz et al., 1986).
2. Used the evaluated scale as a gold standard for itself: Conners' Rating Scales-Revised manual (Conners, 1997), Conners' Abbreviated Teacher Rating Scale (Tarnowski et al., 1986), and Swanson, Nolan, and Pelham Rating Scale (Atkins et al., 1985).
3. Misuse of discriminant analysis, i.e., used the original sample in the validation of a discriminant analysis, rather than using a fresh sample: Conners' Teacher Rating Scale-Revised (Conners et al., 1998b), Conners' Parent Rating Scale-Revised (Conners et al., 1998a), Conners/Wells Adolescent Self-Report of Symptoms (Conners et al., 1997), Conners' Rating Scales-Revised manual (Conners, 1997), and Wender Utah Rating Scale (Ward et al., 1993).

Relative Risk of ADHD Versus Normal Controls

Because QEEG is considered a quantitative, physiologic measure of baseline brain functioning, it is of interest to provide a comparison with similar quantitative measures, such as genetic and environmental risk factors. Relative risk is a variable that can be used to provide the probability of ADHD occurring in groups with either the presence or absence of a particular factor. The relative risks for a number of genetic and environmental factors have been estimated from published values presented in a recent review (Bradley and Golden, 2001) using ADHD prevalence of 5% to produce estimates relative to the general population (Table 7). The presence of the QEEG trait as a risk factor (76.6) was derived from previous studies examining group differences between ADHD and controls (normal children, adolescents, and adults) (Monastra et al., 2001, 1999).

Differences Among the Included EEG Studies

The meta-analysis is a statistical exercise, and one potential concern is that the included studies may not have been compatible due to differences in medication effects, mental state, drowsiness, and reference electrode. Meta-analysis is a standardized method for combining studies of different designs, different populations, and a range of study control factors (refer to Table 2 for differences among the included studies). The inclusion of a formal test of heterogeneity offers the exploration of whether the variability among included studies is due to factors beyond chance (Song et al., 2001). In the test of heterogeneity, the usual statistic is Q, which has a χ^2 distribution (Hardy and Thompson, 1998). The Q for the theta/beta ratio as examined in the current meta-analysis is 1.21 with $P > 0.1$ indicating that heterogeneity is not present among the included studies. A common interpretation of this outcome is that the included studies are

TABLE 5. Studies Included in the EEG and ADHD Reviews of AAN, AHCPR, and AAP Examined per Inclusion Criteria of the Current Meta-Analysis

Study	Review	Findings Related to EEG Power and ADHD	Critical Exclusion Criteria
1. Chabot et al., 1996	1	N/A (did not report EEG power)	DSM-III. Insufficient diagnosis (rating scales). Included subjects in the "ADHD" group who tested negative. Neurometric database (John et al., 1988). *Note: data set from other study (Chabot and Serfontein, 1996)*
2. Kuperman et al., 1996	2, 3, 4	Increased beta activity*	DSM-III-R. Insufficient diagnosis (rating scales). Screened entire school populations
3. Harmony et al., 1995	1	N/A (did not examine ADHD)	Classified by ability with reading and writing
4. Lahat et al., 1995	2, 3, 4	N/A (did not examine EEG power)	Measured brain auditory evoked potential
5. Levy and Ward, 1995	1	N/A (review; no original data)	Review no original data
6. Suffin and Emory, 1995	1	Some had excess theta.[†] Some had excess alpha*	DSM-III-R. Diagnosis not described. Controls from neurometric database (John et al., 1988)
7. Newton et al., 1994	2, 3	N/A (did not examine EEG power)	Measured evoked response potential
8. Matsuura et al., 1993	2, 3, 4	More slow wave activity[†]	DSM-III-R. Classification by referral with no further description of diagnosis
9. Valdizan and Andreu, 1993	2, 3	N/A (did not report EEG power)	Did not report EEG power. Diagnosis not described
10. Galin et al., 1992	1	N/A (did not examine ADHD)	Classified by presence of dyslexia
11. Mann et al., 1992	1	Increased slow activity. Decreased beta activity. Prediction of ADHD[†]	DSM-III-R Insufficient diagnosis (rating scales)
12. Robaey et al., 1992	2, 3	N/A (did not examine EEG power)	Measured evoked response potential
13. Byring et al., 1991	1	N/A (did not examine ADHD)	Classified by ability to spell
14. Satterfield et al., 1990	2, 3	N/A (did not examine EEG power)	Measured evoked response potential
15. Flynn et al., 1989	1	N/A (did not examine ADHD)	Classified by presence of dyslexia
16. Rumsey et al., 1989	1	N/A (did not examine ADHD)	Classified by presence of dyslexia
17. Harmony et al., 1988	1	N/A (did not examine ADHD)	Examined EEG maturation
18. Byring, 1986	1	N/A (did not examine ADHD)	Classified by ability to spell
19. Fein et al., 1986	1	N/A (did not examine ADHD)	Classified by presence of dyslexia
20. Sutton et al., 1986	1	N/A (did not examine ADHD)	Measured evoked response potential
21. Yingling et al., 1986	1	N/A (did not examine ADHD)	Classified by presence of dyslexia
22. Holcomb et al., 1985	2, 3	N/A (did not examine EEG power)	Measured evoked response potential
23. Thatcher and Lester, 1985	1	N/A (did not examine ADHD)	Examined effects of nutrition and environmental toxins
24. Johnstone et al., 1984	1	N/A (did not examine ADHD)	Classified by presence of dyslexia
25. Fein et al., 1983	1	N/A (did not examine ADHD)	Classified by presence of dyslexia
26. Ahn et al., 1980	1	N/A (did not examine ADHD)	Classified by presence of learning disability and risk for neurologic disorders
27. Duffy et al., 1980b	1	N/A (did not examine ADHD)	Classified by presence of dyslexia
28. Duffy et al., 1980a	1	N/A (did not examine ADHD)	Classified by presence of dyslexia
29. Colon et al., 1979	1	N/A (did not examine ADHD)	Classified by presence of dyslexia
30. Hughes and Park, 1958	1	N/A (did not examine ADHD)	Classified by presence of dyslexia

