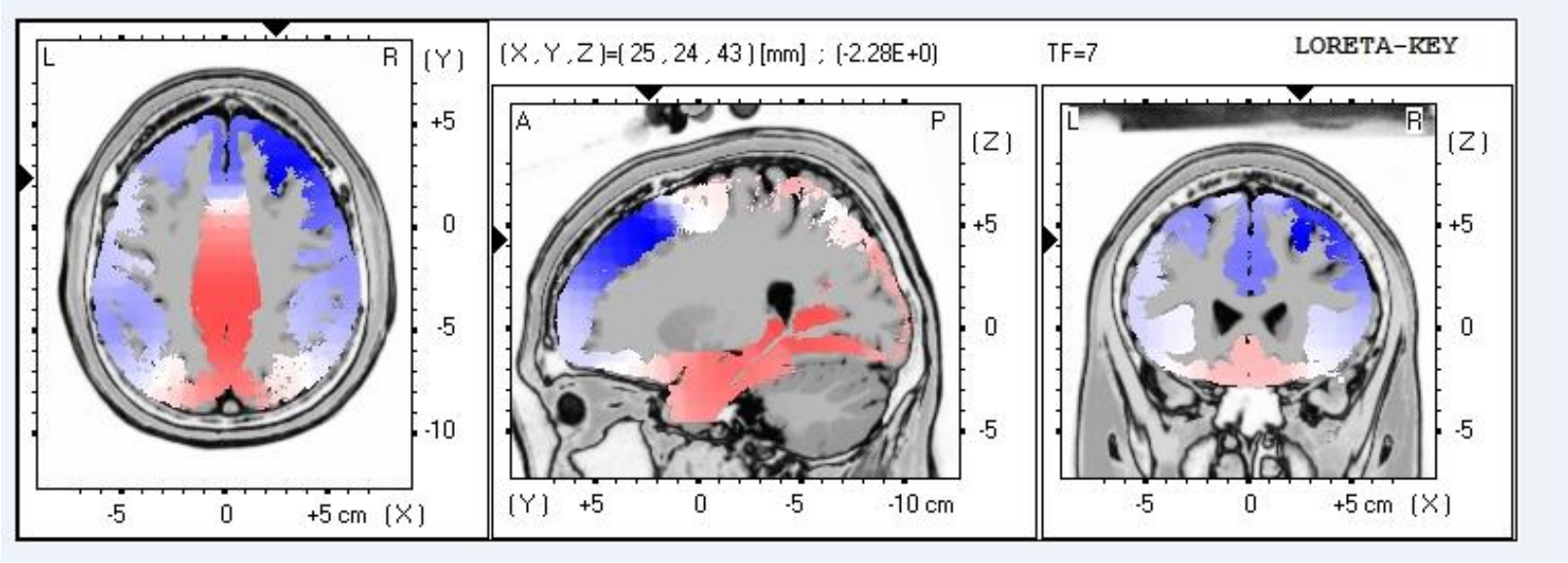
TBI & NFB

Richard Soutar, Ph.D.

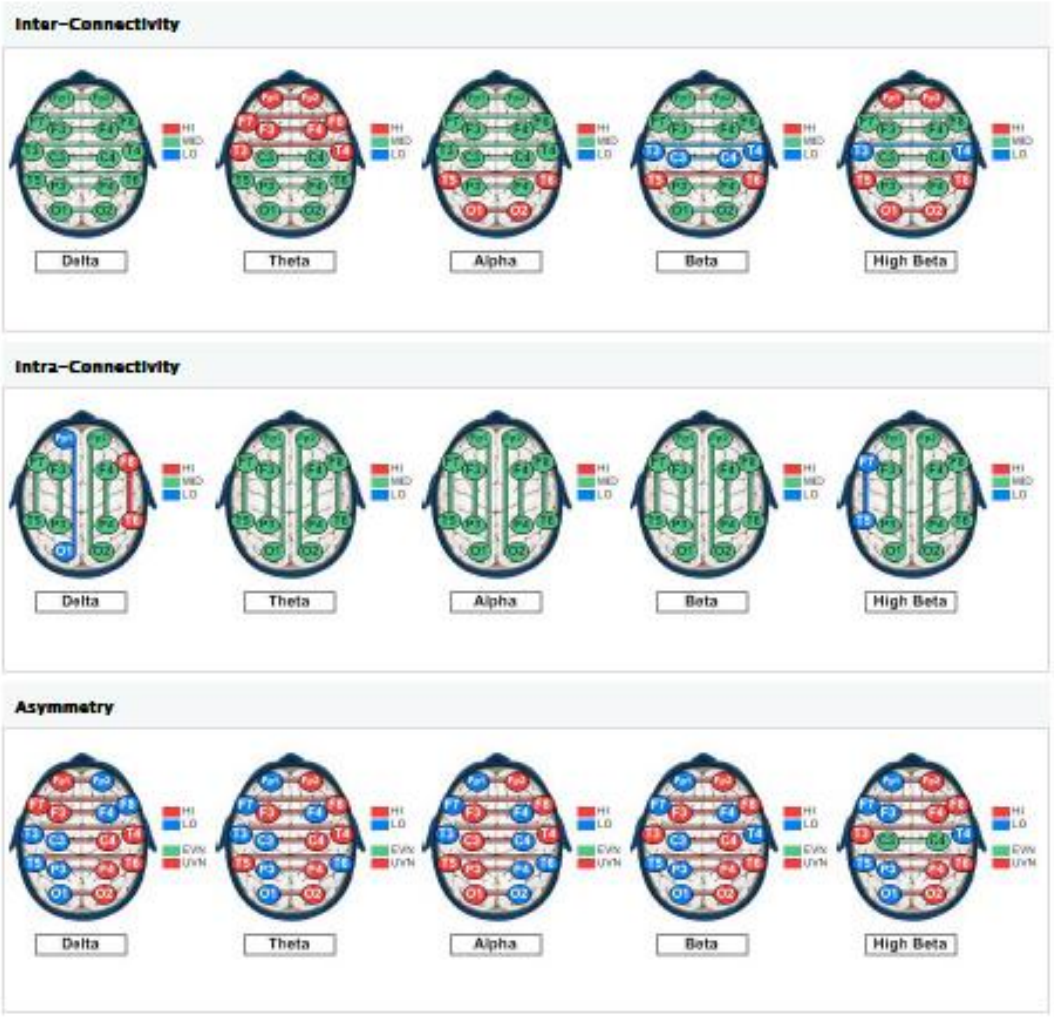
Trauma Map


Absolute Power
VHI
HI
OK
LO
VLO
Delta
Theta
Alpha
Beta
High Beta
Dominant Frequency
FAST
MID
SLO
Delta
Theta
Alpha
Beta
High Beta

LORETA IMAGE



Connectivity



Metabolic Profile

Metabolic Analysis

Score	Metabolic Category	Symptoms Reported
8	Gall Bladder	Indigestion Itchy Skin Reddened Skin Dry or flaky skin
6	Blood Sugar	Headaches Numbness Agitation Caffeine Dependent
5	Kidney	Headaches Joint pain
4	Somatic	Headaches Back pain Numbness Tingling
4	Pituitary	Headaches
3	Liver	Muscle Aches & pains Generalized Itching Loss of Appetite
1	Adrenals	Headaches
1	Gastrointestinal	Indigestion

Pre Post TOVA

Analysis Table	Quarter				Half		Total
	1	2	3	4	1	2	
RT Variability msec	127*	97*	100*	126*	117*	114*	115*
Std Deviation (Z)	<-4*	<-4*	-2.51*	-4.00*	<-4*	<-4*	<-4*
Standard Score	<40*	<40*	62*	40*	<40*	<40*	<40*
Response Time msec	424*	484*	438*	453*	454*	446*	448*
Std Deviation (Z)	-1.67*	-2.82*	-3.22*	<-4*	-2.32*	-3.80*	-3.71*
Standard Score	74*	57*	51*	<40*	65*	42*	44*
d' (DPrime)	8.53	8.53	3.80	2.91	8.53	3.29	4.18
Std Deviation (Z)	0.96	0.72	-1.51	-3.00	1.49	-2.26	-2.51
Standard Score	114	110	77	55	122	66	62
Commission Errors	0.00%	0.00%	8.33%	22.22%b	0.00%	15.28%	3.40%
Std Deviation (Z)	0.64	0.36	0.14	-1.01b	1.00	-0.58	-0.36
Standard Score	109	105	102	84b	115	91	94
Omission Errors	0.00%	0.00%	0.79%	1.59%*	0.00%	1.19%*	0.93%*
Std Deviation (Z)	0.00	0.00	-0.93	-2.00*	0.00	-2.93*	-2.93*
Standard Score	100	100	86	70*	100	56*	56*

[ ] = Invalid b = Borderline result * = Significantly Deviant Result

The T.O.V.A. test results (below) are a quarter by quarter analysis of the test. These results, in combination with the ADHD Score (below and on Form 4) determine the T.O.V.A. Interpretation (see Form 1).

Test Results	*	*	*	*	*	*	*

Test Results Key: N = Within normal limits assuming average intelligence
* = Not within normal limits B = Borderline ? = Not interpretable

ADHD Score = -8.77

Analysis Table	Quarter				Half		Total
	1	2	3	4	1	2	
RT Variability msec	79*	73*	97*	75	81*	87*	87*
Std Deviation (Z)	-2.06*	-1.89*	-2.28*	-0.73	-3.56*	-1.85*	-1.78*
Standard Score	69*	71*	65*	89	46*	72*	73*
Response Time msec	419*	477*	413*	435*	448*	424*	429*
Std Deviation (Z)	-1.56*	-2.65*	-2.48*	-3.61*	-2.18*	-3.12*	-3.12*
Standard Score	76*	60*	62*	45*	67*	53*	53*
d' (DPrime)	8.53	8.53	5.86	8.53	8.53	6.18	6.77
Std Deviation (Z)	0.96	0.72	-0.10	3.11	1.49	0.52	0.57
Standard Score	114	110	98	146	122	107	108
Commission Errors	0.00%	0.00%	5.56%	0.00%	0.00%	2.78%	0.62%
Std Deviation (Z)	0.64	0.36	0.53	1.35	1.00	1.13	1.19
Standard Score	109	105	107	120	115	116	117
Omission Errors	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
Std Deviation (Z)	0.00	0.00	0.07	0.00	0.00	0.07	0.07
Standard Score	100	100	101	100	100	101	101

[ ] = Invalid b = Borderline result * = Significantly Deviant Result

The T.O.V.A. test results (below) are a quarter by quarter analysis of the test. These results, in combination with the ADHD Score (below and on Form 4) determine the T.O.V.A. Interpretation (see Form 1).

