

Olfaction as Physical Examination Biomarker for Residual Neurological Damage Due to Mild TBI (mTBI) Associated with Combat Explosions

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Disclosures

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None

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Disclaimer

Any opinions or conclusions presented are those of the author and do not necessarily reflect those of the Department of Veterans Affairs.

Background

- **Combat mild TBI in OIF/OEF is often associated with PTSD , neurological deficits, impaired sleep and pain (headache)**
- **Epidemiological connection between mTBI and PTSD**

Questions/Issues –

- **1) What is the most sensitive physical exam test for residual deficits from a mTBI?**
- **2) How Can CNS damage associated with impaired olfaction predispose to PTSD?**

**2091 OIF/OEF
veterans**

**Initial screen
18.4% +**

385

**Agree to 2nd level
screen - 90.9%**

350

**2nd level
Screen + 60%**

210

**Agree to
Further
Eval -
84.8%**

**Study Group
126 Veterans
6% of initial group**

178

**Clinician-confirmed mTBI with
Combat mTBI and ≥ 1 LOC
70.1%**

Rationale - Identifying residual neurological injury following mTBI in a clinic setting may direct mTBI care.

Methods: 50 element neurological examination included a quantitative olfaction test (BSIT-12, Sensonics, Haddon Hts NJ).

PTSD severity assessed by PCL-M

Montreal Cognitive Assessment test (MOCA)

Study Groups: OIF – Iraq, OEF - Afghanistan

OIF/OEF mTBI + LOC Group (n=126)

OIF/OEF mTBI w/o LOC Group (n=52)

OIF/OEF injury w/o TBI (n=21)

Civilians with mTBI + LOC (n=21) without LOC (21)

Civilians without TBI (n=21)

Reduced Olfaction was the most sensitive test in a 50 element battery that could be performed in an examining room

Frequencies of abnormalities on neurological testing, PTSD and MOCA scores

Patient Group	Deficit on Examination*	Deficits other than olfaction*	PTSD*	MOCA Scores*
Combat mTBI & LOC (126)	65 (52%) All had ↓ smell	29 (23%)	83 (66%)	25.1 ± 0.18
Combat mTBI w/o LOC (52)	0 (0%)	0 (0%)	5 (9.6%)	28.8± 0.29
Combat w/o TBI (21)	0 (0%)	0 (0%)	2 (9.5%)	28.7 ± 0.31
Civilian mTBI & LOC (21)	2 (9.5%)	1 (4.8%)	1 (4.8%)	28.4 ± 0.23
Civilian mTBI w/o LOC (21)	0 (0%)	0 (0%)	0 (0%)	28.8 ± 0.24
Civilian w/o mTBI (21)	0 (0%)	0 (0%)	0 (0%)	28.9± 0.29

*Probabilities for comparisons to veterans who had mTBI + LOC in combat, all p<0.001

OIF/OEF mTBI + LOC Group (n=126)

mTBI + LOC - Neurological Deficits:

olfaction – 65

balance – 14

eye movements – 13

motor – 2

sensory – 2.

All 65 with NDs had impaired olfaction, 41 (63%) had only impaired olfaction.

80/126 veterans had abnormal Neuro Exam, MOCA test (≤ 27) testing

	MOCA Testing	
Neurological Testing	Abnormal	Normal
Abnormal	64	1
Normal	15	0

Neurological examination: olfaction – 65, balance – 14, eye movements – 13, motor – 2 and sensory – 2. Just 3 veterans (4%) had impaired olfaction as their only abnormality

Neuropsychological Testing

- **Minnesota Multiphasic Personality Inventory (MMPI-2)**
- **Wide Range Achievement Test 4th Ed (WRA-4)**
- **information & letter-number subtests Weschler Adult Intel Scale (WAIS-III)**
- **Stroop Color Name and Color Word tests**
- **Paced Auditory Serial Addition test**
- **Auditory Consonant Trigram test**
- **Trail Making test parts A and B**
- **Controlled Oral Word Association Test (F-A-S and animal naming)**
- **Language function - Boston Naming test**
- **Porteus Maze test**
- **Wisconsin Card Sort test**
- **Rey Complex Figure test**
- **Weschler Memory Scale (WMS-III)**
- **California Verbal Learning Test (CVLT-II)**
- **Test Of Memory Malingering**
- **Beck Depression & Anxiety Inventories**

