Chapter 6
Neurofeedback for Autistic Disorders: Emerging Empirical Evidence

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6.1 Introduction

Autistic spectrum disorders are a heterogeneous group of pervasive developmental disorders including autistic disorder, Rett disorder, childhood disintegrative disorder, pervasive developmental disorder-not otherwise specified (PDD-NOS), and Asperger's disorder. Children with ASD demonstrate impairment in social interaction, verbal and nonverbal communication, and behaviors or interests (American Psychiatric Association 2000). ASD may be comorbid with sensory integration difficulties, mental retardation, or seizure disorders. Children with ASD may have severe sensitivity to sounds, textures, tastes, and smells. Cognitive deficits are often associated with impaired communication skills (National Institute of Mental Health; NIMH, 2006). Repetitive stereotyped behaviors, perseveration, and obsessionality, common in ASD, are associated with executive deficits. Executive dysfunction in inhibitory control and set shifting have been attributed to ASD (Schmitz et al. 2006). Seizure disorders may occur in one out of four children with ASD, frequently beginning in early childhood or adolescence (National Institute of Mental Health; NIMH, 2006).

Autistic disorder includes the following triad of symptoms: (1) impaired social interaction, failure to develop peer relationships, or lack of initiating spontaneous activities; (2) deficits in communication including delay in or lack of spoken language, inability to initiate or sustain conversation with others, stereotyped repetitive use of language, or idiosyncratic language; and (3) restricted repetitive and stereotyped behavior, interests, inflexible adherence to routines or rituals, and repetitive motor patterns (e.g., hand or finger flapping or twisting) (American Psychiatric Association 2000).

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Individuals with Asperger's disorder frequently have high levels of cognitive functioning, engage in literal pedantic speech, experience difficulty comprehending implied meaning, exhibit problems with fluid movement, and manifest inappropriate social interactions. 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, persons with childhood disintegrative disorder and Rett disorder both have normal periods of early development followed by loss of previously acquired skills. Common features among all these conditions include communication and social skill deficits. There is considerable variability in terms of onset and severity of symptomatology within the autistic spectrum of disorders (Siegel 1996; Attwood 1998; Hamilton 2000; Sicile-Kira 2004; McCandless 2005).

Research reviewing the epidemiology of autism (Centers for Disease Control and Prevention 2009) reported between 1 in 80 and 1 in 240 children in the United States diagnosed with the disorder. A report of just 3 years ago (Centers for Disease Control and Prevention 2009) suggested a prevalence of 1 in 110 and as high as 1 in 70 boys. In their most recent report, the CDC (2012) suggests that the rate has risen to 1 in 88. ASDs are five times more likely in boys for which it is seen in 1 out of 54 male children. According to Blaxill (2004), the rates of ASD were reported to be <3 per 10,000 children in the 1970s and rose to >30 per 10,000 in the 1990s. This rise in the rate of ASD constituted a tenfold increase over a 20-year interval in the United States. With increased prevalence comes a need to design and empirically validate effective treatments for those impacted by autistic disorders.

Research studies utilizing electroencephalogram (EEG) and single photon emission computed tomography (SPECT) have provided evidence for a neuropathological basis of ASD. A review of numerous EEG studies reported the rate of abnormal EEGs in autism ranged from 10 % to 83 %, while the mean incidence was 50 %. Atypical EEGs often predict poor outcomes for intelligence, speech, and educational achievement (Hughes and John 1999). In a more recent review of research, Rippon et al. (2007) proposed a model of reduced connectivity between specialized local neural networks and overconnectivity within isolated neural assemblies in autism. Disordered connectivity may be associated with an increased ratio of excitation/inhibition in key neural systems. Anomalies in connectivity may be linked to abnormalities in information integration. 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, while altered perfusion in the right medial temporal lobe was associated with the obsessive desire for sameness (Ohnishi et al. 2000). Children with autism commonly display executive functioning deficits in planning, cognitive flexibility, and inhibition. These executive deficits are associated with dysfunctional integration of the frontal lobes with other brain regions and thus also impact upon social, behavioral, and cognitive function (Hill 2004).

Functional neuroimaging studies have also linked social cognition dysfunction and language deficits in autism to neural substrates (Pelphrey et al. 2004; Welchew et al. 2005). During a sentence comprehension test, individuals with autism showed less functional connectivity between Broca's and Wernicke's areas relative to a

control group, suggesting a lower degree of information organization and neural synchronization during language tasks (Just et al. 2004). A review of neuroimaging studies has found key brain structures including the amygdala, superior temporal sulcus region, and fusiform gyrus to function differently in individuals with autism than in controls (McAlonan et al. 2005).

Parents of children with ASD select many different methods of treatment, with an average of seven different therapies being utilized (Green, Pituch, Itchon, Choi, O'Reilly, and Sigafoos, 2006). Speech therapy (70 % of parents) was the most commonly selected treatment, followed by psychopharmacological treatment (52 % of parents). Other treatments included visual schedules (43 %), sensory integration (38 %), and applied behavior analysis (36 %). Special diets were implemented by 27 % of parents and 43 % utilized vitamin supplements. While there may be some benefit to these treatments, many do not lead to long-lasting changes and/or have risks associated with their implementation. The potential benefits and risks of the major treatments for ASD are summarized below.

6.2 Treatments Often Used for ASDs

Other than neurofeedback, the most common treatments used for these children include applied behavior analysis (ABA), pharmacotherapy, special diets, vitamin supplements and enzymes, chelation, and hyperbaric oxygen therapy. Applied behavior analysis (ABA), a form of behavior modification, is the method of treatment with the most empirical support for treating ASD. The goal of this therapy is to improve social interaction, behavior, and communication (Bassett et al. 2000). ABA is firmly based on the principles of operant conditioning and measures small units of behavior to build more complex and adaptive behaviors through reinforcement. Typically, imitation, attention, motivation, and compliance are targeted early (Couper 2004). Efficacy has been demonstrated across multiple studies with variations on the technique (Schopler and Reichler 1971; Lovaas et al. 1973; Ozonoff and Cathcart 1998; Herbert et al. 2002; Ben-Itzchak and Zachor 2007) with follow-up studies showing ongoing improvements as a result (McEachin et al. 1993). Unfortunately, not all ABA studies have had such positive outcomes (Anderson, Avery, DiPietro, Edwards, and Christian, 1987).

In their clinical practice guidelines report, the New York State Department of Health Early Intervention Program recommended that ABA and other behavioral interventions be included in the treatment of autism. They specify that intensive behavioral programs should include a minimum of 20 h of intervention with a therapist per week. Furthermore, the guidelines state that parents should be included in the intervention and that they be trained in the use of behavioral techniques to provide additional instruction at home with regular therapist consultation. Although promising, intensive behavioral programs are costly and require extensive time on the part of the therapist as well as the family, and debates are ongoing about who should pay for such services (Couper 2004).

Although behavior therapy improves social, cognitive, and language skills, a year or more of intensive training has been used in most research studies that have demonstrated improvement. Furthermore, a strong commitment by parents to complete therapeutic programs is necessary to achieve positive outcomes. While behavioral treatment methods show the most empirical support to date, there remains a need for additional therapies, which may be more easily administered and used in conjunction with the behavioral methods described. It is important to note that though research has been promising, there has been great variability between studies in their results and outcome measures have often been questionable (e.g., IQ scores, returning to regular classrooms). And this approach appears to be more effective with those who are higher functioning (i.e., higher IQ), meaning that lower functioning individuals are often left out, even though they are perhaps in greatest need of treatment.

Pharmacological interventions have also been utilized to treat individuals with ASD. A study conducted at the Yale Child Study Center found that 55 % of a group of 109 individuals with a PDD were taking psychotropic medication, with 29.3 % taking more than one medication (Martin, Scahill, Klin, and Volkmar 1999). The most common medications were antidepressants (32.1 %), followed by stimulants (20.2 %) and neuroleptics (16.5 %). The objectives of psychopharmacological treatment for autism include decreasing the core symptoms of autism, decreasing anxiety and overfocus, improving social skills, reducing aggressive self-injurious behavior, increasing the effects of other interventions, and improving the quality of life for the child and their family. There is no single medication known to be beneficial to all children with ASD nor that has specifically been developed for individuals with autistic spectrum disorder.

Psychostimulant medications are often used with children who are autistic due to its success in the treatment of ADHD (Jensen et al. 2007). Despite this, stimulant use in children who are autistic remains controversial and largely unproven in terms of efficacy (Research Units on Pediatric Psychopharmacology Autism Network 2005). A newer class of neuroleptic, referred to as atypical antipsychotics, reportedly improves social interaction and decreases aggression, irritability, agitation, and hyperactivity (Barnard et al. 2002). They have fewer extrapyramidal adverse side effects than haloperidol and thioridazine. However, most children experience a substantial weight gain within the first months of treatment (Committee on Children with Disabilities 2001). Risperidone and Abilify are the only drugs approved by the FDA to treat the symptoms (irritability) of autism. A recent meta-analysis of three randomized controlled trials found that the drug was effective in treating the symptoms of irritability and aggression (Jesner et al. 2007). The authors concluded that although risperidone may be beneficial, its use must be weighed against its adverse effects, most notably weight gain, and that long-term follow up is needed prior to determining its efficacy in clinical practice. The long-term effects of risperidone are estimated at 1 year (Zuddas et al. 2000) with a relapse rate of 12.5–25 % (Research Units on Pediatric Psychopharmacology Autism Network 2005; Troost et al. 2005). Santangelo and Tsatsanis (2005) reported that there are currently no drugs that produce major improvement in the core social or pragmatic language deficits in autism, although several have limited effects on the behavioral features of the disorder.

The use of SSRI agents for the treatment of repetitive, stereotypical, and perseverative behaviors has also been explored (McDougle et al. 1995; Geller et al. 2001). Findings from such studies have been mixed at best (Cook et al. 1992; Hollander et al. 2005). While some studies report "success," responders often include from 49 to 69 % of the samples (McDougle et al. 1996, 1998; DeLong et al. 2002; Owley et al. 2005). In other studies, the positive response rate is significantly lower than this (McDougle et al. 2000; Couturier and Nicolson 2002; Martin et al. 2003). Based on the research cited, it appears that the limited benefits of psychopharmacology come at the cost of side effects and rebound of aggressive behavior when medication is discontinued. Furthermore, these drugs appear to be only treating certain symptoms and typically not the core symptoms of ASD. Many children require multiple medications to improve their symptoms, and often the benefits do not outweigh the side effects. In addition to patients responding to highly variable doses, the majority of studies reviewed indicate that not all children with ASD respond to these various medications, and there is no good explanation for why some are considered responders and some are not. In summary, the research published thus far suggests that some medications may be helpful in managing some of the behavioral disturbances seen in autism.

