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Chapter 3
QEEG-Guided Neurofeedback for Autism: Clinical Observations and Outcomes

Michael Linden and Jay Gunkelman

3.1 QEEG-Guided Neurofeedback

During the more than 40 year history of EEG biofeedback, now also called neurofeedback (NF), the approach has been used clinically to address attentional problems in attention deficit-hyperactivity disorder (ADHD). Initially, NF was based on the theta/beta ratio, which was measured with eyes open, at the vertex, or the Cz electrode in the International 10–20 Electrode placement system. Generally, the early NF work was based on enhancing beta and reducing the slower theta content (Monastra et al. 1999).

In a review article of NF studies with ADHD spanning 1976-2004, NF provided clients who learn the control of the EEG using NF improvements in hyperactivity, attentional control, impulsivity, and even improved IQ scores (Monastra et al. 2005). This was also confirmed in a more recent meta-analysis of NF in ADHD applications (Arns et al. 2009).

The efficacy of NF in ADHD is now considered well established based on the peer-reviewed published research studies. The efficacy is based on the design characteristics and predictive power of the studies reviewed, including features like the use of matched controls, randomization into treatment condition, independent replication, and improvement in both behavioral and physiological measures. The conclusion was not merely that NF was effective at treating ADHD, but based on the studies' effect sizes, it was a more powerful intervention than medications were.

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However, most of the NF studies these conclusions were based upon did not use a full QEEG to guide the intervention, but were either based on a standard protocol or based on single-channel ratio-based metrics. Interestingly, there is much less literature support for QEEG-guided protocols than for behaviorally or symptom-based approaches.

3.2 Epilepsy and NF

NF applications for epilepsy have a long and well-proven efficacy since the 1960's showing that NF can reduce and occasionally eliminate epileptiform activity in the EEG and the convulsions seen behaviorally. These positive outcomes are seen even in intractable epilepsy where medications have not proven effective (Sterman et al. 1974; Kotchoubey et al. 2001).

In epileptic clients, the literature is more supportive of the use of a full 19-electrode EEGs and even QEEG analysis, with most of Sterman's more recent human research based on the full EEG/QEEG. The American Academy of Neurology and the American Clinical Neurophysiology Society both support the use of QEEG analysis of the EEG in epilepsy and evaluation of epileptiform discharges, including spike dipole analysis and spectral analysis (Nuwer 1997).

Generally in NF the spectral features of the epileptiform discharges are targeted for suppression, with either sensorimotor rhythm (SMR) or slow cortical potential (SCP) based NF training done (Sterman 2000).

3.3 PDD/Autism Treatment Emerges from Attention and Epilepsy Success

In NF there are many who use the technique to help normalize EEG features and will apply the NF experimentally to many disorders, and some practitioners do not even refer to diagnostic issues, but rather are oriented to EEG optimization without the pejorative of a diagnosis.

In autistic spectrum disorders (ASD) and pervasive developmental disorders (PDD), attentional and hyperactivity complaints are common, and the incidence of paroxysmal "epileptiform" discharges in the EEG is estimated at over 40 % conservatively (Gabis et al. 2005), with some suggesting even higher rates of paroxysmal activity. Given the history of success in self-regulation for clients who have epileptiform activity, as well as attentional regulation, many have tried to work with PDD/ASD, as reviewed recently (Coben et al. 2010; Haines and Colletti 2012).

The NF treatment is not specific to autism, but rather oriented to optimizing the brain function each client already has, whether it presents with epileptiform content or rhythmic alterations more like ADHD, anxiety or learning disabilities. The ultimate goal of applying NF to ASD is to improve brain functioning while minimizing side effects. Improvement in brain function can lead to easier success with other therapies, such as those approaches that focus on speech, aggressive behavior, and social skills.

If we use an appropriately conservative perspective with respect to efficacy claims, then NF must be seen as an emerging application, not an established technique for treating ASD with a proven efficacy literature. This is especially true if you use the efficacy criteria adopted by the NF field. These newer emerging applications obviously require further research, with stronger research designs, before claims of actual clinical efficacy can be made (La Vaque et al. 2002).