80/126 veterans had abnormal Neuro Exam, Neuro Psych testing or both

Neuropsychological Testing

Neurological Testing	Abnormal	Normal
Abnormal	59	6
Normal	15	0

Abnormalities on parts of the neurological examination: olfaction – 65, balance – 14, eye movements – 13, motor – 2 and sensory – 2. Among the 65 veterans with abnormalities on neurological examination, 41 (63%) had only impaired olfaction. Just 3 veterans (4%) had impaired olfaction as their only abnormality

Headaches more frequent in Veterans with persisting deficits

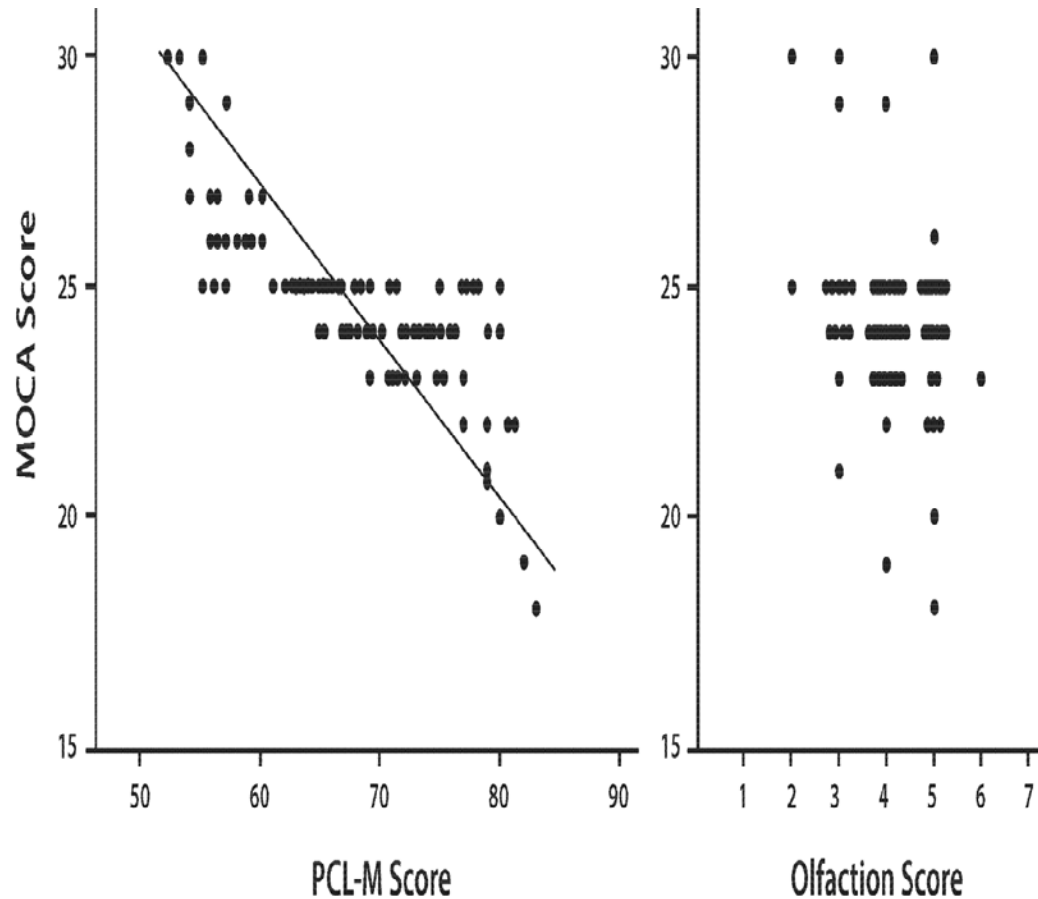
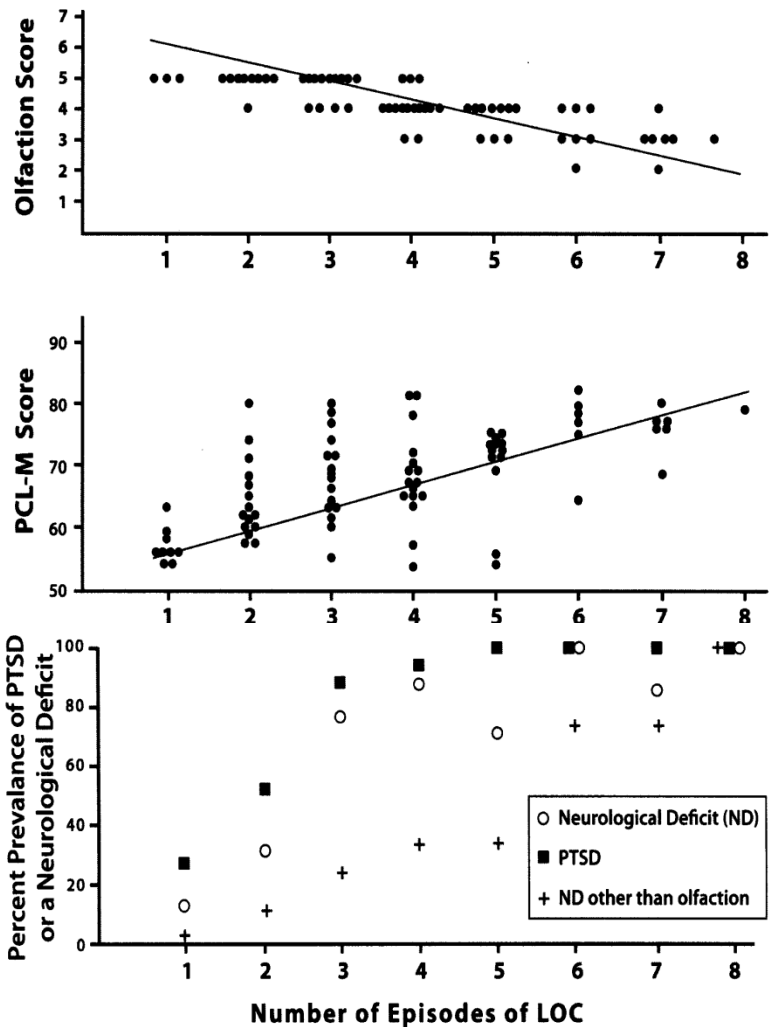
Headache Frequency Based Upon Neurocognitive Deficit	Tension	Migraine	Mixed
Neurocognitive Deficit (74/80) 93%	30 (41%)	14 (19%)	30 (41%)
Normal Neuro Exam & Neuropsychological Testing (6/46) 13%	6 (100%)	0 (0%)	0 (0%)
OR = 82.2 95% CI 24.9 – 272			

IHS criteria defines post-traumatic headaches as 2nd headaches. The separation into tension-like, migraine-like and mixed is based on IHS criteria for the primary headaches

