Chronic Traumatic Encephalopathy (CTE)

Kevin M. Barrett, MD, FAAN
Associate Professor & Vice-Chair of Neurology
Mayo Clinic Florida
Disclosure

Relevant Financial Relationship(s)
NONE

Off Label Usage
NONE
Objectives

• Understand diagnostic criteria for CTE
• Evaluate patient with suspected CTE
• Recognize limitations in current understanding of CTE risk factors and susceptibility
Vignette

• Former rugby player committed suicide by fire arm at age 46
• Began playing at age 16, continued for more than 20 years
• Never diagnosed with concussion and never missed a game because of a head injury
• Teammates reported that he was “confused” on the field many times because of a head injury but kept playing
Vignette (cont)

• in his early 30s:
  • Personality changes - overreacted and became stressed out and anxious about minor things that previously did not bother him
  • Would forget to pick up his daughter from school
  • Word-finding difficulties and became less communicative with family
  • Stopped paying the family’s bills
  • Periods of depression became increasingly longer
  • Developed a “short fuse”, paranoia about his wife’s fidelity
  • Threatened his wife with a baseball bat
  • Frequent and severe headaches 6 months before he died
  • Excessive alcohol use 2 years before his death
Vignette (cont)

• In the months before he died, he told his best friend he want to learn how to shoot a gun

• Previously expressed he was against suicide throughout his life and had never expressed suicidal ideation…
Chronic Traumatic Encephalopathy (CTE)

• Progressive syndrome in retired boxers
  • *Punch drunk syndrome*, first described in 1928
  • *Dementia pugilistica*, described in 1973

• CTE
  • Pathologically defined neurodegenerative disorder *associated* with repetitive concussive or subconcussive head injury
CTE

• 2002 – neuropathologically confirmed case of CTE in former professional football player renewed interest

• Has now been observed in
  • Athletes who suffered concussions
    • Boxing, wrestling, football, hockey
  • Military personnel who have experienced direct impact or primary/secondary blast injuries
Required for Diagnosis of Chronic Traumatic Encephalopathy

◆ The pathognomonic lesion consists of phosphorylated tau (p-tau) aggregates in neurons, astrocytes, and cell processes around small vessels in an irregular pattern at the depths of the cortical sulci

Supportive Neuropathologic Features of Chronic Traumatic Encephalopathy

◆ P-tau–related pathologies

◊ Abnormal p-tau immunoreactive pretangles and neurofibrillary tangles preferentially affecting superficial layers (layers II–III), in contrast to layers III and V as in Alzheimer disease

◊ In the hippocampus, pretangles, neurofibrillary tangles, or extracellular tangles preferentially affecting CA2 and pretangles and prominent proximal dendritic swellings in CA4. These regional p-tau pathologies differ from the preferential involvement of CA1 and subiculum found in Alzheimer disease

◊ Abnormal p-tau immunoreactive neuronal and astrocytic aggregates in subcortical nuclei, including the mamillary bodies and other hypothalamic nuclei, amygdala, nucleus accumbens, thalamus, midbrain tegmentum, and isodendritic core (nucleus basalis of Meynert, raphe nuclei, substantia nigra, and locus coeruleus)

◊ P-tau immunoreactive thorny astrocytes at the glial limitans most commonly found in the subpial and periventricular regions

◊ P-tau immunoreactive large grainlike and dotlike structures (in addition to some threadlike neurites)

◆ Non–p-tau–related pathologies

◊ Macroscopic features: disproportionate dilatation of the third ventricle, septal abnormalities, mamillary body atrophy, and contusions or other signs of previous traumatic injury

◊ Transactive response DNA-binding protein 43 (TDP-43) immunoreactive neuronal cytoplasmic inclusions and dotlike structures in the hippocampus, anteromedial temporal cortex, and amygdala

Age-related P-tau Astrogliopathy That May Be Present; Nondiagnostic and Nonsupportive

◆ Patches of thorn-shaped astrocytes in subcortical white matter

◆ Subependymal, periventricular, and perivascular thorn-shaped astrocytes in the mediobasal regions

◆ Thorn-shaped astrocytes in amygdala or hippocampus

<table>
<thead>
<tr>
<th>Stage</th>
<th>Pathology</th>
<th>Clinical Signs and Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Perivascular phosphorylated tau neurofibrillary tangles in focal epicenters at the depths of sulci in frontal cortex</td>
<td>Headache and loss of attention and concentration</td>
</tr>
<tr>
<td>II</td>
<td>Stage I plus neurofibrillary tangles in superficial cortical layers adjacent to the focal epicenters, the nucleus basalis of Meynert, and locus coeruleus</td>
<td>Depression and mood swings, explosivity, loss of attention and concentration, headache, and short-term memory loss</td>
</tr>
<tr>
<td>III</td>
<td>Stage II plus mild cerebral atrophy; septal abnormalities; ventricular dilation, concave third ventricle, depigmentation of locus coeruleus and substantia nigra; dense p-tau pathology in the cortex, medial temporal lobe, diencephalon, brainstem, and spinal cord</td>
<td>Cognitive impairment with memory loss, executive dysfunction, loss of attention and concentration, depression, explosivity, and visuospatial abnormalities</td>
</tr>
<tr>
<td>IV</td>
<td>Stage III plus further cerebral, medial temporal lobe, hypothalamic, thalamic, and mammillary body atrophy; septal abnormalities; ventricular dilation; pallor of substantia nigra and locus coeruleus; p-tau in widespread regions, including white matter, with prominent neuronal loss, gliosis of cortex, and hippocampal sclerosis</td>
<td>Dementia with profound short-term memory loss, executive dysfunction, attention and concentration loss, explosivity, and aggression; most also show paranoia, depression and impulsivity, and visuospatial abnormalities; many also have parkinsonism, speech, and gait abnormalities</td>
</tr>
</tbody>
</table>

