Tuning the Traumatized Brain, Mind, and Heart: LORETA Z-Score Neurofeedback and Heart Rate Variability Biofeedback for Chronic PTSD

A dissertation research study for
The College of Integrative Medicine and Health Sciences
Saybrook University

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The Traumatized Mind

- Emotional dysregulation
- Intrusive memories
  - Flashbacks
  - Nightmares
- Avoidance and withdrawal
- Alterations in reactivity and arousal
  - Hyperarousal
  - Dissociation
- Negative changes in cognition
The Traumatized Brain

- Abnormalities in both the function and structure of the brain
- Need to target these underlying roots
- Heterogenous disorder = heterogenous findings in neuroimaging research
  - 636,120 possible clinical presentations
- Variations related to type of trauma, age, duration, attachment relationships, comorbidities, substance use, etc.
The Traumatized Brain

- Decreased gray matter volume:
  - Left, medial region of frontal cortex
  - Lateral orbitofrontal cortex
  - Right inferior parietal cortex
  - Bilateral isthmus of the cingulate cortex
  - Right, middle region of the cingulate gyrus
  - Insular cortex
The Traumatized Brain

- Alteration in brainwave patterns:
  - Increased right hemispheric beta power
  - Higher peak alpha frequency
  - Increased alpha asymmetry in frontal and parietal regions
  - Reduced theta activity (4-5 Hz) over the right temporal lobe
  - Reduced theta activity (6-7 Hz) bilaterally in prefrontal regions
  - Excess theta activity (4.5-7.5 Hz) in premotor and parietal regions
  - Theta hyperconnectivity between the right superior parietal, right middle temporal, and left frontal lobules
  - Heightened sensitivity of the amygdala/imbalances with mPFC
The Traumatized Brain

- Altered functional connectivity within Default Mode Network
- Over-engagement/altered connectivity of Salience Network
- Failure to properly recruit Central Executive Network
- Decreased resting-state functional connectivity in CEN
Neurofeedback!
Systematic Review on Neurofeedback for PTSD

- 10 studies (n = 213)
- Variety of modalities, populations, and measurement tools
- Primary outcomes:
  - Medium to large effects on PTSD symptoms and/or EEG
  - F/U: Improvements maintained in majority of trainees
    - 3 studies, 1-26 mos
- Most small, uncontrolled, convenience samples
LORETA Z Score Neurofeedback (LZN F)

- Only 1 small case series reported on LZN F for PTSD
- A fairly new, technologically-advanced modality of EEG biofeedback
- 19 electrodes and Low Resolution Electromagnetic Tomography Analysis (LORETA) 3D source imaging
  - Train specific regions deeper within the cortex
  - Train multiple regions simultaneously
  - Train connectivity patterns between regions / entire networks
- More targeted/comprehensive/indiv? More efficient outcomes?
Primary Purpose

- To generate preliminary data on the effectiveness of LZNF training for:
  - Reducing PTSD symptoms
  - Normalizing neural activation patterns
  - Improving autonomic regulation
Research Design

AN OVERVIEW OF THE METHODS, TOOLS, AND PROTOCOLS
Pretest-Posttest Control Group Design

CONTROL GROUP

OUT OF CONTROL GROUP
HRV Biofeedback (HRVB) as Active Control

- Electrocardiography (ECG) and respiration sensor
- Train the heart to produce higher levels of Heart Rate Variability
  - A measure of beat-to-beat heart rate intervals
- ACTIVE = previously found effective for reducing PTSD
  - More ethical than sham for sensitive populations
  - Closely matched to LZNF condition
    - e.g., time at rest, therapist, A/V feedback based on physiology, etc.
The Traumatized Heart

- Human heart contains ~ 40,000 neurons
- In constant communication with brain
- HRV associated with autonomic regulation
- Low HRV in individuals with PTSD
Sample Demographics