Conclusions and Caveats

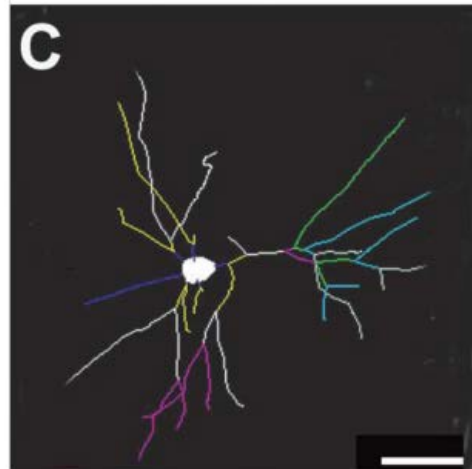
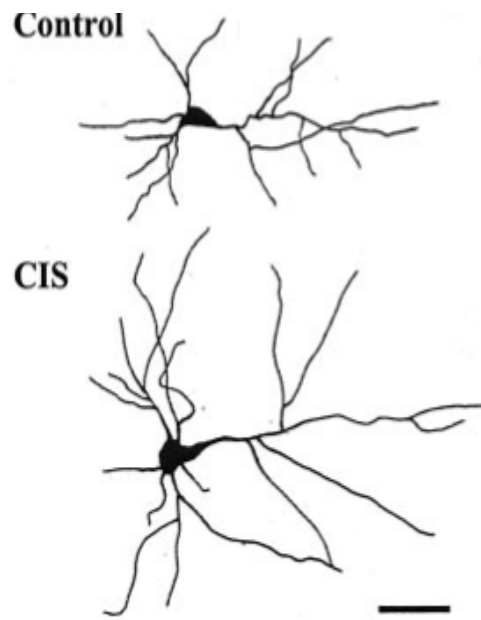
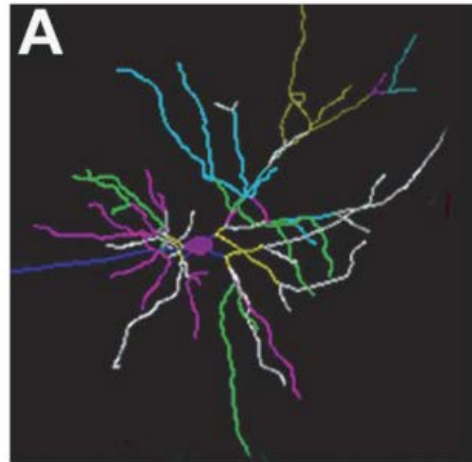
1. Olfaction is a Physical Examination Biomarker for prior mTBI
2. Study combat subjects were evaluated 2+ years after the initial TBI
3. The subjects were identified based on progressive screening – people who were not symptomatic were not identified
4. Veterans who sought care with VA were often having adjustment issues associated with PTSD – 86% divorce rate
5. Unclear how well Olfaction will work in other study populations.

Both Olfaction and PTSD Severity Correlated with # of episodes of LOC – But PTSD Severity had the Strongest Correlation with Cognitive Performance



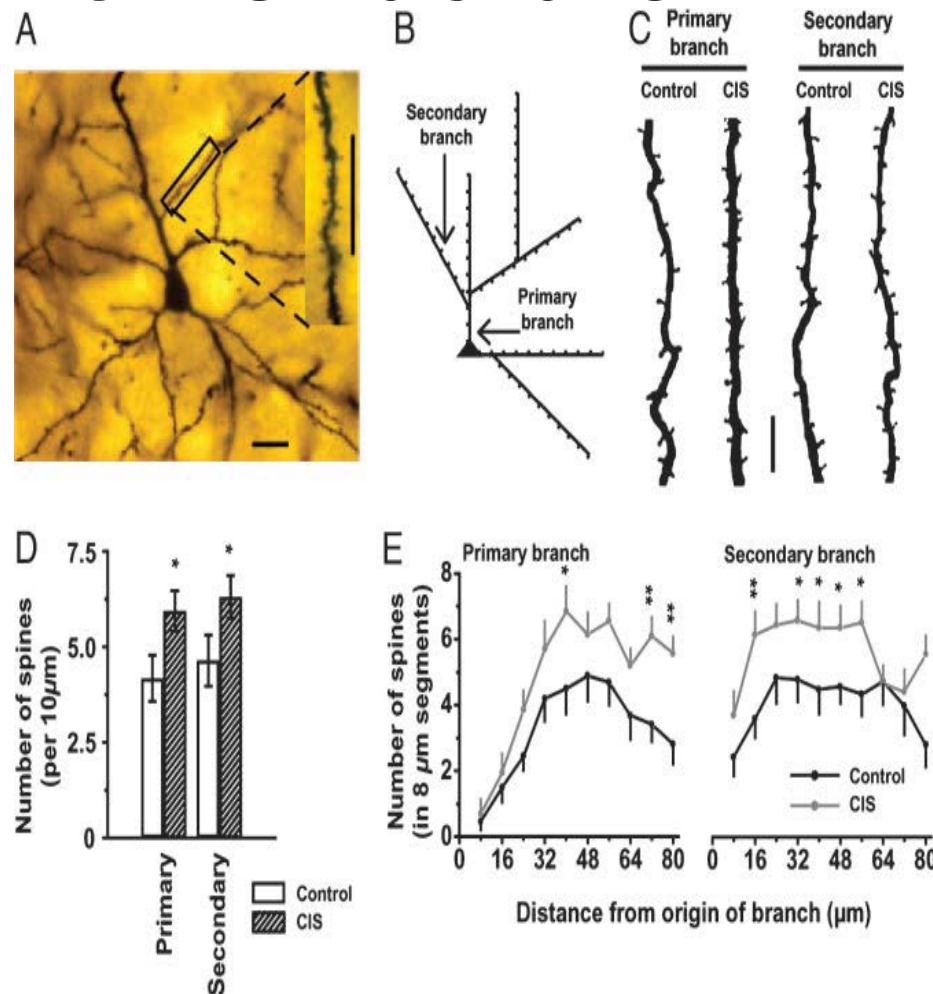
Note that the above figure shows data from subjects with PTSD or impaired olfaction (olfaction score <7)

