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Traumatic Brain Injury – Behavioral Health ECHO

UW Medicine | Psychiatry and Behavioral Sciences

TBI and After: Psychosis, Movement disorders, and CTE

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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:

- ✓ Jennifer Erickson DO
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- ✓ David Minor
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- ✓ Lauren Miles

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Objectives

1. What is Traumatic Brain Injury (TBI)?

2. What are the neurological and neuropsychiatric sequela of TBI? How should I think about psychosis and movement disorder?

3. What is Chronic Traumatic Encephalopathy (CTE)?

4. What are risks for CTE? What are preventative strategies?

A Case

- N.E. is a 38 year old man. He is a professional featherweight boxer who began fighting at age 16. He retired at age 23 due to tremor and unsteadiness. He does not drink alcohol.
- He has been knocked out twice. Once for 1 hour.
- On exam: staggering gait, masklike facial expression, manual tremor, normal intelligence
- Work-up: Blood Wassermann reaction negative, serological and spinal fluid testing negative
- Conclusion: paralysis agitans due to punch drunk

PUNCH DRUNK *

HARRISON S. MARTLAND, M.D.
NEWARK, N. J.

JOUR. A. M. A.
OCT. 13, 1928

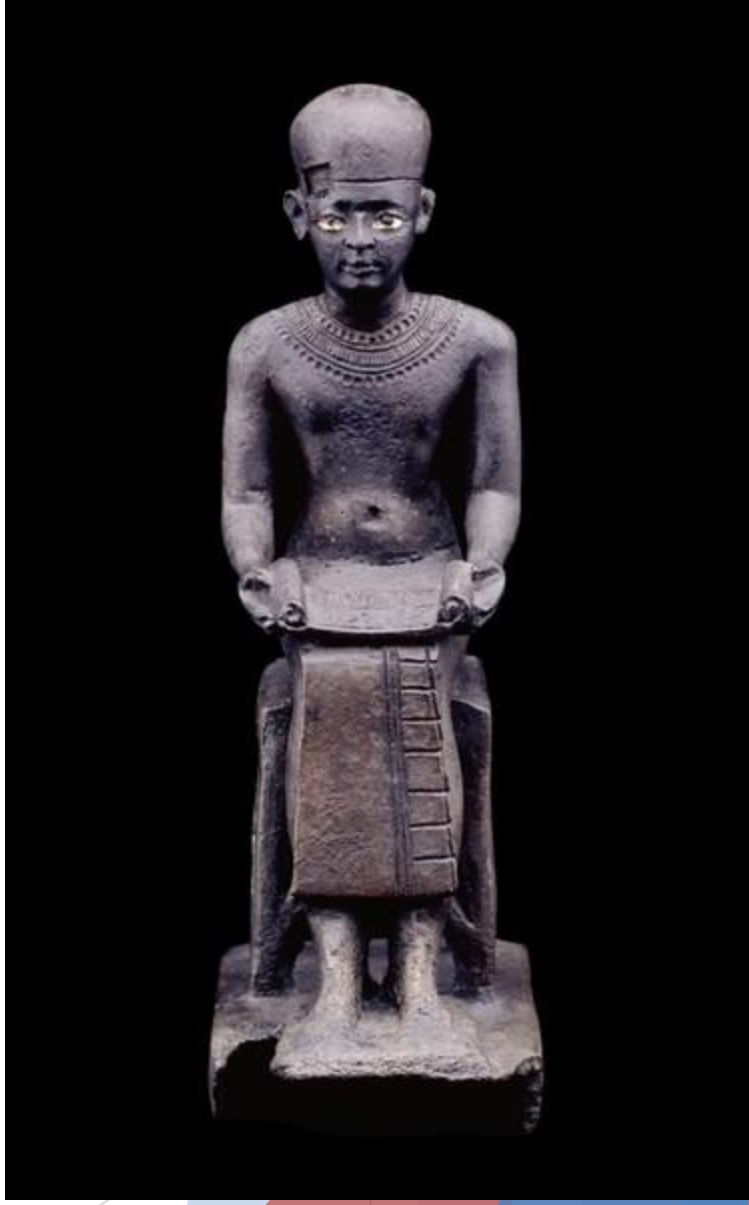
List of Fighters Known by One Promoter to be "Punch Drunk"

No.	Initials	Class	Has Fought	Present Condition
1	B. N.	LHW	Joe Gans	Parkinsonian syndrome
2	J. D.	HW	Weinert, Fulton	Drags leg; bad shape
3	J. T.	LW	Leonard, Kansas, Dundee, Tendler	Drags leg; talks slow
4	B. B.	LW	Walker, Tendler	Punch drunk
5	W. J.	LW	Dundee, Leonard	Punch drunk
6	F. J.	HW	Willard, Weinert	Punch drunk
7	A. W.	LW	.....	Asylum
8	B. M.	HW	Moran, Tunney	Asylum
9	J. G.	HW	Sharkey, Jeffries, Fitzsimmons, Johnson	Asylum
10	C. S.	MW	.....	Asylum
11	J. C.	....	.....	Drags leg; talks slow; thinks slow
12	J. R.	....	.....	Punch drunk
13	M. D.	....	.....	Punch drunk; almost blind
14	C. C.	....	.....	Punch drunk
15	T. S.	....	.....	Punch drunk
16	J. S.	....	.....	Punch drunk
17	R. S.	....	.....	Punch drunk
18	S. M.	....	.....	Punch drunk
19	P. J. G.	....	.....	Punch drunk
20	T. T.	....	.....	Punch drunk
21	B. M.	....	.....	Punch drunk
22	J. H.	....	.....	Punch drunk
23	D. P.	....	.....	Punch drunk

