

26

INFRA-SLOW FLUCTUATION (ISF) TRAINING FOR AUTISM SPECTRUM DISORDERS

Mark Llewellyn Smith, Leo Leiderman, and Jackie de Vries

Abstract

There is growing evidence that the symptoms of Autism Spectrum Disorder have been improved with Infra-slow Fluctuation neurofeedback training. This form of neurofeedback focuses on the slowest oscillations in the human cerebral cortex. These low frequencies have been associated in research with the coordination of neuronal network communication including networks that regulate social, emotional, and sensory processing. Autonomic response was one of the first behaviors linked with ultra-slow frequencies in animal research. The concomitant research and clinical outcomes provide a rationale for the use of ISF training for individuals with Autism Spectrum Disorder.

Recent research suggests that the core symptoms of Autism Spectrum Disorder (ASD), which include restricted reciprocal social interaction, deficits in communication, repetitive behaviors, and sensory sensitivity, are associated with abnormalities in neural connectivity (Billeci et al., 2013; Cantor, Thatcher, Hrybyk, & Kaye, 1986; Coben, Clarke, Hudspeth, & Barry, 2008; Duffy & Als, 2012; Khan et al., 2013; Monk et al., 2009). Disordered connectivity interferes with the normal synchronization of neuronal networks and compromises communication within and between networks of function. This produces abnormal processing of sensory inputs necessary for normal behavior. Altered connectivity within the Default Mode Network has been linked to ASD behavioral deficits, with weaker connectivity between posterior and frontal regions correlated to poorer social functioning and stronger connectivity between posterior and right temporal regions associated with repetitive behaviors (Lynch et al., 2013; Monk et al., 2009). Moreover, the functional rigidity that characterizes hyperconnected brain networks may provide an explanation for the sensory entrapment of the sensitive autistic brain in a painfully intense world (K. Markram & Markram, 2010; H. Markram, Rinaldi, & Markram, 2007).

Neurofeedback as a therapeutic intervention for autism was first reported in a single case study in 1995 that utilized a theta/beta ratio training (Sichel, Fehmi, & Goldstein, 1995). This was followed by several studies whose main protocol was similar (Jarusiewicz, 2002; Kouijzer, de Moor, Gerrits, Buitelaar, & van Schie, 2009; Kouijzer, van Schie, de Moor, Gerrits, & Buitelaar, 2010). The Mu Rhythm was the object of brain training in two recent studies (Pineda et al., 2008; Pineda, Juavinett, & Datko, 2012). Quantitative Electroencephalogram (QEEG) guided neurofeedback for autism began with a small group of children diagnosed with Asperger's Syndrome (Scolnick, 2005). A quantitative analysis determined each child's protocol, a variation of the initial theme of rewarding low beta and

suppressing slower activity. QEEG guided training has been employed to address the remediation of abnormal coherence (Coben, 2007; Coben et al., 2008; Coben & Myers, 2008; Coben & Padolsky, 2007).

Infra-slow Fluctuation (ISF) training is a form of neurofeedback that focuses on the slowest frequencies in cortex. Research proposes that the infra-slow activity is endogenously driven neuronal activity that is crucial in shaping brain network connectivity (Vanhatalo, Voipio & Kaila, 2005). This low-frequency regime has been postulated to coordinate neuronal activity between cortico-cortical networks (Buzsaki, 2006) and play a central role in the control of gross cortical excitability (Hiltunen et al., 2014). Recent research suggests that infra-slow oscillations (ISO) are embedded in and determinant of the excitability cycle of faster frequencies (Ko, Darvas, Poliakov, Ojemann, & Sorensen, 2011; Vanhatalo et al., 2004).

In 1976, Pfurtscheller made the first observations of embedded infra-slow oscillations in the alpha frequency band in the human EEG (Pfurtscheller, 1976). Later studies expanded on this work, identifying fluctuations in the frequencies from 4–30 Hertz that were power-law autocorrelated in time scales from tens to hundreds of seconds. Higher frequencies (100–150 Hz) recorded directly from cortex revealed robust power-law scaling of ISOs in amplitude and coherence (Ko et al., 2011; Linkenkaer-Hansen, Nikouline, Palva, & Ilmoniemi, 2001).

The Default Mode Network (DMN), first labeled and defined by Raichle (Raichle et al., 2001), is theorized to be engaged in the maintenance of a sense of self. This functional definition reflected a key insight of early research that associated elements of the DMN with self-referential processing (Buckner, Andrews-Hanna, & Schacter, 2008; Raichle et al., 2001; Raichle & Snyder, 2007). The Medial Prefrontal Cortex (MPC), part of the DMN, becomes active during the interpretation and prediction of others' beliefs, intentions, and desires, a central deficit in ASD. Additionally, this region becomes active, along with the right Fusiform Gyrus, during facial recognition. Both processes have been linked to core deficits of social and communication impairments.