Ψ Stress Alters VMpfc and Amygdala neuron structure

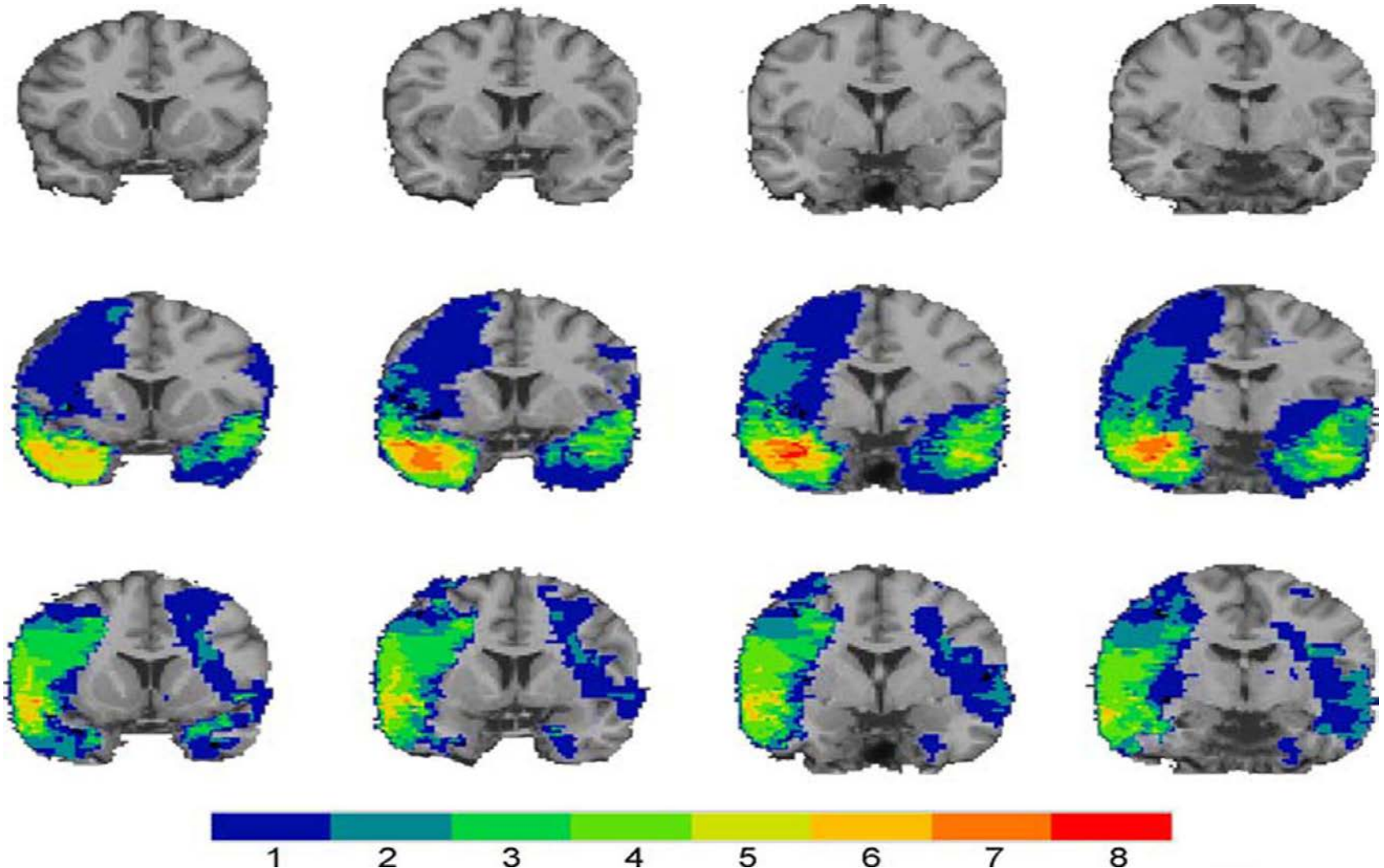


The Journal of Neuroscience, 2002, 22(15):6810–6818
 Chronic Stress Induces Contrasting Patterns of Dendritic Remodeling in Hippocampal and Amygdaloid Neurons