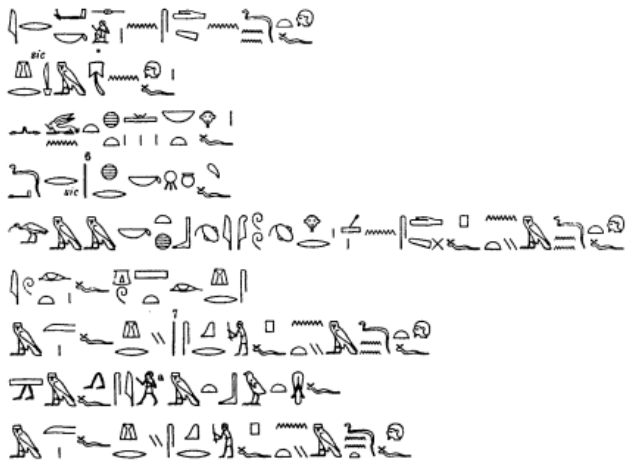
Edwin Smith Surgical Papyrus

- The Old Kingdom (2780 – 2200 BC)
- Author was likely a surgeon following Egyptian armies. Suggested to be Imhotep (“father of Egyptian medicine”)

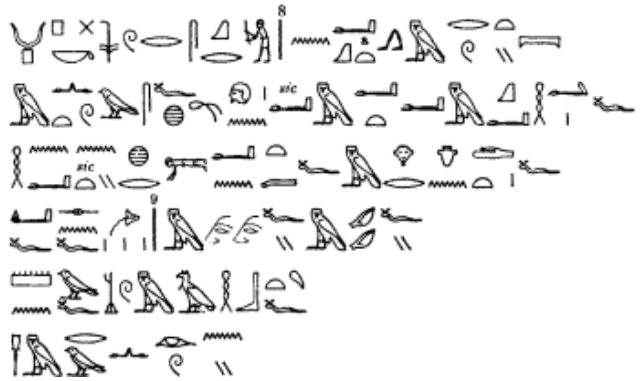
- “An ailment which I will treat”
- “An ailment with which I will contend”
- “An ailment not to be treated”



Case 8 – Instructions concerning a smash in his skull under the skin of his head



If thou examines a man having a **smash of his skull**, under the skin of his head, while there is nothing at all upon it, thou shouldst palpate his wound. Shouldst thou find that there is a swelling protruding on the outside of that smash which is in his skull, while his **eye is askew because of it, on the side of him having that injury** which is in his skull; and **he walks shuffling with his sole, on the side of him having that injury** which is in his skull.



Thou shouldst account him one whom something entering from outside smitten, as one who does not release the head of his shoulder-fork, and one who does not fall with his nails in the middle of his palm; while he discharges blood from both his nostrils and from both his ears and he suffers with stiffness in his neck. **An ailment not to be treated**.

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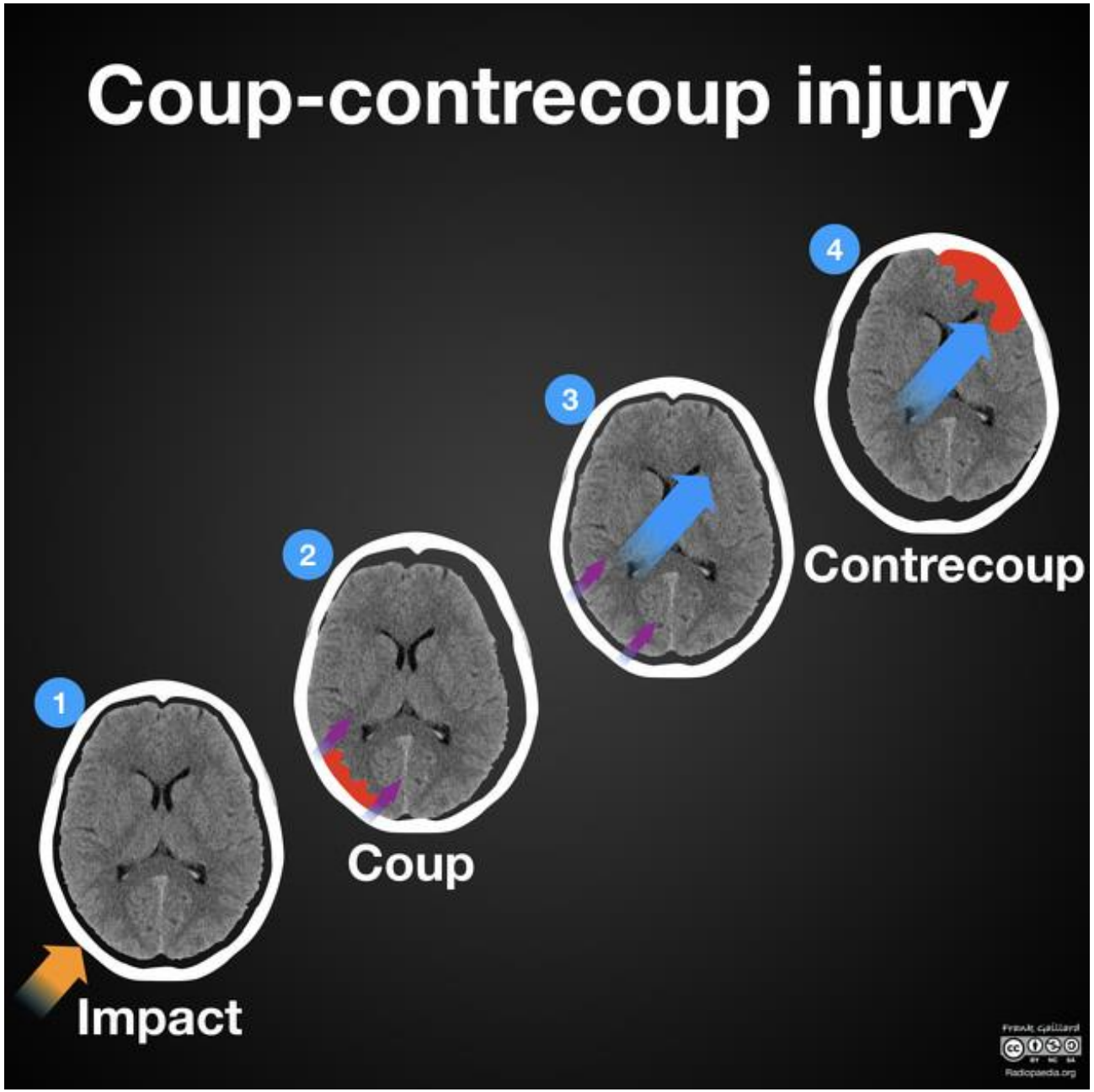
Coup-contrecoup injury
1
2
3
4
Impact
Coup
Contrecoup
Radiopaedia.org

