Neurofeedback and qEEG-Personalized Medicine

Deborah R. Simkin, M.D.
Clinical Assistant Professor
Emory University School of Medicine

Joel Lubar, PhD
Professor Emeritus
University of Tennessee
CAM – Neurofeedback

Part 1

1. History of surface NF, especially as it pertains to ADHD and seizures
2. Studies of Surface NF
3. Enduring Effects
3. Controversies
4. Personalized Medicine - Use of qEEG to determine subtypes for ADHD.

Part 2. Next lecture

5. NF protocol determination and responders to medications
6. AAP approval NF for ADHD
7. Surface NF in regards to autism
8. Role of NF and qEEG in view of the new NIMH Research Domain Criteria (RDoC)
9. Conclusions
Summary of 1st Lecture

When RCT are eliminated that has methodological flaws, the ES using SMR, SCP and TBR NF for ADHD increased to a moderate effect for hyperactivity (.71) and high ES for attention (1.0) and impulsivity (0.94).

Studies were not randomized and had small N.

Use of qEEG is very promising to treatment match.
Summary 1st Lecture

• NF has not only shown enduring effects up to 2 years after NF has been completed, NF has shown continued improvement especially in attention and hyperactivity compared to controls.
Controversies of DBPC studies and Solutions

• From this work, a Phoenix has risen:
• The same collaborative group that came together to look at errors in research have been awarded the first 5 year DBPC NIH grant to study ADHD (PI is Dr. Arnold)
• 140 children ages 7-10
• Will identify (as in Monastra’s study) Theta/Beta ratio >5 at Cz or Fz EO
• Meeting Connor’s Rating Scale (parent and teacher) >1.5 SD
Controversies and Solutions

- Using Monastra/Lubar ADHD assessment suite
- Using same criteria suggested by Dr. Lubar for the Sham
- Train down theta (4-8 Hz) and up train beta (13-21 Hz) at Cz or Fz
- 38 sessions 3x/wk.
- 6, 13 and 25 month follow up
- 19 channel EEG/ERP
- IVA test
- WIAT-II screener
- Conners-3
- Sleep Habits questionnaire
- Functional Assessment Chklst
- Sluggish Cognitive Tempo
Controversies and Solutions

• Specific Aims and outcomes:
  • Test whether NF has specific benefit for ADHD
  • Whether the benefit persists
  • Whether the commonly accepted and RDoC arousal/regulation biomarker for responsiveness, excess electroencephalographic (EEG) theta-beta power ratio (TBR), is valid.

• In addition, (LORETA) will be used to identify deep brain changes as outcomes and mediators
Use of qEEG subtypes to determine NF protocols

- B. NF protocols using qEEG.
- Arns (2012) - Based on qEEG data one of 4 NF protocols selected:

1. **Frontocentral Theta/Beta** protocol - when excess theta was observed at midline site at FZ, FCz or Cz where activity was maximal using Z scores, Theta dec/Beta inc protocol was used unless:
   
   a. Beta was already in excess - in this case only theta was dec.
   
   b. Or Theta was nl but beta dec, then beta was rewarded
Use of qEEG and subtypes to determine NF protocol

• 2. *Frontocentral alpha* protocol - If there was excess frontocentral alpha (esp during eyes open or EO) then midline site where the activity was greatest was chosen and downtrained. If no excess beta or beta spindles, then beta was rewarded

• 3. *Beta downtraining* protocol - If excess beta or beta spindles were present then site where these were maximal was selected - exact training frequency established from qEEG single Hz in zones and downtrained
Use of qEEG and subtypes-to determine NF protocol

• 4. *Low voltage EEG* —If observed, SMR protocol was used *(either rewarding SMR spindles with a .25 duration or SMR/theta at C3/C4. If dec alpha power was noted on Eyes Closed (EC), alpha uptraining was done at Pz with EC (Johnston, 2005)*)