Even with the conservative perspective held by many in the field, clinical interest in the use of neurofeedback for ASD has been heightened by several case series and some small studies which all showed very promising results (Jarusiewicz 2002; Coben and Hudspeth 2006; Coben et al. 2010; Thompson et al. 2010). Linden is one of the primary investigators in a current study comparing QEEG-guided versus standard NF with students with ASD. Linden's research over the past decade has measured the effects of NF on not only QEEG measures, but intelligence (IQ), attention, hyperactivity and diffuse tensor imaging (DTI), a structural measure of connectivity.

3.4 QEEG-Guided NF for Autism Spectrum Disorder

To understand the QEEG-guided NF approach that we recommend for ASD clients, it is important to first recognize that the practice of NF has evolved dramatically over the past 40 years, as stated above. In the early days, NF was based on symptoms alone, without QEEG guidance. This symptom-driven protocol approach was fraught with problems, including unexpected session outcomes, iatrogenic effects in clients, and protocol redesigns that often appeared to be merely random second-guessing.

Given the variance seen in the underlying pathophysiology of ASD clients, it seems rational to expect that any treatment guided by nothing more than symptomatology will eventually be problematic. QEEG subtype analysis and well-designed NF interventions resolved many of these problems. This modern approach to NF in ASD based on measurements of bioelectrical behaviors matches well with cortical areas of the brain that correspond to the behavioral mechanisms seen in most developmental disorders.

Importantly, it became apparent to those looking at the QEEG in autism that there were many different "subgroups" of EEG findings, rather than a single underlying EEG presentation. This heterogeneity is especially true for the complex spectrum of clinical findings often referred to as the "autisms." In more recent years, researchers and clinicians have begun to develop a system of doing NF protocols based on genetically correlated clusters of EEG findings.

Gunkelman had hypothesized that these EEG clusters might be based on underlying genetics and these resultant endophenotype clusters will respond as a group to specific medications and/or to specific NF interventions (Johnstone et al. 2005).

The therapeutic approach which will provide efficacious intervention is predicted by the endophenotype(s) which the client manifests. Thus, the EEG phenotype selects the protocol and this protocol prediction system enhances the clinical outcome.

3.5 Subtypes or Endophenotypes

The EEG/QEEG can be used to identify the endophenotype(s) involved in any individual's EEG. There is a high inter-rater reliability, generally over 90 % concordance in untrained raters. There are a limited number of phenotypes (11), and they predict almost all of the variance in the EEG (Johnstone et al. 2005). The original phenotype paper was based on retrospective modeling, though the model now has prospective validation done in both medication prediction, such as predicting stimulant efficacy in ADHD, and NF outcomes, as seen in the current QEEG-guided NF studies (Arns et al. 2009). These EEG phenotypes predict effective treatment approaches independent of the DSM diagnosis, as seen in the phenotype paper on addiction treatment outcomes (Gunkelman and Cripe 2008).

Others also evaluated EEG subgroups associated with clinical DSM groupings. Chabot and others at NYU (Chabot et al. 1996) first identified two EEG-based subtypes in children with ADHD: (1) excess theta and (2) excess alpha. These subgroups predicted medication efficacy. In later work they also added "excessive beta" as they broke the initial two groupings into even more subgroups. Interestingly, in our experience this beta subtype one of the most common subtypes present in those with ASD, usually does not respond well to stimulant medications, or to NF protocols which are stimulating, as predicted in the phenotype model.

John and Prichep at NYU have also done cluster analysis in DSM groupings, gaining insight into the pathophysiology of various conditions, such as obsessive-compulsive disorder (OCD). In the DSM, there is only one form of OCD. Cluster analysis found a slow cluster which was not SSRI responsive and an alpha cluster that was SSRI responsive. Gunkelman has seen beta spindles as another cluster, and this group has a negative response to SSRI, not merely a lack of clinical response. The neurometric approach was also used to identify clusters in normal population within the Nx-link database of normal subjects developed by John and Prichep. A database of normal subjects is comprised of individuals with all phenotypes mixed into a grand average of the groups.