Test Results	*	*	*	*	*	*	*	*

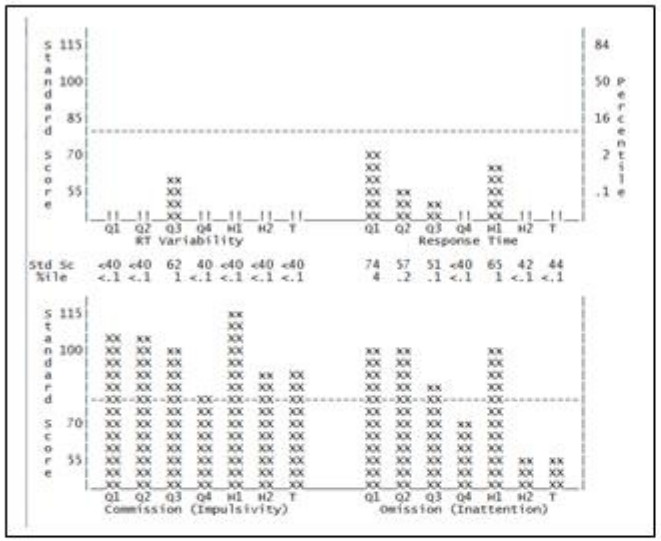
Test Results Key: N = Within normal limits assuming average intelligence
* = Not within normal limits B = Borderline ? = Not interpretable

ADHD Score = -3.44

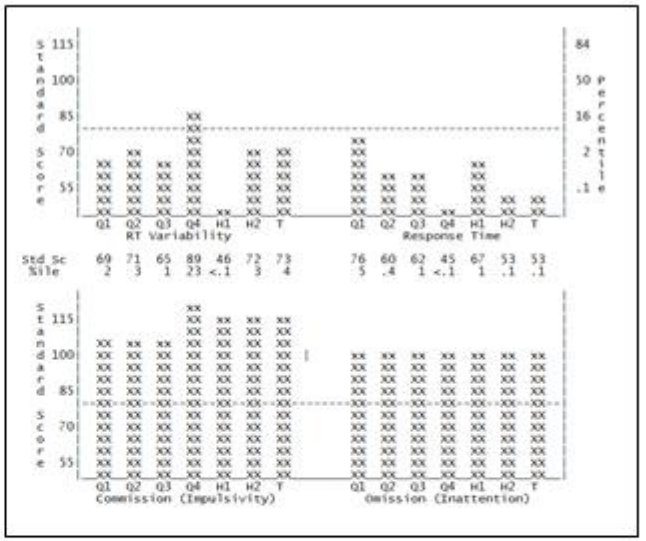
36% Overall Change

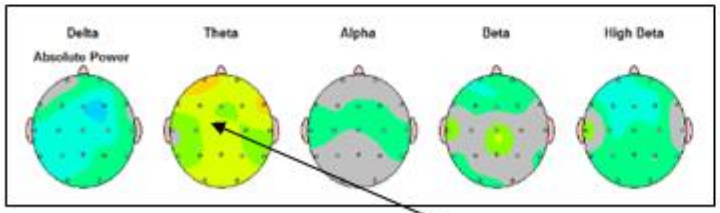
Pre Post TOVA

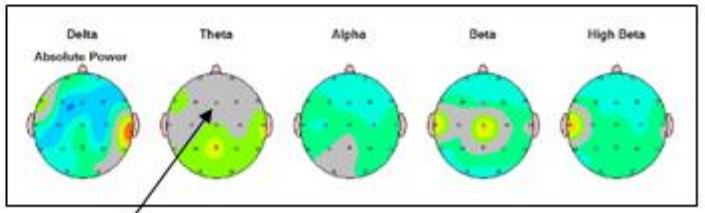
Pre Tests



Post Tests







Grey = Normal Range

Theta Reduction

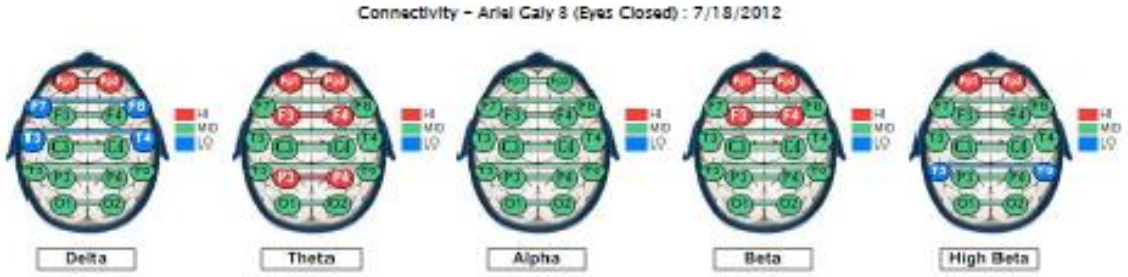
Pre Post Multiple Trauma Sub-concussive

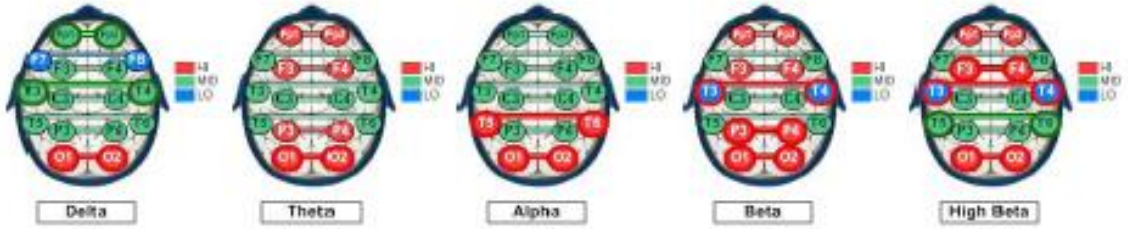
28% Overall Change

Absolute Power - Ariel Caly Post TBI (Eyes Closed) : 8/8/2012

Page 1 of 3

Increase Connectivity Problems





Tau Proteins & TBI

Articles

Initial CSF total tau correlates with 1-year outcome in patients with traumatic brain injury

M. Öst, MD, K. Nylén, MD, L. Csajbok, MD, A. Olsson Öhrfelt, PhD, M. Tullberg, MD, PhD, C. Wikkelsö, MD, PhD, P. Nellgård, MD, PhD, L. Rosengren, MD, PhD, K. Blennow, MD, PhD and B. Nellgård, MD, PhD

ABSTRACT

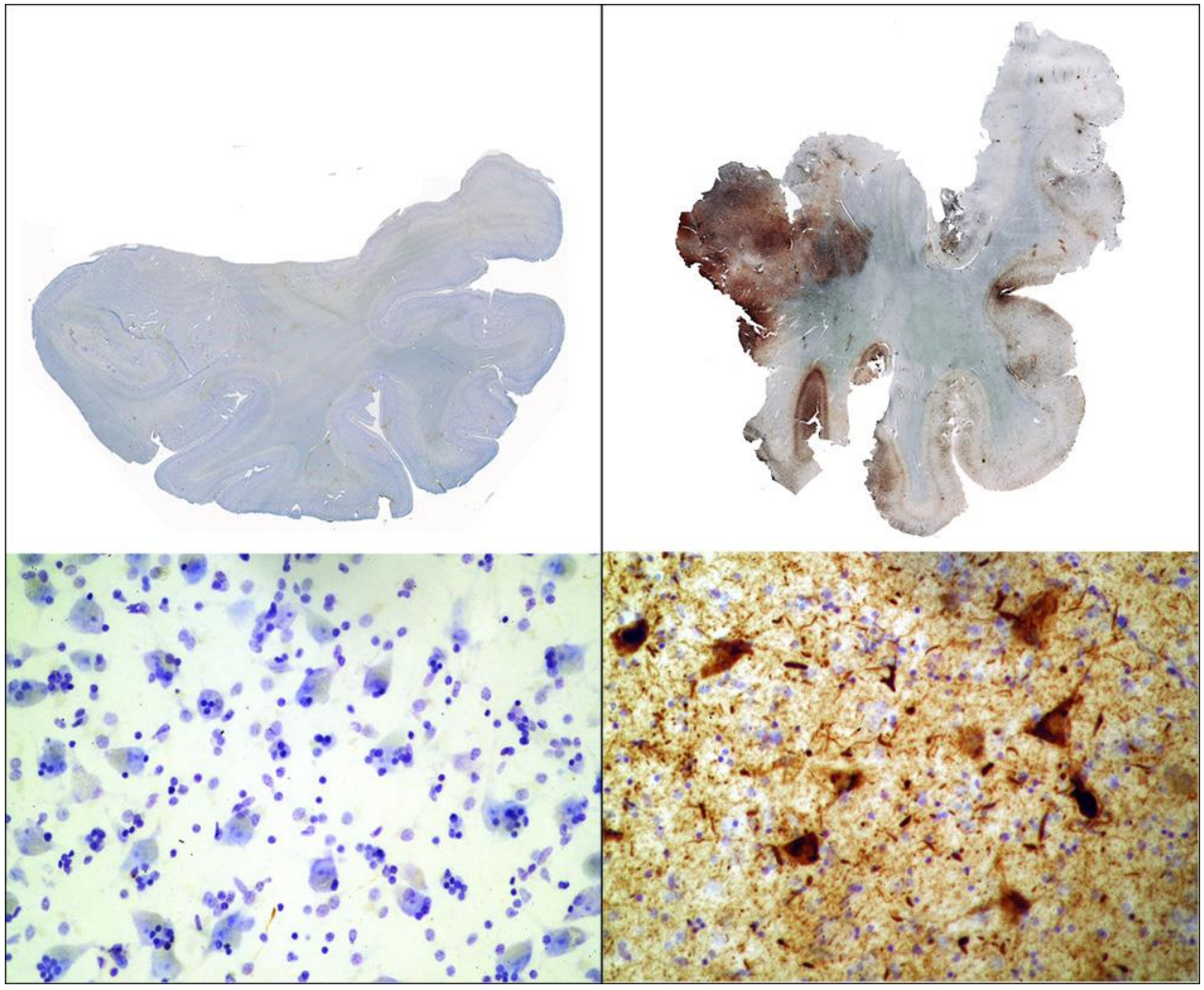
Objective: We investigated if tau, microtubular binding protein, in serum and ventricular CSF (vCSF) in patients with severe traumatic brain injury (TBI) during the initial posttraumatic days correlated to 1-year outcome.

Methods: Patients with severe TBI (n = 39, Glasgow Coma Scale score ≤8) were included. We measured serum and vCSF total tau on days 0 to 14, using ELISA. vCSF total tau correlated to 1-year Extended Glasgow Outcome Scale (GOSE), the NIH Stroke Scale (NIHSS) neurologic status, and the Bartel Daily Living Index. Patients (n = 20) with normal pressure hydrocephalus (NPH) served as reference.

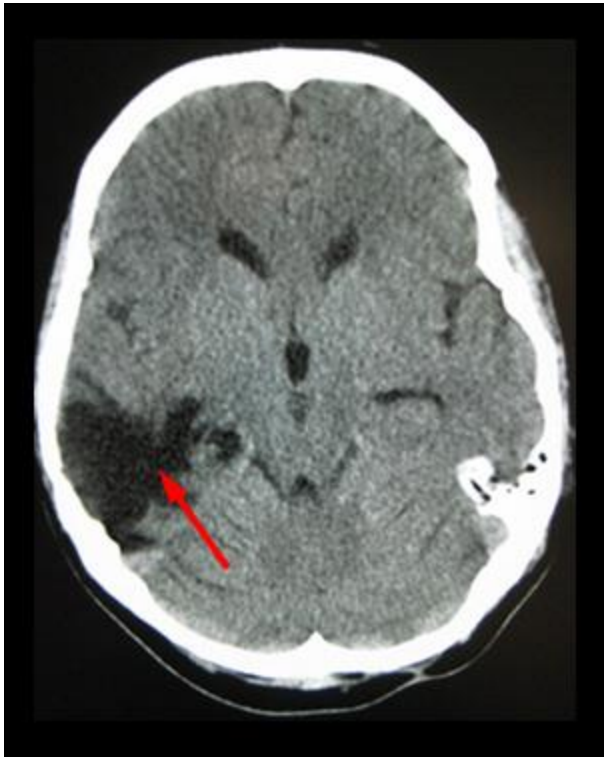
Results: Higher levels of tau were found in TBI patients vs patients with NPH. A correlation was found between initial vCSF total tau and GOSE levels ($R = 0.42$, $p < 0.001$) but not between vCSF total tau and NIHSS or Bartel scores at 1 year. A vCSF total tau level of >2,126 pg/mL on days 2 to 3 discriminated between dead and alive (sensitivity of 100% and a specificity of 81%). A vCSF total tau level of >702 pg/mL on days 2 to 3 discriminated between bad (GOSE 1 to 4) and good (GOSE 5 to 8) outcome (sensitivity of 83% and a specificity of 69%). Patients with GOSE 1 (dead) had higher vCSF total tau levels on days 2 to 3 ($p < 0.001$) vs both surviving patients (GOSE 2 to 8) and those with NPH. Total tau was not detected in serum throughout the study.