• 5. *If no clear qEEG deviations, and or if sleep problems were a main complaint, SMR was used on side where 12-15Hz activity was lowest.*

In all protocols, EMG inhibits were employed where EMG (55-100Hz) had to be kept below 5-10 uV
Use of qEEG and subtypes-to determine NF protocol

• Results:

**Fig. 1** Clinical effects over time for the total group of ADHD/ADD patients at pre-treatment, halfway treatment and post-treatment (averages plus SEM) for ATT and HI. All time effects were significant ($p \leq .001$)
Use of qEEG and subtypes-to determine NF protocol

Fig. 3 ES for the different studies mentioned in the introduction and the ES obtained from the current study, with on the left ES for ATT and on the right ES for hyperactivity. Note that ES for hyperactivity for this study was based on a combined HI scale.
Use of qEEG and subtypes-Summary 1st lecture

- ES for Attention was 1.78 and for Hyperactivity was 1.22
- Recent meta analysis of effects of stimulants medication in ADHD found ES 0.84 for Ritalin for ATT (Faraone and Buitelaar, 2009)
- In addition, an anterior individual alpha peak frequency (iAPF) was related to improvement of depressive symptoms.
- Slow anterior iAPF at baseline predicted poor treatment response on comorbid depressive complaints.
Use of qEEG and subtypes

• In addition, an anterior fast individual alpha peak frequency (iAPF) was related to improvement of depressive symptoms.

• In fact, fast iAPF is associated with better memory performance and more efficient NF training.

• Slow anterior iAPF at baseline predicted poor treatment response to antidepressants, stimulants and antipsychotics.
Use of qEEG and subtypes-to determine NF protocol

Fig. 2 Improvement on comorbid depressive symptoms for the patients across time (time effects: $p = .003$; Left) and the significant correlation between the frontal iAPF and the percentage improvement in BDI scores ($p = .002$; $r = 0.851$; Right)
Use of qEEG to determine response to meds

- **D. Determining responders to stimulants**

- A series of studies which investigated the value of EEG markers for predicting treatment outcome to stimulant medication in ADHD and personalizing neurofeedback treatment in ADHD will be presented.

  - The 1st study demonstrated specific EEG markers associated with non-response (slow alpha frequency) and response (excess Theta and Alpha) to stimulant medication.

  - The 2nd study demonstrated that personalizing neurofeedback treatment based on the EEG-phenotypes from study 1 resulted in a response rate of 76% (ES=1.78) and normalizations in sleep, ERPs and EEG.

- (Arns, et al, 2012)
• Use of qEEG to determine response to meds

F. Use of ERP’s to determine stimulant response (Ogrim et al 2014)

• ERP’s in humans can be divided into 2 categories.
Use of qEEG to determine response to meds

E. Other studies show that effect of stimulants:

First, what do we know about stimulants?

- Stimulant responders have excess theta (slow wave activity)
- Also, stimulants decrease theta, increase beta and
- Improve deviant ERP (Loo et al, 2005).
Use of qEEG to determine response to meds

ERP’s

• A. The early waves, peaking roughly within the first 100 milliseconds after stimulus, are termed ‘sensory’

• B. In contrast, ERPs generated later after the stimulus are termed ‘cognitive’ or ‘endogenous’ ERPs as they examine information processing or ability to inhibit (ie P3).
The P300 component is understood to reflect a higher cognitive response to unexpected and/or cognitively salient stimuli.
qEEG and Subtypes

• F. 3 parameters predicted response to stimulants”

• 1. excess theta is typical for RE

• 2. The amplitude of the IC cue P3, generated in the parietal-occipital distribution, was normal in REs to stimulants

• but significantly smaller in non-Res (may reflect process of orienting in parietal area BA 5)

• innervated by NE and therefore may respond to atomoxetine)
qEEG and Subtypes

3. Whereas the centrally distributed IC P3 no-go early was smaller in REs to stimulants than in non-REs and controls and is generated by the supplementary motor area of PFC (BA 6)

• inhibits motor response-
• BA 6 = area dense in dopamine system, therefore, frontal lobe dysfunction and responsive to stimulants.

