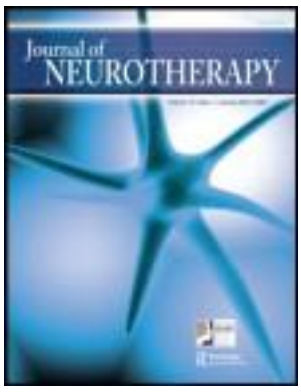

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Assessment-Guided Neurofeedback for Autistic Spectrum Disorder

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Assessment-Guided Neurofeedback for Autistic Spectrum Disorder

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ABSTRACT. *Background*. Research reviewing the epidemiology of Autism (Medical Research Council, 2001) indicated that approximately 60 per 10,000 children (1/166) are diagnosed with Autistic Spectrum Disorder (ASD). Jarusiewicz (2002) published the only controlled study documenting the effectiveness of neurofeedback for Autism based on one outcome measure. The present study extended these findings with a larger sample size, broader range of assessments, and physiological measures of brain functioning.

Methods. Assessment-guided neurofeedback was conducted in 20 sessions for 37 patients with ASD. The experimental and control groups were matched for age, gender, race, handedness, other treatments, and severity of ASD.

Results. Improved ratings of ASD symptoms reflected an 89% success rate. Statistical analyses revealed significant improvement in Autistics who received Neurofeedback compared to a wait list control group. Other major findings included a 40% reduction in core ASD symptomatology (indicated by ATEC Total Scores), and 76% of the experimental group had decreased hyperconnectivity. Reduced cerebral hyperconnectivity was associated with positive clinical outcomes in this population. In all cases of reported improvement in ASD symptomatology, positive treatment outcomes were confirmed by neuropsychological and neurophysiological assessment.

Conclusions. Evidence from multiple measures has demonstrated that neurofeedback can be an effective treatment for ASD. In this population, a crucial factor in explaining improved clinical outcomes in the experimental group may be the use of assessment-guided neurofeedback to reduce cerebral hyperconnectivity. Implications of these findings are discussed. doi:10.1300/J184v11n01_02

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KEYWORDS. Neurofeedback, QEEG analysis, infrared (IR) imaging, neuropsychological assessment, Autistic Spectrum Disorder, Autism, Asperger's Syndrome, executive deficits, hyperconnectivity, hypoconnectivity

INTRODUTION

In recent years, Autistic Spectrum Disorder (ASD) has shown a dramatic increase in prevalence. A review of prevalence survey research for ASD (identified by DSM-IV criteria for Autism, Asperger's Syndrome, and Pervasive Developmental Disorder-Not Otherwise Specified) across the United States and the United Kingdom reported rates of ASD substantially increased from prior surveys indicating 5 to 10 per 10,000 children to as high as 50 to 80 per 10,000 (equivalent to a range of 1 in 200 to 1 in 125 children with ASD) (Blaxill, 2004). Another review of research on the epidemiology of Autism (Medical Research Council, 2001) indicated that approximately 60 per 10,000 children (equivalent to a range of 1 in 166 children) are diagnosed with Autistic Spectrum Disorder.

Autism is defined as a neurodevelopmental disorder characterized by impairment in social interaction and communication. Historically, Kanner and Asperger introduced the term Autism (Kanner & Eisenberg, 1956; Asperger, 1991/1944). Further research concluded that Autism can be categorized as part of a spectrum of heterogeneous disorders. This continuum of disorders is characterized by a broad range of abilities and levels of severity. The common feature of Autistic Spectrum Disorder (ASD) is qualitative impairment in social and communication domains, as well as imaginative development (Wing & Gould, 1979). More current research indicates that Autism is one of a range ofrelated Pervasive Disorders including: Asperger's Disorder, Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS), Childhood Disintegrative Disorder (CDD), and Rett's Disorder (Medical Research Council, 2001).

The triad of symptoms including impaired communication, social skills, and imaginative development formed the basis for the current international classification systems–International Classification of Diseases (ICD-10; WHO, 1993) and Diagnostic and Statistical Manual, 4th edition (DSM-IV; APA, 1994). Both diagnostic systems characterize ASD as a disorder of early onset (before the age of 3), with impairment in social interaction, communication and imagination, as well as restricted interests and activities (Medical Research Council, 2001).

The heterogeneity within the spectrum of Autistic Disorders has led researchers to propose a division of Autism into subgroups: (1) Low, medium, and high-functioning; and (2) Non-regressive and regressive subtypes differentiated by age of onset. Regressive Autism occurs in 15-40% of children with ASD. This disorder is characterized by normal development for 15-19 months followed by loss of vocabulary, reduced social interaction and responsiveness, and sometimes repetitive play behavior (Medical Research Council, 2001).

In some cases, children with Autism may never develop patterns of typical speech. Their speech may be inflexible and unresponsive to the context. Speech may be limited to echolalia or narrow topics of specialized knowledge. Communicative impairment includes nonverbal cues such as eye contact, facial expression, and gesture. Social behaviors are often characterized by lack of interaction; play lacks cooperation and imagination and is narrowly focused on repetitive activities (Belmonte et al., 2004).

Executive deficits associated with Autism have been attributed to frontal lobe dysfunction resulting in perseveration and the inability to shift attention. Weak central coherence (a preference for local detail over global processing) has been attributed to individuals with Autism to explain their superior ability to attend to details. In addition, weak central coherence also predicts the tendency of people with Autism to have deficits in understanding global systems or the relation between the parts and the whole (Baron-Cohen, 2004).

The other subdivisions of Autistic Spectrum Disorder include: Asperger's Disorder, Pervasive Developmental Disorder-Not Otherwise Specified, Childhood Disintegrative Disorder,

and Rett's Disorder. Individuals with Asperger's Syndrome frequently have high levels of cognitive function, speech is characterized by literal pedantic communication, difficulty comprehending implied meaning and fluid motion, as well as inappropriate social interaction. Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS) reflects deficits in language and social skills which do not meet the criteria of other disorders. In contrast, Childhood Disintegrative Disorder and Rett's Disorder both have normal periods of early development followed by loss of previously acquired skills. Most of the conditions described involve deficits in communication and social skills, however they vary considerably in terms of onset and severity of symptomatology included within the Autistic Spectrum of Disorders (Attwood, 1998; Hamilton, 2000; McCandless, 2005; Sicile-Kira, 2004; Siegel, 1996).

Current research suggests that Autistic Spectrum Disorders may be associated with functional disconnectivity between brain regions. There is evidence for anomalies in the functional connectivity of the medial temporal lobe (Baron-Cohen, 2004; Belmonte et al., 2004). Abnormalities were found specifically in the functional integration of the amygdala and parahippocampal gyrus (Welchew et al., 2005). This points to the need for therapeutic interventions which address ASD as a neurodevelopmental and brain disorder.

Recent survey research reported on the therapies that parents most frequently selected for their children with Autistic Spectrum Disorder (Green et al., 2006). The majority of parents reported utilizing as many as seven different treatment modalities to ameliorate their children's symptoms of Autism. These include speech therapy (the most common), visual schedules, sensory integration, applied behavior analysis, medications, special diets, andvitamin supplements (Green et al., 2006).