Conclusion: The increase in ventricular CSF (vCSF) total tau probably reflects axonal damage, known to be a central pathologic mechanism in traumatic brain injury (TBI). These results suggest that vCSF total tau may be an important early biochemical neuromarker for predicting long-term outcome in patients with a severe TBI.

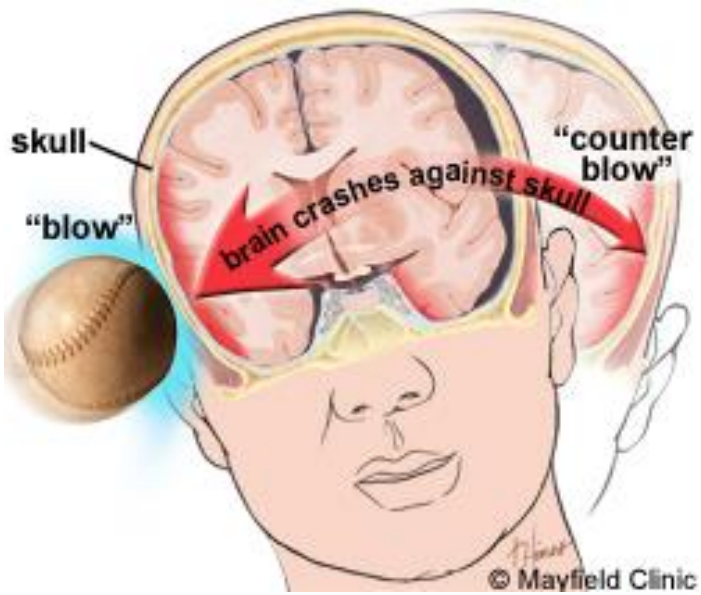
Healthy vs Tau Protein

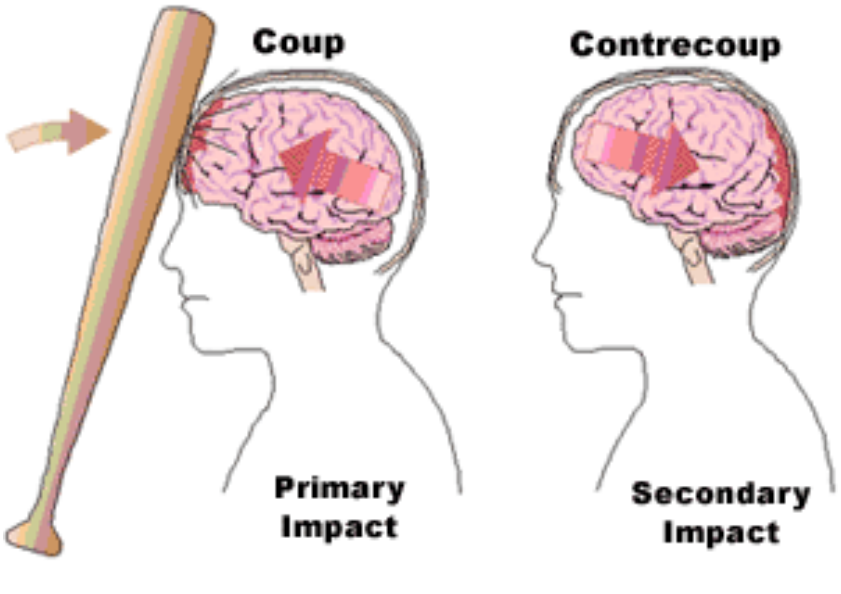


Multiple Sub-concussive Tau Development

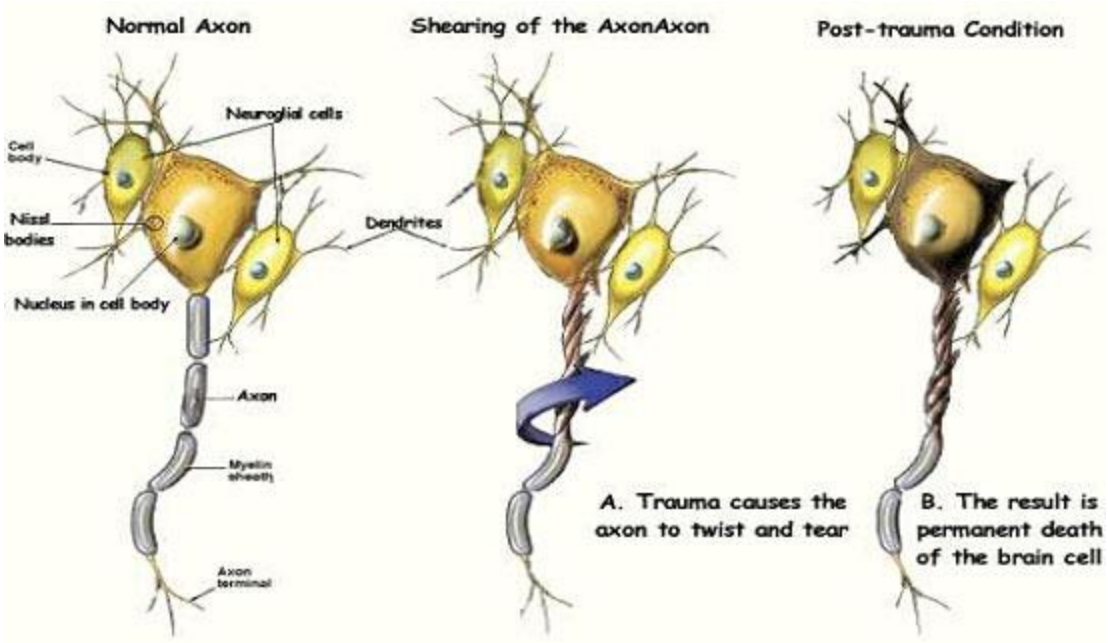


Coup Contrecoup





Axonal Shearing



Compensation

Transcallosal Inhibitory Control

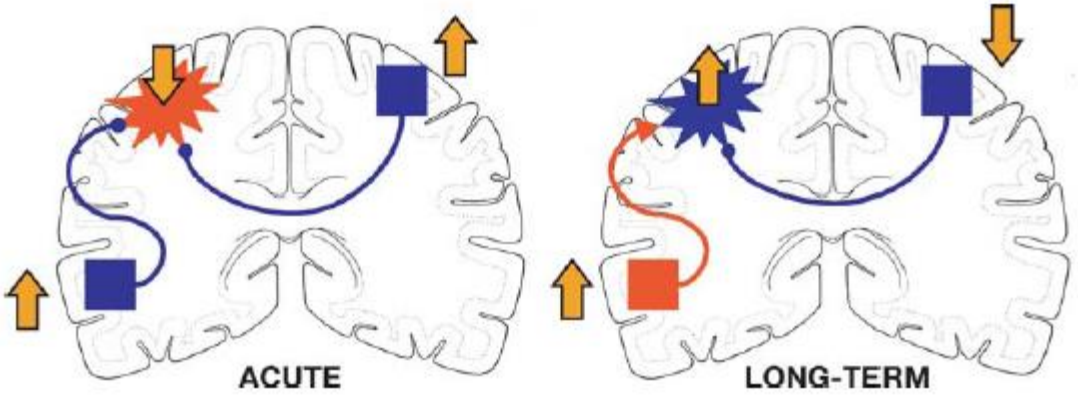


Figure 5

Schematic illustration showing that in the acute phase after a stroke, increased inhibitory input (within or across the hemispheres) may limit the extension of the lesion. Increased excitability (increased glutamatergic activity and reduced GABAergic activity) and postischemic LTP harbor an otherwise increased risk for further damage. However, after the acute phase, and once the injury is stable (long-term), excitatory input increases excitability and may further increase the efferent (e.g., motor) output. In contrast, inhibitory input at chronic stages is a maladaptative strategy, and the resulting functional outcome may be undesirable, with limited behavioral restoration. Note that the sources (intra- or interhemispheric) of such inputs may differ across neural systems and across individuals. Nevertheless, this provides a road map for neuromodulatory interventions whose aims differ in the acute and long-term stages (*block arrows indicate a desirable increase or decrease in excitability*).

Compromised regions in one hemisphere are invaded by the contralateral homologous region and managed until pyramidal, supporting cells or network functions recover and begin activating again.

Pascual-Leon, 2005

Adaptive Response To Trauma

Compromised regions or nodes increase and decrease connections to supportive networks depending on node valence in network constellations.

Modeling Lesions in Human Brain

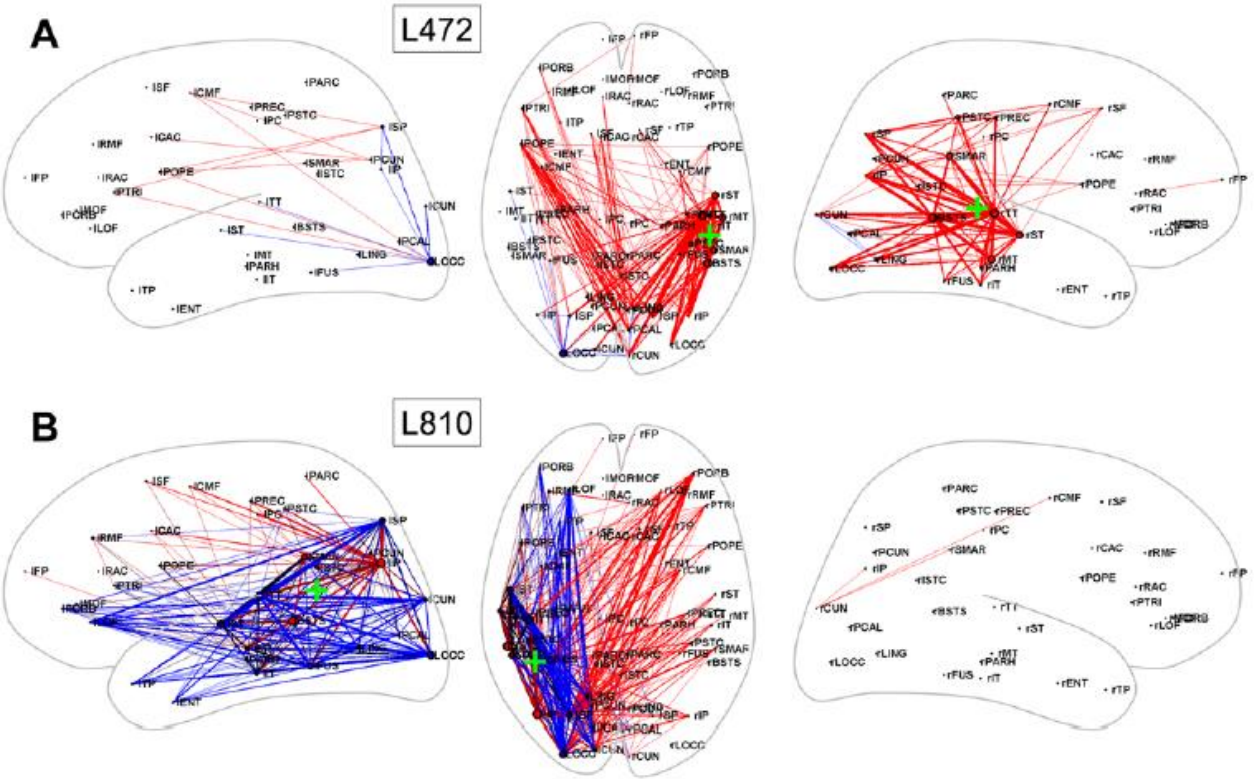


Figure 5. Dynamic effects of lesions near the temporo-parietal junction. (A) L472. (B) L810. For plotting conventions see legend to Figure 4.
doi:10.1371/journal.pcbi.1000408.g005

Alstott, 2009

Delta Correlates

- Abnormal delta: Cortical disconnect from subcortical and brainstem networks (Gloor et al, 1977).
- .5-2.5 polymorphic delta is usually an indicator of white matter damage.
- FIRDA- Frontal Intermittent Rhythmic Delta- Dysfunction of thalamocortical connections esp dorsal medial nucleus. Often shows up in toxic or metabolic encephalopathy.
- Synchronous delta bursts are common with decreasing blood sugar.
- Reducing acetylcholine generates delta in the cortex (Schaul,1978)
- Diffuse Frontal Delta in toxic and metabolic disorders. (Dyro, 1989).

