PET in TBI and PTSD

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Disclosures

• None
Background

- According to Center for Disease control there are:
  - 1.7 million new cases of TBI reported yearly in the US among civilians.
  - 1.35 million Emergency room visits
  - 275,000 hospitalization
  - 40% long term disabilities
- Between 2000-2013 around 280000 service members have been diagnosed with a TBI
HEADS UP

Keeping children and teens healthy and safe is always a top priority. Whether you are a parent, youth sports coach, school coach, school professional, or health care provider, this site will help you recognize, respond to, and minimize the risk of concussion or other serious brain injury.

A Fact Sheet for High School Sports Officials

Officials, learn how you can help keep athletes safe

I need to know...
- How to get concussion training
- How to get the HEADS UP app
- What a concussion is
- How to return to activities
- Signs and symptoms of a concussion
- Concussion danger signs
- Brain injury safety tips and prevention

I am a...
- Youth Sports League
# CONCUSSION

**A Must Read for NFL Players**

Let’s Take Brain Injuries Out of Play

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## Concussion Facts

- Concussion is a brain injury that alters the way your brain functions.
- Concussion can occur from a blow to the head/neck, contact with another player, or contact with the ground, object or another player.
- Most concussions occur without being knocked unconscious.
- Severity of injury depends on many factors and is not known until symptoms resolve and brain function is back to normal.
- All concussions are not created equally. Each player is different, each injury is different and all injuries should be evaluated by your team medical staff.

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## Concussion Symptoms

Different symptoms can occur and may not show up for several hours. Common symptoms include:

- Confusion
- Headache
- Amnesia / Difficulty remembering
- Balance problems
- Irritability
- Dizziness
- Difficulty concentrating
- Sleep disturbances
- Nausea

Symptoms may worsen with physical or mental exertion (e.g., lifting, computer use, reading).

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## Why Should I Report My Symptoms?

- Practicing or playing while still experiencing symptoms can prolong the time to recover and return to play.
- Unlike other injuries, there may be significant consequences of “playing through” a concussion. Repetitive brain injury, when not treated promptly and properly, may cause permanent damage to your brain.

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## What Should I Do If I Think I’ve Had a Concussion?

**Report it.** Never ignore symptoms even if they appear mild. Look out for your teammates. Tell your Athletic Trainer or Team Physician if you think you or a teammate may have had a concussion.

**Get Checked Out.** Your team medical staff has your health and well being as its first priority. They will manage your concussive injuries according to NFL / NFLPA Guidelines which include being fully asymptomatic, both at rest and after exertion, having normal neurologic examination, normal neuropsychological testing, and clearance to play by both the team medical staff and the independent neurologic consultant.

**Take Care of Your Brain.** According to the CDC, “Traumatic brain injury can cause a wide range of short- or long term changes affecting thinking, sensation, language, or emotions.” These changes may lead to problems with memory and communication, personality changes, as well as depression and the early onset of dementia. Concussions and conditions resulting from repeated brain injury can change your life and your family’s life forever.

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**Work smart. Use your head, don’t lead with it. Help make our game safer. Other athletes are watching...**

*For more information about traumatic brain injury and concussion, go to http://www.cdc.gov/concussion*
Movies about TBI and PTSD

- The Hurt Locker (2008)
- Head Games (2012)
- The Crash Reel (2013)
- Concussion (2015)
Challenges in evaluating TBI

• Complex causes of injury
  • Direct trauma to the cortex
  • Acceleration, Deceleration and rotational injuries due to sudden skull movements causes axonal injury
  • Damage due to hematomas and associated hypo-perfusion
  • Blast exposure damages

• Comorbidities
• Acute vs. chronic effects
• Genetic factors
Challenges in evaluation of military TBI and PTSD

• Comorbidities
• Substance abuse
• Accurate history
PET imaging overview

• Patient’s preparation
  • Rest vs. task based

• Image acquisition
  • 2D or 3D
  • Static vs. Dynamic

• Image Analysis
  • Qualitative
  • Quantitative
    • ROI vs. Voxel Based
ROI Based analysis

• Widely used
• Easier to implement and use
• Several commercial and non-commercial products are available
• High inter- and intra-observer variability
Voxel Based analysis

- Each voxel is an ROI
- Regarded as gold standard
- Harder to implement
PET versus SPECT: strengths, limitations and challenges

Arman Rahmima and Habib Zaidib

• Sensitivity: PET has 2 to 3 times higher sensitivity than SPECT. SPECT allows longer acquisition time due to longer half-life.