Reprinted with permission from Budson AE, Solomon PR,\(^{18}\) using data from McKee AC, et al, Brain.\(^{13}\) © 2016 Elsevier, Inc.
<table>
<thead>
<tr>
<th>Stage</th>
<th>Pathology</th>
<th>Clinical Signs and Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Perivascular phosphorylated tau neurofibrillary tangles in focal epicenters at the depths of sulci in frontal cortex</td>
<td>Headache and loss of attention and concentration</td>
</tr>
<tr>
<td>II</td>
<td>Stage I plus neurofibrillary tangles in superficial cortical layers adjacent to the focal epicenters, the nucleus basalis of Meynert, and locus coeruleus</td>
<td>Depression and mood swings, explosivity, loss of attention and concentration, headache, and short-term memory loss</td>
</tr>
<tr>
<td>III</td>
<td>Stage II plus mild cerebral atrophy; septal abnormalities; ventricular dilation, concave third ventricle, depigmentation of locus coeruleus and substantia nigra; dense p-tau pathology in the cortex, medial temporal lobe, diencephalon, brainstem, and spinal cord</td>
<td>Cognitive impairment with memory loss, executive dysfunction, loss of attention and concentration, depression, explosivity, and visuospatial abnormalities</td>
</tr>
<tr>
<td>IV</td>
<td>Stage III plus further cerebral, medial temporal lobe, hypothalamic, thalamic, and mammillary body atrophy; septal abnormalities; ventricular dilation; pallor of substantia nigra and locus coeruleus; p-tau in widespread regions, including white matter, with prominent neuronal loss, gliosis of cortex, and hippocampal sclerosis</td>
<td>Dementia with profound short-term memory loss, executive dysfunction, attention and concentration loss, explosivity, and aggression; most also show paranoia, depression and impulsivity, and visuospatial abnormalities; many also have parkinsonism, speech, and gait abnormalities</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage</th>
<th>Pathology</th>
<th>Clinical Signs and Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Perivascular phosphorylated tau neurofibrillary tangles in focal epicenters at the depths of sulci in frontal cortex</td>
<td>Headache and loss of attention and concentration</td>
</tr>
<tr>
<td>II</td>
<td>Stage I plus neurofibrillary tangles in superficial cortical layers adjacent to the focal epicenters, the nucleus basalis of Meynert, and locus coeruleus</td>
<td>Depression and mood swings, explosivity, loss of attention and concentration, headache, and short-term memory loss</td>
</tr>
<tr>
<td>III</td>
<td>Stage II plus mild cerebral atrophy; septal abnormalities; ventricular dilation, concave third ventricle, depigmentation of locus coeruleus and substantia nigra; dense p-tau pathology in the cortex, medial temporal lobe, diencephalon, brainstem, and spinal cord</td>
<td>Cognitive impairment with memory loss, executive dysfunction, loss of attention and concentration, depression, explosivity, and visuospatial abnormalities</td>
</tr>
<tr>
<td>IV</td>
<td>Stage III plus further cerebral, medial temporal lobe, hypothalamic, thalamic, and mammillary body atrophy; septal abnormalities; ventricular dilation; pallor of substantia nigra and locus coeruleus; p-tau in widespread regions, including white matter, with prominent neuronal loss, gliosis of cortex, and hippocampal sclerosis</td>
<td>Dementia with profound short-term memory loss, executive dysfunction, attention and concentration loss, explosivity, and aggression; most also show paranoia, depression and impulsivity, and visuospatial abnormalities; many also have parkinsonism, speech, and gait abnormalities</td>
</tr>
</tbody>
</table>

CHRONIC TRAUMATIC ENCEPHALOPATHY
Tau Protein: Amygdala (McKee et al. 2009)

Healthy Brain  Football Player  Boxer
Memory impairment (85%)
Executive dysfunction (79%)
Attention and concentration difficulties (73%)
Sadness/depression (64%)
Hopelessness (64%)
Explosivity (58%)
Language impairment (58%)
Visuospatial difficulties (55%)
"Out of control" (52%)
Physically violent (52%)
Verbally violent (49%)
Impulse and control problems (46%)
Suicidal ideation/attempts (30%)
Motor symptoms (30%)


b Percentage of individuals with autopsy-proven chronic traumatic encephalopathy who had each feature at presentation.
General Criteria for Traumatic Encephalopathy Syndrome (TES) (all five criteria must be met)