The DMN has been shown to be characterized by high gamma band coherence at infra-slow frequencies. According to Ko, this “spectral” coherence, similar to comodulation, forms the neuro-physiological basis of the DMN (Ko et al., 2011). More broadly, the phase of the infra-slow activity appears to be coordinated with the excitability cycle of faster frequencies (Monto, Palva, Voipio, & Palva, 2008). Homologous regions of the human cerebral cortex have been described as coordinated by coherent fast and ultra-slow spontaneous rhythmic activity that reflects the communication between and among large-scale functional networks (Liu, Fukunaga, de Zwart, & Duyn, 2010). Noting a similar correlation to the Blood Oxygen Level Dependent signal, researchers have recently concluded that infra-slow frequencies arise from cellular mechanisms including glia, neurons, and blood. These oscillations reflect the same underlying physiological phenomena: a superstructure of interrelating slow activity that coordinates the integration of active neuronal networks (Palva & Palva, 2012).

Poor sensory processing in the autistic brain has a host of consequences. Researchers have theorized that the disorder is characterized by overwhelmingly painful sensory perceptions that are experienced as emotionally charged and traumatic. This painful hyper-perception leads to obsessively detailed information processing of fragments of the world and a defensive decoupling of the autistic individual from a painfully intense world (H. Markram et al., 2007; K. Markram & Markram, 2010).

This excruciatingly extreme sensory world is made more so, according to the researchers, due to a hyper-active amygdala. Citing animal research that suggests Valproic Acid exposed rat off-spring exhibit autistic traits, the researchers identify a hyper-active amygdala as the agent responsible for generating enhanced anxiety and fear processing (K. Markram, Rinaldi, Mendola, Sandi, & Markram, 2007). The amygdala is a central part of neuronal networks that mediate emotional and social behavior. Situated in the temporal lobe, this brain region participates in the interpretation of emotional and socially significant cues in the environment. Responsible for the creation, retrieval, and modulation of fear memory, the amygdala regulates anxiety through the modulation of autonomic and hormonal responses (LeDoux, 2003).

The earliest research observed the infra-slow band to increase in amplitude when subjects were exposed to stress producing stimuli (Aladjalova, 1957, 1964). These researchers theorized that the increase in amplitude of the infra-slow oscillations reflected the Hypothalamus's reparative, parasympathetic response. In addition to organizing neuronal networks, Aladjalova's research suggests that the efficacy of ISF neurofeedback for autism may lie in its impact on the Autonomic Nervous System.

ISF training turns on the selection of an Optimum Frequency for each client. This frequency is chosen through the identification of an autonomic response to the training in session. Peripheral measures of autonomic function such as finger temperature and skin conductance are utilized, as is heart rate variability. These measures and a close scrutiny of emergent state shifts within session guide the clinician through trial and error to a state of autonomic balance. Reductions in anxiety, better affect regulation, improved language skills, and enhanced social interaction are common outcomes for autistic clients treated with ISF training.

Infra-slow Fluctuation training has produced remarkable behavioral successes with ASD clients in a manner consistent with the proposed functional significance of these slow oscillations. Addressing the networks involved with a sense of self, productive language, sensory processing, and social interaction has produced profound changes in behavior. These networks demonstrate significantly improved information sharing in post-treatment QEEGs. Normalization of activation within these functional regions has also been demonstrated in post hoc analysis.

Two case studies follow. The first is a high-functioning person on the Autism Spectrum who might have carried an Asperger's diagnosis before the release of DSM5. The second is a client diagnosed PDD-NOS, a category that has also been subsumed by Autism Spectrum Disorder. These cases are emblematic of ISF training in that both individuals exhibited notable changes in behavior specifically in autonomic arousal, social interaction, and language skills. The brain mapping reveals significant remediation of activation and extraordinary improvements in network information sharing.

Case Study 1

Pt is a 29-year-old single male on the Autism Spectrum with a long history of being non-communicative; limited interpersonal relations; shyness; limited emotional abilities to express self/connect with others; was selectively mute during latency age years and had sensory issues. He was placed in a gifted program in elementary and middle schools, doing well academically in all school settings. In addition he complained of ongoing problems concentrating; confusion; difficulty making decisions; low self-esteem; decrease interest in others; being disorganized; conflict avoidance and being unable to solve personal issues. He has a history of three psychiatric hospitalizations to address increased paranoia and agitation and is being treated with a neuroleptic.

