MRI In TBI And PTSD

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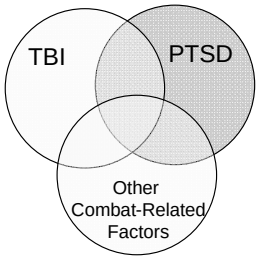
TBI - Problem Statement

- Most knowledge from hospitalized civilians
- TBI in returning veterans can be different
  - In many cases less severe
  - Much less documentation
  - Diagnosis relies on symptomatology
  - Symptoms overlap with PTSD
  - TBI and PTSD may co-exist
- Huge need for biomarkers of TBI and PTSD
- Our MRI studies are in progress!

Overall Goal For MRI

- Objective detection of TBI and PTSD
- Improve differential diagnosis
- Predict progression
- Assess efficacy of therapeutic interventions
- Monitor treatment
- Elucidate mechanisms

Veteran TBI – Specific Issues

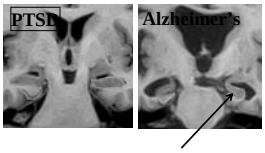


MRI In PTSD: The Hippocampus

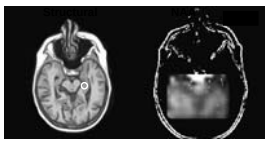
- **Plays an important role in**
  - **Memory (declarative, spatial, and contextual)**
  - **Perception of chronic pain**
- **Plasticity modulated by stress hormones (animal studies)**
  - **Suppressed neurogenesis in the dentate gyrus**
  - **Remodeling of dendrites in the CA3 region**
  - **Elevated excitability of hippocampal neurons**
- **Problems**
  - **Findings of hippocampal atrophy in PTSD have been inconsistent**
  - **Alterations are subtle**
  - **Normal aging and many brain disorders are also associated with alterations in the hippocampus**

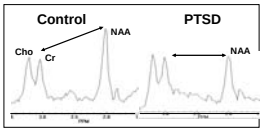
Hippocampus in PTSD

Structural MRI | **Proton MR Spectroscopy (1H MRS)**



Hippocampal Atrophy





→Atrophy in PTSD is subtle

→ Reduction of NAA, a marker of viable neurons, is substantial but highly variable

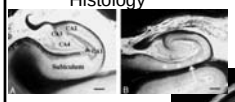
MRI Of Hippocampal Subfields

- **Refine hippocampal measurements by imaging its subfields**
- **Determine if PTSD impacts specific hippocampal subfields**

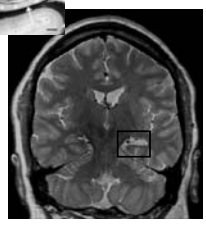
- **HYPOTHESES**
  - **The dentate gyrus is selectively reduced in PTSD**
  - **The pattern of reduced subfields in PTSD is different from that in aging and other brain disorders, e.g. Alzheimer's disease**

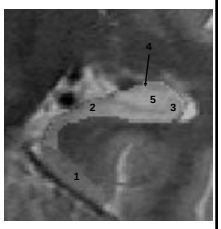
High-Field MRI of Subfields

Histology



4 Tesla MRI





Dentate

1: ERC; 2: Subiculum; 3: CA1; 4: CA1-CA2,
5: CA3 & Dentate gyrus

Subfield Volumes In PTSD

17 PTSD positive
19 PTSD negative

Differential Effects of Age And PTSD

PTSD ——
Control ·····

Total Hippocampal Volumes

Subfields In Other Conditions

By Susanne Mueller et al. Neuroimage. 2008;42(1):42-8

Table 1. Subfield and Total Hippocampal Volumes in mm3

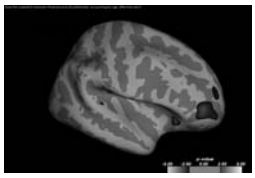
	Control N = 47	MCI N = 14	AD N = 14
ERC	202.4 ± 54.0	168.4 ± 48.0	145.0 ± 53.4*
Subiculum	200.2 ± 36.1	184.7 ± 38.1	154.2 ± 44.9*
CA1	331.4 ± 47.0	285.1 ± 42.5*	264.4 ± 63.1*
CA1-2 transition	20.5 ± 5.5	15.1 ± 3.4 *	14.1 ± 3.8*
CA3&DG	224.4 ± 37.7	227.2 ± 24.3	230.3 ± 54.7
Total Hippocampus	5520.6 ± 770.4	5154.9 ± 817.7	4450.8± 1285.2*