Research has suggested that individuals with autism may not properly metabolize the proteins in casein (dairy) and gluten (wheat and related grains) resulting in an opioid effect on the brain as they enter the bloodstream (Reichelt, 2001). Use of a gluten–casein-free diet has been shown to lead to positive outcomes in some children with autism (Knivsberg et al. 2002; Cade et al., 1999; Reichelt and Knivsberg, 2003). However, more recently, Elder et al. (2006) conducted a rigorous double-blinded controlled trial of the GFCF diet in autism. Fifteen (12 boys, 3 girls) children with ASD between the ages of 2 and 16 were studied over the course of 12 weeks. The researchers reported no significant differences between groups on their primary measure, the Childhood Autism Rating Scale, while parents reported improvement in their children. The researchers noted that the children were quite heterogeneous (which may have masked any group differences) and noted the relatively small sample size. One of the major problems with the GFCF diet is that it may lead to reduced bone cortical thickness (Hediger et al. 2008). Indeed, in this study, boys between the ages of four and eight who were autistic showed an 18.9 % deviation in metacarpal bone cortical thickness, which was nearly twice that of boys on minimally restricted or nonrestricted diets. Furthermore, the GFCF diet may induce nutritional imbalances by limiting the foods that may be eaten. It has also been shown to increase the risk of becoming overweight/obese (Mariani et al. 1998).

Vitamin supplements and enzymes have been proposed as another treatment for autistic-related symptoms. One supplement that has generated a great deal of interest as a treatment for autism is the gastrointestinal hormone secretin. After receiving much heated attention in the media, a comprehensive review of research studies utilizing secretin to treat autism was conducted by Esch and Carr (2004). Seventeen quantitative studies were reviewed, encompassing approximately 600 children, ages 2–15, and 12 adults with ASD. Only one of the studies reviewed found a causal relationship between secretin administration and amelioration of autistic symptoms across various treatment variables (type of secretin, dosage potency, frequency), observation

times, and participant characteristics (e.g., GI status, severity of ASD, age, history of medication use). Twelve of the thirteen placebo-controlled studies reviewed obtained negative results. Despite the lack of empirical support for secretin, parents of autistic children continue to seek out secretin treatment from their physicians (Esch and Carr 2004). The reviewers attempted to explain this by the media attention that secretin received early on, coupled with the fact that parents of these children are often desperate to find a treatment for this debilitating condition. In addition to secretin, it has been suggested that the consumption of omega-3 fatty acids may have a positive effect on the symptoms of autism (Amminger et al. 2007). These highly unsaturated fatty acids are essential for normal brain development and functioning (Wainwright 2002), and some studies have found fatty acid deficiencies in children who are autistic (Bell et al. 2000; Vancassel et al. 2001; Bell et al. 2004). Amminger and colleagues (2007) recently completed a double-blind, randomized controlled trial of omega-3 fatty acid supplementation in children who were autistic. They found that with administration of 1.5 g/day, the treatment group showed no significant change in hyperactive behaviors including disobedience, distractibility, and impulsivity, relative to the control group. Potential limitations to this study include that it was conducted with only 12 subjects, and preselection of these subjects was based on high irritability scores based on the Aberrant Behavior Checklist (Aman et al. 1985).

Anecdotal reports that methyl-B_{12} (methylcobalamin) injections may improve the symptoms of autism have been plentiful; however, there have been very few controlled research studies to support the efficacy of this treatment. The only published study found by the authors was an open trial of methyl-B_{12} conducted in Japan with 13 children with autism, ranging from 2 to 18 years of age (Nakano et al. 2005). Dosages of 25–30 g/kg/day were administered for between 6 months and 25 months. The authors found a significant increase in the intelligence and developmental quotients, as well as improvement on the Childhood Autism Rating Scale (Schopler, Reichler, DeVellis, and Daly, 1980). Even after the children were divided into subgroups based on age and intelligence, these effects did not diminish. This was not a controlled study, however. In contrast, a preliminary report of a double-blind crossover study presented at the American Academy of Child and Adolescent Psychiatry conference revealed no significant benefits in the 14 patients in their study after 3 months (Deprey et al. 2006). Specifically, there were no differences between the methyl-B_{12} injections and the placebo on the Clinical Global Impression Scale Improvement, Peabody Picture Vocabulary Test, or Social Communication Questionnaire verbal results.

A controversial theory to explain the increase in incidence of ASDs over the past 30 years is that it is related to environmental factors such as exposure to heavy metals (Bradstreet et al. 2003), mercury (Hg) in particular. The medical literature indicates that autism and Hg poisoning have numerous similarities in their symptom profiles, including psychiatric disturbances, speech, language, and hearing difficulties, sensory impairment, and cognitive difficulties (Bernard et al. 2000). In autism, heavy metal toxicity seems to occur from a decreased ability to excrete heavy metals (Adams et al. 2009). Because of this, some health-care providers are performing chelation therapy, which utilizes dimercaptosuccinic acid (DMSA) to clear the body of mercury and other toxic metals.

Results of a study by Holmes (2001) suggest that chelation therapy may be effective only for young children with autism (under age six), with minimal benefit for older children and adolescents (Kirby 2005). Recently, Adams et al. (2009) reported the results of a 2-phase study intended to determine the efficacy of DMSA/glutathione in treating children with autism. Overall, there were rated improvements in 3 of every 4 children with 11 % showing a worsening of symptoms. Chelation therapy is considered by some to be a risky treatment, and there have even been reports of death following chelation therapy in autism (Sinha et al. 2006).

Direct treatment of brain anomalies in autism has also been pursued with the use of hyperbaric oxygen therapy (HBOT). Among other brain abnormalities that have been identified, numerous studies using PET and SPECT have shown cerebral hypoperfusion in autism (George et al. 1992; Mountz et al. 1995; Ohnishi et al. 2000; Starkstein et al. 2000; Zilbovicius et al. 2000), leading to the hypothesis that HBOT may be beneficial in the treatment of autism (Rossignol and Rossignol 2006). HBOT involves the inhalation of 100 % oxygen in a pressurized chamber, usually above one atmosphere absolute (ATA). It has been shown that HBOT can lead to improved functioning in various neurological populations that show cerebral hypoperfusion including stroke (Nighoghossian et al. 1995), cerebral palsy (Montgomery et al. 1999), chronically brain injured (Golden et al. 2002), and even a teenage male with fetal alcohol syndrome (Stoller 2005). It has been suggested that the increased oxygen delivered by HBOT could counteract the hypoxia caused by hypoperfusion and lead to a reduction in symptoms of autism. Preliminary support for this treatment was reported by Rossignol and Rossignol (2006). While a study by Rossignol et al. (2007) showed empirical support for the possible benefits of HBOT for autistic children, another study (where parents were blinded to the treatment) by Granpeesheh et al. (2010) showed no significant benefits.

In summary, this review of the autism treatment literature reveals there are no treatments, except possibly behavior therapy, that have been well validated or that have exhibited favorable long-term results. In addition, many forms of intervention include the possibility of adverse effects, require long-term use, or were not developed specifically for autistic spectrum disorders. Neurofeedback represents an alternative that may have the potential to decrease symptomatology on a long-term basis with little risk of harm.

6.3 Neurofeedback for ASD

Neurofeedback is designed to use sophisticated computer technology to train individuals to improve poorly regulated brain-wave patterns. In EEG biofeedback, information regarding brain-wave activity is fed to a computer that converts this information into game-like displays that can be auditory, visual, or both. During a typical session, EEG electrodes (which measure brain waves) are placed on the scalp and earlobe(s). Individuals instantly receive feedback about the amplitude and/or synchronization of their brain waves and learn to improve their brain-wave

Table 6.1 EEG frequency bands [adapted from Demos (2005) and Thompson and Thompson (2003a, b)]

Name	Frequency	Normal occurrence	Significance
Delta	0.5–3.5 Hz	Deep sleep and infants	Sign of significant brain dysfunction, lethargy/drowsiness, or cognitive impairment
Theta	4–7.5 Hz	Young children, drowsiness, some aspects of learning	Slowing often related to attention/ cognitive impairments, internal focus
Alpha	8–13 Hz	Eyes closed, relaxation, self-awareness	Excessive alpha during demand states can be a sign of difficulties with learning, emotional stability, relating to the environment, or others
Beta	13–30 Hz	Fast activity associated with alertness and activity	Excessive beta is often associated with anxiety, irritability, and poor integration
Gamma	>30 Hz	May be associated with problem solving and memory consolidation	Unknown

functioning. The only way to succeed at the games involved is for children to control and improve their brain-wave patterns (following an operant-conditioning paradigm). In research and clinical treatment for children with ADHD, this conditioning process has resulted in improvements that have persisted for up to 5–10 years or more (e.g., Lubar 1995).

Individuals who participate in EEG biofeedback learn to inhibit brain-wave frequencies that may produce negative symptoms and enhance specific frequencies that produce positive results. Table 6.1 displays the typical EEG brain-wave frequency bands and lists their normal occurrences and respective significance [information adapted from resources contained in Demos (2005) and Thompson and Thompson (2003a, b)]. Within these general frequency bands, there may also be more detailed breakdowns of EEG activity. For example, mu-rhythm abnormalities are associated with excesses in the alpha-frequency band and have a characteristic morphologic and topographic distribution (Coben and Hudspeth 2006). Subdivisions of beta power have also been presented and related to clinical characteristics (Rangaswamy et al. 2002).

Individuals with poorly regulated cortical activity can learn to develop a fluid shift in brain waves to meet task demands utilizing neurofeedback. Through the process of operant conditioning, this treatment modality can result in improvement of brain-wave patterns as well as behavior. These changes in EEG patterns have been shown to be associated with regulation of cerebral blood flow, metabolism, and neurotransmitter function (Lubar 1997).