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Traumatic Brain Injury (TBI)

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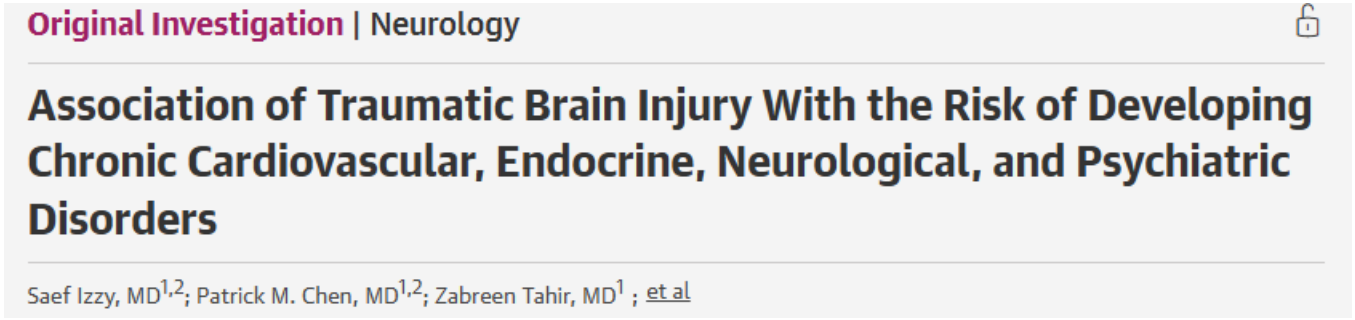
Why care?

- Can impact people of all ages

- Accounts for 2.5 million ED visits, hospitalizations, and deaths
  - 87% treated and discharged from ED
  - 11% hospitalized and discharged
  - 2% died

- Associated with multiple complaints recent or remote to the trauma.


Original Investigation | Neurology

Association of Traumatic Brain Injury With the Risk of Developing Chronic Cardiovascular, Endocrine, Neurological, and Psychiatric Disorders

Saef Izzy, MD[1,2]; Patrick M. Chen, MD[1,2]; Zabreen Tahir, MD[1] ; et al

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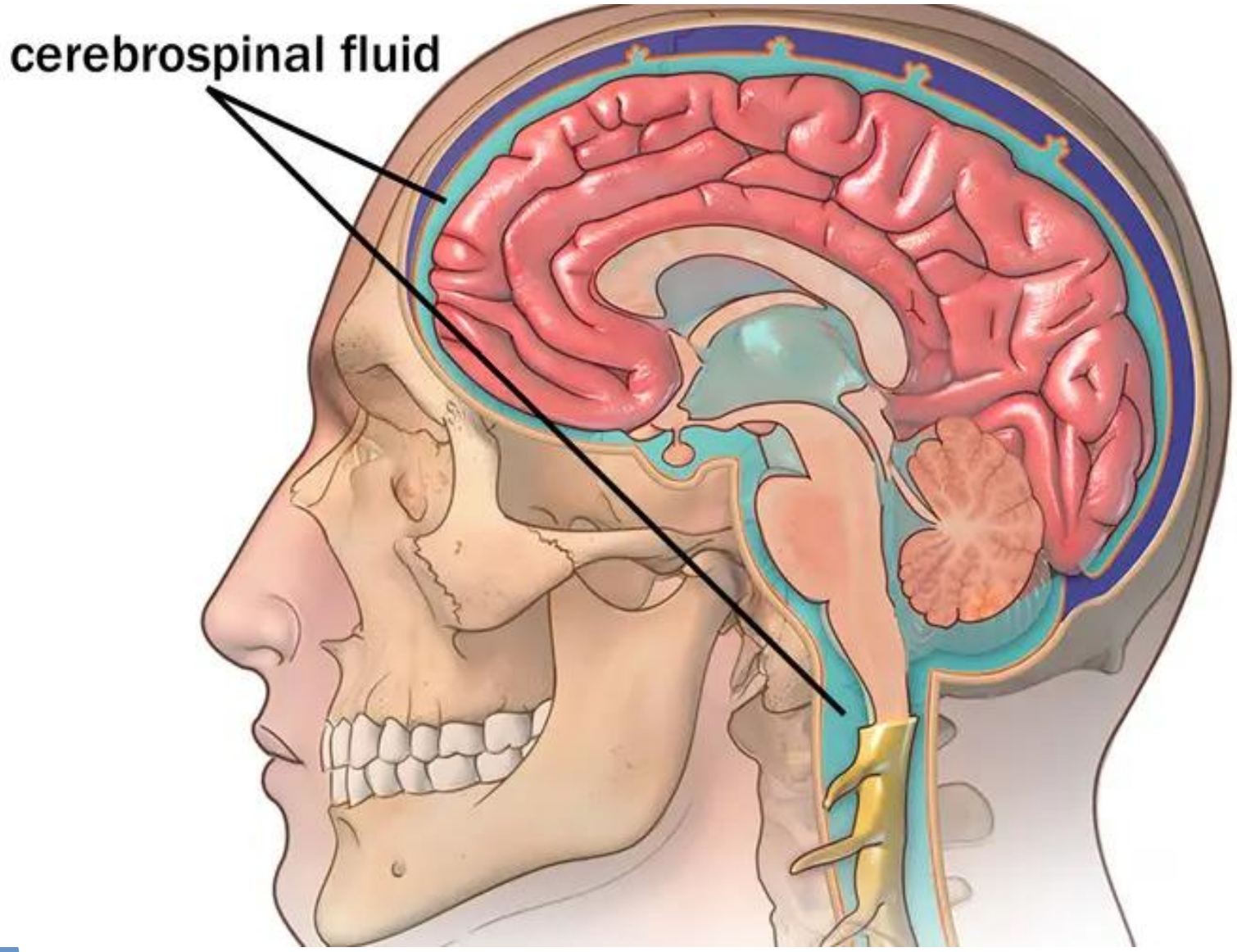

