Combat- Related PTSD: A Developmental and Historical Perspective
Objectives

• Brief historical review of combat-related post-traumatic stress syndrome
• Functional neuroanatomy of PTSD
• Role of prefrontal dysfunction and/or immaturity on affect modulation and impulse control, with focus on aggression
Historical PTSD

• Samuel Pepys (1666, six months after the ‘great fire’ of London):
  — "I cannot sleep a night without great terrors of the fire; and this very night could not sleep to almost two in the morning through great terrors of the fire."

Bentley S. A Short History of PTSD: From Thermopylae to Hue Soldiers Have Always Had A Disturbing Reaction To War. The VVA Veteran March/April 2005 (reprint from January 1991)
Civil War: ‘Nostalgia’ or ‘Neurasthenia’

• ‘Insane’ soldiers were put on trains with no supervision, the name of their home town or state pinned to their tunics; others were left to wander about the countryside until they died from exposure or starvation

• By 1863 the number of ‘insane’ soldiers simply wandering around was so great there was a public outcry, and in 1864 the War Department ordered that these men be transferred to hospital until their families could come for them

World War I: ‘Shell Shock’

• Symptoms included violent tremors, staring eyes, unexplained blindness, deafness, paralysis...
• defective control of temper, tendency to weep on slight provocation; timidity, lessened power of attention, defective memory and will power
World War I: ‘Shell Shock’

• 1917: Army Surgeon General’s Office develops a treatment protocol:
  – Immediate intervention
  – Psychiatrists in units when possible
  – ‘Simple’ treatment: rest, warm shower, food
  – Expectation of quick return to battle

• 12.5% of soldiers were put out of action for psychiatric reasons
World War II: ‘Combat Fatigue’

- “Unit Cohesion” recognized as a protective factor
- Intensity and duration of combat exposure seen as contributors
- Symptoms seen as cowardice by many officers

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George Patton and Combat Fatigue

• In 1943, at a tent hospital in Sicily, Gen. George Patton slapped a soldier with his gloves, and dragged him out of the tent by the collar, ejecting him with a kick in the backside

• “Don't admit this son-of-a-bitch... You hear me, you gutless bastard? You're going back to the front!”

• The man was later diagnosed with malaria
Vietnam: ‘Stress Response Syndrome’

- Stress Response Syndrome was included in the first DSM (1952), which was based on the War Department Technical Bulletin “Medical 203”
- Psychiatric evacuations rose from 4.4% to 60% during the course of the war*
- 1968: if symptoms lasted more than 6 months, they were deemed a ‘pre-existing condition’ and not service-connected
  - Much delay in treatment resulted
  - Appeals continue into the present

*Franklin D. Jones, Chapter 3: War Psychiatry. Department of the Army, 1995
US Wars: Average Age of Combatants

- Revolutionary War: 32 at Lexington, 26 at Valley Forge, 21 at end
- Civil War: 26
- Spanish-American War (1898): 27
- WWI: 23-25
- WWII: 24-26
- Korean War: 23-25
- Vietnam War: 19
- Iran and Iraq: 27 (active duty), 33 (National Guard)
- Afghanistan: 26 (average age of those KIA)
Prefrontal Cortex

• can represent things not currently in environment
  – abstract thinking, sense of future and past
• that part of the front of your brain that doesn’t move anything if it’s stimulated
• necessary for “executive functions”
Executive Functions

• Setting a goal, planning
• Initiating tasks, maintaining focus
• Keeping track of time
• Keeping track of more than one thing
• Making mid-course corrections in work
• Predicting the result of possible choices
• Thinking clearly even when emotional
• Controlling impulses
Prefrontal Cortex Development

• The human PFC is not completely myelinated until MUCH later than in other mammals
  — In chimpanzees, PFC myelination is completed as sexual maturity is reached

• Without PFC inhibitory input, humans’ very survival depends on close adult supervision
  — Why did we evolve this way?
Human Prefrontal Development

Cognition Without Control

- “Learning vs. Performance” theory
  - Having decades of parental supervision allows us to learn and explore while protected from consequences
  - Increases likelihood of novel experiences, chance discoveries, novel conjunctions (innovation)
  - Executive functions mature only when we need to perform independently (or so it is hoped..)

Cognition without Control: When a little frontal lobe goes a long way
Cognition Without Control

- Exploration without inhibition or judgment
  - Sticking non-food items in our mouths, forks in electrical outlets
- Language learning free from internal “noise” about formalized rules
- Novel conjunctions
  - Light is a particle AND a wave
  - Using bicycle-building skills to make a flying machine

Cognition Without Control...

- Adults with ADHD (and thus less inhibitory downflow from the PFC) often perform better on ‘thinking outside the box’ puzzles.

PTSD: Brain Circuits

- Anterior cingulate cortex
- Ventromedial PFC
- Amygdala
- Hippocampus

- CHANGES IN “FUNCTIONAL CONNECTIVITY”
Anterior Cingulate Cortex (ACC)

• Contains specific processing modules for cognitive and emotional information
• Integrates input from other brain regions
  – Motivation
  – Evaluation of error
• Modulates cognitive, motor, endocrine, and visceral responses
Anterior Cingulate in PTSD

- Emotional Counting Stroop test
- Vietnam veterans with and without PTSD (n=16, all right-handed)
- Terms were combat-related, general negative, and neutral
- fMRI showed lack of activation in rostral ACC in the presence of emotionally relevant stimuli in PTSD

Ventromedial PFC

• Highly active during emotionally charged reasoning
  – (dorsolateral PFC more active during emotionally neutral reasoning)

• Evaluates probable outcome of behaviors
  – Attaching positive or negative valence
Ventromedial PFC in PTSD