*Contradictory to meta-analysis.
[†]Consistent with meta-analysis.
1, AAN & ACNS; 2, AHCPR; 3, AAP (2000); 4, AAP (2001).

compatible for the estimation of a single underlying effect size (Sutton et al., 2000).

Because of reported concerns of the low power of the Q test for heterogeneity, we have used a recommended *P* value cutoff of 0.1 to increase the power (Hardy and Thompson, 1998). In addition, we have included subgroup analyses to further explore the studies for potential sources of heterogeneity. Subgroup analysis can be used to identify moderator variables that may be associated with the outcomes of the studies by examining changes in effect sizes, in this case standardized in units of standard deviation. With this in mind, we have exam-

ined substantive factors known to influence theta power, including medication, drowsiness, and mental state (see Table 2 for differences among studies). Further, EEG method factors were evaluated including the study choices of frequency range, electrode sites, reference electrode, and EEG variable definitions (differences listed in Tables 2 and 3). The studies also differed in the form in which the data were reported, which determined the meta-analytic method used to derive the effect size (Table 3). Therefore the different analytical methods were evaluated as potential sources of variability. Results of the various subgroup analyses follow below.

TABLE 6. Comparison of QEEG and Behavior Rating Scales: Detection of Traits in ADHD Versus Controls

Trait	Measurement Technique	Presence of Trait(s) in ADHD (Predicted Sensitivity)	Absence of Trait(s) in Controls (Predicted Specificity)
Theta/beta ratio trait	QEEG*	90%	94%
	QEEG[†]	86%	98%
Behavioral traits	Child behavior checklist (CBCL), combined, $(T \geq 65)$[‡]	76%	69%
	CBCL, inattentive, $(T \geq 65)$[‡]	81%	69%
	CBCL, tested by discriminant analysis[§]	65%	49%
	CBCL, parent, inattentive	56%	63%
	CBCL, parent, combined	78%	63%
	CBCL, teacher, inattentive	56%	60%
	CBCL, teacher, combined	53%	60%
	Behavior assessment system for children (BASC), parent, inattentive	81%	68%
	BASC, parent, combined	82%	68%
	BASC, teacher, inattentive	73%	80%
	BASC, teacher, combined	60%	80%
	BASC, parent, tested by discriminant analysis[§]	74%	44%
	Devereaux Scales of Mental Disorders (DSMD), combined, $(T \geq 65)$[‡]	80%	78%
	DMSD, inattentive, $(T \geq 65)$[‡]	78%	78%
	Early Childhood Inventory-4 (ECI-4), parent[‖]	66%	57%
	ECI-4, teacher[¶]	68%	69%
	ADHD–IV, teacher, inattentive, $(\geq 90\%)$[#]	67%	80%
	ADHD–IV, teacher, combined, $(\geq 90\%)$[#]	80%	80%
	ADHD–IV, parent, inattentive, $(\geq 93\%)$[#]	83%	49%
	ADHD–IV, parent, combined, $(\geq 93\%)$[#]	84%	49%

*Monastra et al., 2001.
[†]Monastra et al., 1999.
[‡]Eiraldi et al., 2000.
[§]Doyle et al., 1997.
[‖]Vaughn et al., 1997.
[¶]Sprafkin et al., 2002.
[#]DuPaul et al., 1998.