The Research Units on Pediatric Psychopharmacology (RUPP) Autism Network (2005a; 2005b) has conducted two separate studies related to the use of Risperidone and Methylphenidate. In the first of these studies (RUPP Autism Network, 2005a), Risperidone was effective in reducing irritability, but with side effects and a significant relapse rate. In the Methylphenidate study (RUPP Autism Network, 2005b), 49% of the sample was considered positive responders, but with significant non-responders and an 18% side effect rate. Behavior therapy is another frequently implemented treatment for children with Autism. Smith et al. (2000) demonstrated that intensive treatment conducted over two to three years was successful in improving IQ and language functions. Sallows and Graupner (2005) observed a significant improvement in 48% of the subjects. Rapid learners were in regular education by age 7. The best outcomes were associated with the capacity for imitation, social responsiveness, and language.

Although behavior therapy improves social, cognitive and language skills, years of intensive training are required before children can attain positive treatment outcomes. Parents who select behavior therapy for their children with Autism appear to be highly motivated and committed to completion of the program.

Other interventions that has been studied in terms of efficacy include vitamin, mineral, and enzyme supplementation. Adams and Holloway (2004) conducted a randomized, double-blind placebo controlled study to investigate the effects of a multivitamin/mineral supplement on ASD (n = 20). The results indicated that 84% of their sample had improved sleep and gastrointestinal symptoms, but there was a side effect rate of 18%. Chez et al. (2002) found that L-carnosine supplementation led to improved ratings of behavior, socialization and communication.

When vitamin and mineral deficiencies are treated, there can be improvement in certain conditions co-occurring with Autism such as gastrointestinal and sleep disorders.However, some children with Autism may have allergic reactions to certain forms or dosages of vitamin and mineral supplementation. Therefore, careful monitoring of dosage levels and adjustments are required.

Special diets are another biomedical non-drug intervention which were found to be effective in the treatment of Autism. Reichelt and Knivsberg (2003) found that a gluten- free/casein-free diet followed over four years led to improvements in cognitive, social, language, and behavioral domains. The total number of children who improved following the dietary

intervention was not reported in the study. Therefore, percentage of improvement for the group receiving the intervention could not be calculated.

Based on research reporting the co-occurrence of gastrointestinal conditions with Autism, secretin (a gastrointestinal hormone) has also been studied as a treatment for Autism. Roberts et al. (2001) investigated the effects of repeated doses of intravenous secretin on 64 children diagnosed with Autism in a randomized, placebo controlled study. Following treatment, receptive and expressive language improved in both groups but the amount of improvement did not distinguish between groups. However, parents anecdotally reported the following changes: sleep improvement in 7 children (10.9%), 4 of whom had diarrhea according to the GI questionnaire (6.25%), toilet training in 3 shortly after the injection (4.68%); and more connectedness in 5 children (7.8%). Twenty-one percent of children receiving secretin injections had generalized flushing in the neck, face or chest immediately following the injection (Roberts et al., 2001).

Another condition that can co-occur with Autism is heavy metal toxicity which involves excessive levels of mercury. Chelation therapy utilizes Di-mercaptosuccinic- Acid (DMSA) to clear the body of mercury or other toxic metals. Bradstreet et al. (2003) conducted a case control study of mercury toxicity in children with Autistic Spectrum Disorders (n = 221). Following an oral chelating agent, urinary mercury concentrations were significantly higher in 221 children with Autistic Spectrum Disorders than in 18 normal controls ($p < .0002$). Vaccinated children with ASD had significantly higher urinary mercury concentrations then did vaccinated controls ($p < .005$).

Holmes (2001) documented the progress of children with Autism (n = 85; 40 aged 1-5 yrs.; 25 aged 6-12 yrs.; 16 aged 13-17 yrs.; and 4 aged >18 yrs.) treated with chelation (DMSA+ lipoic acid) for at least four months. Marked improvement in behavior, language, and social interaction was noted in 35% of children 1-5 years of age. Moderate improvement was found in 39% of children aged 1-5, 28% of children aged 6-12 and 6% of children aged 13-17. However, 52% of children aged 6-12, 68% of children aged 13-17 made only slight improvement, and 75% of individuals over 18 made no improvement. The results of the Holmes study indicate that chelation therapy was effective for children with Autism under the age of six.In contrast, the majority of older children and adolescents did not benefit from this treatment (Kirby, 2005). Holmes (2001) noted that younger patients excreted larger quantities of mercury than did older patients which may explain this discrepancy in treatment outcomes.

Rimland (2005) in association with the Autism Research Institute collected responses from 23,700 parents of children with Autism rating the efficacy of biomedical drug and non-drug interventions. The benefit to harm ratios for several of the therapies discussed previously are listed below in Table 1.

As shown in Table 1, the most effective rated treatments are chelation, digestive enzymes, and gluten-/casein-free diets. These findings are based on parent report only and additional research is necessary to provide further support for these findings. Special diets can also result in improved ASD symptoms, however regression in symptoms can occur after discontinuation of the diet (Reichelt & Knivsberg, 2003). Digestive enzymes must also be continued to maintain improved treatment outcomes. Vitamin therapy and secretin may also be beneficial, however some children with Autism may have allergic reactions to secretin and certain forms of vitamin and mineral supplementation (Adams & Holloway, 2004; Roberts et al. 2001).

TABLE 1. Benefits to Harm Ratios

Treatments	Ratios
Risperidal	3.0: 1
Ritalin	0.7:1
Haldol	0.9: 1
Thorazine	0.7: 1
B6 with Magnesium	10: 1
Digestive Enzymes	20: 1
Intravenous Secretin	6.7: 1
Gluten-/Casein-Free Diet	20: 1
Chelation	35: 1

Note. All benefit to harm ratios listed are modified from Rimland (2005) based on parent ratings of biomedical interventions.

The least effective rated treatments for ASD were Ritalin, Risperidal, Thorazine, and Haldol. Although neuroleptics (i.e., Thorazine and Haldol) may reduce dysfunctional behaviors associated with ASD, adverse side effects such as sedation, irritability, and extrapyramidal dyskinesias limit the use of these medications (Committee on Children with Disabilities, 2001). In addition, side effects can include weight gain (for Risperidal), decreased appetite and difficulty falling asleep (for Ritalin). There may also be a rebound of aggressive behavior when medication is discontinued (RUPP Autism Network, 2005a; RUPP Autism Network, 2005b).

In comparison, neurofeedback is a non-invasive therapeutic intervention which has been shown to enhance neuroregulation and metabolic function (Coben, 2005b, 2005c). In contrast to behavior therapy, positive treatment outcomes as a result of neurofeedback training are achieved over the course of several months rather than a year or more of intensive training.Neurofeedback has no adverse side effects while psychopharmacological interventions, as well as certain vitamin/mineral supplementation and secretin are associated with side effects. The therapeutic treatment outcomes of neurofeedback training are maintained over time and do not reverse after treatment is withdrawn (Linden, Habib, & Radojevic, 1995; Lubar et al., 1995; Monastra et al., 2005; Tansey, 1993) as in drug therapy, diet therapy, and supplementation with vitamins, minerals, and enzymes.