Identifying clusters in ADHD was also done by Chabot and Prichep, when they analyzed their approximately 400 ADHD clients from earlier work (Chabot et al. 1996). In their later work, they found 11 clusters within the heterogeneous ADHD clinical group. More recently, we found that the EEG clusters predicted medication response in ADHD to stimulants (Arns et al. 2008), with the slower frontal cluster responding to dopamine reuptake inhibitors.

3.5.1 Endophenotypes Seen in Autism

Early in the application of NF to the autisms, a series of cases was passed through a single EEG laboratory. The presence of a variety of clusters was identified by Gunkelman, and this was discussed with others in the field, including Linden. The phenotypic clusters were initially only observed as general groupings, and only later

was their rate or incidence actually estimated and presented in talks and workshops between 2004 to 2013 at various scientific meetings. Linden's current research at UC San Diego is gathering additional data on these endophenotypes' prevalences.

The presence of slow EEG activity, frequently delta activity, was commonly reported in autism, as also seen in some with learning disabilities. This makes rational sense when seen as evidence of white matter disturbance(s), commonly observed in many clients with an autism spectrum diagnosis. More recently, researchers have seen white matter disturbances with DTI that provides better images of white matter than a static MRI scan (Groen et al. 2011). In Linden's clinical experience, ASD individuals, especially those younger having abnormally high delta activity, often were very active, impulsive, and at times aggressive.

Epileptiform paroxysms are common in autisms, as noted earlier in this chapter. In our experience the distribution of the EEG spectral disturbance often correlates directly with the clinical presentation. Left hemispheric involvement is more likely to involve language disturbances, and if the discharges are seen within the right hemisphere, then a more Asperger syndrome-related presentation is more likely clinically. Frontal discharges often disturb the higher functions of attentional and affective regulation and more posterior and parietal discharges involving disturbances of sensory processing.

Beta spindles are very common in autism, and as classically seen in EEG since initially described by Frederic Gibbs (Stone and Hughes 1990), they represent an easily kindled or irritable cortex with a lower threshold for discharges. This may be seen as sensory hypersensitivity with beta spindles present more posteriorly and parietally in the sensory cortex, though other symptoms appropriate to the cortical regions involved are also seen, such as behavioral explosiveness and difficulty with emotional gating with a right frontal beta spindle distribution. According to Linden's clinical experience and research, this endophenotype pattern often correlates with anxious, overfocused, perseverative and obsessive behaviors.

Temporal changes such as slower content or alpha which suggest a local disturbance may impact language function on the left as well as verbal memory function. The right temporal changes are associated with spatial, prosodic, and nonverbal comprehension and memory functions, such as facial expression, body language, and other emotional contextual perception and comprehension tasks; this right temporal emphasis is commonly seen in individuals with Asperger syndrome. Auditory cortex is deeply embedded temporally at the temporal-parietal junction, and occasionally these areas may also be involved associated with temporal findings.

Mu rhythm (Mu) is seen centrally in a disproportionate percentage of clients with autism, estimated as high as 70 % (Pineda et al. 2008). In Pineda's work, Mu is seen as an effect of a fronto-central disconnection associated with the mirror neuron system. When there are mirroring behaviors, Mu desynchronizes and is not seen in the spectral displays in the EEG waveforms. Though Mu is not considered evidence of any neurologically specific issues such as a lesion, demyelination, and vascular issue, it does suggest a functional disturbance. As classically observed in EEG, Mu is eliminated with even the intent to move.

Low-voltage slow EEGs are seen in a minority of those with autism, and though not specific, in EEG the finding is classically associated with toxic or metabolic encephalopathies, and these clients seem to respond well to medical management such as with methyl-B12, chelation and hyperbaric oxygen and rarely even have been seen to have thyroid or immune system disturbances (Neubrander et al. 2012). Theoretically, this low voltage may be related to environmental factors such as vaccines, pollution, and pesticides.

Coherence changes have been seen in autism, suggesting possible connectivity issues, and these also appear to reflect the symptoms of the client with fronto-central changes associated with the findings of Mu and the right and left temporal changes reflecting language or emotional comprehension presentations clinically. Both hypercoherence and hypocoherence may be observed.