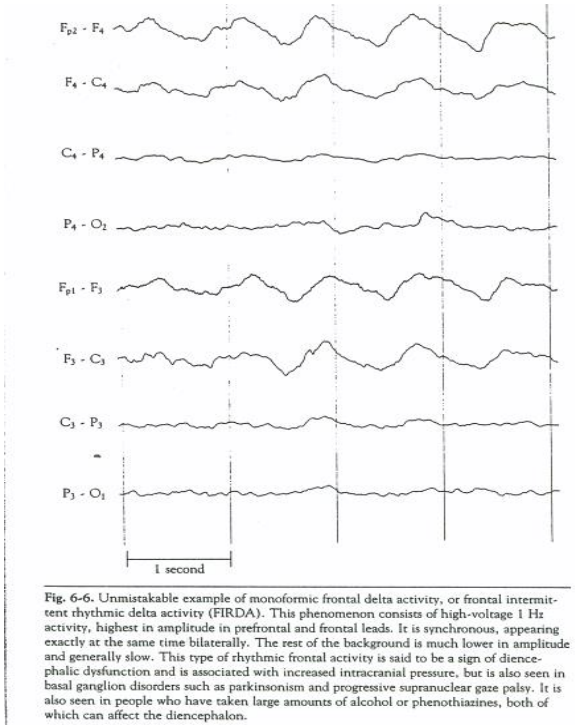
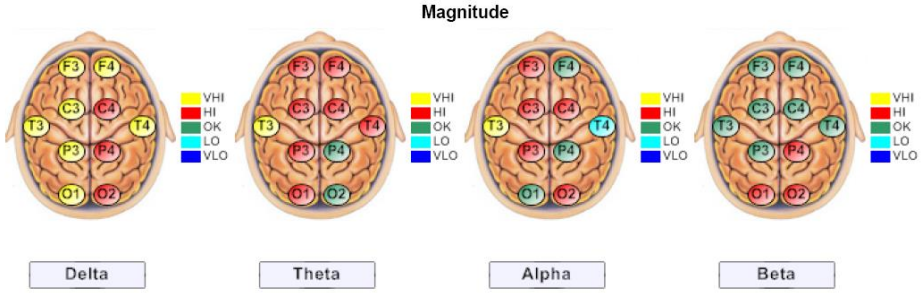
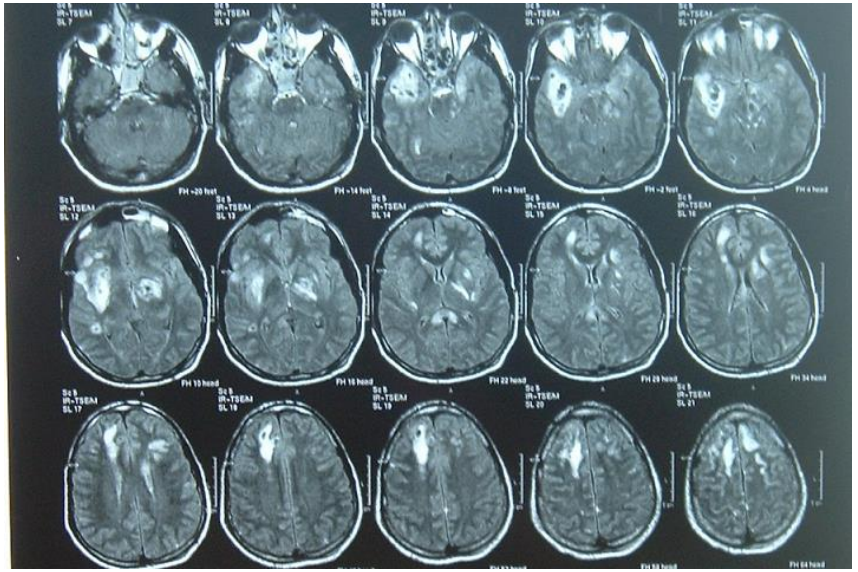


Fig. 6-6. Unmistakable example of monoformic frontal delta activity, or frontal intermittent rhythmic delta activity (FIRDA). This phenomenon consists of high-voltage 1 Hz activity, highest in amplitude in prefrontal and frontal leads. It is synchronous, appearing exactly at the same time bilaterally. The rest of the background is much lower in amplitude and generally slow. This type of rhythmic frontal activity is said to be a sign of diencephalic dysfunction and is associated with increased intracranial pressure, but is also seen in basal ganglion disorders such as parkinsonism and progressive supranuclear gaze palsy. It is also seen in people who have taken large amounts of alcohol or phenothiazines, both of which can affect the diencephalon.



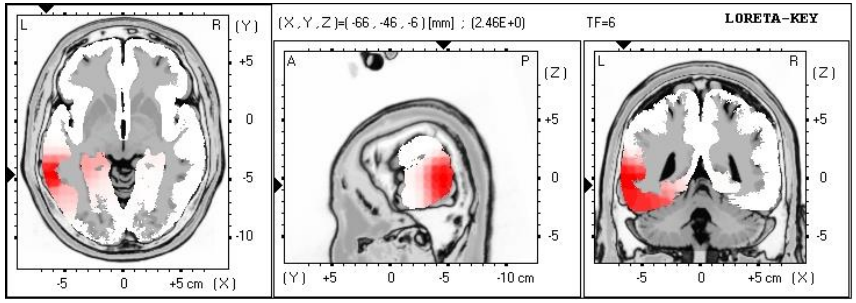
Training Upstream or Downstream

- Damage to one area may have a greater or lesser effect on other areas depending on the degree of participation in the processing network.
- Its impact may be further affected by available alternate routes of processing.



LORETA 6Hz

Brodmann area 22 is most impacted by the dorsal lateral network damage. Of the many regions trained, training in this region had the most impact on his entire system.



Neurological Report

Cognition

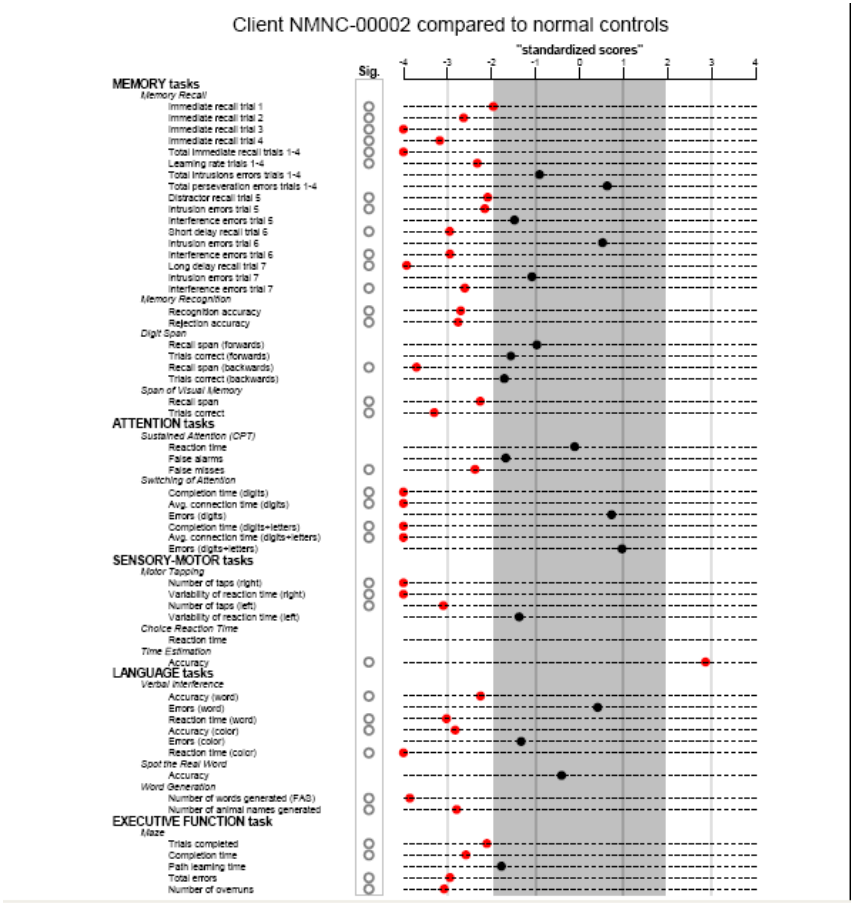
Test	Deficit
1. Memory Recall and Recognition	●
2. Digit Span	●
3. Span of Visual Memory	●
4. Sustained Attention (CPT)	●
5. Switching of Attention	●
6. Motor Tapping	●
7. Choice Reaction Time	
8. Time Estimation	
9. Verbal Interference	●
10. Spot the Real Word	
11. Word Generation	●
12. Maze	●

● = deficit compared to matched controls (see Appendix 1.3 for details)

