TBI-BH ECHO

Traumatic Brain Injury – Behavioral Health ECHO

UW Medicine | Psychiatry and Behavioral Sciences

TBI-BH ECHO 2026

Neuropsychiatric and neurocognitive disorders after TBI

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Project ECHO

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Speaker Disclosures

No conflicts of interest

- **The following series planners have no conflicts of interest:**
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  - Jess Fann, MD
  - Cherry Junn, MD
  - Chuck Bombardier, PhD
  - Cara Towle, MSN, RN, MA

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Objectives

1. Grasp a basic understanding of localization theory and neurological networks
2. Understand the mechanisms and pathophysiology of TBI
3. Understand the neuropsychiatric sequalae of TBI and an approach to treatment
4. Understand the association between TBI and neurodegeneration

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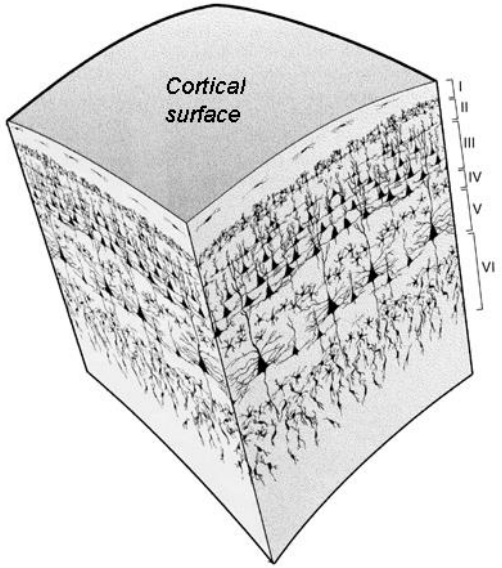
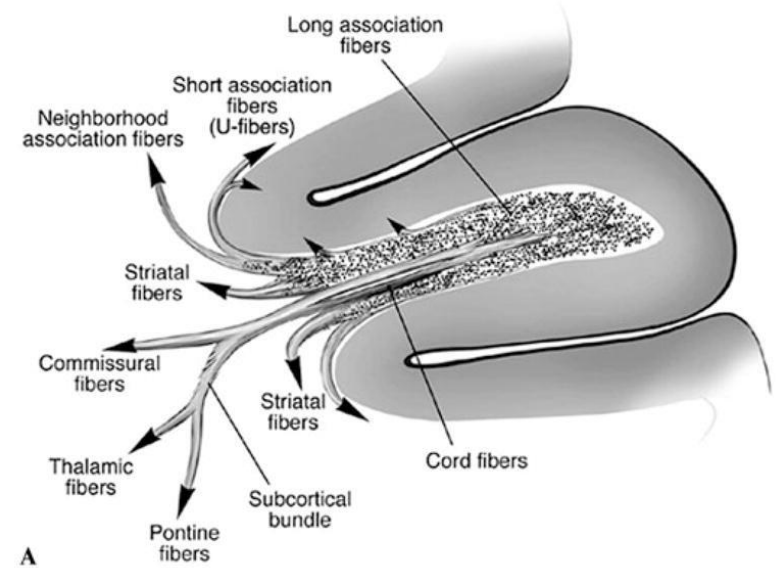
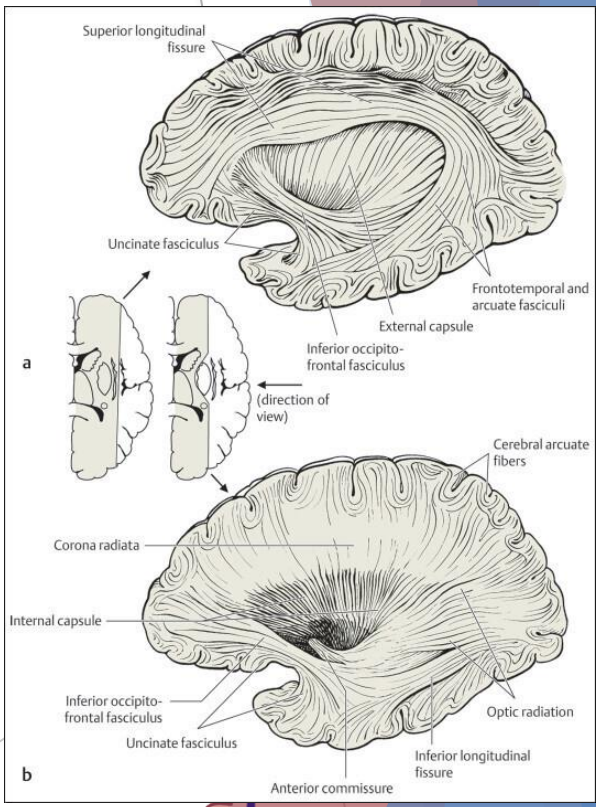
Localization theory

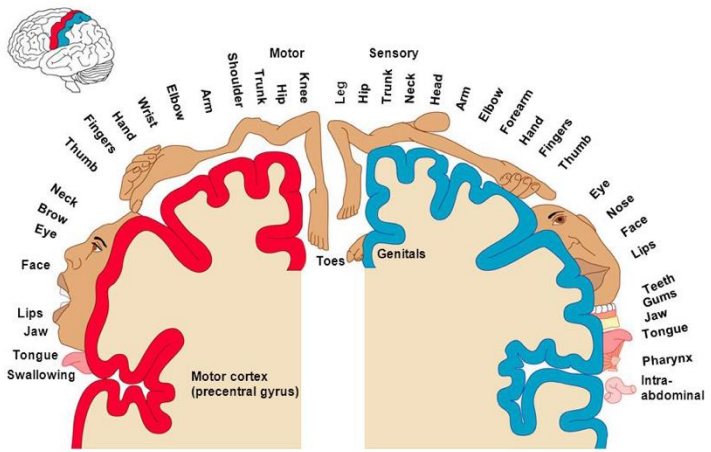
- A patient presents with a symptom or set of symptoms
- Generate a set of hypotheses about what part(s) of the nervous system may be involved
- Use the exam to empirically challenge those hypotheses and yield a localization
- Historical features (speed of onset, evolution, exacerbating or alleviated factors) contextualized by the localization generate the differential diagnosis
- Ancillary testing (MRI, EEG, EMG) probe the likelihood of different diagnoses in the differential