In 1994, Cowan and Markham conducted the first case study of neurofeedback with Autism. QEEG analysis was performed on an 8 year old girl diagnosed with high functioning Autism during eyes open and at rest. The findings indicated an abnormally high amount of alpha (8-10 Hz) and theta (4-8 Hz) activity predominately in the parietal and occipital lobes. Based on these results, a neurofeedback protocol was designed to suppress the ratio of theta and alpha (4-10 Hz) to beta (16-20) EEG activity at central and parietal sites using a bipolar (sequential) montage (two scalp electrodes and one ear reference electrode). The findings following 21 neurofeedback sessions included: increased sustained attention, decreased autistic behaviors (inappropriate giggling, spinning), improved socialization based on parent and teacher reports. There were also substantial improvements in the Test of Variables of Attention (TOVA) for measures of inattention (omission), impulsivity (commission) and variability. A follow-up TOVA was administered two years later. All scores were within normal limits. In addition, the girl continued to maintain positive social interactions as reflected by engaging in team sports.

Other researchers have also reported positive treatment outcomes or normalizing trends for children with Autism or Asperger's Syndrome treated with neurofeedback (Sichel et al., 1995; Scolnick, 2005). However, these studies utilized only single case or small group designs without control groups. Thompson and Thompson (1995) conducted research on neurofeedback combined with metacognitive strategies for a group of boys (n = 15; aged 8-14). Nine of the children met criteria for Asperger's Syndrome and the others met criteria for Attention Deficit Disorder and Learning Disabilities. All 15 boys improved as indicated by parent-teacher interviews, academic function and sustained visual and auditory attention.

Jarusiewicz (2002) published the only group study documenting the efficacy of neurofeedback for Autistic Disorders. Forty participants responded to a request to participate in the research. Only 12 of the 20 experimental group children completed 20 or more sessions (range 20-69; mean = 36 sessions) necessary for data analysis. Measurement of treatment outcome was based on the use of only one assessment measure–the Autism Treatment Evaluation Checklist (ATEC). The initial protocols were reward at site C-4 referenced to the contralateral ear in the 10-13 Hz range or lower depending on each child's ATEC score. Inhibits were set at 2-7 Hz and 22-30 Hz. The 2-7 Hz inhibit was selected due to the significant levels of delta and theta found in the spectrals of all the children in the study. This protocol was applied to 57% of the children with adjustments as necessary (Jarusiewicz, 2002).

For children that experienced problems with vocalization during training, an F7 electrode placement with a right ear reference was utilized. The protocol included augmenting 15-18 Hz and inhibiting 2-7 Hz and 22-30 Hz. When children were able to maintain training without

demonstrating signs of overarousal, additional five minute increments were provided until the session reached 30 minutes in duration. This protocol was administered 15% of the time, and was frequently followed by the C4 electrode placement and initial protocol for calming effects (Jarusiewicz, 2002).

For children who required assistance in enhancing socialization and communication skills, a bipolar F3-F4 electrode placement was employed. A 7-10 Hz to 14.5- 17.5 Hz augment and 2-7 Hz and 22-30 Hz inhibit protocol was utilized. This protocol was employed 12% of the time, and it was discontinued if giggling and inappropriate laughter occurred (Jarusiewicz, 2002).

For children who experienced emotional instability, a bipolar T3-T4 electrode placement was implemented, beginning with 9-12 Hz rewards and inhibits at 2-7 Hz/ 22-30 Hz. Protocol frequencies were adjusted up or down if further reduction of anxiety, sadness, and hyperactivity were necessary. The protocol was employed 13% of the time. Children received one to three training sessions per week, with two sessions per week as the most common frequency of sessions.

Children with Autistic Spectrum Disorder who completed neurofeedback training attained a 26% average reduction in the total ATEC rated autism symptoms in contrast to 3% for the control group. Parents reported improvement in socialization, vocalization, anxiety, schoolwork, tantrums, and sleep while the control group had minimal changes in these domains (Jarusiewicz, 2002).

Further research on methods of developing effective neurofeedback protocols for children with Autistic Spectrum Disorders is needed. Autism encompasses a broad range of symptoms (e.g., anomalies in communication, social behavior, cognitive and motor function, seizure activity, obsessive compulsive behavior, atypical sleeping and eating patterns), therefore one single assessment measure may not provide sufficient data to accurately target specific sites associated with dysfunction and disregulation. Coben's (2005a, 2005b, 2005c) research has shown that improved outcomes can result from assessment providing multiple data points to guide the development of individualized neurofeedback protocols which target specific brain regions to increase activation, symmetry, and interconnectivity.

In the present study, we seek to extend Jarusiewicz' findings with a larger sample size and broader range of measures to evaluate treatment outcome. The assessments utilized included: neuropsychological tests, ratings of behavior and executive function, Quantitative EEG (QEEG) analysis, Infrared imaging to accurately target dysfunctional or disregulated regions in need of remediation, as well as parent rating of treatment outcome. Treatment protocols were assessment-based and individualized for each child receiving neurofeedback training.

METHOD

Participants

Thirty-seven children diagnosed with Autistic Spectrum Disorder (ASD) participated in the study and served as the experimental group. There were 12 participants in the wait-list control group similarly diagnosed with ASD. The experimental and control groups were matched based on age, gender, race, handedness, other treatments, and severity of ASD as indicated by the Autism Treatment Evaluation Checklist (ATEC). The experimental group received assessment-guided neurofeedback training for at least 20 sessions. Of the initial 38 patients that began the study, only one patient dropped out prior to completion of the study. No new treatments were undertaken by any participants during the course of the study. Procedures were explained to parents and informed consent was obtained for their children to participate in the study. Refer to Table 2 for the demographics of the neurofeedback group and Table 3 for the demographics of the control group.

As shown in Table 4, the ASD diagnoses for the experimental group were as follows: 56.8% (n = 21) had Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS); 18.9% (n = 7) Autism; 13.5% (n = 5) Asperger's Disorder; and 10.8% (n = 4) Childhood Disintegrative Disorder. The majority of participants (75.7%) were diagnosed with PDD-NOS or Autism.

TABLE 2. Demographics of Neurofeedback Group

Age	Gender	Race	Handedness	Number of Meds	Total ATEC Score
Mean 8.92 years	31 Males	36 Caucasian	27 Right	22 None	Mean 45.161
	6 Females	1 Asian-American	5 Left	8 One	
Range 3.92-14.66 years			5 Mixed	5 Two	Range 12-100
				2 Three	

Note. Total ATEC Score was computed from the Autism Treatment Evaluation Checklist (ATEC; Rimland & Edelson, 2000).

TABLE 3. Demographics of Control Group

Age	Gender	Race	Handedness	Number of Meds	Total ATEC Score
Mean 8.19 years	10 Males	12 Caucasian	9 Right	8 None	Mean 45.25
	2 Females		2 Left	2 One	
Range 5.83-10.92 years			1 Mixed	1 Two	Range 20-72
				1 Three	

Note. Total ATEC Score was computed from the Autism Treatment Evaluation Checklist (ATEC; Rimland & Edelson, 2000).

TABLE 4. ASD Diagnoses for the Neurofeedback Group

Autism	PDD-NOS	CDD	Asperger's Disorder
7	21	4	5

Note. ASD=Autistic Spectrum Disorder; PDD-NOS=Pervasive Developmental Disorder-Not Otherwise Specified; CDD=Childhood Disintegrative Disorder.