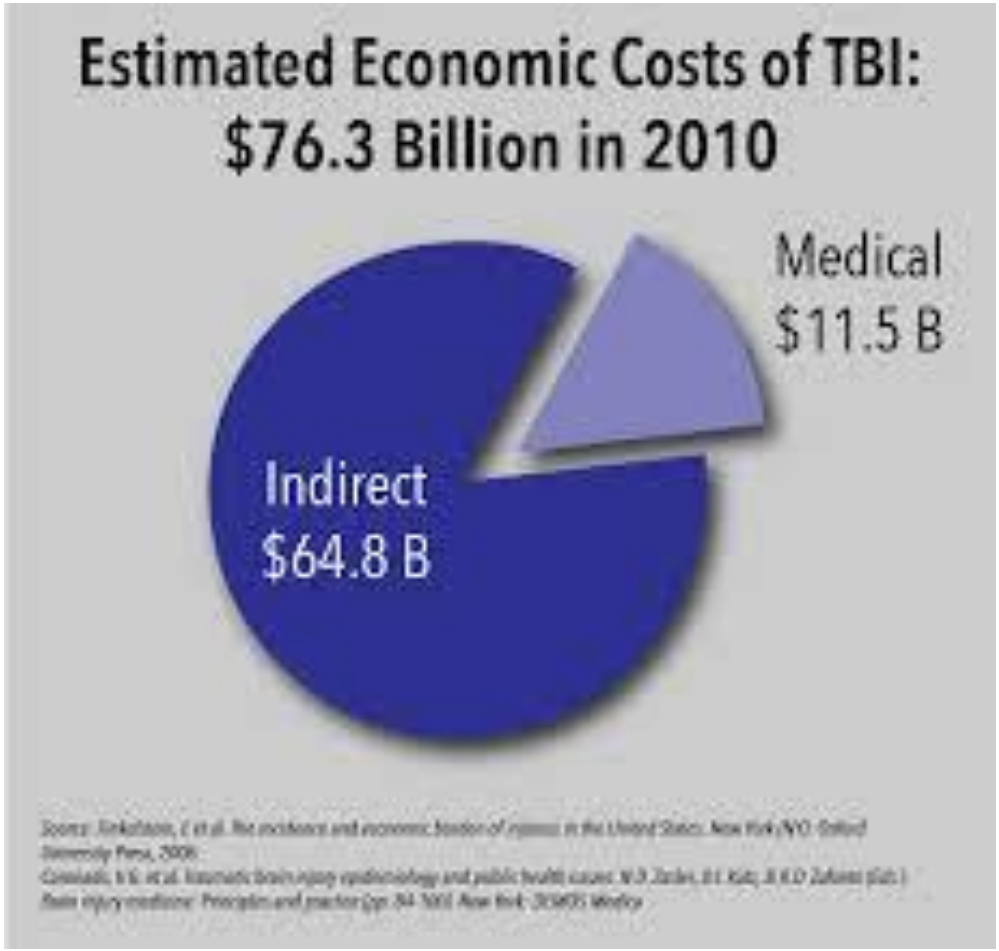
The table above shows deficits found in each test (1–12).

The list below summaries what the practical significance of that deficit is considered to be:

1. Ability to learn and remember new tasks based on verbal information. Critical, central everyday skill.
2. Ability to hold, retain and operate on new verbal information. Skills crucial to most everyday, verbal tasks requiring memory. Everyday examples include remembering telephone numbers and shopping lists.
3. Ability to hold and retain new spatial information. Skills crucial to most everyday, non verbal tasks requiring memory. Examples include navigation, operating industrial machines.
4. Ability to detect and respond to significant change under conditions requiring vigilance. Fundamental everyday skills e.g. train, plane, automobile, computer and equivalent machine operations.
5. Part 1: Simple ability to attend. Part 2: Ability to sustain and control the direction of attention. Critical activity for everyday multitasking skills e.g. management, driving.
6. Everyday motor skills such as typing and machine operation.
9. Part 1: Simple reading ability. Part 2: Ability to control impulses; behavioural control.
11. Ability to generate and articulate thoughts and ideas in a systematic manner.
12. Ability to plan, strategize and implement complex tasks involving visuospatial information.



Part 2


Estimated Economic Costs of TBI:
$76.3 Billion in 2010
Medical
$11.5 B
Indirect
$64.8 B

Rating Trauma Is Tricky

Severity of traumatic brain injury[13]

	GCS	PTA	LOC
Mild	13–15	<1 day	0–30 minutes
Moderate	9–12	>1 to <7 days	>30 min to <24 hours
Severe	3–8	>7 days	>24 hours

PTA- Post Traumatic Amnesia

LOC- Loss of Consciousness

More Than Physical Trauma

Int. J. Mol. Sci. **2014**, *15*, 1216-1236; doi:10.3390/ijms15011216

OPEN ACCESS
International Journal of
Molecular Sciences
ISSN 1422-0067
www.mdpi.com/journal/ijms

Review

Neuroprotective Strategies for Traumatic Brain Injury: Improving Clinical Translation

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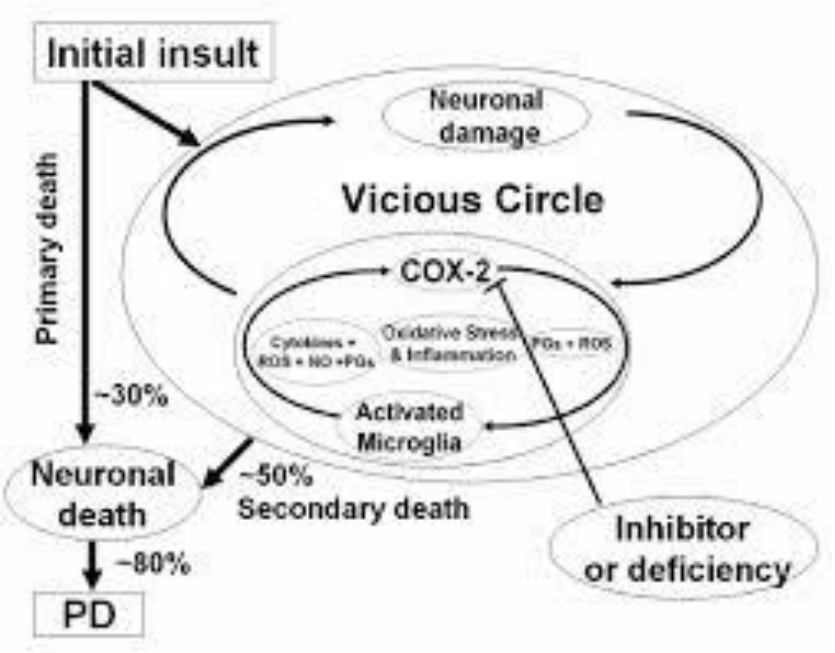
Received: 11 December 2013; in revised form: 7 January 2014 / Accepted: 13 January 2014 / Published: 17 January 2014

Abstract: Traumatic brain injury (TBI) induces secondary biochemical changes that contribute to delayed neuroinflammation, neuronal cell death, and neurological dysfunction. Attenuating such secondary injury has provided the conceptual basis for neuroprotective treatments. Despite strong experimental data, more than 30 clinical trials of neuroprotection in TBI patients have failed. In part, these failures likely reflect methodological differences between the clinical and animal studies, as well as inadequate pre-clinical evaluation and/or trial design problems. However, recent changes in experimental approach and advances in clinical trial methodology have raised the potential for successful clinical translation. Here we critically analyze the current limitations and translational opportunities for developing successful neuroprotective therapies for TBI.

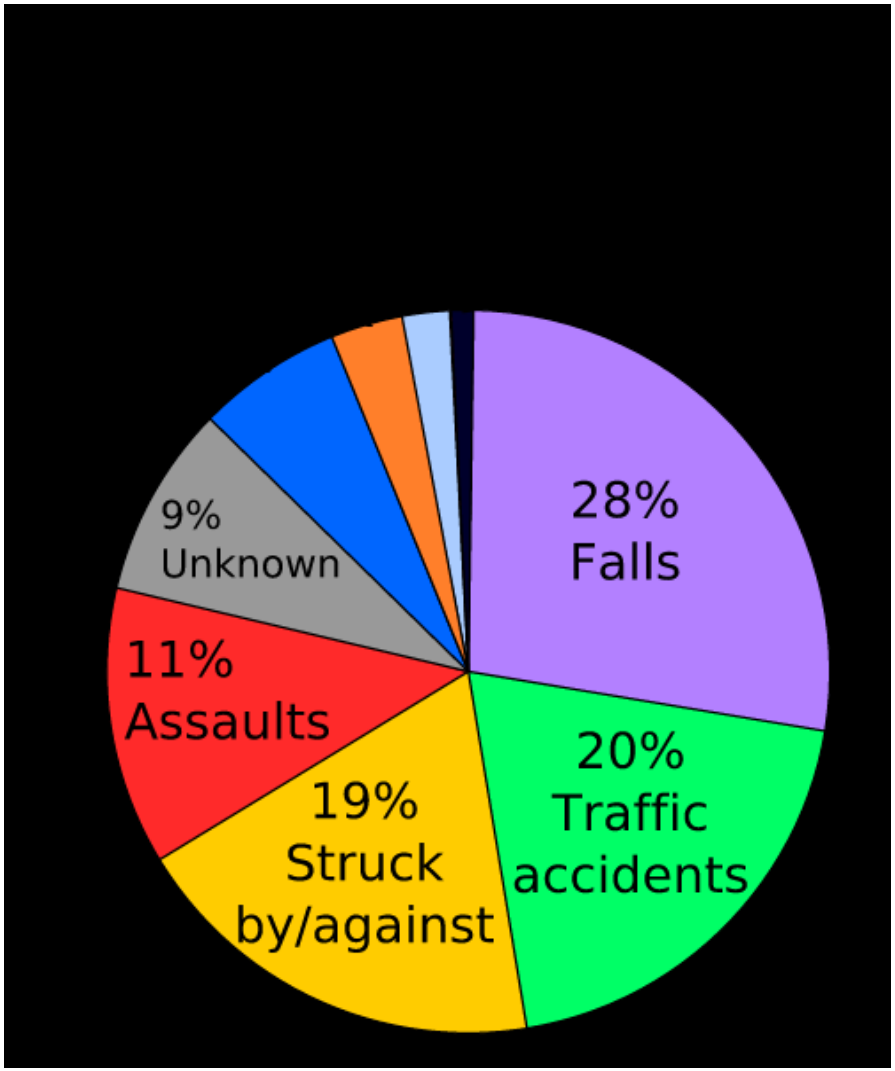
TBI is a degenerative disorder

"TBI must not be considered an acute or static disorder, but a complex and chronic neurodegenerative condition."



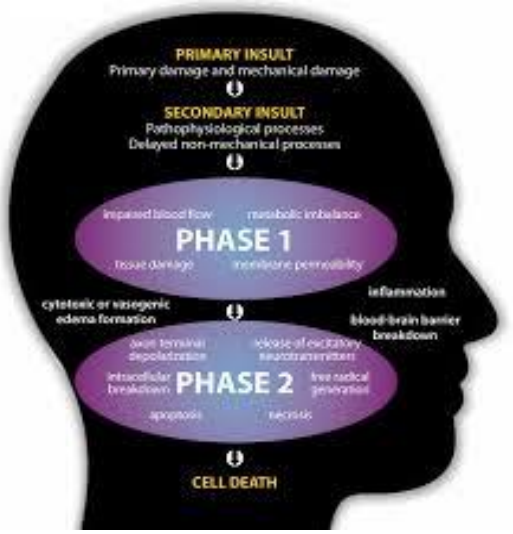
Primary Impact

The primary injury can be described as the mechanical damage occurring at the time of trauma to the neurons, axons, glia and blood vessels through shearing, tearing and stretching .



