Chronic Traumatic Encephalopathy and the Athlete

Update from the Boston University Center for the Study of Traumatic Encephalopathy

CSTE
Boston University Center for the Study of Traumatic Encephalopathy

• Robert Cantu, M.D.
  – Clinical Professor of Neurosurgery, BU School of Medicine
  – Co-Founder and Medical Advisory Board Chairman, Sports Legacy Institute
  – Chief of Neurosurgery Service and Director of Sports Medicine, Emerson Hospital
  – Co-Director, Neurologic Sports Injury Center, Brigham and Women’s Hospital

• Ann McKee, M.D.
  – Associate Professor of Neurology and Pathology, BUSM
  – Director, Neuropathology Core and Brain Banks of the Boston University Alzheimer’s Disease Center (ADC), Framingham Heart Study, New England Centenarian Study
  – Director, Neuropathology Service, New England Veterans Administration Medical Centers

• Chris Nowinski
  – President and Founder, Sports Legacy Institute
  – Former Harvard Football Player and Professional Wrestler
  – Author of Head Games: Football's Concussion Crisis

• Robert Stern, Ph.D.
  – Associate Professor of Neurology, BUSM
  – Co-Director, Alzheimer’s Disease Clinical and Research Program
  – Acting Director, Clinical Core, BU ADC
Center for the Study of Traumatic Encephalopathy

A Collaboration Between Sports Legacy Institute and Boston University School of Medicine

Established September 2008

**Goal of CSTE:** To study the long-term effects of sports-related brain trauma

1. Establishment of Brain Donation Registry (C.O.N.T.A.C.T.)
   - Current or retired athletes (pro and college), with and without history of concussion, to agree to donate brain and spinal cord tissue following death and to be interviewed by phone annually.

2. Conduct Longitudinal Clinical Research
   - In-depth examinations of retired athletes, including neuropsychological, psychiatric, and neurological assessments, as well as brain MRI (DTI, fMRI) and lumbar punctures (to measure proteins in cerebrospinal fluid), electrophysiological studies, and genetics. Study longitudinally and examine brains following death.

3. Create a Brain Bank
   - Brain and spinal cord tissue repository (at the Bedford VAMC) for the examination of the underlying neuropathology associated with repetitive brain trauma in athletes.
Non-Amyloid AD?

• We propose that some (perhaps, many) cases hitherto diagnosed both clinically and neuropathologically as AD are, in fact, examples of CTE.

• Furthermore, the reported and widely accepted increased risk of AD following TBI is actually due to the inclusion of such CTE cases that were erroneously diagnosed as AD.

• Interestingly, in a recent report, Nelson and colleagues (2009) at the University of Kentucky ADC queried the 5108 cases in the NACC Neuropathology Registry and found that ~5% demonstrated medial temporal lobe NFTs in the presence of little or no amyloid plaques.

• Is it possible that some (perhaps many) of these cases may have had CTE (head trauma history for these cases would not have been available and, of course, were not reported)?
Dementia Pugilistica

First described in boxers by Martland in 1928

Chronic Traumatic Encephalopathy (CTE)

- Believed to be caused by repeated trauma to brain, including mild concussions and subconcussive blows.
- Progressive neurodegenerative disease, distinct from Alzheimer’s.
  - Tauopathy
- Early Symptoms:
  - memory and cognitive difficulties
  - depression
  - impulse control problems and behavior change
- Symptoms begin months or years after concussions and continue to worsen
- Eventually leads to full-blown dementia
- Perhaps the only fully preventable cause of dementia
<table>
<thead>
<tr>
<th>#</th>
<th>age</th>
<th>sex</th>
<th>highest level of sport</th>
<th>reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>75</td>
<td>M</td>
<td>Professional Boxing</td>
<td>Journal of Neuropathology and Experimental Neurology, July 2009</td>
</tr>
<tr>
<td>2</td>
<td>80</td>
<td>M</td>
<td>Professional Boxing</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>45</td>
<td>M</td>
<td>NFL Football</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>45</td>
<td>M</td>
<td>NFL Football</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>18</td>
<td>M</td>
<td>High School Football</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>66</td>
<td>M</td>
<td>NFL Football</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>49</td>
<td>M</td>
<td>NFL Football</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>40</td>
<td>M</td>
<td>College Football</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>75</td>
<td>M</td>
<td>Professional Boxing</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>35</td>
<td>M</td>
<td>NFL Football</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>80</td>
<td>M</td>
<td>NFL Football</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>70</td>
<td>M</td>
<td>NHL Hockey</td>
<td></td>
</tr>
</tbody>
</table>
CTE in Football players (11)
5 reported in literature (1 from BU); our 6 additional cases