Procedure

A diagnostic interview was conducted with the parents to ascertain core behavioral, cognitive and social/emotional issues of concern as part of a comprehensive neurodevelopmental history. Following the interview, neurobehavioral rating scales were administered which included: the Autism Treatment Evaluation Checklist (ATEC), Gilliam Asperger's Disorder Scale (GADS), Gilliam Autism Rating Scale (GARS), Behavior Rating Inventory of Executive Function (BRIEF), and Personality Inventory for Children (PIC-2). Baseline measures also included neuropsychological evaluation of executive, attentional, visual-perceptual, and language functioning. All participants also underwent Quantitative EEG (QEEG) analysis. Another measure of underlying cortical activity was Infrared (IR) imaging. IR imaging assesses the thermoregulation of specific brain regions which is associated with metabolic activity and regional Cerebral Blood Flow (rCBF). IR imaging was conducted prior to and following each training session. All other assessments were administered prior to and following treatment.

Materials

Assessment Instruments

At the completion of the study, parents rated the effectiveness of assessment-guided neurofeedback. An index of Parental Judgment of treatment efficacy was computed to provide a benefit-harm ratio. The index consisted of three categories of Parental Judgment: 1. Improved; 2. No Change; and 3. Worse. The Parental Judgment Ratings were compared to those calculated by Rimland (2005) for other therapeutic approaches to ASD (as previously described).

The Autism Treatment Evaluation Checklist (ATEC; Rimland & Edelson, 2000) was developed as a valid means of assessing the effectiveness of treatments for Autism. The ATEC consists of a one-page checklist to evaluate the severity of the core symptoms of Autism as rated by parents or primary caretakers. The instrument is divided into four subtests consisting of: 1. Speech/Language/Communication (14 items); 2. Sociability (20 items); 3. Sensory/Cognitive Awareness (18 items); and 4. Health/Physical/Behavior (25 items). The Autism Research Institute developed an Internet scoring procedure that computes the four subscale scores and a total ATEC score. The severity of disorder is reflected by higher subscale and total scores.

The ATEC was normed on the first 1,358 ATEC forms submitted to the Autism Research Institute by mail, fax, or Internet. The Pearson split-half coefficients reflecting internal consistency were: Scale I: Speech .920; Scale II: Sociability .836; Scale III: Sensory/Cognitive Awareness .875; Scale IV: Health/Physical/Behavior .815; and ATEC Total: .942. The ATEC was shown to be a reliable measure with strong internal consistency indicating that items within each scale measure the same domain of behavior. Therefore, pre-treatment

ATEC scores can be reliably compared with post-treatment scores.

The Gilliam Asperger's Disorder Scale (GADS; Gilliam, 2001) is a behavioral rating scale. The GADS consists of 32 items divided into four subscales including: Social Interaction (10 items); Restricted Patterns of Behavior (8 items); Cognitive Patterns (7 items); and Pragmatic Skills (7 items).

The GADS was normed on a sample of 371 individuals (aged 3-22; males n = 314/ Females n = 57) diagnosed with Asperger's Disorder from across 46 states, the District of Columbia, Canada, Great Britain, Mexico, Australia, and other countries. Internal consistency reliability coefficients ranged from .87 to .95 for total Asperger's Disorder Quotient across samples of children with and without identified disabilities. The test- retest reliability for the Asperger's Disorder Quotient is .93 ($p < .01$). These results indicate that the GADS has a high level of stability for use as a pre-/post-treatment measure of individuals with Asperger's Disorder. Construct validity was indicated by analyses finding that: GADS scores are minimally related to age; items on the subscales are representative of behaviors associated with Asperger's Disorder; persons with other diagnoses score differentially; GADS scores are strongly related to each other and performance on other tests that screen for serious behavioral disorders; and the GADS can discriminate among individuals with Asperger's Disorder and those with behavioral disorders.

The Gilliam Autism Rating Scale (GARS; Gilliam, 1995) is a behavioral checklist. The GARS is comprised of four subtests (Stereotyped Behaviors; Communication; Social Interaction; and Developmental Disturbances) of 14 items each. The scale was normed on a sample of 1,092 children and young adults (aged 2-28) across 46 states, the District of Columbia, Puerto Rico, and Canada.

The internal consistency reliability coefficients for all subtests and total Autism Quotient range from .88 to .96. The stability or test-retest reliability ranges from .81 to .88 for all subtests and total Autism Quotient. These results indicate high levels of stability required for pre-/post-treatment assessment of individuals with Autism. The construct validity was confirmed by analyses finding that: items of the subscales are representative of the behaviors associated with Autism; GARS scores strongly related to each other and to performance on other screening tests for Autism; GARS scores are not related to age; and individuals with other diagnoses score differentially on the GARS.

The Behavior Rating Inventory of Executive Function (BRIEF; Gioia, Isquith, Guy, & Kenworthy, 2000) is a questionnaire completed by parents or teachers of children to assess executive behaviors. The parent and teacher forms of the BRIEF contain 86 items within 8 theoretically and empirically derived clinical scales that measure different aspects of executive functioning: Inhibit, Shift, Emotional Control, Initiate, Working Memory, Plan/Organize, Organization of Materials, and Monitor.

For parent and teacher forms of the BRIEF internal consistency was high ranging from .80 to .98. Test-retest reliability ranged from .80 to .92 across overall indices of Behavioral Regulation, Metacognition, and Global Executive Composite. These results indicate high stability needed for pre-/post-treatment assessment. The validity of the BRIEF is confirmed by factor analysis indicating a two-factor model.

The Personality Inventory for Children, Second Edition (PIC-2; Lachar & Gruber, 2001) is a multidimensional, objective questionnaire developed to evaluate domains of adjustment in children and adolescents. The PIC-2 was normed on a standardization group (N = 2,306) reflecting a cross-section of children in the United States. Data was representative of urban, suburban, and rural areas, across socioeconomic status (SES) (including poor, blue-collar, middle-class, and upper SES status), as well as the major ethnic groups (Asian, Black, Hispanic, Caucasian, Other).

The PIC-2 contains 275 items completed by parents or parent surrogates to identify domains of adjustment consisting of: Cognitive Impairment, Impulsivity & Distractibility, Delinquency, Family Dysfunction, Reality Distortion, Somatic Concern, Psychological Discomfort, Social Withdrawal, and Social Skill Deficits. A Behavioral Summary is made up of the first 96 items of the PIC-2 and contains composite scales (i.e., Externalization, Internalization, Social Adjustment, and Total Score).

The internal consistency ranges from .78 to .95 for the composite scales and the Total Score. Test-retest stability was .89 for all composite scores including the Total Score for nonclinical and clinically referred samples. These results indicate high reliability necessary for pre-/post-treatment assessment. Validity was confirmed by factor analytic studies of the PIC-2 Standard Form Adjustment Subscales which yielded a five factor solution (Externalizing Symptoms; Internalizing Symptoms; Cognitive Status; Social Adjustment; and Family Dysfunction) and a two factor solution for the Behavioral Summary Short Adjustment Scales (Externalizing and Internalizing).