1. History of multiple impacts to the head based upon the type of injury and source of exposure

   Types of injuries
   
   - Mild traumatic brain injuries or concussions, minimum of four
   - Moderate or severe traumatic brain injury
   - Subconcussive trauma

   Source of exposures
   
   - Involvement of high-exposure contact sports for minimum of 6 years, including at least 2 at college level or higher
   - Military service
   - History of any other significant exposure to repetitive hits to the head
   - For moderate/severe traumatic brain injury, any activity resulting in the injury

2. No other neurologic disorder present that likely accounts for all clinical features

3. Clinical features must be present for a minimum of 12 months

4. At least one core clinical feature must be present and considered a change from baseline

5. At least two supportive features must be present
Must have at least one injury type and one exposure type from the list below

◆ Mild traumatic brain injury or concussion, minimum documented four episodes

◆ Moderate or severe traumatic brain injury, two episodes, defined as loss of consciousness of at least 30 minutes with alteration of consciousness or mental state of more than 24 hours, posttraumatic amnesia of more than 24 hours and Glasgow Coma Scale score of less than 13\textsuperscript{14}

◆ Subconcussive trauma

◆ High-exposure contact sport involvement (including, but not limited to, boxing, football, ice hockey, lacrosse, rugby, wrestling, or soccer) for a minimum of 6 years (at least 2 of which are at college level or higher)

◆ Military service including blasts or other explosions as well as noncombat exposure to explosives or to combatant or breach training

◆ Repetitive hits to the head including, but not limited to, domestic abuse and head banging or door breaching by police

\textsuperscript{a} Data from Montenigro PH, et al, Alzheimers Res Ther.\textsuperscript{22}
Core Clinical Features of TES (at least one must be met)

1. Cognitive: difficulties in cognition as reported by either self or informant, by history, or clinician’s report of decline and substantiated by impairment on standardized tests
2. Behavioral: emotionally explosive, physically and/or verbally violent
3. Mood: feeling overly sad, depressed, and/or hopeless

Supportive Features of TES (at least two must be present)

1. Impulsivity: impaired impulse control as demonstrated by new behaviors
2. Anxiety: history of anxious mood, agitation, excessive fears, or obsessive and/or compulsive behavior
3. Apathy: loss of interest in usual activities, loss of motivation and emotions, and/or reduction in voluntary goal-directed behaviors
4. Paranoia: delusional beliefs of suspicion, persecution, and/or unwarranted jealousy
5. Suicidality: history of suicidal thoughts or attempts
6. Headache: significant and chronic headache, with at least one episode per month for 6 months
7. Motor signs: dysarthria, dysgraphia, bradykinesia, tremor, rigidity, gait disturbance, falls and/or signs for a minimum of 1 year
8. Documented decline: progressive decline in function and/or a progression in symptoms and/or signs for a minimum of 1 year
9. Delayed onset: delayed onset of clinical features after significant head impact exposure, usually at least 2 years and, in many cases, several years after the period of maximal exposure
Chronic Traumatic Encephalopathy (CTE) Diagnostic Classification

1. Probable CTE: meets classification for any TES subtype; progressive course; does not meet diagnostic criteria for another disorder more consistently than TES; has a minimum of one positive potential biomarker for CTE

2. Possible CTE: meets classification for any TES subtype; progressive course; and (1) has not undergone any potential biomarker testing, (2) has had negative results on one or more biomarkers with the exception of tau PET imaging (if tau PET imaging was performed and is negative, necessary classification is “unlikely CTE”), or (3) meets the diagnostic criteria for another disorder that, on its own, could account for the clinical presentation

3. Unlikely CTE: does not meet TES diagnostic criteria or has had a negative tau PET imaging scan or both
# Potential Biomarkers for the Diagnosis of Probable Chronic Traumatic Encephalopathy

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cavum septum pellucidum</td>
<td>Cavum septum pellucidum, cavum vergae, or fenestrations based on neuroimaging study</td>
</tr>
<tr>
<td>Normal CSF amyloid-β levels</td>
<td>CSF amyloid-β levels in the normal range for age rather than in the decreased range, which can be suggestive of Alzheimer disease</td>
</tr>
<tr>
<td>Elevated CSF phosphorylated tau to total tau ratio</td>
<td>CSF phosphorylated tau to total tau ratio above the normal range for age</td>
</tr>
<tr>
<td>Negative amyloid imaging</td>
<td>PET amyloid imaging in the normal range, not suggestive of Alzheimer disease</td>
</tr>
<tr>
<td>Positive tau imaging</td>
<td>PET paired helical filament tau imaging suggestive of abnormal tau deposition; it should be noted that this remains an experimental procedure and requires additional validation before use as a clinical diagnostic tool</td>
</tr>
<tr>
<td>Cortical thinning</td>
<td>Based on MRI measurement, evidence of increased cortical thinning consistent with neurodegeneration</td>
</tr>
<tr>
<td>Cortical atrophy</td>
<td>Based on MRI or CT, generalized cortical atrophy beyond that expected for age, particularly in the frontal, thalamic, hippocampal, and/or amygdalar regions</td>
</tr>
</tbody>
</table>

CSF = cerebrospinal fluid; CT = computed tomography; MRI = magnetic resonance imaging; PET = positron emission tomography.