In his initial QEEG brain map hypocoherence was noted in the delta, theta, and alpha bands (Figure 26.1). This disordered neural information sharing was observed telescoping from the right hemisphere regions of the parietal and temporal lobes. Excessive power in theta was evident at 4–7 Hertz with most deviance in bilateral central and temporal lobes (Figure 26.2).

ISF therapy began three times a week for the first month wherein he was optimized with bipolar placements at the bilateral temporal lobes. He then opted to be seen two times a week and had a combined right temporal, right parietal followed by a bilateral temporal lobe ISF therapy protocol. His third protocol first combined the right prefrontal and right temporal lobe, followed by the right temporal and right parietal areas, and finished by training the bilateral temporal regions. At the time of his second QEEG he had received a few sessions of his fourth protocol: right temporal lobe and right lateral frontal lobe, followed by right temporal and right prefrontal, and finished with the right temporal and right parietal areas. His second QEEG, after less than three months of ISF therapy, revealed a near complete normalization of network information sharing (Figure 26.3). The excessive

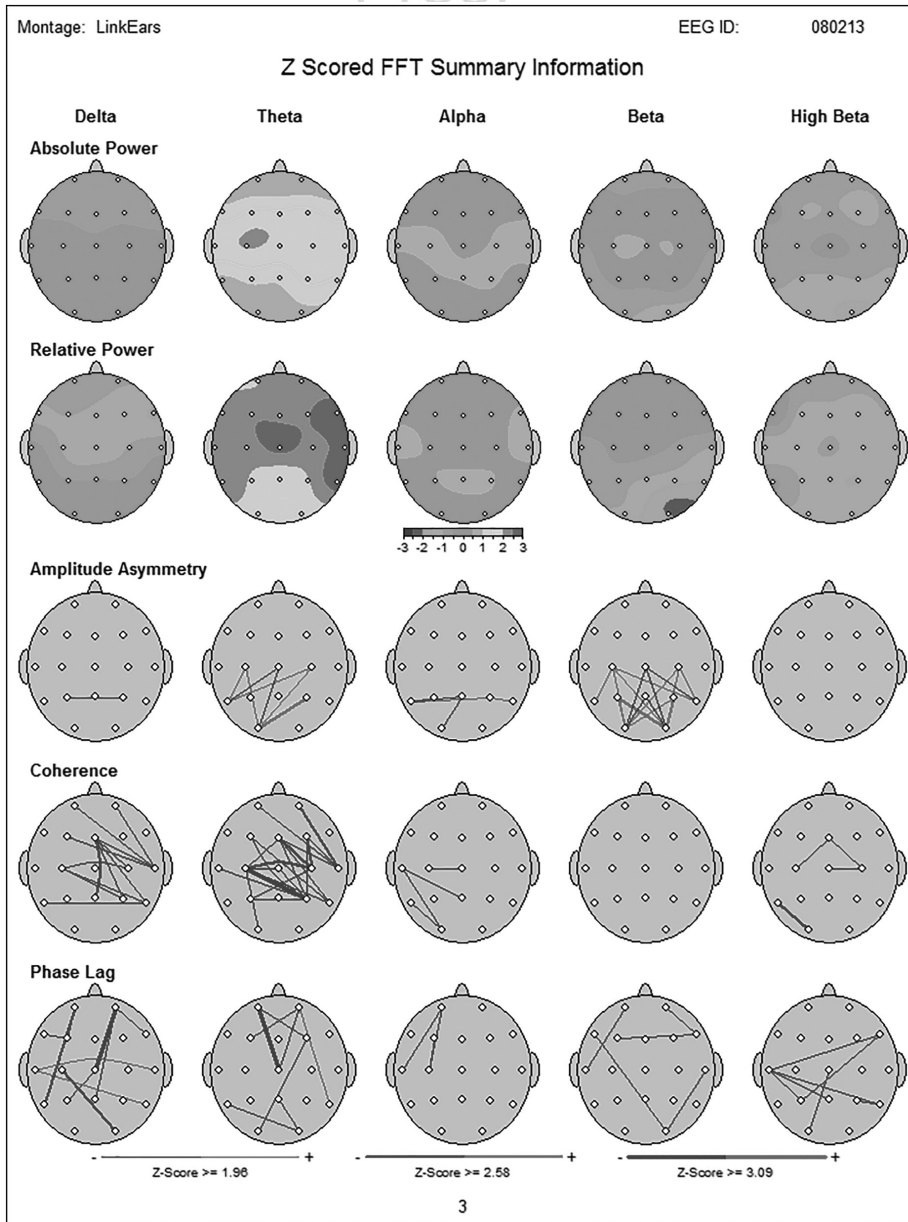


Figure 26.1 Pre-treatment QEEG summary maps. Excess theta band absolute power. Hypocoherence in all bands but the beta band. Most deviance in the delta and theta bands with telescoping hypocoherence from right hemisphere parietal and temporal areas.