Neuropsychological testing has been sufficiently validated as a reliable procedure for evaluating cognitive functions (Lezak, 1995) and was utilized for this purpose in our study. Neuropsychological measures constituting composite indices of attention, visual-perceptual, executive function, and language skills (Delis-Kaplan Executive Function System; NEPSY; Integrated Visual and Auditory Continuous Performance Tests; and others) were administered to assess pre-/post-treatment levels of attention, visual-perceptual, language, and executive function. All Neuropsychological measures used, including the Delis-Kaplan Executive Function System (D-KEFS; Delis, Kaplan, & Kramer, 2001), Developmental Neuropsychological Assessment (NEPSY; Korkman, Kirk, & Kemp, 1998), Comprehensive Test of Visual Functioning (CTVF; Larson, Buethe, & Vitali, 1990), Rey Complex Figure Test and Recognition Trial (RCFT; Meyers & Meyers, 1995), Expressive One-Word Picture Vocabulary Test (EOWPVT; Upper-Extension; Gardner, 1983), Expressive One-Word Picture Vocabulary Test-Revised (EOWPVT-R; Gardner, 1990), and The Integrated Visual and Auditory Continuous Performance Test (IVA; Sanford & Turner, 2002), have demonstrated adequate reliability and validity.

Quantitative EEG (QEEG) involved recording and digitizing EEG based on the International 10/20 System of electrode placement utilizing the Deymed Diagnostic (2004) TruScan 32 Acquisition EEG System. (Refer to Table 5 for specifications.)

TABLE 5. Specifications

	TruScan 32 EEG System*	**NeuroCybernetics EEGer Neurofeedback Training System****
Number of Channels	32	2 channels of EEG data at 256 Hz
Sampling Stored data	128, 256, 512, or 1024 Hz.	All sampling is done by external EEG amplifiers/ converters at 256 Hz.
Analog Sampling Frequency	4,096 Hz per channel.	
Encoders		Thought Technology Encoders
Maximal Input DC Offset:	± 250 mV	
Filtering	Equivalent input noise is 1 mVp-p.	Filter coefficients were precomputed and provided in 1/8 Hz steps from 0 to 50 Hz.
	0.1 Hz-100 Hz with impedance below 10 K ohm.	Lowpass filters input can be independently specified as 0-40, 0-50, 0-30 Hz to minimize 50 or 60 Hz interference.
	Common Mode Rejection Ratio:102 dB. In Bandwidth 0-60 Hz with all inputs shorted to ground.	
	Isolation Mode Rejection Ratio: 140 dB.	
Power Source:	Four AA Batteries	

Note. Specifications for equipment were obtained from: * Deymed Diagnostic (2004) and ** NeuroCybernetics Inc. (2006).

Data were acquired (during eyes closed/eyes open conditions) using a stretchable electrode cap embedded with 19 sensors with frontal reference, prefrontal ground, and linked ears; attached to the scalp by means of electrode paste. The duration of recording was a total of 20 minutes; 10 minutes in each condition. All data was manually artifacted in NeuroRep (Hudspeth, 1999) and analyzed with the same EEG analysis software including measures of multivariate coherence or connectivity. The neuroelectric eigen image (NEI) can be defined as a 3-D structure which results from the Principal Components Analysis (PCA) of the multichannel (i.e., 19) EEG waveforms. PCA results routinely show that EEG waveforms can be explained by 3 orthogonal waveform components that refer to the lateral, anterior-posterior, and dorsoventral position of recording electrodes. Although every effort is made to situate electrodes at equal distances on the scalp, it is abundantly clear that PCA results show that functional interelelectrode distances are not equal and therefore, must be estimated as vector dis-

tances: squareroot ($dx^2 + dy^2 + dz^2$). Therefore, it can be seen that a connectivity image (CIM) can be constructed as the average interelectrode distances that converge on each of the 19 electrodes, with 3 elements for each edge electrode and 4 elements for internal electrodes. Thus, normative average and standard deviation reference data were computed for the 19 electrode sites of the CIM indices based on 30 normal adults. Statistical comparisons are made with effect size estimates, r = z/squareroot(N), based on methods discussed in Rosenthal & DiMatteo (2001) (W.J. Hudspeth, personal communication, July 25, 2006). Further analyses included measures of absolute and relative power, as well as connectivity processed by the Neurometric Analysis System (NxLink, 2001; John, 1988) and Neuroguide (Thatcher et al., 2003) EEG software (both FDA approved) with age referenced normative databases. A permanent record was made prior to initiation and at the completion of the study for both the assessment-guided neurofeedback group and the control group. The reliability and validity of QEEG has been established (Thatcher et al., 2003).

NeuroCybernetics EEGer Training System (NeuroCybernetics Inc., 2006) was the software utilized to perform assessment-guided Neurofeedback. Hardware included Thought Technology encoders. Sensors (Grass Silver Disc 48" Electrodes with SafeLead protected terminals; Grass SafeLead, 2006) were applied to the patient's scalp to measure EEG activity. The signal is then fed back to the patient in visual and aural form based on relative amplitude/threshold values. The patient learns to inhibit frequencies which are excessively generated and augment frequencies which are targeted for training.

The aural reward rate is limited to 2 Hz so each individual sound is audible to the patient. The aural reward is a prerecorded sound file of a short 1/2 second beep when specified amplitude conditions are met. The visual feedback consists of simple graphics providing a continuous display of the ratio of amplitude to threshold for each stream of data. Visual feedback can be provided in the following game formats: 4mation, Boxlights, Highway, Island, Jumpbox, Mazes, EEG Chomper, Space Race, Cubes, and Starlight (NeuroCybernetics Inc., 2006). (Refer to Table 5 for specifications.)

A ThermoVision A20M camera from FLIR Systems (2006) was used for infrared imaging. As part of the imaging procedure, the camera (mounted on a tripod) was set up approximately two feet from the patient and the thermal image was projected onto a screen. (Please Refer to Table 6 for specifications.)

Infrared (IR) imaging of the prefrontal area was performed prior to and following each neurofeedback training session. IR imaging assesses the levels of thermoregulation. Thermal output is assigned thermal degrees. The levels of thermal activity are associated with underlying metabolic activity and regional Cerebral Blood Flow (rCBF). Research indicates that IR imaging is a valid and reliable measure of brain activity, metabolic processes, and rCBF (Carmen, 2004; Coben, Carmen, & Falcone, 2005a; Coben, 2005b; Coben, 2005c; Toomin et al., 2004).

Neurofeedback Protocols

Training protocols were based on the combined use of all assessment information with a heavy emphasis on initial QEEG which included analysis of absolute, relative power, and connectivity measures. Protocols included primarily sequential (bipolar) or interhemispheric montages individualized for each patient. The focus was on reducing hyperconnectivity

TABLE 6. Specifications for ThermoVision A20M

Field of View:	25 degrees X 19 degrees/ 0.3 m.
Detector Type:	Focal plane array (FPA) uncooled microbolometer.
Spectral Range:	7.5 to 13 microns
Thermal Sensitivity:	At 50/60 Hz : 0.12 degrees C at 30 degrees C.
Accuracy (% of reading):	± 2 degrees C or ± 2%.
Individual Emissivity Settings:	Individually settable.
Measurement Corrections:	Reflected ambient, distance, relative humidity, external optics. Automatic, based on user input.
Power Source:	AC operation: AC adapter 110/220 VAC. 50/60 Hz (included). DC operation: 12/24V nominal , <6W.

Note. Relevant specifications of the ThermoVision A20M

which was frequently observed in posterior-frontal to anterior-temporal regions. These protocols remained constant during the training period of 20 sessions and were conducted twice weekly. For each patient, the neurofeedback protocols were determined based on regions of maximal hyperconnectivity. For example, one patient had maximal hyperconnectivity in the right frontal region primarily in alpha. A protocol was designed for this patient to reward alpha (the frequency range of maximal hyperconnectivity) and inhibit low and higher frequency EEG activity at F8/F7.

