Module XV-D: Brain Fitness Therapies

TBI/PTSD ASSESSMENT AND TREATMENT

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Disclosures

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TBI/PTSD Assessment and Treatment

Learning Objectives

1. Attendees will be introduced to non-invasive brain imaging technologies applied to TBI and PTSD.
2. Attendees will be introduced to neuro-networks implicated in PTSD.
3. Attendees will be introduced to brain computer interface treatments for TBI and PTSD.

Test Questions (multiple choice; T/F)

1. A 3-tesla fMRI is ideal for white matter damage detection of the type commonly seen with deceleration and blast exposure injuries to the brain. T/F
2. One of the heart rate variability measures found to be low among those with PTSD and TBI is the SDNN. T/ F
3. Three primary neuro-networks implicated in PTSD are
    a) default mode, salience, executive
    b) default mode, salience, motor sensory
    c) Salience, executive, motor sensory

Answers: 1) F; 2) T 3) a

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Mounted and Dismounted IED blasts

M1 Abrams – 63 tons

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PTSD is more than just exposure to a few life threatening events.

- combat tempo
- 130^0 degree heat
- “moon dust”
- loss of best friends
- pushing through chronic pain

IED Blast Waves

1. **Primary blast trauma:**

   The shock wave causes injury to gas-filled organs like the lungs and bowels and can cause the eardrum to rupture. It can also cause brain damage.

2. **Secondary blast trauma:**

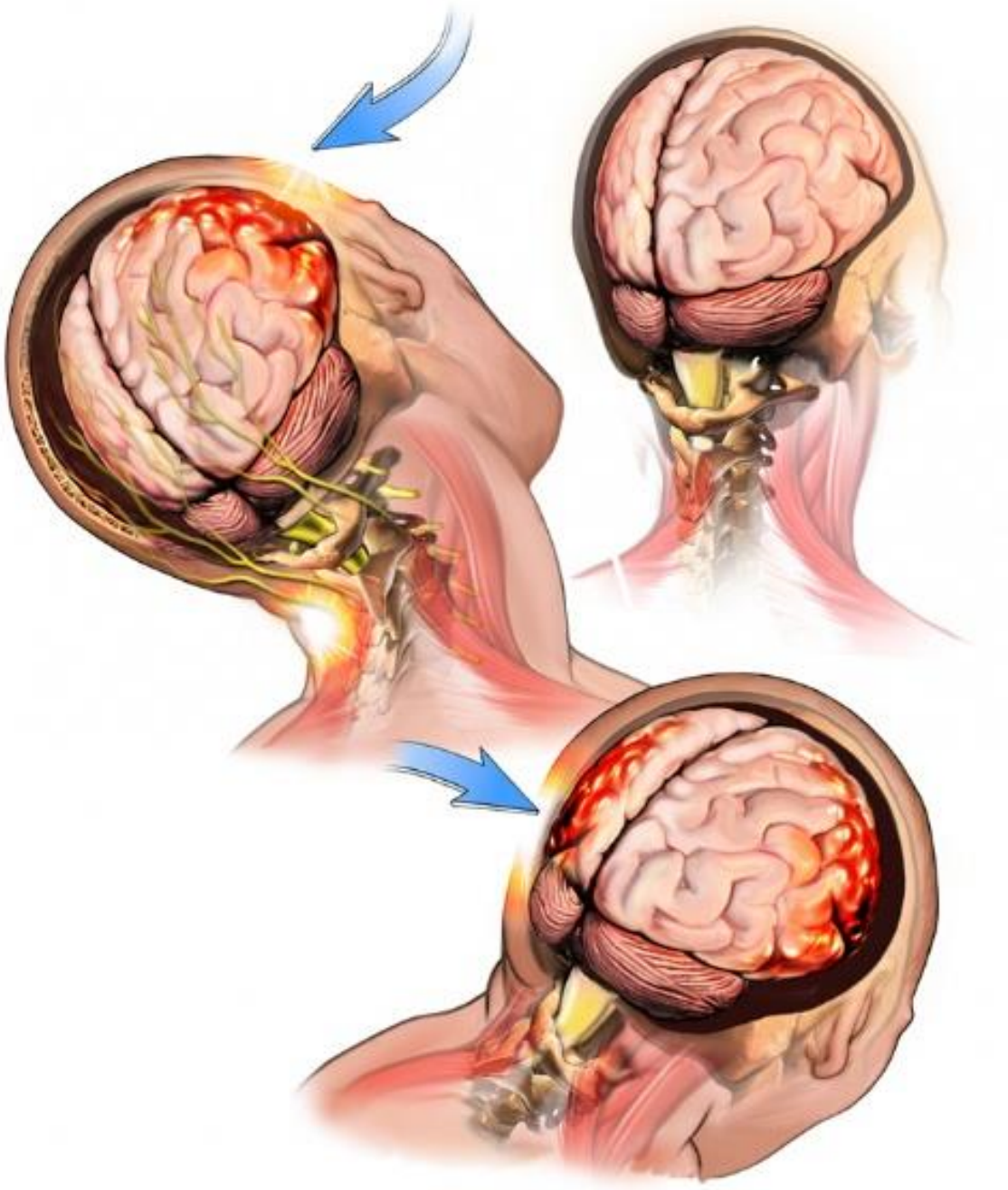
   These are injuries sustained when service members are hit with debris travelling at high speeds after the detonation.

3. **Tertiary blast injuries:**

   Blast winds trailing the primary shock wave can amputate limbs or throw people into the air.

4. **Quaternary blast injuries:**

   These result from high heat and exposure to noxious chemicals associated with the fire that follows the detonation.



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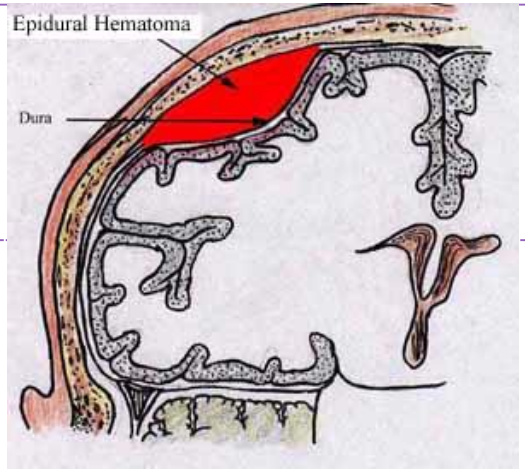
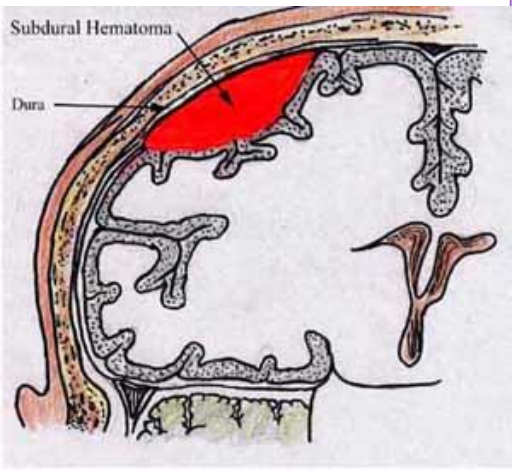
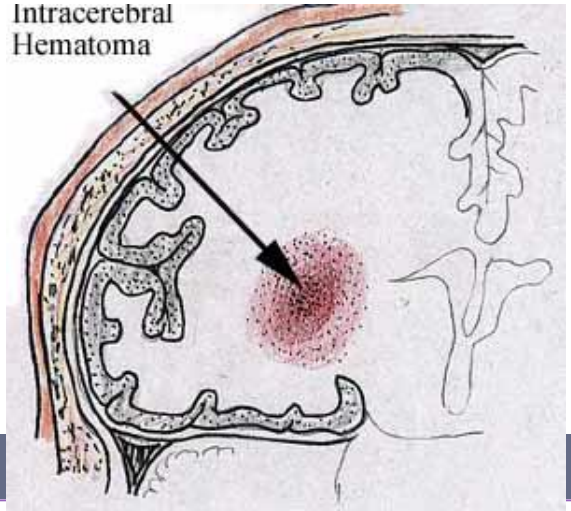


An **epidural hematoma** forms between the skull and the dura mater, the tough outer membrane that covers the brain. Epidural hematomas are most commonly seen in conjunction with a skull fracture. If the hematoma is not removed it can cause brain damage by putting pressure on the brain.

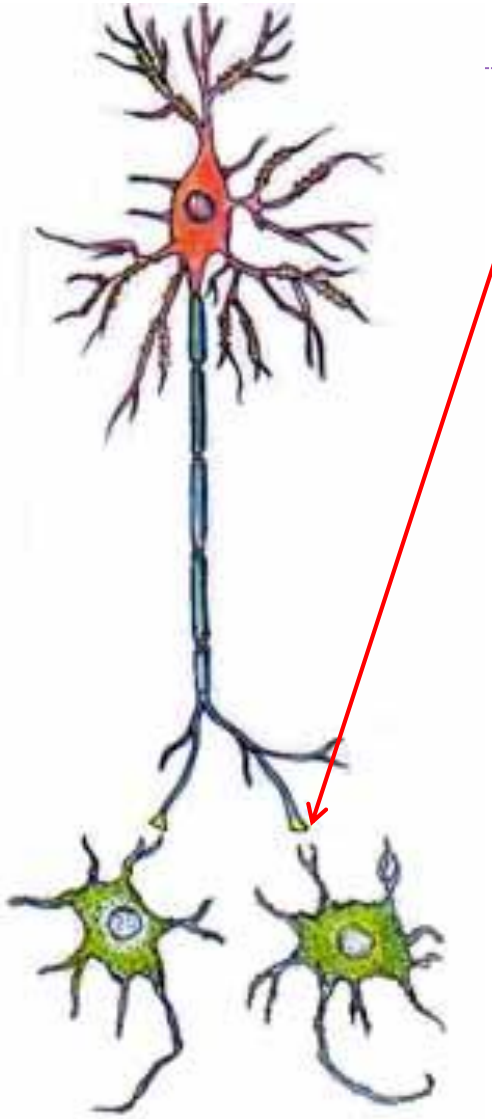


A **subdural hematoma** forms between the dura mater and the underlying membranes that cover the brain. These hematomas are seen most often in association with direct damage to the brain. Symptoms from hematomas may appear immediately or gradually as blood seeps out of torn blood vessels



Intracerebral hematomas result from accumulation of blood within the brain caused by bleeding in and around the brain

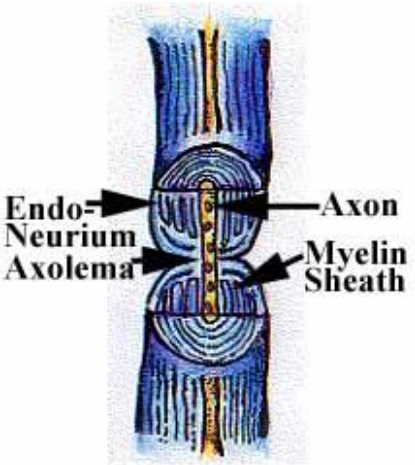
Normal Axonal Function



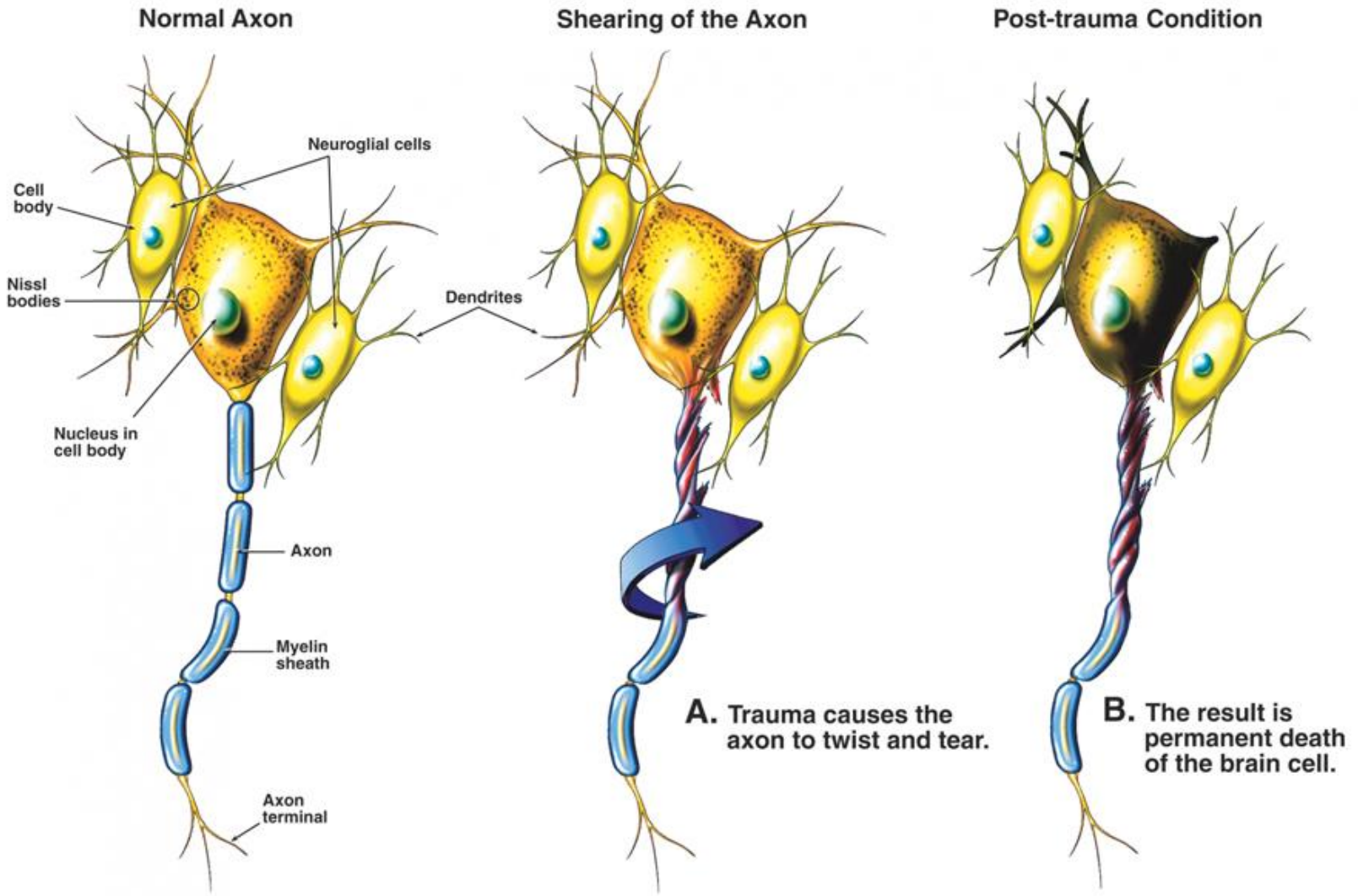
Here you can see how one neuron connects to another neuron.

There is a very small gap between the bouton (end of the neuron) and the dendrites of the neuron to which it connects.

Electrical impulses travel from the cell body down through the axon until they reach the bouton. The impulses are conveyed chemically from the bouton to the dendrites by substances called neurotransmitters.



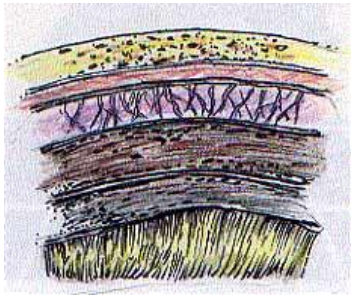
This shows a close up of an axon that has <u>not</u> been injured.



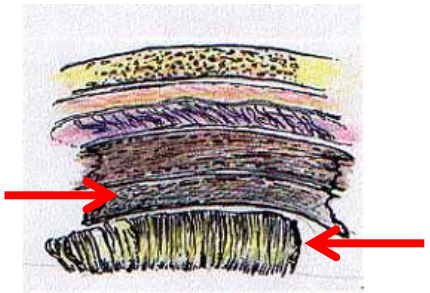
Diffuse Axonal Injury

- Primary pathological feature in all levels of brain injury
- Functional injury
- Not detectible on MRI or CT
- Decreased brain arousal & function

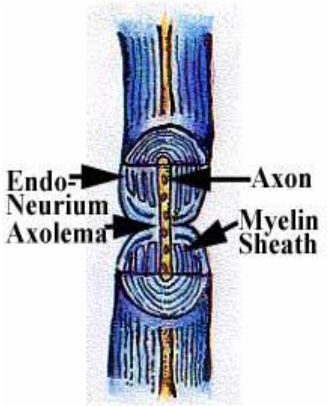
Healthy Neuron



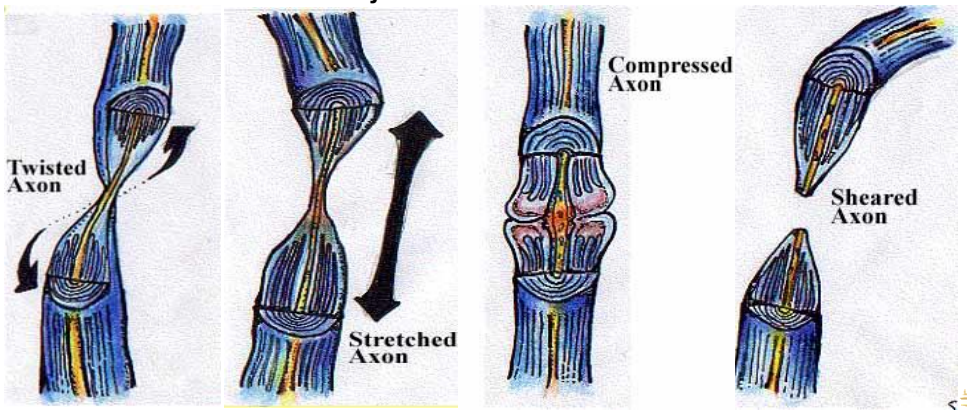
Shearing



Healthy Neuron



DAI Injured Neurons



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Axon Damage is **not** so easy to locate

- This kind of injury does not always show up on a typical CT or MRI scans and symptoms are often subtle and progress slowly.
- As a result patients are undiagnosed and misdiagnosed in part because loss of consciousness is not a prerequisite for mTBI.
- Rating scales and other neurological and functional examination methods, including *standard* EEG assessment, often produce false negative results (missed diagnoses) because they fail to measure ***multiple systems***.