TABLE 7. Comparison of QEEG and Relative Risk Factors for ADHD

Factor	Relative Risk
Emotional stress during pregnancy*	2.3
Maternal smoking*	2.9
D4 gene polymorphism*	3.3
Low birth weight (<1500 g)*	3.5
Early injurious accident*	5.6
Surgery first month of life*	19.9
QEEG: increased theta/beta ratio[†]	76.6

*Bradley and Golden, 2001.
[†]Monastra et al., 2001, 1999.

In the current meta-analysis the effect sizes were calculated, when possible, using published mean and standard deviation data or data provided by the studies' authors. When the original data were not available, conversion of F-statistics or P values was used. Because it has been reported that the F/P conversion method would typically result in a substantial under-

estimation of effect size (Glass et al., 1981), this was the first area to be evaluated, to account for this factor when analyzing the remaining factors. The effect size for theta power using the mean and standard deviation meta-analytic method is 1.81, and for the method of F/P conversion is 0.72, representing 1.09 standard deviations of difference between methods. Because of this noteworthy difference between meta-analytic methods, the most effective means to analyze the remaining factors is to first subgroup the studies by meta-analytic method applied, and then compare effect sizes by the further factor.

Of the 19 effect size results reported in the current meta-analysis (Table 3), 2 were not derived from relative power, but rather from absolute power. Both of these absolute power results were derived by the F/P conversion method, therefore the comparison was performed within that analytical subgroup. The effect size for the F/P conversion studies using theta absolute power is 0.57, compared to 0.81 for relative power, representing a difference of 0.24 standard deviations between the EEG variable choices.

The one study that used a chin electrode for reference rather than linked ears was in the F/P subgroup. There was a

0.21 standard deviation difference between effect sizes within the subgroup based on reference choice for theta power. With only one study using chin reference, these study results could be removed from the total meta-analysis for the sake of comparison, resulting in an effect size for theta power of 1.40 compared to a total meta-analytic result of 1.31. This outcome shows a difference of 0.09 standard deviations for inclusion versus exclusion of the one study using chin reference.

One study reported control of drowsiness, whereas the other studies did not report presence or absence of methods in this area. The one study that reported control of drowsiness was part of the F/P subgroup and had a 0.21 standard deviation difference in theta power in comparison to studies within the F/P subgroup not reporting drowsiness control. Removal of the one controlled study resulted in a difference of 0.09 standard deviations for theta power relative to the total meta-analytic result.

Studies varied by the selection of sets of electrodes for their analyses. However most of the studies observed significant differences in theta and beta power variables between ADHD and normal controls at each included electrode. In fact, 18 of the 19 effect sizes reported in the meta-analysis were based on significant differences at all included electrodes in the studies. One effect size result from only one study was based on significant differences at a portion of the electrodes observed in that study. Removal of this study from the meta-analysis results in 0.09 standard deviations of change in the pooled effect size for theta power.

The factor of medication is the simplest to evaluate because two repeated studies from the same research group differed in their reported inclusion criteria for medication use. Of importance to note is that all patients were reported to be off medications at the time of the EEG recordings; however, the time of washout for medication users varied. One study required no previous history of medication use, whereas the other required at least 12 hours of washout for medication users. These two inclusion criteria represent the extreme ends of medication control when applied in the studies. These two studies focused on the theta/beta ratio, and there was a 0.49 standard deviation difference between effect sizes of the two studies. It is important to note that there was one study included in the meta-analysis that did not report control of medication. Removal of this study from the meta-analysis led to a 0.06 standard deviation difference in the effect size for theta power.