• Coincidence detection in PET improves image quality, shorter scans, and improved temporal resolution.

• Spatial resolution in PET is generally better, but limited by photon non-collinearity and positron range.

• Dynamic imaging is more superior in PET.
Is there a preference for PET or SPECT brain imaging in diagnosing dementia? The views of people with dementia, carers, and healthy controls

Claire Bamford, Kirsty Olsen, Chris Davison, Nicky Barnett, Jim Lloyd, David Williams, Michael Firbank, Helen Mason, Cam Donaldson and John O’Brien

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* p < .05  *** p < .001

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doi:10.1177/1041610215001039
Radiotracer Used in Evaluation of TBI

• Metabolism
• Amyloid
• Inflammation
• Dopaminergic pathways
• Taupathy
FDG PET in TBI

Discordance Between FDG Uptake and Technetium-99m-HMPAO Brain Perfusion in Acute Traumatic Brain Injury

Nuclear Medicine Section, Departments of Radiology and Neurology, St. Vincent’s Hospital and Medical Center of New York, New York Medical College at Valhalla, New York

- 28 yo female h/o MVA 2 days prior to PET imaging
- Resting FDG PET normal uptake
- Tc99m HMPAO SPECT on day 3 demonstrates hypoperfusion to bilateral frontal lobes

• 21 TBI patients with cerebral contusion in acute phase (3.1 days)
• Reduced whole brain hexokinase activity including uninjured cortex
• Impaired glucose transport in the area immediately around the contusion
• A subgroup of 7 patients showed increased FDG uptake in the peri-contusional areas likely due to regionally increased hexokinase activity.
• 12 Veterans with pure blast induced and 12 with blunt brain trauma.
• Both group had lower scores in neuropsychological assessments and standard Health Survey.
• The Blast-induced TBI group demonstrated greater deficit in attentional control and regional brain metabolism in FDG PET in the right superior parietal region.
33 blast-exposed Veterans with average 21.2 TBIs (lifetime)
A statistically significant negative correlation between number of Blast-related mild TBIs and cerebellar metabolism
Additional readings

FDG-PET imaging in mild traumatic brain injury: a critical review
Kimberly R. Bynes¹,², Colin M. Wilson³,⁴, Fiona Brabazon⁵, Ramona von Leden⁶, Jennifer S. Jurgens⁵,⁶, Terrence R. Oakes⁷ and Reed G. Selwyn¹,⁴*

Neuroimaging assessment of early and late neurobiological sequelae of traumatic brain injury: implications for CTE
Mark Sundman¹, P. Murali Doraiswamy²,³ and Rajendra A. Morey**
Clinical Cases

• Case 1:
  • 27 year old with history of blast exposure
    5 years prior to FDG PET/CT
  • Number of TBIs: one
  • No loss of consciousness
Case2

- 24 year old male with history of blast exposure
- 5+ TBI with LOC
- Baseline FDG PET/CT one year after the last TBI
- Follow up FDG PET/CT 4 years after the first scan
Trigeminal nerve stimulation for the treatment of mild traumatic brain injury
Langevin JP¹, Gaines D², Choi E², Krahl SE³, Berenji G²

Reported anxiety and depression before and after TNS

Anxiety improved for both subjects. Subject 2 also had an improvement in depression symptoms. Both subjects reported substantial improvement in post-traumatic headaches.

Self-assessment of cognitive functioning

Both subjects reported cognitive improvements on the PAOF. Subject 2 reported substantial improvements in the memory and language dimensions.

Baseline and post-treatment resting ¹⁸FDG PET

Both subjects showed an increase in metabolism after 8 weeks of daily TNS treatment in the following regions: the dorsolateral prefrontal cortex (DLPFC), the medial frontal gyrus (MFG), the orbitofrontal cortex (OFC) and the medial prefrontal cortex (mPFC).
Beyond FDG
• 11C PIB PET in 15 TBI patients 1 to 361 days after a TBI and 11 control subjects
• Autoradiography and Immunocytochemistry for Beta-amyloid in brain tissue in 16 patients, died 3 hours to 56 days after a TBI and 7 controls
• TBI group demonstrate increased Beta-amyloid in cortical gray matter and the striatum