3.5.2 The Incidence of Phenotypes

Recently, we used EEG/QEEG to estimate the prevalence of these subtypes in children with autism. In our experience, the excess beta spindling phenotype or subtype is the most common (70 %). The beta spindles seen in the phenotype model are identified both visually and in spectral analysis. Coherence changes are also commonly observed (70 %). Paroxysmally abnormal EEGs are seen in about 40 % of cases, with epileptiform spike activity more common than many may assume merely by looking at the incidence of convulsions in this population. As mentioned, the excessive slow content is common, with an estimated incidence of 30 % in autism. The low-voltage slow pattern suggesting toxic or metabolic issues comprises only 10 % of the cases in our population.

Coben and colleagues (2012) recently showed five "subtypes" in the cases they researched in autism. They used relative EEG power and looked at 91 individuals on the autism spectrum and 310 normal controls. They report excesses of beta and alpha in about one-fourth of the ASD sample (26.5 % and 25.3 %); they have also described subtype patterns of coherence or connectivity.

3.6 Predictive Validity

Obviously, EEG patterns are not simplistic, and linear models of real brain function are not even close to a proper reflection of reality. Even with our EEG-based endophenotype approach, more than one pattern is commonly evident. The search for a single biomarker in the ASD is no longer a realistic expectation. In the presence of a variety of findings, the important feature of any model explaining the observed findings is that it must have some predictive validity. The model should at least predictively correlate with symptoms and preferably also with the proper treatment approach to deal with the symptoms and their underlying neurophysiology.

On a case basis, the EEG phenotypes seem to correlate well with each individual's clinical presentation, and even though these phenotypic clusters cut across the DSMIV-TR categories and are not considered diagnostically specific, this phenotype framework can be used to guide a personalized approach to medicine or NF through its ability to predict treatment responses (Johnstone et al. 2005; Gunkelman 2006; Arns et al. 2008).

The phenotype model was tested in ADHD with the goal of predicting stimulant medication efficacy. The phenotype model was shown to be predictive of effective response for stimulant medication in the children, with 49 ADHD subjects studied against 49 matched controls (Arns et al. 2008). The phenotype approach has also been used in other DSM applications effectively to predict effective treatment approach.

3.7 QEEG-Guided Neurofeedback

QEEG-guided NF normalizes poorly regulated brain regions that are the neural representation of specific clinical presentations (Arns et al. 2008, 2009). With ASD, this means that the treatment approach is personalized to match each individual's phenotypic pattern(s) and clinical presentation. The goal of the initial NF with ASD is to correct amplitude abnormalities and balance brain functioning. Following these initial interventions, many of the coherence findings will have normalized, though some areas may remain either hyper- or hypocoherent. These remaining findings, which were resistant to initial interventions, are then subjected to coherence neurofeedback, which is intended to improve the connectivity and plasticity between brain regions where residual changes in coherence remain.

When treating clients with conditions as heterogeneous as autism, obviously an EEG/QEEG baseline is required to properly designing a personalized NF treatment plan. The QEEG identifies a client's phenotype pattern(s). Using those patterns to guide subsequent neurofeedback or medication management, it becomes possible to develop a customized NF treatment approach that normalizes and optimizes each individual's EEG.

These tailored interventions have protocol-specific effects, such as left temporal lobe interventions affecting speech and language communication, right temporal interventions affecting social and emotional functions, and frontal interventions influencing attention, and central and posterior abnormalities can influence sensory and motor functions. Our specific outcomes clinically include significant speech and communication improvement, less aggressive behavior, calmer demeanor, increased attention, improved eye contact, and increased socialization. Many of our clients have generally been able to reduce or eliminate their medications following completion of NF based on the phenotype model, with the exception of anticonvulsant medication in some with residual paroxysms. This is not unexpected because currently there is no medication that has been specifically developed for ASD.

3.8 Not All *Z*-Score Outliers Are Abnormal

EEG results are compared with a normative reference population to evaluate which measured values differ from the mean values. Due to the plethora of statistical comparisons done when processing an EEG through the QEEG databases, it is highly likely that divergence from the mean will be seen merely due to multiple statistical comparisons. This is especially true as the categories that we evaluate quantitatively increase: now including not merely absolute and relative power and connectivity but also bursts metrics, multivariate analysis, and many other features. With this increase in statistical manipulation and lack of correction for these rapidly expanding number of metrics, when we see a divergence it is most important to focus on the validity of any given divergence, as the statistical likelihood of a random outlier has dramatically increased. Patterns of deviation are needed when correction for multiple comparison is not performed in order to assure any observed deviation is a real outlier and not due to the statistical manipulations.