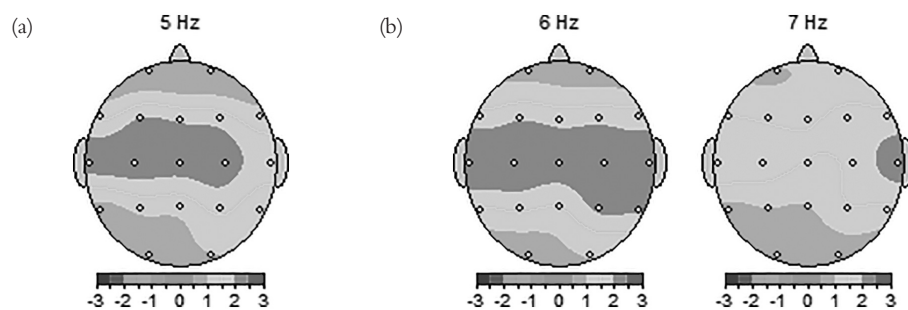


Figure 26.2 Pre-treatment QEEG single Hertz bins revealing near global excess absolute power in the theta band at 5–7 Hertz.

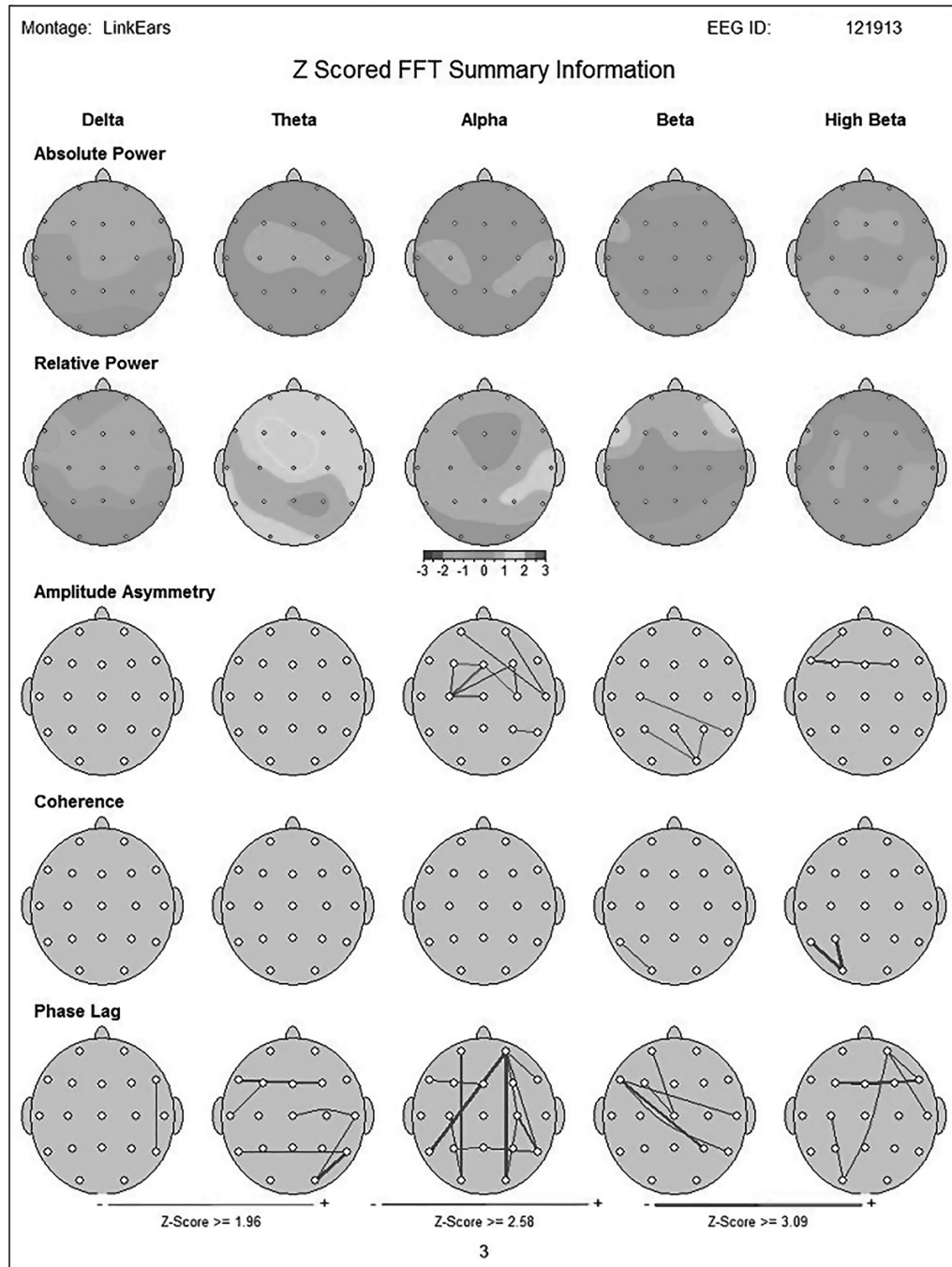


Figure 26.3 Post-treatment QEEG. Complete regulation of absolute power in the theta band. Complete normalization of coherence in the delta, theta, and alpha bands. Some minor hypocoherence in the beta and high beta bands.

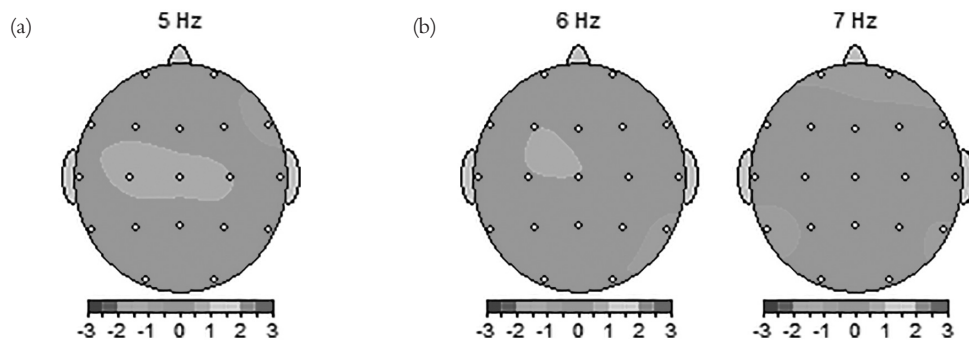


Figure 26.4 Post-treatment QEEG. Near total normalization of power in the theta band single Hertz bins at 5–7 Hertz.

power in the theta band revealed in the first QEEG was observed to be normal in the second brain mapping (Figure 26.4).

After ISF sessions, the client frequently gave a 24-hour report like the following: “feeling relaxed, mental clarity, energetic, calm, and alert. I am also noticing higher quality information coming through my senses which is useful for music.” Interpersonally he reported feeling less fear relating to others, left his cognitive behaviorist for a therapist who was more relational, began co-ed dance lessons in New York City, and began dating.

Case Study 2

G was six years old when he appeared with his mother for an intake appointment. He came in preoccupied by two miniature robots that he moved around on a tiny pad. In that first meeting there was no greeting, no eye contact, and no communication. The client had retreated to the solace of a 6" × 6" world which held his full attention. G had low physical tone, speech delays with articulation issues, trouble focusing, significant acting out behaviors, explosive anger, anxiety, and carried a PDD-NOS diagnosis.

The client was enrolled in a special education school specific to low functioning ASD children whose curriculum included academic subjects. He was one of twelve students with two teachers. In the first year of neurotherapy G was treated with traditional forms of neurofeedback plus the Low Energy Neurofeedback System (LENS). He made little progress. He was assessed for heavy metals and began a lead and mercury chelation detoxification regimen. After approximately a year on this detox protocol, ISF neurofeedback was started.

For the first month, the client was trained with ISF neurofeedback once per week. Following the first month we shifted G to a twice per week schedule over the next three months. He was then put on a twice per week supervised home training schedule for the duration of treatment. During this time, and throughout his nearly two years of ISF neurofeedback training, G was treated with a host of interventions by allied health practitioners that included detoxification, reflex integration, and a gluten free diet.

