Infra-slow Fluctuation Training
For Autism Spectrum Disorder

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Typical Neurofeedback

• Focused on voluntary control of EEG parameters:
  – Power Training
  – Zscore training
  – sLORETA training
  – SCP training
• Teaches clients to make big thing small and small things big
  – Rewards brain electrical activity when the EEG value exceeds or is below a value set by the practitioner
Infra-slow Fluctuation Training

- State Discrimination Training:
  - Reflection of ISF activity causes the client to “feel” something
  - “Training” is merely a display of the ISF signal
  - No direction or quantity of the signal is desired
  - Client focus: reporting state change
- During training:
  - Trainer optimizes session through frequency adjustments
  - The subject responds with increased awareness of his/her physiological state—state shifts
  - Subject is taught to identify optimal states of physiological response
- Once identified, repetitions of optimized training operantly condition desired behavioral change

Infra-slow Fluctuation Training

- Trains the Infra-slow Fluctuations of Alternating Current (AC) current measured in microvolts
- That are driven by Direct Current (DC) fluctuations measured in milivolts
- DC coupled amplifier
  - Atlantis/Discovery
  - Other manufacturers make DC coupled amps
- Single channel bipolar montage
- Ag/AgCl electrodes
  - Silver/Silver Chloride

ISF is Bipolar Training

- In bipolar training the reference lead is placed on the head not the ear
- Bipolar = imaging/training the difference between two signals
- All EEG training is bipolar training
- Due to design of amplifiers: differential
- Referential training fiction: ear is silent to EEG
Differential Amplifier Output
(Common Mode Rejection)

Zero Output

Non-Zero Output

Definition of Terms

• Direct Current (DC) current flows in one direction
  Batteries/motors
  Brain activity
• Alternating Current (AC) flow of current alternates between (+) and (-)
  Household electricity
  Brain waves

DC the Steady State Potential

• DC is a standing potential measured in mV
• This potential fluctuates in voltage up and down
• It is these shifts that are imaged in the frequency domain in ISF training
• Feedback is given on the frequency equivalent of the DC shift
• Much of the time
HE’S GETTING TECHNICAL AGAIN!

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DC Cushion
- DC gives the AC current “bounce”
- DC acts like a trampoline and allows current to continue to bounce/shift on the DC like a kid on a trampoline
- AC amplifiers allow one big bounce and stop like a kid who jumps up from and lands on the floor

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More Bounce with DC!

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Definitions

• Slow Cortical Potential (SCP): changes in the cortical polarization of the EEG, lasting from 100 ms up to several seconds. It is part of the Direct Current signal
• Research defines Infra-slow Fluctuations (ISF): < .1 hertz
  — ISF is Alternating Current
  — ISF is not SCP but may reflect SCP activity
  — ISF training is executed with a Direct Current (DC coupled) amplifier
• Clinical ISF frequencies trained: From 0.002 to 0.012
  — We do not train .0001

Definitions Cont.

• AC amplifier: filters and amplifies the alternating current and excludes DC
  — Most Neurofeedback amplifiers
• DC amplifier: filters and amplifies AC + DC
• Atlantis & Discovery, Nexus, are DC coupled amplifiers
• Both Atlantis & Discovery can be operated in AC only mode
  — Z Score Training/Traditional Neurofeedback

Definition of Terms

• All brain electrical activity contains both AC & DC unless one is filtered out
**Protocol is Data Driven**

- Typical Bipolar montage
  - 1 channel 3 electrodes
  - Cannot image the activity under each electrode site
- ISF Electrode array:
  - 3 Channels-5 electrodes
  - 2 channel linked ears
  - 1 channel Bipolar montage executed in software
  - Simultaneous referential/bipolar montages
- Allows for:
  - Z-score monitoring
  - Amplitude monitoring at each site
  - SCP monitoring