Absence of evidence is not always evidence of absence.

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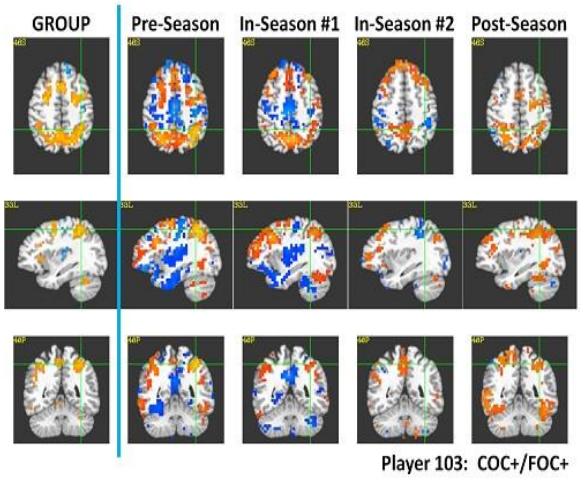
fMRI



Technology:

- Functional magnetic imaging
- Measure changes in oxidization
- High spatial resolution
- **Low** temporal resolution (~ 2sec)
- **Expensive**
- **Highly specialized facility**

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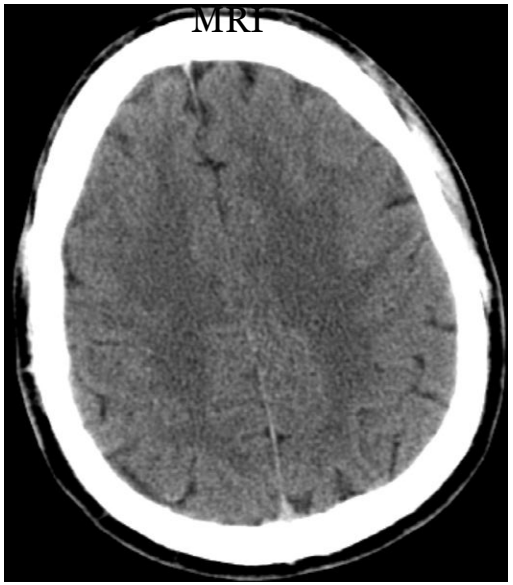
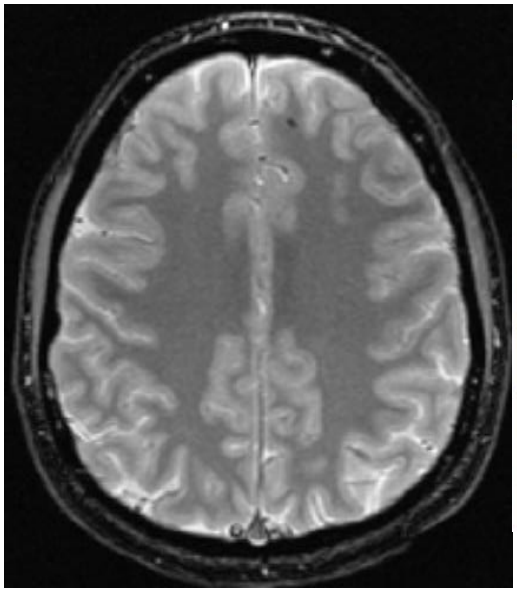
3T detects twice as many microhemorrhages as 1.5T

CT

MRI



3 tesla



At 7 Tesla, which is almost five times the field strength of most clinical MR scanners, the inherent heightened sensitivity to microvasculature can provide a major advantage by allowing the detection of very small vessels

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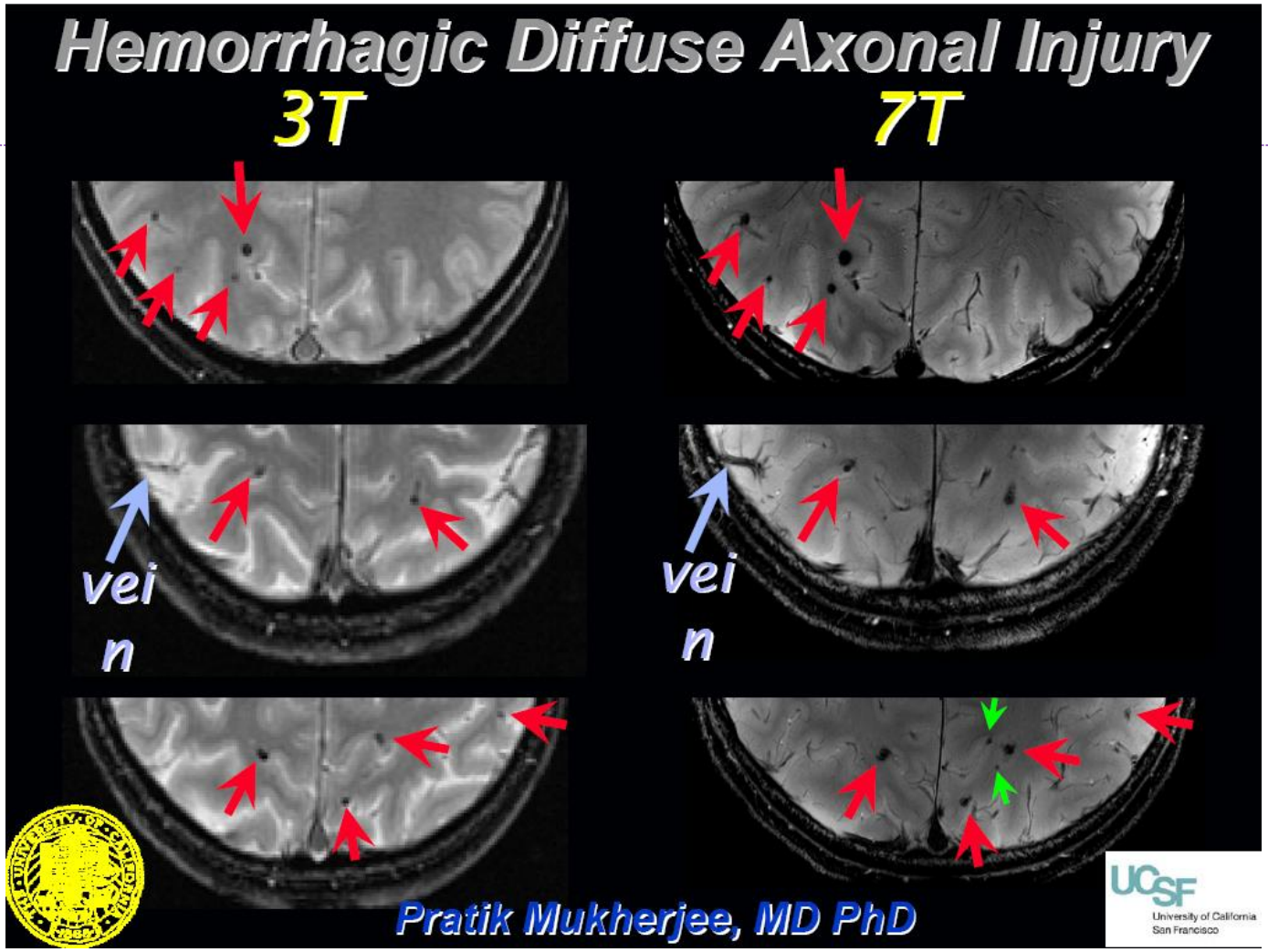

Lee H, Wintermark M, Gean A, Ghajar J, Manley G, Mukherjee P. *J Neurotrauma 2008; 25:1049-56*
Niogi S, Mukherjee P, Ghajar J et al., *AJNR 2008; 29:967-73*

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“Using functional MRIs to show the part of the brain that is active during fear and other traumatic emotions, we can see and measure the physiologic changes that occur during trauma." "These MRIs are telling us that the cause of PTSD is physical in nature, and not simply a 'psychological condition.'“

In a paper published in 2009, Lipov proposed a mechanism that trauma leads to an increase in nerve growth factor. "That leads to sprouting of the sympathetic nerves, which leads to increased production of norepinephrine and that makes people anxious."

Dr. Eugene Lipov, a Chicago-area anesthesiologist

While very helpful, MRI/DTI have high cost, lack of portability, and somewhat invasive.

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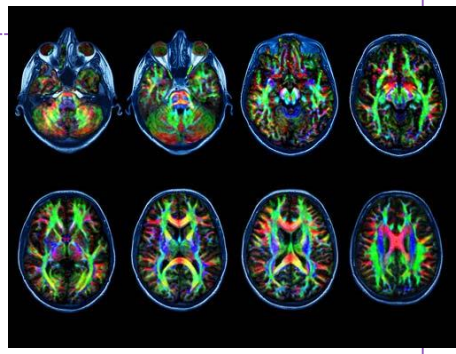
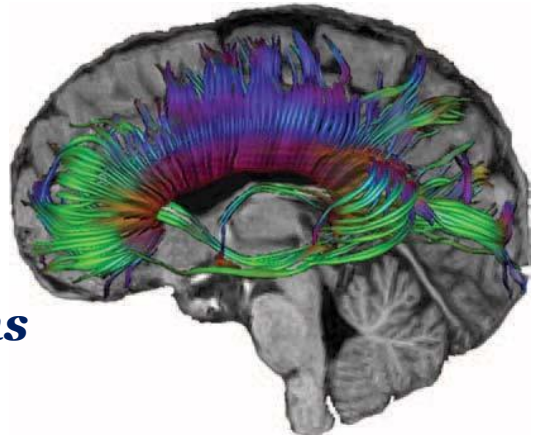
Diffusion Tensor Imaging (Basser et al., 1994)
– Is sensitive to microstructural changes within white matter tracts, which may improve the detection of axonal injury



Arfanakis et al. AJNR (2002) and many other studies
– can localize axonal shearing injury to specific white matter tracts, for structure-function correlation



Le et al. Neurosurgery (2005) and other studies
– can provide quantitative pathophysiological information that might be useful for determining prognosis and monitoring therapeutic interventions in TBI

McDonald et al. NEJM (2011)
– injuries still resolving after 12mo

Fibers running between the front and back are blue, those between right and left are red, and those running between the brain's interior and exterior are green

PRE-PUBLICATION EXECUTIVE SUMMARY

POSITION STATEMENT ACCEPTED FOR PUBLICATION IN
THE CLINICAL NEUROPSYCHOLOGIST

Official Position of the Military TBI Task Force on

The Role of Neuropsychology and Rehabilitation Psychology in the Evaluation, Management and Research of Military Veterans with Traumatic Brain Injury[1]

APPROVED by:
American Academy of Clinical Neuropsychology (AACN)
American Psychological Association Division 40 (Neuropsychology)
American Psychological Association Division 22 (Rehabilitation Psychology)
National Academy of Neuropsychology (NAN)

In summary, the increased prevalence and complexity of TBI in the current military combat setting creates a unique set of immediate challenges that require experts to develop *new, innovative methods for injury evaluation and treatment*. Beyond the front lines, similar challenges will be encountered in the post-deployment evaluation of veterans with mTBI

NEED: quick objective measure of cognitive operations

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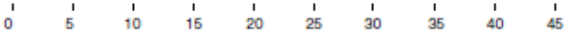
Self-Report tests have their place....

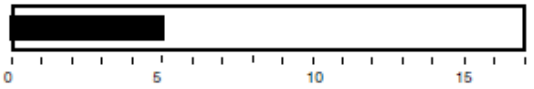
Posttraumatic Stress Diagnostic Scale

PTSD Diagnosis ☐ YES ■ NO ☐ Incomplete Information

Symptom Severity Score: 7



Number of Symptoms Endorsed: 5



Symptom Severity Rating: MILD

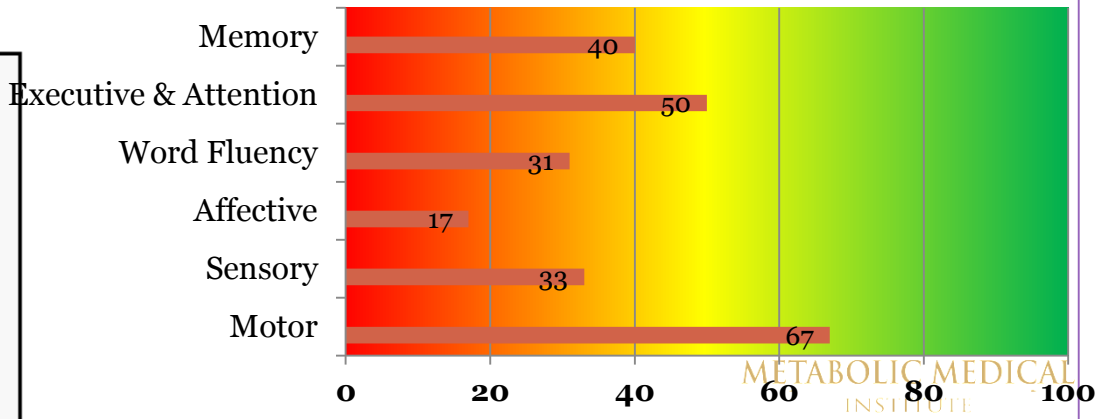
Level of Impairment in Functioning: NO IMPAIRMENT

Was the Criterion Met?

YES	NO	Incomplete Information	*DSM-IV* Criterion
■	☐	☐	A: Exposure to a traumatic event
■	☐	☐	B: Reexperiencing symptoms
☐	■	☐	C: Avoidance symptoms
■	☐	☐	D: Arousal symptoms
■	☐	☐	E: Symptom duration of 1 month or more
☐	■	☐	F: Distress or impairment in functioning

The PCL is a 17-item self-report measure of the 17 DSM-IV symptoms of PTSD. Respondents rate how much they were "bothered by that problem in the past month". Items are rated on a 5-point scale ranging from 1 ("not at all") to 5 ("extremely"). There are several versions of the PCL. The original PCL is the PCL-M (military). The PCL-M asks about problems in response to "stressful military experiences." The PCL-S (specific) asks about problems in relation to an identified "stressful military experience." The PCL-C (civilian) is for civilians and is not focused on any one traumatic events. Instead it asks more generally about problems in relation to stressful military experiences. A total score (range 17-85) is obtained by summing the scores from each of the 17 items. A second way to score the PCL-M is to follow the DSM-IV criteria.

1	Repeated, disturbing memories, thoughts, or images of a stressful military experience from the past?	4 - Quite a bit
2	Repeated, disturbing dreams of a stressful military experience from the past?	4 - Quite a bit
3	Suddenly acting or feeling as if a stressful military experience were happening again (as if you were reliving it)?	5 - Extremely
4	Feeling very upset when something reminded you of a stressful military experience from the past?	5 - Extremely
5	Having physical reactions (e.g. heart pounding, trouble breathing, or sweating) when something reminded you of a stressful military experience from the past?	4 - Quite a bit
6	Avoid thinking about or talking about a stressful military experience from the past or avoid having feelings related to it?	4 - Quite a bit
7	Avoid activities or situations because they remind you of a stressful military experience from the past?	4 - Quite a bit
8	Trouble remembering important parts of a stressful military experience from the past?	5 - Extremely
9	Loss of interest in things you used to enjoy?	5 - Extremely
10	Feeling distant or cut off from other people?	5 - Extremely
11	Feeling emotionally numb or being unable to have loving feelings for those close to you?	5 - Extremely
12	Feeling as if your future will somehow be cut short?	1 - Not at all
13	Trouble falling or staying asleep?	5 - Extremely
14	Feeling irritable or having angry outbursts?	3 - Moderately
15	Having difficulty concentrating?	5 - Extremely
16	Being "super alert" or watchful on guard?	5 - Extremely
17	Feeling jumpy or easily startled?	5 - Extremely
	PCL-M Total Score	**74**



EMDR

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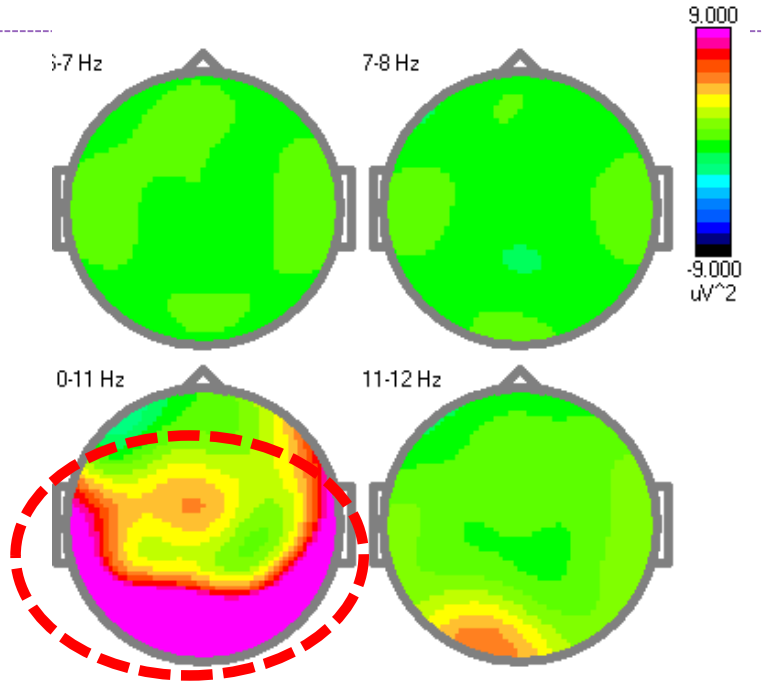
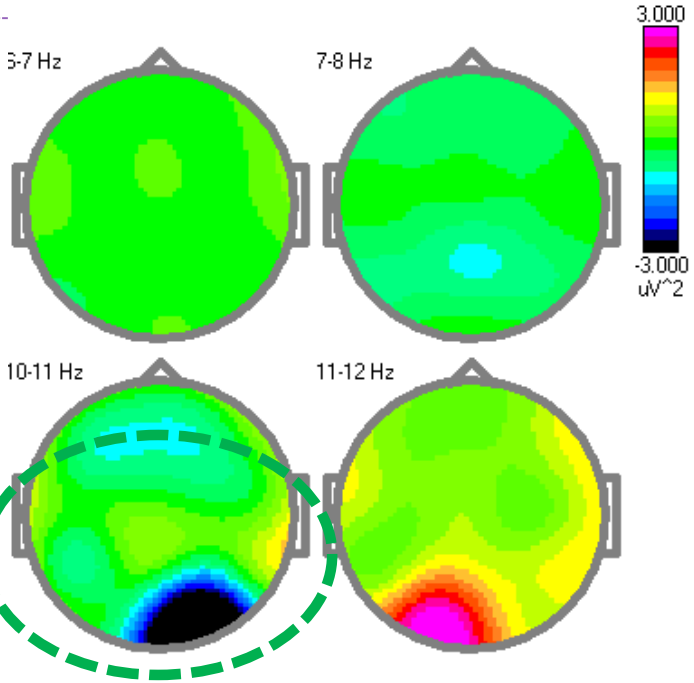
EMDR