 A Vyas, R Mitra, S Rao, S Chattarji

J. J. Radley et al. / Neuroscience 125 (2004) 1–6 (pfc pyramidal cell)

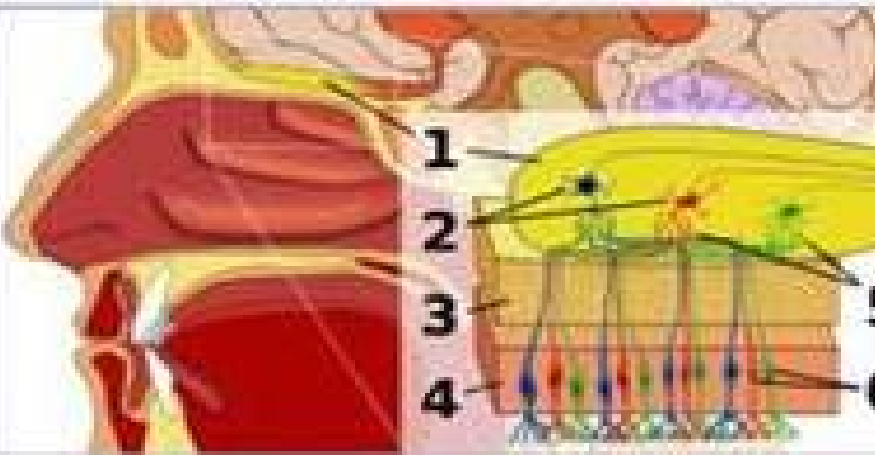
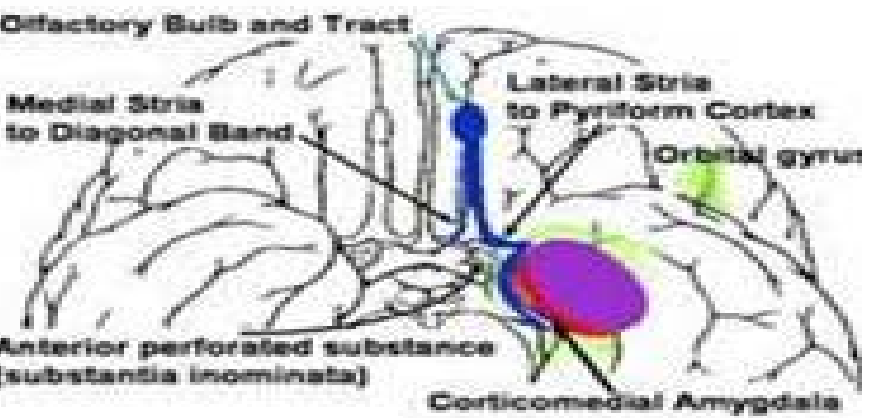