When recording EEG, the eyes closed condition was used by one research group, whereas eyes open with a fixed gaze task was used by the others. Eyes closed produced an effect size of 2.49 for the theta/beta ratio, predicting sensitivity and specificity of 91% in ADHD versus normal controls, and eyes open with fixed gaze task resulted in an effect size of 3.34 with a prediction of 95% for sensitivity and specificity. Two of the investigators incorporated additional tasks with eyes open. However, when examining fixed gaze task versus the other tasks such as reading, listening, and drawing, the theta/beta ratio of the normal controls did not change significantly. The theta/beta ratio of ADHD subjects did not change significantly between fixed gaze and other

tasks, except for a slight increase with the final task in a series of four tasks (Monastra et al., 1999). Because there was no reported randomization in the order of the task series in the experimental design, the significance of this slight increase due to this task is inconclusive. The bottom line is that reading and listening tasks produced the same theta/beta ratio outcome as fixed gaze task, supporting that fixed gaze is sufficient to control mental state to the degree necessary to produce the consistent results observed by the current meta-analysis in the effect size and the Q statistic results. Due to lingering questions in the literature on the effect of mental state on EEG, investigation of further controls of mental state are recommended, however in light of the above results, absence of further mental state controls does not detract from the support of the meta-analysis to the hypothesis of consistency among studies.

In summary, the overall heterogeneity analysis indicates that the included studies are compatible for meta-analysis despite the noted differences among studies. An exploratory subgroup analysis indicated that three differences among the included studies resulted in changes in the meta-analytic results of approximately 0.5 standard deviations or greater, due to: 1) meta-analytic technique required for effect size derivation, 2) eyes open versus eyes closed, and 3) control of medication. The influence of the meta-analytic technique has been well documented and is an accepted part of the meta-analytic practice. Utilization of this technique is known to typically produce an underestimation of effect, leading to a more conservative meta-analytic estimate (Glass et al., 1981). The factor of eyes open versus eyes closed is worthy of note, as it has been demonstrated that although only a 0.5 standard deviation shift may be observed, the predicted sensitivity and specificity are shifted as well with a reduction when using eyes closed data. Control of medication has been recognized as an important control factor for EEG studies, as supported in the current meta-analysis by the 0.5 standard deviation difference between effect sizes of repeated studies with different medication control. The implication from these studies is that the residue of stimulant present after 12 hours of washout and possible effects of medication withdrawal were at most responsible for a 0.49 difference in standardized effect. Although the other evaluated factors weren't demonstrated to have major effects on the meta-analysis, it is widely accepted that these other factors such as drowsiness may have an effect on theta power. Although subgroup analysis may provide insights into variability among studies, it is recommended when applied post hoc that the analysis be considered exploratory and interpreted with caution (Hardy and Thompson, 1998; Song et al., 2001). Therefore, it remains important in future studies to investigate standardized methods of control of factors which may influence the outcome variables examined in this meta-analysis.

Age Patterns of ADHD

Age range is another potential source of heterogeneity among studies, but the overlapping of age ranges among the included studies did not allow for further subgroup analysis in the current meta-analysis. Therefore, we provided a separate evaluation by the comparison of changes in theta/beta ratio and in ADHD behavioral symptoms with age. It has been observed that QEEG measures vary over time with matura-

tion and development (Clarke et al., 2001a, b). With this in mind, group differences in the theta/beta ratio trait of ADHD versus normal controls have been previously explored using a separation of subjects by age groups (Monastra et al., 2001, 1999). In these studies, it was recognized that the theta/beta ratio varies with age for both ADHD and normal control subjects.

On a related note, behavioral and cognitive studies have shown that ADHD symptoms recede to an extent with age (Biederman et al., 1996 , 2000; Bradley and Golden, 2001; Hill and Schoener, 1996; Seidman et al., 1997). In support, a mathematical model has been precisely fit to the diagnostic results of 8 longitudinal clinical studies (N = 595) demonstrating the age decline of full ADHD diagnosis per DSM-III-R and DSM-III criteria (Hill and Schoener, 1996). An additional clinical study has repeated these results (N = 128) using DSM-III-R criteria (Biederman et al., 2000).

To investigate whether the QEEG and behavioral symptom changes of ADHD over time are associated, we have provided a comparison of the ADHD behavioral and cognitive changes relative to the QEEG data for ADHD at different age ranges. To accommodate this goal, the results of the QEEG and the age decline studies have been averaged for the same age ranges—6 to 11 years, 12 to 15 years, 16 to 20 years, and 21 to 30 years—standardized in terms of percent retention, and adjusted to the same reference point. Percent retention refers either to the persistence of meeting full ADHD diagnostic criteria, or to the persistence of an increased theta/beta ratio in ADHD relative to a normal baseline for aging. The values for the 6 to 11 years age range were chosen as the reference point against which percent retention was calculated for the other age ranges.