- 8 died suddenly in middle age (8/11 = 73%):
  (age at death, 36-80 years; m = 45 years)
- 7 of the 11 experienced tragic deaths (64%):
  3 from suicide
  2 substance abuse
  1 during a high-speed police chase
  1 accidental gunshot while cleaning his gun
10 years of professional football

Death in his 80s with dementia

Severe II and III ventricular dilatation

Brain weight: 1450 gms
10 years of professional football

Death in his 80s with dementia

Brain weight: 1560 grams

Cavum septum pellucidum
10 years of professional football

Death in his 80s with dementia

Marked medial temporal atrophy
Shrinkage of the mammillary bodies
pallor of the substantia nigra
Microscopic Pathology of CTE

Neurofibrillary degeneration
Extensive tau-immunoreactive NFTs, glial tangles, and neurites throughout the brain

Widespread distribution:
- Cerebral cortex – frontal and temporal lobes
- Medial temporal lobe – amygdala, hippocampus, entorhinal cortex
- Subcortical white matter
- Thalamus, hypothalamus, mammillary bodies
- Brainstem
- Spinal cord
Microscopic Pathology of CTE

Unique pattern of involvement:

- **Superficial cortical laminae: layers II and III**
- Perivascular
- Patchy, irregular
- Prominent glial tangles
- Often greatest at sulcal depths
- Dotlike, spindle-shaped neurites
- Subcortical white matter
CTE: Tau immunoreactive NFTs

Cerebral cortex – primarily the frontal and temporal lobes

Medial temporal lobe – amygdala, hippocampus, entorhinal cortex
CTE: Tau immunoreactive NFTs
Subcortical Nuclei

Hypothalamus
Mammillary bodies

Thalamus
CTE: Tau immunoreactive NFTs

Brainstem and Spinal cord

Substantia Nigra  Locus ceruleus

Midbrain  Pons  Medulla  Cord
World Champion Boxer

death at age 73 years, profoundly demented

Tau immunohistochemistry

No Aβ
Football player: 10 years in NFL
death at age 45 years: memory loss, confusion, executive dysfunction

No Aβ

Tau immunohistochemistry
Football player: 16 years in NFL
death at age 66 years: memory loss, confusion, executive dysfunction, profound apathy
Football player: 9 years in NFL
depth at age 45 years: depression, poor decision making, substance abuse

Orbital frontal  Hippocampus  Temporal  Amygdala

Aß: rare diffuse plaques
High school football player

Death at age 18. Cognitively intact. Focal evidence of perivascular tau
Chronic Traumatic Encephalopathy in Football Players

- To date, all 11 brains from college and professional football players that we have studied have shown evidence of CTE
Not Just Athletes…

• Although CTE is most commonly found in athletes, many individuals are susceptible: epileptics, persons who suffer falls, accidental blows from moving objects, motor vehicle accidents, and military veterans (blast injuries)
Collaborators Wanted
Acknowledgments

Andrew Budson, M.D.
Dan Daneshvar, M.A.
Brandon Gavett, Ph.D.
E. T. Hedley-Whyte, M.D.
Patrick Hof, M.D.
Carol Kubilus
Daniel Perl, M.D
Hoon Rhyu, Ph.D.
Hyo Soon-Lee, M.D.
Megan Wulff, B.A.

And all the athletes, living and deceased, who have participated in our research
Funding sources

Boston University School of Medicine

NIA: Boston University Alzheimer’s Disease Center
  P30 AG13846
  supplements

National Operating Committee on Standards in Athletic Equipment (NOCSAE)

Department of Veteran’s Affairs