Aside from the reliability of the EEG sampled for analysis, the underlying validity of the findings is also critical. Although a statistical divergence may be associated with an actually abnormal finding, there are two other possibilities. Divergent values also may be due to:

1. A compensatory mechanism that helps the brain with another abnormal feature
2. A unique skill or performance state that is not compensatory for any other finding (such as very fast alpha and superior declarative memory performance or EEG changes associated with meditation)

3.9 CNS Arousal and Frequency "Tuning"

Databases are not very adept at describing divergence when the usual banded activity shifts outside an expected frequency range. There are multiple statistical divergences seen due to frequency drifting outside normally expected ranges. As an example, a normal amount of power and coherence seen as a normal pattern of alpha, if merely slowed to 7 Hz without coherence or power alterations, will be seen as excessive theta (not slowed alpha) and as hypercoherent (when coherence was not altered), merely due to the database's expectation of the alpha power and coherence pattern at a higher frequency range. The database will not say that this is a frequency issue but that the coherence and power pattern is in a normative range. The databases will say the content is hypercoherent and that there is excessive power in theta. In this case, the statistical divergences in coherence and power would be distractions from the real task of speeding up the 7 Hz slowed alpha activity.

Shifts in the underlying frequency tuning in the EEG are described as a phenomenon called "brain-rate." This term is coined and mathematically defined by Pop-Jordanov of the Macedonian Academy of Science and Art (Pop-Jordanova and Pop-Jordanov 2005). The frequency shifts are associated with variations in the CNS arousal level.

These frequency-shift-related statistical divergences which are not meaningful may even be directly a distraction from the real issue. This shows that for the clinician the important task is to track both clinical and behavioral changes during training and correlate these with the EEG/QEEG findings. The clinician's oversight assures that the features being normalized with neurofeedback were actually more than just statistical outliers and that the findings are not merely compensatory, in which case the client's presentation would worsen with the neurofeedback.

The use of QEEG-based NF with ASD is becoming a highly personalized and apparently successful treatment option to address the behaviors we see impacted by these disorders, and this approach continues to be very promising to deal with undiagnosed epileptiform activity, speech and communication, aggressive behavior, irritability, poor attentional skills, poor eye contact, and impaired socialization that comprise much of autism spectrum's clinical presentation.

The addition of QEEG-directed NF to the clinical armamentarium has given a significant percentage of our patients the ability to begin moving on the road to recovery, and improvements are seen in the majority of clients with ASD. Many of them have gone much farther than they would have ever been expected to with the other treatments available. This is especially true if we were without the insight into the client's pathophysiology associated with their individual presentation which the QEEG provides. This is especially clear with the identification of epileptiform findings when they are unexpected due to absence of behavioral convulsion.

Cases with episodes of epileptiform "subclinical seizures," if and when identified, suggest a clinical trial of anticonvulsant medication or appropriate NF, even with cases that do not have a history of convulsive seizure activity. This would never be the case without the insight the EEG/QEEG testing provides. Historically, only children with documented convulsive activity are prescribed anticonvulsants. The approximate 40 % of cases with autism which have epileptiform content would seldom have received appropriate anticonvulsant medication without these findings. The use of anticonvulsant medication is becoming more accepted for children on the autism spectrum who do not have convulsions but who have paroxysmal EEG brain wave activity to at some point be given a clinical trial of anticonvulsant therapy, especially when other treatments are not producing positive results. It is not uncommon for parents to report that the addition of an anticonvulsant medication or appropriate NF protocol to their child's treatment regimen resulted in increased language, better vigilance, improved attention, cognition, and positive behavioral changes as the EEG function normalizes.

Through the use of EEG/QEEG, we are now more successful in choosing appropriate treatment approaches and protocols which are personalized for each client. Through the knowledge of the client's phenotype(s), we have been able to target specific treatments rather than "blindly prescribing" a clinical approach based on behavior alone, as is commonly done by those psychiatrists and neurologists who do not obtain EEG/QEEG to help guide their work. The long-term goal of neurofeedback with ASD is to improve brain functioning long-term without side effects. This neurological improvement also leads to better success with other treatments and therapies such as speech, behavior, occupational therapy, and social skills.