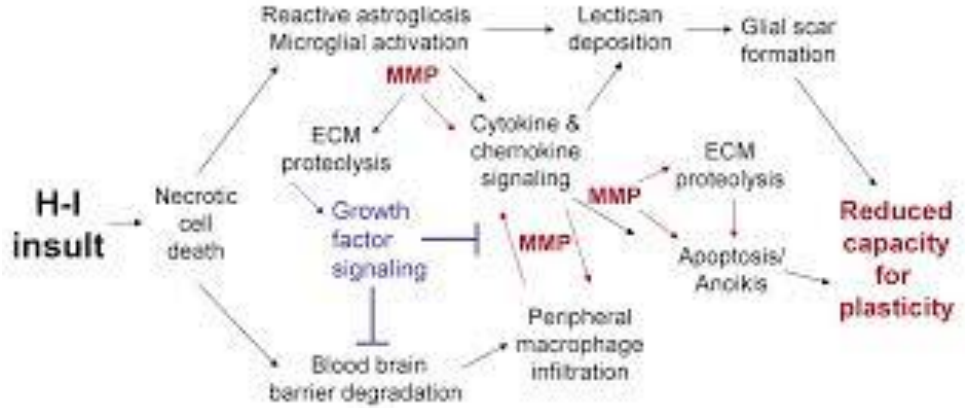
Secondary Cascades

Such events pave the way for secondary pathophysiological cascades that include biochemical, metabolic and physiological changes such as spreading depression, ionic imbalance, release of excitatory neurotransmitters, mitochondrial dysfunction, and activation of inflammatory and immune processes, among others.

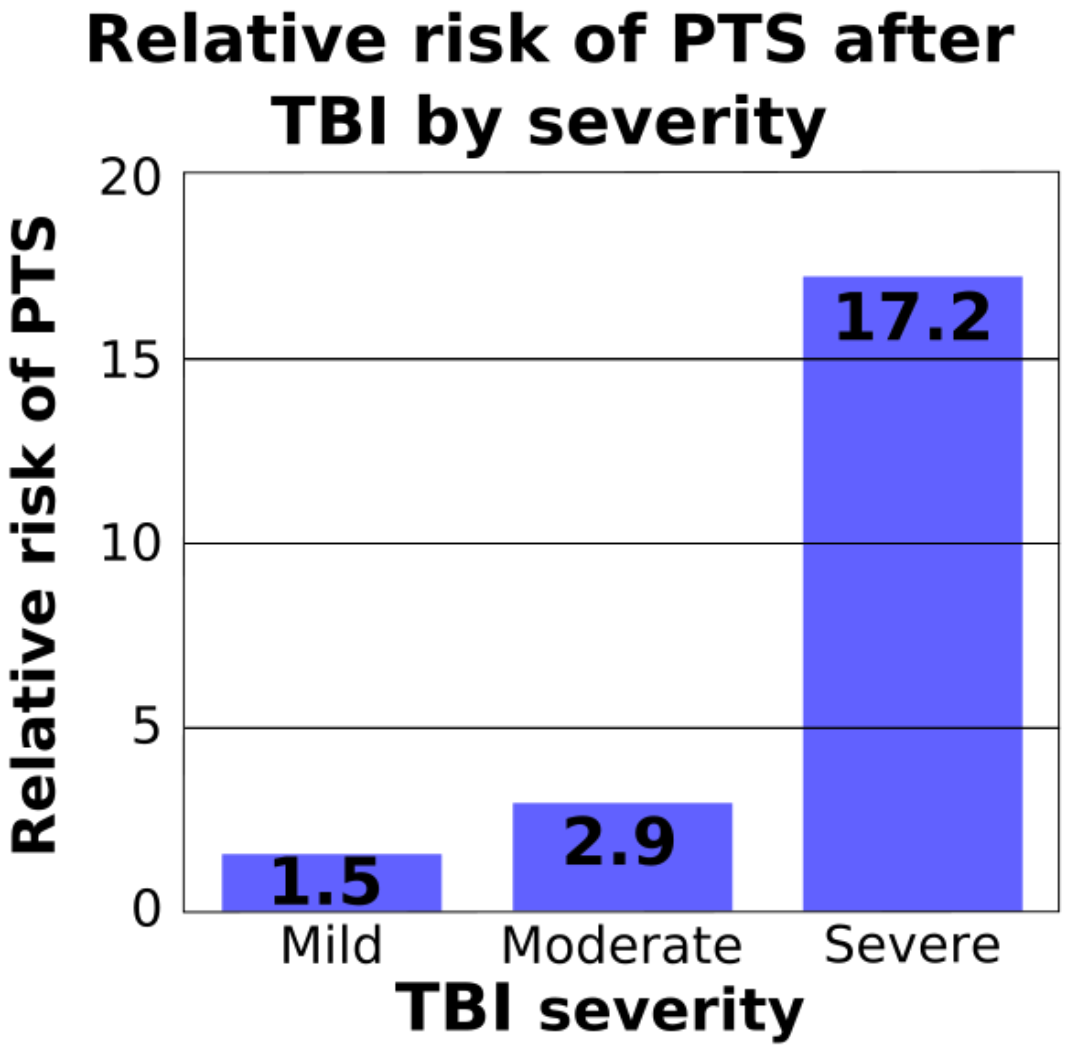


Secondary Effects

- Some of the more important secondary injury mechanisms involve:
- Activation of neuronal cell death pathways,
- Microglial and astrocyte activation,
- Neurotoxicity.
- Notably, chronic inflammation following CNS trauma providing a mechanistic link between acute and chronic neurodegeneration.



Seizure Risk



Back Up Networks

frontiers in
SYSTEMS NEUROSCIENCE

ORIGINAL RESEARCH ARTICLE
published: 24 February 2011
doi: 10.3389/fnsys.2011.00009

Prefrontal compensatory engagement in TBI is due to altered functional engagement of existing networks and not functional reorganization

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Functional neuroimaging studies of traumatic brain injury (TBI) have demonstrated altered neural recruitment, specifically within prefrontal cortex (PFC). This is manifest typically as increased recruitment of homologous regions of PFC (e.g., right ventrolateral PFC during performance of a verbal working memory task, possibly in response to damage involving the left PFC). The behavioral correlates of these functional changes are poorly understood. We used fMRI and multivariate analytic methods to investigate changes in spatially distributed activity patterns and their behavioral correlates in a sample of TBI patients with diffuse axonal injury (DAI, but without focal injury) and matched healthy controls. Participants performed working memory tasks with varying memory load and executive demand. We identified networks within left and right PFC that uniquely and positively correlated with performance in our control and TBI samples respectively, providing evidence of compensatory functional recruitment. Next we combined brain–behavior and functional connectivity analyses to investigate whether compensatory brain changes were facilitated by functional reorganization (i.e., recruitment of brain regions not engaged by our control sample) or altered functional engagement (i.e., differential recruitment of similar brain regions between the two groups based on task demands). In other words, does altered recruitment represent the instantiation of novel neural networks to support working memory performance after injury or the unmasking of extant, but behaviorally latent, functional connectivity? Our results support an altered functional engagement hypothesis. Areas within PFC that are normally coactivated during working memory are behaviorally relevant at an earlier stage of difficulty for TBI patients as compared to controls. This altered functional engagement, also evident in the aging literature, is attributable to distributed changes owing to significant DAI.

Keywords: traumatic brain injury, fMRI, working memory, functional connectivity, partial least squares, diffuse axonal injury

NFB Can Alter Structural Degradation

Clinical EEG and Neuroscience
00(0) 1-8

DOI: 10.1177/1550059413476031
eeg.sagepub.com
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Neurofeedback Training Induces Changes in White and Gray Matter

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Abstract

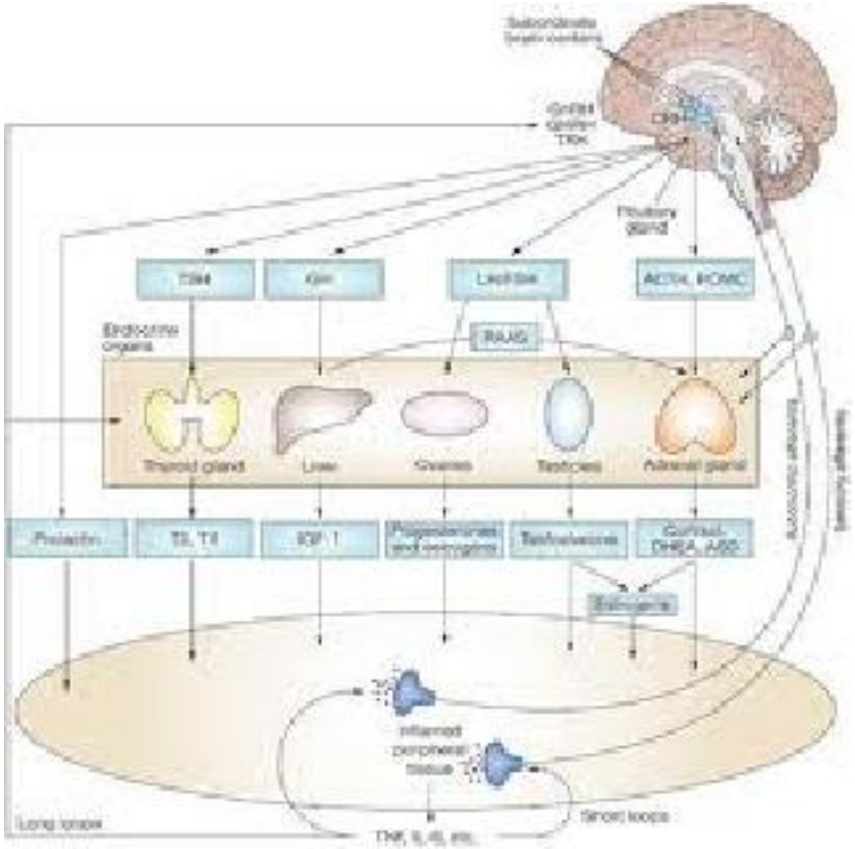
The main objective of this structural magnetic resonance imaging (MRI) study was to investigate, using diffusion tensor imaging, whether a neurofeedback training (NFT) protocol designed to improve sustained attention might induce structural changes in white matter (WM) pathways, purportedly implicated in this cognitive ability. Another goal was to examine whether gray matter (GM) volume (GMV) might be altered following NFT in frontal and parietal cortical areas connected by these WM fiber pathways. Healthy university students were randomly assigned to an experimental group (EXP), a sham group, or a control group. Participants in the EXP group were trained to enhance the amplitude of their β1 waves at F4 and P4. Measures of attentional performance and MRI data were acquired one week before (Time 1) and one week after (Time 2) NFT. Higher scores on visual and auditory sustained attention were noted in the EXP group at Time 2 (relative to Time 1). As for structural MRI data, increased fractional anisotropy was measured in WM pathways implicated in sustained attention, and GMV increases were detected in cerebral structures involved in this type of attention. After 50 years of research in the field of neurofeedback, our study constitutes the first empirical demonstration that NFT can lead to microstructural changes in white and gray matter.

Keywords

neurofeedback, structural magnetic resonance imaging, white matter, gray matter, sustained attention

TBI- Endocrine Effects
Neuroendocrine Dysfunction (NED)

- 80% of Adult Growth Hormone deficiencies are likely due to TBI.
- Chronic hormone deficiency occurs in 30-40% of patients after TBI, with 10-15% of patients having more than one deficiency.
- 15% of TBI patients develop gonadal hormone deficiencies and 10-30% develop hypothyroidism.
- Adrenal deficiency is common.
- 30% have elevated prolactin levels.



Mild TBI

Every Day Head Bumps

Approximately 15 percent of patients with mild TBI experience persistent symptoms

Of the approximate 15 percent who experience a mild TBI and remain symptomatic, an estimated 15-30 percent develop NED .

The Majority of the symptoms are related to pituitary and thyroid dysregulation.