Neurofeedback is a noninvasive treatment with no known significant or lasting negative side effects that has been shown to enhance neuroregulation and metabolic function in ASD (Coben and Padolsky 2007). Positive neurofeedback treatment outcomes are often achieved over the course of several months, in contrast to behavior therapy, which often takes a year or more of intensive training. Furthermore, the therapeutic treatment outcomes of neurofeedback training with individuals with

ADHD (increased attention, reduced impulsivity, and hyperactivity) have been reported to be maintained over time and not reverse after treatment is withdrawn as in drug therapy and diet therapy (Tansey 1993; Linden et al. 1996; Monastra et al. 2005; Lubar, Swartwood, Swartwood, and O'Donnell, 1995).

Over 30 years of research on using neurofeedback to treat ADHD has consistently shown that it leads to improvements in attention, impulsivity, hyperactivity, and IQ (see Monastra et al. 2005, for a review and analysis). This success was the foundation for the emergence of using neurofeedback with ASD.

6.3.1 QEEG Evaluation and Autistic Spectrum Disorder

Quantitative electroencephalographic (QEEG) evaluation or "brain mapping" is an assessment procedure designed to pinpoint anomalies in brain function (Hammond 2005). QEEG analyses measure abnormalities, instabilities, or lack of proper communications pathways (connectivity) necessary for optimal brain functioning. QEEG maps, collected using 19 electrodes based on the international 10–20 system (Jasper 1958), reflect quantitative analyses of EEG characteristics of frequency, amplitude, and coherence during various conditions or tasks. These data can be statistically compared to an age-matched normative database to reveal a profile of abnormalities. Such regions and aspects of dysfunctional neurophysiology may then be targeted specifically through individualized neurofeedback protocols.

QEEG analyses are conducted to assess underlying neurophysiological patterns related to the symptoms and challenges of children with ASD. In addition, assessment of the raw EEG can be used to evaluate neurological abnormalities such as seizure disorders, which are common in children with autism. QEEG data are important for developing the most individualized, specific, and successful neurofeedback protocols for patients with ASD (Coben and Padolsky 2007; Linden 2004).

Coben et al. (2013) identified five relative power subtypes in individuals with autism. However, they noted that many types of dysfunction overlap in people with autism, and most reveal a combination of findings. In over 83 % of the individuals with autism, connectivity anomalies could be identified when compared to the normative group. Coben and Myers (2008) used QEEG multivariate connectivity data to develop a typology of autism connectivity patterns including (1) patterns of hyperconnectivity across bilateral frontotemporal regions and between left hemisphere locations and (2) hypoconnectivity involving orbitofrontal, frontal to posterior, right posterior, or left hemisphere sites. A pattern of hypoconnectivity that underlies a mu-rhythm complex was identified as well.

6.3.2 Neurofeedback: Case Studies, Case Series, and Group Pilot Studies

There have been numerous case and group pilot studies conducted with clients diagnosed with autistic spectrum disorders. In general, these studies have shown

that neurofeedback improved symptomatology and these improvements were maintained at follow-up. For a more thorough review of these, please see Coben et al. (2010b).

6.3.3 Controlled-Group Studies of Neurofeedback for ASD

There have been two approaches to the research done related to neurofeedback and ASD. Kouijzer and her colleagues have researched the effects of power training and Coben and his colleagues the effects of coherence training. The first study of Kouijzer and colleagues (2009b) investigated the effects of neurofeedback in children with autism. It included 14 children from 8 to 12 years old with a pervasive developmental disorder—not otherwise specified (PDD-NOS)—diagnosis. Excluded were children with an IQ score below 70, children using medication, and children with a history of severe brain injury or comorbidity such as ADHD or epilepsy. Participants were divided into treatment and wait-list control group according to the order of applying. During baseline (Time1), all participants were evaluated using QEEG and a range of executive function tasks, and parents completed behavior questionnaires (CCC and Auti-R). After neurofeedback training (Time2), or a comparable time interval for the wait-list control group, QEEGs and data on executive functions and social behavior were re-collected. One year after ending treatment (Time3), follow-up data including QEEGs, executive function tasks, and behavior questionnaires were collected in the treatment group. Participants in the treatment group had neurofeedback training twice a week, until 40 sessions were completed. In each session, participants were rewarded when inhibiting theta power (4–8 Hz) and increasing low beta power (12–15 Hz) at scalp location C4 according to a protocol including seven 3 min intervals of neurofeedback training separated by 1 min rest intervals. After 40 sessions of neurofeedback, 70 % of the participants in the treatment group had effectively decreased theta power and increased low beta power. Repeated measures MANOVA on the executive functions data collected at Time1 and Time2 revealed a significant interaction between treatment and control group, indicating improvement of participants in the treatment group on tasks measuring attention skills, cognitive flexibility, set shifting, concept generation/inhibition, and planning. Using repeated measures MANOVA to compare questionnaire data collected at Time1 and Time2 revealed a significant interaction effect between treatment and control group, indicating improvement in nonverbal communication and general communication. Time2 Auti-R questionnaire data evaluating changes in behavior over the last 6 months showed significant improvement in social interactions, communication skills, and stereotyped and repetitive behavior for the treatment group, but not for the control group.

In a second study by Kouijzer and colleagues (2010), several methodological improvements were implemented to better identify the effects of neurofeedback. A randomized wait-list control group design was used, and the study was conducted at the schools of the participants ($n = 20$). Participants were 8–12 years old and

had diagnoses of autism, Asperger's disorder, or PDD-NOS. Participants in the treatment group had 40 individual neurofeedback sessions using an individualized treatment protocol based on an initial QEEG. However, all treatment protocols included theta inhibition at fronto-central scalp locations. Treatment response was evaluated by QEEG measures taken during rest and task conditions, a range of executive function tasks, and social behavior questionnaires filled out by parents and teachers. All data were collected before (Time1) and after treatment (Time2) and at 6 months follow-up (Time3).

Results of the study showed that 60 % of participants decreased theta power within 40 sessions of neurofeedback. Additionally, repeated measures MANOVA on QEEG data revealed a significant interaction between treatment and control group, indicating a decrease in theta power in the treatment group in two out of four QEEG conditions. Repeated measures MANOVA on Time1 and Time2 executive function data showed a significant interaction between treatment and control group for cognitive flexibility, indicating improvement in cognitive flexibility in the treatment group compared to the control group. Repeated measures MANOVA showed a significant interaction effect for social interactions and communication skills, indicating that parents of participants in the treatment group reported significant improvement in social interactions and communication skills, whereas less or no improvement was reported by parents of children in the control group.

Coben and his colleagues began researching the effects of coherence/connectivity training on autistic symptoms about 6 years ago. Coben and Padolsky (2007) published a study investigating the effects of neurofeedback treatment for autistic disorders. The study included 49 children on the autistic spectrum, with 37 participants receiving QEEG connectivity-guided neurofeedback and 12 participants in a wait-list control group. Treatment included 20 sessions performed twice per week. The control group was matched for age, gender, race, handedness, other treatments, and severity of ASD. According to the parents, there was an 89 % success rate for neurofeedback and an average of 40 % reduction in core ASD symptomatology. There were significant improvements on neuropsychological measures of attention, visual–perceptual skills, language functions, and executive functioning. Importantly, reduced cerebral hyperconnectivity was associated with positive clinical outcomes, and in all cases of reported improvement, positive outcomes were supported by neurophysiological and neuropsychological assessment.

Mu-rhythm abnormalities are a sign of mirror neuron dysfunction, which is thought to be the case in many children with autism (Oberman et al. 2005). In two studies focused on reducing abnormal mu rhythms in children with autism, Pineda and Hecht (2009) found that according to parents, participants showed a small but significant reduction in symptoms but increased ratings of sensory-cognitive awareness. In another study related to mu rhythms, Coben and Hudspeth (2006) studied fourteen children with ASD who were identified as having significantly high levels of mu activity and a failure to suppress mu during observational activity. They all received assessment-guided neurofeedback, with a strong focus on aspects of mu power and connectivity. The participants were nonrandomly assigned to an interhemispheric bipolar training ($n = 7$) or a coherence training ($n = 7$) group designed to

increase connectivity between central regions and the peripheral frontal cortex. All patients were given neurobehavioral and neuropsychological testing and QEEG assessment. Both groups of patients improved significantly on neurobehavioral and neuropsychological measures. However, only in the coherence training treatment group was mu activity significantly reduced. Increased coherence was associated with diminished mu and improved levels of social functioning. Lastly, Coben (2007) conducted a controlled neurofeedback study focused on intervention for prominent social skill deficits based on a facial/emotional processing model. Fifty individuals with autism were included in these analyses, and all had previously had some neurofeedback training. All patients underwent pre- and post-treatment neuropsychological, QEEG, and parent rating scale assessments. Twenty-five individuals were assigned to either an active neurofeedback or a wait-list control group, in a randomized fashion. The two groups were matched for age, gender, race, handedness, medication usage, autistic symptom severity, social skill ratings, and visual–perceptual impairment levels. Neurofeedback training was QEEG connectivity guided and included coherence training (along with amplitude inhibits) between maximal sights of hypocoherence over the right posterior hemisphere. The group that received the coherence training showed significant changes in symptoms of autism, social skills, and visual–perceptual abilities such that all improved. Regression analyses showed that changes in visual–perceptual abilities significantly predicted improvements in social skills. EEG analyses were also significant, showing improvements in connectivity and source localization of theta power related to brain regions (fusiform gyrus, superior temporal sulcus) associated with enhanced visual/facial/emotional processing.

In the seven controlled-group studies that have been completed, a total of 214 individuals with autism have been studied and positive results reported in each study. These findings have included positive changes as evidenced by parental report, neuropsychological findings, and changes in the EEG (Coben 2007). Both Coben and Padolsky (2007) and Yucha and Montgomery (2008) have viewed these data as demonstrating a level of efficacy of "possibly efficacious" based on the standards put forth by the Association for Applied Psychophysiology and Biofeedback (AAPB 2006). Added to these initial findings of efficacy is preliminary evidence that the effects of neurofeedback on the symptoms of autism are long-lasting (1–2 years) (Coben 2009; Kouijzer et al. 2009a). While these findings are initially encouraging, there are many limitations that prevent firm conclusions to be drawn from the data collected thus far.