Pre-EMDR:
faster alpha
Excessive beta 17-30Hz
Insomnia, anxiety, irritability, rage



Post-EMDR (3 sessions)
Reduction of alpha by 0.5Hz
Still has excessive beta 17-30Hz
Off all medications, sleeping, feels more connected to wife and children

Maps for absolute power spectra deviations from normality in 1 Hz windows (uV^2)

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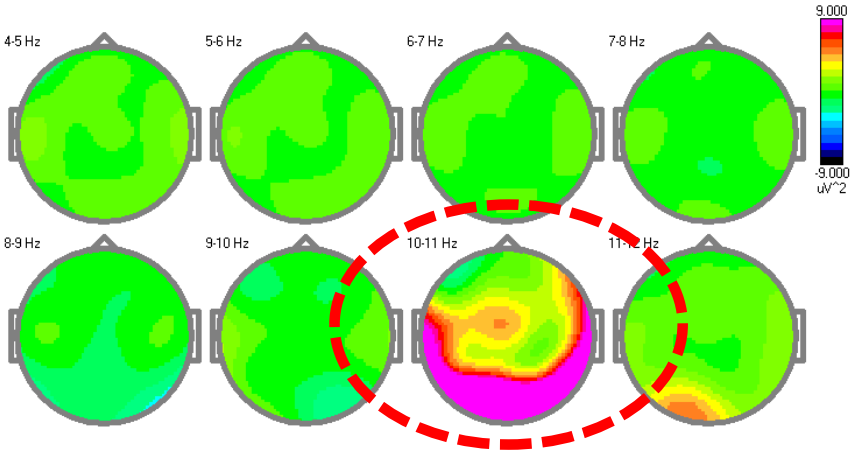
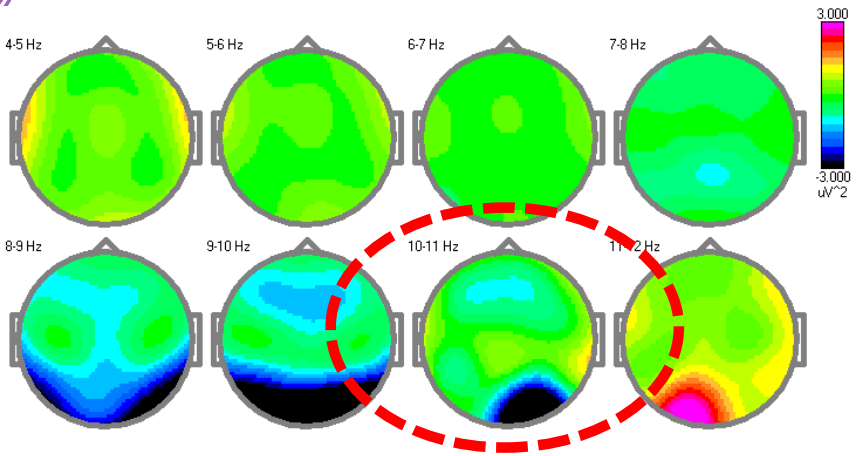
EMDR

But it helped identify areas of interest and track changes



Pre-EMDR

- Insomnia
- Anxiety
- Irritability
- rage



Post-EMDR

- off all medications
- sleeping
- "*I feel more connected to my wife and children*"

Maps for absolute power spectra deviations from normality in 1 Hz windows (uV^2)

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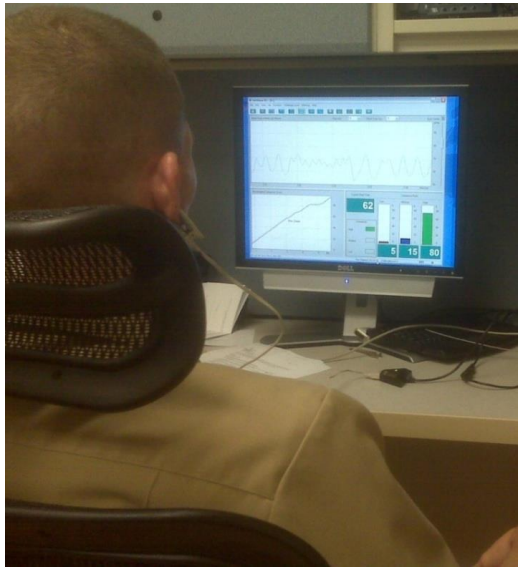
Heart Rate Variability (HRV)

- HRV biofeedback used for…
- anxiety disorders
- Asthma
- Cardiovascular conditions
- chronic obstructive
- pulmonary disorder
- chronic fatigue
- chronic pain
- essential hypertension
- irritable bowel syndrome



HRV biofeedback is "a process of training an active balancing between the sympathetic and parasympathetic branches' effects on the heart rhythm" (Shaffer & Moss, 2006).

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HRV and PTSD

- Vagus (10th cranial) nerve is a conduit for the brain stem to several visceral organs
- The myelinated cardioinhibitory vagal fibers, which originate in the nucleus ambiguus and terminate on the cardiac sinoatrial node, help regulate the heart rate response to stress.
- Removal of the "vagal brake" results in the expression of sympathetic NS influences on the heart
- Amygdala seems to play a roll in the interpretation of stressful experiences and influence vagal response to fear
- Reduced heart rate variability (HRV), a measured as variance in cardiac inter-beat intervals, or power, has been reported in combat-related PTSD.
- Vagal modulation is lacking with PTSD and biofeedback can help improve modulation; however, there seems to also require retraining the interpretation of the stressful experiences. HRV + EMDR

American Heart Journal

Volume 149, Issue 6, June 2005, Pages 1137

Clinical Investigation

Heart rate variability biofeedback as a behavioral neurocardiac intervention to enhance vagal heart rate control

Robert P. Nolan, PhD[a], Markad V. Kamath, PhD[b], John S. Floras, MD, DPhil[c], Jill Stanley, MA[d], Clement Pang, MSc[b], Peter Picton, MASc[c], Quincy R. Young, PhD[e]

Appl Psychophysiol Biofeedback (2009) 34:135–143
DOI 10.1007/s10484-009-9085-2

The Effects of Respiratory Sinus Arrhythmia Biofeedback on Heart Rate Variability and Posttraumatic Stress Disorder Symptoms: A Pilot Study

Terri L. Zucker · Kristin W. Samuelson · Frederick Muench · Melanie A. Greenberg · Richard N. Gevirtz

Appl Psychophysiol Biofeedback (2007) 32:19–30
DOI 10.1007/s10484-006-9029-z

ORIGINAL PAPER

Preliminary Results of an Open Label Study of Heart Rate Variability Biofeedback for the Treatment of Major Depression

Maria Katsamanis Karavidas · Paul M. Lehrer · Evgeny Vaschillo · Bronya Vaschillo · Humberto Marin · Steven Buyske · Igor Malinovsky · Diane Radvanski · Afton Hassett

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- High prevalence of depressed SDNN among those with pain, PTSD, mTBI Tan, et al. (2009; 2011)
- PTSD patients, lower HRV measures Sahar, (2001)
- PTSD patients show elevated VLF and low HF Wahbeh & Oken (2012)
- Fluoxetine (Prozac) and HRV Biofeedback helps improve (increase) HRV Cohen, H, (2000), Tan (2011)

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HRV and PTSD

HRV parameter	PTSD $n = 52$	No-PTSD $n = 29$	Statistics
LF peak frequency (Hz)	0.09 ± 0.02	0.08 ± 0.02	$F(2,78) = 2.85$; $p = 0.06$[a]
LF absolute power (ms^2)	407.9 ± 533.7	620.6 ± 1,123.9	$F(2,78) = 4.69$; $p = 0.01$[a]
LF power (normalized units)	63.3 ± 17.7	68.1 ± 16.0	$F(2,78) = 3.87$; $p = 0.03$[a]
HF peak frequency (Hz)	0.21 ± 0.07	0.23 ± 0.06	$F(2,78) = 26.5$; $p<0.00005$[a]
HF absolute power (ms^2)	237.9 ± 438.6	236.9 ± 395.9	$F(2,78) = 1.21$; $p = 0.30$[a]
HF power (normalized units)	36.7 ± 17.7	31.8 ± 16.0	$F(2,78) = 3.87$; $p = 0.03$[a]
LF/HF ratio	2.4 ± 2.0	2.9 ± 1.9	$F(2,78) = 1.02$; $p = 0.32$[a]
Respiration	15 ± 0.6	15 ± 0.8	$F(1,84) = 0.68$, $p = 0.41$

The PTSD group had lower high-frequency HRV

Meaning= more sympathetic arousal

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- minimal-contact therapies have demonstrated efficacy for the greatest variety of anxiety diagnoses when accounting for both attrition and compliance
- **computerized treatments** have been shown to be a less-intensive, cost-effective way to deliver empirically validated treatments for a variety of psychological problems and to enhance peak-performance.

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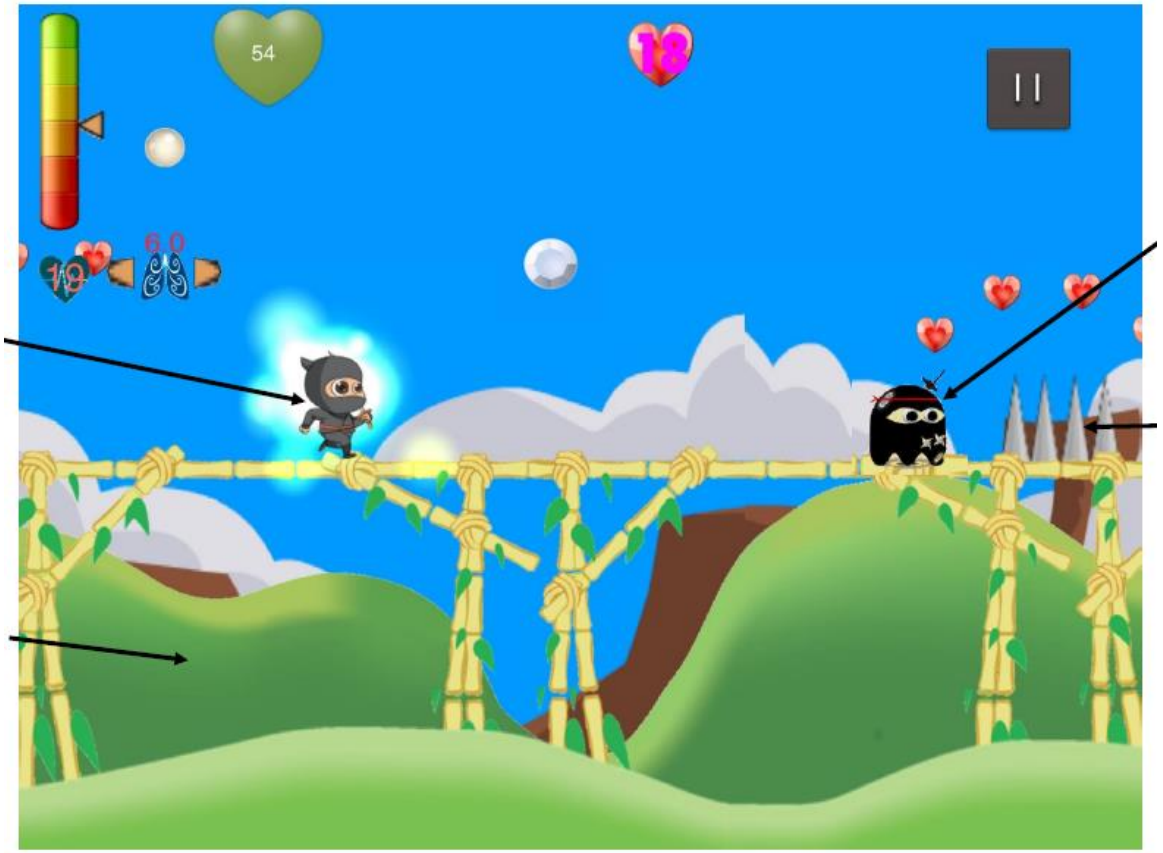
Home-Use & Rx: HRV Biofeedback



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Why Use Biofeedback?

Biofeedback appeals to people for a variety of reasons:

- It's noninvasive.
- It may reduce or eliminate the need for some medications.
- It may be a treatment alternative for those who can't tolerate medication side effects.
- It may be an option when medications haven't worked well.
- It may be an alternative to medications for some conditions during pregnancy.
- It helps people take charge of their health and this “active” role may have its own therapeutic benefit.

Biofeedback

- Is a technique you can use to learn to control or improve the body's various physiological functions – specifically **heart rate variability** and **brainwave activity**.
  - Non-invasive
  - Painless
  - Medication free
  - Effective intervention
    - Efficacious since the 1960's.
    - Research based

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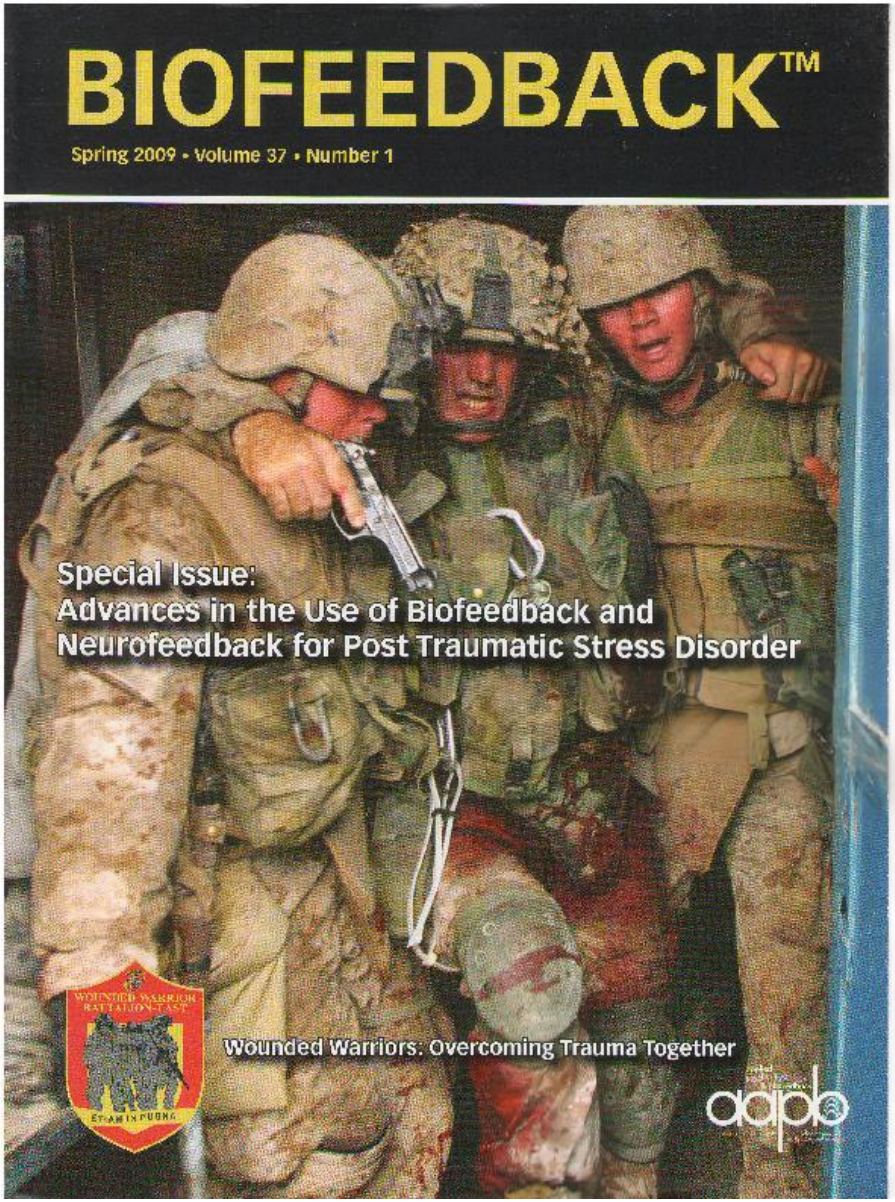
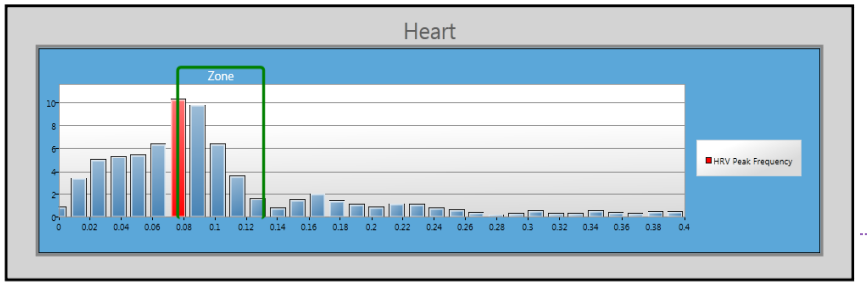
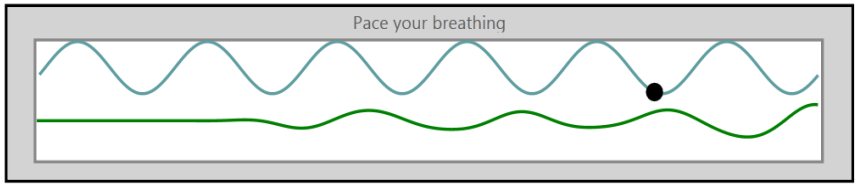
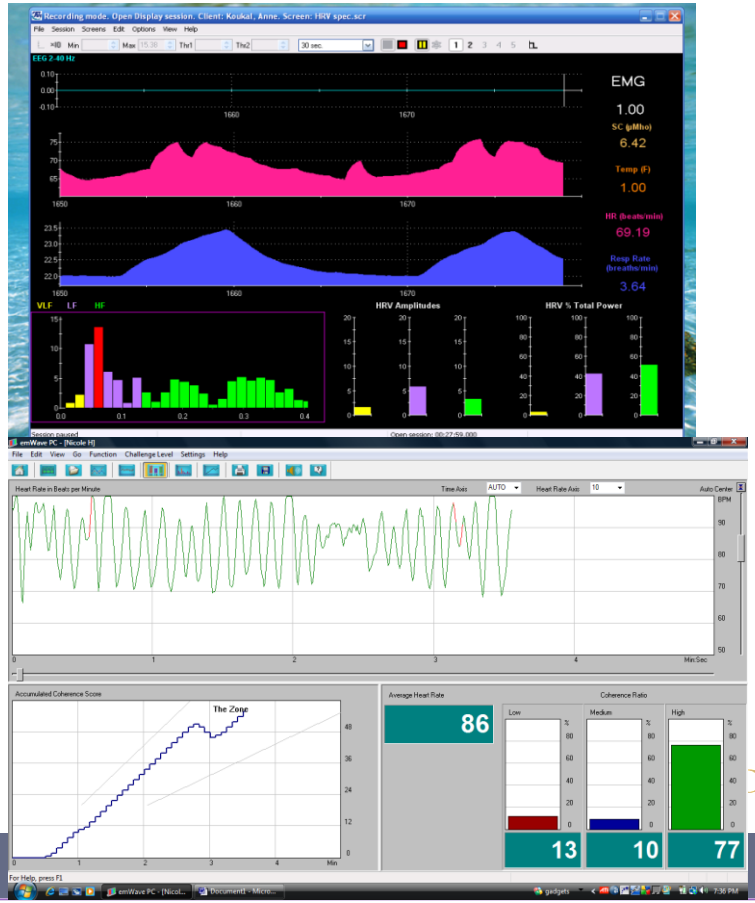
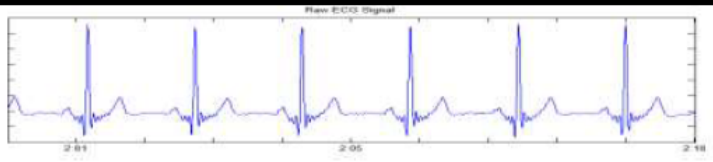
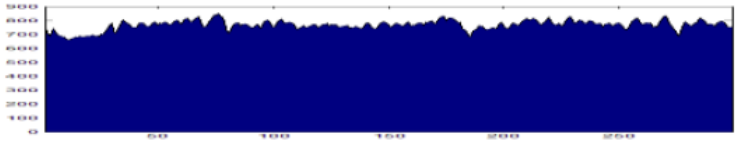