- Random sampling from Denver/Boulder area
- 24 adults enrolled
  - Ages 30-60, mean ~44
  - Multiple traumas (min 3, mean ~6 direct experiences)
    - 15 sexual trauma, 14 physical assault, 12 childhood abuse/neglect, 11 life-threatening illness/injury, 8 natural disaster, 3 combat veterans, 2 first-responders
  - 6+ months passed since the traumatic event
Sample Demographics

- Criteria for inclusion less rigorous than many other PTSD studies
  - Majority diagnosed with at least one comorbidity
    - e.g., anxiety disorder, depression, bipolar, ADHD, etc.
  - Challenging for interpretations/generalizations
  - More ecological validity
    - Approx. 80% with PTSD have at least 1 comorbidity
- Eligible individuals alternately assigned to LZNF or HRVB
  - Completers: LZNF n = 12, HRVB n = 11 (1 dropout)
LZNFF Protocol Design

- Symptom checklist-functional neural network match (SCL-FNM) method

Networks Tab:
- Default
- Salience
- Executive

Z-Tunes

All metrics:
- Amplitude
- Coherence
- Phase
- Phase Lock
- Phase Shift
HRVB Protocol Design

- Determined participant’s heart’s resonant frequency
  - set breath pacer to that rate
- Feedback based on HRV amplitude
Both Groups: Sessions and Feedback

- 2 assessment sessions
- 15 training sessions, 20 min each (4 rounds of 5 minutes)
- Audio and visual feedback:
  - Movie with zoom/volume features (Zukor Multimedia Player)
  - HRVB screen also contained breath pacer
  - Manually adjusted threshold to maintain 40-60% reward
  - i.e., LZNF 25-35 rewards per minute
What is the effect of 15 sessions of LZNF training, as compared to 15 sessions of HRVB training, on mental health symptoms, HRV metrics, and deviated neural networks in adults with chronic PTSD?
Statistical Analyses

- To answer... 7 dependent variables and 10 hypothesis sets
- To test hypotheses/effectiveness of the interventions:
  - Non-parametric counterparts to paired and independent samples t-tests: Wilcoxon and Mann-Whitney U analyses
  - Signed rank – better for heterogenous samples/outliers
- Cohen’s $d$ effect sizes
Results

PRINCIPLE FINDINGS FOR EACH OUTCOME MEASURE
Outcome Measure 1: PTSD Symptoms

PTSD Checklist for DSM-V (PCL-5)

Null hypothesis 1. There is no difference between the LZNF and HRVB groups in the amount of pre-post change in PCL-5 scores.

Alternative hypothesis 1. There is a statistically significant difference between the LZNF and HRVB groups in the amount of pre-post change in PCL-5 scores.
Outcome Measure 1: PTSD Symptoms

- LZNF pretest to posttest PTSD symptoms
  - Significantly lower in posttest, Wilcoxon $p = .003$
    - Pretest: $M = 46.17$, $SD = 14.23$; posttest: $M = 18.08$, $SD = 12.65$; Cohen’s $d = 2.09$

- HRVB pretest to posttest PTSD symptoms
  - Significantly lower in posttest, Wilcoxon $p = .006$
    - Pretest: $M = 49.82$, $SD = 10.16$; posttest: $M = 31.18$, $SD = 13.53$; Cohen’s $d = 1.40$
PCL-5 difference between groups non-significant, $p = .414$, $d = 0.57$
Outcome Measure 2: Physiological Anxiety Symptoms

Beck Anxiety Inventory (BAI)

Null Hypothesis 2. There is no difference between the LZNF and HRVB groups in the amount of pre-post change in BAI scores.

