PET and DTI imaging of brain injury

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Scope of TBI

• More than 1.7 million in US have TBI annually with 75 to 85% having mild
  – CDC 2010
• May be underestimate since many do not see doctor
• Signature war wound from Aghanistan and Iraq
Conventional imaging studies insensitive

- Often normal on CT scans, typical MRI sequencing
- Look for macroscopic changes in brain
PET scans and DTI scans

• PET = positron emission tomography
  – Shows regional brain function
    • E.g. frontal lobe activity
• DTI = diffusion tensor imaging
  – Shows white matter tract integrity
    • E.g. corpus callosum
DTI

Diffusion Tensor Imaging
DTI is much more sensitive than conventional MRI
Diffusion tensor imaging

• Water diffusion normally is random and the same in all directions,

• In white matter fiber tracts, water diffusion is hindered perpendicular to the tract and higher in direction parallel to fiber

• More sensitive at detecting signs of traumatic brain injury than older MRI sequences, looks for microstructural changes
Diffusion tensor imaging superior at detecting signs of DAI

- DAI, diffuse axonal injury
- After mild traumatic brain injury, DAI results in impairment of axoplasmic transport and damage to axon
Diffuse axonal injury can cause shortening
DTI and FA maps
DTI

- FA map
  - Red = left to right
  - Blue = top to bottom
  - Green = front to back
DTI = Diffusion tensor imaging

• Can assess integrity of white matter
• FA = fractional anisotropy
  – Value between 0 to 1
  – Higher values indicate more white matter tracts integrity
• Tractography
  – Determining the path of the white matter tracts
DTI in TBI has been studied extensively

• Over 80 articles published on DTI abnormalities noted in traumatic brain injury subject in peer reviewed journals
• First article in mTBI published in 2002 by Arfanakis and colleague in 5 pts vs. 10 controls
Mild traumatic brain injury and DTI


• 46 pts with mild TBI vs. 29 Healthy volunteers
  – 20 of the 46 were studied 4.05 days after injury
  – 26 were studied 5.7 years after injury

• Significant reduction in corpus callosum, internal capsule and centrum semi-ovale seen in post acute and chronic mild TBI patients vs. normal controls
Tractography differs between normal controls and TBI
Traumatic brain injury, Case 1

- Mid 40 male
- Struck by vehicle
- Complaint of word finding problems, headaches, blurred vision, cognitive difficulties
- Can’t remember to do things he used to do
- Neuropsych difficulties
  - Slower cognitive processing
  - Impaired memory
DTI Z maps high sensitivity and high specificity

- 28 controls compared to 18 TBI patients
- FA were calculated for each subject
- FA Z maps were calculated for each subject (control and TBI) vs. the 28 controls
- The Z-maps were evaluated blindly and categorized into control or TBI
- The blind categorization was then checked for accuracy and rates of tp, tn, fp, fn were calculated
- 95% sensitivity (tp/(tp+fp)) was found
- 98% specificity (tn/(tn+fn)) was found
- (Lee, Keumsil; Tsai, Varin, Potkin, S,; Wu, J)
- Supported by FBIRN and NIH
Negative z-map showing significant difference between normals and controls in corpus callosum
TBI lower than normal controls in other tracts

- Cingulum
- Internal capsule
- Superior longitudinal fasiculus
POSITRON = Positive Electron

- Most electrons are negative
- Positive electron = form of antimatter
- When positrons combine with electrons, you get matter-antimatter conversion to release tremendous energy
  
  \[ E = mc^2 \]

- Similar to Star Trek’s USS Enterprise starship engine
Normal CT, MRI; decreased frontal activity in brain trauma

• Ruff et al. 1994 (Brain Injury 8:297-308)
• N=9
• Corroboration found between positive neuropsychological findings and PET
• Findings primarily in frontal and anteriotemporal regions
• No differences with reported loss of consciousness vs. those without
Normal MRI, CT scan; Abnormal PET in brain injury

• Peer reviewed scientific article
• Mattioli et al., 1996, Cortex 32:121-129
• PET scan showed evidence of brain injury
• Patient showed abnormal neuropsych evaluation
• Patient had normal CT and MRI scan
• PET scan more sensitive than MRI or CT
Cyclotron

- 22 ton instrument
- Accelerates subatomic particles to near speed of light velocity
- Bombard target to create positron emitter (fluorine-18)
Radiochemist attaches to sugar

- Fluorine-18 is attached to sugar-like compound (deoxy-glucose) FDG
- Hot cell is used for synthesis
Intravenous line

• Small plastic tube used to introduce tracer
Positron Annihilation

Detector

Photon

511 keV

Photon

Detector

Positron Range

Positron Emission

180°
PET SCANS generally accepted

• PET scans used for over thirty years
• 1000’s of articles using PET scans to assess brain function
• Generally accepted for study of brain function by scientific community
Clinical Uses of PET scanning