Conclusion:

1. So NL P3 in parietal area (BA 5) = response to stim
2. Smaller amp P3 in parietal = non responder to stim. = possible atomoxetine responder
3. P3 amp smaller in central area (BA 6) responds to stimulants-area dense in dopamine receptors = frontal lobe dysfunction & responsive to stimulants
BRODMANN (SKIL)
qEEG and Subtypes

***In addition, in the Ogrim study: Comorbid autism, anxiety and LD did not prevent response to stimulants but did increase risk to side effects. Therefore, notion that co morbidity decreases medication effects may be partly due to increased risk for side effects.
qEEG and Subtypes to determine response to meds

- G. Another study showed that stimulants increase beta in responders and decreases beta in non responders (Clark et al, 2003, Loo et al, 2004)
- Ogrim’s study agreed with this
Several multicenter large-scale studies are underway that are also measuring EEG amongst other biomarkers

1. the EMBARC study (Establishing Moderator and Biosignatures of Antidepressant Response in Clinical Care) in Depression (one diameter uses LORETA analysis of Anterior Cingulate to determine responders (inc. theta) vs non-responders)

2. iSPOT studies (International Study to Predict Optimized Treatment Response) in Depression and ADHD.
The first half of these data have currently been collected and the first data analyses are underway and expected to be published in the first half of this year and replicated in the second half.

These data will be available to selected academics to test their specific hypotheses related to the potential prognostic value of EEG (or other biomarkers such as genomics, fMRI, heart rate, DTI, MRI, etc.).

These new initiatives will hopefully add the prognostic use to diagnostic approaches in the multidimensional deployment of EEGs in research and clinical practice.
Practice Wise-NF 1st line intervention for ADHD-not approved by AAP

- **RCT** Studies influencing the decision included:

  - Beauregard, M., & Levesque, J. (2006). Functional magnetic resonance imaging investigation of the effects of neurofeedback training

MRI research using NF

- Ghaziri, et al, 2013-treatment , control and sham group ages 18-30 healthy participants
- Sham received feedback of sessions from members of EXP group
- Treatment group trained to enhance beta 1 at F4 and P4
- Higher scores on visual and auditory attentional performance on Integrated Visual Auditory continuous performance test-sham only had improvements in visual attention

- MRI demonstrated increased fractional anisotrophy was measured in Working memory pathways implicated in sustained attention and Grey Matter Volume increases were detected in cerebral structures involved in frontal and parietal cortical areas connected by these WM fiber pathways.
Autism-Kouijer et al, 2009

- Autistic spectrum disorder in youth has been examined in 2 NF studies.

- In one, 14 children (ages 8-12) were evaluated using qEEG, executive function tests and parent rating scales, then randomized to surface NF or waitlist control.

  - Time1=baseline, Time 2=end of study, **Time 3=1 year later**.

- **NF rewarded inhibiting theta (4-8 Hz) and increasing low beta (12-15 Hz) at scalp location C4.**

- After 40 sessions, 70% of participants had effectively reduced theta (p<0.05) and increased low beta (p<0.05) activity.
Autism-Kouijer et al, 2009

- These participants demonstrated significant improvements in several neuropsychological indices such as:
  - attention (Test of Sustained Selective Attention),
  - verbal inhibition (Stroop),
  - planning (Tower of London) and
  - cognitive flexibility (Trail Making),
- and some participants showed nonverbal and verbal communication, social interaction and stereotypic behaviors, with improvements sustained at one year follow-up.