Alternative Hypothesis 2. There is a statistically significant difference between the LZNF and HRVB groups in the amount of pre-post change in BAI scores.
Outcome Measure 2: Physiological Anxiety Symptoms

- **LZN F Pretest to Posttest Anxiety**
  - Posttest anxiety significantly lower, Wilcoxon $p = .003$
  - Pretest: $M = 25.50$, $SD = 8.08$; Posttest: $M = 9.83$, $SD = 6.52$; Cohen’s $d = 2.13$

- **HRVB Pretest to Posttest Anxiety**
  - Posttest anxiety significantly lower, Wilcoxon $p = .018$
  - Pretest: $M = 24.91$, $SD = 8.77$; Posttest: $M = 18.18$, $SD = 8.95$; Cohen’s $d = 0.76$
Outcome Measure 2: Physiological Anxiety Symptoms

- BAI difference between groups statistically non-significant, $p = .214$, $d = .94$
Neural Network Analyses

- Exported all LORETA current source density z scores to Excel (71,820 metrics) → separated metrics of 3 networks
- Z scores negative and positive and thus cancel out
  - Converted to absolute scores
- Dampening effects of multiple metrics
  - Several Brodmann areas per network, 1-30 Hz = 600-780 metrics per network
    - E.g., average of $3.5 + 1.5 + 0.5 / 3 = 1.83$
  - Used total number of significant absolute z-scores ($z > 1.96$)
LZNF Responders

- Canceling effects of increases/decreases in significant z-scores between participants
  - Further analyzed LZNF Responders subset (n = 9) to assess size and significance of effect w/o canceling
    - Responders = LZNF participants whose overall number of significant z scores decreased from pretest to posttest (by any amount)
Outcome Measure 3: Default Mode Network (DMN)

**Null hypothesis 3.1.** There is no difference in the amount of pre-post change in total significant LORETA CSD z-scores in the DMN between the LZNf and HRVB groups.

**Alternative hypothesis 3.1.** There is a significant difference in the amount of pre-post change in total significant LORETA CSD z-scores in the DMN between the LZNf and HRVB groups.
Outcome Measure 3: Default Mode Network (DMN)

- **Null hypothesis 3.2.** There is no difference between the pre-intervention and post-intervention total significant LORETA CSD z-scores in the DMN of Responders within the LZNF group.

- **Alternative hypothesis 3.2.** There is a significant difference between the pre-intervention and post-intervention total significant LORETA CSD z-scores in the DMN of Responders within the LZNF group.
Outcome Measure 3: Default Mode Network (DMN)

- LZNFL Pretest to Posttest DMN
  - Total significant z-scores lower in posttest (Pretest $M = 70.50$, $SD = 105.04$; Posttest $M = 54.33$, $SD = 96.13$; Cohen’s $d = 0.27$)
  - Not significant, Wilcoxon $p = .213$

- HRVB Pretest to Posttest DMN
  - Significant z-scores lower in posttest (Pretest $M = 74.27$, $SD = 73.82$; Posttest: $M = 68.27$, $SD = 81.18$; Cohen’s $d = 0.08$)
  - Not significant, Wilcoxon $p = .790$
Outcome Measure 3: Default Mode Network (DMN)

- Pre-post difference between LZN F and HRVB groups was non-significant, $p = .713$, $d = 0.17$
Outcome Measure 3: Default Mode Network (DMN)

- LZNFR Responders pretest-posttest difference in DMN:
  - Pretest $M = 86.22$, $SD = 117.24$; posttest $M = 49.89$, $SD = 108.95$
Outcome Measure 3: Default Mode Network (DMN)

- LZNF Responders showed large, statistically significant pre-post improvement in the DMN, Wilcoxon $p = .012$, $d = .96$
Outcome Measure 3: Salience Network (SN)

- **Null hypothesis 4.1.** There is no difference in the amount of pre-post change in total significant LORETA CSD z-scores in the SN between the LZNF and HRVB groups.

- **Alternative hypothesis 4.1.** There is a significant difference in the amount of pre-post change in total significant LORETA CSD z-scores in the SN between the LZNF and HRVB groups.
Outcome Measure 4: Salience Network (SN)

- **Null hypothesis 4.2.** There is no difference between the pre-intervention and post-intervention total significant LORETA CSD z-scores in the SN of Responders within the LZNF group.