*Modified from Montenigro PH, et al, Alzheimers Res Ther. © 2014 The Authors*
# Potential Biomarkers for the Diagnosis of Probable Chronic Traumatic Encephalopathy

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cavum septum pellucidum</td>
<td>Cavum septum pellucidum, cavum vergae, or fenestrations based on neuroimaging study</td>
</tr>
<tr>
<td>Normal CSF amyloid-β levels</td>
<td>CSF amyloid-β levels in the normal range for age rather than in the decreased range, which can be suggestive of Alzheimer disease</td>
</tr>
<tr>
<td>Elevated CSF phosphorylated tau to total tau ratio</td>
<td>CSF phosphorylated tau to total tau ratio above the normal range for age</td>
</tr>
<tr>
<td>Negative amyloid imaging</td>
<td>PET amyloid imaging in the normal range, not suggestive of Alzheimer disease</td>
</tr>
<tr>
<td>Positive tau imaging</td>
<td>PET paired helical filament tau imaging suggestive of abnormal tau deposition; it should be noted that this remains an experimental procedure and requires additional validation before use as a clinical diagnostic tool</td>
</tr>
<tr>
<td>Cortical thinning</td>
<td>Based on MRI measurement, evidence of increased cortical thinning consistent with neurodegeneration</td>
</tr>
<tr>
<td>Cortical atrophy</td>
<td>Based on MRI or CT, generalized cortical atrophy beyond that expected for age, particularly in the frontal, thalamic, hippocampal, and/or amygdalar regions</td>
</tr>
</tbody>
</table>

CSF = cerebrospinal fluid; CT = computed tomography; MRI = magnetic resonance imaging; PET = positron emission tomography.

Vignette - revisited

- Former rugby player committed suicide by fire arm at age 46
- Pathologists diagnosed stage II Chronic Traumatic Encephalopathy at autopsy

- Clinical features > 15 years
- Cognitive, behavioral, and mood changes
- Impulsivity
- Anxiety
- Paranoia
- Suicidality
- Headache
- Documented decline
- Delayed onset
Evaluation - Clinical

• History of repetitive head trauma - with or without concussion
  • Contact sports
  • Military service
  • Domestic abuse
  • Assault
  • Motor vehicle accidents

• Behavioral, mood, cognitive, and possible motor symptoms

• Temporal profile and impact on activities of daily living
Evaluation - Clinical

• Neurologic examination with focus on:
  • Mental status survey

• Motor evaluation
  • Fasciculations or upper motor neuron signs

• Gait evaluation
  • Parkinsonism
CTE patients have history of *repetitive or subconcussive head injury* and *more memory loss* than bvFTD.

CTE patients with behavioral changes often manifest *explosivity* and *disinhibition*.

Parkinsonism is *late feature* of CTE, if present.
Symptomatic Treatment

• No FDA approved treatment for CTE
• Empiric treatment for symptomatic management
  • Acetylcholinesterase inhibitors – memory
  • Selective serotonin reuptake inhibitors – mood
  • Memantine – attentional issues in advanced dementia
  • Atypical antipsychotics – violence and disinhibition
Epidemiology

• True incidence and prevalence of CTE unknown
• Mayo Clinic Brain Bank (n=1721)
  • 32% prevalence in contact sports athletes
  • 0% prevalence in controls w/o TBI or contact sports (n=162)
  • 0% prevalence in individuals with single TBI (n=33)

• 2-4 million sports related concussions/year in US
• Estimated age of onset 30-65 years on average
CTE Overlap

- 55% AD
- 19% LBD
- 13% FTLD-TDP-43
- 6% FTLD-Tau
- 5% MND
- 3% Pure CTE

CONTINUUM: LIFELONG LEARNING IN NEUROLOGY
Susceptibility Factors/Biomarkers

• Apolipoprotein ε4 allele
• Cognitive reserve
• PET imaging with tau tracers
• CSF biomarkers
Conclusions

• Science of CTE is advancing rapidly

• Some amount of repetitive head injury combined with unknown genetic, exposure, and other susceptibility factors leads to CTE

• Future state may include validated clinical consensus criteria and biomarkers (tau PET imaging) to diagnose individuals during life
barrett.kevin@mayo.edu
Traumatic Brain Injury in Older Adults
How is TBI different in older adults?