BIOFEEDBACK™
Spring 2009 • Volume 37 • Number 1
Special Issue:
Advances in the Use of Biofeedback and
Neurofeedback for Post Traumatic Stress Disorder
Wounded Warriors: Overcoming Trauma Together
aapb


Heart
Zone
HRV Peak Frequency


Pace your breathing

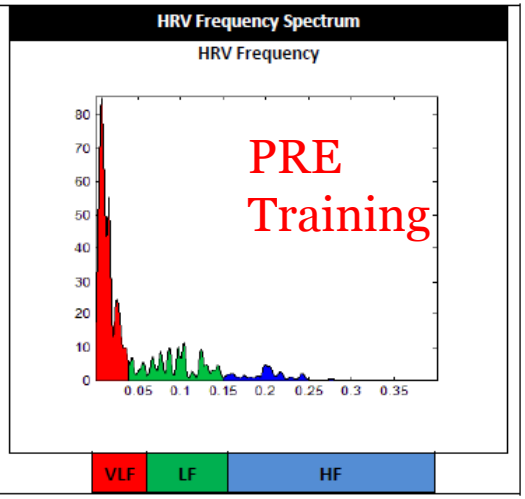

EMG
1.00
SC (µMho)
6.42
Temp (F)
1.00
HR (beats/min)
69.19
Resp Rate (breaths/min)
3.64
HRV Amplitudes
HRV % Total Power
The Zone
86
13
10
77

MEASURE

Assessment Metric	Cardiac Waveforms and R-R Variability
Cardiac Waveform (P-Q-R-S wave)	
Heart Rate Variability (Rhythmicity)	

Neuro-Cardiac Stability	Patient Score	Normal Range
Heart Rate (bpm)	78	55-80
QTc interval	394.4	male < 440 ms female < 460 ms
QRS duration	0.066	0.06 - 0.12 sec

Autonomic Balance	Patient Score	Normal Range
Autonomic Balance (SDNN (ms))	32.07	75-150
Total Power	594.0	>2000
Very Low Frequency (ms^2)	395.5	low
Low Frequency (ms^2)	149.0	highest
High Frequency (ms^2)	49.5	low



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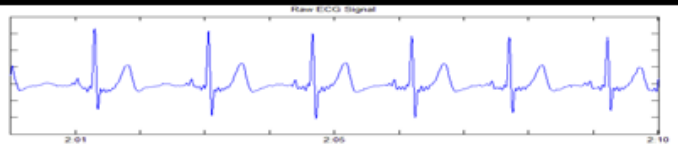
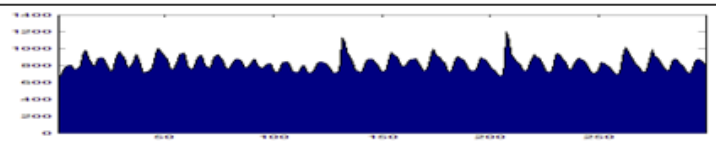
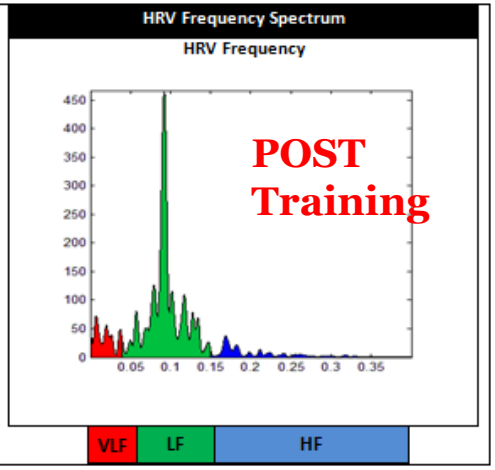
RE-MEASURE

Assessment Metric	Cardiac Waveforms and R-R Variability
Cardiac Waveform (P-Q-R-S wave)	
Heart Rate Variability (Rhythmicity)	

Neuro-Cardiac Stability	Patient Score	Normal Range
Heart Rate (bpm)	73	55-80
QTc interval	426.7	male < 440 ms female < 460 ms
QRS duration	0.092	0.06 - 0.12 sec

Autonomic Balance	Patient Score	Normal Range
Autonomic Balance (SDNN (ms))	70.25	75-150
Total Power	3394.9	>2000
Very Low Frequency (ms²)	443.7	low
Low Frequency (ms²)	2625.2	highest
High Frequency (ms²)	326.0	low



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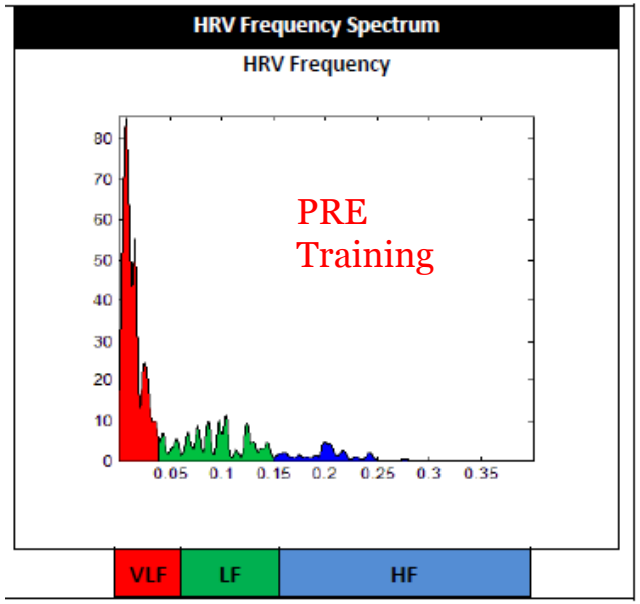
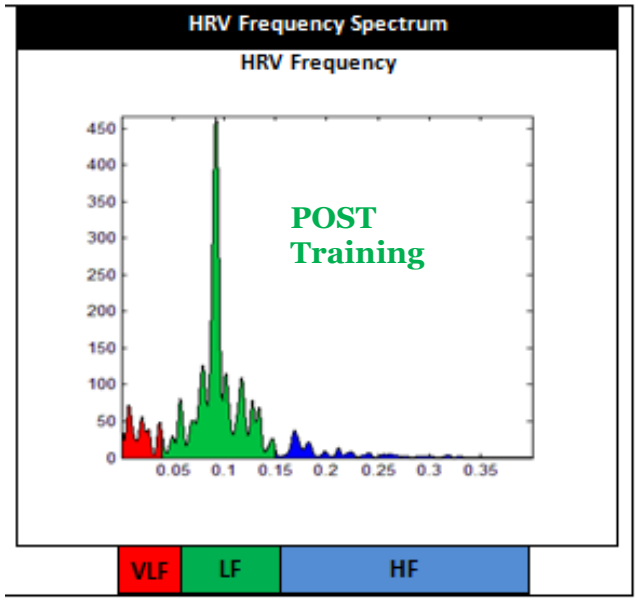
MEASURE





Events: Rocket attack with LOC, IED Blast in vehicle, IED dismounted. Symptoms: Anxiety, headaches, dizziness, blurred vision, startled response to loud noises, tinnitus, panic attacks, night sweats, nightmares, memory loss

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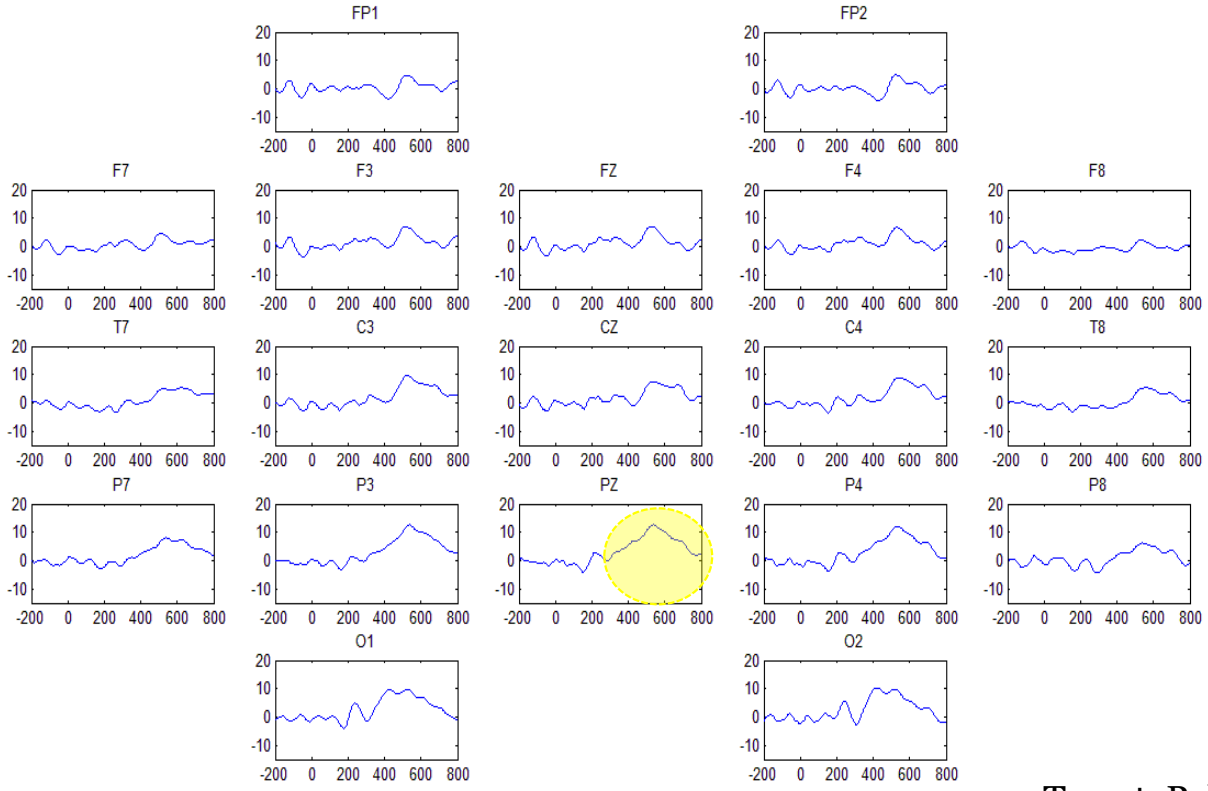
TBI and ERPs

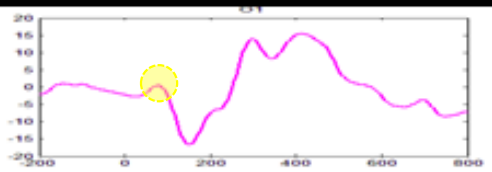
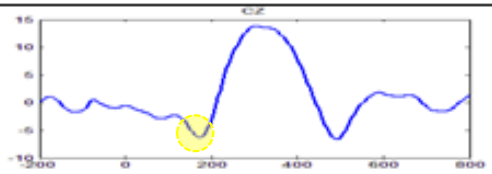
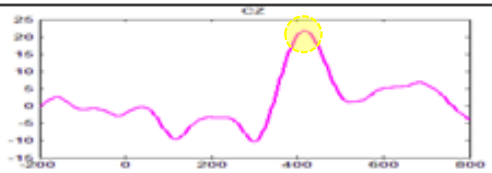
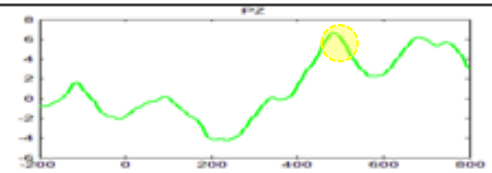
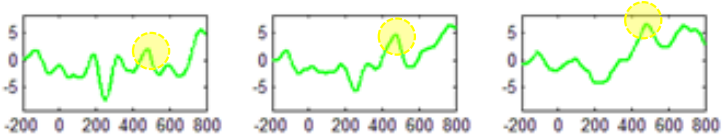
ERP amplitude is similarly lower with longer latency

In addition to the midline ERPs we like to see the whole head under stimulus conditions and task demand conditions.

Deceleration injury from deceleration injury: **weak discrimination of target from standard, very late P3b, poor amplitude morphology**



Target: P3b

	ERP Component	Amplitude and Latency	
1.	**P1 (visual)** **Function**: Sensory System. Information processing - primary visual cortex. checkerboard		76 ms 0.5 uV Excepted Range <200ms
2.	**N1 (auditory)** **Function**: Sensory System. Auditory processing, perceptual processing white noise		184 ms -5.7 uV Excepted Range <250ms
3.	**P3a** **Function**: Executive System. Impulsivity, action suppression checkerboard		416 ms 21.8 uV Excepted Range <450ms
4.	**P3b engagement** **Function**: Executive System. Working memory, stimulus interpretation, engagement operation for performing actions large circle		484 ms 6.6 uV Excepted Range <450ms
5.	**Midline Gradient:** P3b - target	 Fz: 2.0 uV Cz: 4.6 uV Pz: 6.6 uV	

P300 and PTSD Findings

Most brain disorders affect the fundamental cognitive operations of attention allocation and immediate memory, and therefore influence P300 amplitude or latency.