- **Alternative hypothesis 4.2.** There is a significant difference between the pre-intervention and post-intervention total significant LORETA CSD z-scores in the SN of Responders within the LZNF group.
Outcome Measure 4: Salience Network (SN)

- **LZNFL Pretest to Posttest SN**
  - SN z-scores lower in posttest (Pretest $M = 82.00$, $SD = 119.83$; Posttest $M = 54.42$, $SD = 102.05$; Cohen’s $d = 0.49$)
  - Non-significant, Wilcoxon $p = .092$

- **HRVB Pretest to Posttest SN**
  - SN z-scores lower in posttest (Pretest: $M = 89.09$, $SD = 82.74$; Posttest: $M = 74.91$, $SD = 115.85$; Cohen’s $d = 0.14$)
  - Non-significant, Wilcoxon $p = .625$
Outcome Measure 4: Salience Network (SN)

- SN pre-post difference between LZNF and HRVB groups was non-significant, $p = 1.00$, $d = 0.18$
Outcome Measure 4: Salience Network (SN)

- LZNF Responders pretest-posttest difference in SN:
  - Pretest $M = 101.67$, $SD = 133.38$; posttest: $M = 51.44$, $SD = 117.30$
Outcome Measure 4: Salience Network (SN)

- LZNF Responders showed very large, statistically significant improvement in the SN, Wilcoxon $p = .008, d = 1.32$
Outcome Measure 5: Central Executive Network (CEN)

- **Null hypothesis 5.1.** There is no difference in the amount of pre-post change in total significant LORETA CSD z-scores in the CEN between the LZNF and HRVB groups.

- **Alternative hypothesis 5.1.** There is a significant difference in the amount of pre-post change in total significant LORETA CSD z-scores in the CEN between the LZNF and HRVB groups.
Outcome Measure 5: Central Executive Network (CEN)

- **Null hypothesis 5.2.** There is no difference between the pre-intervention and post-intervention total significant LORETA CSD z-scores in the CEN of Responders within the LZNFG group.

- **Alternative hypothesis 5.2.** There is a significant difference between the pre-intervention and post-intervention total significant LORETA CSD z-scores in the CEN of Responders within the LZNFG group.
Outcome Measure 5: Central Executive Network (CEN)

- **LZNF Pretest to Posttest CEN**
  - CEN z-scores lower in posttest (Pretest $M = 66.17$, $SD = 99.79$; Posttest $M = 42.50$, $SD = 81.27$; Cohen’s $d = 0.59$)
  - Non-significant, Wilcoxon $p = .084$

- **HRVB Pretest to Posttest CEN**
  - CEN z-scores lower in posttest (Pretest $M = 66.00$, $SD = 69.42$; Posttest $M = 57.75$, $SD = 94.41$; Cohen’s $d = 0.10$)
  - Non-significant, Wilcoxon $p = .790$
Outcome Measure 5: Central Executive Network (CEN)

- CEN pre-post difference between the LZNF and HRVB groups non-significant, $p = .414$, $d = 0.29$
Outcome Measure 5: Central Executive Network (CEN)

LZNFRS Responders pretest-posttest difference in CEN:

- Pretest: $M = 83.44$, $SD = 110.48$; posttest: $M = 43.11$, $SD = 95.11$
Outcome Measure 5: Central Executive Network (CEN)

- LZNF Responders showed very large, statistically significant improvement, Wilcoxon $p = .008$, $d = 1.33$
A Picture Worth 1000 words: NF111

Before:

After:
A Picture Worth 1000 Words: NF111

Sample of LORETA at 12 Hz

Before:

After:
A Picture Worth 1000 words: NF115

Before:

After:
A Picture Worth 1000 Words: NF115

Sample of LORETA at 28 Hz

Before:

After:
A Picture Worth 1000 words: NF121

Before:

After:
A Picture Worth 1000 Words: NF121

Sample of LORETA at 29 Hz

Before:

After:
A Picture Worth 1000 words: NF131

Before:

After:
A Picture Worth 1000 Words: NF131

Sample of LORETA at 15 Hz

Before:

After:
Outcome Measure 6: Heart Rate Variability (SDNN)

- HRV Standard Deviation of the NN Interval (SDNN)
  - **Null hypothesis 6.** There is no difference in the amount of pre-post change in the HRV metric SDNN between the LZNF and HRVB groups.
  - **Alternative hypothesis 6.** There is a significant difference in the amount of pre-post change in the HRV metric SDNN between the LZNF and HRVB groups.
Outcome Measure 6: Heart Rate Variability (SDNN)

- **LZNF Pretest to Posttest SDNN**
  - SDNN slightly lower in posttest (Pretest $M = 37.82$, $SD = 23.51$; Posttest $M = 36.53$, $SD = 18.32$; Cohen’s $d = .11$)
  - Non-significant, Wilcoxon $p = .814$

- **HRVB Pretest to Posttest SDNN**
  - SDNN higher in posttest (Pretest $M = 24.90$, $SD = 11.97$; Posttest $M = 29.82$, $SD = 17.73$; Cohen’s $d = 0.36$)
  - Non-significant, Wilcoxon $p = .182$
Outcome Measure 6: Heart Rate Variability (SDNN)

- SDNN pre-post difference between the LZNF and HRVB groups non-significant, $p = .266$, $d = 0.58$
Outcome Measure 7: Heart Rate Variability (RMSSD)

- **Root Mean Square of the Successive Differences (RMSSD)**

  - **Null hypothesis 7.** There is no difference in the amount of pre-post change in the HRV metric RMSSD between the LZNF and HRVB groups.

  - **Alternative hypothesis 7.** There is a significant difference in the amount of pre-post change in the HRV metric RMSSD between the LZNF and HRVB groups.
Outcome Measure 7: Heart Rate Variability (RMSSD)

- **LZNF Pretest to Posttest RMSSD**
  - RMSSD lower in posttest (Pretest $M = 34.41$, $SD = 17.32$; Posttest $M = 31.51$, $SD = 12.74$; Cohen’s $d = 0.25$)
  - Non-significant, Wilcoxon $p = .530$

- **HRVB Pretest to Posttest RMSSD**
  - RMSSD higher in posttest (Pretest $M = 22.18$, $SD = 12.13$; Posttest: $M = 23.93$, $SD = 16.77$; Cohen’s $d = 0.12$)
  - Non-significant, Wilcoxon $p = .722$
Outcome Measure 7: Heart Rate Variability (RMSSD)

- RMSSD pre-post difference between the LZNf and HRVB groups non-significant, $p = .551$, $d = 0.50$
Discussion

AN OVERVIEW OF THE SIGNIFICANCE OF THE RESEARCH FINDINGS
Tuning the Traumatized Brain

- Overall decrease in deviated brainwave activity in all groups following only 15 sessions of LZNF training
  - Difference between LZNF and HRVB not significant
    - Canceling effects of significant z-score increases/decreases
- LZNF Responders (75% of LZNF): Large to very large, significant effects in all three neural networks
What about the Non-Responders?