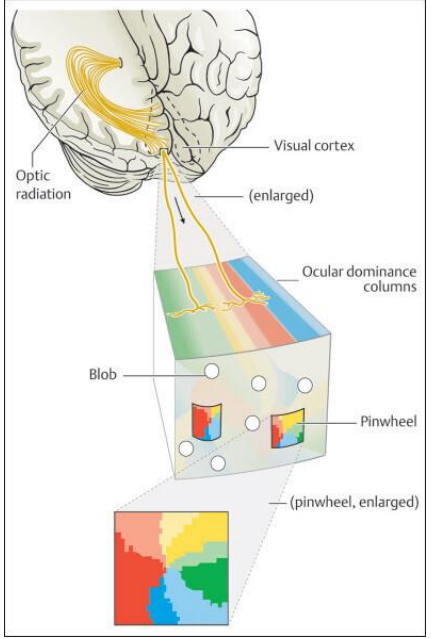
The nervous system is organized into networks of interconnected brain regions

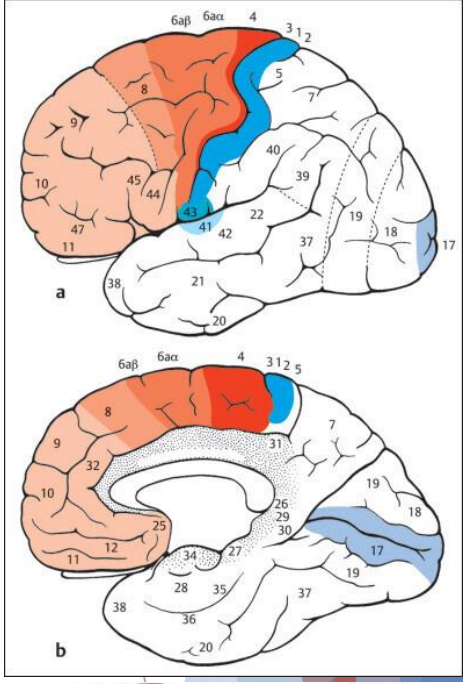







Motor
Sensory
Shoulder
Arm
Elbow
Wrist
Hand
Fingers
Thumb
Trunk
Hip
Knee
Leg
Neck
Brow
Eye
Face
Lips
Jaw
Tongue
Swallowing
Toes
Genitals
Head
Forearm
Eye
Nose
Face
Lips
Teeth
Gums
Jaw
Tongue
Pharynx
Intra-
abdominal
Motor cortex
(precentral gyrus)


Optic
radiation
Visual cortex
(enlarged)
Ocular dominance
columns
Blob
Pinwheel
(pinwheel, enlarged)


6aβ
6aα
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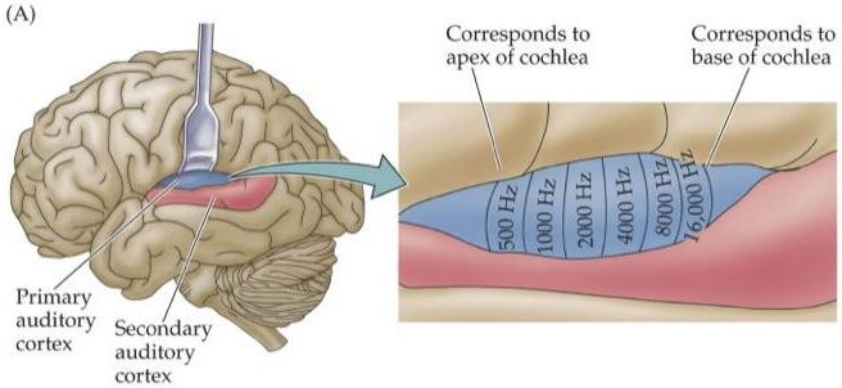
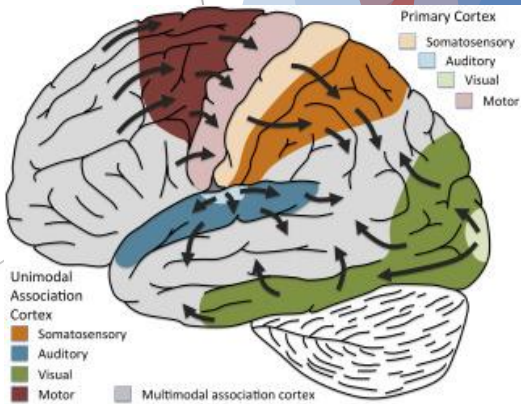
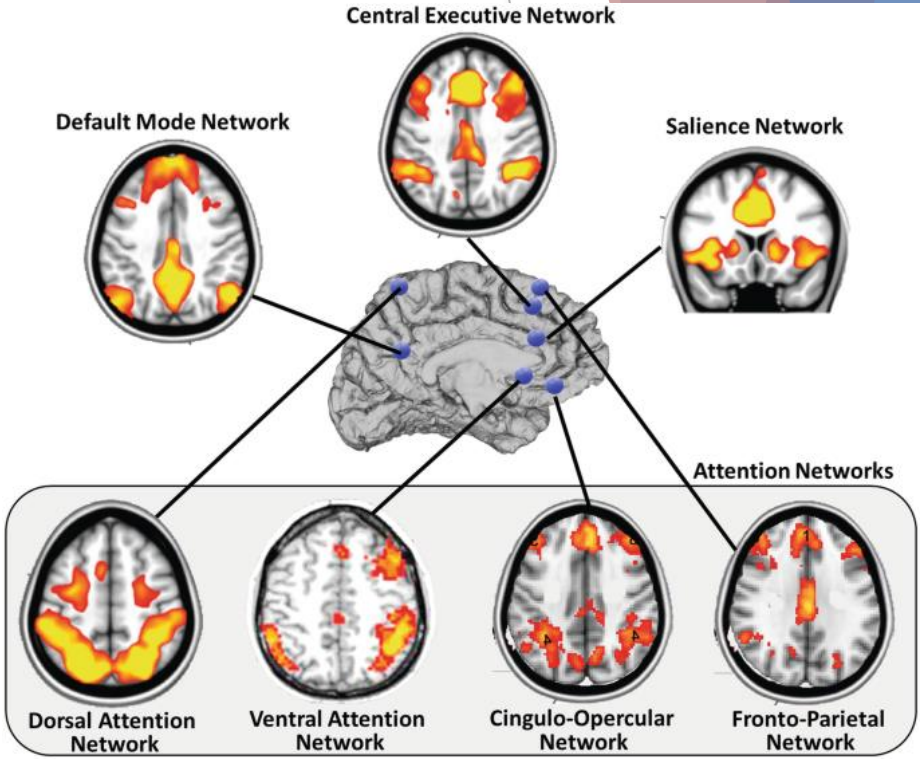