- Low arousal individuals have smaller amplitudes compared to high-arousal individuals who have larger components (Brocke, 2004; De Pascalis, 2004)
- frontal lobe and hippocampal integrity are necessary for P3a generation (Knight, 1996) and hippocampus is diminished with PTSD.
- ERP findings have demonstrated increased frontal lobe activity for the detection of rare or physically alerting stimuli (McCarthy, Luby, Gore, Goldman-Rakic, 1997; Potts, Liotti, Tucker, & Posner, 1996)
- P3b amplitude is positively correlated with hippocampal size relative to the temporal lobe size. This outcome implies that larger hippocampal size is associated with larger P300 amplitudes (Polich, 2004)

P3b amplitude/latency: PTSD Findings

Reduced P3b amplitude and elongated latency (index of cognitive impairment, attention deficits, working memory)

- reduced allocation of information processing to stimuli
- Reduced processing of neutral information if exposed to trauma

  ** *However, there is high amplitude P3b during enhanced or excess processing (trauma exposure primer triggers this)*

However, when there is a combat-related "primer" we see increased P3b

- this seems to be due to an increased anxious arousal state induced by the "primer" or combat stimulus
  - I don't use aversive images for ethical reasons but often the artillery is very loud and shakes the building so this has been anecdotal and consistent with research that used combat images as distractors

A problem with most studies is the lack of discrimination and reporting of P3a and P3b
Task difficulty also needs to be assessed as this will alter amplitude

P3a amplitude/latency: PTSD Findings

P3a amplitude is reduced and longer latency

- may be due to re-experiencing symptoms
- may reflect a failure to inhibit irrelevant stimuli

With a combat-related "primer" we see increased P3a amplitude and longer latency

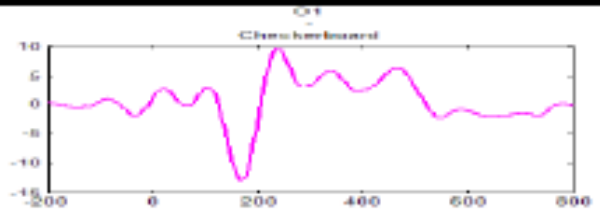
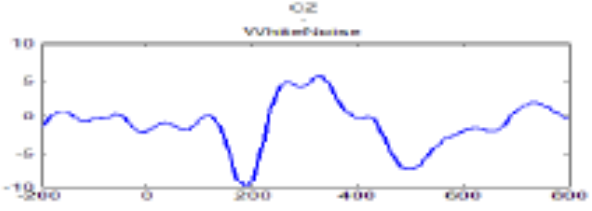
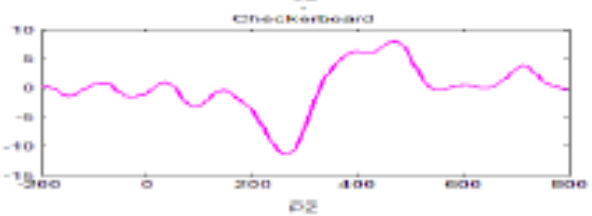
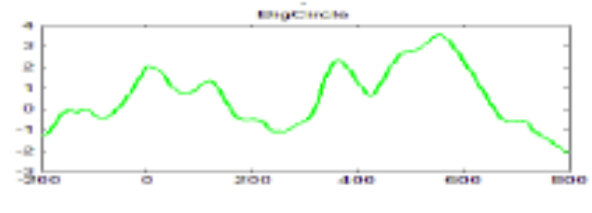
- processing is reduced for neutral stimuli but enhanced for trauma-combat stimuli

A problem with most studies is the lack of discrimination and reporting of P3a and P3b
Task difficulty also needs to be assessed as this will alter amplitude

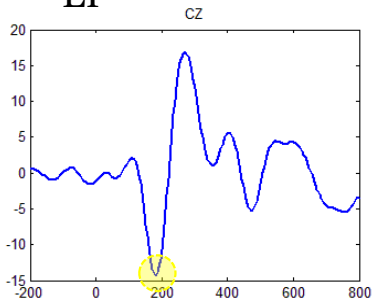
PTSD, mTBI from several blast exposures 2009

Low amplitude P3b (target)
Longer latency P3b (target)
Longer latency P3a (distractor)

Non combat images (primer)

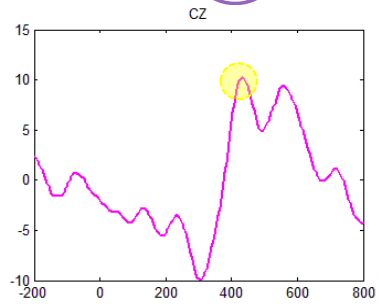
ERP Component	Amplitude and Latency	Patient Score
P1 (visual)		104 ms 2.9 uV
N1 (auditory)		188 ms -9.9 uV
P3a		472 ms 7.9 uV
P3b		556 ms 3.5 uV

N1 – auditory EP



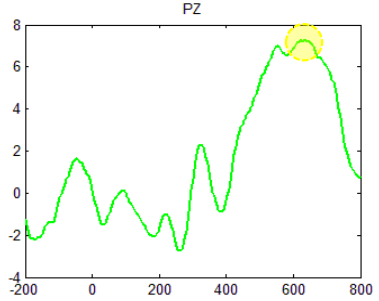
184ms -14.2uV

P3a – attention



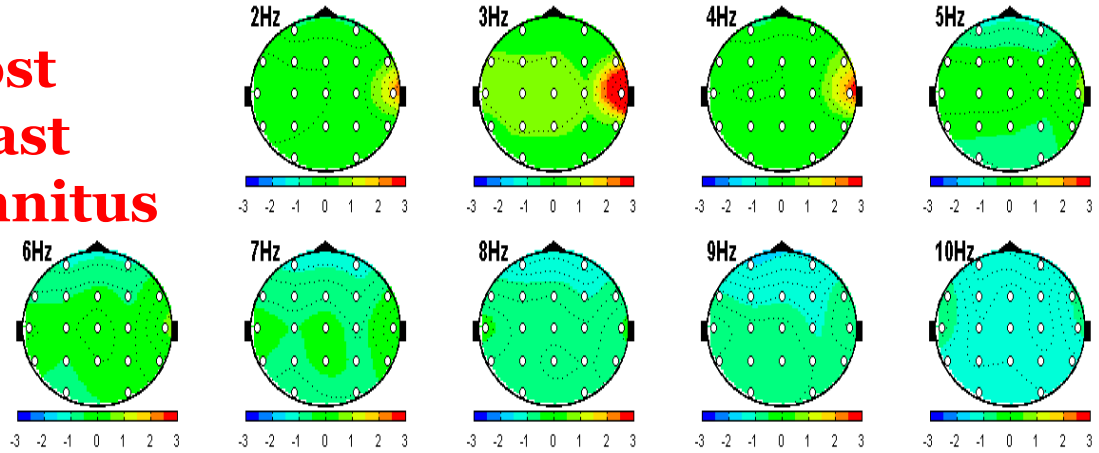
432ms 10.3uV

P3b – engagement



620ms 7.2uV

Post blast tinnitus



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Elevated Peak Alpha

Appl Psychophysiol Biofeedback. 2013 March ; 38(1): 57–69. doi:10.1007/s10484-012-9208-z.

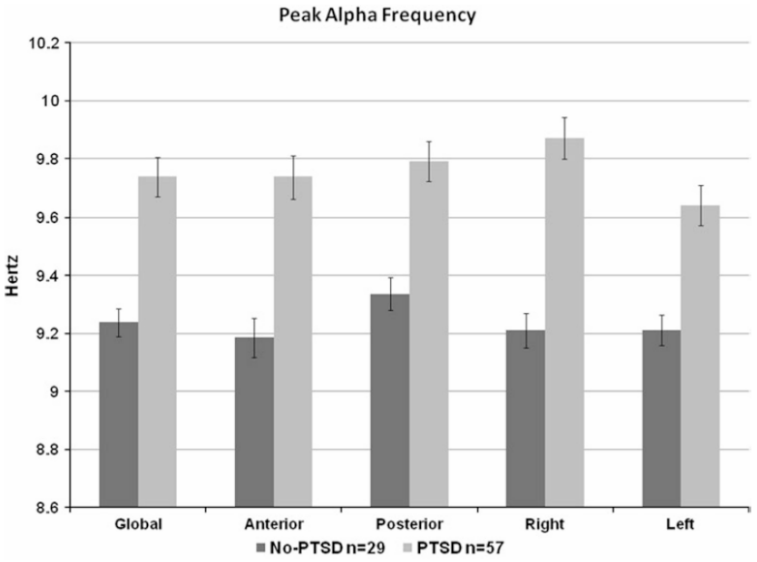
Peak High-Frequency HRV and Peak Alpha Frequency Higher in PTSD

Helané Wahbeh and **Barry S. Oken**
Department of Neurology, Oregon Health & Science University, 3181 S.W. Sam Jackson Park Rd., Portland, OR 97239, USA

Helané Wahbeh: wahbehh@ohsu.edu

Abstract

Posttraumatic stress disorder (PTSD) is difficult to treat and current PTSD treatments are not effective for all people. Despite limited evidence for its efficacy, some clinicians have implemented biofeedback for PTSD treatment. As a first step in constructing an effective biofeedback treatment program, we assessed respiration, electroencephalography (EEG) and heart rate variability (HRV) as potential biofeedback parameters for a future clinical trial. This cross-sectional study included 86 veterans; 59 with and 27 without PTSD. Data were collected on EEG measures, HRV, and respiration rate during an attentive resting state. Measures were analyzed to assess sensitivity to PTSD status and the relationship to PTSD symptoms. Peak alpha frequency was higher in the PTSD group ($F(1,84) = 6.14$, $p = 0.01$). Peak high-frequency HRV was lower in the PTSD group ($F(2,78) = 26.5$, $p<0.00005$) when adjusting for respiration rate. All other EEG and HRV measures and respiration were not different between groups. Peak high-frequency HRV and peak alpha frequency are sensitive to PTSD status and may be potential biofeedback parameters for future PTSD clinical trials.



There were no group differences in delta, theta, alpha, or beta EEG amplitudes.

Peak alpha global was different between groups with the PTSD group having a higher peak alpha frequency.

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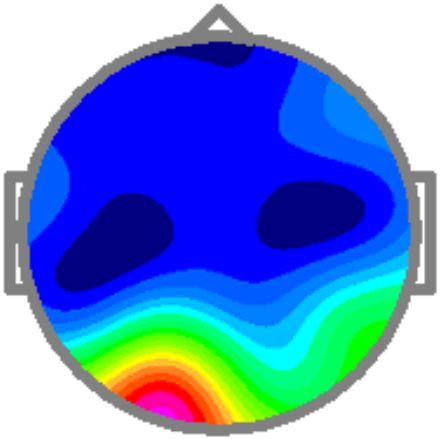
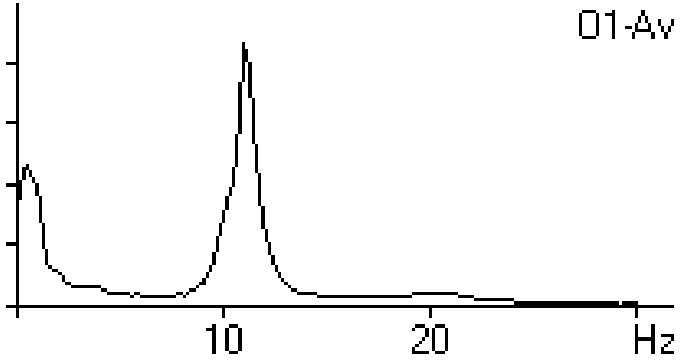
Faster individual posterior peak alpha (not diagnostic)



11Hz peak alpha



Thalamic generated posterior alpha is typically faster than frontal alpha due to the more direct or faster thalamo-cortical-thalamic loop circuit.

Navy Corpsman with PTSD pre-treatment baseline (EC)

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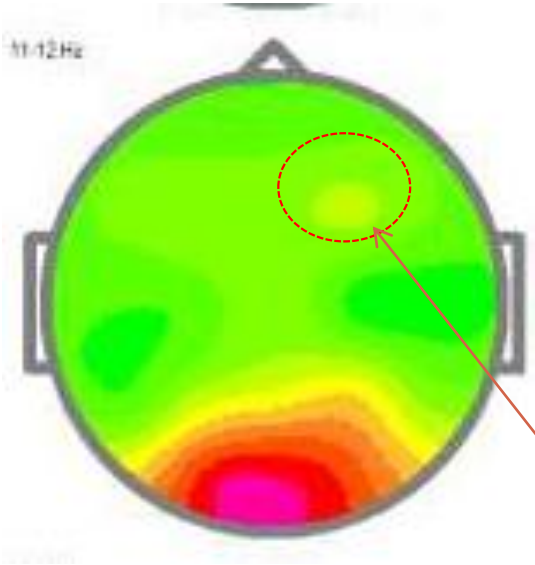


Elevated fast alpha (11-12Hz) appears to be a correlated biomarker for over activation of the central nervous system and is seen in the occipital region (visual cortex).
It is not diagnostic (doctors w/o PTSD often have 11-12Hz)

This will be seen clinically as “brain speed increase or rumination” when eyes are closed which of course makes it hard to sleep.

Because there is also over abnormality over the right DLPFC this is likely going to be seen ***emotional regulation*** dysfunction (e.g., sudden and seemingly unprovoked anger, even rage).

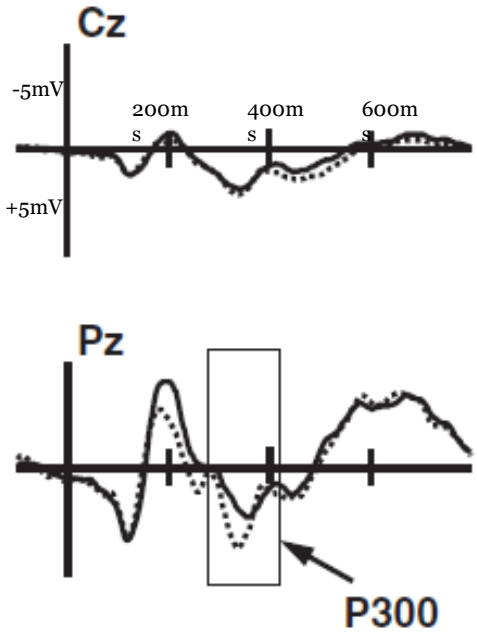
Wang *et al. BMC Neuroscience* 2013, **14**:115
http://www.biomedcentral.com/1471-2202/14/115

BMC Neuroscience

RESEARCH ARTICLE Open Access

EEG biofeedback improves attentional bias in high trait anxiety individuals

Sheng Wang, Yan Zhao, Sijuan Chen, Guiping Lin, Peng Sun and Tinghuai Wang*



* P300 amplitude was larger for emotional pictures (fear and sadness) than for neutral pictures in anxious.

* P300 delay can be interpreted as reflecting the sustained negative-related emotion processing among those with anxiety traits

PERFORMANCE IMPLICATIONS:
Brain processing speed is hindered among those with anxiety, something that can impact performance.
ERPs can measure this condition

Neurofeedback helped normalize the brain, fixing this bias or trait anxiety hindrance to performance

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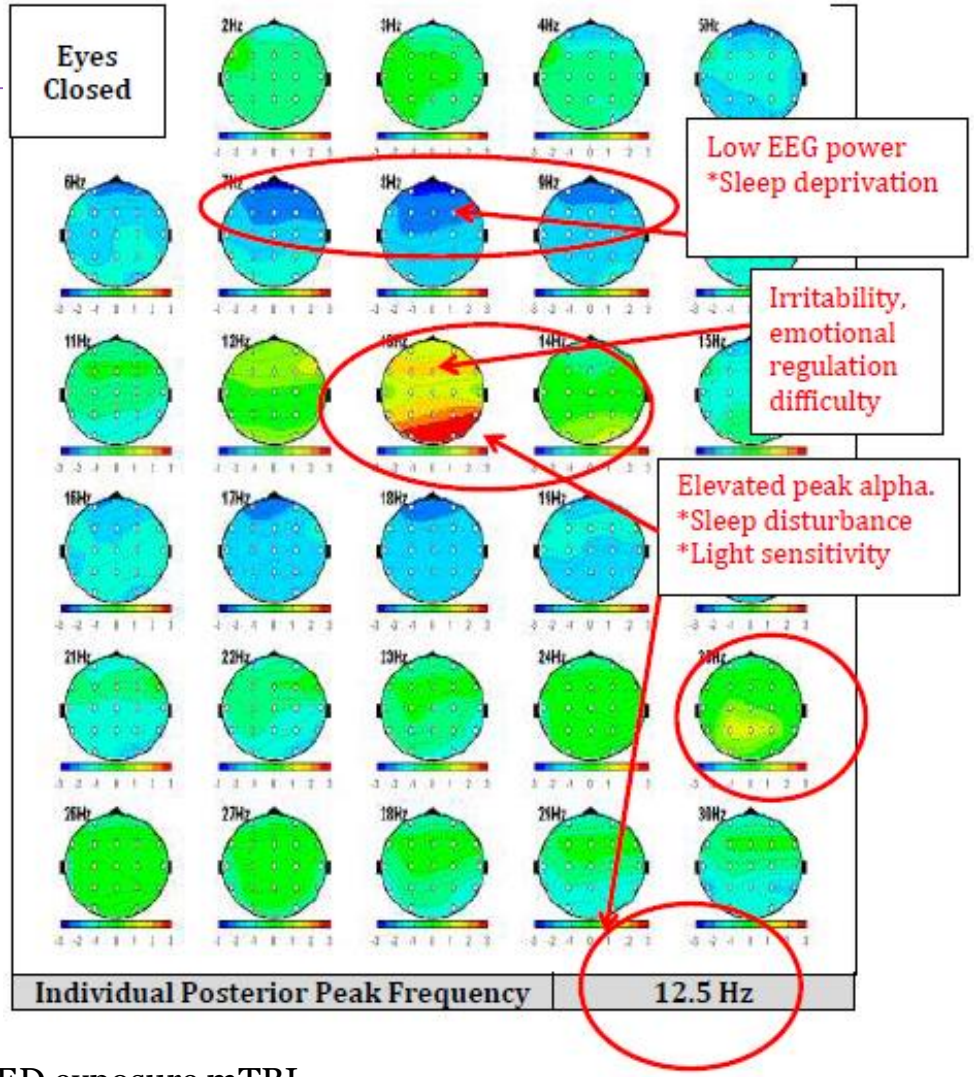
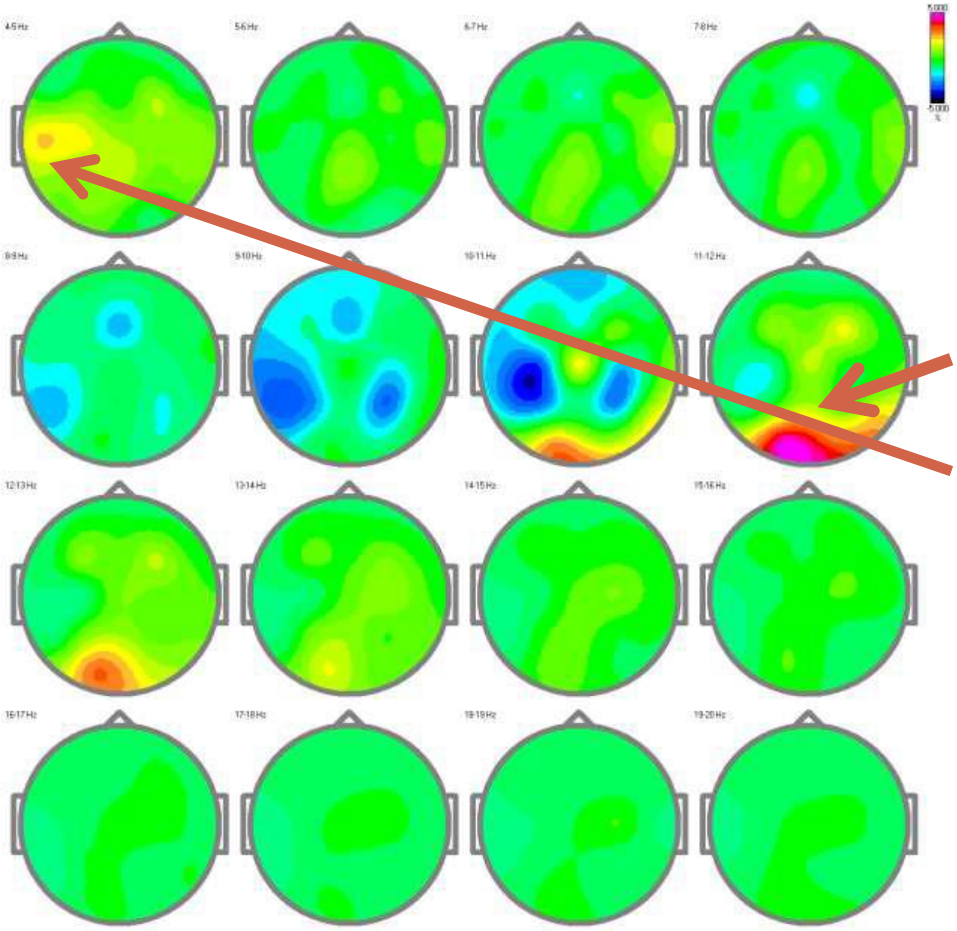
Elevated peak alpha is observed with PTSD

Frontal impairment is correlated with *emotional dysregulation;* orbitofrontal cortex is involved positive or negative reception of the emotional value of actions



EOD Tech: PTSD w/ hx of IED exposure mTBI

IMI METABOLIC MEDICAL INSTITUTE



Fast alpha in occipital region seen clinically with insomnia.