- 25% of total LZNFE group \((n = 3)\)
- “Non-responders” for the sake of distinguishing/consistency
  - **However…**
    - Brains did show changes, just not in expected direction
      - Initial low amplitude → overall increases in power
      - Z-score increases primarily in alpha band
        - Associated with feelings of calmness
        - All 3 reported pre-post improvements in symptoms
Responders vs. Non-Responders

- What makes the difference?
  - Healing process always linear (i.e., toward neurotypical) or sometimes dynamic?
    - Compensatory mechanisms
  - Brain-Computer Interface illiteracy/inefficiency?
    - Differences in brain that make self-regulation of neural activity more challenging
      - Improve assessment/methods to overcome
  - Only a matter of time?
Tuning the Traumatized Mind

- PTSD and anxiety symptoms decreased significantly by very large amounts in both groups
  - Larger effects than prior research
  - Less sessions than traditional (15 vs. 40)
  - Difference between groups not significant, medium to large effects of group type
Tuning the Traumatized Heart

- Exploratory: first to assess HRV changes following LZNF training
  - Effects small and not statistically significant
    - Ceiling effect in 3 LZNF participants with high baseline HRV
- Future assessments:
  - During training
  - Under stress
  - During stress recovery
Tuning the Traumatized Mind

- Qualitative reports on pre-session questionnaires:
  - Improved mood/more positive outlook
  - Increased ability to manage stress
  - Less reactivity to negative/stressful situations
  - More calm and peaceful
  - Decreased nightmares/improved sleep quality
  - Increased mental clarity
  - Increased ability to feel and process emotions
  - Healthier relationships
  - Returned sense of humor
Limitations/Recommendations

- Confounding variables:
  - Placebo/nocebo
  - Hawthorne effect
  - Dual roles and desire to please/support the researcher
  - External psychotherapy, medication, and substances
  - External life stressors (e.g., exposure to triggers, job loss, seasonal shifts, etc.)
  - Diurnal variables (e.g., sleep quality)
  - Physiological variables (e.g., hormonal shifts)
  - Non-cerebral artifact (e.g., EMG, etc.)
  - Slow, diaphragmatic breathing
Limitations/Recommendations

- Small sample
  - Increased probability for Type II error (failure to reject false null)
  - Potentially underpowered for statistical significance on measures with smaller effect sizes
- HRVB as active control
  - Unblinded (future may connect to both technologies for all sessions to blind participant)
  - Large effect harder to achieve statistical significance between groups
- Heterogeneity: set inclusion parameters/clustering
Limitations/Recommendations

- LZNF protocol only individualized to an extent to keep reproducible and quantifiable
- Only regions within selected networks, automated SCL-FNM method
  - Future research: use as starting point with manualized clinical adjustments
  - Clinical practice: should not replace clinical judgement/expertise
An Integrative Approach

- Add a 3rd group: Combined LZNF and HRVB group
- Target cortical/subcortical regions from different angles
- HRV closely linked to solitary nucleus of brainstem
  - connections to various cortical regions involved in DMN, SN, and CEN
- HRVB “bottom up” (peripheral → subcortical → cortical)
- LZNF “top down” (cortical → subcortical → peripheral)
- Higher-level regulatory functions
An Integrative Approach

- Combine with other neurofeedback/modulation modalities
  - Traditional amplitude training for empowerment/training self-regulation skills
  - Alpha-Theta for processing/integrating memories
  - Functional magnetic resonance imaging neurofeedback for deeper subcortical structures
  - Neurostimulation/neuromodulation tools to assist/“show the way”
  - LZNF for specificity and comprehensive network connectivity training
Conclusions

- Both LZNF and HRVB training were highly effective for reducing symptoms in adults with chronic PTSD.
- LZNF was largely effective for normalizing deviated brainwave activity within targeted neural networks in 75% of participants.
- LZNF produced these significant outcomes after only 15 sessions (less than traditional).
- Although differences between groups were not statistically significant, which may have been partially related to the canceling effects and small sample, this study did provide preliminary data on the specificity of each intervention.
  - Overall effect sizes larger in LZNF group for both symptom questionnaires and all three neural networks, larger in HRVB group for both HRV metrics.
- Dropout rates very low (0 LZNF, 1 HRVB).
- Future research should explore added benefits of integrating approaches.
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References

▶ 240 references...too many for these slides!
(Will email reference list upon request)
Let’s Connect!

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Questions/Comments