* p<0.05 compared to controls

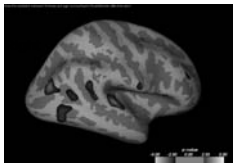
ERC, entorhinal cortex; CA1-2 transition, CA1-CA2 transition zone (definition see text); CA3&DG, CA3 and CA4 together with dentate gyrus

AD : Alzheimer's disease
MCI: Mild cognitive impairment, a transitional condition to AD

Subfields And Cortical Thickness in PTSD



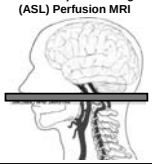
Correlation between a smaller CA1 and thicker orbitofrontal cortex

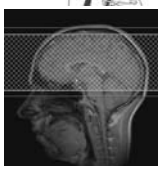


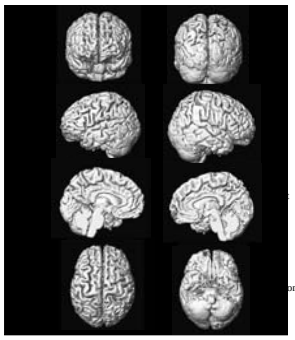
Effect of aging on cortical thickness

Cortical *Hyper*-Perfusion in PTSD

Arterial Spin Labeling (ASL) Perfusion MRI



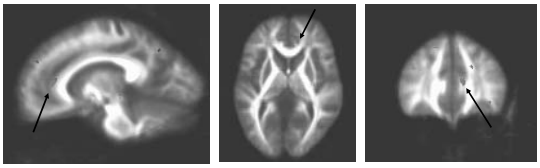




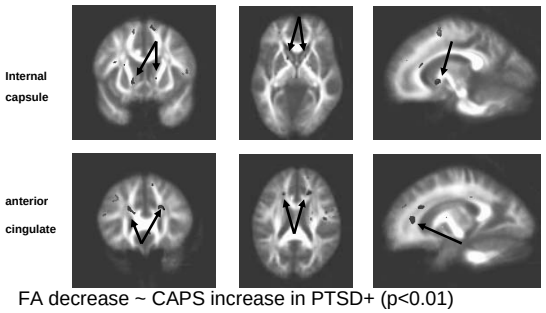
White Matter Disintegration in PTSD

Using Diffusion Tensor Imaging

Reduction of fractional anisotropy (FA) as a function of dentate/CA3 volume



WM Degradation and PTSD Severity



FA decrease ~ CAPS increase in PTSD+ ($p<0.01$)

Conclusions

- A volume reduction of dentate/CA3 in PTSD is consistent with suppressed neurogenesis under chronic stress
- Dentate/CA3 reductions are not seen in normal aging, MCI and AD and therefore might be specific for PTSD
- Correlations between dentate/CA3, thickness of cortical regions, and white matter degradation suggests that PTSD impacts brain networks

Impact

- MRI of dentate/CA3 could be a PTSD marker to help
  - improving PTSD diagnosis
  - differentiating between PTSD and disorders with similar syndromes
  - assessing efficacy of treatments, specifically those that target proliferation of neurogenesis
  - advancing the understanding of PTSD mechanisms

Challenges For MRI in TBI

- **Regional heterogeneity**
  - **Group analysis may lack sensitivity**
  - **Individual tests could be more effective**
  - **Establish robust single subject statistics**
  - **Multivariate MRI, using structural perfusion, diffusion and spectral imaging together could improve power**
- **Scale Variability**
  - **Large scale versus small scale dilemma in detecting alterations**
  - **Image analysis on a variable scale maybe a solution, i.e using entropy and complexity measures**

FA decrease ~ CAPS increase in PTSD+ ($p<0.01$)

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