**ISF Metrics & Current Training Screen**

- DC/SCP=Direct Current/Slow Cortical Potential
  - Measured in millivolts (thousandths of a volt) "mV"
- ISF=Infra-slow Fluctuations
  - Measured in microvolts (millionths of a volt) "uV"
- Optimum Frequency @ T3/T4 = right side ISF dominant 
- left side ISF greater negative gradient or less positive gradient
- Optimum Frequency reduction is negativity at both sites become less active
ISF Training

- Turns on discovering an Optimum Frequency (OF) for each client
- The most common OF from 0.002 to 0.012
- Some outliers are higher, some lower
- Provide feedback on small changes in the amplitude of the signal both increase and decrease
- Feedback equates to relative phase of the signal

ISF Training

- Not encouraging increase or decrease of ISF amplitude
- Providing info to the brain about change in the signal’s amplitude
- Info causes state shifts—Autonomic
- Seek optimum behavioral state: most alert/most relaxed
- Looking for parasympathetic response—in most cases
- Use peripheral measures:
  - Finger temp
  - GSR
  - Capnometry
- Use physiological response while shifting frequency and 24-hour report to determine optimization

What is reinforced in Infra-slow Fluctuation Training?

- Provide info on the change in amplitude of the signal compared to a damped average
  - Not simply rewarding an increase in amplitude
  - Not inhibiting or enhancing the signal
- Providing data on a ratio of amplitude increase and decrease/ratio of change
- This data may reflect the relative phase of this slow moving signal
- Mirror the Infra-slow energy
The ISF Training Paradigm

• Basic:
  – ISF combined with 1-40 hertz inhibits

• More advanced:
  – ISF training/Z-score inhibits
    • A ceiling and floor
  – ISF combined inhibit/enhance protocol
    • QEEG based
  – ISF sLORETA
    • Full cap

Name Change: Infra-low Frequency to Infra-slow Fluctuation. Why?

• Infra-slow does not train an oscillatory event
  – 0.020 does not train an 8.3 minute oscillation
• ISF images fluctuations in amplitude measured in uV of infra-slow frequencies that reflect changes in amplitude of DC voltage shifts measured in mV
• Consonant with the research
• Differentiates ISF from the Othmer’s approach
  – Othmer AC amplifier until 2013
    • HD = High Definition
    • A true DC coupled amp
  – ISF Atlantis Amplifier DC amp since 2006 at introduction
  – No optimum frequency equivalent

Origin of the Signal
Infra-slow Oscillations (ISO)

- Hughes(2011)
  - ISF is part of the local field potential
  - Thalamus consistently reveals ISOs.
  - ISOs can be observed in slices in isolated thalamic nuclei maintained in vitro.
  - Proposed that in addition to Thalamic Nuclei, Astrocytes are the origin of ISOs
• There is evidence that ionic shifts between the compartments of blood and tissue in the cortex gives rise to potential gradients across the blood-brain barrier and contribute to these slow oscillations
• Hemodynamic origin as measured by fMRI/BOLD signal
Origin of the ISF Signal

- Palva and Palva (2012) have determined that the "Ultradian Rhythm" (< 0.01 Hz) in EEG recordings, BOLD signals, neuronal activity levels, and behavioral time series are likely to image the same fundamental phenomenon; a superstructure of oscillatory ISFs that regulate both the excitatory level of functional networks and the integration between them.
ISF Power Law Correlated

- Nir (2008) described a 1/f-like power distribution of <.1 activity
- A power law posits a functional relationship between two quantities.
  - The infra-slow signal quantities:
    - Frequency
    - Microvolts

ISF Research & Function

- Aladjalova (1957, 1964)
  - ISF becomes intensified, increases in amplitude, by agents that elicit a defense reaction similar to the response to "stress"
  - Aladjalova proposed a role for the ISF in hypothalamic functioning/autonomic function
  - She theorized that the increase in amplitude reflected the Hypothalamus's reparative, parasympathetic, response.

