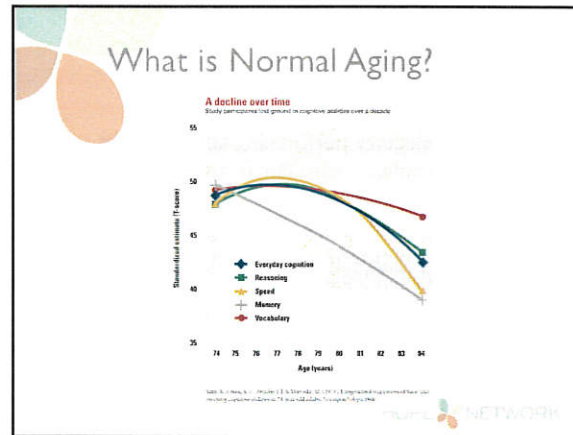


Aging and Brain Injury

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HOPE NETWORK
NEURO REHABILITATION

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Aging Metrics...

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Normal Aging

- Brain volume peaks in the early 20's
 - Nerves shrink and atrophy
 - Dendrites are lost
 - Lower cerebral blood flow (CBF).
- Less plasticity to shift neural substrate for varied needs.
- CBF decline is most evident in the frontal lobes
 - Reduced verbal fluency
 - Reduced executive function for planning and organization.
- CBF also declines in the parietal cortex and medi-temporal areas (hippocampus). (memory and constructional skills).

APA.org/research/action/memory.changes.aspx

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Memory loss is not the same as Alzheimer's Disease

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Dementia of the Alzheimer's Type (DAT)

- 60 – 80% of dementia diagnoses
- Mild** initial symptoms are failures to make new memories, rapid forgetting, and confusion and creation of alternative memories. Mood problems of under-arousal.
- Middle** symptoms add confusion, speech and activity performance problems, mood irritability.
- Late** presentation is wholesale memory impairment for old and new information, complete loss of ADL capacity.
- 10 – 15 years from diagnosis to finish. Often diagnosis is delayed 5 years from onset.

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10 Warning Signs of DAT (American Neurological Association)

1. Memory loss
2. Difficulty performing familiar tasks
3. Problems with language
4. Disorientation to time and place
5. Poor or decreased judgment
6. Problems with abstract thinking
7. Misplacing things
8. Changes in mood or behavior
9. Changes in personality
10. Loss of initiative

alzheimer's association
alz.org | 1.800.272.3900

What is normal age related memory loss?

Age-related memory loss is an encoding and retrieval weakness. It is not a "storage limit."

<u>Less Preserved:</u>	<u>More Preserved:</u>
Episodic Source Flashbulb	Semantic (words and facts) Procedural

Psychologists call this Mild Cognitive Impairment (MCI) when it is somewhat more than normal.

(Craik, 1994)

Normal aging brains (cont.)

- Interference vulnerabilities
 - Distraction
 - Brittleness
- Slower processing speed.
- Many cognitive skills are diminished further or in proportion to the presence of anxiety which becomes more prominent with age.
- Only occasional lapses of memory, language, confusion, orientation.

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What's Normal Compensations with age?

- It is NORMAL to blend memory skill training (practicing neumonics) with compensatory strategies (keys by the door, take a picture where you parked) to adjust for age related memory decline.
- It is NORMAL to emphasize good brain health to mitigate age related cognitive decline.
 - Aerobic Exercise (vigorous if possible)
 - Mental exercise (does no harm, may help)
 - New intellectual challenges (volunteer, languages, musical instruments, games and puzzles)
- It is NORMAL to have increased fatigue. People typically pace their lifestyle to accommodate this over time.

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Aging with General Neuropathic conditions.