Eighty-nine percent of the 37 patients had sequential (bipolar) versus unipolar montages. Ninety-four percent of the sequential (bipolar) montages included frontal or temporal electrode sites including F8-F7, Ft8-Ft7, T4-T3, or F7-F8. In one case, F6-F5 was applied and in the other F4-F3. Reward bands ranged anywhere from 5-16 Hz. A delta inhibit protocol as low as 1-2 Hz Ranging to as high as 6 Hz was utilized for 92% of the patients. In 100% of patients, a high beta inhibit protocol was applied ranging from 18-50 Hz with the greatest overlap at 18-30 Hz.A third inhibit ranging within a 7-14 Hz range was utilized for 68% of the patients.

RESULTS

Treatment efficacy was analyzed by calculating difference scores between pre- and post-treatment clinical variables. These differences scores were tested for significance with ANOVA measures comparing changes in the experimental versus control conditions. Significant findings suggest therapeutic changes in the experimental subjects and little to no change for wait list control participants. The alpha level for rejecting the null hypothesis was set at a stringent p equal to or less than 0.01 to guard against chance discoveries.

The experimental group was composed of 37 patients diagnosed with ASD; 84% were males, 16% female, 97% Caucasian, and 3% Asian-American.Seventy-three percent were right-handed, 13.5% left-handed, and 13.5% had mixed hand dominance. Fifty-nine percent of patients did not take medication; 22% were taking one medication, 14% two medications, and 5% three medications. Of the initial 38 patients that began the study, only one patient dropped out prior to completion of the study. Please refer to Table 2 for demographics.

No significant differences were noted between the experimental and control group for age ($F(1, 47) = .795$, $p = .377$), gender (Kolmogorov-Smirnov $Z = .014$, $p = 1.00$), race (Kolmogorov-Smirnov $Z = .081$, $p = 1.00$), handedness ($\chi^2(1, N = 49) = .044$, $p = .833$), number of medications ($F(1, 47) = .003$, $p = .954$), ATEC score ($F(1, 41) = .000$, $p = .991$), and other treatments ($F(1, 47) = .123$, $p = .752$). Eighty-three percent of controls were males and 17% were females. All controls were Caucasian. Seventy-five percent were right-handed; 17% left- handed; and 8% had mixed hand dominance. Sixty-seven percent did not take medication; 12% were taking one medication; 8% were taking two medications; and 8% were taking three medications. Please refer to Table 3 for demographics.

Over the course of the study, patients in the control group made no significant changes in parent rating of symptom severity ($t(11) = .276$, $p = .788$) and in neuropsychological (attention) ($t(11) = .343$, $p = .738$) measures. Parental Judgment of Treatment Outcome ($\chi^2(1, N = 12) = 5.333$, $p = .021$) for the control group showed a trend indicating a lack of success or improvement. There was also a trend for cerebral hyperconnectivity to increase in the control group [($M = -.012$, $SD = .018$), $t(11) = -2.179$, $p = .052$]. These trends were the opposite pattern of that observed in the experimental group.

Parental Judgment of Treatment Outcome

Following treatment, improvement (decrease) in ASD symptoms was reported by parents for 89% ($n = 33$) of the experimental group. This rate of improvement is significantly different than that found in the control group (Kolmogorov-Smirnov $Z = 2.167$, $p = .000$) in which 83% reported no change. All positive treatment outcomes reported by parents were confirmed by neuropsychological and neurophysiological assessment. There were no reports of symptoms worsening. The benefit to harm ratio was calculated at 89:1 exceeding all

currently available therapies or treatments for ASD.

Parent Ratings

Table 7 below shows the pre-/post-treatment results of parent ratings of ASD indicating that patients in our sample had initial ATEC Total Scores primarily in the mild to moderate ranges of severity. A trend toward positive skewedness and lower initial Total ATEC Scores associated with milder levels of ASD symptoms was noted (Shapiro-Wilk Coefficient p = .0330). The majority of initial ATEC Scores (88%) were mild to moderate (0-79th percentile), however there were six participants in the moderate to severe range (59th-89th percentile).

Following neurofeedback training, a significant reduction in ASD symptomatology was reported on the ATEC (F (1, 40) = 18.360, p = .000) representing a 40% reduction in ASD symptoms. This finding was confirmed by significant reductions in ASD behaviors, executive deficits, and symptomatology associated with ASD following treatment as reported on the: GADS (F (1, 37) = 13.914, p = .001) BRIEF(F (1,40) = 9.852, p = .003), and the PIC-2 (F (1,42) = 8.488, p = .006) as shown in Table 7.

NEUROPSYCHOLOGICAL TESTING

As indicated by Table 8 below, there were highly significant improvements for the experimental group on composite measures of attention (F (1, 30) = 20.701, p = .000), visual perceptual functioning (F (1, 27) = 16.382, p = .000), and executive function (F (1, 36) = 13.048, p = .001). Although the sample size for participants completing the language assessment was small, improvement in language skills reached statistical significance as well (F (1, 14) = 28.891, p = .000).

Infrared (IR) Imaging: First Session

As shown in Table 9 below, the experimental group showed a trend towards enhancement in the minimum or lowest thermal reading (F (1, 44) = 3.192, p = .081) and a significant decrease in the range of thermal degrees (F (1,44) = 8.488, p = .006) as a result of their first session. These findings indicate that even in the first session, patients in the experimental group were able to elevate their metabolic activity and regulate the range or variability of output.

IR Imaging: Last/20th Session

By the 20th session, there was a trend towards a decrease in the range of thermal degrees (F (1, 43) = 6.500, p = .014) indicating a continuation of self- regulation of metabolic activity or thermal regulation. Please refer to Table 10.

Evidence of Enduring Change: Comparison of First and 20th/ Last Session

As indicated by Table 11 below, throughout the course of treatment, the experimental group showed a trend towards an increase in the minimum thermal reading (F (1, 44) =4.335, p = .043) and reduction in the range of thermal de-

TABLE 7. Percent Ratings for Neurofeedback Group

Initial Total ATEC	**%ile**	**Severity**
Range= 28.000-56.500	**9th -39th%ile**	**Mild-Moderate**
Pre-ATEC Total	**Post-ATEC Tot al**	**Significance (p)**
Mean=46.100	**Mean=27.733**	**p < .000**
Pre-GADS ADQ	**Post-GADS ADQ**	**Significance (p)**
Mean=83.852	**Mean=72.519**	**p < .001**
Pre-BRIEF GEC	**Post-BRIEF GEC**	**Significanc (p)**
Mean=71.700	**Mean=64.767**	**p < .003**
Pre-PIC-2 TOTC	**Post-PIC-2 TOTC**	**Significance (p)**
Mean=71.250	**Mean=64.250**	**p < .006**

*Note. ATEC=Autism Treatment Evaluation Checklist; GADS ADQ=Gilliam Asperger's Disorder Scale Asperger's Disorder Quotient; BRIEF GEC=Behavior Rating Inventory of Executive Function Global Executive Composite; PIC-2 TOTC =Personality Inventory for Children Second Edition Total Composite

TABLE 8. Neuropsychological Testing* for Neurofeedback Group

Pre-Attention	**Post-Attention**	**Significance (p)**
Mean z= -1.859	**Mean z=-0.571**	**p < .000**
Pre-Visual Perceptual	**Post-Visual Perceptual**	**Significance (p)**
Mean z= - 2.483	**Mean z= -1.584**	**p < .000**
Pre-Executive	**Post-Executive**	**Significance (p)**
Mean z= -1.818	**Mean z= -0.783**	**p < .001**
Pre-Language	**Post-Language**	**Significance (p)**
Mean z= -1.928	**Mean z= -0.798**	**p=.000**

*Note. All neuropsychological testing consisted of composite scores for indices of attention, visual perceptual, executive, and language domains.