(A)
Corresponds to
apex of cochlea
Corresponds to
base of cochlea
500 Hz
1000 Hz
2000 Hz
4000 Hz
8000 Hz
16,000 Hz
Primary
auditory
cortex
Secondary
auditory
cortex


Primary Cortex
Somatosensory
Auditory
Visual
Motor
Unimodal
Association
Cortex
Somatosensory
Auditory
Visual
Motor
Multimodal association cortex

- Cognition and behavior are supported by the activity of anatomically distributed networks
- Cognitive problems and behavioral problems can be understood as network-level problems



TBI: From the macroscopic to the microscopic and back again

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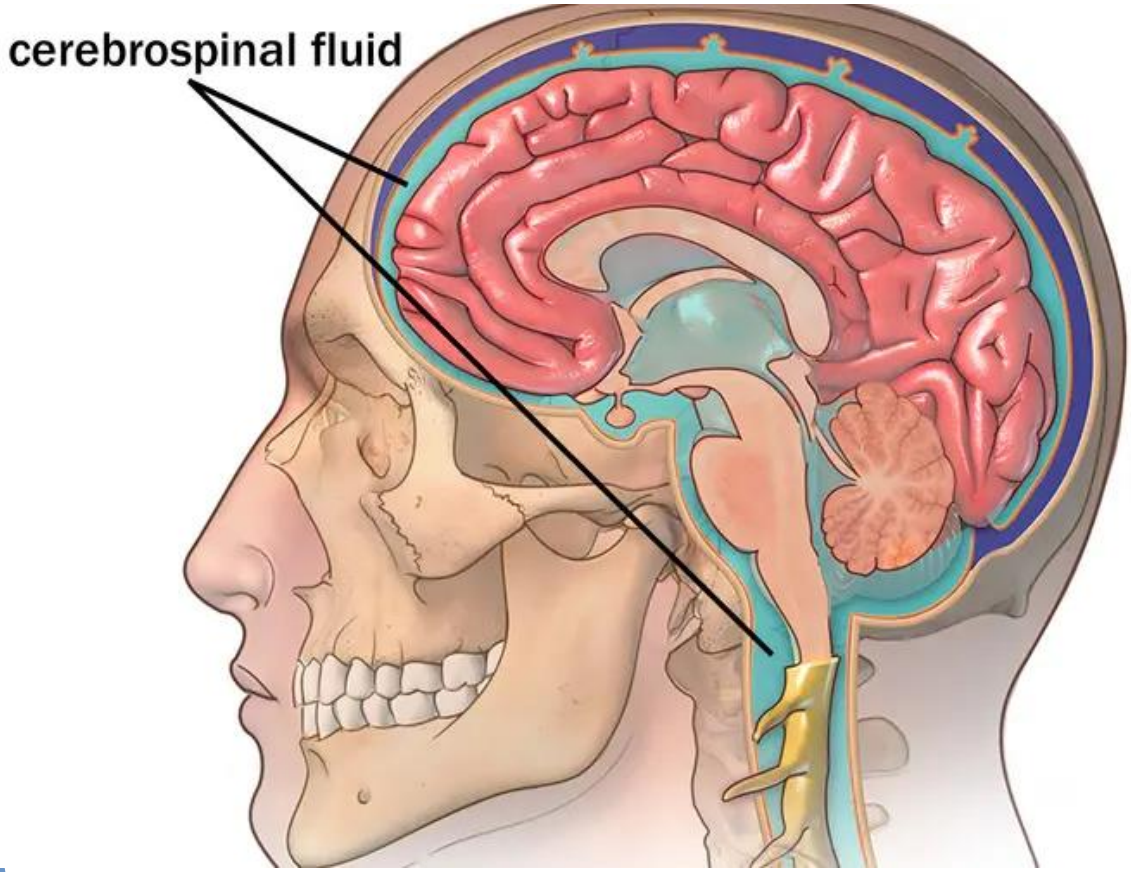