- Epidemiology
- Mechanism of injury
- Morbidity and mortality
- Functional outcomes

- Age-related brain changes
- Age-related cognitive outcomes
Epidemiology of TBI

• Significant cause of death and disability in US
  • Over 5 million Americans living with disability related to TBI

• 1.7 million TBI cases per year

• More than 80,000 ED visits each year in those 65 and older
  • 75% of these require hospitalization
  • Those 75 and older have highest rates of hospitalization and death

• 52,000 deaths

• TBI-related deaths are 1/3 of all trauma related deaths

Hirshon, 2013
Epidemiology of TBI

- TBI incidence: 2 peaks

- 15-24 years old

- 70 years and older
  - Falls are leading cause in older adults (51%) and MVCs are second (10%)
  - Severe disability and death rates for those 15-24 years old are about 50% of that for those 55 and older

Hukkelhoven, et al., 2003
Epidemiology of TBI

• Male: female injury rates

• In younger adults males are much more likely than females to sustain TBI

• At around age 65, there is equal risk

• After 80, women are more likely to have TBI

Dams-O’Connon, 2013; Walker, 2013
Epidemiology of TBI in older adults

• TBI affects approximately 524 out of 100,000 older adults in US; 538 per 100,000 for younger adults

• But, number of older adults is on rise…

Rapoport, 2008; Walker 2013
Epidemiology: Aging in America

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 65 years (millions)</td>
<td>33.5</td>
<td>36.2</td>
<td>53.2</td>
<td>75.2</td>
</tr>
<tr>
<td>Percent of total population</td>
<td>12.8</td>
<td>12.6</td>
<td>16.5</td>
<td>20.3</td>
</tr>
<tr>
<td>≥ 85 years (millions)</td>
<td>3.6</td>
<td>4.9</td>
<td>6.5</td>
<td>13.6</td>
</tr>
<tr>
<td>Percent of total population</td>
<td>1.4</td>
<td>1.7</td>
<td>2.0</td>
<td>3.7</td>
</tr>
</tbody>
</table>

US Bureau of Census, 2008
Epidemiology of TBI

• National Trauma Data Bank (Level 1 and 2 trauma centers)

• Adults over 65 had highest rates of TBI-related hospitalization

• There was an increase of 25% in trauma center admissions for people over 75 with TBI between 2007 and 2010

• Annual hospital charges for treating TBI patients 65 and over in 2010 was over $2 billion

Dams-O’Connor, 2013
Epidemiology of TBI in older adults

- Older adults are hospitalized more often
- Older adults have 2x the mortality from TBI

Rapoport, 2008; Walker 2013
Injuries are different

• Injuries in older adults are different from younger adults
• An estimated 85% of older adults’ TBIs are mild to moderate in severity

Kim, 2011; Rapoport, 2008; Walker 2013
Injuries are different

• In older adults than younger adults
• more common:
  • Subdural hematomas
  • Diffuse axonal injury
  • Focal contusions

• Might be because MVCs involving older adults tend to be lower speed. Crashes between vehicles and pedestrians involving older adults tend to occur at crosswalks and parking lots, can be low velocity
• Assaults can occur too

Kim, 2011; Walker, 2014
Injuries are different

- Older adults may have other health problems that affect the recovery
- The older adult brain has a decreased ability to repair itself

Kim, 2011
Mechanism of injury

In younger individuals, motor vehicle crashes are the most common cause of TBI.

In older individuals, falls account for the highest proportion of TBIs.

Kim, 2011
Falls

Falls are the 5\textsuperscript{th} leading cause of death in people 65 and over.

Falls lead to 70\% of accidental deaths in people over 75

Falls are leading cause of hospitalization in individuals over 70

Kim, 2011; Testa, 2005.
TBI sequelae

- Compared to younger adults with TBI, Older adults with TBI (on average)
  - Undergo more in-hospital procedures (including imaging and neurosurgery)
  - Have longer acute care hospital stays
  - are more likely to require continued medical care

- For every 10 years of age, there is a 40-50% increase in the odds of a poor outcome as a result of TBI

Dams-O’Connor, 2013; Walker, 2013
Increased mortality/ morbidity after TBI in older adults

• In older vs younger patients, these are more common
  • Cardiac problems
  • Pulmonary problems
  • Multisystem organ failure

• There might be decreased tolerance for blood pressure issues and hypoxia/ pulmonary issues with age

Walker, 2013
TBI morbidity/ mortality

- Older adults are more susceptible to medical complications
  - Cerebrovascular events in setting of trauma related hypotension
  - Adverse effects of anemia due to blood loss in trauma
  - More likely to have pulmonary/ cardiac complications

Kim, 2011; Walker, 2013
TBI Mortality Sequelae

• Compared to younger people, older adults with TBI have:

• Higher mortality (acute and long term)
Mortality and TBI in older adults

- Older adults (55 and over) who completed acute rehabilitation for TBI, in TBI Model Systems Database
- Comparison of patients who died 1-4 years later with patients who didn’t die
- Increased mortality was associated with
  - Abnormal gait
  - Prescriptions for respiratory medications
  - Diabetes mellitus
  - More medications

Hirshon, 2013
TBI Functional Sequelae

• Compared to younger people, older adults with TBI have:
  
  • Poorer short term functional outcomes
  • Worse functional outcome
  • Greater levels of disability

Testa, 2005; Walker, 2013
Sequelae: Functional outcome

- Study of 272 patients (195 had TBI and 82 had orthopedic injuries)

- Older patients with TBI may have a greater likelihood of becoming physically and financially dependent on others