Left temporal slow content seen with tinnitus

Kluetsch et al., 2014 found that alpha amplitude reduction biofeedback (neurofeedback) was able to produce less alpha and also a significant increase (“rebound”) in resting-state alpha rhythm amplitude. This rebound (PTSD subjects) was related to increased calmness, greater default mode network connectivity, and enhanced Salience Network connectivity.

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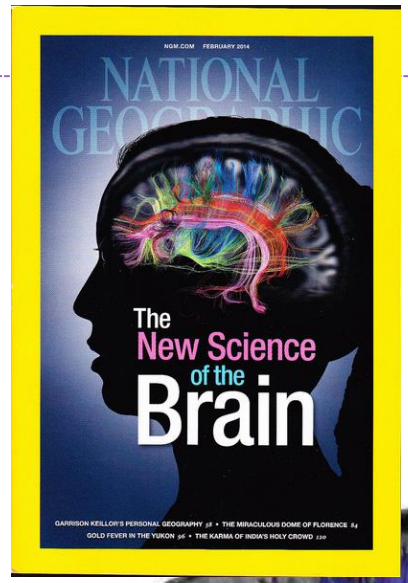
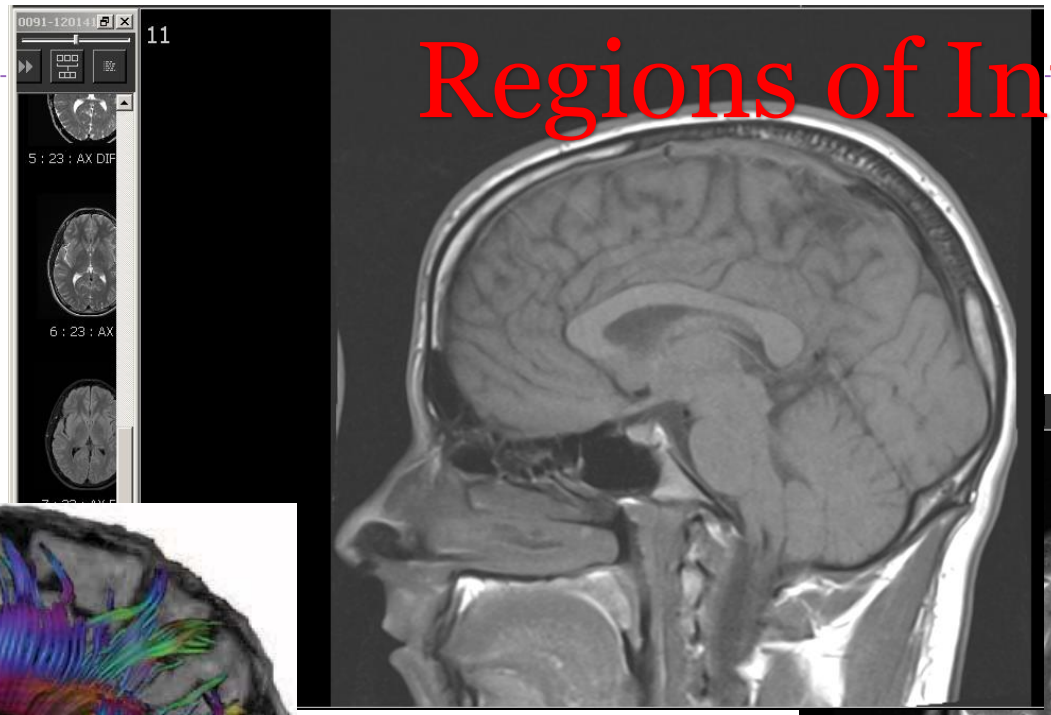
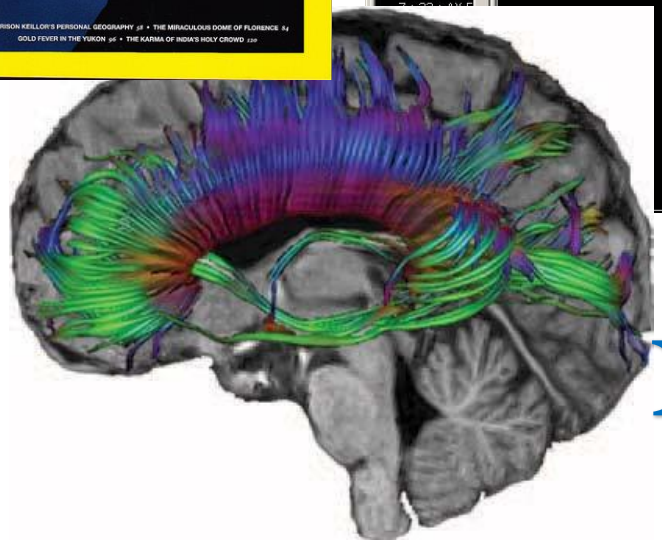
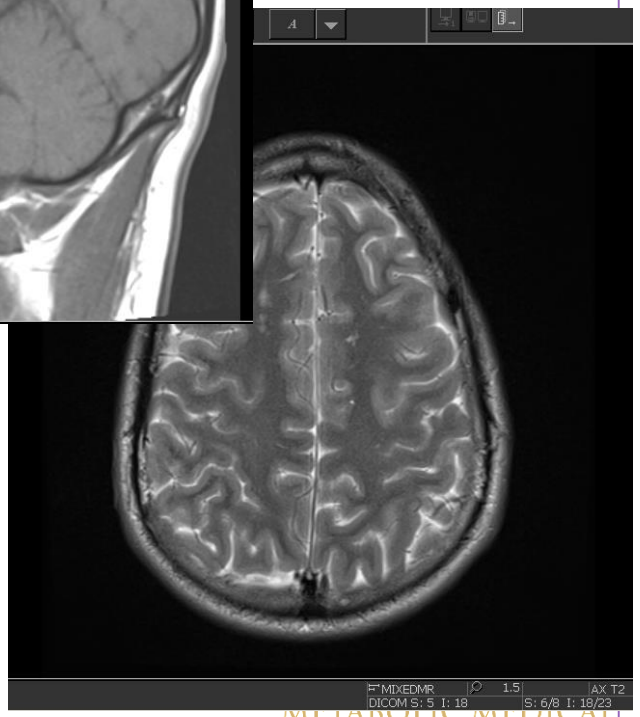
Regions of Interest







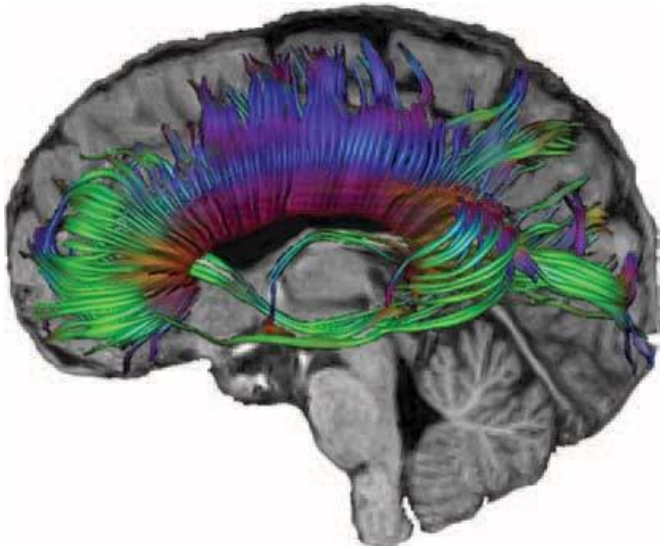
Networks



Neuronetworks & PTSD

Restoring large-scale brain networks in PTSD and related disorders: a proposal for neuroscientifically-informed treatment interventions

Ruth A. Lanius[1,2*], Paul A. Frewen[1,2], Mischa Tursich[1], Rakesh Jetly[3] and Margaret C. McKinnon[4,5,6]



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European Journal of Psychotraumatology 2015, 6: 27313

Default Mode

Acta Psychiatr Scand 2009: 1–8
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DOI: 10.1111/j.1600-0447.2009.01391.x

ACTA PSYCHIATRICA SCANDINAVICA

Default mode network connectivity as a predictor of post-traumatic stress disorder symptom severity in acutely traumatized subjects

Lanius RA, Bluhm RL, Coupland NJ, Hegadoren KM, Rowe B, Théberge J, Neufeld RWJ, Williamson PC, Brimson M. Default mode network connectivity as a predictor of post-traumatic stress disorder symptom severity in acutely traumatized subjects.

Objective: The goal of this study was to investigate the relationship between default mode network connectivity and the severity of post-traumatic stress disorder (PTSD) symptoms in a sample of eleven acutely traumatized subjects.
Method: Participants underwent a 5.5 min resting functional magnetic resonance imaging scan. Brain areas whose activity positively correlated with that of the posterior cingulate/precuneus (PCC) were assessed. To assess the relationship between severity of PTSD symptoms and PCC connectivity, the contrast image representing areas positively correlated with the PCC was correlated with the subjects' Clinician Administered PTSD Scale scores.
Results: Results suggest that resting state connectivity of the PCC with the perigenual anterior cingulate and the right amygdala is associated with current PTSD symptoms and that correlation with the right amygdala predicts future PTSD symptoms.
Conclusion: These results may contribute to the development of prognostic tools to distinguish between those who will and those who will not develop PTSD.

R. A. Lanius[1,2], R. L. Bluhm[1], N. J. Coupland[3], K. M. Hegadoren[4], B. Rowe[5], J. Théberge[1,6,7,8], R. W. J. Neufeld[9], P. C. Williamson[1,2], M. Brimson[1]

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Key words: post-traumatic stress disorder; neuroimaging; anxiety

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Accepted for publication March 23, 2009

Default mode alterations in posttraumatic stress disorder related to early-life trauma: a developmental perspective

Judith K. Daniels, PhD; Paul Frewen, PhD; Margaret C. McKinnon, PhD; Ruth A. Lanius, MD, PhD

Daniels, Frewen, Lanius — Division of Neuropsychiatry, Department of Psychiatry, Schulich School of Medicine and Dentistry, University of Western Ontario, London, Ont. McKinnon — Mood Disorders Program, St. Joseph's Healthcare, Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, and the Kunin-Lunenfeld Research Unit, Baycrest, Toronto, Ont.

Introduction

Recently, altered default mode network (DMN) connectivity in individuals with posttraumatic stress disorder (PTSD) has been related to prolonged childhood maltreatment.[1] An emerging body of literature also describes the developmental differentiation of the DMN in healthy children.[2–6] Critically, developmental changes in the DMN may parallel those observed in other associated domains, including self-referential processing, autobiographical memory, prospection and theory of mind, which are thought to rely on many of the same underlying processes and neural substrates implicated in the DMN.[7] Moreover, deficient DMN connectivity in adults with childhood maltreatment–related PTSD appears similar to patterns of DMN connectivity observed in healthy children aged 7 to 9 years. Here, we propose that early-life trauma may interfere with the developmental trajectory of the DMN and its associated functions.[8–11]

posterior cingulate cortex (PCC), anterior cingulate cortex (ACC), middle temporal gyrus, inferior parietal cortex and medial prefrontal cortex (mPFC). It has been hypothesized that the brain maintains the "default mode" in the absence of cognitive demands,[12–14] possibly to facilitate a state of readiness to respond to environmental changes.[15] Other authors link DMN activity to self-referential processing[16,17] and the so-called "stream of consciousness," as key DMN regions like the PCC and the mPFC have been shown to subserve introspective mental imagery, self-reflection and self-awareness. By contrast, the inferior lateral parietal cortex has been implicated in embodied cognition.[8–11,18]

Development of the DMN during the first 12 years of life

Developmental studies have been conducted to map the unfolding of the DMN in the maturing brain. Critically, DMN

mPFC, ACC, PCC, middle temporal gyrus, inferior parietal cortex

(BA 8-12, 21, 23-25, 31-33, 39, 40)

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Networks impaired with PTSD

Network	Key Functions	Structures	Symptoms
Central Executive	verbal learning and executive functioning	DLPFC	Executive and cognitive dysfunction
Salience	Directing behavior for the appropriate response	Dorsal ACC, Frontoinsular cortex (insula)	Hyper- or hypoarousal, sensitivity to internal stimuli
Default Mode	Self referential processing, autobiographical memory, and social cognition	PCC, medial PFC	Hindered or altered sense of self

frontoparietal network appears to be in a state of hypofunction with PTSD

The anterior insula of the SN is thought to mediate the engagement of the CEN and disengagement of the DMN, and thus the dynamic interplay between externally- and internally-focused attention and cognitive-affective processing

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Adapted from: Lanius et al (2015) European Journal of Psychotraumatology, 6: 27313

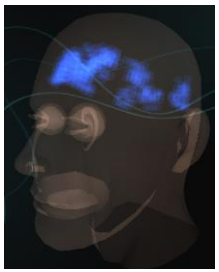
Default Mode Network Connectivity Predicts Sustained Attention Deficits after Traumatic Brain Injury

Valerie Bonnelle,[1,2] Robert Leech,[1] Kirsi M. Kinnunen,[3] Tim E. Ham,[1] Cristian F. Beckmann,[1,4] Xavier De Boissezon,[5,6,7] Richard J. Greenwood,[8] and David J. Sharp[1]

- Attention impairment is associated with activation increase in the Default Mode Network -- particularly within the precuneus and posterior cingulate cortex which forms the central node in the DMN of the brain

- TBI often results in diffuse axonal injury not seen with MRI, which produces cognitive impairment by disconnecting nodes in distributed brain networks

PERFORMANCE IMPLICATIONS: Default Mode Network can be trained using source localization neurofeedback, and thereby improve the network and be a method to address post-blast axonal injury that has disrupted networks

Attention/Vigilance (P3a)		576 ms 23.8 uV		BA 23 31 32 10 39

MEASURE ---------- TRAIN

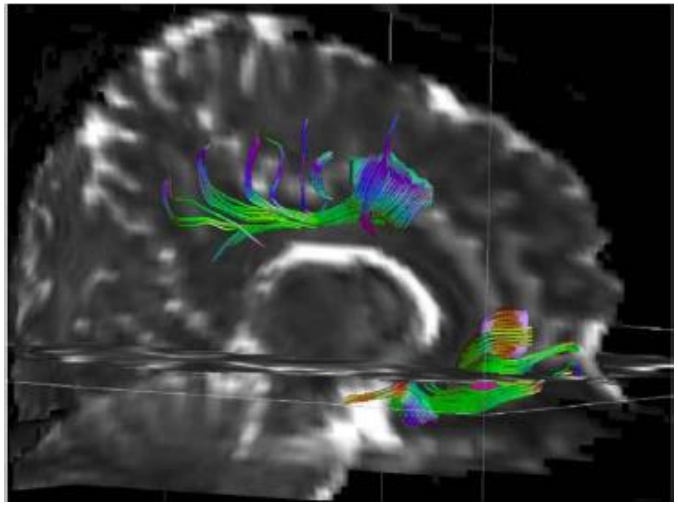
Available online at www.sciencedirect.com
ScienceDirect
Neural Networks 19 (2006) 1422–1429
Neural Networks
www.elsevier.com/locate/neunet
2006 Special Issue