List of Hormones Affected

FSH	**Follicle-Stimulating hormone**
GH	**Growth hormone**
IGF 1	**Insulin-like growth factor 1**
LH	**Luteinizing hormone**
TSH	**Thyroid-stimulating hormone**

Deficiency Symptoms

Growth hormone: Increased abdominal fat mass, fatigue, decreased vigor and concentration, decreased lean body mass, dyslipidemia, anxiety, depression, impaired judgment

Gonadotropin: Males — infertility, decreased libido, erectile dysfunction, decreased muscle mass, decreased exercise tolerance, anemia and testicular atrophy. Females — amenorrhea, sexual dysfunction, breast atrophy

Corticosteroid: Adrenal crisis, hypoglycemia, hyponatremia, myopathy, anemia, depression, fatigue, anxiety, apathy, weight loss, loss of libido

Thyroid hormone: Decreased energy, depression, cold intolerance, weight gain, fatigue, poor memory, muscle cramps, constipation, myopathy, hypotension, bradycardia, neuropathy, skin, hair and voice changes

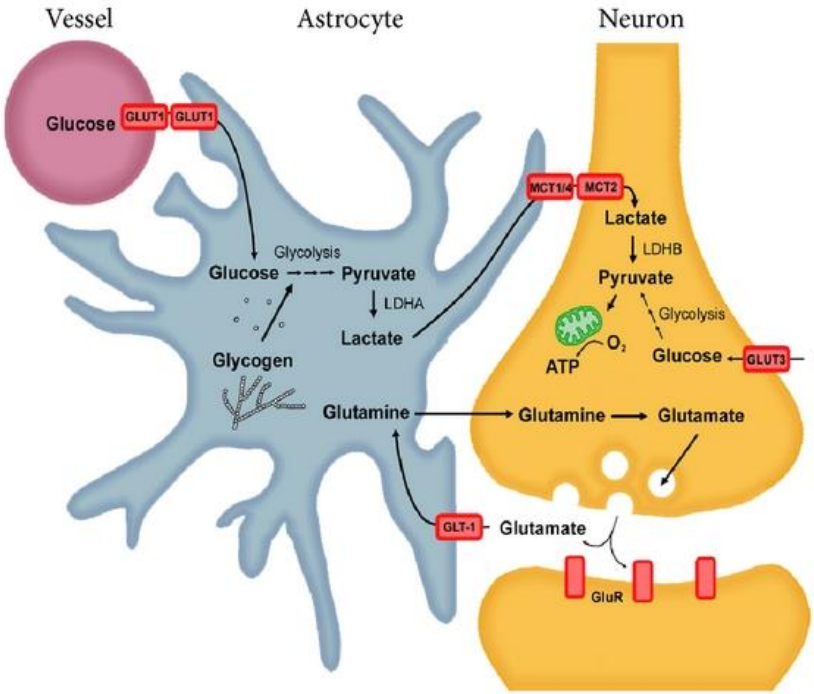
Prolactin: Males — decreased libido, impotence. Females — amenorrhea, oligomenorrhea, galactorrhea, infertility, hot flashes, vaginal dryness, hirsutism (in post menopausal women). Both — sudden onset of depression

Antidiuretic hormone: Excessive urination, dehydration, excessive thirst, hypernatremia (potentially leading to weakness, altered mental status, coma, seizures)

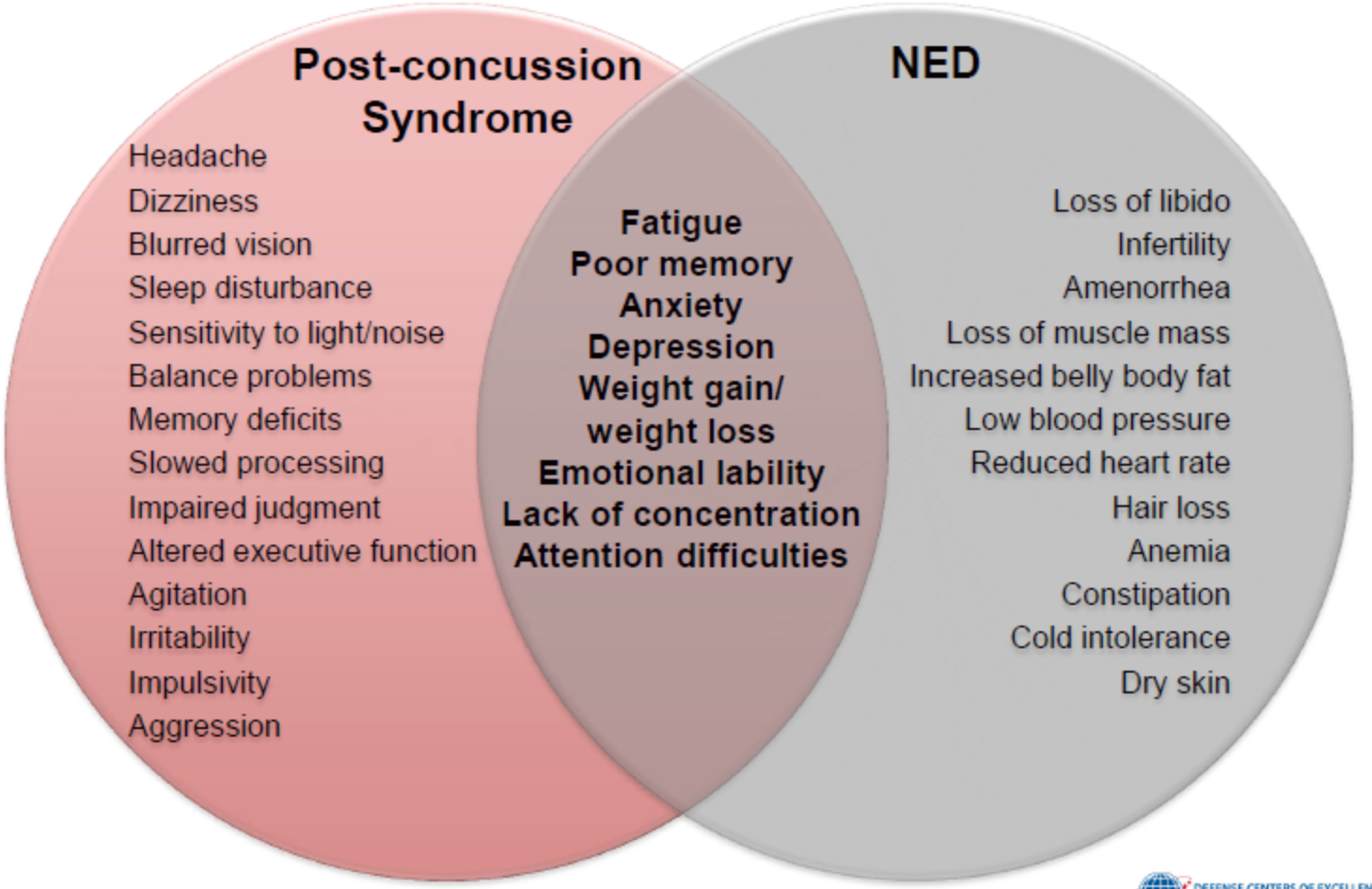
IGF-1 & Glucose Regulation

Insulin-like growth factor (IGF-1) IGF-1 deals with the functional use of glucose in the brain.

IGF-1 depletion causes disruption in lipid and microtubule metabolism, leading to impaired neuronal, somatic, and dendritic growth.



Symptom Overlap

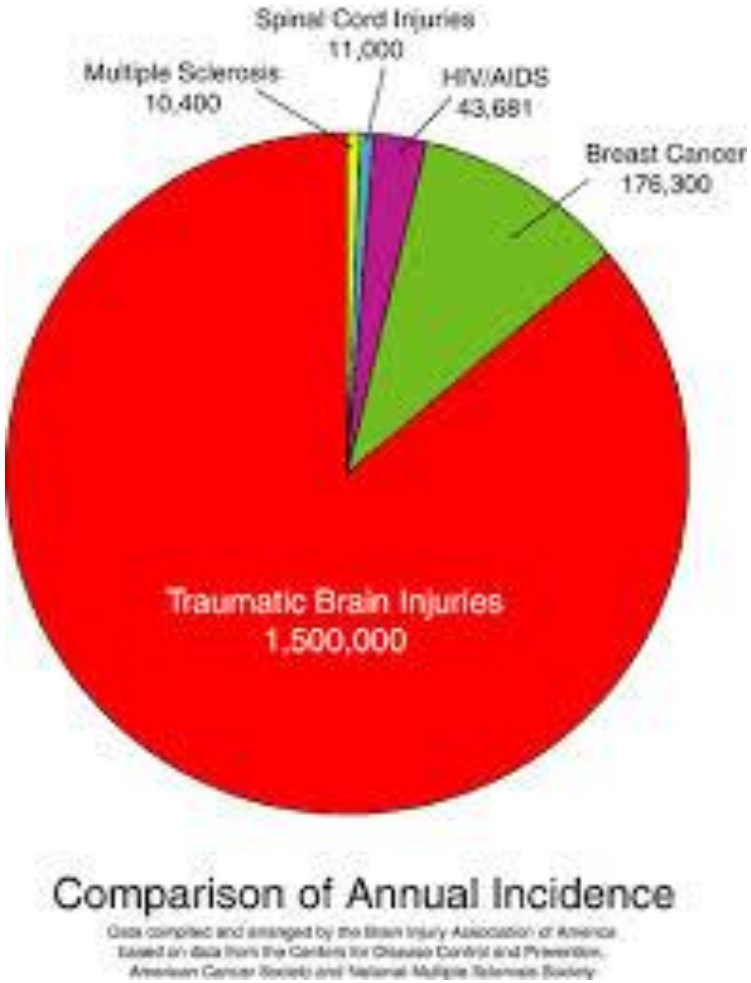


If Symptoms of Mild TBI persist beyond 3 months, then NED is likely present.

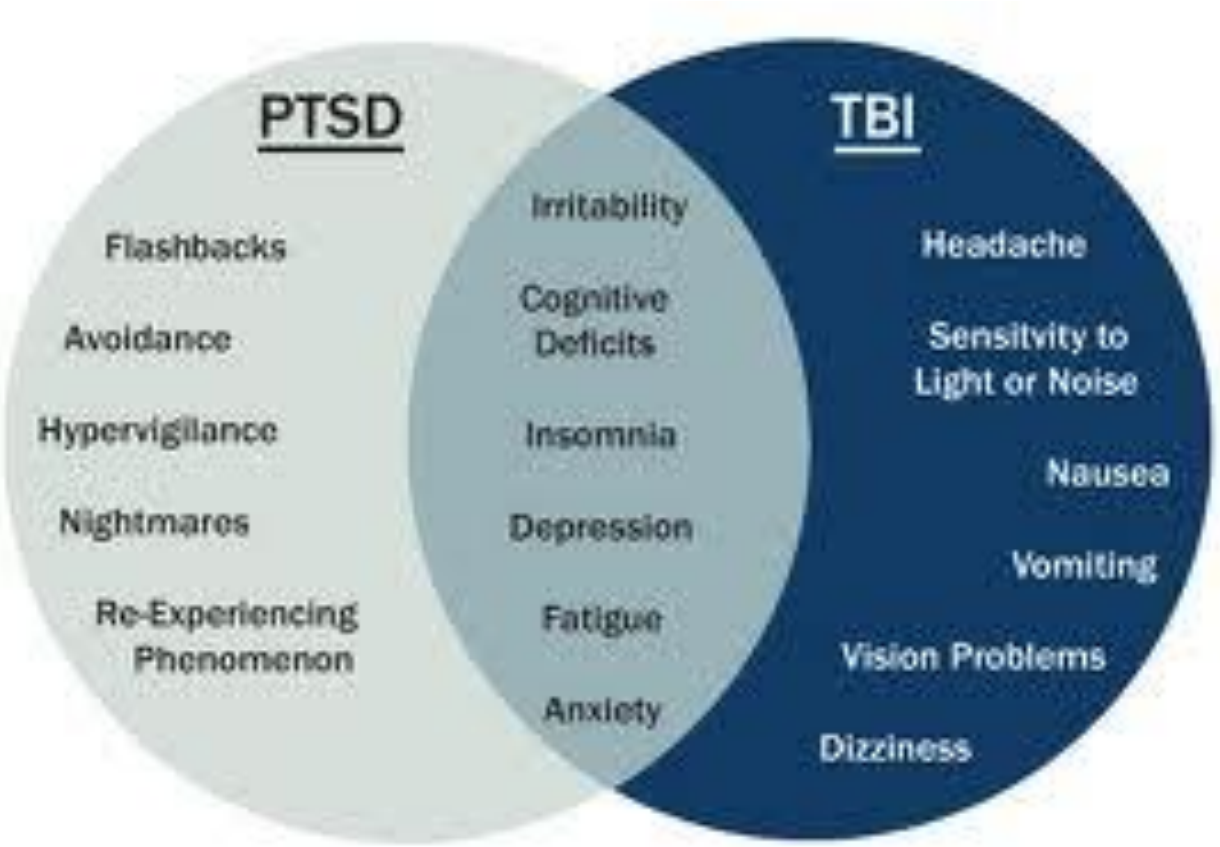
30 Year TBI Follow UPs

- 48% Axis 1 Problems
- Depression 27%
- Alcohol Abuse 12%
- Panic Disorder 8%
- Phobias 8%