- This is likely affected by injury severity

Mosenthal, 2004; Testa, 2005
Sequelae: functional outcome

- Study of people over 55 vs younger than 55
- Matched for injury severity and gender
- Older group had
  - Significantly longer mean length of rehabilitation stay
  - Higher total rehabilitation charges
  - Slower rate of improvement on functional measures
  - Higher rate of discharge to nursing home

Cifu, 1996; Walker, 2013
Long term recovery from TBI in older adults

- Older age group (over 40 in this study)
  - Less severely injured (GCS)
  - Slightly more disabled at discharge from rehabilitation
  - Age had significant negative influence on disability scores (DRS) 5 years after TBI

=> Older adults showed greater decline over first 5 years after TBI than younger patients

De la Plata, 2008
Functional outcome

• No difference between groups in discharge disposition
  • Community vs. institutional setting

=> Although older patients needed significantly longer and more costly rehabilitation stays, their postdischarge dispositions were compatible with younger patients

Cifu, 1996
Functional outcome

- TBI model systems data:
  - Almost all individuals over 65 who received acute inpatient rehabilitation:
    - Achieved significant functional improvement
    - 2/3 were discharged to community setting
    - Nearly 85% were in community setting 1 year later

Walker, 2013
Functional outcome

• Injury severity is important

• In cases of TBI uncomplicated by multiple trauma, older adults have potential to achieve functional outcomes comparable to younger patients

• May take longer and at greater expense

Mosenthal, 2004
Aging and the brain

• Age-associated cell changes occur after about age 40

• Age-related cerebral atrophy results from
  • Loss of neurons
  • Decrease in neuronal volume
  • Loss of synapses
Aging and the brain

• There may be a decrease in synthesis of nerve growth factor, making neuronal repair more difficult.

• This may have implications for plasticity during recovery.

Kim, 2011
Aging and the brain

• Age-related cerebrovascular changes can lead to reduction in cerebral perfusion and reduced regional cerebral metabolism.

Kim, 2011
Aging and the brain

• Overall brain shrinkage due to atrophy increases the space between the brain and skull

• Then vessels are more likely to be exposed to shearing forces in TBI.

Kim, 2011
Aging and TBI

Age-related factors:
- Mobility
- Functional loss
- Hearing/vision loss
- Memory problems
- Health problems
- Loss of independence
- Reduced income
- Depression
- Social withdrawal

TBI-related factors:
- Mobility
- Functional loss
- Memory/cognitive problems
- Sensory impairments
- Health problems
- Loss of independence
- Reduced income
- Depression
- Social withdrawal

Traumaticbraininjury.net
Neurochemical changes in aging

• Decreased acetylcholine and impairment in acetylcholine activity.
• Decreased serotonergic function.
• Decreased norepinephrine function.
• Decreased dopaminergic activity and function.

• These changes may predisposed older adults to cognitive and affective changes after TBI

Kim, 2011
Aging

- Aging brain may be more vulnerable to damage
  - More significant injury can result from a mild blow
- Less “reserve”
- Pre-existing medical conditions
- Polypharmacy issues
- Deficits are more pronounced
- Poorer functional outcomes
- Cognitive decline

Dams-O’Connor, 2013; Kim, 2011
Cognitive outcome

• Older adults are at risk for poorer cognitive outcome following TBI

• It’s possible that cognitive impairment predisposed the injury or that there’s some decreased cognitive reserve present

• Effects of medications need to be carefully considered

Kim, 2011; Testa, 2005
Neuropsychological Outcome

- Executive control
- Processing speed
- mTBI versus moderate/severe TBI

- Performance of middle aged individuals with TBI mirrors senior citizens without TBI
- Increased risk for brain atrophy

Salib and Hillier, 1997; De Deyn, 1999
Objective 2

• Describe the process of rehabilitation, including recommendations for best practice, and community reintegration in older adults with TBI.
TBI rehabilitation in older adults

- Rehabilitation evaluation
- Functional assessment
- Interventions need to be appropriate for medical and overall functional status
- Preventing falls and additional injuries
Rehabilitation evaluation after TBI in older adult

• Start in ICU to determine acute needs, start long term planning
• Continue throughout course in other settings

Walker, 2013
Rehab evaluation after TBI in older adult

- Preinjury activity level
- Cognitive issues
- Behavioral issues
- Chronic medical conditions

- Important in planning intensity of therapies and setting goals
Rehab evaluation after TBI in older adult

- Cognitive and behavioral status
- Ability to tolerate physical and mental activities
- Impairments: eg hemiparesis, dysphagia, incontinence, impaired cognition
- Functional level: mobility status, ADL abilities
Activities of Daily Living (ADL)

self-care activities:

bathing/showering
bowel and bladder management
Dressing
eating (including chewing and swallowing)
feeding
functional mobility
personal hygiene and grooming
sleep/rest
toilet hygiene
Instrumental Activities of Daily Living (IADL)

Activities focused on interaction with environment

- caring for children, pets and other people
- communication device use
- community mobility
- financial management and maintenance
- home management
- meal preparation and cleanup
- safety procedures
- emergency responses
Nutrition/ swallowing

• Dentures
• Dysphagia
• Electrolytes/ vitamin levels
• Calorie counts
• Hydration status
Social history