Yu, Lei; Boyle, Patricia A.; Segawa, Eisuke; Leurgans, Sue; Schneider, Julie A.; Wilson, Robert S.; Bennett, David A. Residual decline in cognition after adjustment for common neuropathologic conditions. *Neuropsychology*, Vol 29(3), May 2015, 335-343. <http://dx.doi.org/10.1037/neu0000159>

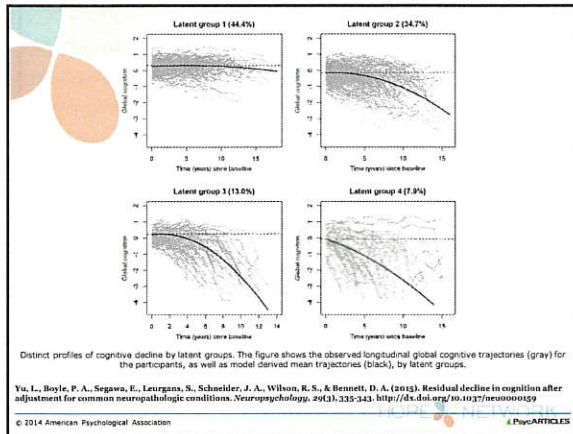
- 876 Autopsied participants (of 2800 enrolled) for 2 cohort studies of aging. (Religious Orders Study and the Rush Memory and Aging Project)
- Annual clinical evaluations and brain donation upon death. 1994- present.
- All free of dementia at baseline.

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Trajectory of cognitive decline from a model without mixture ($k = 1$). The figure shows the raw cognitive data (gray) and fitted values (dark gray) from a linear mixed model ($k = 1$) for a random sample of 100 participants. The black curve corresponds to the fitted mean trajectory.

Yu, L., Boyle, P. A., Segawa, E., Leurgans, S., Schneider, J. A., Wilson, R. S., & Bennett, D. A. (2015). Residual decline in cognition after adjustment for common neuropathologic conditions. *Neuropsychology*, 29(3), 335-343. <http://dx.doi.org/10.1037/neu0000159>

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Yu, et al (2015)

- The declining groups showed:
 - More depressive symptoms
 - More social isolation
 - Reduced engagement of physical and cognitive challenges
 - Physiological markers of reduced cognitive reserve.

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Reason for Hope?

- Dementia has declined in persons over age 65 between 2000 and 2012
- Observational study
- ? Better control of risk factors?
- ? Better educational attainment?

Langa, K, Larson, E, Crimmins, E, Faul, J, Levine, D, Kabeto, M, & Weir, D. (2017). A Comparison of the Prevalence of Dementia in the United States in 2000 and 2012. *JAMA Internal Medicine*, 177, 51-58. doi: 10.1001/jamainternmed.2016.6807

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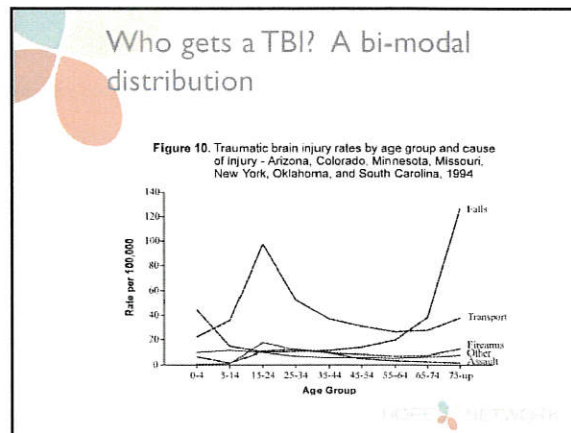
Lessons from the general aging literature:

- The cognitive contributions of burdens are additive and independent.
 - (consider that PTSD shows 2 x the Alzheimer's Disease risk and add that to what we will learn of TBI)
- Sub-clinical and mixed pathologies are common.
- Some people have the markers (e.g. plaques) but no symptoms
- Heterogeneity is more powerful than all the known cognitively impairing influences, accounting for 60% of the variance of outcome scores. (Yu, et. al., 2015).
- Some people (the largest group!) don't really experience substantial decline.