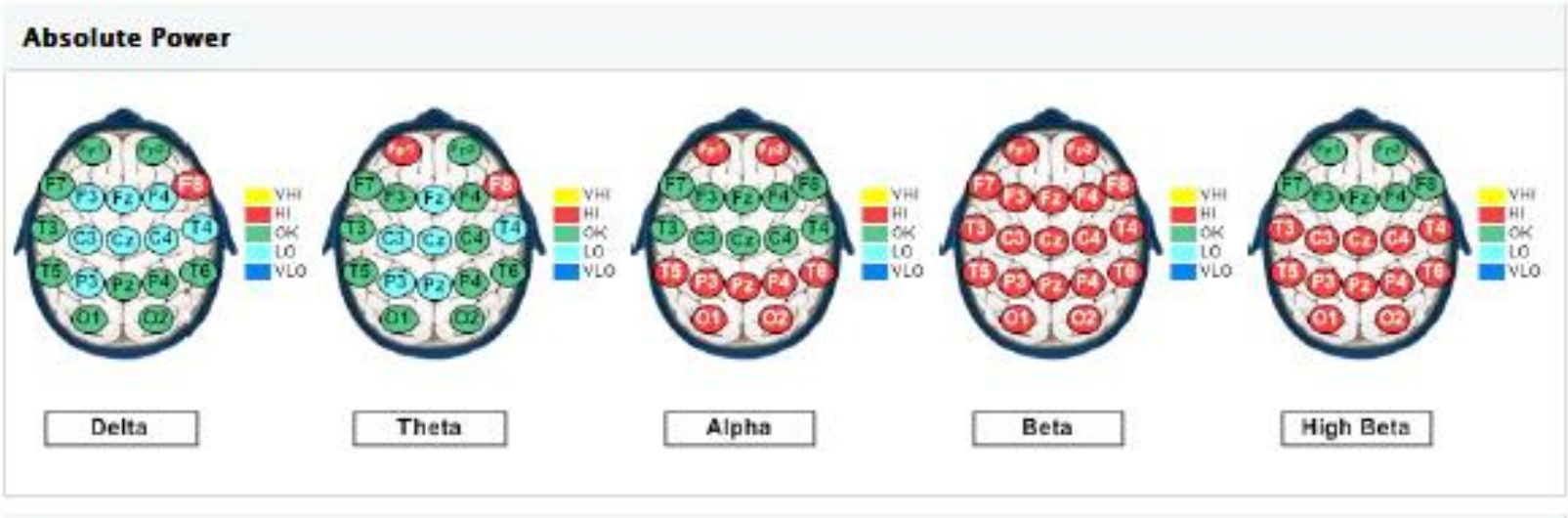
- 23% Axis 2 Disorders



TBI & PTSD

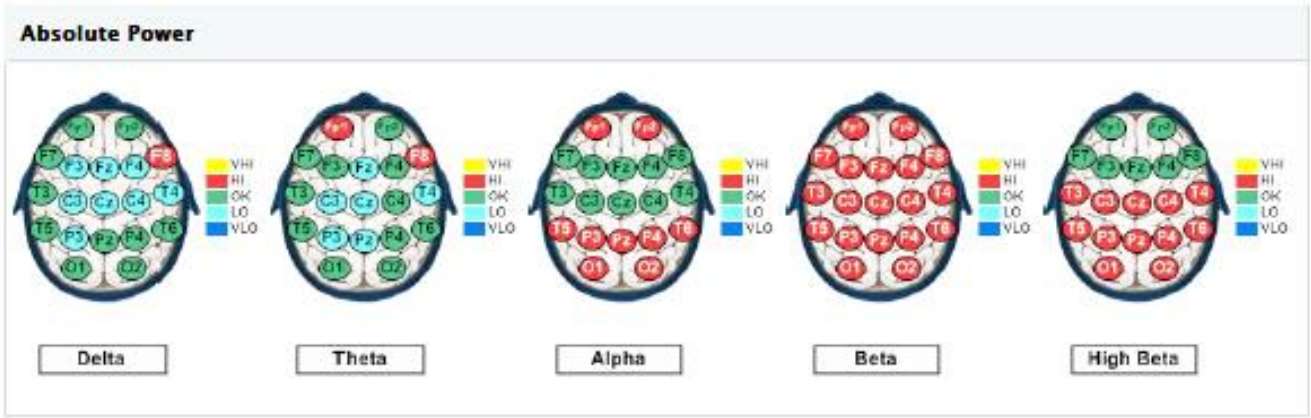

PTSD
Flashbacks
Avoidance
Hypervigilance
Nightmares
Re-Experiencing Phenomenon
Irritability
Cognitive Deficits
Insomnia
Depression
Fatigue
Anxiety
TBI
Headache
Sensitvity to Light or Noise
Nausea
Vomiting
Vision Problems
Dizziness

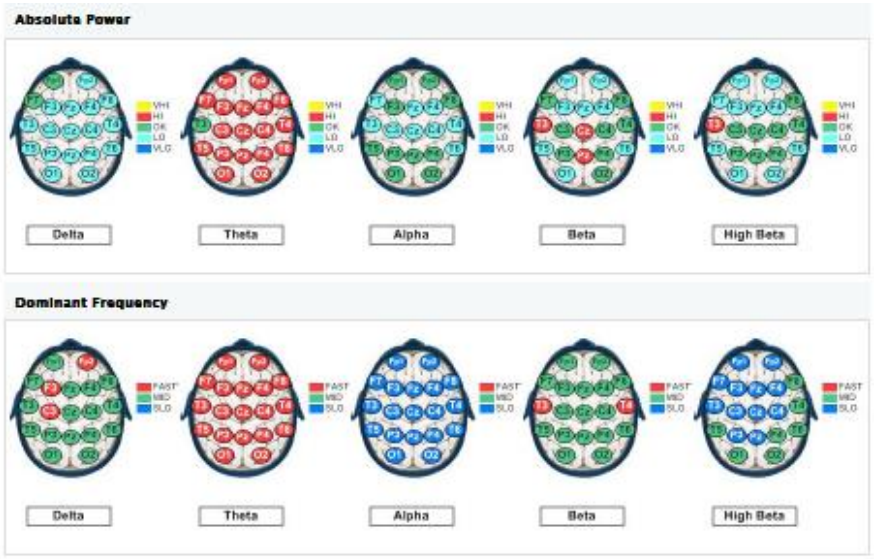
Multiple Sub Concussive Case (NED)



With PTSD

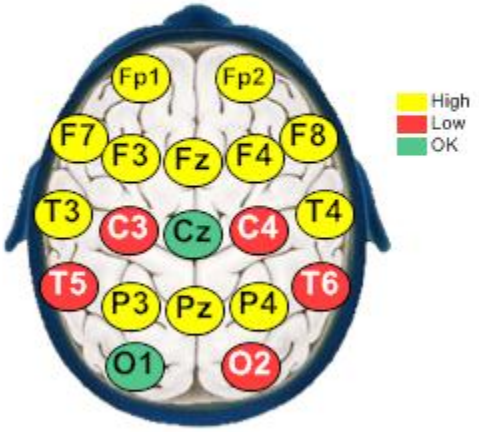
Different Trauma Patterns





CEC Analysis

Cognitive / Emotional Checklist Assessment



CEC Response Assessment

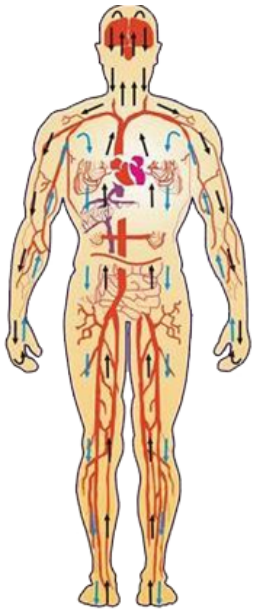
Category	Response Count	Average Response	Category Score
Attention	10	2.30	23.00
Memory	13	1.92	25.00
Impulsive	6	2.00	12.00
Depression	5	2.20	11.00
Anxiety	12	2.50	30.00

* Red indicates an abnormally high score.

Metabolic Analysis 1

Metabolic Assessment

Probability	Score	Metabolic Category	Symptoms Reported
	40	Pituitary	Headaches Insomnia Menstrual irregularity Excessive menstrual bleeding
	26	Kidney	Headaches Joint pain Dry mouth Fatigue Excessive Thirst
	36	Adrenals	Headaches Heart palpitations Insomnia Dizziness Shaking or tremor Fatigue Non-restorative sleep Weakness
	20	Thyroid (hypo)	Sexual indifference Fatigue Cold all the time Weight Gain Morning Headaches Hair Thinning
	19	Thyroid (hyper)	Heart palpitations Insomnia Heart racing Dizziness Night Sweats Trembling Weight loss
			Headaches Nausea Dizziness Shaking or tremor Numbness



Metabolic Analysis 2

	28	Blood Sugar	Numbness Visual blurring Agitation Irritable with missed meals Crave Sweets Eating relieves fatigue Caffeine Dependent
	16	Cardio-Vascular	Heart palpitations Fatigue Sleepiness Chest Pains Shortness of Breath Ringing in Ears
	23	Gastrointestinal	Abdominal bloating Abdominal pain Stomach Pain Nausea Constipation Indigestion Diarrhea Food intolerances Heartburn
	19	Liver	Nausea Diarrhea Sexual indifference Sudden weight fluctuation Fatigue Muscle Aches & pains Excessive Thirst Dark Urine Light Colored Stools Generalized Itching Loss of Appetite

Metabolic Analysis 3

	12	Gall Bladder	Food intolerances Heartburn Indigestion Itchy Skin Greasy food distress Dry or flaky skin
	18	Somatic	Headaches Lump in throat Back pain Numbness Spasms Tingling Extremity pain Chest Pains Shortness of Breath Excess sweating Shock sensation Tics-verbal or motor Restless Legs

Probability Legend

Minimal Low Moderate High