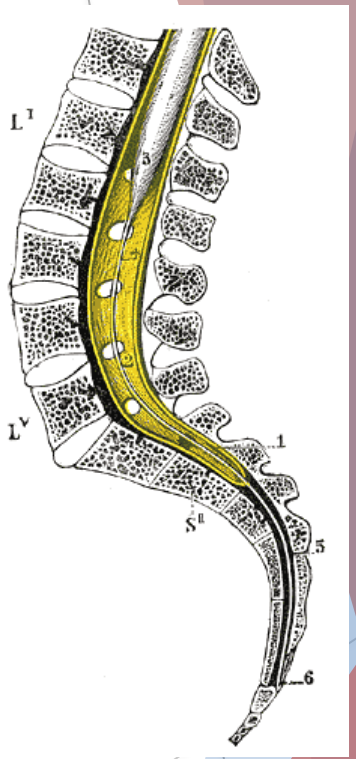

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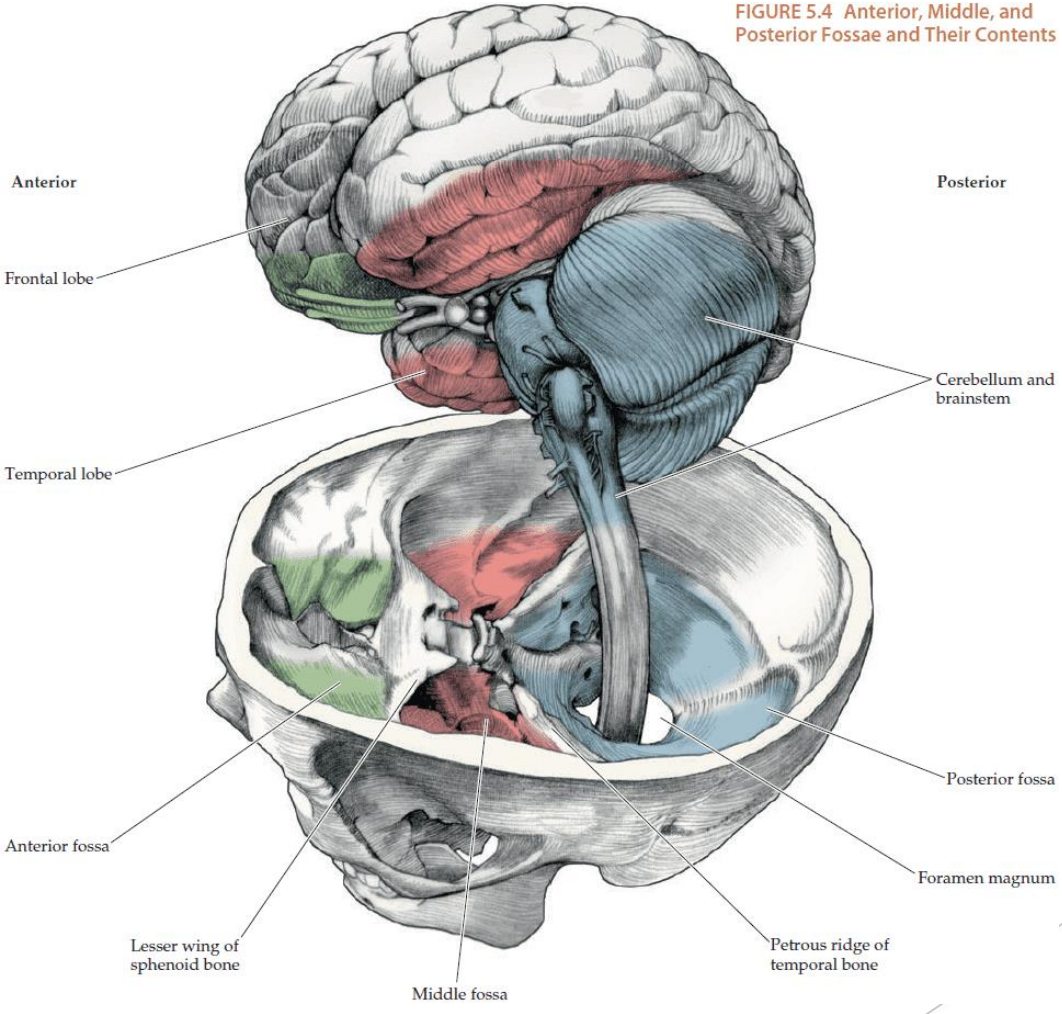
FIGURE 5.4 Anterior, Middle, and Posterior Fossae and Their Contents



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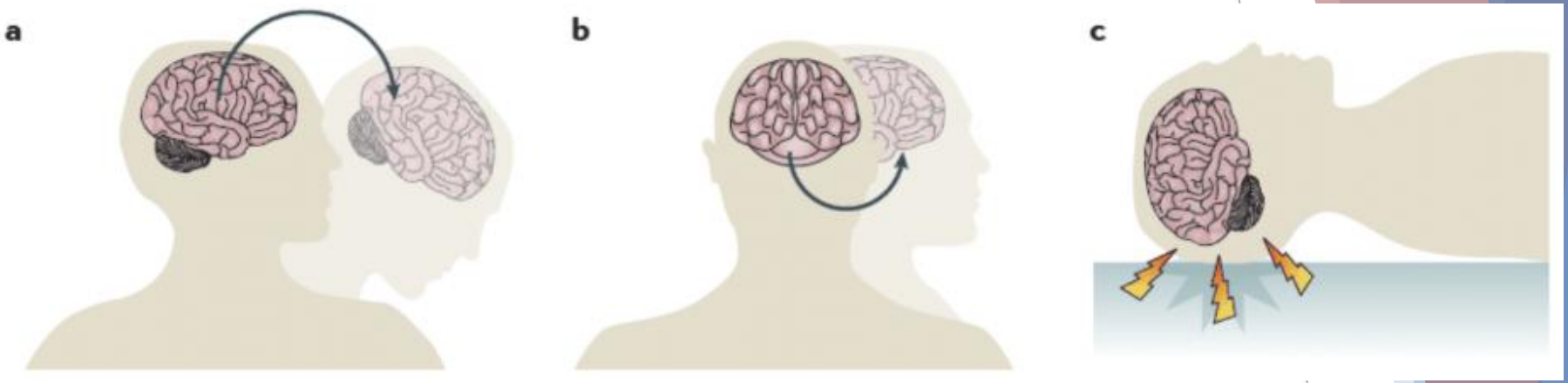
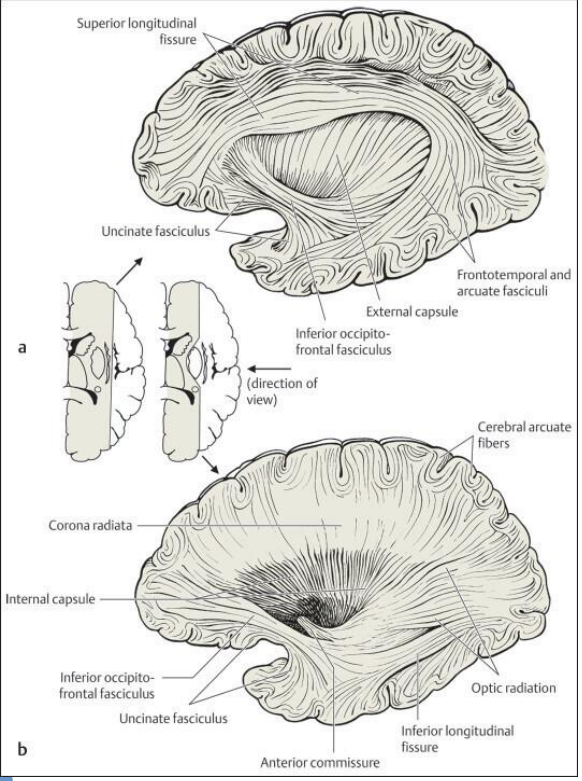


	Mild TBI	Moderate TBI	Severe TBI
Structural Brain Imaging	Normal	Normal or Abnormal	Normal or Abnormal
Loss of Consciousness	0-30 min	30 min to 24H	>24H
Altered Mental State	≤24H	>24H	>24H
Post-traumatic Amnesia	≤1 Day	1-7 Days	>7 Days
Glasgow Coma Scale score	13-15*	9-12*	<9*