Damage to Amygdale ↓PTSD



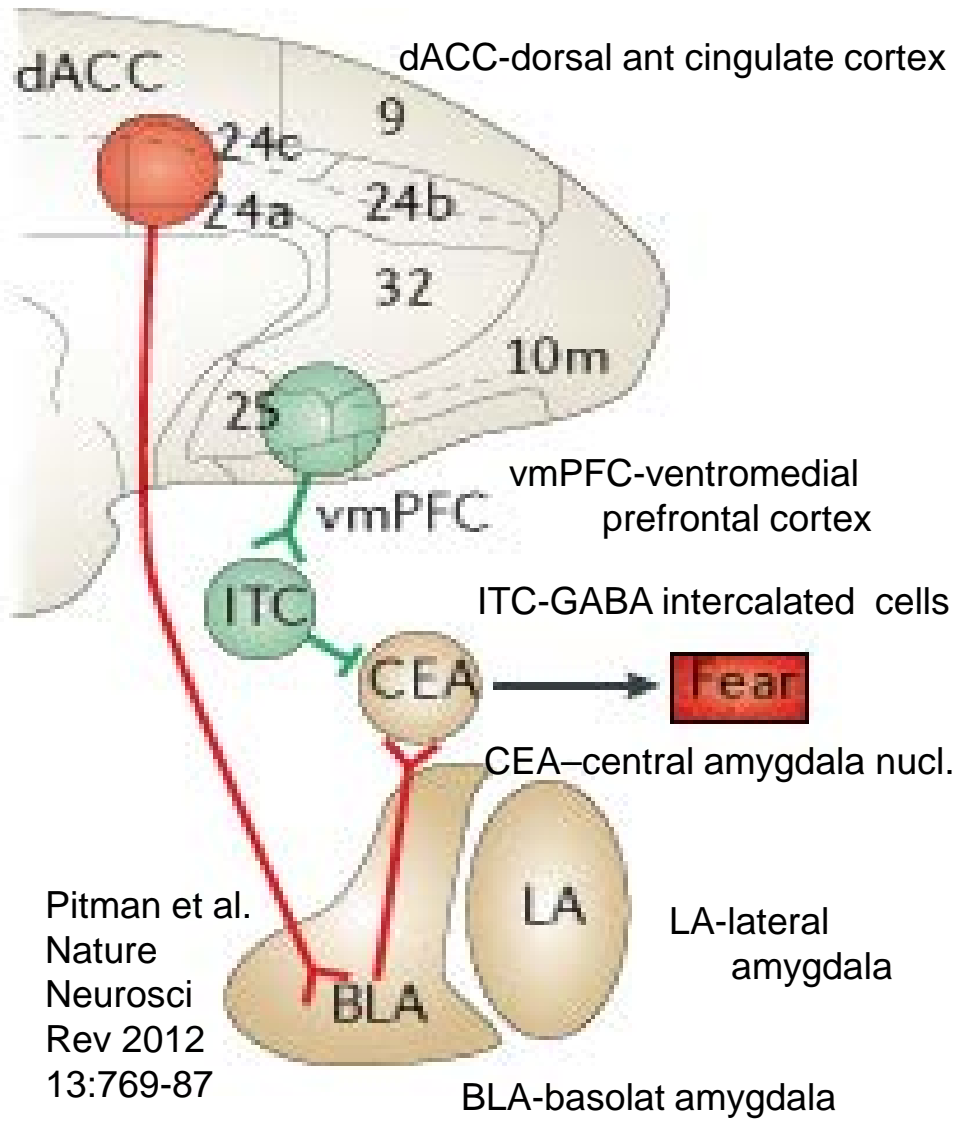
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Olfaction Processing is near ventromedial PreFrontal Cortex and may serve as a marker for vmPFC damage, which can predispose to PTSD developing after trauma by removing the modulating influence of vmPFC on the Amygdala