G progressed in so many ways: he was able to participate in karate classes and his physical coordination was greatly improved. He would come into the office and head right for the bungee trampoline where he would burn off some energy performing karate moves in the air before starting his neurofeedback training session. As time progressed he was writing his letters, starting to read, and doing math. His articulation improved and his temper began to diminish. He completed approximately eighty sessions of ISF neurofeedback at termination of treatment. Given G's performance in

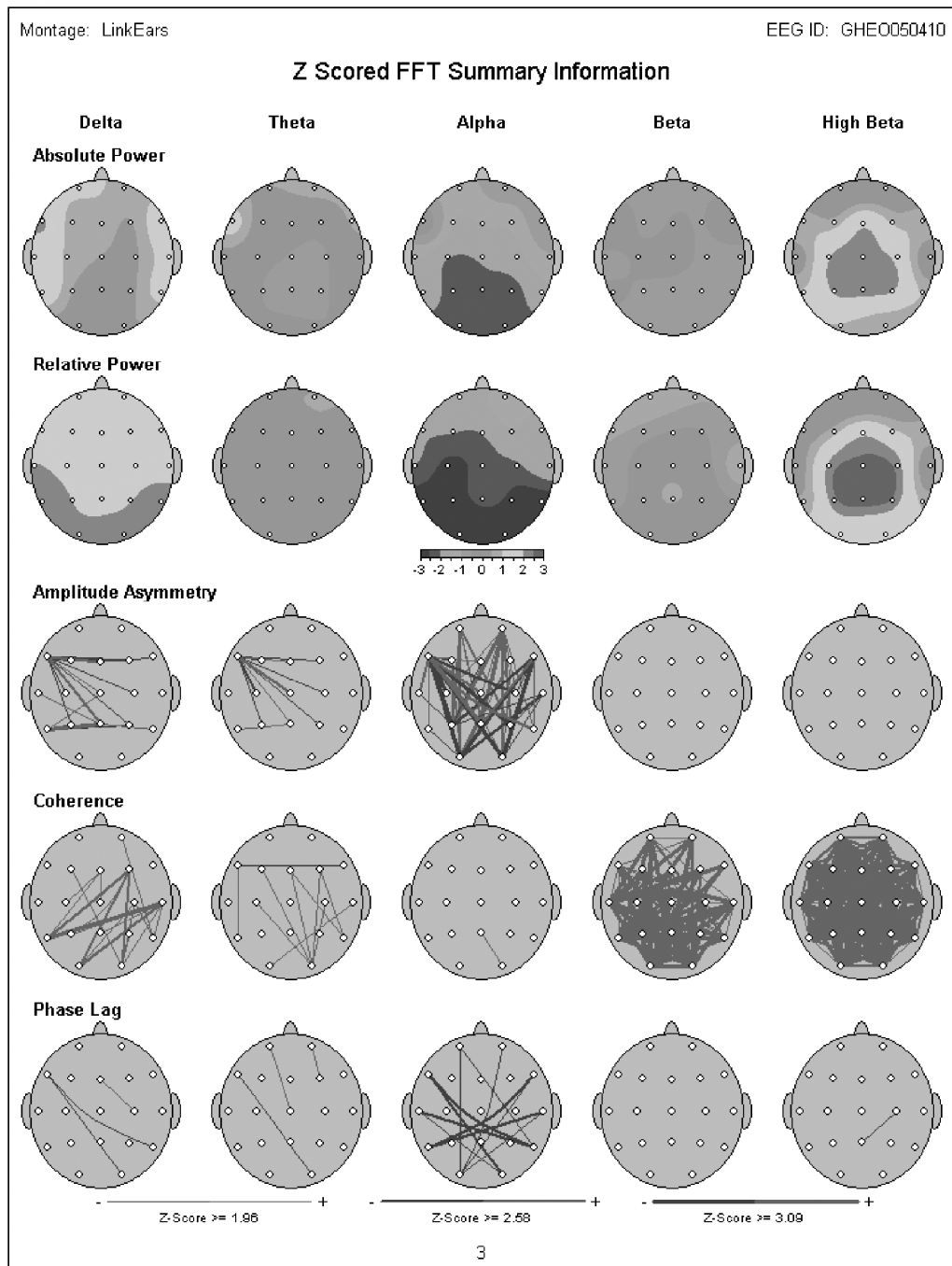


Figure 26.5 QEEG summary maps at intake. Note the hypercoherence in all bands with a global expression in the beta and high beta bands. This map reveals excess high beta absolute power.