• Hypoactivation of the medial PFC extending back to the ventral ACC (linked with amygdala changes)
• Impaired outcome predictions
• Impaired cortical oversight of bodily responses
Dorsolateral Prefrontal Cortex

• Anterior: attention and action inhibition
• Posterior: action execution (including fear responses) and working memory
• Crucial to impulse control

Cieslik E et al: Is There "One" DLPFC in Cognitive Action Control? Evidence for Heterogeneity From Co-Activation-Based Parcellation. Cerebral Cortex 2012 Aug 23
Dorsolateral Prefrontal Cortex

• Very active during emotion-regulating cognitive strategies
• Counterbalances strong affect to allow for optimal cognition
• Does not reach adult dimensions until well into the 3rd decade of life

Dorsolateral Prefrontal Cortex in PTSD

• Smaller in size, hypoactive
• PTSD-specific expression of over 800 mitochondrial-targeted genes in the dlPFC
• These genes are also associated with apoptosis (programmed cell death) in various neurological disorders

Amygdala

• More than a “fear center”
• It is a “what the heck?” center, computing the salience of incoming stimuli
• Most active during ambiguity or uncertainty
• Modulates- and is modulated by- other brain regions’ processing activity- a sort of Grand Central Station
The Amygdala in PTSD

- Men with PTSD vs. trauma-exposed men without PTSD (n= 26)
- PTSD group: increased amygdala activation and decreased medial PFC activation with fearful face exposure
  - Medial PFC important in extinction
- PTSD group: increased reaction, decreased habituation to fearful face exposure

The Amygdala in PTSD.

• Adrenal stress hormones increase noradrenergic transmission in basolateral complex of amygdala (BLA)
  – Normally offset by GABA downflow from PFC
• In PTSD, there is reduced GABA (inhibitory) receptor binding in BLA
  – Enhanced memory of events under stress
  – Impaired working memory

The Hippocampus

• Head Librarian for your neocortex
  – Acts as the brain’s search engine (finds your book)
  – Helps integrate newly acquired memories into long-term storage (re-shelves books in an orderly way, discards duplicates)
  – Navigates outer AND inner space and keeps maps of the routes
  – Generates your brain’s largest coordinated bursts of activity, triggering morphological changes
Mapping and the Hippocampus

- London taxi drivers vs. bus drivers: all were right handed, male, and 32-62 years old
- Did the taxi drivers self-select because of superior mapping ability?
- The taxi drivers’ posterior hippocampal volume increased with time on the job

The Hippocampus in PTSD

• Impaired contextualization of memory
• Inefficient working memory
• Inefficient memory
  – Loud noises which do NOT signify incoming fire may leave little impression
• Core affect is over-determined by remembered events and under-determined by the here-and-now
How Do We Control Our Impulses?

- Ratings of impulse control and fMRI data
- Size and activity of right vm-PFC correlated with impulse control via connections with the ACC and amygdala
- Among other functions, vm-PFC drives autonomic responses to *anticipated* results of action choices

Impulsive Aggression

- Patients with Intermittent Explosive Disorder and controls (NOT PTSD)
- fMRI while viewing angry faces
- Higher amygdala activity, lower OFC activity
- “Failed to demonstrate amygdala-OFC coupling”

Coccaro E et al. *Amygdala and orbitofrontal reactivity to social threat in individuals with impulsive aggression* Biological Psychiatry 08/2007; 62(2):168-78
Aggression and CR-PTSD

- Cross-sectional self report data
- Impulsive aggression
  - Not anger, hostility, or premeditated aggression
- Higher in veterans with PTSD (70%) than without PTSD (29%)

Teten A et al. Military Medicine, Vol 175 No 6, June 2010
Intimate Aggression and CR-PTSD

- 63% of male Vietnam veterans reported some act of intimate aggression in the last year (1995)
- Veterans without PTSD had same rate as in general population (different studies)

Case Reports of Response to ADHD Meds in CR-PTSD

- Methylphenidate enhanced extinction of contextual fear in one study
- 3 patients with refractory PTSD responded to stimulant therapy*
- Guanfacine can be helpful in nightmares

Veteran Unemployment Data

- May 2012, Gulf War II era Veterans’ unemployment rates compared to national data
  - ages 18-24, 23.5% (vs. 12.9%)
  - ages 25-34, 14.7% (vs. 8.2%)
  - ages 35-44, 6.4% (vs. 6.8%)
  - ages 45-54, 7.5% (vs. 6.4%)

Bureau of Labor Statistics
Developmental Issues

• the prefrontal cortex remains very plastic until the mid- to late-20’s

• experience and survival pressures affect the “shape” of the PFC
  – relative strength of various “circuits”
  – affective and cognitive thresholds

• consider a mostly-baked cake: tilt the oven rack for the last 15 minutes of baking...
Divergent Life Experience

• Civilian peers spend crucial early adulthood years developing
  – self care skills
    • trial and error mastery of sleep and food needs
    • capacity for substance intake
  – financial independence
    • budgeting and planning
    • navigating job interviews, socialization re: appropriate dress and comportment
Divergent Life Experience

• most civilian 18-25 year olds are performing ‘with a net’
  – they lose jobs, run out of money, get arrested, or stranded in foreign countries
  – showing back up at family home is the norm is this age group
  – most will become successively more able to navigate independently

• a bad choice in combat may lead to injury or death
Summary

• injury to brain structures, causing deficits in executive function, leads to functional impairment in PTSD

• younger soldiers with PTSD may experience more functional impairment for 2 reasons
  – still-developing prefrontal brain structures
  – injury occurs before civilian life skills can be consolidated