First, these studies have largely included nonrandomized samples. It is possible that an unknown selection bias exists which could have impacted the findings. Second, none of these studies have included participants or therapists/experimenters who were blind to the condition. Knowledge of group placement could have impacted the findings such that those in treatment (and their parents) would be prone to report significant changes. Third, there has been no attempt to control for placebo effects, attention from a caring professional, or expectations of treatment benefit. A randomized, double-blinded, placebo-controlled study is clearly needed to further demonstrate efficacy.

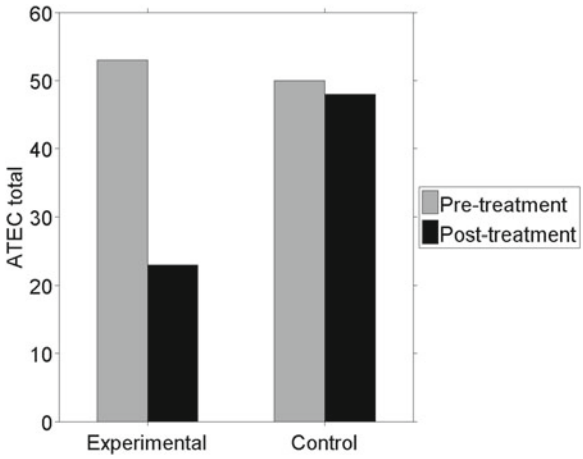

Fig. 6.1 Pre- and post-treatment ATEC scores

In terms of generalization of these findings to the larger population of individuals who are autistic, very young children and adults have not been well represented in these group studies. Lastly, there is the question of whether neurofeedback may be applicable to persons who are lower functioning or who have more severe symptoms associated with autism. These populations also should be the focus of future investigations.

6.3.4 Efficacy of Connectivity-Guided Neurofeedback for Autistic Spectrum Disorder

Recently, Coben (2009) presented on a study of the effects of an entire course of connectivity-guided neurofeedback treatment on autistic children. This included 110 subjects on the autistic spectrum, with 85 in the experimental and 25 in the control (wait-list) group. The mean age of these subjects was 9.7 years (range 4–20 years). Seventy-seven percent of these subjects were not on medication at the time, while 14 % were on one medication, 7 % on two medications, and 1 % on three medications. The mean IQ of this group was 93 (range 50–130). The mean ATEC score was 50 (range 40–170). There were no significant differences between the experimental and control groups for age, gender, handedness, race, medications, IQ, or ATEC scores.

The experimental group underwent an average of 74 neurofeedback sessions. They were assessed using QEEG, neuropsychological testing, and parent rating scales before treatment and then again after treatment. In order to evaluate the efficacy of neurofeedback treatment for reducing ASD symptomatology, the subjects' scores on the ATEC and neuropsychological testing were compared before and after treatment. A univariate analysis of variance (ANOVA) revealed that ATEC scores changed significantly after treatment ($F = 117.213$; $p < 0.0001$; see Fig. 6.1). Furthermore, 98.8 % of parents reported a reduction in ASD symptoms on the ATEC after treatment.

On objective neuropsychological testing, 100 % of subjects demonstrated some degree of improvement. An ANOVA revealed improvements on tests of visual–perceptual skills ($F=53.6$; $p<0.0001$), language abilities ($F=31.24$; $p<0.0001$), attentional skills ($F=54.04$; $p<0.0001$), and executive functioning ($F=15.65$; $p=0.00015$). In fact, visuoperceptual skills improved 43 %, language abilities improved 47 %, attentional skills improved 56 %, and executive functioning improved 48 %.

Once it was determined that the therapy was efficacious, the next question investigated was whether it had greater efficacy depending on level of functioning or severity of autistic symptoms. We investigated the effects of pretreatment ATEC and IQ scores on treatment outcome by dividing the groups into quartiles based on ATEC and IQ scores and reanalyzing the data. There were no significant differences for any of these analyses. This revealed that (1) ASD symptomatology improved with treatment regardless of IQ and (2) severity of ASD symptoms did not affect treatment outcomes. These results suggest that neurofeedback is an effective treatment regardless of the child's intellectual ability or severity of symptoms, at least within the parameters of the subjects that were included in this study.

6.3.5 Enduring Effects of Neurofeedback on Children with ASD

Both Kouijzer and Coben, along with their respective colleagues, have studied the enduring effects of neurofeedback after the treatment period has ended. One year follow-up data from Kouijzer et al.'s original study demonstrated enduring effects of neurofeedback treatment (Kouijzer et al. 2009a). Repeated measures MANOVA on the executive function task scores at Time2 and Time3 indicated maintenance of cognitive flexibility, planning skills, and verbal inhibition, improvement of attention, and marginally significant improvement of motor inhibition. No significant decreases in executive function skills were found after 1 year. Repeated measures MANOVA comparing Time1 and Time3 data confirmed maintenance of these effects. Analysis revealed significant increases of all executive functions that improved after neurofeedback treatment, i.e., attention skills, cognitive flexibility, inhibition, and planning. Figure 6.2 shows Time1, Time2, and Time3 scores of the treatment group on tests for attention, cognitive flexibility, inhibition, and planning.

Analysis of behavior questionnaires filled out by parents at Time2 and Time3 showed no loss of nonverbal communication and general communication (CCC), social interactions, communication skills, and stereotyped and repetitive behavior (Auti-R). Comparing Time1 and Time3 behavior questionnaires (CCC) confirmed the positive effect for nonverbal communication, but not for general communication. Figure 6.3 shows Time1, Time2, and Time3 questionnaire data (CCC) for general communication and nonverbal communication of the treatment group.

Detailed information about the results of this study can be found in the original paper (Kouijzer, de Moor, Gerrits, Buitelaar et al. 2009).

Analysis of the 6-month follow-up data from their second study (Kouijzer, van Schie, de Moor, Gerrits, and Buitelaar 2009) revealed enduring effects of

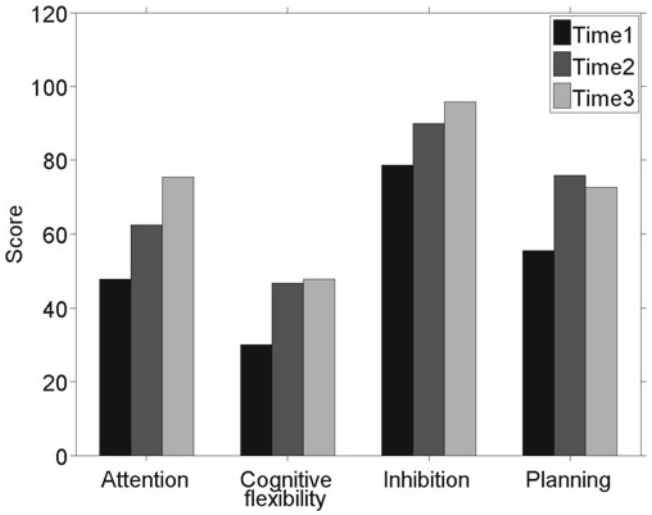

Fig. 6.2 Time1, Time2, and Time3 data of the treatment group on executive function tasks

neurofeedback treatment. Repeated measures MANOVA was used to compare the scores on executive function tasks at Time2 and Time3 and showed no significant changes, suggesting that participants maintained the same levels of executive functioning for at least 6 months. Repeated measures MANOVA comparing Time1 and Time3 data confirmed the previously described effects by revealing a significant increase of cognitive flexibility for the treatment group but not for the control group. Figure 6.4 shows Time1, Time2, and Time3 scores of the treatment and control group on cognitive flexibility.

Repeated measures MANOVA comparing the scores on behavioral questionnaires at Time2 and Time3 showed no effects of group or time, indicating maintenance of the effects in social behavior that were reached 6 months earlier. Repeated measures MANOVA comparing Time1 and Time3 questionnaire data confirmed this effect by showing a significant interaction, suggesting decreases in problem scores on behavior questionnaires for the treatment group, but not for the control group. Figure 6.5 shows Time1, Time2, and Time3 questionnaire data of social interactions and communication skills of treatment and control group.

More detailed information about the results of this study can be found in the original paper (Kouijzer et al. 2009a).

Both studies discussed above indicate maintenance of the effects in executive functions and social behavior from 6 months to 1 year after ending neurofeedback treatment.

A similar study with findings which can be considered complementary to those of Kouijzer and colleagues was recently conducted by Coben at his New York clinic (Coben et al. 2010a). This study assessed 20 patients with ASD in order to investigate long-term clinical effects of neurofeedback in terms of behavioral and

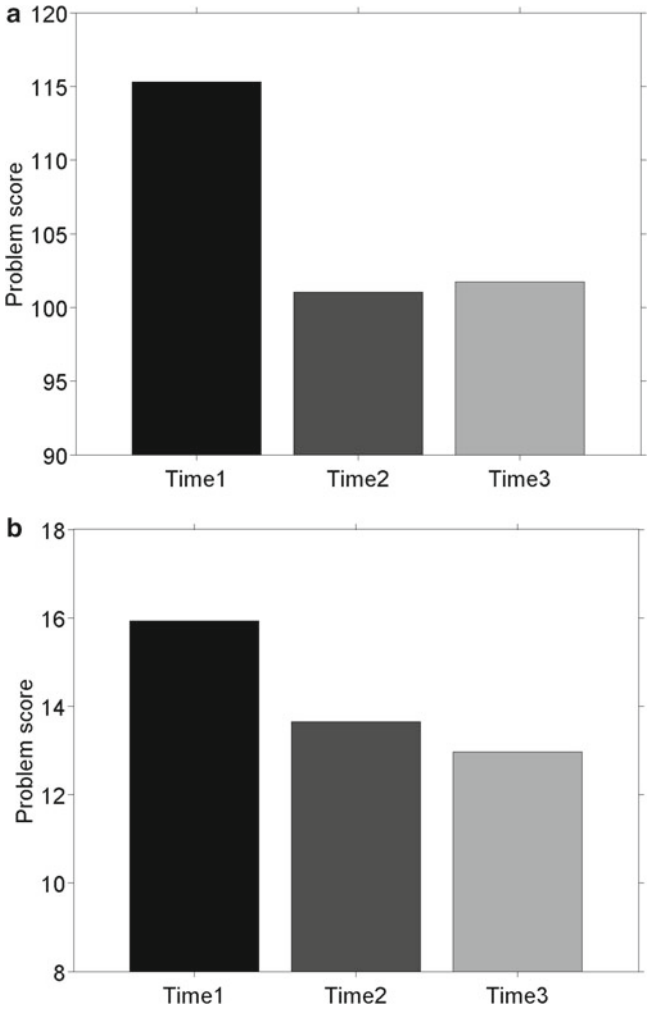

Fig. 6.3 Time1, Time2, and Time3 data of the treatment group on social behavior: general communication (**a**) and nonverbal communication (**b**)

neuropsychological measures. The subject pool for this study was predominately male (16 out of 20 individuals) and all Caucasian. The mean age was 9.53 years, with a range of 5–10 years. Most subjects (80 %) were medication free, with only one subject taking more than two medications. Handedness was mostly right handed ($n = 16$) with one left handed and 3 ambidextrous subjects. Subjects were administered parent rating scales, including the Autism Treatment Evaluation Checklist (ATEC; Rimland and Edelson 2000), the Personality Inventory for Children (PIC-2; Lachar and Gruber 2001), the Behavior Rating Inventory of Executive Function (BRIEF; Gioia, Isquith, Guy, and Kenworthey, 2000), and the Gilliam Asperger's Disorder Scale (GADS; Gilliam 2001). Subjects were also administered