• Living situation
• Vocational history
• Any alcohol/drug history
• Community resources
FUNCTIONAL INDEPENDENCE MEASURE (FIM) OUTCOME TOOL

- Helps us measure progress toward functional goals
- Main Components
  - Motor
  - Cognitive

SUNY Buffalo, 1996
FIM Scoring

Levels:

• 7 - complete independence
• 6 - modified independence (with use of device)
• 5 - supervision
• 4 - minimal assistance (patient does 75-100% of task)
• 3 - moderate assistance (patient does 50-75% of task)
• 2 - maximal assistance (patient does 25-50% of task)
• 1 - total assistance (patient does less than 25% of task)
FIM Motor

Self Care:
• eating
• grooming
• bathing
• dressing- upper body
• dressing-lower body
• toileting

Sphincter control:
• bladder management
• bowel management

Transfers:
• bed, chair, wheelchair
• toilet
• tub, shower
• Locomotion:
• walk/ wheelchair
• stairs

SUNY Buffalo, 1996
FIM Cognitive

Communication:
- comprehension
- expression

Social cognition:
- social interaction
- problem solving
- memory

SUNY Buffalo, 1996
Rehabilitation issues

• Sensory: optimize vision and hearing with adaptive equipment
Rehabilitation issues

• Self-care
  • Organize therapies around older adult’s preinjury habits and routines
  • Incorporate their own clothes/ utensils into familiar routines

Walker, 2013
Rehabilitation issues

• Mobility and balance
  • May take older adult longer to recover these functions
  • Premorbid issues with cognition, sensation, strength and balance likely play a role
  • They may have decreased tolerance for intensive therapy sessions
    • Lower endurance
    • More muscle and joint stiffness

Walker, 2013
# Falls Risk Factors

<table>
<thead>
<tr>
<th>Category</th>
<th>Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>SENSORY</td>
<td>Impaired vision, Impaired proprioception, Impaired vestibular function, Peripheral neuropathy</td>
</tr>
<tr>
<td>MUSCULOSKELETAL</td>
<td>Muscle weakness, Arthritis</td>
</tr>
<tr>
<td>CARDIOVASCULAR</td>
<td>Postural hypotension, Cardiac arrhythmia</td>
</tr>
<tr>
<td>CENTRAL NERVOUS SYSTEM</td>
<td>Dementia, Depression, Movement disorders</td>
</tr>
</tbody>
</table>

Kim, 2011; Walker 2013
Falls prevention

Short term factors
- Acute illness
- Alcohol abuse
- Medication effects
- Other transient or episodic conditions or events

Walker, 2013
Falls prevention

Activity related factors
- Tripping while
  - Walking
  - Climbing ladders
  - Descending stairs
- Other activities

Walker, 2013
Falls prevention

Environmental factors: objects or other environmental elements that predispose a person to falls

- throw rugs
- poor lighting
- poorly fitting shoes or clothes
Home eval/ caregiver education

- Home evaluation by members of the rehabilitation team can
  - Assess architectural barriers
    - Doorways, stairs, rugs
    - Furniture arrangements
    - Lighting
  - Train caregivers on safe mobility practices in the home environment

Walker, 2013
Secondary TBI prevention

Risk factors also predispose older adults to
Motor vehicle crashes
pedestrian mishaps
recreational injuries

Walker, 2013
Secondary TBI prevention

- Management of medical comorbidities
- Regulation of medications
- Providing ongoing education
Psychosocial Functioning

• Community reintegration
  • Severity of injury
  • Age
  • Level of disability
  • Challenging behavior

• Environmental factors
  • Transportation
  • Attitudes
  • Barriers
Independence after TBI

- Fewer comorbid conditions
- Access to home modification
- Home support services
- Male gender
- Age
- Shorter acute care length of stay
Increasing Barriers with Age

- Functional capabilities decrease
- Additional medical problems may emerge
- Social roles and relationships may change
- Higher rates of psychological problems
  - Depression, addiction, suicide
- Problems with housing and community access
- Lack of social support
- Aging and caregiver issues
Persistent Affective and Behavioral Symptoms

- Insert research from
- Sleep problems
- Substance use disorders
- Major depression
- Anxiety disorders - PTSD and panic disorder
- High comorbidity
  - 44% of individuals presenting with two or more Axis I diagnoses

Colantonio, 2004; Hibard, 1998; Hoofien, 2001
Objective 3

• Discuss at least two significant themes in the current research literature regarding the potential association between TBI and dementia.
TBI & Alzheimer’s Disease (AD)

• There seems to be some association between previous head injury and the risk of developing Alzheimer’s disease

• Increased risk in those
  • Age 55 with moderate to severe TBI
  • Age 65 with mild TBI

Fleminger, 2003; Graves, 1990; Mortimer, 1985
TBI & Alzheimer’s Disease (AD)

- Multiple case control studies have been performed
- Statistically significant association between head trauma and Alzheimer’s
  - 130 matched pairs in Washington State, 1980-1985, in a dementia clinic, retrospectively asked about TBI
  - Minneapolis VA, 1980s, 78 Veterans with Alzheimer’s and 124 control subjects. Statistically significant higher TBI in the AD group

Graves, 1990; Mortimer, 1985
TBI and dementia

- TBI from 2005-2011 in state of California
- Retrospective analysis, 51800 patients

- There was an increased risk for dementia in:
  - Patients over 55 who had moderate to severe TBI
  - Patients over 65 with mild TBI

- Compared with trauma patients who did not sustain TBI

Gardner, 2014
TBI and dementia

- TBI from 1934 to 1984, 1283 cases
- Olmstead County
- Time to onset of Alzheimer’s disease was studied.