3.10 Neurofeedback Research with Autism

3.10.1 Pilot and Case Studies

Two pilot group studies of neurofeedback for ASD have been conducted. In the first (Jarusiewicz 2002), twelve children each were assigned to an experimental or a control group. The experimental group received a mean of 36 treatment sessions (range = 20–69). Treatment protocols were based on standard EEG frequencies and locations. The Autism Treatment Evaluation Checklist (ATEC) (Rimland and Edelson 2000) was used to assess outcome. Children who completed NF training attained an average 26 % reduction in the total ATEC rated autism symptoms in contrast to 3 % for the control group. Parents reported improvement in socialization, vocalization, anxiety, schoolwork, tantrum behavior, and sleep habits, while the control group had minimal changes in these domains. However, the outcome measure used is based on only parent report with no other objective measures utilized.

The second pilot study of the effects of neurofeedback was conducted by Kouijzer et al. (2009a, b). Fourteen children with ASD, seven in the treatment and seven in the wait-list (no treatment) control group, were matched for age, gender, and IQ scores, but were not randomly assigned. The treatment group received 40 sessions of neurofeedback on the right sensory motor strip. Theta activity (4–7 Hz) was inhibited, while sensorimotor (SMR) activity (12–15 Hz) was rewarded. Pre- and posttreatment assessment consisted of EEG learning curves, QEEG analyses, tests of executive functioning, and behavior rating scales (CCC-2, Dutch Autism Scale). The findings showed that the neurofeedback-trained group demonstrated significant improvement in attentional control, cognitive flexibility, and goal setting compared to the control group. Results of parent rating scales also showed improvements in social interaction and communication skills. These changes were associated with improvements in EEG learning curves.

Interestingly, this same research group performed a 12-month follow-up of the treated patients with ASD (Kouijzer et al. 2009a). Both changes in executive functioning and behavior were maintained suggesting that neurofeedback may have long-lasting effects for children with autism as it has been shown by Lubar (1991) and Monastra et al. (2005) to have with students with ADHD. These pilot studies have shown positive results, but caution should be exercised as their sample sizes were quite small. Nevertheless, the optimism regarding their findings has led to more controlled research with larger sample sizes.

3.10.2 Controlled Group Studies of Neurofeedback for ASD

In the largest published, controlled study to date of neurofeedback for autistic disorders, Coben and Padolsky (2007) studied 49 children on the autistic spectrum. The experimental group included 37 children that received QEEG-guided neurofeedback

(20 sessions performed twice per week), and the wait-list control group included 12 children that were matched for age, gender, race, handedness, other treatments, and severity of ASD. A broad range of assessments were utilized including parental judgment of outcome, neuropsychological tests, behavior rating scales, QEEG analyses, and infrared imaging. Treatment protocols were assessment based (including QEEG power and coherence) and individualized for each child receiving neurofeedback training with a specific focus on the remediation of connectivity anomalies. Based on parental judgment of outcome, there was an 89 % success rate for neurofeedback and an average 40 % reduction in core ASD symptomatology based on parent rating scales. There were also significant improvements, as compared to the control group, on neuropsychological measures of attention, executive functioning, visual-perceptual processes, and language functions. Reduced cerebral hyperconnectivity was associated with positive clinical outcomes in this population. In all cases of reported improvement in ASD symptomatology, positive outcomes were confirmed by neuropsychological and neurophysiological assessment. The benefit to harm ratio, which is regularly utilized to determine if a treatment is successful and safe, was 91:1, the highest of any treatment for ASD studied to date.

Two studies have focused on abnormal Mu rhythms (previously discussed) (Oberman et al. 2005) in children with autism with neurofeedback. In a series of two experiments, Pineda and colleagues (Pineda et al. 2008) studied 27 children with high-functioning autism. In study 1, eight high-functioning males were randomly assigned to an experimental ($n=5$) or placebo ($n=3$) group. One subject dropped out of the experimental group midway through the training. Neurofeedback training included 30 thirty-minute sessions with rewards for Mu-like activity (8–13 Hz) and inhibits for EMG (30–60 Hz) at C4 (right central location). Parent rating scales (ATEC) (Rimland and Edelson 2000) showed small changes (9–13 %) in two of the four experimental participants. These pilot data should be considered preliminary due to the very small sample size.