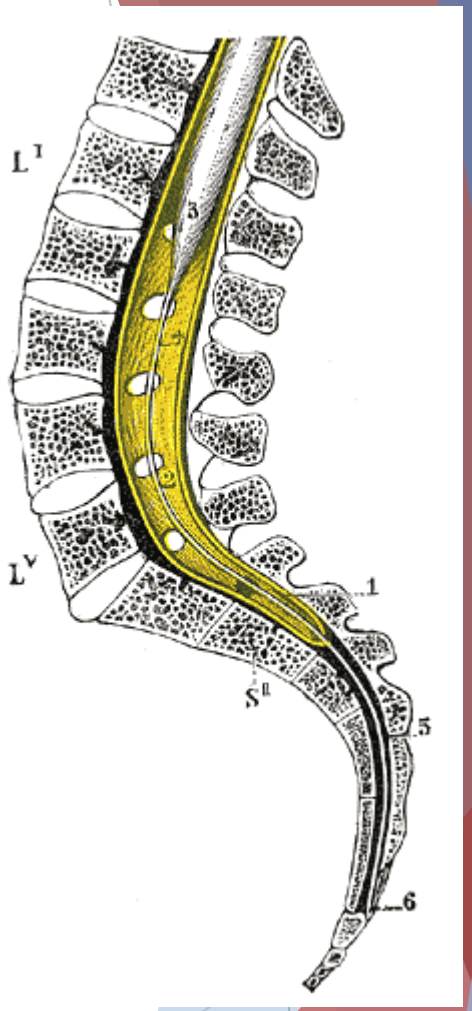

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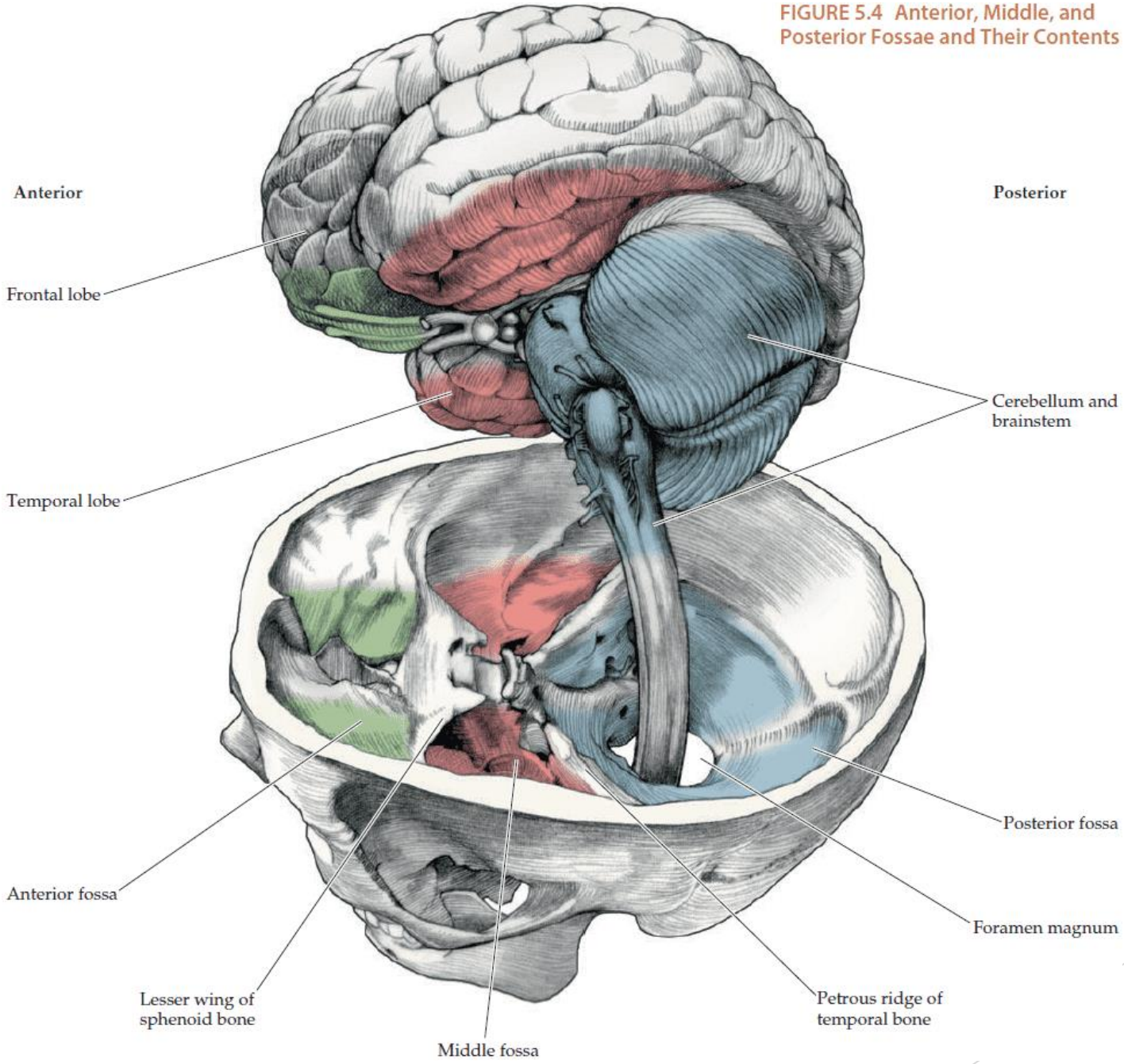
FIGURE 5.4 Anterior, Middle, and Posterior Fossae and Their Contents