- (Coben et al, 2014, Kouijzer et al, 2009)
Autism-Kouijer et al, 2009

- Attention skills, $p < 0.05$
- Set-shifting, $p < 0.05$
- Inhibition $p < 0.05$
- Verbal inhibition $p < 0.05$
- Motor inhibition and planning, $p < 0.05$
Autism- Kouijzer et al, 2009-Time 3=1 yr

Figure 15.2 Time1, Time2, and Time3 data of the treatment group on executive function tasks.
Figure 15.3 Time1, Time2, and Time3 data of the treatment group on social behavior.
In a second study, 60% of 20 NF participants with autism decreased theta and showed significant improvements over the waitlist controls in cognitive flexibility, social interactions and communication that endured 6 months after treatment on follow up (Coben et al, 2014, Kouijzer et al, 2010).

Time 1=baseline, Time 2=after end of treatment and Time 3=6 months
Autism-Kouijer et al., 2010 - Time3 = 6 mos

Figure 15.5 Time1, Time2, and Time3 data of treatment and control group on social behavior.
Predominately male (male16;female4) and all Caucasian.
The mean age was 9.53, with a range of 5-10.
Most subjects (80%) were medication free, with only one subject taking more than two medications.
Subjects were administered parent rating scales, including the:
  - Autism Treatment Evaluation Checklist (ATEC; Rimland & Eldelson, 2000),
  - Personality Inventory for Children (PIC-2; Lachar & Gruber, 2001),
  - Behavior Rating Inventory of Executive Function (BRIEF; Gioia, Isquith, Guy & Kenworthy, 2000), and the
  - Gilliam Asperger’s Disorder Scale (GADS; Gilliam, 2001).
Autism, Coben, 2012

• Frontal and local (short neuronal paths hyperconnectivity has been shown to be present in autistic samples (Li, Xue, Ellmore, Frye, & Wong, 2012; Wass, 2011).

• In addition, there is other recent data showing hypoconnectivity in long distance and posterior to anterior or temporal regions in autistics.

• Multivariate Coherence technique targeted:
  • (1) right hemisphere (temporal) hypocohерences across all frequency bands,
  • (2) hypercoherences in the alpha band over prefrontal regions, and
  • (3) right parietal-posterior temporal hypercoherences in the theta and alpha frequency bands.
Autism-Enduring Effect of Neuropsychological Benefits
Coben et al, 2014

• Subjects were also administered neuropsychological assessments covering domains of attention/executive functioning, language, and visuo-spatial 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 re-evaluated and pre-and post-treatment scores were compared for significance.

• After re-evaluation, neurofeedback was withheld for 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.
Figure 15.6 Clinical improvements among subjects as assessed by the parents rating scales of ATEC, BRIEF, GADS, and PIC-2 for pre-, post-treatment, and follow-up periods.
Figure 15.7 Graph showing the clinical improvements among the domains of attention/executive functioning, language, and visuo-spatial processing as assessed by neuropsychological evaluations at pre-, post-treatment and follow-up periods.
Summary

• Use of the TBR and multivariate NF not only improves symptoms associated with autism, the effects continue to improve up to one year.
• Longer outcome studies are needed to determine if the effects sustain
• For multivariate NF, there was a correlation to improvement on DTI (presented Coben, ISNR, 2014)
• However, the N’s were small
Not all FDA approved technology is the same


- Good news-FDA sanctioned objective biological brain marker into Psychiatry and Pediatrics

- Bad news-it may inadvertently be over-used simplistically as a diagnostic tool.

Theta/Beta ratio is a poor diagnostic measure, in 25–30% of ADHD patients this measure is consistently found to deviate and it has been repeatedly shown that excess theta is associated with a favorable treatment outcome to stimulant medication and neurofeedback (Arns et al., 2012), suggesting that Theta/Beta ratio might serve a prognostic rather then a diagnostic purpose.” (Editorial Clinical Neurophysiology, 2014)
Closest 10-10 Electrode position to each Brodmann area

- Area LEFT RIGHT
  - ba01 C3 C4
  - ba02 C3 C4
  - ba03 C3 C4
  - ba04 C3 C4
  - ba05 C1 CP2
  - ba06 FC3 FC4
  - ba07 P1 P2
  - ba08 F1 F2
  - ba09 AF3 AF4
  - ba10 FP1 FP2
  - ba11 AF7 FPz
  - ba17 O1 O2
  - ba18 O1 O2
  - ba19 PO7 PO4
  - ba20 FT9 FT10