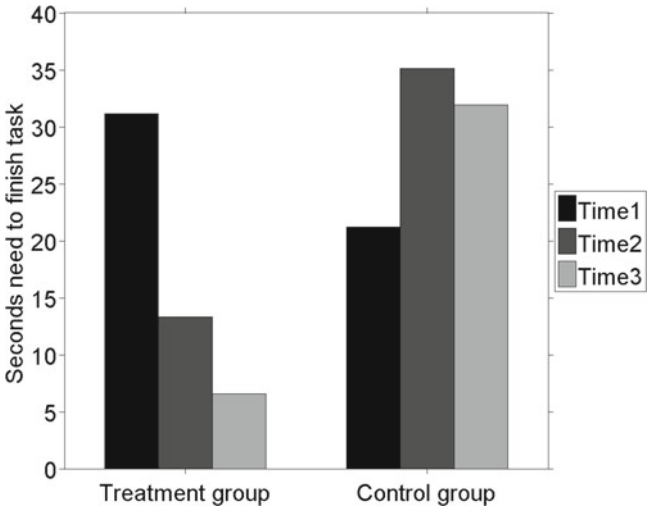

Fig. 6.4 Time1, Time2, and Time3 data of treatment and control group on cognitive flexibility

neuropsychological assessments covering domains of attention/executive functioning, language, and visuospatial processing. After baseline assessments were collected, all subjects underwent at least 40 sessions of neurofeedback training, with an average of 64.5 completed sessions among all subjects. Upon completion of therapy, subjects were reevaluated and pre- and post-treatment scores were compared for significance. After reevaluation, neurofeedback was withheld for between 5 months and 22 months (mean 10.1 months), while no other treatments were administered. Following this break in treatment, subjects were evaluated once again in the same fashion as previously described. Their latter scores were then compared to scores obtained at the end of active neurofeedback training (Time2).

All statistical computations were performed in the statistical package SPSS. Scores prior to treatment on parent rating scales were compared for significance to scores obtained after treatment had ended. Analysis of pre- and postscores obtained from the ATEC revealed significant changes following neurofeedback training. Likewise, changes in scores on the GADS prior to and following treatment were found to be significant. Significant changes were also found to be present following treatment among scores from the BRIEF as well as the PIC-2. Interestingly, when subjects were reassessed following the 5-month to 22-month period of no neurofeedback training, no significant changes were found on any parent rating scale administered (Fig. 6.6). This suggests that changes in parent ratings that were improved by neurofeedback training remained stable during this follow-up period.

Neuropsychological evaluations encompassing the domains of attention, executive functioning, language, and visuospatial processing were also analyzed for significant differences. Significant changes from pre- to post-treatment scores were found among all three domains assessed: attention/executive functioning, language, and visuospatial processing. Interestingly, significant therapeutic changes were also

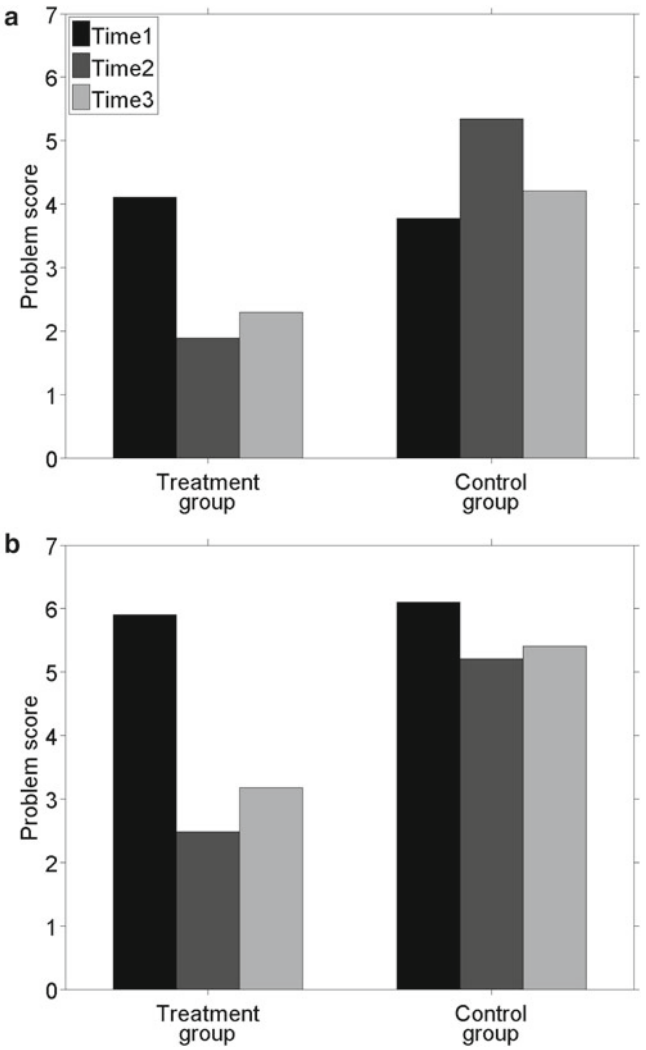

Fig. 6.5 Time1, Time2, and Time3 data of treatment and control group on social behavior: social interactions (**a**) and communication skills (**b**)

found after subjects were reevaluated after a lengthy (5–22 months) absence from neurofeedback training. These occurred in the areas of attention, language, and visuospatial processing (Fig. 6.7). This would suggest that neurofeedback training not only led to objective gains in neuropsychological functioning but that these enhancements in functioning continued to improve over the follow-up period when no treatment was being received.

The results of this present study were quite interesting. First, our findings add to the wealth of studies that have shown that from pre- to posttreatment conditions,

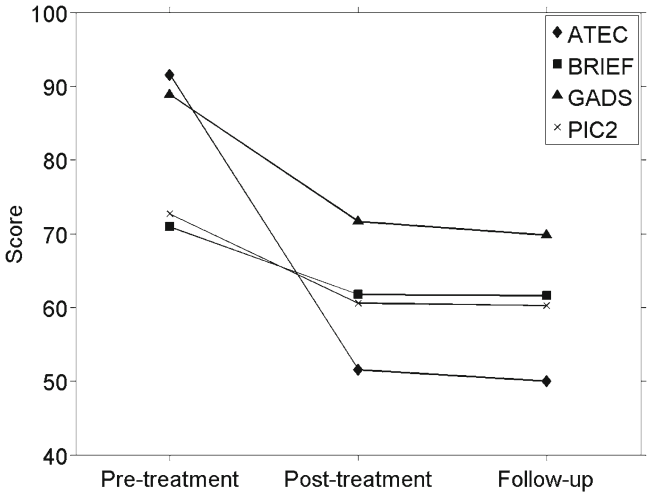

Fig. 6.6 Graph showing the clinical improvements among subjects as assessed by the parents rating scales of ATEC, BRIEF, GADS, and PIC-2 for pretreatment, post-treatment, and follow-up periods

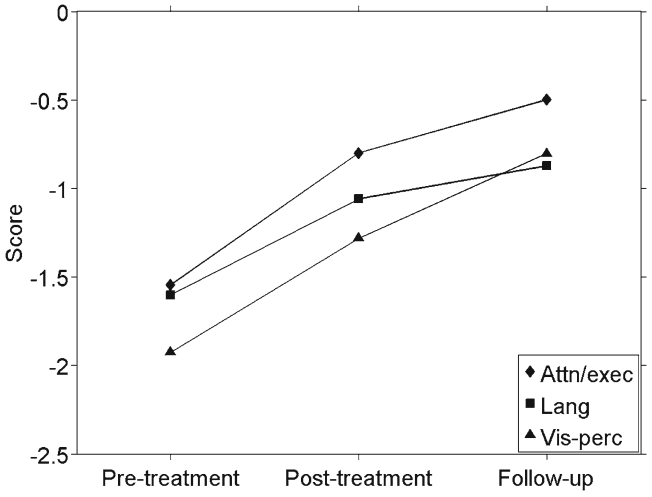

Fig. 6.7 Graph showing the clinical improvements among the domains of attention/executive functioning, language, and visuospatial processing as assessed by neuropsychological evaluations at pretreatment, post-treatment, and follow-up periods

neurofeedback is an effective therapy for treating individuals with autistic spectrum disorders. Additionally, these results show that this treatment was effective in limiting autistic behavioral deficits as well as deficits of a more neuropsychological nature. Furthermore, as our analysis shows, there were no significant increases in autistic pathology when subjects were reevaluated after neurofeedback was

withheld. This finding supports previously found evidence that neurofeedback is capable of creating stable changes within autistic subjects that are not likely to rapidly degrade when treatment ends (Jarusiewicz 2002, p. 749; Coben 2007, p. 740).