  Supporting a role in the Neuroendocrine system:

  - ISF is associated with Hypothalamic-Pituitary secretory activity
  - An increase in amplitude of ISF coupled with the release of the Luteinizing Hormone
  - Released by the Hypothalamus a LH surge triggers ovulation and stimulates production of testosterone

ISF & Higher Frequencies

- Kekovic (2012) ISOs
  - Found significant coupling between ISOs and higher frequencies
  - Concluded from spectral coherence analysis that ISOs have an important role in the synchronization of neuronal networks

- Vanhatalo (2004)
  - ISOs are embedded in and determinant of the excitability cycle of higher frequencies
  - Established a role for ISOs in the control of gross cortical excitability
  - The phase of the ISO robustly correlated with the amplitude of higher frequencies.
ISF as Embedded Frequency

- Vanhataloo Cont.
  - Slow fluctuations are tightly associated with K complexes (wave form during stage 2 sleep) and inter-ictal activity (epileptiform discharges)
- Vanhataloo (2005) became so convinced of ISOs centrality in cortex he stated that any attempt to attenuate the signal eliminates the most salient features of the human EEG

ISF & DMN & Attention

- Ko (2011)
  - Default Mode Network (DMN) high gamma band (65-110 hz) coherence at ISO frequencies
  - Coherence centered at 0.014 hz
- Monto (2008)
  - Strong correlation between a subject’s ability to detect a sensory stimuli and the phase of the slow frequency signal

ISF & Attention

- Broyd (2011)
  - Found attention induced deactivations of the ISF signal do not occur in DMN areas in ADHD
  - Suggests ADHders get stuck in self-referential processing
  - Unable to turn off DMN when appropriate
- Mairena (2012), Dong (2012)
  - Supported Monto & Broyd’s research
  - Behavioral performance is correlated with ISOs
ISF & Sleep

• ISOs become prominent during sleep
• Picchioni (2011)
  – ISOs organize a broad dissociation of cortical and sub-cortical activities during sleep
  – Organize positive correlations between Cerebellum, Thalamus, Basil Ganglia, lateral neocortices, & Hippocampus
  – Suggested a role in the organization of sleep-dependent neuroplastic processes generally
  – Consolidation of episodic memory specifically

ISF & Function

➢ Case reports corroborate the research
➢ Sleep
➢ Memory
➢ Migraines
➢ Attention Disorders
➢ Sexual dysfunction
➢ PTSD
➢ Autism
➢ RAD
➢ Affective Disorders

How is ISF Training Conceptualized?

• Largely symptom driven
• Three distinct but broad categories
  – Homeostatic Deficits of brain state
  – Developmental Disorders & Trauma
  – Arousal and Activation Disorders
• Use QEEG to identify treatment responders and to assess treatment efficacy
• QEEG is an aid to beginning electrode placement but is not definitive
QEEG Analysis & ISF Treatment

- Developmental Disorders & Trauma
- Florid symptomatic expression
  - Anxiety
  - RAD
  - PTSD
- Autism
- Substantial hypercoherence
- Often start T4/P4

QEEG Analysis & ISF Low Power/Hypocoherence

- Often Instabilities
- QEEG indicators:
  - Global insufficient power
  - Hypocoherence abnormalities
  - Argues for T3/T4 starting placement
  - Often tolerates only inter-hemispheric placements

Mixed Hypo/Hyper Coherence Mixed Slowed/Accelerated Phase

- Anxiety
- Symptom dictates T4/P4
- QEEG suggests interhemispheric T3/T4
- Start T4/P4, if not good switch to T3/T4
- If mixed response add in T3/T4 to T4/P4
Autism Definition DSM IV

• DSM-IV
  – Autistic patients fall into four categories:
    • Autism Spectrum Disorder (ASD)
    • Asperger’s Disorder
    • Pervasive Developmental Disorder (PDD)
    • Childhood Disintegrative Disorder (CDD)
  – These categories were not consistently applied across clinics and treatment centers