In the second study, 19 children with high-functioning ASD were randomly assigned to an experimental ($n=9$) or placebo ($n=10$) group. One very positive addition to this study was the verification of their diagnoses by administering the Autism Diagnostic Observation Schedule (ADOS) (Lord et al. 2000) and the Autism Diagnostic Interview–Revised (ADI-R) (Rutter et al. 2003). Neurofeedback training was similar to study one except the reward band was now 10–13 Hz. Parent ratings showed a small but significant reduction in symptoms (ATEC Total score). However, of interest was an increase in ratings of Sensory/Cognitive Awareness in excess of 40 % that did not occur in the placebo control group. According to their parents, participants improved in some areas and worsened in others, and these areas of improvement may be based upon the frequencies and locations trained.

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 the Mu rhythm activity and a failure to suppress Mu during observational activity. They all received assessment-guided (QEEG guided) neurofeedback, with a strong focus on aspects of Mu power and connectivity. The participants were non-randomly

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, 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.

Coben (2008) 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. All patients underwent pre- and post-NF neuropsychological, QEEG, and parent rating scale assessments. Fifty individuals were each assigned equally to an active neurofeedback and wait-list control group, in a nonrandomized 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. QEEG analyses were also significant, showing improvements in connectivity and source localization of brain regions (fusiform gyrus, superior temporal sulcus) associated with enhanced visual/facial/emotional processing.

In the five controlled group studies that have been completed, a total of 180 individuals with autism have been studied with 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 2008). Both Coben and Padolsky (2007), Yucha and Montgomery (2008) and Coben, Linden & Meyer (2010) 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). 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) (Kouijzer et al. 2009b; Coben and Myers 2010).

Pineda and Linden are currently conducting research at the University of California at San Diego (UCSD). They are investigating QEEG, fMRI, and DTI results of both QEEG-guided and Mu neurofeedback in both ASD and typical students. ASD and typical students were all treated with 60 h (45 forty-five minute sessions) of neurofeedback. Some of the students received QEEG-guided neurofeedback and the other half Mu suppression NF. The NF for both groups was administered using consistent scripts utilizing Thought Technology software and hardware. Preliminary results are indicating more significant improvements in DTI (volume)

related to connectivity between brain regions for ASD students compared to typical students. These DTI results would support previous research of improved connectivity in students with ASD from NF.

3.10.3 Limitations

While the findings to date are initially encouraging, there are limitations that prevent firm conclusions. 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 past studies (except the current study at UCSD) 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 effects from a caring professional, or expectations of treatment benefit; however, in the current UCSD study (Pineda and Linden unpublished findings) typical students completed neurofeedback as a control group. A randomized, double-blinded, placebo-controlled study, although complicated and difficult to do, would be optimal to further demonstrate efficacy.

Another unknown is that very young children (less than four years of age) and adults have not been represented, in these studies, so generalization to the current population is not possible. These populations should be also the focus of future research investigations especially because children are currently being diagnosed at before the age of one.

Furthermore, ASD individuals who are lower functioning or who have more severe symptoms associated with autism have not been included in most of the research to date, although clinicians, including the authors, have had successful treatment outcomes. Overall, the use of QEEG to assess subtype patterns of ASD is important in both the diagnosis and treatment selection and success.

3.11 NF Research with ASD Conclusion

Even with the conservative perspective held by many in the field, clinical interest in the use of neurofeedback for ASD has been heightened by several case series and research studies. If an appropriately conservative perspective with respect to efficacy claims is taken, then neurofeedback must be seen as an emerging application. This is especially true if you use the efficacy criteria adopted by the field of neurofeedback. These newer emerging applications obviously require further research, with stronger research designs, before claims of actual clinical efficacy can be made. However, the use of QEEG-guided neurofeedback with ASD is becoming a highly individualized and successful treatment option and continues to be very promising.

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