Of potentially even greater interest, this study found that during the period in which subjects were receiving no treatment, positive clinical neuropsychological gains were still being manifested within the domains of attention, executive functioning, language, and visuospatial processing. Thus, even without continued treatment, subjects apparently were continuing to improve in these realms. An important implication of this finding is that neurofeedback may indeed change the autistic brain to work in novel and more efficient ways, and these changes may continue to progress even after the treatment has ended. This finding helps further the claim that neurofeedback creates specific neurophysiological changes within the autistic brain (Coben et al. 2009). This is in stark contrast to other commonly administered treatments for autism. For example, Lovaas et al. (1973, p. 1145) performed a study in which applied behavioral analysis (ABA) was administered to a group of children with autism. Upon completion of ABA training, the experimenters reported positive gains in terms of clinical improvements in behavioral deficits. Subjects were then reevaluated between 1 and 4 years later, and subjects who did not continuously receive ABA training had significantly regressed. As our current findings demonstrate, there is no evidence of regression among any of our subjects receiving neurofeedback training. In terms of drug therapies, there is no evidence to our knowledge that would indicate that medications result in enduring clinical gains for subjects with autism when medication is withheld. In fact, numerous studies indicate that prolonged medication use has detrimental effects on autistic individuals (Malone 2002, p. 1149; Anderson et al. 2010).

In terms of the limitations of the current study, the participants consisted of a selected pool of subjects. Subjects were placed in groups by choice of the experimenter rather than by random assignment. When subjects are chosen in that manner, there may be a degree of selection bias associated. We would also recommend that this experiment be replicated with more neuropsychological assessments and parent rating scales included in order to more widely assess the effects of neurofeedback training. This type of investigation could broaden the present findings and help determine if there are other correlations or significant predictors we might not have considered. Also, we would recommend a study with a greater gap between the end of treatment and reevaluation of subjects. Doing this, we believe, would help to assess nature and extent of any positive clinical gains found in subjects when they are no longer receiving treatment, as well as test more fully the limits of enduring effects of neurofeedback treatment.

6.4 Discussion

There are few interventions with proven efficacy for children with autism. Behavioral modification interventions currently have the most empirical support, while pharmacologic interventions, hyperbaric oxygen, and vitamin supplementation have

shown some potential. It is our opinion that neurofeedback is in a similar position with respect to efficacy for ASD, but more research is needed. Neurofeedback is an intervention that may prove to be efficacious in the treatment of symptoms of autism. At present, it should be viewed as possibly efficacious with potential as is the case with most interventions used with this population. Measuring brain-related changes that may occur as a result of neurofeedback is one way of demonstrating its efficacy and mechanism of action. Additional well-designed, more rigorous studies and longer follow-up periods should be included in the future to measure the efficacy of neurofeedback in treating children on the autistic spectrum.

In addition, there is growing evidence that neurofeedback is a therapy capable of creating enduring changes in children with autism. A therapy that can lead to long-lasting effects for children with developmental disorders (and perhaps continuing improvement even after the treatment is stopped) is an enormous asset for children with developmental disorders. Most contemporary treatments require prolonged and lengthy treatment sessions. For example, ABA training can require up to 40 h a week over several months to be effective (Howard 2005, p. 1132). Furthermore, drug therapies usually require years of medication in order to maintain efficacy. In addition, some children require incremental increases in dosages over a period of years for medication use to be clinically viable. Our current results and those of others discussed in this chapter indicate that neurofeedback therapy can reach clinical efficacy relatively quickly and positive gains can be retained for months after treatment has stopped. Outside of the clinical implications, there are ancillary benefits supporting the use neurofeedback. For example, the financial aspects of this treatment should be considered. Presently, the United States alone spends upward of $3.2 million for the care and treatment for a single individual with autism, a figure that equates to $35 billion annually (Ganz 2006).

Results of the studies reviewed in this chapter also provide evidence for the safety of neurofeedback. All studies reported no instances of subjects worsening or showing any side effects while undergoing this treatment over an extended period of time. Moreover, there was no evidence of negative side effects when neurofeedback was ceased. In fact, the opposite was found across all studies. This, again, is contradictory to other interventions, most notably drug therapies, which have documented adverse reactions within this population and often have failed to demonstrate positive effects on primary symptoms (Kidd 2002). Investigations into other contemporary treatments (i.e., diet and chelation therapies) have failed to yield adequate evidence in regard to their safety or efficacy (McDougle et al. 2000; Doja and Roberts 2005; Elder et al. 2006).

We speculate that the enduring effects of neurofeedback in children with developmental disorders are the result of this treatments' ability to change the brain in a therapeutic manner. Recently, Coben and colleagues reported specific neurophysiological changes in terms of coherence within and between specific neural regions following neurofeedback treatment for children with autism spectrum disorder (Coben et al. 2009). We would argue that neurofeedback training causes specific neurophysiological changes within the brain, which in turn contribute to the long-lasting effects of this treatment, and this fosters the continued growth and development of cognitive functions. Moreover, we suggest that more research be conducted

into the precise neural areas clinically affected by neurofeedback in an effort to more fully understand the efficacy of neurofeedback for children with developmental disorders. In summary, results of the studies examined add to the growing wealth of investigations into the efficacy of neurofeedback as a treatment for children with developmental disorders. Moreover, these results have found this treatment to be effective over an extended period of time. Consistent with these results, we recommend future studies be conducted that assess the enduring effects of neurofeedback over even longer treatment spans.

References

Adams JB, Baral M, Geis E, Mitchell J, Ingram J, Hensley A, Zappia I, Newmark S, Gehn E, Rubin RA, Mitchell K, Bradstreet JJ, El-Dahr J (2009) Safety and efficacy of oral DMSA therapy for children with autism spectrum disorders: part A—medical results. BMC Clin Pharmacol 9:16

Aman MG, Singh NN, Stewart AW, Field CJ (1985) The aberrant behavior checklist: a behavior rating scale for the assessment of treatment effects. Am J Ment Defic 89:485–491

American Psychiatric Association (2000) Diagnostic and statistical manual of mental disorders. American Psychiatric Publishing, Washington, DC

Amminger GP, Berger GE, Schäfer MR, Klier C, Friedrich MH, Feucht M (2007) Omega-3 fatty acids supplementation in children with autism: a double-blind randomized, placebo-controlled pilot study. Biol Psychiatry 61:551–553

Anderson SR, Avery DL, DiPietro EK, Edwards GL, Christian WP (1987) Intensive home-based early intervention with autistic children. *Education and Treatment of Children*, 10:352–366

Association for Applied Psychophysiology & Biofeedback (2006). Efficacy: How we rate theefficacy of our treatments or how to know if our treatments actually work. Retrieved February 22, 2006 from http://www.aapb.org/i4a/pages/index.cfm?pageid = 3336

Attwood T (1998) Asperger's syndrome: a guide for parents and professionals. Jessica Kingsley, London

Barnard L, Young AH, Pearson J, Geddes J, O'Brien G (2002) A systematic review of the use of atypical antipsychotics in autism. J Psychopharmacol 16:93–101

Bassett K, Kazanjian A, Green CJ (2000) Autism and Lovaas treatment: a systematic review of effectiveness evidence. British Columbia Office of Health Technology Assessment, Vancouver

Bell JG, Sargent JR, Tocher DR, Dick JR (2000) Red blood cell fatty acid compositions in a patient with autistic spectrum disorder: a characteristic abnormality in neurodevelopmental disorders? Prostaglandins Leukot Essent Fatty Acids 63:21–25

Bell JG, MacKinlay EE, Dick JR, MacDonald DJ, Boyle RM, Glen ACA (2004) Essential fatty acids and phospholipase A_2 in autistic spectrum disorders. Prostaglandins Leukot Essent Fatty Acids 71:201–204

Ben-Itzchak E, Zachor DA (2007) The effects of intellectual functioning and autism severity on outcome of early behavioral intervention for children with autism. Res Dev Disabil. 2007 May-Jun; 28(3):287–303

Bernard S, Enayati A, Binstock T, Roger H, Redwood L, McGinnis W (2000) Autism: a unique type of mercury poisoning. Accessed http://whale.to/a/autism7.html

Blaxill MF (2004) What's going on? The question of time trends in autism. Public Health Rep 119:536–551

Bradstreet JJ, Geier DA, Kartzinel JJ, Adams JB, Geier MR (2003) A case-control study of mercury burden in children with autistic spectrum disorders. J Am Physicians Surg 8:76–79

Cade R, Privette M, Fregly M, Rowland N, Sun Z, Zele V, et al (1999) Autism and schizophrenia: Intestinal disorders. Nutritional Neuroscience, 2:57–72

Centers for Disease Control and Prevention (2009) Prevalence of autism spectrum disorders—autism and developmental disabilities monitoring network, United States, 2006. Morb Mort Wkly Rep 58(SS-10):1–20

Centers for Disease Control and Prevention (2012) Prevalence of autism spectrum disorders—autism and developmental disabilities monitoring network, 14 sites, United States, 2008. Morb Mort Wkly Rep 61(SS-3):1–19

Coben R (2007, September) Autistic spectrum disorder: a controlled study of EEG coherence training targeting social skill deficits. Presented at the 15th annual conference of the international society for neurofeedback and research, San Diego, California.

Coben R (2009) Efficacy of connectivity guided neurofeedback for autistic spectrum disorder: controlled analysis of 75 cases with a 1 to 2 year follow-up. J Neurother 13:81

Coben R, Hudspeth W (2006) Mu-like rhythms in autistic spectrum disorder: EEG analyses and neurofeedback outcome. In: 14th Annual conference of the international society for neuronal regulation, Atlanta

Coben R, Myers TE (2008) Connectivity theory of autism: use of connectivity measures in assessing and treating autistic disorders. J Neurother 12:161–179

Coben R, Padolsky I (2007) Assessment-guided neurofeedback for autistic spectrum disorder. J Neurother 11:5–23

Coben R, Sherlin L, Hudspeth WJ, McKeon K (2009) Connectivity guided EEG biofeedback for autism spectrum disorder: evidence of neurophysiological changes. J Autism Develop Disord (under review).