- Traumatic brain injury evaluation
- Hypoxic brain injury
  - E.g. carbon monoxide poisoning or hypovolemic shock
- Toxic brain encephalopathy
- Electrical shock injury
- Parkinson’s disease
- Epilepsy lesion location in presurgical evaluation
- Cerebrovascular disease (Stroke) and assessment of recovery
- Differential diagnosis of Alzheimer’s disease and other memory disorders
- Neuropsychiatric assessment (e.g. schizophrenia)
- Differential diagnosis of brain tumor and radiation treatment
Mild TBI

- Associated with “chronic postconcussive condition”
- Complaints include: headache, dizziness, poor concentration, poor memory, fatigue, irritability
- May be debilitating
- Often no abnormality on MRI or CAT scan
Clinically significant asymmetry in brain metabolism

- Analogous to asymmetry in face
- Signifies neural abnormality
TBI IMAGING

- PET scans are more sensitive at detecting injuries than CAT or MRI scans
- Well documented with over 45 articles on functional brain imaging being useful in assessment of TBI
Functional brain study done for injury incurred years earlier

- Ruff et al. 1994 (Brain Injury, 8: 297-308) average time lapsed between minor traumatic brain injury and PET clinical evaluation = 29.2 months

- Gross et al. 1996, (Journal Neuropsychiatry and Clinical Neurosciences, 8:324-334) studied 20 patients mild traumatic brain injury with mean time lapsed between injury and PET scan of 3.5 years
No-contact mild brain injury

• Roberts 1995 (Brain Injury 9:427-436) reported that a no-contact injury (whiplash-type injury) had abnormal PET scan findings when done 4 years post injury
TBI IMAGING

- PET scans often show frontal or temporal decrease
- PET scans often show occipital increase (may be apparent compensatory change)
- Can be correlated with neuropsychological testing deficits
- Written about in major textbook for psychiatry as accepted medical imaging tool to assess brain injury (Wu et al. 2000)
Use of PET scan to evaluate mild traumatic brain injury taught in other major textbooks
Patient with traumatic brain injury

- Mid 30 year old male in rollover accident
- Has normal MRI
- Has abnormally decreased orbitofrontal and hippocampal metabolism
- Has abnormal WSCT < 5%ile in conceptual level
- Had < 5% percentile in verbal fluency
- Abnormal frontal neuropsych scores
- Mildly impaired visual memory impairment on complex figure drawing test
- Mildly impaired on Rey Auditory verbal learning test
PET report

• Will indicate if scan is consistent with referring diagnosis
• PET scan by itself is not diagnostic
• Corroborative tool
Clinical correlation report

- Not necessary if PET scan report is normal
- Other sources of PET abnormalities include:
  - Stroke
  - Dementia
  - Epilepsy
  - Schizophrenia
  - Cancer
- Review of other clinical records can be used to narrow differential diagnostic issues for abnormal PET scan
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PET scan and neuropsychological testing

• PET scan discussed in textbook for neuropsychologist as accepted tool for assessment of brain function

• In textbook “Clinical syndromes in adult neuropsychology: The practitioner’ handbook” (Editor, R.F. White, 1992)

• In chapter “Neuropsychological evaluation of traumatic brain injury (Morse and Montgomery)
Cross modality validation of functional brain imaging with neuropsychological findings

• Ruff 1994 revealed “corroboration between the positive neuropsychological findings confirmed on the PET”

• Gross 1996 found “abnormal local cerebral metabolic rates were significantly correlated statistically with overall neuropsychological test results”
Traumatic case RC

- Car struck by debris
- Neuropsych testing deficits
  - Impairment in memory
  - Impairment in information processing (digit symbol)
- Changes in emotional function
  - Much more irritable
Patient RC DTI vs. normal

Corpus callosum  patient

Corpus callosum
Significant decrease in z score in FA in corpus callosum on patient RC
Decrease in FA in midsagittal corpus callosum
PET scan of patient RC TBI shows qualitative decrease in parietal cortex relative to frontal cortex

Patient RC

Normal control
Statistical comparison

Patient RC

Statistical Z-map
Statistical z-map for PET

- PET FDG z maps have 5% false positive error rate for statistical z map
- PET FDG z-maps have over 90% sensitivity in detecting abnormalities in patients with TBI
Patient IL

• Motor vehicle accident
• Clinical symptoms
  – Fogginess, impaired attention
• Neuropsych deficits
  – Slowed processing speed
Patient IL  DTI significant decrease in FA
Decreased fiber track length in corpus callosum

Patient IL

Normal
PET scan negative z score map

Patient IL
Sig negative decrease in PET
Conclusion

• PET and DTI are clinically useful and complementary imaging methods which are sensitive for mild traumatic brain injury with persistent cognitive and emotional deficits in chronic time