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"Insult to Injury": Now let's add in the effect of a traumatic brain injury...

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Which injury are we talking about?

- Mild Injuries**
 GCS: 13-15
 LOC: none to 30 min.
 PTA: <24 hrs.
 Negative CT/MRI findings
 Transient symptoms resolving in days to 1-2 months.
- Moderate to Severe**
 GCS: 12 or lower
 LOC: >30 min
 PTA: >24 hrs.
 Typically positive CT/MRI findings
 Clinical improvement, but some permanent changes in function.
 Includes Mild Complicated TBI

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Recovery patterns from TBI

Alzheimer's & Dementia: The Journal of the Alzheimer's Association 2014 10, S174-S181 DOI: 10.1016/j.jalz.2014.04.006 Terms and Conditions

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Which aging person are we talking about?

- Injured as a child/young adult and now old.
- Injured as an older adult.

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Injured as an older adult

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Outcomes for older adults with newly acquired TBI

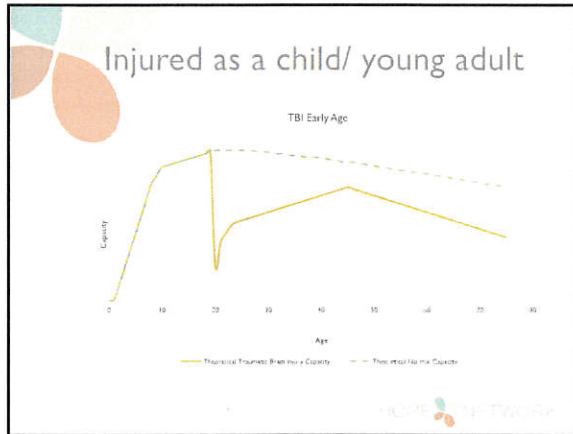
- Longer LOS, slower progress in rehabilitation (Frankel, et. al., 1976)
- More likely to D/C to Nursing than Rehab (Miller & Pentland, 1989)
- Higher TBI mortality (Harrison-Felix, et. al., 2004)
- Higher influence of fatigue on performance
- Higher rates of long-term disability (Cifu, et. al., 1996)
- More impairments in cognition and behavior. Poorer functional outcomes. (Rapoport, et. al., 2006)

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From the new PBE studies:

- 10 centers, 2130 patients. Real world research.
- "A consistent predictor of [lack of] discharge to home."
- "In all cases, the higher the age, the worse the outcome."
- "Higher age predicted poorer motor outcome at 9-month follow-up in all subgroups, and had a similar effect on cognitive outcome, but only for the lowest 3 levels of admission FIM cognitive score"
- (Corrigan, J., Horn, S, et al, 2015) APM&R

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Outcomes for remote TBI older adults

- Reasonably static physical limitations
- Personality change remains persistent or amplified
- Psychosocial disabilities prominent
- Anxiety and depression
- Social isolation
- Impaired quality of life
- Work and social handicaps

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Risk factors exacerbating TBI adjustment with aging

- Immobility
- osteoporosis, balance, falls.
- Swallowing problems.
- Metabolic syndrome.
- Depression.
- Cognitive challenges (reduced functional adaptation).
- Reduced cognitive reserve for Mild Cognitive Impairment.
- Reduced attention to regular health maintenance.
- Resulting premature decreased function and increased mortality.

THE METABOLIC SYNDROME

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Moderator variables for TBI outcomes: Age at injury

- Predicts reduced functional independence
- Predicts reduced social participation
- Fatigue has a greater role in outcome
- There are less perceived barriers (because they avoid challenges)

“Should we slow down because we are getting older, or hurry up because we are not getting any younger?”

Sendroy-Terrill, et. al., 2010

Moderator variables for TBI outcomes: Time since injury

- Predicts reduced physical function
- Predicts reduced cognitive function
- Predicts reduced societal role participation

Sendroy-Terrill, et. al., 2010


Moderator variables for TBI outcomes: Injury Severity

- The **strongest factor** predicting outcome in older adults with TBI.
- Affects cognitive, physical and social functioning.