*Best score achieved in the first 24H after trauma



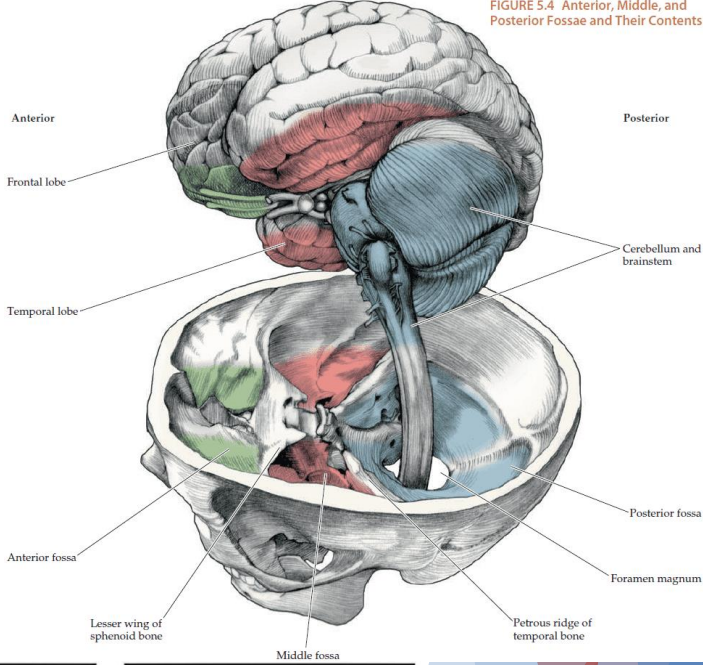
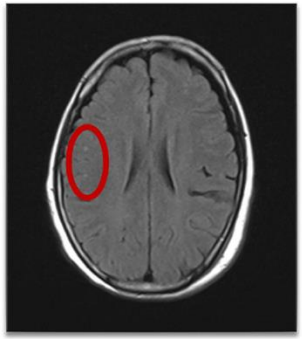
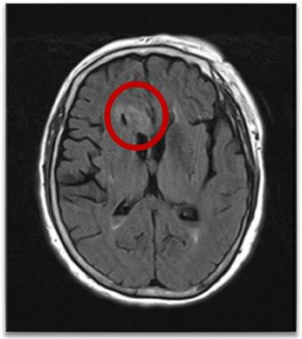


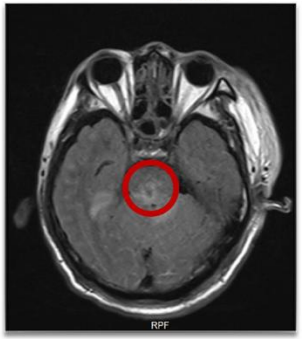
FIGURE 5.4 Anterior, Middle, and Posterior Fossae and Their Contents



DAI grade 1



DAI grade 2



DAI grade 3

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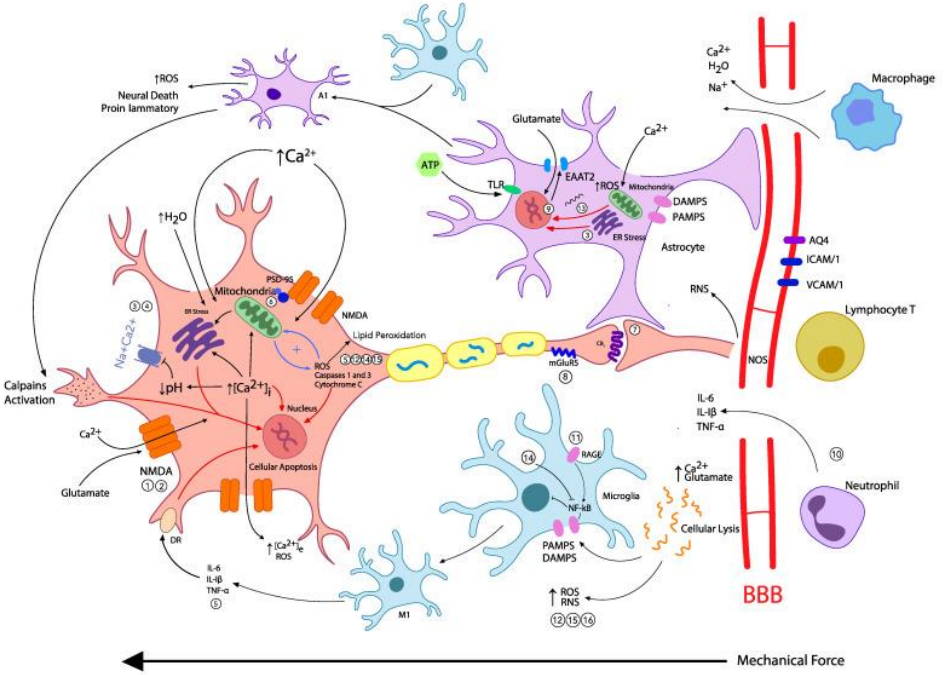
Pathophysiology

- Mechanical deformation of neurons leads to large release of neurotransmitters like glutamate as well as activation of immune system
- Glutamate activity increases intracellular movement of calcium
- Initiation of intracellular processes that lead to cytotoxicity and cell death



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TBI context

- TBI patients are not a random sample of the general population
  - Higher rates of pre-injury psychiatric illness and substance use
  - This can complicate rehabilitation and treatment
- The meaning of the injury
  - Individuals with pride in intelligence or who depend on intelligence for work may be devastated by small decrement
- Psychosocial supports
  - Pain, communication impairment, social disconnection

Factors	Biological	Psychological	Social
Predisposing vulnerabilities	Illness and disease. History of previous functional symptoms.	Personality traits. Poor attachment/coping style. Emotional disorder.	Adverse life events or stressors. Childhood neglect. Difficulties in interpersonal relationships. Symptom modelling. Financial difficulties/deprivation.
Precipitating mechanisms	Physical injury or state (eg, drug side effect). Abnormal physiological event (eg, hyperventilation and sleep paralysis).	Panic attack. Perception of life event as traumatic/negative.	Adverse life events or stressors.
Perpetuating factors	Plasticity in sensory and motor pathways leading to abnormal movement patterns. Deconditioning. Fatigue. Chronic pain.	Illness beliefs (person and significant others). Feeling disbelieved. Maladaptive behaviours. Co-morbidities including anxiety and depression.	Diagnostic uncertainty (eg, ongoing medical investigations). Reliance on care and benefits. Compensation claims. Ongoing social stressors (eg, relationship difficulties, financial hardship and loss of roles).