Coben R, Arns M, Kouijzer MEJ (2010a) Enduring effects of neurofeedback in children. In: Coben R, Evans JR (eds) Neurofeedback and neuromodulation techniques and applications. Academic, London, pp 403–422

Coben R, Linden M, Myers TE (2010b) Neurofeedback for autistic spectrum disorder: a review of the literature. Appl Psychophysiol Biofeedback 35:83–105

Coben R, Chabot RJ, Hirshberg L (2013) EEG analyses in the assessment of autistic disorders. In: Casanova MF, El-Baz AS, Suri JS (eds) Imaging the brain in autism, pp 349–370. Springer, New York

Committee on Children with Disabilities (2001) Technical report: the pediatrician's role in the diagnosis and management of autistic spectrum disorder in children. Pediatrics 107:e85

Cook EH Jr, Rowlett R, Jaselskis C, Leventhal BL (1992) Fluoxetine treatment of children and adults with autistic disorder and mental retardation. J Am Acad Child Adolesc Psychiatry 31:739–745

Couper J (2004) Who should pay for intensive behavioural intervention in autism? A parent's view. J Paediatr Child Health 40:559–561

Couturier JL, Nicolson R (2002) A retrospective assessment of citalopram in children and adolescents with pervasive developmental disorders. J Child Adolesc Psychopharmacol 12:243–248

DeLong GR, Ritch CR, Burch S (2002) Fluoxetine response in children with autistic spectrum disorders: correlation with familial major affective disorder and intellectual achievement. Dev Med Child Neurol 44:652–659

Demos JN (2005) Getting started with neurofeedback. W.W. Norton, New York, NY

Deprey LJ, Brule N, Widjaja F, Sepheri S, Blank J, Neubrander J, et al (2006) Double-blind placebo-controlled, cross-over trial of subcutaneous methylcobalamin in children with autism: preliminary results. Poster presented at the annual meeting of the American academy of child and adolescent psychiatry, San Diego, CA, October

Doja A, Roberts W (2006) Immunizations and autism: A review of the literature. The Canadian Journal of Neurological Sciences, 33:341–346

Elder JH, Shankar M, Shuster J, Theriaque D, Burns S, Sherrill L (2006) The gluten-free, casein-free diet in autism: results of a preliminary double blind clinical trial. J Autism Dev Disord 36:413–420

Esch BE, Carr JE (2004) Secretin as a treatment for autism: a review of the evidence. J Autism Dev Disord 34:543–556

Ganz ML (2006) The costs of autism. In: Moldin SO, Rubenstein JLR (eds) Understanding autism: from basic neuroscience to treatment. CRC Press, Boca Raton, pp 475–498
Geller DA, Hoog SL, Heiligenstein JH, Ricardi RK, Tamura R, Kluszynski S, Jacobson JG, Fluoxetine Pediatric OCD Study Team (2001) Fluoxetine treatment for obsessive-compulsive disorder in children and adolescents: a placebo-controlled clinical trial. J Am Acad Child Adolesc Psychiatry 40:773–779
George MS, Costa D, Kouris K, Ring HA, Ell PJ (1992) Cerebral blood flow abnormalities in adults with infantile autism. J Nerv Ment Dis 180:413–417
Gioia GA, Isquith PK, Guy SC, Kenworthy L (2000) Behavior rating inventory of executive function. Lutz, FL: Psychological Assessment Resources
Gilliam JE (2001) Gilliam asperger's disorder scale examiner's manual. Austin, Texas: Pro-Ed.
Golden ZL, Neubauer R, Golden CL, Greene L, Marsh J, Mleko A (2002) Improvement in cerebral metabolism in chronic brain injury after hyperbaric oxygen therapy. Int J Neurosci 112:119–131
Granpeesheh D, Tarbox J, Dixon DR, Wilke AE, Allen MS, Bradstreet JJ (2010) Randomized trial of hyperbaric oxygen therapy for children with autism. Res Autism Spectr Disord 4:268–275
Green VA, Pituch KA, Itchon J, Choi A, O'Reilly M, Sigafoos J (2006) Internet survey of treatments used by parents of children with autism. Research in Developmental Disabilities 27:70–84
Hamilton LM (2000) Facing autism: giving parents reasons for hope and guidance for help. WaterBrook Press, Colorado Springs, CO
Hammond DC (2005) "Neurofeedback with anxiety and affective disorders." *Child and adolescent psychiatric clinics of North America* 14.1 (2005): 105
Hediger ML, England LJ, Molloy CA, Yu KF, Manning-Courtney P, Mills JL (2008) Reduced bone cortical thickness in boys with autism or autism spectrum disorder. J Autism Dev Disord 38:848–856
Herbert JD, Sharp IR, Gaudiano BA (2002) Separating fact from fiction in the etiology and treatment of autism. Sci Rev Ment Health Pract 1:23–43
Hill EL (2004) Executive dysfunction in autism. Trends Cogn Sci 8:26–32
Hollander E, Phillips A, Chaplin W, Zagursky K, Novotny S, Wasserman S, Iyengar R (2005) A placebo controlled crossover trial of liquid fluoxetine on repetitive behaviors in childhood and adolescent autism. Neuropsychopharmacology 30:582–589
Holmes AS (2001) Chelation of mercury for the treatment of autism. Forum on alternative and innovative therapies for children with developmental delays, brain injury and related neurometabolic conditions and disorders. http://www.healing-arts.org/children/holmes.htm. Accessed 30 Mar 2010
Howard JS, Sparkman CR, Cohen HG, Green G, Stanislaw H (2005) A comparison of intensive behavior analytic and eclectic treatments for young children with autism. *Research in Developmental Disabilities*, 26(4):359–383
Hughes JR, John ER (1999) Conventional and quantitative electroencephalography in psychiatry. J Neuropsychiatry Clin Neurosci 11:190–208
Jarusiewicz B (2002) Efficacy of neurofeedback for children in the autistic spectrum: A pilot study. Journal of Neurotherapy, 6(4):39–49
Jasper HH (1958) The ten–twenty electrode system of the International Federation. Electroencephalogr Clin Neurophysiol, 10:371–5
Jeffrey S Anderson, Nicholas Lange, Alyson Froehlich, Molly B DuBray, T Jason Druzgal, Michael P Froimowitz, Andrew L Alexander, Erin D Bigler, Janet E Lainhart (2010) Decreased left posterior insular activity during auditory language in autism American Journal of Neuroradiology, 31, 1:131–139
Jensen PS, Arnold LE, Swanson JM, Vitiello B, Abikoff HB, Greenhill LL, Hechtman L, Hinshaw SP, Pelham WE, Wells KC, Conners CK, Elliott GR, Epstein JN, Hoza B, March JS, Molina BSG, Newcorn JH, Severe JB, Wigal T, Gibbons RD, Hur K (2007) 3-year follow-up of the NIMH MTA study. J Am Acad Child Adolesc Psychiatry 46:989–1002
Jesner OS, Aref-Adib M, Coren E (2007) Risperidone for autism spectrum disorder. Cochrane Database Syst Rev 2007:CD005040

Just MA, Cherkassky VL, Keller TA, Minshew NJ (2004) Cortical activation and synchronization during sentence comprehension in high-functioning autism: evidence of underconnectivity. Brain 127:1811–1821

Kidd PM (2002) Autism, an extreme challenge to integrative medicine, part II: medical management. Altern Med Rev 7:472–499

Kirby D (2005) Evidence of harm: Mercury in vaccines and the autism epidemic: A medical controversy. New York: St. Martin's Press

Knivsberg A-M, Reichelt K-L, Høien T, Nødland M (2002) A randomised, controlled study of dietary intervention in autistic syndromes. Nutr Neurosci 5:251–261

Kouijzer MEJ, de Moor JMH, Gerrits BJL, Buitelaar JK, van Schie HT (2009a) Long-term effects of neurofeedback treatment in autism. Res Autism Spectr Disord 3:496–501

Kouijzer MEJ, de Moor JMH, Gerrits BJL, Congedo M, van Schie HT (2009b) Neurofeedback improves executive functioning in children with autism spectrum disorders. Res Autism Spectr Disord 3:145–162

Kouijzer MEJ, van Schie HT, de Moor JMH, Gerrits BJL, Buitelaar JK (2010) Neurofeedback treatment in autism: preliminary findings in behavioral, cognitive, and neurophysiological functioning. Res Autism Spectr Disord 4:386–399

Lachar D, Gruber CP (2001) Personality inventory for children, second edition. Los Angeles, CA: Western Psychological Services

Linden M, Habib T, Radojevic V (1996) A controlled study of the effects of EEG biofeedback on cognition and behavior of children with attention deficit disorder and learning disabilities. Biofeedback Self Regul 21:35–49

Linden M (2004) *Case studies of QEEG mapping and neurofeedback with autism*. Presented at the 12th Annual Conference of the International Society for Neuronal Regulation, Fort Lauderdale, Florida

Lovaas OI, Koegel R, Simmons JQ, Stevens Long J (1973) Some generalization and follow-up measures on autistic children in behavior therapy. J Appl Behav Anal 6:131–165

Lubar JF (1995) Neurobiological foundation for neurofeedback treatment of attention deficit hyperactivity disorder (ADD/HD). Biofeedback 25(10):4–23

Lubar JF, Swartwood MO, Swartwood JN, O'Donnell PH (1995) Evaluation of the effectiveness of EEG training for ADHD in a clinical setting as measured by TOVA scores, behavioral ratings, and WISC-R performance. Biofeedback&Self-Regulation, 20(1):83–99

Lubar JF (1997) Neurobiological foundation for neurofeedback treatment of attention deficit hyperactivity disorder (ADD/HD). Biofeedback 25(10):4–23

Malone RP, Maislin G, Choudhury MS, Gifford C, Delaney MA (2002) Risperidone treatment in children and adolescents with autism: short-and long-term safety and effectiveness. Journal of the American Academy of Child & Adolescent Psychiatry, 41(2):140–147

Mariani P, Viti MG, Montuori M, La Vecchia A, Cipolletta E, Calvani L, Bonamico M (1998) The gluten-free diet: a nutritional risk factor for adolescents with celiac disease? J Pediatr Gastroenterol Nutr 27:519–523

Martin A, Scahill L, Klin A, Volkmar FR (1999) Higher functioning pervasive developmental disorders: Rates and patterns of psychotropic drug use. Journal of the American Academy of Child and Adolescent Psychiatry, 38:923–931

Martin A, Koenig K, Anderson GM, Scahill L (2003) Low-dose fluvoxamine treatment of children and adolescents with pervasive developmental disorders: a prospective, open-label study. J Autism Dev Disord 33:77–85

McAlonan GM, Cheung V, Cheung C, Suckling J, Lam GY, Tai KS, Yip L, Murphy DGM, Chua SE (2005) Mapping the brain in autism: a voxel-based MRI study of volumetric differences and intercorrelations in autism. Brain 128:268–276

McCandless J (2005) Children with starving brains: a medical treatment guide for autism spectrum disorders. Bramble Books, Putney

McDougle CJ, Kresch LE, Goodman WK, Naylor ST, Volkmar FR, Cohen DJ, Price LH (1995) A case-controlled study of repetitive thoughts and behavior in adults with autistic disorder and obsessive-compulsive disorder. Am J Psychiatry 152:772–777