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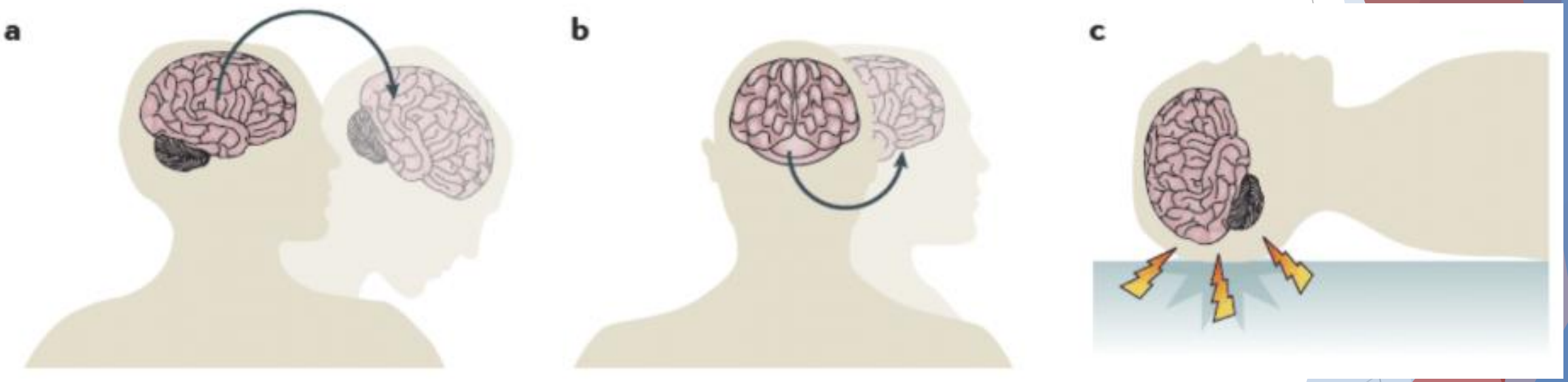
Mechanism



Linear

Rotational

Impact/Deceleration

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TBI classification

	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

Complicated mild TBI = mild TBI + imaging abnormality

Mild TBI prognosis

- 70-80% of TBIs are mild
- In majority of cases, symptoms improve within 10 days.
- Cognitive performance typically improves within 3 months. If continued issues then typically in attention, memory, and processing speed.
- Despite this it is common for patients to report symptoms which they believe are from a TBI
- Important to consider the base rate of any classical “post-concussive symptom” in the general population before attributing it to TBI

When to get neuroimaging after mild TBI

- If concussion is suspected -> Needs neurological examination

- Abnormal neurological exam (including gait)
- Progressive headache
- Recurrent vomiting
- Loss of consciousness >1 minute
- Prolonged anterograde amnesia (problem forming new memories)
- Seizure
- Skull fracture
- Age >60
- Intoxication
- Coagulopathy

After TBI

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Consider not only the injury, but the head that is injured

- Patients with TBI are not a random sample of the general population
- This cohort (excluding elite athletes) has higher rates of pre-injury psychiatric illness
- Not surprisingly, combining psychiatric vulnerability with TBI frequently worsens underlying psychiatric disorder
- This complicates rehabilitation and recovery

Section of Psychiatry

President—T. A. Ross, M.D.

[*April* 13, 1937]

Mental Disorder Following Head Injury

By C. P. Symonds, M.D.

- "…one of the symptoms in the state of post-traumatic dementia is an exaggeration of pre-existing traits in the mood and personality…the injury creates a situation of invalidism and incapacity to which the patient reacts in terms of his individual make-up."
-
- "Illness of the manic-depressive type, however…may develop, in a way which suggests very strongly that it is a direct result of the organic disturbance."

Neurobiopsychosocial approach

- Overarching approach is an integration of
  - What is known about neurobiology of TBI
  - Specific injury profile
  - Context of pre-injury history
  - Context of meaning of the injury to the individual
  - Patient's network of support

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).

Is there a post-concussive syndrome?