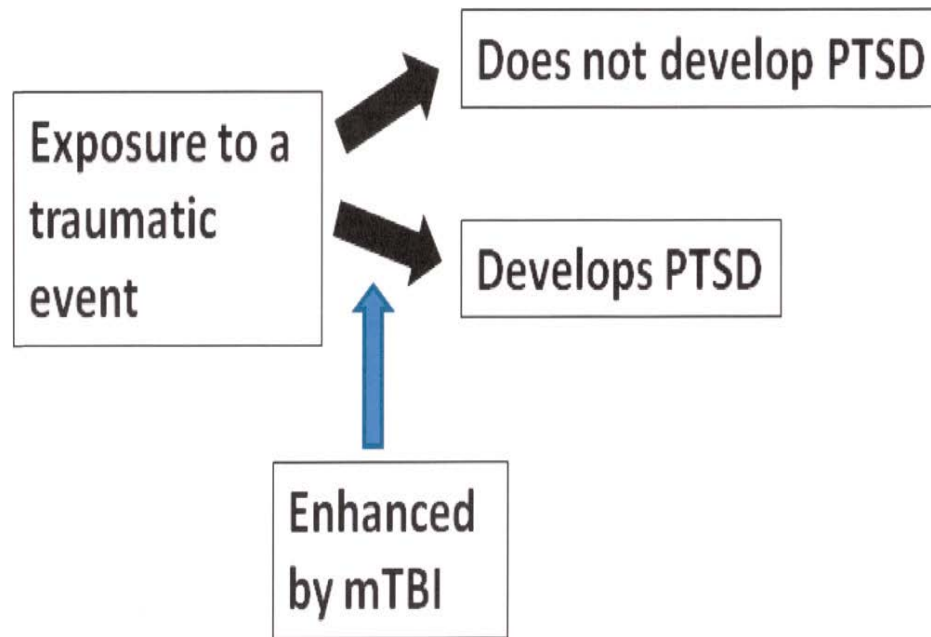
Human olfactory system. 1: Olfactory bulb 2: Mitral cells 3: Bone 4: Nasal epithelium 5: Glomerulus (olfactor) 6: Olfactory receptor cell

Note - the Combat Veterans were evaluated >1 year after TBI –impaired olfaction was likely due to olfactory bulb damage



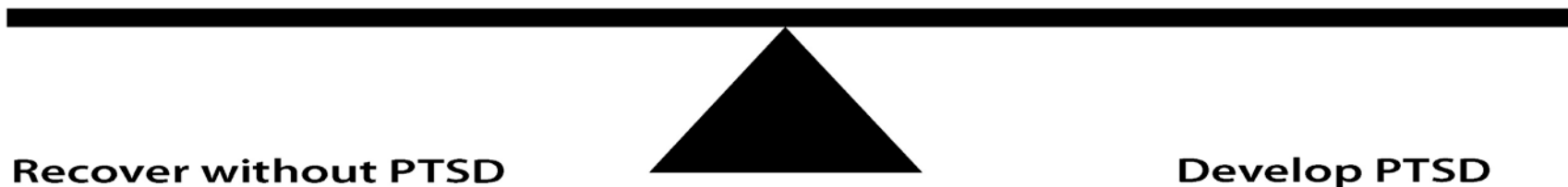
Pitman et al.
Nature
Neurosci
Rev 2012
13:769-87

Role of TBI in PTSD Genesis?



Amygdala destruction
Good Pain Control
Strong Support System
Psychological Resiliency

Soft Neurological Signs
mTBI
Psychological Trauma



Recover without PTSD

Develop PTSD

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Thank You

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