- Observed time to Alzheimer’s was shorter in patients with TBI than in patients without TBI

Nemetz, 1999
TBI and dementia

US Veterans, 55 and older

Retrospective cohort study, 188764 patients 2000-2012

16% of those with TBI developed dementia
10% of those without TBI developed dementia

-> TBI in older Veterans seems associated with increased risk of dementia

Barnes, 2014
TBI & Alzheimer’s Disease (AD)

• There seems to be a synergistic effect between traumatic brain injury and apolipoprotein E4 status
  • Heterozygous (has one allele) or homozygous (has two alleles)
  • There be correlation between apo E and amount of beta amyloid buildup

• This appears to confer higher risk of developing Alzheimer’s disease

Mayeux, 1995
TBI & AD

• Study of 236 community dwelling older adults
• TBI alone not associated with increased risk of Alzheimer’s disease
• History of TBI AND Apo E allele was associated with 10 fold increase in risk for AD

Mayeux, 1995
TBI and dementia

• Evidence points to this fact:
  • After TBI, Alzheimer’s may occur earlier than without TBI in patients who were predisposed to Alzheimer’s

In patients not predisposed to AD, NO increase in risk for AD after TBI
Dementia Risk

• Other factors to consider:
  • TBI severity (moderate/severe)
  • Age

• History of TBI *along with* brain changes associated with normal may exacerbate cognitive decline

• Important to remember that individuals with dementia do not usually have a history of TBI and survivors of TBI do not invariably acquire dementia later in life
Mild traumatic brain injury (mTBI)

- Loss of consciousness up to 30 minutes
- Change in mental status/ amnesia for up to 24 hours
- Head CT with no acute intracranial abnormality
- Acute symptoms can occur immediately or within a few minutes

Peskind, 2013
Common acute symptoms of mTBI

- Loss of consciousness
- Headache
- Confusion
- Lightheadedness/ dizziness
- Vertigo
- Blurred vision/ eye strain
- Tinnitus
- Fatigue
- Mood/ behavioral changes
- Altered memory, concentration, attention, thinking

Peskind, 2013
Mild TBI and dementia

• International Collaboration on Mild Traumatic Brain Injury Prognosis

• Systematic review

-> There is a lack of evidence of increased risk of dementia after mTBI in adults

Godbolt, 2014
Compound effect of multiple mTBI

• In a study of Veterans who’d had mTBI
  • More than 90% with more than 5 episodes had neurological symptoms
  • Less than 20% with 1 episode had neurological symptoms

• Service members with multiple mTBIs had higher frequency of depression, anxiety and post-traumatic stress than people with one mTBI

• Combat mTBI may be different from civilian though

• Interval between mTBIs may be important

Peskind, 2013
Chronic Traumatic Encephalopathy

- Symptoms can develop with in a few years of the injury in some people
- There is usually a period of some 8 years or more between injury and symptoms

Peskind, 2013
Chronic Traumatic Encephalopathy

• The exact relationship between concussions and CTE remains ambiguous and remains under study

• CTE on neuropathological examination is NOT INEVITABLE
  • Even with
    • History of multiple concussions eg from a contact sport
    • Positive clinical presentation before death

Tartaglia, 2014
Chronic Traumatic Encephalopathy

- We don’t know who will be affected
- We don’t know the actual risk

- Risk may be higher for
  - repetitively injured
  - Injuries involving high velocity/ large amount force

Peskind, 2013
Cognitive Reserve

• Strategies to increase cognitive reserve may be helpful in preventing exacerbated decline after TBI
  • What is it?
  • Helps to withstand brain diseases of old age
  • Ability to adapt/route using alternative pathways
Increasing Cognitive Reserve

• Physical activity
• Challenge yourself
  • Learn something new
  • Foreign language, skill, hobby
  • Use your non-dominant hand
• Social activity
• Reduce stress
What we can do

Primary Prevention
What we can do

• Address risk of falls
• Seatbelts
• Bike helmets
• Motorcycle safety
• Playground safety
• Driving issues
  • Avoiding driving distracted, impaired, fatigued
What we can do

Secondary Prevention
What we can do

• Identify injuries when they occur
• Provide appropriate care
• Follow “return to play” and return to activity guidelines
• Appropriate safety precautions during activities

Peskind, 2013
Why do we need baseline neurocognitive assessments in sports?

• “Nobody in football should be called a genius. A genius is a guy like Norman Einstein.”

-- Football commentator and former player, Joe Theisman
Conclusions