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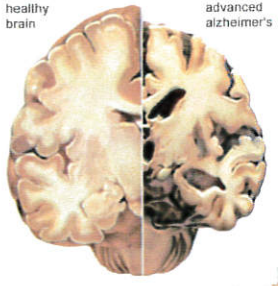
Moderator variables for TBI outcomes: Gender factors

- Women report disproportionately more fatigue
- Women experience more work-related environmental barriers.



Sendroy-Terrill, et. al., 2010

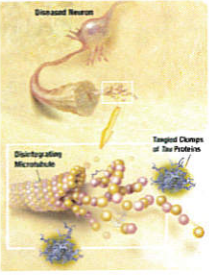
Does TBI cause Alzheimer's Disease (DAT)?



healthy brain advanced alzheimer's

Caution: Advanced Neurobiology:

- TBI does trigger deposits of amyloid- β plaques that build up between nerve cells (Lye and Shores, 2008) and neurofibrillary tangles, or Tau Proteins that build up inside cells (Jurya, et al, 2007) that are hallmarks of DAT.
- An inflammatory response that is part of the neurochemical cascade following injury also contributes to DAT development (Holmes et al, 2009).



Diseased Neuron
Amyloid- β Plaques
Neurofibrillary Tangles
Tangled Clumps of Tau Proteins
Disrupting Microtubule

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Parkinson's Disease (PD) and TBI

- Again, not cause and effect, but some relationships.
- Twin studies of WWII vets support the higher risk of PD after TBI (Goldman et al, 2006).
- The risk is injury severity modulated (Bower, et al, 2003)

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Chronic Traumatic Encephalopathy

- Lots of new attention
- A lot less conclusive science



CONCUSSION
CHRISTMAS

NFL

HCPN NETWORK


CTE conclusions:

- A pattern of chronic neurodegenerative changes in a population exposed to repetitive, cumulative sub-clinical brain insults.
- Formerly known as Dementia Pugilistica ("Punch Drunk")
- Marked by behavioral features of irritability, impulsivity, aggression, depression, suicidality, and some cognitive changes
- MANY confounding lifestyle variables.
- Appears to represent early advance of MCI

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Cut to the conclusions on DAT..

- No relationship to mild TBI
- No strong association to what we understand as CTE
- Not a cause and effect with TBI
- Appears to be an *association* of Dementias of aging and TBI
- Not a certainty. 2.3x – 4x DAT risk likely in moderate to severe TBI (Vincent et. al., 2014)
- Appears to accelerate DAT





Aging with a brain injury

- For mTBI, many symptoms resolve in weeks or months., they almost always resolve to never present a problem again.
- Physical disabilities persist, but are not the biggest challenge for the older adult with TBI
- Personality and psychosocial function are often the biggest barrier.
- Anxiety and depression continue to intensify over time.
- (Senroy-Terrill et al, 2010) (and WMBIN 2008)




So, with no complications, what is it like to age with a brain injury?


Brain Injury as a Chronic Disease

A Chronic Disease is:

- Permanent
- Has non-reversible pathological alterations
- Requires special training for rehabilitation
- May require long periods of observation, supervision, or care.




- Masel, B. E., and DeWitt, D. (2010) Traumatic brain injury: a disease process, not an event. *Journal of Neurotrauma*, 27, 1529-1540.