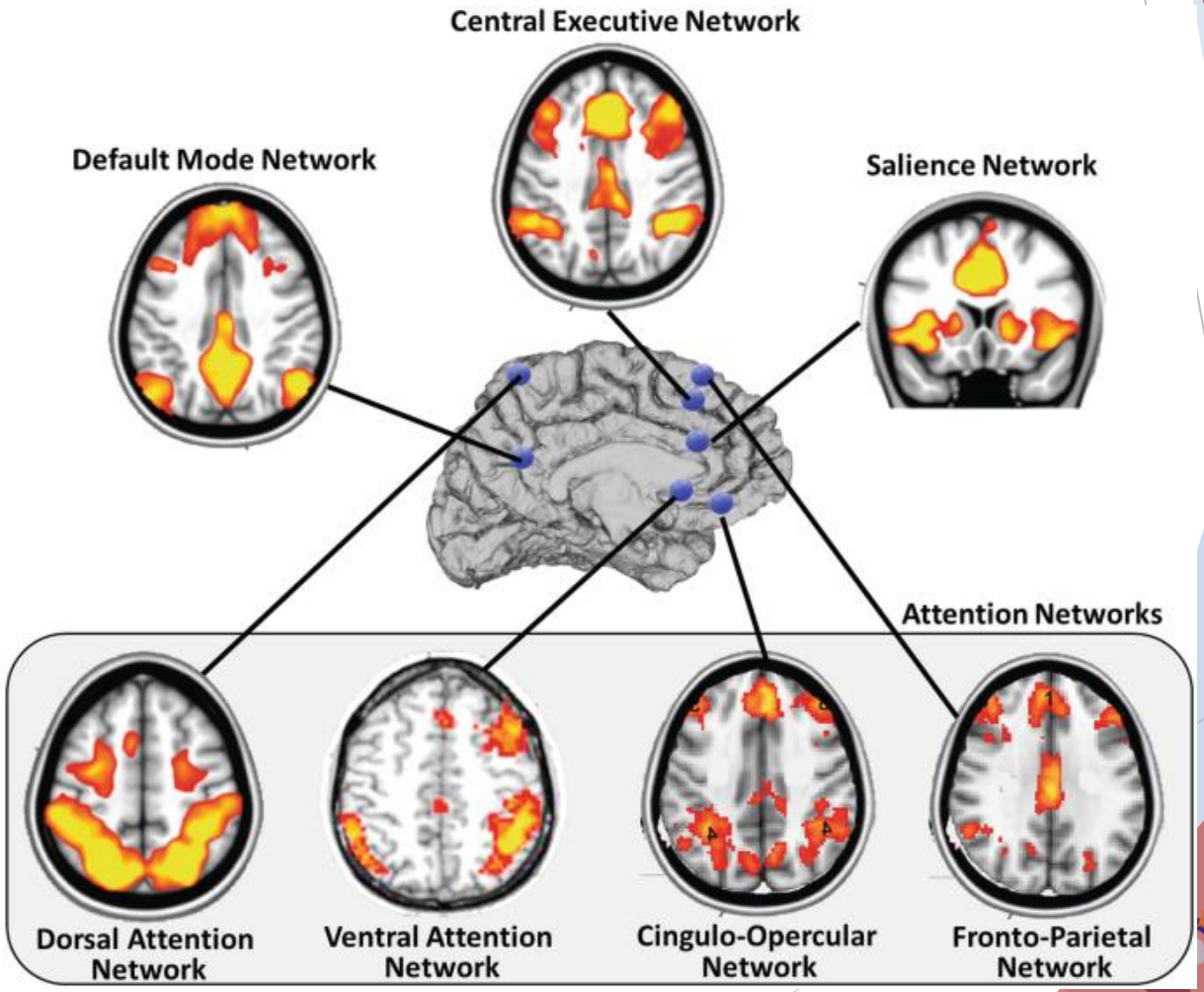
- DSM5: Neurocognitive disorder due to traumatic brain injury
- ICD-10: Post-concussive syndrome
- Fatigue, sleep disturbances, headache, dizziness, irritability, affective disturbances, apathy or personality changes x3 months or longer

- Reported incidence varies wildly

- To “lump” or to “split”
  - Lump: Multiple symptoms after TBI are a syndrome with common underlying mechanism. Therefore, there is a unifying etiology and particular treatment to ameliorate that syndrome.
  - Split: Multiple symptoms after TBI have distinct mechanisms that share an initiating event. Therefore, a careful look at the typology of each symptom will afford proper diagnosis and treatment (eg dizziness related to labyrinthine trauma or headache due to cervical muscle strain)

Cognitive behavioral networks

- Cognition and behavior are supported by networks
- Cognitive problems and behavioral problems are network problems