2014 Jan;71(1):23-31
• 28 participants (9TBI, 9 control, 10 Alzheimer’s Disease
• 11 months to 17 years post moderate to severe TBI
• C11 PIB (Pittsburgh Compound B) was found in TBI in the posterior Cingulate and cerebellum.
• In TBI the distribution of Amyloid overlaps, but different from AD
• The difference suggests a mechanistic link between TBI and the development of neuropathologic features of dementia

2016 Mar 1;86(9):821-8
Detection of brain amyloid β deposition in patients with neuropsychological impairment after traumatic brain injury: PET evaluation using Pittsburgh Compound-B

Nobuyuki Kawai, Masahiko Kawanishi, Nobuyuki Kudomi, Yukito Maeda, Yuka Yamamoto, Yoshihiro Nishiyama & Takashi Tamiya

- 12 Chronic TBI patients with neuropsychological impairment
- 11C PIB PET 5 to 12 months after TBI
- Only 3 positive PETs
- No Correlation between 11C-PIB deposits and severity of symptoms
- Concluded the finding does not support Beta-amyloid deposits progress over time after TBI

2013;27(9):1026-31
• Serial imaging of severe TBI after 1, 12 and 24 months
• 18F-Florbetapir PET compared to normal control
• In both cases there was an initial increase in florbetapir uptake in some areas of the brain including caudate, hippocampus and precuneus, which decreased over time
• The authors concluded 18F-Florbetapir PET may be useful in monitoring Amyloid dynamics after severe TBI and may be predictive of cognitive deficits.
9 subjects: 4 control, 3 with history of TBI and 2 with mild cognitive impairment

In one TBI subject increased uptake of $^{18}$F-T807/$^{18}$F-AV-1451 was seen in posterior corpus callosum

In MCI subjects increased uptake is noted in occipital, parietal, temporal cortices and posterior cingulate gyrus, precuneus, and mesial temporal cortex

2017 Mar;58(3):484-491
• 39 year old retired football player with 22 concussions
• Subject had progressive neuropsychiatric symptoms
• $^{18}$F-T807/AV1451 PET showed retention in gray-white matter junction. SUV analysis showed increased uptake in bilateral cingulate, occipital and orbitofrontal cortices
• $^{18}$F florbetapir was negative
• Authors concluded tauopathy imaging may be promising tool to detect and diagnose Chronic Traumatic Encephalopathy (CTE)
9 former NFL players and 9 age matched control
11C-DPA-713 PET tracer, which binds to the translocator protein (TSPO)
Increased uptake in supramarginal gyrus and right amygdala with varied performance of memory and verbal learning
Concluded there may be a relationship between TSPO (a marker of brain injury and repair) expression and cognitive decline
Dopaminergic function in patients with posttraumatic parkinsonism:

An $^{18}$F-dopa PET study

N. Turjanski, MD; A.J. Lees, MD, FRCP; and D.J. Brooks, MD, FRCP

- 6 patients with Posttraumatic parkinsonism (PTP), 32 age matched normal control and 18 patients with idiopathic Parkinson's Disease (PD)
- $^{18}$F-dopa PET imaging revealed 40% reduction of uptake in caudate and putamen of PTP patients compared to control
- Study concluded $^{18}$F-dopa may help to differentiate PTP from idiopathic PD

1997 Jul;49(1):183-9
FDG PET was performed in PTSD subjects:

- 19 Danger-based traumas
- 26 Non-danger based traumas
- 26 combat control
- 24 civilian controls

In Danger-based group higher metabolism in the right amygdala compared to the control, while non-danger had higher metabolism in precuneus compared to the danger-based group.

Relation between PTSD symptoms severity and regional metabolism was also different in danger-based and non-danger-based groups.

The study suggests a biological basis to consider subtyping PTSD according to the nature of the traumatic context.

2016 Feb;11(2):234-42
Conclusion

• PET is a great research tool for evaluation of individual with TBI or PTSD. However additional large scale studies are needed to evaluate its clinical applications.

• PET is a useful for evaluating individual cases and can be helpful in longitudinal studies as well as treatment response evaluation.

• FDG is the most widely used tracer in evaluation of patients with TBI and PTSD; however new tracers have great potential to impact clinical application of PET.
• Which statement is true regarding PET for evaluation of TBI and PTSD:

1. PET is widely used in clinical evaluation of TBI and PTSD.

2. FDG is the only PET tracer used in evaluation of TBI and PTSD.

3. PET has been used in research related to TBI and PTSD and can be helpful in longitudinal studies and treatment response.
References