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DSM 5

• The DSM 5:
  – The four classifications of DSM IV are collapsed into one broad catch all: Autism Spectrum Disorder
  – Symptoms:
    • Fall on a continuum
      – Mild: the old Asperger’s group
      – More severe
        » PDD
        » CDD
    – Must show symptoms from early childhood even if they are recognized later

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Autism Definition DSM 5

• A highly varied developmental disorder
  – Typically characterized by:
    • Deficits in:
      – Reciprocal social interaction
        » Difficulty building and maintaining friendships
      – Verbal and non-verbal communication
        » From functionally non-verbal to:
        » Misreading non-verbal interactions
        » Inappropriate in conversation
    • Restricted interests
    • Repetitive behaviors
      – Overly dependent on routine
      – Tics
      – OCD
Autism and the Brain

- Research:
  - ASD associated with abnormalities in neural connectivity
    - Local and global
  - In our field:
    - Cantor
    - Thatcher
    - Coben
  - Ubiquitous in the larger neuroscience field

Connectivity & Research in Autism

Disordered connectivity in research both:
- Increased
- Decreased

Disordered connectivity:
- Complication normal network synchronization
- Throttles or alters communication among networks
- Negatively impacts behavior associated with affected networks

In QEEG:
- Increased connectivity = hypercoherence
- Decreased connectivity = hypocoherence

Among autistic clients in ISF treatment, the vast majority reveal hypercoherence

Autistic Client QEEG

11 year old boy

Notice the hypercoherence in all bands.

This is the typical QEEG that we see among ASD clients.
Autism is a Profound Dysautonomia

- Produced by:
  - Abnormal neuronal network communication
    - Affects all behavioral domains
- Exacerbated by:
  - Poor sensory processing
    - Trapped in a painful sensory world (Markham, 2007, 2010)
  - In combination with Autonomic dysregulation

Autism & ISF Training

- Majority start T4/P4
- Right hemisphere focus
- Epileptiform activity
  - T3/T4
- Other sites:
  - T4/T6 facial recognition/social contact
  - T4/F8 language/prosody
  - T4/Fp2 emotional lability
Autism ISF Training

• OCD behaviors
  – T4/Fz
  – Fz/Pz
  – T4/Fp1
• Left hemisphere training later in treatment course
• Sites dependent on symptoms
• Attention:
  – T3/Fp1
  – T3/F3
• Learning difficulties:
  – T3/P3
  – T3/T3
  – T3/O1
• OCD behaviors
  – T3/Fp1

The Child School Neurofeedback Program
Roosevelt Island, New York

The Child School

• Established 1973
• School for children with learning disabilities
• 8:1:1 student to teacher & teacher assistant ratio
• Multi-disciplinary approach that includes:
  – Psychologists, speech pathologists, and occupational therapists
Neurofeedback Program

- Staff:
  - John Ferrera, PhD Program Director/neurotherapist
  - Mark L. Smith, LCSW Clinical Director
  - Jason Park, MS Neurotherapist
  - Xian Zhang, PhD Researcher
- Program initiation: April 2011

Neurofeedback Program

- 17 students were enrolled 6-15 years of age
- Two broad groups:
  - Pervasive Developmental Disorders (PDD)
    - Includes children with Autism
  - Emotionally Disturbed (ED)
    - Anxiety
    - Or another mood related disorder
- All participants were having difficulty meeting academic and/or social demands of the school environment
  - Extreme cases—students at risk of forced transfer to a different school

Neurofeedback Program

- Students also grouped by amount of difficulty:
  - High Risk
  - Moderate Risk
  - Low Risk
- All trained with Infra-slow Fluctuation training
- Average number of NF sessions: 23
- All trained without QEEG guidance
- Assessed with pre/post Child Behavior Check List
Neurofeedback Program

Participants from the ED group (7 total) included three students with a combination of social and generalized anxiety, three students with reactive attachment disorder, and one student with atypical form of bipolar depression.

Participants from the PDD group (10 total) included children diagnosed to be on the autistic spectrum. The group included students with high functioning Autism and Asperger’s syndrome.