The comparison has been represented in Fig. 1. Although visual inspection shows that the patterns in the graph are not perfectly overlapping, statistical analysis shows that
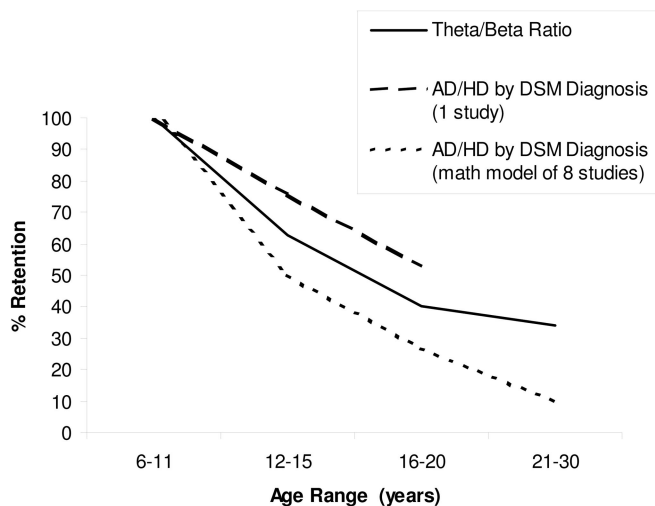
the QEEG data follows age-related changes of the Biederman et al. study (Pearson correlation coefficient, 0.993, $P = 0.078$, 3 data points) and of the mathematical model that had been fit by Hill and Schoener to 8 diagnostic studies (Pearson correlation coefficient, 0.996, $P = 0.004$, four data points). Our analysis of these results supports the observation that ADHD behavior as defined by DSM criteria and ADHD physiology as represented by QEEG conform to a mathematically similar age dependent attenuation. In other words, the QEEG trait tracks changes in ADHD symptom presentation with age.

DISCUSSION

The results of this meta-analysis support the conclusion that a theta/beta ratio increase is a commonly observed trait in ADHD relative to controls (normal children, adolescents, and adults) and that the QEEG trait follows age-related changes in ADHD symptom presentation. A number of related issues not directly addressed by the meta-analysis need consideration.

Specificity of QEEG in Differential Diagnosis

The focus of the meta-analysis on studies of ADHD versus normal controls limits the generalizability of the results. Because the evaluated QEEG trait is known to arise with other conditions (Coutin-Churchman et al., 2003; Hughes and John, 1999), the specificity of QEEG in differential diagnosis of ADHD remains unknown. Further, because the presence of comorbidities is considered to be common with ADHD (Goldman et al., 1998), the effect of comorbid conditions on the QEEG trait requires future investigation. Although the professional guidelines of the AAP may provide recommendations about the clinical use of ADHD rating scales based on studies of ADHD versus normal controls, it remains important from an evidence-based medicine standpoint to demonstrate whether quantifiable traits are specific to a disorder when examined versus other disorders. For instance, it is important to note that increased theta is considered a nonspecific EEG abnormality that may appear in a number of disorders, such as epilepsy, polysubstance dependence, dementia, alcoholism, and schizophrenia (Coutin-Churchman et al., 2003; Hughes and John, 1999). Theta increases and beta decreases may be seen in a wide range of disorders that are on the differential diagnosis of ADHD. This includes developmental delays and focal or generalized injuries or dysgenesis from a variety of causes. The theta and beta traits' roles in the differential diagnosis of ADHD remain to be clarified. Coutin-Churchman et al. discussed with their findings that the preferred emphasis for clinical applications of EEG may be in its integration as one piece of information in the complete clinical picture. Therefore, it remains of considerable importance to investigate QEEG as it would be applied in the clinical setting in the differentiation of ADHD from other disorders that may be mistaken for ADHD.

One preliminary study has compared the theta/beta ratios of subjects with ADHD to a pool of subjects with oppositional defiant disorder, mood disorder, or anxiety disorder but not ADHD (N = 209). Seventy-eight percent of ADHD subjects demonstrated the trait of an increase in the theta/beta ratio, whereas 97% of subjects with the other disorders did not display this trait (Rabiner, 2001). These preliminary results suggest the importance of further clinical research to examine QEEG in the

FIGURE 1. *Quantitative EEG results follow age-related changes in ADHD diagnosis.* Plots constructed from published results: theta/beta ratio (Monastra et al., 2001, 1999), ADHD by DSM-III-R criteria (Biederman et al., 2000), and a mathematical model of retention of ADHD diagnoses from eight studies using DSM-III and DSM-III-R criteria (Hill and Schoener, 1996).

differential diagnosis of ADHD to determine its degree of generalizability to clinical populations.