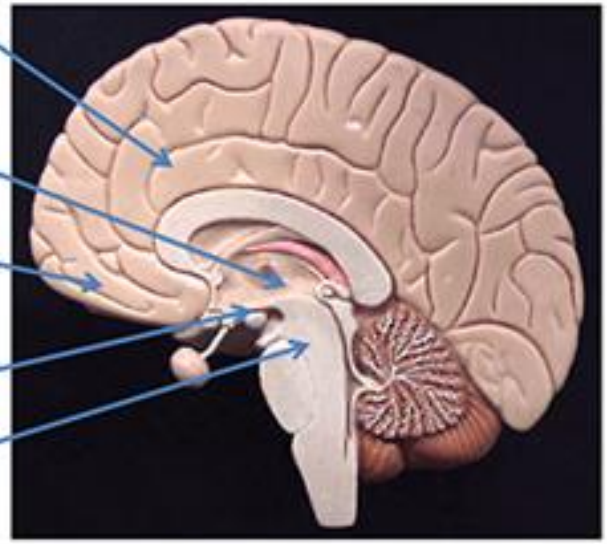
Anterior cingulate cortex:
Apathy

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



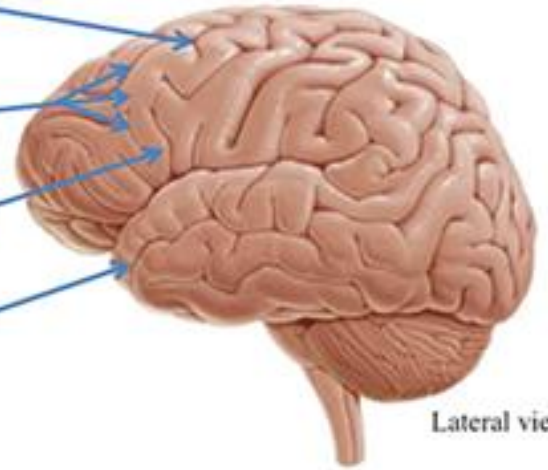
Medial view

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

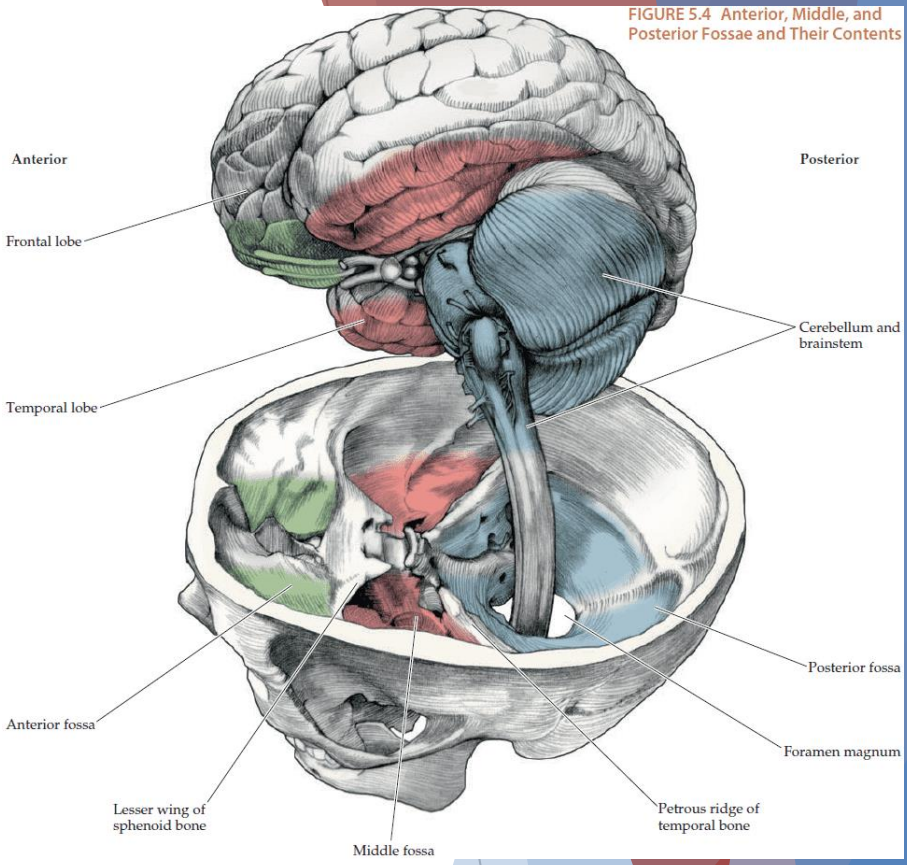
Anterior, polar temporal cortex:
Disturbances in semantic memory, facial, social and emotional processing, impaired social/ empathic function



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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Post TBI Psychosis

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Post-TBI Psychosis – Epidemiology

- Prevalence 1-9 % (three times general population)
- 50% within 1 year of injury. 50% within 5 years of injury.
- If presentation is delayed, unlikely that TBI is sole factor

- Challenging to make sure connection with TBI
- Best case: Absence of psychotic symptoms or prodromal symptoms before TBI. New onset psychosis in months following TBI.

Post-TBI Psychosis – Important points

- 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

Post-TBI Psychosis – Clinical Features

- Delusional Disorder
  - Capgras (familiar people replaced by imposter)
  - Reduplicative paramnesia (familiar place is duplicated elsewhere)
  - Delusional jealousy, Cotard syndrome (delusion of being dead/dying), somatic delusions, Fregoli (different unfamiliar people are actually one person in disguise)
  - Less common to have negative symptoms

- Schizophrenia-like psychosis
  - Auditory and visual hallucinations
  - Persecutory delusion
  - Less common to have negative symptoms

Post-TBI Psychosis - Treatment

- No FDA approved intervention. Approach is “treatment by analogy”
- 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