Neuropsychiatric and neurocognitive sequelae and their treatments

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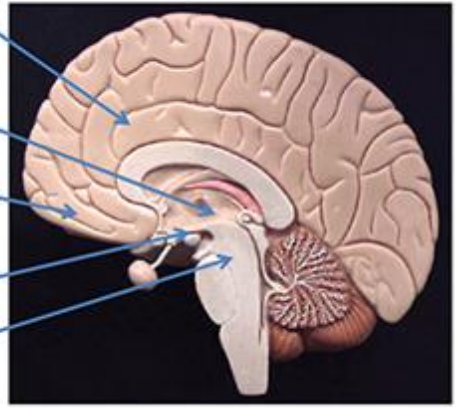
Anterior cingulate cortex:
Apathy

Entorhinal-hippocampal complex:
Impaired attention, working memory, declarative memory (lateral to this medial sagittal view)

Ventral frontal cortices:
Disinhibition, irritability, emotional dysregulation, agitation, aggression

Amygdala:
Affective placidity, Kluver-Bucy-like presentations; occasionally, anxiety

Reticular system:
Impaired arousal, inattention



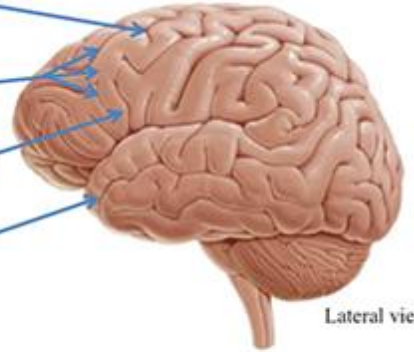
Medial view

Dorsolateral prefrontal cortex:
Impairments in executive control of attention, memory, language, motor planning, sequencing, set shifting, abstraction, judgment, insight

White matter:
Slow, inefficient information processing; impaired functions supported by the areas connected

Inferolateral prefrontal cortex:
Working memory impairments

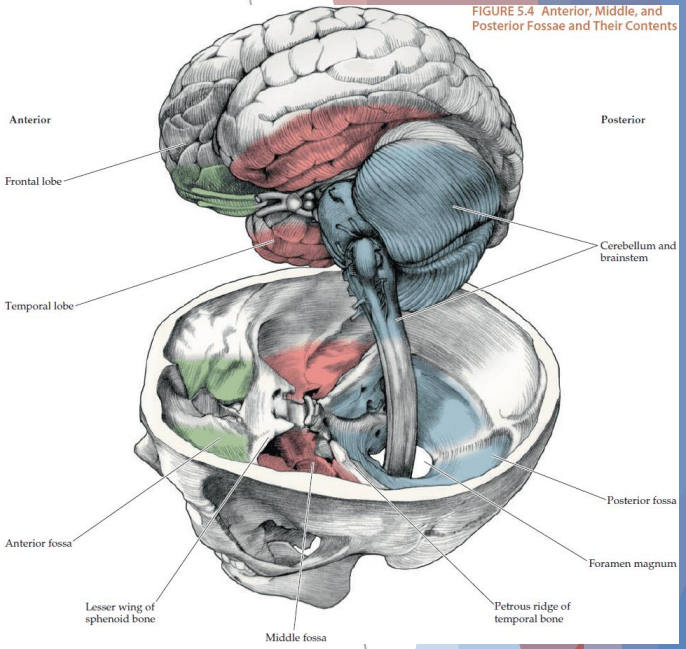
Anterior, polar temporal cortex:
Disturbances in semantic memory, facial, social and emotional processing, impaired social/ empathic function



Lateral view

Source: Arthur J. Barsky, David A. Silbersweig, Robert J. Boland:
Depression in Medical Illness
www.neurology.mhmedical.com

FIGURE 5.4 Anterior, Middle, and Posterior Fossae and Their Contents



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General therapeutic principles

- No FDA approved medication for post-TBI conditions
  - "Treatment-by-analogy"
  - Treat inattention following TBI similarly to inattention of ADHD
- Choose medications which benefit multiple issues
  - Methylphenidate for inattention AND depression
  - Amitriptyline for agitation AND insomnia AND headache (although watch cognitive impact)
  - VPA for agitation AND seizure
- Start low, go slow. May be unusually sensitive to psychotropic medications
- Stay the course. Adequate dose, adequate duration
- TBI is a dynamic process.
  - Treatments that work in acute/subacute phase may be less useful in chronic phase (for example amantadine)

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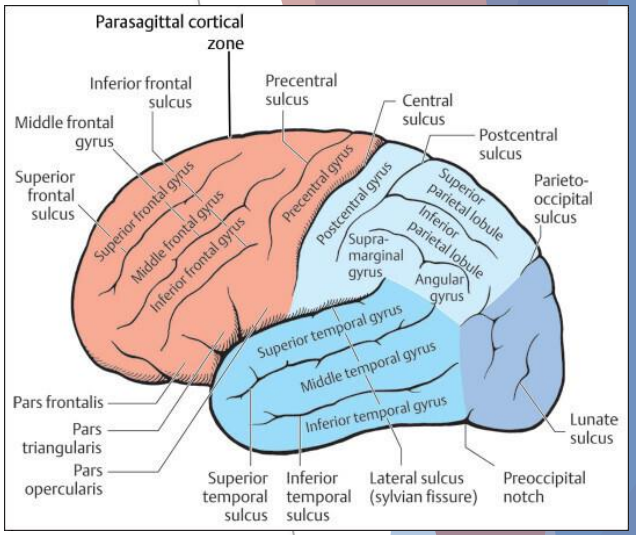
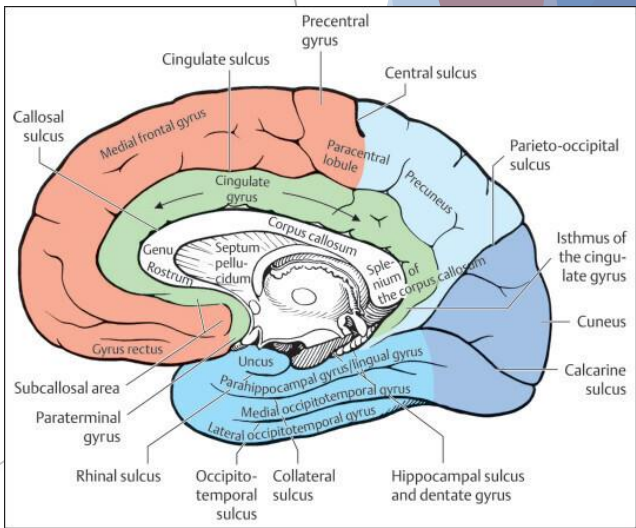
General therapeutic principles