Heterogeneity of ADHD

We reported above the examination of heterogeneity among included studies. However, part of the controversy of ADHD lies with the heterogeneity of the disorder, which has been marked by a varied response in ADHD patients to medication (Baumgaertel et al., 1995; Cantwell, 1996; Overmeyer et al., 1999; Wolraich et al., 1996), and has been observed as well in some QEEG studies by variations in the QEEG patterns between statistical clusters of ADHD subjects (Clarke et al., 2001c, 2002b). With regards to medication, only 60% to 75% of DSM-IV–diagnosed ADHD subjects respond to methylphenidate (Elia, 1993; Nash, 2000; Spencer et al., 2000). In other words, within the ADHD population there are subgroups of good and poor responders to methylphenidate, raising the question of whether there is a QEEG difference between these subgroups. Differences in medication response associated with EEG were initially observed around 75 years ago by Herbert Jasper, who reported increased frontal theta power in stimulant medications responders (Cutts and Jasper, 1939; Jasper et al., 1938). Within the scope of the literature search of the current review, studies of the brain electrical activity of methylphenidate responders have been reported as far back as the early 1970s, with seven pre–DSM-IV studies appearing (see Table 4). Five of the seven studies observed that methylphenidate responders have the pattern of an increase in QEEG slowing. More recently, in a DSM-IV study, ADHD subjects were separated into groups characterized by good or poor response to methylphenidate, and compared against normal controls as well. With an estimated effect size of 3.5, the mean theta/beta ratio was of notable difference between subgroups of good and poor responders. Correspondingly, the effect size for ADHD good responders versus normal controls was 4.9 (Clarke et al., 2002a). These QEEG results support the presence of heterogeneity within the disorder along the lines of medication response.

Other issues of heterogeneity in ADHD have been addressed in terms of QEEG. Some studies have investigated more elaborate statistical analyses of QEEG, resulting in the further partitioning of ADHD subjects into electrophysiologic subtypes *within* the DSM-IV subtypes. Such research has demonstrated heterogeneity within the ADHD population in the form of three electrophysiologic subtypes for the ADHD combined subtype (Clarke et al., 2001c) and two electrophysiologic subtypes for the ADHD inattentive subtype (Clarke et al., 2002b), which for the purposes of this review, shall be referred to as the five electrophysiologic subtypes of ADHD. The question that arises relative to the results of the current meta-analysis is whether an increase in the theta/beta ratio is a characteristic of each of these five subtypes.

What the studies observed is that four of the five electrophysiologic subtypes have the pattern of an increase in theta power and a decrease in beta power, representing approximately 90% of all ADHD subjects. These general changes in theta and beta power coincide with previous studies finding about 90% sensitivity for the presence of a raised theta/beta ratio in ADHD patients versus normal children, adolescents, and adults (Monastra et al., 2001; Monastra et al., 1999). Although the four

subtypes are consistent for general changes in theta and beta power, the differences between groups were delineated by degree of change in theta and beta power, as well as other changes in QEEG beyond the scope of this review (for further details, refer to studies of Clarke et al. (2001c, 2002b).

The fifth electrophysiologic subtype did not demonstrate an increase in the theta/beta ratio, but rather was marked by a distinct increase in frontal beta power. This subtype represents approximately 10% of ADHD subjects, or 15% to 20% of the ADHD combined subtype (Chabot and Serfontein, 1996; Clarke et al., 1998, 2001c, d, e). The effect size for this variable is 4.1, at a level supporting that there is a distinct departure from normal in brain electrical activity for this electrophysiologic subtype. These results imply that the QEEG trait of an increased theta/beta ratio might be present in 90% of the ADHD population, and the remainder may express a QEEG trait of an increase in frontal beta power.

CONCLUSIONS

Meta-analytic results of 9 DSM-IV studies and the results of 29 pre–DSM-IV studies support that a theta/beta ratio increase is a commonly observed trait in ADHD relative to controls (normal children, adolescents, and adults). By statistical extrapolation, the effect size of 3.08 predicts a sensitivity and specificity of 94%, which is similar to values predicted by retrospective studies examining ADHD and normal controls in group comparisons. The QEEG trait also follows age-related changes in ADHD symptom presentation. Because it is known that this trait may arise with other conditions, we recommend a prospective study covering differential diagnosis to examine generalizability to clinical applications.

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