TABLE 9. Pre-/Post-IR Imaging in the First Session for the Neurofeedback Group

1st Pre-Min Mean	1st Post-Min Mean	Significance (p)
93.523	93.903	.081
1st Pre-Range Mean	1st Post-Range Mean	Significance (p)
4.032	3.291	.006

* Note. Min=Lowest thermal reading; Max=Highest thermal reading.

TABLE 10. Pre-/Post-IR Imaging of Last/20th Session for the Neurofeedback Group

20th Pre-Range Mean = 3.573	20thPost-Range Mean= 3.161	Significance (p) .014

* Note. Min=Lowest thermal reading; Max=Highest thermal reading.

TABLE 11. Pre-/Post-IR Imaging: Comparison of 1st and 20th Session

1st Pre-Min Mean	20th Pre-Min Mean	Significance (p)
93.523	94.368	.043
1st Pre-Range Mean	20th Pre-Range Mean	Significance (p)
4.032	3.574	.050

* Note. Min=Lowest thermal reading; Max=Highest thermal reading.

grees (F (1, 44) = 4.049, p = .050). The experimental group enhanced metabolic activity (i.e., thermal regulation), regulated this output, and maintained these changes by the 20th session of neurofeedback. Change in thermal regulation occurred both within sessions and across sessions suggesting that change in metabolic regulation was enduring.

QEEG Connectivity

A total of 76% of the experimental group had a decrease in cerebral hyperconnectivity.Reduced hyperconnectivity patterns were statistically significant for the Total CIM score averaged across all 19 electrode sites (F (1,35) = 10.790, p = .002) and a trend was noted across the Beta frequency band (F (1, 35) = 5.316, p = .027). In this population, reduction in cerebral hyperconnectivity was associated with positive clinical outcomes.

Predictors of Response to Therapy

As shown in Table 12 below, Kurtosis and Skewedness for the percentage of change in ATEC Total Scores were not significant indicating an even spread of scores approximating a normal distribution. Additional regression analyses ruled out confounding variables extraneous to the effect of treatment (severity of ASD as measured by Pre-ATEC Total [F (1, 28) = .23, p = .6338]; age [F (1, 28) = 1.83, p = .1868]; and number of medications [F (1, 28) = .46, p = .5014].

DISCUSSION

The major findings of our study included an 89% success rate with a 40% reduction in core ASD symptoms, as a result of assessment-guided neurofeedback training over 20 sessions. Significant improvement was noted for the experimental group on measures of attention, executive, visual perceptual and language functions. IR imaging confirmed elevated metabolic activity even within the initial treatment session. Enduring change was indicated by enhanced metabolic activity, regulation of output, and maintenance of changes within and across the 20th treatment session. The benefit to harm ratio of 89:1, exceeded all current treatments for ASD as surveyed by Rimland (2005). Seventy-six percent of the experimental group had a decrease in hyperconnectivity patterns. Reduced hyperconnectivity as well as enduring change in metabolic activity confirmed neurophysiological change following neurofeedback. The experimental and control groups

TABLE 12. Predictors of Response to Therapy

ATEC Total Mean= 38.770 Median= 38.750 Range= 20.000-52.543	Kurtosis p=.4419	Skewedness p=.4295
Pre-ATEC Total	R^2 .01*	Significance (p) .6338
Age	.06*	.1868
Number of Medications	.02*	.5014

Note.. ATEC=Autism Treatment Evaluation Checklist. *R^2 = percentage of total variance in percentage of change in ATEC Total Score

were matched for age, gender, race, handedness, other treatments, and severity of ASD. The variables extraneous to the treatment effect were controlled and did not interact with the effect of assessment-guided neurofeedback. In addition, regression analyses ruled out the effect of intervening variables (severity of ASD, age, and number of medications) interacting with the treatment effect. Therefore, it was likely that assessment-guided neurofeedback was the causative factor in improving ASD symptomatology as confirmed by neurobehavioral, neuropsychological, and neurophysiological findings.

The purpose of our research was to replicate the previous controlled neurofeedback study conducted by Jarusiewicz (2002). This is the second controlled study to demonstrate improvement in the core symptoms of ASD following neurofeedback. Our study provides support for positive treatment outcomes of neurofeedback for ASD based on multiple measures, including the demonstration of neurophysiological changes.

The five levels of treatment efficacy which provide guidance for applied psychophysiologic research have been outlined (Monastra, 2005) as follows:

Level 1: "Not empirically supported" rating assigned to treatments supported by evidence from only case studies in non-peer-reviewed journals and anecdotal reports.

Level 2: "Possibly efficacious" rating given to treatments investigated in at least one study with sufficient statistical power and well-identified outcome measures but lacking randomized control groups.

Level 3: "Probably efficacious" rating assigned to treatments which demonstrate beneficial effects in multiple observational studies, clinical studies, wait list control studies, and within-subject and between-subject replication studies.

Level 4: "Efficacious" rating given to treatment studies containing a no-treatment control, alternative treatment, or placebo control group using randomized assignment proven statistically superior to the control or equivalent treatment with well-defined procedures facilitating replication. Positive treatment outcomes are confirmed by at least two independent studies.

Level 5: "Efficacious and specific" rating assigned to treatments that demonstrate statistically superior results compared to a placebo, medication, or other treatment in at least two independent studies.

Our research– the second controlled study to report a positive treatment outcome of neurofeedback for ASD–supports neurofeedback as possibly efficacious; the second level of efficacy rating as defined by the Association for Applied Psychophysiology & Biofeedback (AAPB, 2006). This rating describes research containing sufficient statistical power, well identified outcome measures, however lacking a randomized control group.

Our study may be the first step in establishing a Level 3 criteria rating of neurofeedback as probably efficacious in the treatment of ASD. We replicated another controlled study (Jarusiewicz, 2002). A broader range of outcome measures confirmed the reduction of ASD symptomatology following neurofeedback. Further research is necessary utilizing randomized control groups to establish neurofeedback as an efficacious treatment for ASD.

Our research, in contrast to Jarusiewicz' (2002) study, demonstrated greater improvement in clinical outcomes following assessment-guided Neurofeedbackreflected by a 40% compared to 26% reduction of ASD symptoms in fewer sessions (20 versus an average of 36). This finding indicates a 54% increase in treatment efficacy and a 44% decrease in the number of sessions required for positive treatment outcome.