- Aggressively manage other issues: sleep, mood disorder, substance abuse, chronic pain, migraine
- Cognitive, social, physical stimulation
- Speech therapy for cognitive rehab
- Rehab psych (typically through PM&R clinic)
- Consider the biopsychosocial model to guide a logic for understanding the patient's situation and where improvements could be made

Dysexecutive and neurobehavioral issues: “their personality has changed”

- Executive dysfunction
- Impulsivity
- Irritability, agitation, aggression
- Emotional lability
- Disordered motivation





Treatment considerations: Cognition

SPECIAL COMMUNICATION · Volume 107, Issue 4, P753-760, April 2026 Download Full Issue

Practice Guideline for Methylphenidate Use in Persons With Traumatic Brain Injury: Report of the American Congress of Rehabilitation Medicine

David B. Arciniegas, MD [a,b] · Ronald T. Seel, PhD [c] · Stephen N. Macciocchi, PhD [d] · ... · Douglas I. Katz, MD [h] · Tolu O. Oyesanya, PhD, RN [i] · Amy K. Wagner, MD [j] ... Show more

- **Methylphenidate**
  - **Indication: Disordered attention, processing speed, working memory, executive function, depression**
    - **Helpful for depressive symptoms especially if rapid response is desired**
  - **Goal dose: 0.3 mg/kg BID**
    - **Start 5 mg QD or BID. Increase in increments of 5 mg every 3-7 days**
  - **Not associated with treatment-related seizures even in those with post-traumatic epilepsy**
  - **Avoid in setting of: high opioid use, pregnancy, substance use, cardiovascular disease, certain psychiatric conditions (schizophrenia, bipolar, severe anxiety)**
- **Acetylcholinesterase inhibitor? (donepezil, rivastigmine)**
  - **Mixed data**
  - **May help with post-traumatic memory loss**

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Treatment considerations: Irritability, agitation

- Propranolol
  - Typically, first line
- Clonidine
- Anti-epileptic drugs (valproic acid, carbamazepine)
- Antidepressants (sertraline, escitalopram, amitriptyline)
- Antipsychotics (quetiapine, risperidone, olanzapine)
  - Caution: lowered seizure threshold, EPS, cognitive impact

Treatment considerations: Emotional lability

- SSRIs (sertraline, escitalopram, citalopram, fluoxetine)
- SNRIs (venlafaxine, duloxetine)
- Lamotrigine

Treatment considerations: Disorders of motivation

- All based on small studies:

- Methylphenidate
- Amantadine
- Bromocriptine
- Donepezil
- Fluoxetine

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Psychiatric Disorders

- Depression
- Anxiety
- Mania
- PTSD
- Psychosis

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Treatment considerations: Depression and Anxiety

- Depression
  - Sertraline, citalopram, escitalopram, fluoxetine
    - Placebo component likely
    - Sertraline, citalopram, escitalopram preferred due to less anticholinergic effects
  - Methylphenidate
    - At least as effective as sertraline with added benefit to fatigue and cognition

- Anxiety
  - SSRI/SNRI
  - Buspirone
  - Psychotherapy

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Treatment considerations: PTSD

- SSRI/SNRI
- Prazosin for PTSD-nightmares
- Caution with benzodiazepines
  - Sedation, inattention, impaired memory
  - Inhibition of prefrontal cortex -> disinhibition with worsening impulsivity

Treatment considerations: Psychosis

- Post-injury delirium can be associated with psychosis. Should resolve.
- Consider post-traumatic epilepsy with peri-ictal or postictal psychosis.
- Separate from other causes of psychosis such as schizophrenia or neurodegenerative conditions
  - Schizophrenia: more often have negative symptoms
  - Neurodegenerative: more often involve visual hallucinations, cognitive issues, progressive

Treatment considerations: Psychosis

- Anti-psychotics +/- anticonvulsant, anti-depressant

- Special considerations
  - If seizures or mood disorder present treat those as starting point
  - If traumatic-epilepsy is present then careful with anti-psychotics given lowered seizure threshold
  - May be more susceptible to adverse effects (sedation, anticholinergic effects, extrapyramidal symptoms)
  - Aggressively manage other issues: sleep, mood disorder, substance abuse, chronic pain, migraine

TBI and neurodegeneration

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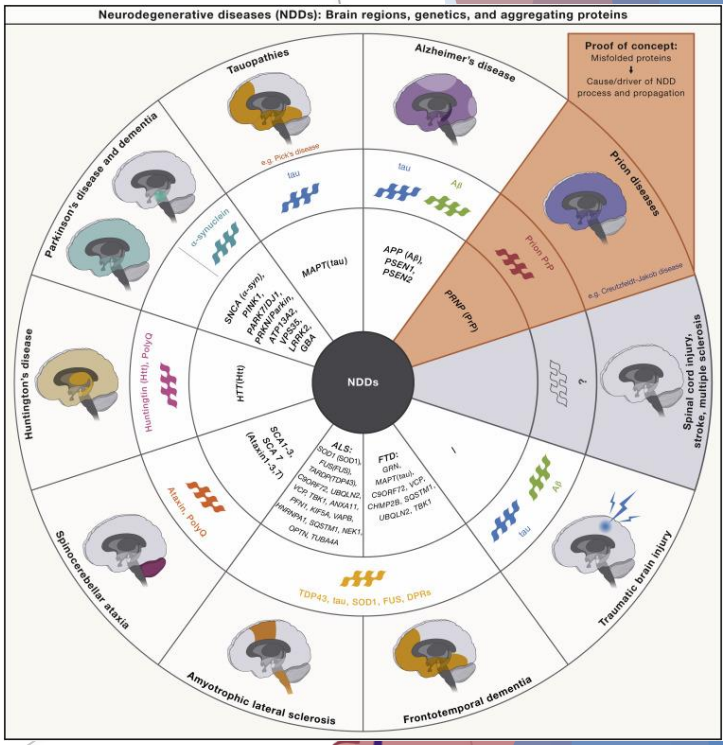
Brief neurodegeneration terminology

- Mild Neurocognitive Disorder (Mild Cognitive Impairment
- Major Neurocognitive Disorder (Dementia)

- Alzheimer Disease (Beta-amyloid, 3R/4R Tau)
  - Amnestic, PCA, lvPPA, dysexecutive, behavioral, CBS
- Lewy Body Disease (synuclein)
  - Dementia with Lewy Bodies, PCA
- Frontotemporal lobar Degeneration (3R Tau, 4R Tau, TDP-43, FUS)
  - bvFTD, svPPA, nfvPPA, PSP, CBD
- Chronic Traumatic Encephalopathy (3R/4R Tau)
  - Traumatic Encephalopathy Syndrome



Wilson et al. Hallmarks of neurodegenerative diseases. 2023.