McDougle CJ, Naylor ST, Cohen DJ, Volkmar FR, Heninger GR, Price LH (1996) A double-blind, placebo-controlled study of fluvoxamine in adults with autistic disorder. Arch Gen Psychiatry 53:1001–1008

McDougle CJ, Brodkin ES, Naylor ST, Carlson DC, Cohen DJ, Price LH (1998) Sertraline in adults with pervasive developmental disorders: a prospective open-label investigation. J Clin Psychopharmacol 18:62–66

McDougle CJ, Kresch LE, Posey DJ (2000) Repetitive thoughts and behavior in pervasive developmental disorders: treatment with serotonin reuptake inhibitors. J Autism Dev Disord 30:427–435

McEachin JJ, Smith TH, Lovaas OI (1993) Long-term outcome for children with autism who received early intensive behavioral treatment. Am J Ment Retard 97:359–391

Monastra VJ, Lynn S, Linden M, Lubar JF, Gruzelier J, La Vaque TJ (2005) Electroencephalographic biofeedback in the treatment of attention-deficit/hyperactivity disorder. Appl Psychophysiol Biofeedback 30:95–114

Montgomery DL, Goldberg J, Amar M, Lacroix VJ, Lecomte JM, Lambert J, Vanasse M, Marois P (1999) Effects of hyperbaric oxygen therapy on children with spastic diplegic cerebral palsy: a pilot project. Undersea Hyperb Med 26:235–242

Mountz JM, Tolbert LC, Lill DW, Katholi CR, Liu H-G (1995) Functional deficits in autistic disorder: characterization by technetium-99 m-HMPAO and SPECT. J Nucl Med 36:1156–1162

Nakano K, Noda N, Tachikawa E, Urano M, Miyuki T, Nakayama T, Sasaki K, Osawa M (2005) A preliminary study of methylcobalamin therapy in autism. J Tokyo Women's Med Univ 75:64–69

National Institute of Mental Health (2006) Autism spectrum disorders (pervasive developmental disorders). Retrieved 12 Feb 2010 from http://www.nimh.nih.gov/health/publications/autism/complete-index.shtml

Nighoghossian N, Trouillas P, Adeleine P, Salord F (1995) Hyperbaric oxygen in the treatment of acute ischemic stroke. Stroke 26:1369–1372

Oberman LM, Hubbard EM, McCleery JP, Altschuler EL, Ramachandran VS, Pineda JA (2005) EEG evidence for mirror neuron dysfunction in autism spectrum disorders. Cogn Brain Res 24:190–198

Ohnishi T, Matsuda H, Hashimoto T, Kunihiro T, Nishikawa M, Uema T, Sasaki M (2000) Abnormal regional cerebral blood flow in childhood autism. Brain 123:1838–1844

Owley T, Walton L, Salt J, Guter SJ Jr, Winnega M, Leventhal BL, Cook EH Jr (2005) An open-label trial of escitalopram in pervasive developmental disorders. J Am Acad Child Adolesc Psychiatry 44:343–348

Ozonoff S, Cathcart K (1998) Effectiveness of a home program intervention for young children with autism. J Autism Dev Disord 28:25–32

Pelphrey K, Adolphs R, Morris JP (2004) Neuroanatomical substrates of social cognition dysfunction in autism. Ment Retard Dev Disabil Res Rev 10:259–271

Pineda JA, Hecht E (2009) Mirroring and mu rhythm involvement in social cognition: are there dissociable subcomponents of theory of mind? Biol Psychiatry 80:306–314

Rangaswamy M, Porjez B, Chorlian DB, Wang K, Jones KA, Bauer LO, Rohrbaugh J, O'Connor SJ, Kuperman S, Reich T, Begleiter H (2002) Beta power in the EEG of alcoholics. Biol Psychiatry 52:831–842

Reichelt K (2001, October) Opioid peptides. Paper presented at the defeat autism now conference, San Diego, CA

Reichelt K, Knivsberg AM (2003, October). Why use the gluten-free and casein-free diet in autism and what the results have shown so far: Peptides and autism. Paper presented at the defeat autism now conference, Portland, OR

Research Units on Pediatric Psychopharmacology Autism Network (2005) Risperidone treatment of autistic disorder: longer-term benefits and blinded discontinuation after 6 months. Am J Psychiatry 162:1361–1369

Rimland B, Edelson SM (2000) Autism treatment evaluation checklist (ATEC). Autism Research Institute, San Diego

Rippon G, Brock J, Brown CC, Boucher J (2007) Disordered connectivity in the autistic brain: challenges for the 'new psychophysiology'. Int J Psychophysiol 63:164–172

Rossignol DA, Rossignol LW (2006) Hyperbaric oxygen therapy may improve symptoms in autistic children. Med Hypotheses 67:216–228
Rossignol DA, Rossignol LW, James SJ, Melnyk S, Mumper E (2007) The effects of hyperbaric oxygen therapy on oxidative stress, inflammation, and symptoms in children with autism: an open-label pilot study. BMC Pediatr 7:36
Santangelo SL, Tsatsanis K (2005) What is known about autism: genes, brain, and behavior. Am J Pharmacogenomics 5:71–92
Schmitz N, Rubia K, Daly EM, Smith AB, Williams SCR, Murphy DGM (2006) Neural correlates of executive function in autistic spectrum disorders. Biol Psychiatry 59:7–16
Schopler E, Reichler RJ (1971) Parents as cotherapists in the treatment of psychotic children. J Autism Child Schizophr 1:87–102
Schopler E, Reichler RJ, DeVellis RF and Daly K (1980) Toward objective classification of childhood autism: Childhood Autism Rating Scale (CARS). Journal of Autism and Developmental Disorders 10(1):91–103
Sicile-Kira C (2004) Autism spectrum disorders: the complete guide to understanding autism, Asperger's syndrome, pervasive developmental disorder, and other ASDs. Berkley Publishing Group, New York, NY
Siegel B (1996) The world of the autistic child: understanding and treating autistic spectrum disorders. Oxford University Press, New York, NY
Sinha Y, Silove N, Williams K (2006) Chelation therapy and autism. BMJ 333:756
Starkstein SE, Vazquez S, Vrancic D, Nanclares V, Manes F, Piven J, Plebst C (2000) SPECT findings in mentally retarded autistic individuals. J Neuropsychiatry Clin Neurosci 12:370–375
Stoller KP (2005) Quantification of neurocognitive changes before, during, and after hyperbaric oxygen therapy in a case of fetal alcohol syndrome. Pediatrics 116:e586–e591
Tansey MA (1993) Ten year stability of EEG biofeedback results for a 10 year old hyperactive boy who failed fourth grade in a class for the perceptually impaired. Biofeedback Self Regul 18:33–44
Thompson M, Thompson L (2003a) The neurofeedback book: an introduction to basic concepts in applied psychophysiology. Association for Applied Psychophysiology and Biofeedback, Wheat Ridge, CO
Thompson L, Thompson M (2003b) Neurofeedback treatment for autistic spectrum disorders: review of 60 cases-principles and outcome. Citation paper presented at the 34th annual meeting of the Association for Applied Psychophysiology and Biofeedback, Jacksonville, FL, March.
Troost PW, Lahuis BE, Steenhuis M-P, Ketelaars CEJ, Buitelaar JK, van Engeland H, Scahill L, Minderaa RB, Hoekstra PJ (2005) Long-term effects of risperidone in children with autism spectrum disorders: a placebo discontinuation study. J Am Acad Child Adolesc Psychiatry 44:1137–1144
Vancassel S, Durand G, Barthélémy C, Lejeune B, Martineau J, Guilloteau D, Andrès CR, Chalon S (2001) Plasma fatty acid levels in autistic children. Prostaglandins Leukot Essent Fatty Acids 65:1–7
Wainwright PE (2002) Dietary essential fatty acids and brain function: a developmental perspective on mechanisms. Proc Nutr Soc 61:61–69
Welchew DE, Ashwin C, Berkouk K, Salvador R, Suckling J, Baron-Cohen S, Bullmore E (2005) Functional disconnectivity of the medial temporal lobe in Asperger's syndrome. Biol Psychiatry 57:991–998
Yucha C, Montgomery D (2008) Evidence-based practice in biofeedback and neurofeedback. Association for Applied Psychophysiology and Biofeedback, Wheat Ridge
Zilbovicius M, Boddaert N, Belin P, Poline J-B, Remy P, Mangin J-F, Thivard L, Barthélémy C, Samson Y (2000) Temporal lobe dysfunction in childhood autism: a PET study. Am J Psychiatry 157:1988–1993
Zuddas A, Di Martino A, Muglia P, Cianchetti C (2000) Long-term risperidone for pervasive developmental disorder: efficacy, tolerability, and discontinuation. J Child Adolesc Psychopharmacol 10:79–90

Biography

Robert Coben, Ph.D., received his doctoral degree in 1991 and has been a licensed psychologist in the state of New York since 1994. He is the director and chief neuropsychologist of NeuroRehabilitation and Neuropsychological Services. His post doctoral training in clinical and rehabilitation neuropsychology was done at the UCLA Medical Center and Cedars-Sinai Medical Center in California. His experience in rehabilitation neuropsychology includes directing two separate inpatient neurorehabilitation programs. He is former director of inpatient and outpatient brain rehabilitation at Staten Island University Hospital. He is an affiliate of Winthrop University Hospital and an affiliated researcher of NYU Medical Center.

Dr. Coben is a member in good standing of the American Psychological Association, International Neuropsychological Society, International Society for Neurofeedback and Research, and the American Association of Psychophysiology and Biofeedback. He is an associate editor for the Journal of Neurotherapy and Frontiers in Child Health and Human Development. He is also an editorial reviewer for the following journals: Journal of Neurotherapy, Journal of Autism and Developmental Disorders, Frontiers in Child Health and Human Development, Clinical Neurophysiology, Neuroimage, and Journal of Psychophysiology. He has edited special issues of journals on EEG Connectivity and more recently an upcoming issue on Applied Neuroscience, Neuromodulation and Neurofeedback. He has also edited a book entitled Neurofeedback and Neuromodulation Techniques and Applications. His research interests include the study of neuropsychology and neurophysiology in the understanding of childhood neurodevelopmental disorders, especially autism, and treatment applications for the same.