  - Area Left Right
  - ba21 T7 T8
  - ba22 T7 T8
  - ba23 Pz Pz
  - ba24 F1 F2
  - ba31 Pz Pz
  - ba32 F1 AFz
  - ba37 P7 P8
  - ba38 FT9 FT10
  - ba39 P5 P6
  - ba40 CP3 CP4
  - ba41 C5 T8
  - ba42 T7 C6
  - BROCA/44R F5 FC6
  - ba45 F8
  - ba46 AF7 F6
  - ba47 F7 F8
### Closest Brodmann area to each 10-10 electrode

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Channels and Function

- **Fp1, Fp2** Prefrontal (Cortex) & F7, Fz, F8
  - I: Executive Cognitive Dysfunction
  - II: ADD Distractibility/Inattention

- **Fp1, F7, F3** Frontal Left (Cortex)
  - I: Depression
  - II: Inability to Feel Positive Emotion
  - III: Learning Disability—Language/Speaking Dysphasia
  - IV: Learning Disability—Language/Writing Dysgraphia

- **Fp2, F4, F8** Frontal Right (Cortex)
  - I: Impulse Control
  - II: Inability to Feel Negative Emotion
  - III: Elevated Anger, Rage, Fear
  - IV: Dissociative Identity Disorder

- **Fpz, Fz** Frontal Midline (Cortex)
  - I: Amotivational
• Fpz, Fz, Cz, Pz  Midline (Limbic\Cingulate)
• I  Obsessive Compulsive Disorder
• II: Oppositional Defiant Disorder
• III: Addiction

• F3, Fz, F4, C3, Cz, C4  Premotor\Motor (Cortex)
• 1a: Hyperactivity Disorder
• 1b: Hypoactivity Disorder
• 1la: Motor Dysfunction--Fine
• 1lb: Motor Dysfunction--Gross

• T3 Temporal Left (Limbic\Amygdala)
• I: Emotional Disorder, Social

• T3, T5 superior Temporal Left (Cortex)
• I: Learning Disability--Auditory; Language Listening
• II: Learning Disability--Auditory; Language Listening, Perception
• **T3, T5 superior\inferior Temporal Left (Cortex)**  
  I: Learning Disability--Auditory; Language Listening, Comprehension

• **T3, T5 superior\inferior Temporal Left (Limbic\Hippocampus)**  
  I: Memory Dysfunction--Auditory, Language\Listening

• **T5 superior\inferior-P3-O1, O2 Temporal-Parietal-Occipital (Cortex)**  
  I: Learning Disability--Visual; Language\Reading  
  II: Learning Disability--Visual; Language\Reading, Perception  
  III: Learning Disability--Visual; Language\Spelling, Perception  
  IV: Learning Disability--Visual; Language\Reading, Comprehension

• **T5 superior\inferior-P3-O1, O2 Temporal-Parietal-Occipital (Limbic\Hippocampus)**  
  I: Memory Dysfunction--Visual, Language\Reading
- C3, Cz, C4  Parietal (Cortex)
  - I: Learning Disability--Somatosensory, Perception

- P3, Pz, P4  Parietal (Cortex)&T5, T6
  - I. Learning Disability--Mathematics
  - IIa: Neurosensory Integration Disorder (Right)
  - IIb: Neurosensory Integration Disorder (Left)

- T4 Temporal Right (Limbic\Amygdala)
  - I: Emotional Disorder, Primary

- T4, T6 superior Temporal Right (Cortex)
  - I: Learning Disability--Auditory; Sound\Voice
  - II: Learning Disability--Auditory; Sound\Voice, Perception