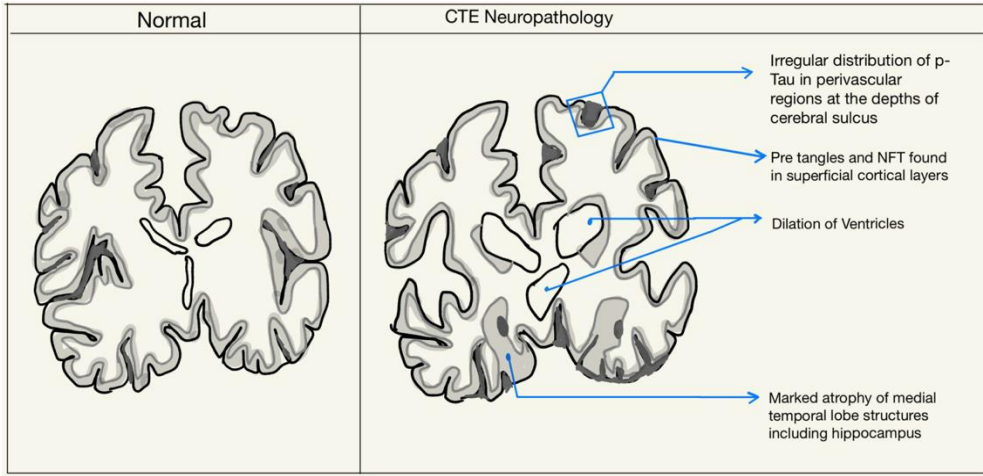
Single TBI and neuro-degenerative disease (non CTE)

- Caution about “reverse causality”
  - Head injury may have occurred because of early stages of neurodegenerative process (falling). Clinician may falsely assume the head injury caused the then noted progressive cognitive impairment.
- Lifetime TBI of any severity increases risk for all-cause dementia, AD, PD, LBD, ALS, FTLD
  - Higher risk in moderate to severe TBI or multiple TBIs
  - 1.2-1.5x increased odds of dementia associated with prior mild TBI
  - Dementia incidence are ~30% higher after TBI compared to non-TBI trauma control

Chronic Traumatic Encephalopathy

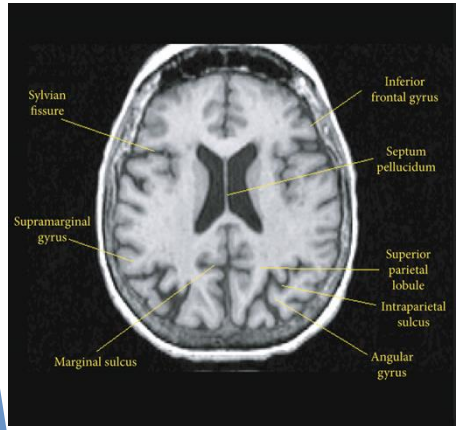
- CTE is a neuropathological diagnosis made at autopsy
  - Defined by presence of phosphorylated tau aggregating in neurons and astrocytes in the depth of cortical sulci
  - It is different then other conditions associated with tau (AD, PSP, CBD, FTD)

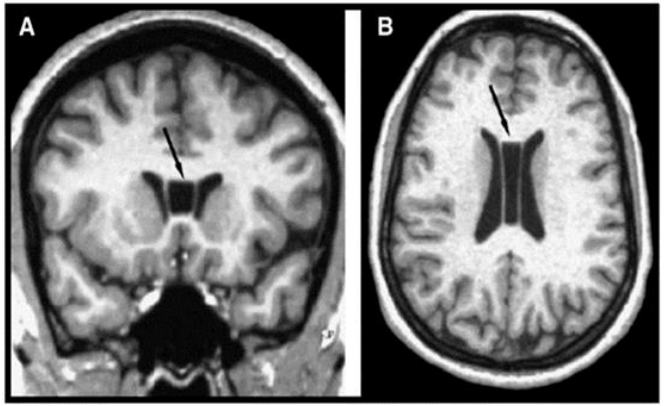
- Traumatic Encephalopathy Syndrome (TES) has been proposed as the clinical syndrome which results from the pathological state of CTE



Traumatic Encephalopathy Syndrome

- Substantial repetitive head injury (>5 years of football with >2 years high school or military exposure or domestic violence or vocation involving head impacts)
- Cognitive decline: Memory loss and/or executive dysfunction
- Neurobehavioral dysregulation: anger issues, impulsivity, irritability/explosivity
- Progressive course
- Supportive: parkinsonism, other psychiatric features (apathy, depression, anxiety)





- Cavum septum pellucidum is the separation of the septal leaflets separating the lateral ventricles.
- Seen in up to 65% of CTE brains
- But it can be seen in ~30% of non head-trauma cohort.

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Challenges with TES/CTE

- No in-vivo biomarker
- Frequent co-pathology
- Cognitive symptoms are common after TBI. Roughly half of mTBI patient report incomplete recovery after 12 months.
- Complexity increases with the elderly given the higher likelihood of preexisting incipient neurodegenerative disease.
  - Symptom onset related to TBI or from culminating neurodegeneration?

- Manage cognitive symptoms, neuropsych symptoms, sleep, pain. Monitor for progressive cognitive syndrome.

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Prevention

- CTE has a clear environmental trigger –> TBI.
- Thus, avoid TBI -> avoid CTE (and lower risk of other neurodegenerative diseases)
- Clinician's role:
  - Neuropathy
  - CV conditions
  - PT for balance therapy or falls clinic
  - Care with meds on Beer's List in the elderly
  - Advocate for seatbelt wearing

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