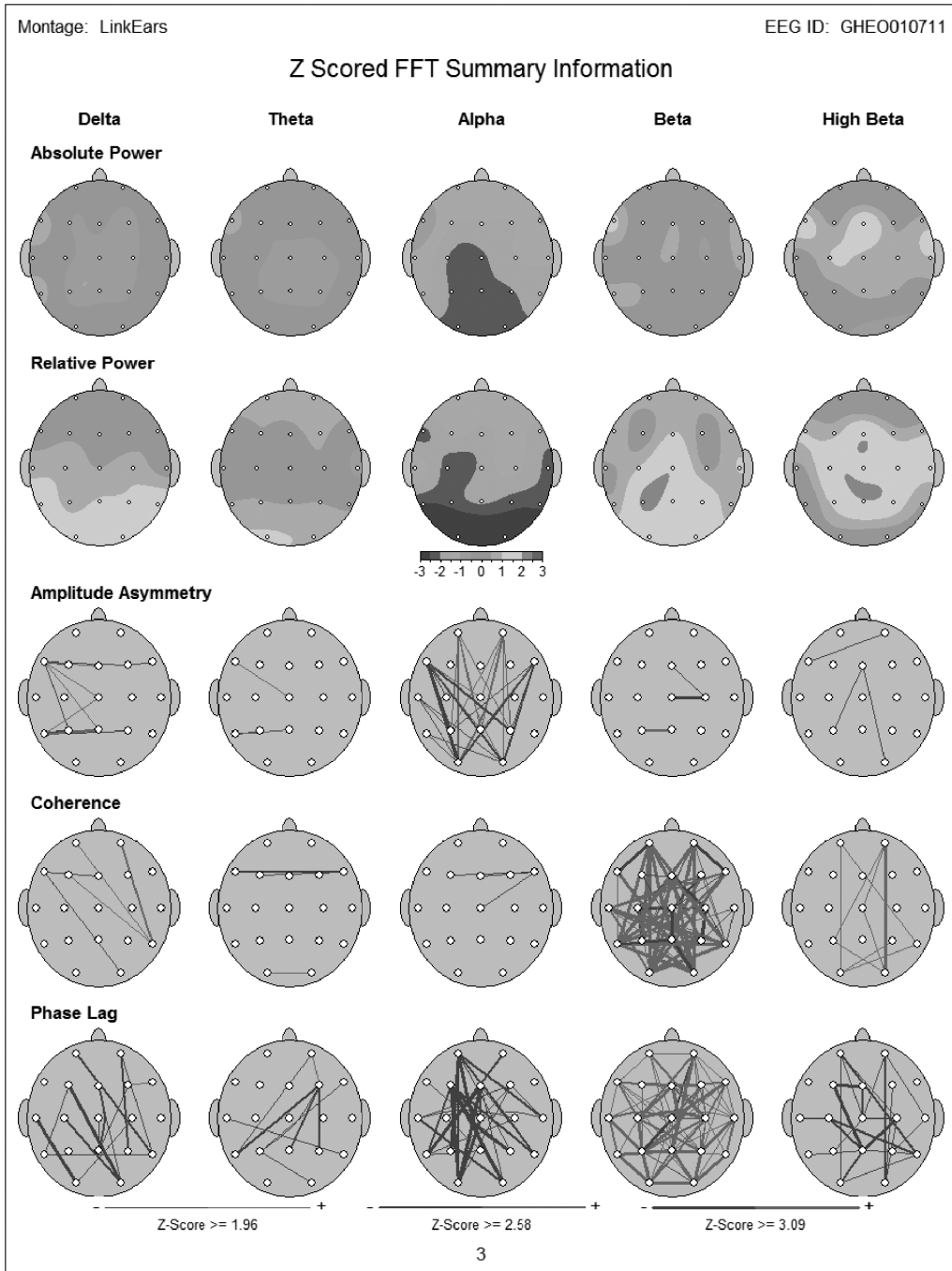


Figure 26.6 2nd QEEG. Mid-treatment summary maps. Note the normalization of delta absolute power, the virtually normalized excess high beta and substantial regulation of coherence abnormalities in the beta and high beta bands.