- T4, T6 superior\inferior Temporal Right (Cortex)
  - I: Learning Disability--Auditory; Sound\Voice, Comprehension
• T4, T6 superior\inferior Temporal Right (Limbic\Hippocampus)
  • I: Memory Dysfunction--Auditory, Sound\Voice

• T6 superior\inferior-P4-O1, O2 Temporal-Parietal-Occipital (Cortex)
  • I: Learning Disability--Visual; Spatial\Facial
  • II: Learning Disability--Visual; Spatial\Facial, Perception
  • III: Learning Disability--Visual; Spatial\Facial, Comprehension

• T6 superior\inferior-P4-O1, O2 Temporal-Parietal-Occipital (Limbic\Hippocampus)
  • I: Memory Dysfunction--Visual, Spatial\Facial

• T4, T6 superior\inferior-P4-O1, O2 Temporal-Parietal-Occipital (Cortex)
  • I: Comprehending Social Cues Dysfunction

Any 10-20 System Placements All Cerebral Lobes (Cortex)
• I: Generalized Anxiety Disorder
• IIa: Sleep Disorder (Hyposomnia)
• IIb: Sleep Disorder (Hypersomnia)
Research Domain Criteria (RDoC) at NIMH-Buckholtz et al, 2012
Low Resolution Electromagnetic Tomography (LORETA) neurofeedback

• Uses qEEG neurofeedback analysis (based on surface NF) that provides an estimation of the location of the deep underlying brain generators, called “modules” or “hubs” (e.g., the anterior cingulate, insula, fusiform gyrus)

• Also uses networks of the patient’s EEG activity within a frequency band.
LORETA NF

- From a historical viewpoint, surface NF is based on 2-4 electrodes.
- Originally Surface NF did not employ the use of Quantitative EEG.

- There are three more types of NF that employ the use of qEEG:
  
  1. Real time Z score NF
  2. Low Resolution Electromagnetic Tomography (LORETA NF)
  3. Functional magnetic resonance imaging (fMRI) neurofeedback’s

- Surface NF involves measuring the amplitude of neurons directly beneath the electrode where 95% of the neurons arise from a distance of 6 cm and all frequencies are mixed together at each electrode.

- However, LORETA uses three-dimensional source localization applied to human qEEG in which the mixture of frequencies under each scalp electrode are unscrambled and linked to three-dimensional sources in the interior of the brain with accuracies of approximately 1 cm in many situations.
History

• LORETA NF uses a different kind of qEEG NF analysis that provides an estimation of the location of the deep underlying brain generators, called modules or hubs (e.g., the anterior cingulate, insula, fusiform gyrus) and networks of the patient’s EEG activity within a frequency band.

• It requires more labor-intensive preparation, because an electrode cap with 19 electrodes must be applied in every session, but it can shorten the length of treatment.

• Coherence training can include multiple areas.

• The goal is to start with symptoms and then link dysregulation in networks of the brain to the patient’s symptoms.
LORETA NF

- It allows the clinician to translate qEEG data into a three-dimensional figure that corresponds with and looks like the images in fMRI that are associated with disease states.

- 3-dimensional EEG biofeedback is then used to reinforce increased stability and efficiency in the nodes and connections between nodes linked to the patient’s symptoms.
Increased slow wave (Theta) activity in the Frontal Lobes commonly seen in ADD.
Excessive Theta waves (4-8 Hz) at the central & left parietal area due to traumatic brain injury, presented in 1 Hz slices. The red color represents increased slow wave activity at the site of the injury.

Before Neurofeedback Treatment:

After Neurofeedback Treatment:
How did all of this occur?