As a Chronic Disease, TBI is associated with negative outcomes:

- Mortality risk factors:
 - 49 x aspiration pneumonia mortality
 - 22-37 x seizure mortality
 - 4 x general pneumonia mortality
 - 3 x suicide mortality
 - 3 x respiratory mortality
 - 2 x as likely to die in the first year to matched controls
 - 7 year reduction in life expectancy


Masel, B. E., and DeWitt, D. (2010)



As a Chronic Disease, TBI is associated with negative outcomes:

- Reduced mobility equates to reduced life expectancy
- Seizure complications 1.5 – 17 times more likely to have them
- Sleep disorders (rates as high as 70%) with cardiac and other implications.
- Neuroendocrine and metabolic implications
- Sexual dysfunction implications
- Chronic bowel and bladder implications (UTI infections, etc.)
- TBI needs to be managed as a Chronic Disease is managed.

Masel, B. E., and DeWitt, D. (2010)



Preventing age related cognitive decline in TBI.

- Mobility
- Socialization
- Cognitive engagement
- Treatment and assessment of normal age-related issues
- Treat and manage TBI as a chronic health condition

Anticipate
Protect
Early intervention
Adapt

Programming for older adults with TBI

- Diet: good nutrition / avoid toxins (tobacco, alcohol, poorly tolerated medication like opiates and benzodiazepines).
- Fitness: not Body Combat™ but some appropriate movement with a focus on aerobic activity.
- Focus on Fall Risk. Assess balance, safety, and injury prevention
- Watch for family caregiver strain. Patient outcomes are tied to Caregiver coping and social support.
- Support partnerships and networks for aging resources
- Don't forget the regular aging protocols (pap smears, mammograms, prostate exams, colonoscopies, cholesterol checks) (Women and minorities may often be overlooked with this.)

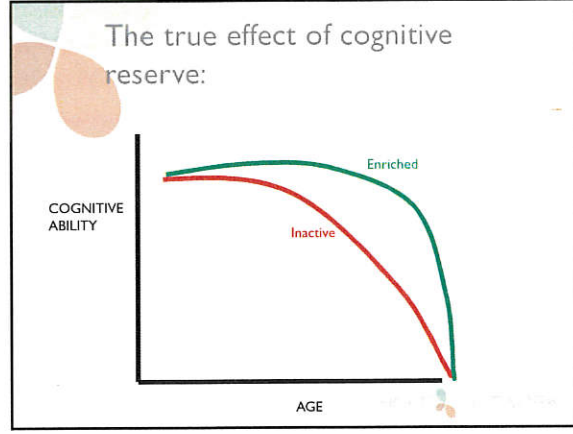
What helps keep an injured brain healthy? Same as a healthy brain!

Cognitive activity that builds COGNITIVE RESERVE. Memory activities, Problem solving and visual skills/puzzles, musical skill, fine motor skills, volunteer work, reading and professional activities.

ACTIVE study showed relatively minimal interventions can have a meaningful effect. (10 75 min training sessions)

Reference: Rebok, G. W., et al. "Ten-Year Effects of the Advanced Cognitive Training for Independent and Vital Elderly Cognitive Training Trial on Cognition and Everyday Functioning in Older Adults." *Journal of the American Geriatrics Society* 2014; DOI: 10.1111/jgs.12607.

- **Physical Activity:** (aerobic exercise) (increases hippocampus size and corresponding gains in memory performance.)
- **Nutrition / general health maintenance** (Healthy bodies, Healthy brains: Blood pressure management and Diabetes management.)
- **Managing Mental Health** (depression and anxiety are associated with significant and irreversible cognitive decline.)



Keep at it! It is hard work but worth it!


Conclusions:

- The person matters more than the injury. Most of the variability is not due to the injury. When it is the injury, it is the severity that matters for aging effects.
- The age at the time of injury means a lot for the effects on outcome in the future.
- TBI is a chronic disease and has lifelong implications for many physical, psychological, and social outcome criteria



More conclusions...

- Personality and social behavioral problems can be the biggest limiting factor for quality of life.
- Mitigating factors of isolation, anxiety, depression, and activity all have a big influence on cognition.
- There are modifiable factors that mitigate age related decline in normal and TBI aging.




Thank You!

- Martin Waalkes, Ph.D., ABPP, CBIS-T





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