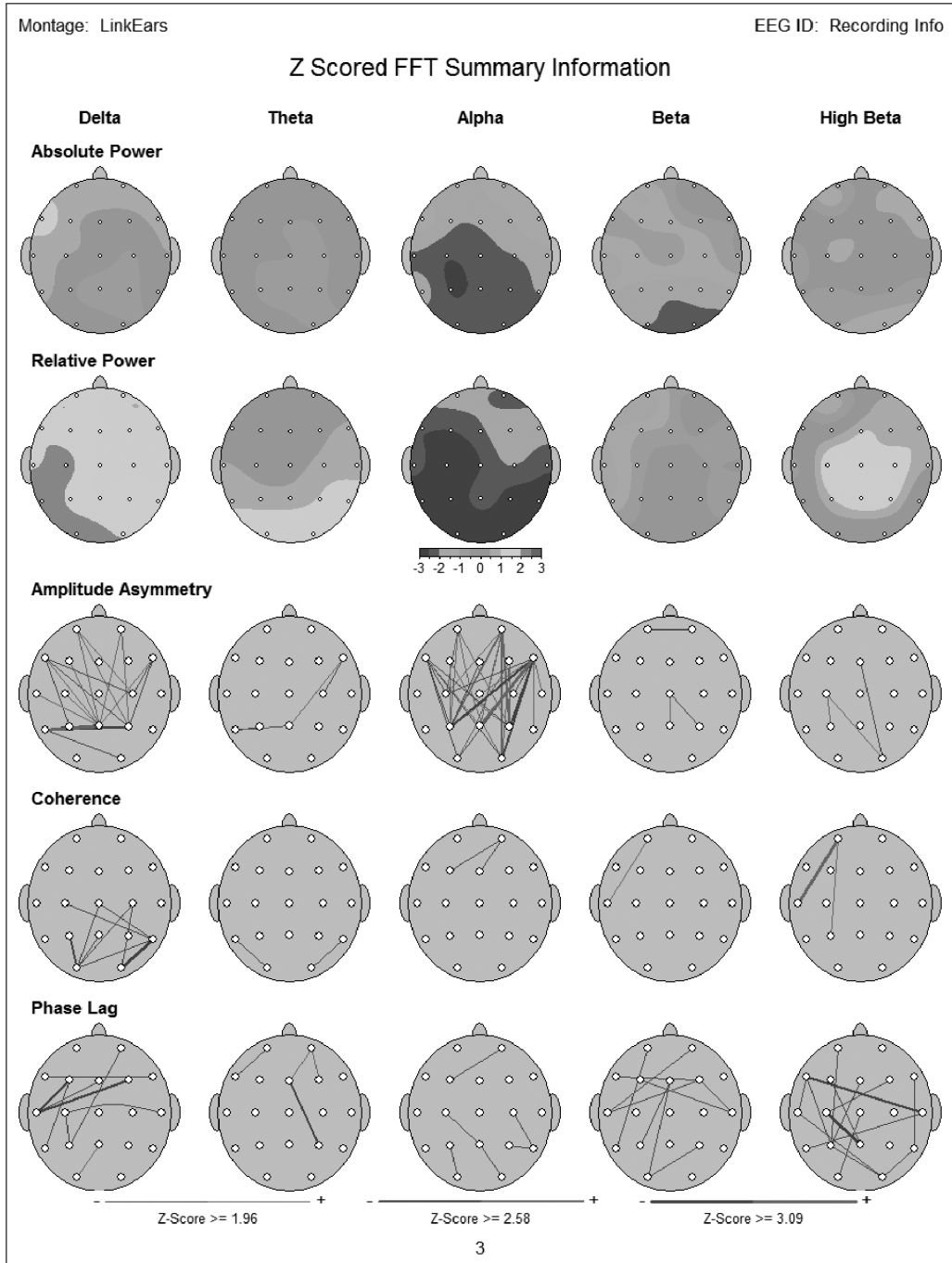


Figure 26.7 Post-treatment QEEG. Note the normalization of coherence values, particularly in the beta and high beta bands.

school, by mid-term of the second year of ISF training, his school began discussing a mainstreaming strategy with his parents. G moved to a mainstream classroom setting with twenty-five students, one teacher, and one aid, the following fall. G performed at grade level and he has been declassified from PDD-NOS to Learning Disabled.

Conclusion

Autism Spectrum Disorder is a neurodevelopmental disorder characterized by impairments in communication, social skills, sensory processing, and behavior. These deficits have been associated in research with abnormalities in neural connectivity. Disordered connectivity interferes with the normal synchronization of neuronal networks negatively impacting communication within and between networks of function. Abnormal network communication may be responsible for the entrapment of the autistic individual in a painfully intense sensory world.

In case studies of ISF neurofeedback training for ASD clients, normalization of network connectivity has been demonstrated with QEEG post hoc analysis in this and other case reports (Smith, 2013). Client, parent report, and behavioral scales have demonstrated symptom improvement (Legarda, McMahon, Othmer, & Othmer, 2011; Smith, Collura, Ferrara, & de Vries, 2014), and ISF training and demonstrable academic progress have been recorded (Smith et al., 2014). Documented behavioral progress combined with network sharing normalization revealed in QEEG post hoc analysis suggest that ISF training should be considered a viable neurofeedback intervention for ASD clients.

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