• In the early 90’s EEG comparisons were age matched to healthy subjects and those with particular disorders=qEEG
• Then PET (Positron Emission Tomography), DTI (Diffuse Tensor Imaging), SPECT (Single Photon Tomography) and MRI (Magnetic Resonance Tomography) was compared to electrical neuroimaging using qEEG (quantitative EEG) and magnetic electroencephalography (MEG).
• This led to the transformation of the EEG to MRI slices which created a 3 D representation of the wave forms to a 3 D picture of the brain that would be seen on an MRI=EEG Tomography
• This is LORETA-Low Resolution Electromagnetic Tomography
• (Thatcher, Applied Neuroscience.com)
Functional magnetic resonance imaging (fMRI) neurofeedback

• Functional magnetic resonance imaging (fMRI) neurofeedback’s advantage is that it can examine functioning at deep subcortical areas of the brain.

• However, the serious practical disadvantage of fMRI neurofeedback is that it is incredibly expensive with equipment that costs approximately $1 million or more and is not portable.
How does Neurofeedback work

Neurofeedback uses subconscious reward systems based on **operant conditioning**.

- When a targeted area of weakness in the brain illicits a desired brain wave rhythm,
- It is paired with a reward,
- The brain learns to change brain wave forms based on the probability of receiving the reward.
• How operant conditioning related to changing the wavelengths on an EEG?

• Synapses produce the EEG.

• All changes in the EEG result from changes in the synapse.

• So any changes in the EEG that occur from operant conditioning involves changes in the synapses.

• Collection of active neurons burst in a synchronized effect (phase lock).

• Followed by a sufficient time (phase shift) to pump neuromodulators (dopamine, norepinephrine) to exceed thresholds necessary to activate long term potentiation, synaptic modification occurs (synapses grow in size and number)

What is phase shift and phase lock?

- Phase shift:

  - Ex- Family at Thanksgiving dinner and unexpected cousin they have not seen in years arrives-change focus from dinner to cousin

- Phase lock: Length of time all neurons are synchronized so that neuromodulation occurs which reinforces certain EEG rhythms-

  - This is what Kandel got the Nobel prize for in 2000. DNA/RNA and protein linkage to LTP and synapse growth and development of new synapses during learning

- Longer the phase shift, the more neurons are recruited and the higher the IQ

- (Thatcher, Applied neuroscience.com)
Phase shift

Phase lock
An EEG is done with eyes closed and open

Then artifact is taken out

Then the brain waves are quantified (qEEG) to determine which are 2 standard deviations above or below the mean (Z scores) when compared to normal individuals
The most Comprehensive EEG and QEEG System Available: Dynamic EEG Databases, Discriminant Functions, Power, Coherence, Phase, Pre vs Post Treatment Statistics, Batch Processing, LORETA, JTFA, Video Integration

Pre vs Post Treatment Statistics And Z Score EEG Biofeedback
# Z Scored FFT Absolute Power

**Intrahemispheric: LEFT**

<table>
<thead>
<tr>
<th></th>
<th>DELTA</th>
<th>THETA</th>
<th>ALPHA</th>
<th>BETA</th>
<th>HIGH BETA</th>
<th>BETA 1</th>
<th>BETA 2</th>
<th>BETA 3</th>
</tr>
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<tbody>
<tr>
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<tr>
<td>F3 - LE</td>
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**Intrahemispheric: RIGHT**

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<th>BETA 3</th>
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<td>1.34</td>
<td>1.07</td>
<td>1.31</td>
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Patient CT scan prior to neurosurgery
Before LORETA NF, HAM-17 = 22, Mini Mental Status = 21
After 22 sessions LORETA NF, HAM-17=8, Mini Mental Status=29
14 Months after completing NF-Ham-17=0,
# Neuropsych testing repeated

<table>
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<tr>
<th>Performance Scale</th>
<th>1999</th>
<th>2004</th>
<th>2014</th>
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<tbody>
<tr>
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<td>11</td>
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<td>Working Memory</td>
<td>104*</td>
<td></td>
<td>89*</td>
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<tr>
<td>Processing Speed</td>
<td>96**</td>
<td></td>
<td>108**</td>
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<tr>
<td>Full Scale IQ</td>
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<td></td>
<td>104</td>
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<tr>
<td>GAI</td>
<td>123</td>
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</table>
After 5 more sessions LORETA NF targeting WM
Before NF
After 22 sessions
After 5 sessions targeting WM using center and maximal voxels with similar standard deviations (fusion)-Fusion appeared to get faster results over 5 sessions than previous NF requiring 22 sessions and after 5 sessions, patient tapered off antidepressant
Pre BRIEF-A