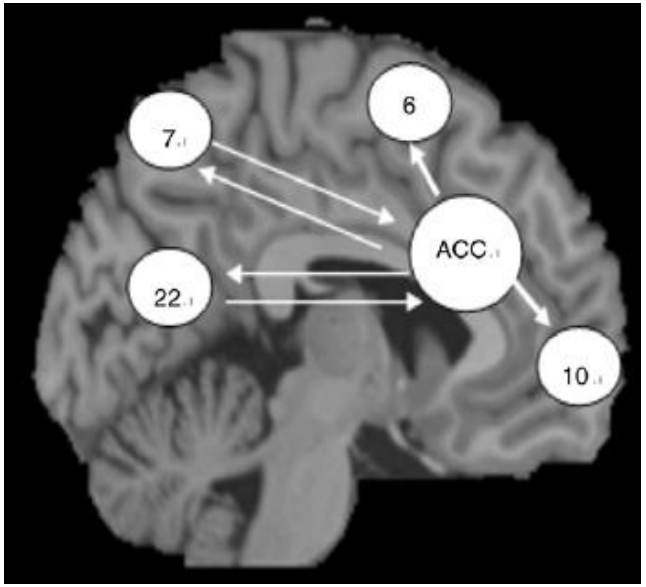
Analyzing and shaping human attentional networks☆

Michael I. Posner[a,*], Brad E. Sheese[a], Yalçin Odludaş[a], YiYuan Tang[b,a]

[a] *Department of Psychology, University of Oregon, Eugene, OR, USA*
[b] *Institute of Neuroinformatics, Dailan University of Technology, China*

Received 30 June 2006; accepted 1 August 2006





Attention Networks

Default Mode Network Connectivity Predicts Sustained Attention Deficits after Traumatic Brain Injury

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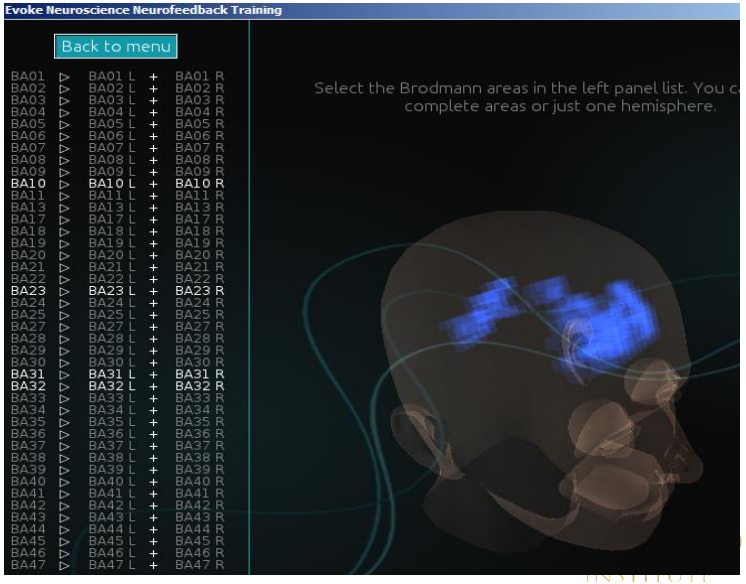
Sleep Quality: Default Mode Network

J Cogn Neurosci. 2010 August ; 22(8): 1637–1648. doi:10.1162/jocn.2009.21331.

The un-rested resting brain: Sleep-deprivation alters activity within the default-mode network

Ninad Gujar[1], **Seung-Schik Yoo**[2], **Peter Hu**[1], and **Matthew P. Walker**[1,*]

Sleep loss triggers imbalance in midline anterior and posterior brain regions associated with the *Default Mode Network*



NeuroImage 91 (2014) 169–176

Contents lists available at ScienceDirect

NeuroImage

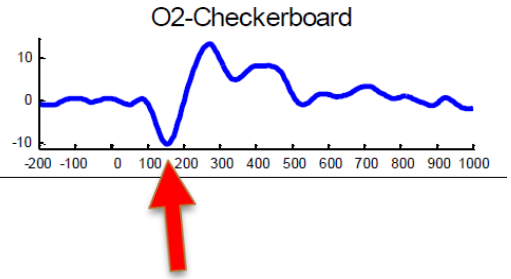
journal homepage: www.elsevier.com/locate/ynimg

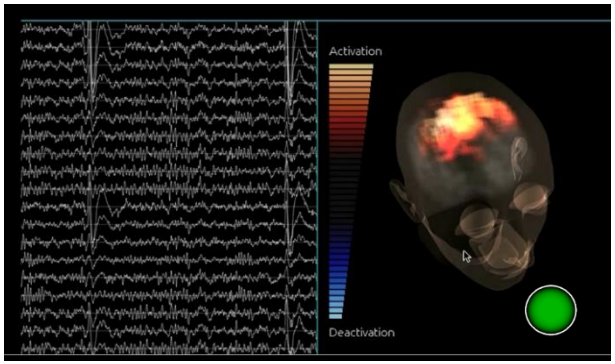
Sleep deprivation reduces the rate of rapid picture processing

Danyang Kong [a], Christopher L. Asplund [a,b], Michael W.L. Chee [a,*]

[a] Center for Cognitive Neuroscience, Neuroscience & Behavioral Disorders Program, Duke-NUS Graduate Medical School, Singapore
[b] Division of Social Sciences (Psychology), Yale-NUS College, Singapore

Sleep deprivation effects on visual processing speed likely result in reduced information processing capacity

ERP Component	Waveform
Visual processing	



Measure ----------Train

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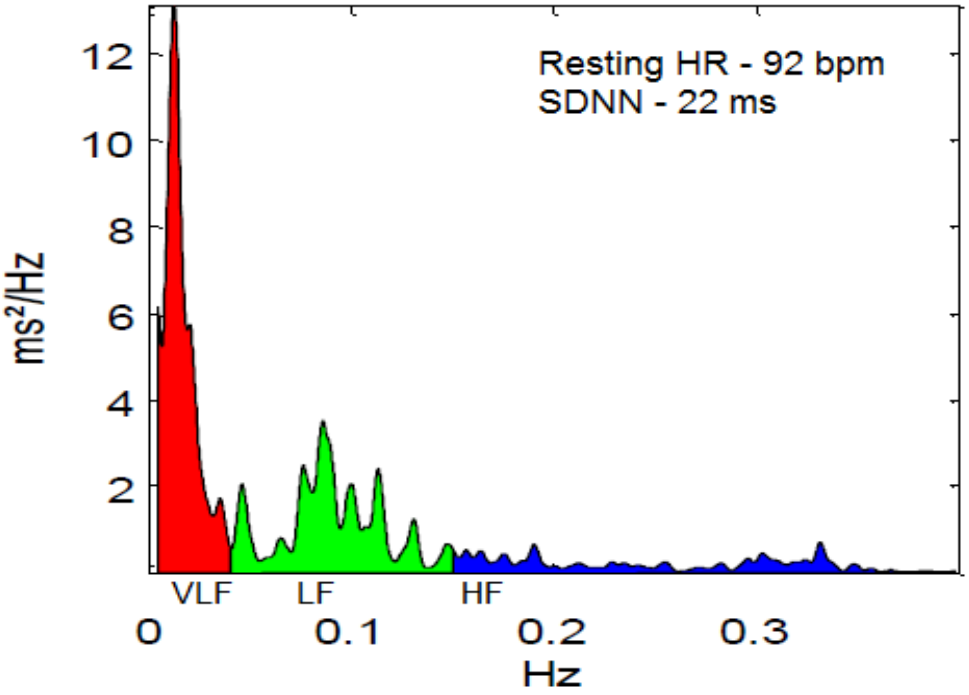
Case: 36yo male with PTSD

10-minute resting ECG. 36yo male diagnosed with PTSD. Heart rate variability power spectra reflecting elevated heart rate, low variability, and elevated sympathetic tone.



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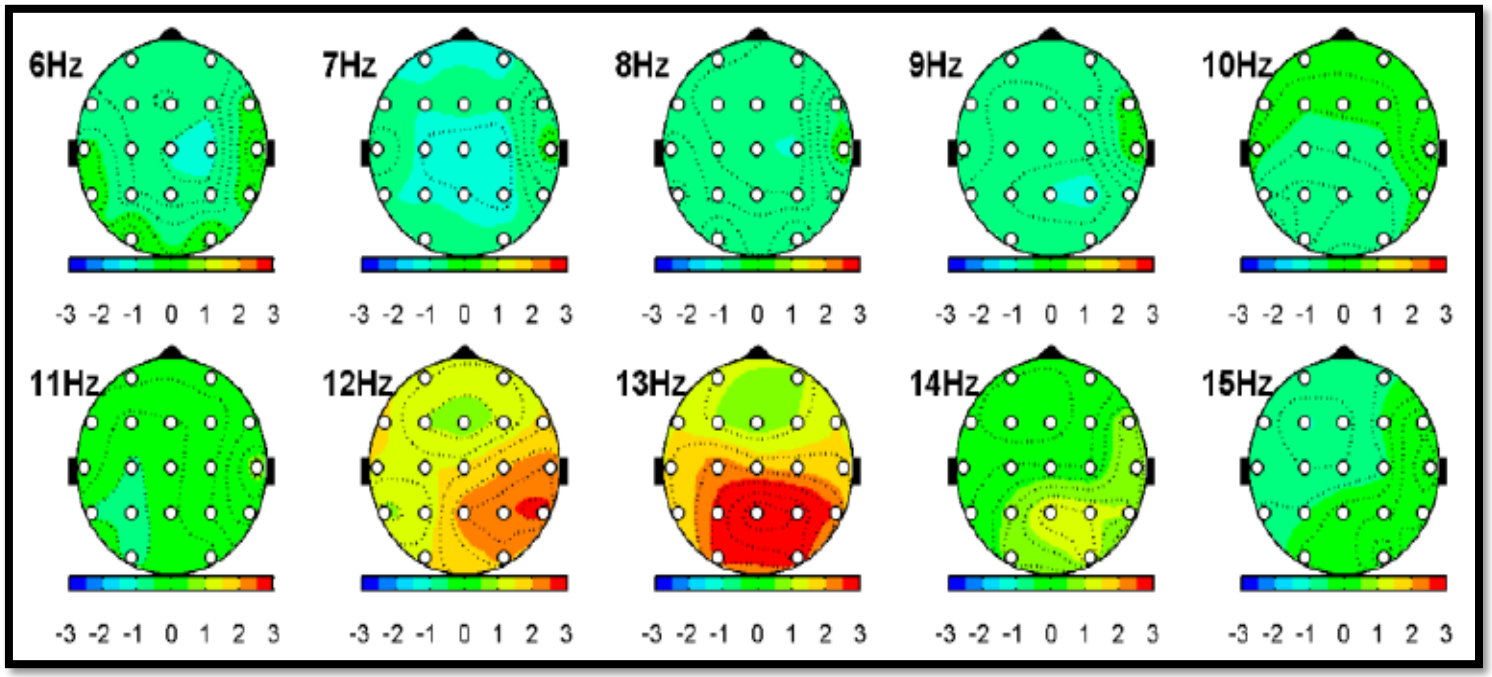
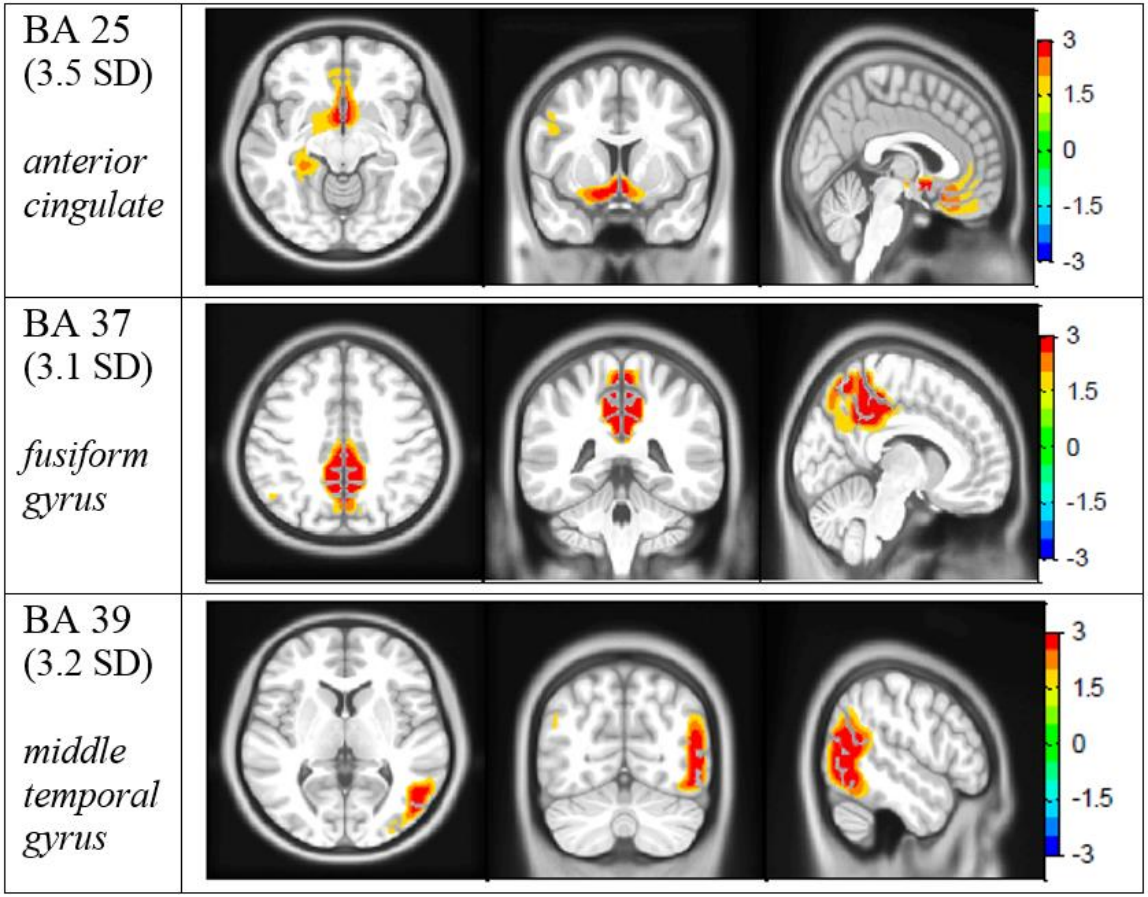
Case: 36yo male with PTSD

36-year old male with PTSD, surface amplitude (eyes closed) deviation from health reference group reflecting elevated 12-13 Hz in parietal region



Case: 36yo male with PTSD

BAs of interest for sLORETA neurofeedback in a 36 year-old male with PTSD



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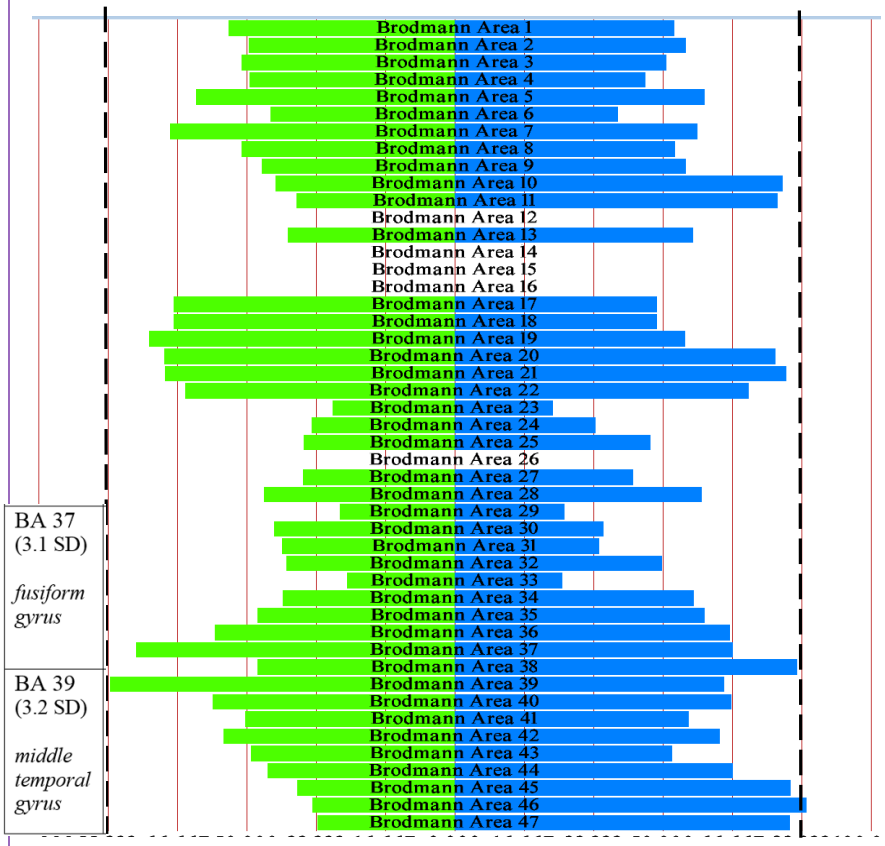
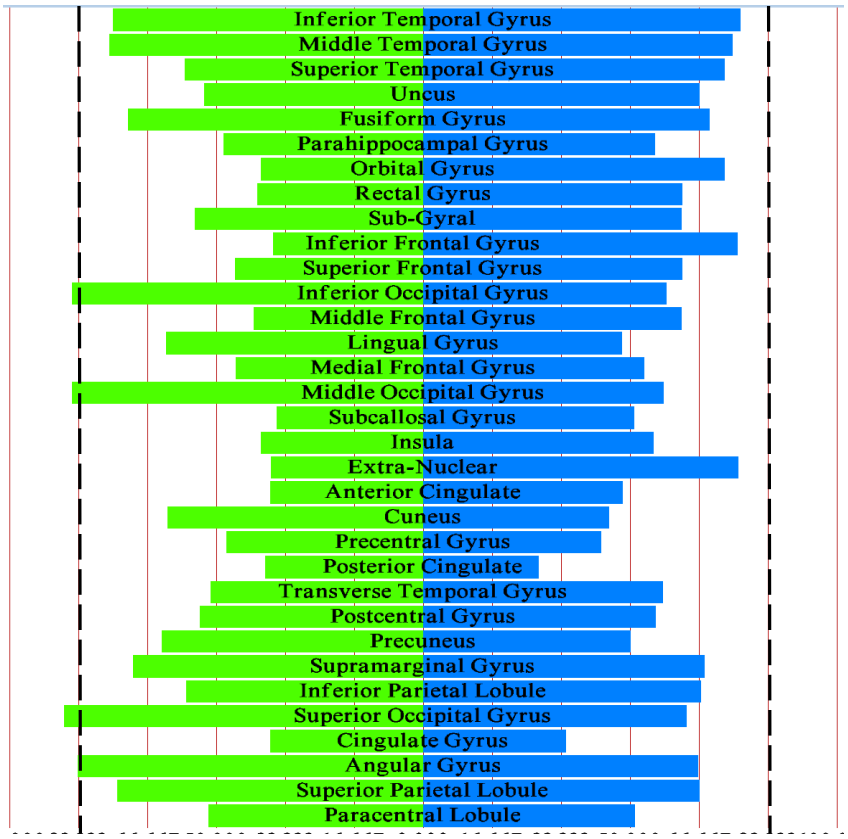
Case: 36yo male with PTSD