Subgroup

Low Risk
Student is making adequate academic and social progress.

Moderate Risk
Student exhibits emotional and/or behavioral difficulties that hinder academic progress and/or leads to behavioral outbursts during school. Student at moderate risk of forced transfer to another school.

High Risk
Exhibits significant emotional and/or behavioral difficulties, including disruptive classroom behaviors, that cause student to miss a significant amount of instructional time. Student at serious risk of forced transfer to another school as a result of disruptive classroom behavior and/or social deficits.

Participant Breakdown

Pre-treatment breakdown of participants by diagnosis and presenting concern

ED Group (7 total)
- Three Students with anxiety:
  - Difficulty initiating and completing tasks
  - Under performing academically
  - Socially isolated
  - Sensory issues
    - Hypersensitive-overreact to seemingly innocuous stimuli (i.e. touch and sound)

ED Group (7 total)
- Remaining four difficulties with:
  - Regulating emotional response to academic or social challenges
  - Led to serious behavioral disruptions and removal from the classroom
  - Sensory seeking-sought out excessive amounts of stimulation

ED Group (7 total)
- High functioning Autism
- Asperger’s syndrome
PDD Group

- 10 total= High Functioning Autism/Asperger’s Syndrome
  - Emotional reactivity
    - Tendency to overreact in response to environmental stressors
    - This hypersensitivity to stressors caused disruptive outbursts which often led to removal from classroom
      - Making consistent attendance in an academic environment difficult
      - Making transitions between different classes and activities challenging

Results

- 14 of 17 students had a positive response that involved either:
  - a significant reduction of behavioral disruptions and/or
  - a reduction or elimination of psychotropic medication and/or
  - improved ability to sustain attention during class and continued academic progress
- One student’s positive results were confounded by initiation of an SSRI
- The other two were status quo at completion of treatment

Child Behavior Check List

- Pre/post CBCL data available for 12 students
- The CBCL is a standardized measure of emotional functioning available in:
  - Parent, teacher, and self-report forms
  - Present group= Pre/post teach rating scales
- Teacher form:
  - 113 questions
  - 3 point Likert scale
CBCL Cont.

Each CBCL item loads onto one or more clinical scales:
- Anxious/depressed
- Depressed
- Somatic complaints
- Social problems
- Thought problems
- Attention problems
- Rule breaking behavior
- Aggressive behavior

And six DSM-oriented scales
- Affective problems
- Anxiety problems
- Somatic problems
- ADHD
- Oppositional defiant problems
- Conduct problems

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MF

- 15 years old, 9th grade. 26 sessions ILF at T4P4. During last 15 sessions, T4T6 was added.
- PDD (Aspergers). Can be very rigid in unstructured situations. Difficulty with transitions. When anxious, he would yell very loudly and refuse to comply with instructions. Above average intelligence, average academic skills.
- Now much calmer and better with transitions. He still has his moments, but they are less frequent and less severe.

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NV

- 12 years old, 7th Grade. 26 sessions ILF at T3T4. During last 15 sessions, T3F3 was added.
- History of severe affective disorder. Extremely depressed and anxious. Cries daily, becomes aggressive toward self and objects (lockers!). Average academic skills, though little confidence and compliance with homework.
- He has showed steady progress, with many blips along the way. He has stopped directing his anger outward at others, however.
- Now completely compliant and finally beginning to make academic and developmental gains.
CBCL Results
For 11 of the 12 students for which CBCL data was available, improvements of greater than one standard deviation on relevant clinical scales.

References

- Ko, A. L., Darva...
References Cont.


References Cont.


ISF Workshops

- New York Metro Region—Secaucus, NJ
  – May 1, 2, 3, 2015
  – Call 212-877-7929
- Munich Germany
  – June 17-19, 2015
  – http://www.neurofeedback-info.de/en/
- Cleveland, Ohio-Stress Therapy Solutions
  – July 2015 exact datesTBA