Profile of BRIEF®-A T Scores - Pre NF

<table>
<thead>
<tr>
<th>T-score</th>
<th>Inhibit</th>
<th>Shift</th>
<th>Emotional</th>
<th>Self Monitor</th>
<th>Initiate</th>
<th>Working Memory</th>
<th>Plan Organize</th>
<th>Task Monitor</th>
<th>Org. of Materials</th>
<th>BRI</th>
<th>Mt</th>
<th>GEC</th>
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<td>83</td>
</tr>
<tr>
<td>Percentile</td>
<td>86</td>
<td>&gt;99</td>
<td>92</td>
<td>80</td>
<td>&gt;99</td>
<td>&gt;99</td>
<td>&gt;99</td>
<td>&gt;99</td>
<td>95</td>
<td>97</td>
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<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Note: Age-specific norms have been used to generate this profile. For additional normative information, refer to the Appendixes in the BRIEF®-A Professional Manual.
Profile of BRIEF®-A T Scores-Post NF
Research Domain Criteria (RDoC) at NIMH

• The primary reason that criterion of clinical significance is used in the DSM 5 and earlier versions is related to: “. . .the absence of clear biological markers or clinically useful measurements of severity for many mental disorders” (DSM-5, page 21)

• A notable attempt to break this circular reasoning is the U.S. NIMH Research Domain Criteria (RDoC) and personalized or precision medicine, in which EEG’s could be used to inform core psychopathological instabilities, rather than investigate the EEG correlate of signs and symptoms that have an “inescapable heterogeneity”
Summary

• LORETA NF has been shown to improve symptoms of depression and PS in very sessions and symptoms continued to improve one year later.

• More research is needed to determine if LORETA NF occurs in fewer sessions with enduring effects.

• If so, NF may become more affordable.
“We should start shifting to better-defined sub-groupings that also make sense from a neurobiological perspective.

For example a more specific characterization e.g. impaired vs. normal default mode function (Helps et al., 2010), impaired vs. normal circadian function (van der Heijden et al., 2005), low vs. high vigilance regulation (Hegerl and Hensch, 2012) etc.”

(Editorial Clinical Neurophysiology, 2014)
Research Domain Criteria (RDoC) at NIMH-Buckholtz et al, 2012
Z Score Neurofeedback Publications
47 studies


**LORETA EEG Biofeedback**


PMID:


Conclusions

• 1. NF has shown to be important as an integrative approach to treating psychiatric disorders

• 2. Early DBPCT studies that did not show effectiveness were often flawed due to a lack of treatment matching and poorly devised protocols, etc.

• 3. However, these early DBPCT set the stage for better designed studies.

• 4. Quantitative EEG opens the door for the ability to determine specific NF protocols better suited to the patient.

• 5. Quantitative EEG can be used as an important tool to determine response to medication

• 6. NF and LORETA NF has been shown to have enduring effects that continue to improve over time
Conclusions

• 7. LORETA NF, as well as, other NF modalities using qEEG fits in with the new directive of NIMH (RDoC)-especially in regards to personalized medicine and the recognition of treatment entities targeting networks.

• 8. Although a DBPC study using TBR has now been funded by NIH and approved for study, the results are >5 years away.

• 9. Meanwhile, RCT’s should continue with many different approaches (SCP, TBR, SMR, LORETA NF, Z score NF, Multivariant Coherence) to determine when these different approaches may be useful in different patients.

• 10. Clinicians should be careful about what amplifiers, software programs and “FDA” approved devices they use.

• 11. Clinicians should be trained in by certified NF clinicians but should continue to see it as another intervention among many other interventions we use (i.e CBT).