Paired Histogram: mean current density over epoch





current density is electrical activity over a cubic unit of space
voxels of the BA (left) or name brain structure (right)over epoch

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P3b amplitude/latency: PTSD Findings

Reduced P3b amplitude and elongated latency (index of cognitive impairment, attention deficits, working memory)

- reduced allocation of information processing to stimuli
- Reduced processing of neutral information if exposed to trauma

However, there is high amplitude P3b during enhanced or excess processing (trauma exposure primer triggers this)

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Neurofeedback

- NFB = *going to the gym*, but for your brain.
- It will strengthen, calm and improve state flexibility.
- There are multiple forms of NFB available:
  - Single Channel
  - LORETA/Brodmann Area Training

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EEG is responsive to operant and respondent (classical) conditioning

Journal of Neurotherapy, 15:292–304, 2011

ISSN: 1087-4208 print/1530-017X online
DOI: 10.1080/10874208.2011.623089

Routledge
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REVIEW ARTICLES

NEUROFEEDBACK AND BASIC LEARNING THEORY: IMPLICATIONS FOR RESEARCH AND PRACTICE

Leslie H. Sherlin[1,2,3], Martijn Arns[4,5], Joel Lubar[6], Hartmut Heinrich[7,8], Cynthia Kerson[9,10,11], Ute Strehl[12], M. Barry Sterman[13]

frontiers in
HUMAN NEUROSCIENCE

HYPOTHESIS AND THEORY ARTICLE
published: 06 November 2014
doi: 10.3389/fnhum.2014.00894

What learning theories can teach us in designing neurofeedback treatments

Ute Strehl*

Institute of Medical Psychology and Behavioral Neurobiology, University of Tuebingen, Tuebingen, Germany

MEDICAL

Neurofeedback

- EEG Biofeedback or Neurofeedback (NFB) is a form of biofeedback.
- Brain training aimed at **improving dysregulated EEG patterns**.
- Dysregulated EEG patterns have been linked to a variety of symptoms and issues, including:
  - Attention/Focus/Concentration
  - Cognitive Impairment related to brain injury or concussion or age
  - Migraines/Headaches
  - Memory
  - Fatigue
  - Poor Sleep
  - Depression or Anxiety

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State Flexibility

- Ever see someone go from depressed (e.g. the other team just scored) to wild elation (e.g. your team just scored and took the lead) in seconds?

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Self-Regulation

- NFB is a passive style of biofeedback and only requires the patient to remain relaxed and focused on achieving success (i.e. feedback **ON**) as much as possible.

- Using this computerized feedback, the brain learns to increase or decrease certain brainwaves that are helpful for improved functioning.
  - Increasing deficient alpha activity for relaxation and quieting the mind.
  - Decreasing excessive theta activity for improved attention and memory.

- The feedback provided tells the brain that it is having success – over time this pattern is learned and permanent!

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BRAIN COMPUTER INTERFACE TRAINING

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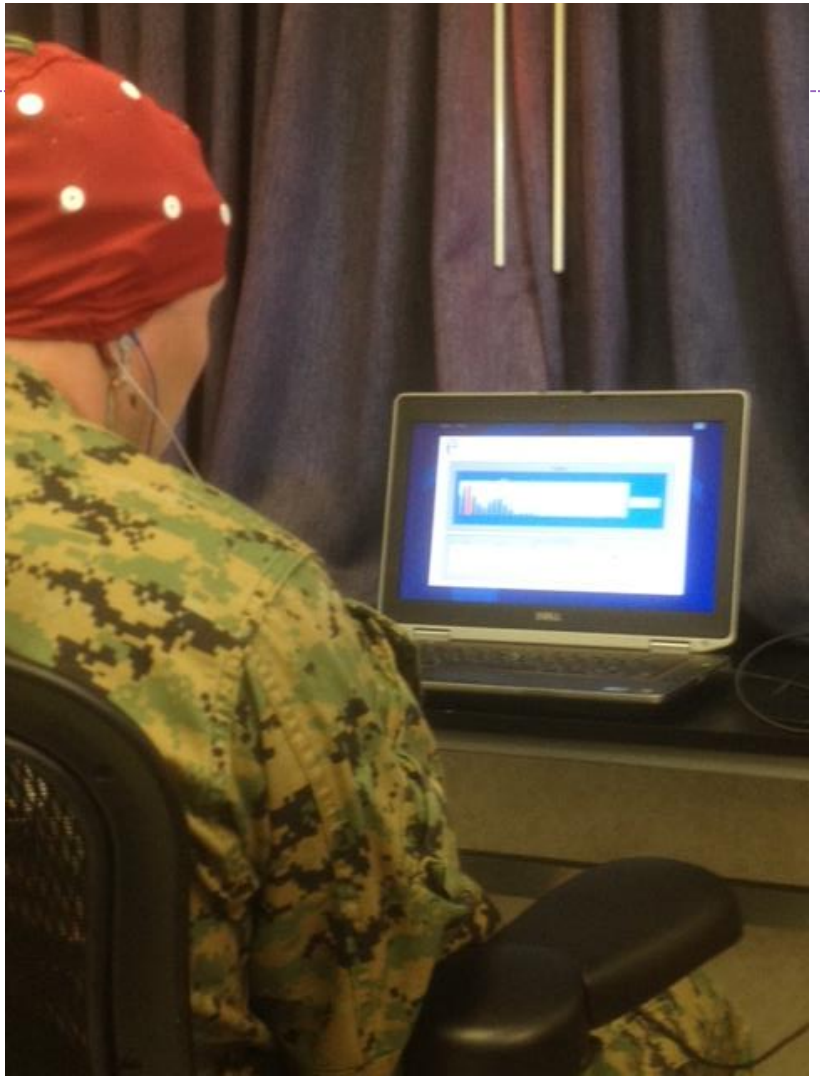

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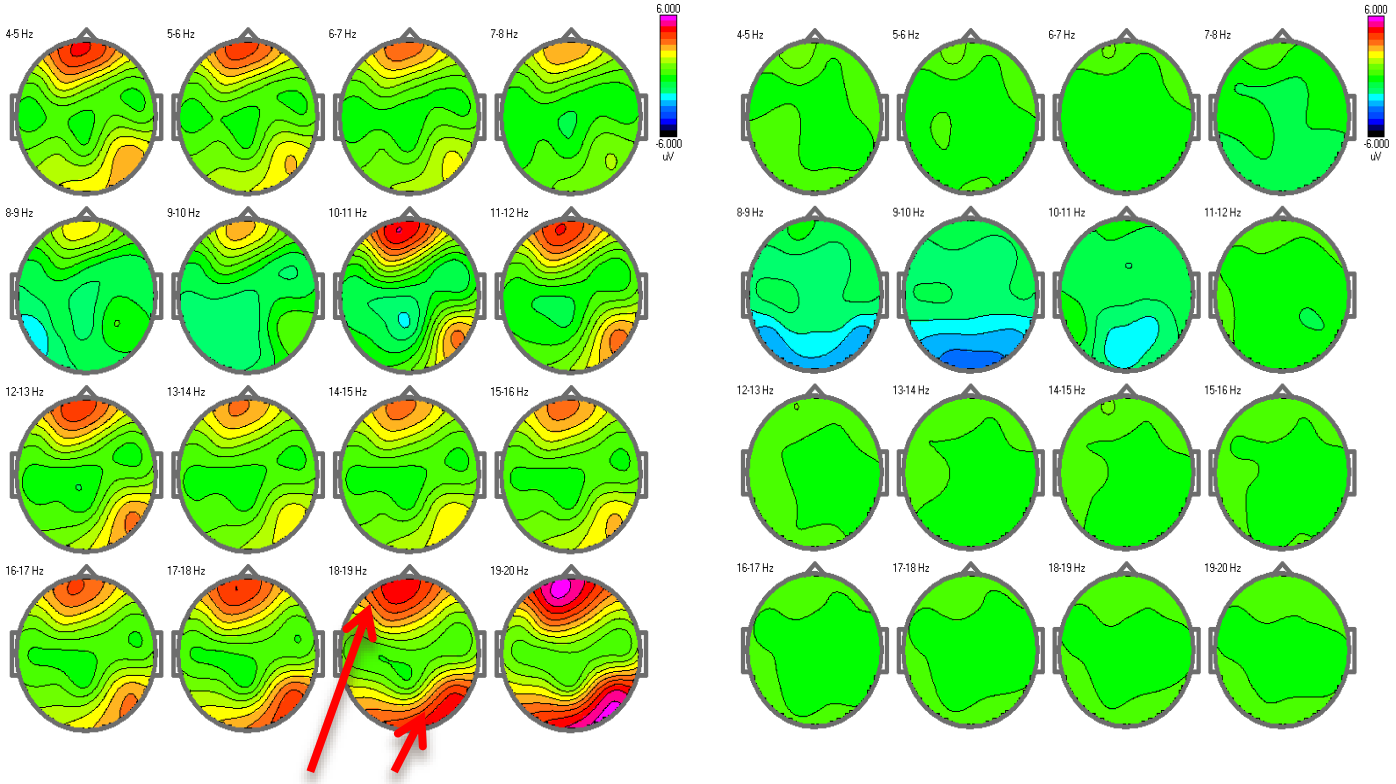
Injury Location & Dysfunction (EEG)

28 yr old male: Pre – Post brain injury rehabilitation (EEG-feedback, HRV, tDCS)



Coup-Contra-coup

Injury Resolution

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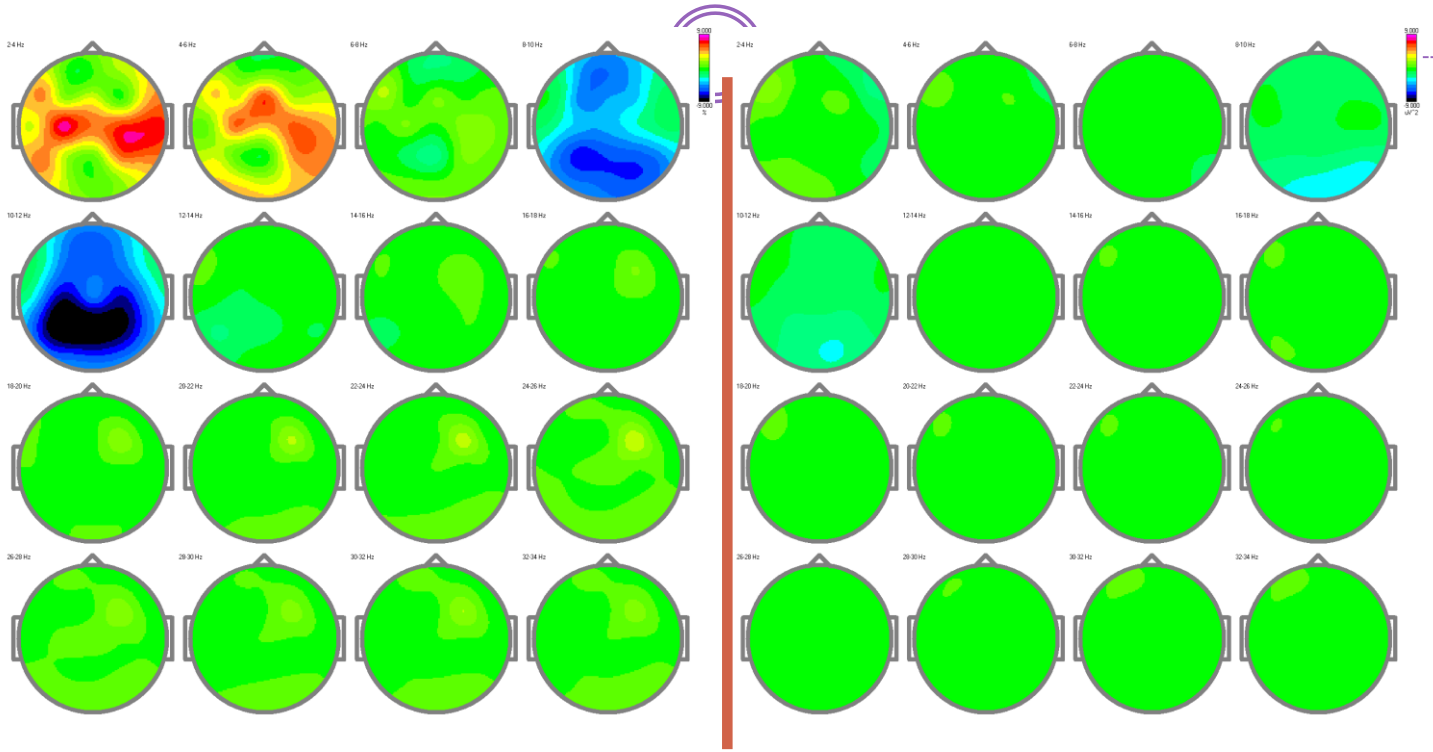
Pre- and Post-31 sessions (EO norm)



3 IED events with LOC one year prior to assessment:

- **May (left)** - Presented with midline vertex and frontal slowing and right DLPFC beta excess: resulting in inattention, emotional regulation difficulty (sudden rage), OCD sx desire to take things started after blast, memory loss, headache, dizziness, nightmares.
- **November (right)** – sleeps without medication, improved attention and memory, improved emotional regulation (reduced rage), remission of obsessions to take things.

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NFK improves recall memory

Memory, 2015
Vol. 23, No. 5, 683–694, http://dx.doi.org/10.1080/09658211.2014.921713

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Influence of electroencephalography neurofeedback training on episodic memory: A randomized, sham-controlled, double-blind study

Jonathan Guez[1,2], Ainat Rogel[1], Nir Getter[1], Eldad Keha[2], Tzlil Cohen[2], Tali Amor[2], Shirley Gordon[3], Nachshon Meiran[3], and Doron Todder[1]

[1]Department of Psychiatry, Beer-Sheva Mental Health Center, Beer-Sheva, Israel
[2]Department of Psychology, Achva Academic College, Beer-Tuvia, Israel
[3]Department of Psychology and Zlotowski Center for Neuroscience, Ben-Gurion University of the Negev, Beer-Sheva, Israel

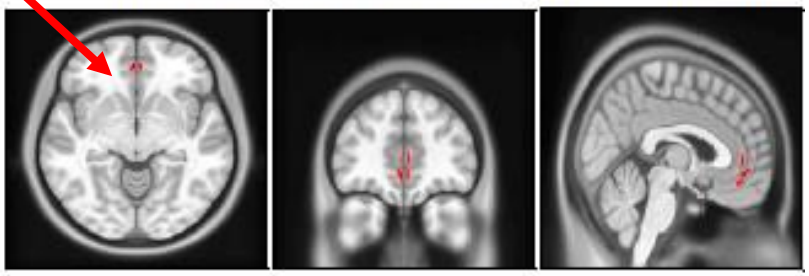
(*Received 4 August 2013; accepted 2 May 2014*)

4D NeuroTraining

- A more sophisticated form of NFB.
- Directly trains the source (Brodmann Area) of deviant brain activity, not just surface location.
- Trains real-time standard deviations or **Z-score** measurements.

Region:	**Medial Frontal Gyrus**
Brodmann Area (BA):	10
Frequency:	6Hz (3.1 SD)
Function:	verbal construction, emotional decision making[190,191]; motor, memory recall, attention, executive function[190,191]
Secondary BA:	32

(L) axial (R) (L) coronal (R) (P) sagittal (A)



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Nutrition & Supplements

N=7; Male post-concussion syndrome; 5-wks 9.6g EFA

Measure	Direction of Change for Clinical Improvement	Value	Z Score	$P < 0.05$ two-tailed	Significance
Global	↑	%	1.084	0.279	NS
Memory	↑	%	0.135	0.893	NS
Executive & Attention	↑	%	1.362	0.173	NS
Word Fluency	↑	%	2.207	0.027	Significant
Affective	↑	%	1.549	0.121	NS
Sensory	↑	%	1.355	0.176	NS
Motor	↑	%	0.944	0.345	NS
Reaction Time	↓	ms	-1.352	0.176	NS
Reaction Time Variance	↓	ms	-1.352	0.176	NS
Omission Errors	↓	%	-1.342	0.18	NS
Commission Errors	↓	%	0.000	1.000	NS
Heart Rate	↓	BPM	1.016	0.31	NS
QRS Duration	↓	seconds	-0.954	0.34	NS
QTc Interval	↓	ms	1.472	0.141	NS
SDNN	↑	ms	1.859	0.063	NS
HRV Total Power	↑	ms2	2.366	0.018	Significant
Visual N1 latency	↓	ms	-1.101	0.271	NS
Auditory N1 latency	↓	ms	-2.023	0.043	Significant
P3a latency	↓	ms	-1.352	0.176	NS
P3b latency	↓	ms	-0.845	0.398	NS
Theta:Beta Ratio	↓	ratio	0.000	1.000	NS
Posterior Peak Frequency	↑	Hz	-0.405	0.686	NS

HRV power

N1 vertex

CLOSE