In contrast to the prior research conducted by Jarusiewicz (2002), the enhanced treatment outcome of assessment-guided neurofeedback may be explained by the following factors: (1) a milder degree of ASD in the experimental group; (2) utilizing multiple data points to target specific brain regions for individualized neurofeedback protocols; (3) sequential (bipolar) protocols in contrast to mostly unipolar protocols employed by Jarusiewicz (2002). It is likely that the first factor–severity of ASD symptoms–can be excluded; as previously discussed, regression analyses as well as the use of a control group ruled out any interaction of this variable with the treatment effect. In addition, the reduction of ASD symptomatology was

also evident for patients (in the experimental group) with the most severe ASD ratings.

The second factor, pertaining to the use of assessment-guided neurofeedback (primarily QEEG), may be a crucial factor in explaining the improved treatment outcomes. Neurofeedback training protocols were based on the combined use of all assessment information with a strong emphasis on initial QEEG analysis of absolute, relative power, and connectivity measures. In contrast, Jarusiewicz (2002) utilized neurofeedback protocols based on symptom complaints of patients. In our study, improved treatment outcomes resulted from assessment providing multiple data points guiding the development of individualized neurofeedback protocols targeting specific brain regions to increase activation and reduce hyperconnectivity.

The use of a sequential (bipolar) montage is another possible factor contributing to improved treatment outcomes in our study. Sequential montages consisting of one active sensor site and one reference site located over brain regions can reinforce interhemispheric communication while reducing hyperconnectivity within and across brain regions. In contrast, Jarusiewicz (2002) frequently utilized monopolar montages consisting of an active sensor site over a brain region and a reference sensor on the ear which targets neurofeedback training to only one brain region. Further research is needed to investigate the impact of sequential compared to unipolar montages on treatment outcomes for neurofeedback in generalas well as protocols specific to individuals with ASD.

Our research found that decreased hyperconnectivity resulted in improved treatment outcomes in an Autistic population. Individualized neurofeedback treatment protocols may address patterns of hyperconnectivity as well as the heterogeneity characterizing ASD. Other researchers investigated the impact of cortical hyperconnectivity on brain anatomy and function. Belmonte et al.'s (2004) model of Autism is characterized by increased local connectivity within the neural assemblies of a specific brain region while there is decreased long-range connectivity with other brain regions. Courchesne and Pierce (2005) described a pattern of over-connectivity (hyperconnectivity) within the frontal lobe and long-distance disconnection (hypoconnectivity) between the frontal lobe and other brain regions associated with ASD. Reduction of long-distance cortical to cortical reciprocal activity and coupling disrupts the integration of information from emotional, language, sensory, and autonomic systems (Courchesne & Pierce, 2005).

Researchers also investigated the impact of mirror neurons on ASD symptomatology. High functioning individuals with ASD failed to suppress Mu wave activity in the mirror neuron system (MNS) as hand movement was observed, while, controls were able to suppress Mu wave activity (Oberman et al., 2005). Lack of MNS activity in area F5 (pars opercularis) was also reported in children with Autism during imitation of emotional expression. Lack of MNS activation during imitation and observation of emotional expression was associated with dysfunction in social domains in both studies (Oberman et al., 2005; Dapretto et al., 2006).

Dysfunctional integration of the frontal lobes with other brain regions is frequently linked to deficits in the executive system. The long-term consequences of deviation from patterns of normal frontal lobe development are atypical patterns of brain connectivity (Hill, 2004). In SPECT scans of children with Autism, abnormal regional cerebral blood flow in the medial prefrontal cortex and anterior cingulate gyrus was related to impaired communication and social interaction. Altered perfusion in the right medial temporal lobe was associated with the obsessive desire for sameness (Ohnishi et al., 2000). Functional neuroimaging studies have linked social cognition dysfunction and language deficits in Autism to neural substrates (Just et al. 2004; McAlonan et al., 2005: Pelphrey, Adolphs, & Morris, 2004; Welchew et al., 2005). In a study utilizing diffusion tensor imaging, disruption of white matter tracts was associated with social cognition found in the following regions: the fusiform gyrus and the superior temporal sulcus linked to face and gaze processing and the anterior cingulate, amygdala, as well as the ventromedial prefrontal cortex associated with awareness of mental states and emotional processing. These impairments may disrupt neural connectivity required for children with Autism

to develop appropriate social skills (Barnea-Goraly et al., 2004).

The aforementioned research confirms that patterns of cortical connectivity have a substantial impact on the social, emotional, and cognitive function of individuals with ASD. Assessment-guided neurofeedback (primarily QEEG) targets brain regions to alter neural connectivity patterns. We have shown that regions of hyperconnectivity can be reduced and that this leads to therapeutic outcomes. Further research should be pursued to investigate the possibility of enhancing connectivity in other, more disconnected, brain regions.Coherence is analogous to the squared correlation coefficient between a pair of EEG waveforms, represented by the temporal voltage oscillations in each waveform. The signals are normalized over the entire record to minimize the influence of signal amplitudes and, thereby, emphasize the relationship between the pair of EEG profiles (Bendat & Piersol, 1980). The exact equation for such a calculation can be found in Bendat and Piersol (1980) Equation 3.43.

Coherence anomalies have been associated with drug resistant epilepsy and mild closed head injury. QEEG-guided coherence training is a form of neurofeedback that has been successfully employed to normalize abnormal QEEG coherence in patients with mild closed head injury and to reduce seizures in refractory epilepsy (Walker, Norman, & Weber, 2002; Walker, 2003).

Treatment goals are based on coherence anomalies identified by QEEG analysis. Increased focal power in a frequency band or increased coherence between brain regions may be downtrained while deficient focal power or decreased coherence between brain regions may be uptrained (Walker, Norman, & Weber, 2002; Walker, 2003: Walker & Kozlowski, 2005). The promising results demonstrated with QEEG-guided coherence training warrant further research with other populations characterized by coherence anomalies such as those with ASD.

In regard to the limitations of our study, the subjects consisted of a selected pool of patients in the experimental group and a wait-list control group. When treatment is selected by patients (via parents), there is the potential for selection bias to interact with the treatment effect. Therefore, randomized assignment of treatment and control groups is needed to confirm that there was no interaction between the treatment effect and subject selection. In addition, comparison with an alternative treatment group would further establish the efficacy of neurofeedback. Long-term follow-up would be beneficial to demonstrate that positive treatment outcomes are maintained over time and we plan to include follow-up findings in future research.

In light of the findings of this study and others regarding the links between cortical connectivity patterns, reduced cerebral blood flow, and executive, behavioral, as well as emotional/social functioning, it would be beneficial for future research to further investigate interhemispheric connectivity (left vs. right hemisphere) comparisons as well as intrahemispheric connectivity between the frontal, temporal, central, parietal, and occipital lobes in Autism and other conditions. Further analysis of the QEEG data will provide information regarding neurophysiological changes that occur as a result of neurofeedback, and we intend to include these findings in future research. In addition, the specificity of neurofeedback treatment protocols for ASD may be enhanced by identifying the effect of: unipolar and sequential montages, levels of absolute and relative power for delta, theta, alpha, and beta activity associated with specific brain regions, as well as exploring whether neurofeedback can alter activity in the mirror neuron system. It would also be advantageous to further explore the impact of assessment-guided neurofeedback on domains of executive, emotional, and behavioral function for groups of individuals with varying functional levels of ASD (i.e., Severe vs. Moderate or Mild) in studies utilizing randomized control groups.Ultimately, clear demonstration of the impact of neurofeedback on the symptoms of autistic disorders requires a randomized controlled trial that is placebo controlled.

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