Post – TBI Movement disorders

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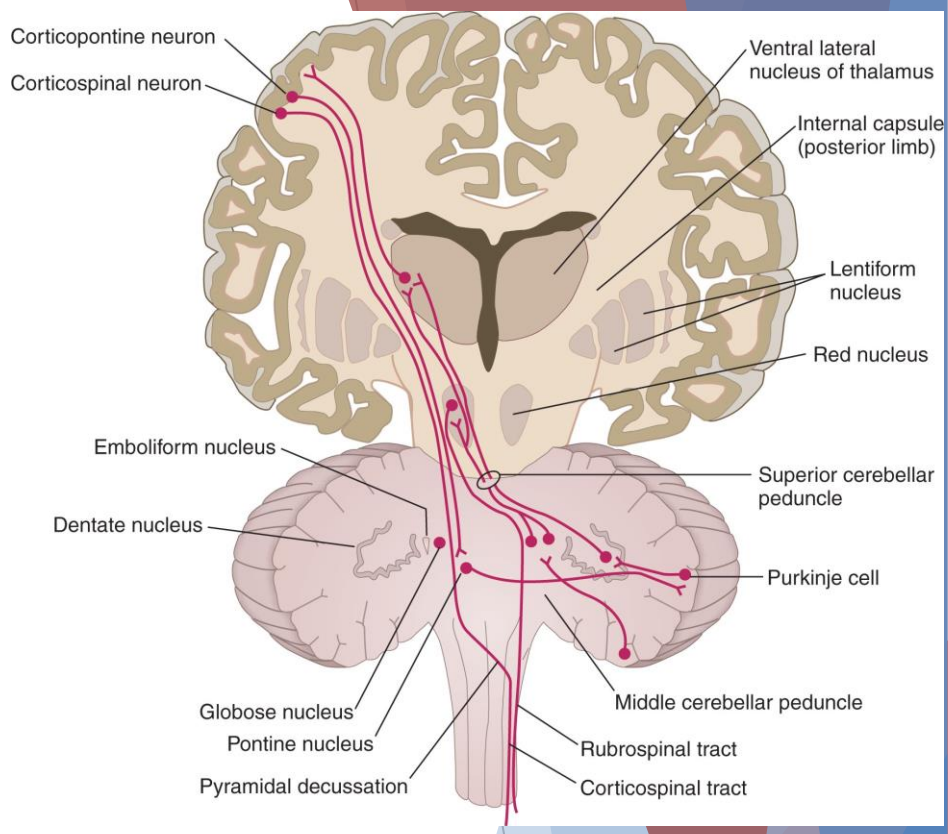
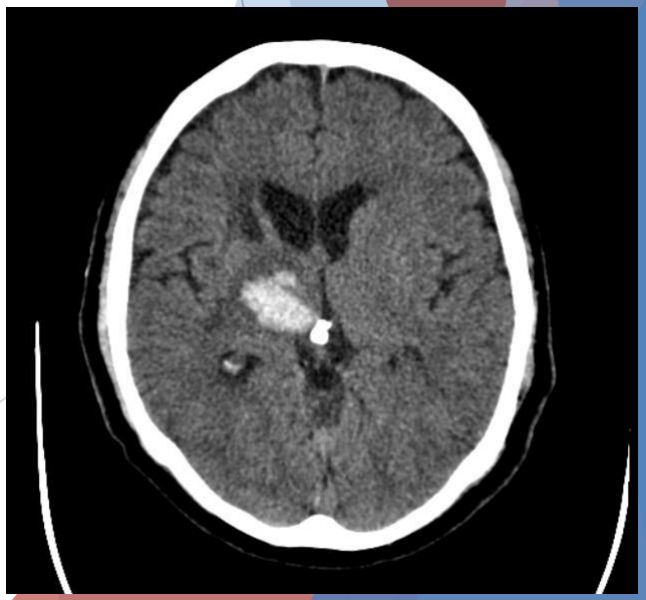
Post-TBI Movement Disorder

- Like psychosis, it is challenging to draw direct connection
- Wide variability in incidence

- Krauss et al.
  - 398 subjects with severe TBI
    - 22% with movement disorder (tremor and dystonia most common)
  - 158 subjects with mild to moderate TBI
    - 10% with movement disorder (tremor mostly)
    - 2% persistent





Characterizing Movement Disorders (phenomenology)

- Hyperkinetic or Hypokinetic?
- If hyper -> rhythmic or irregular?
- If hypo -> Rigid? Contractions? Postures of muscles?
- Paroxysmal or continuous? Are they suppressible?
- Do they occur at rest or with activity?
- Do they occur only during wakeful or persist into sleep?

Hyperkinetic and hypokinetic movement disorders

Tremors	Involuntary, alternating movements involving one or more joints occurring at a regular frequency resulting in "rhythmic oscillations"
Dystonia	Involuntary, slow, sustained contractions of agonist and sometimes also antagonist muscles producing twisting movements and/or abnormal posturing
Chorea	Involuntary, non-rhythmic, abrupt movements resulting from continuous flow of muscle contractions from one muscle group to another resulting in jerky or dance like movements
Athetosis	Involuntary, slow, non-rhythmic, writhing movements with alternating postures in the limbs
Ballism	Involuntary, rapid, non-rhythmic, non-suppressible movements of the proximal joints producing wild, flinging, high-amplitude movements
Myoclonus	Involuntary, sudden, brief muscle contractions (positive myoclonus) or inhibition of muscle contractions (negative myoclonus) leading to shock like movements
Tics	Simple or complex, repetitive, abnormal movements or sounds usually preceded by an uncomfortable feeling or sensory urge that is relieved by carrying out the behavior. Tics can often be easily mimicked and suppressed by short efforts of will
Stereotypy	Simple or complex, repetitive, coordinated, ritualistic movement, posture or utterance that is continuous and purposeless
Bradykinesia	Involuntary slowness or poverty of movement
Rigidity	Involuntary increase in resistance to slow passive movement which is not velocity dependent

Post-TBI Movement Disorder - Treatment

- Exercise, PT, OT, PM&R
- Tremor
  - Beta-blocker, benzodiazepines, primidone, carbidopa-levodopa, anti-convulsants, anticholinergics
- Dystonia
  - Anti-cholinergics, benzodiazepines, baclofen, tizanidine

- Special considerations
  - Careful with anti-cholinergics as these agents can worsen cognitive function
  - Aggressively manage other issues: sleep, mood disorder, substance abuse, chronic pain, migraine

Chronic Traumatic Encephalopathy

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Chronic Traumatic Encephalopathy in a National Football League Player

Omalu, Bennet I. M.D., M.P.H.; DeKosky, Steven T. M.D.; Minster, Ryan L. M.S.I.S.; Kamboh, M Ilyas Ph.D.; Hamilton, Ronald L. M.D.; Wecht, Cyril H. M.D., J.D.

Author Information

Neurosurgery 57(1):p 128-134, July 2005. | ***DOI:*** 10.1227/01.NEU.0000163407.92769.ED

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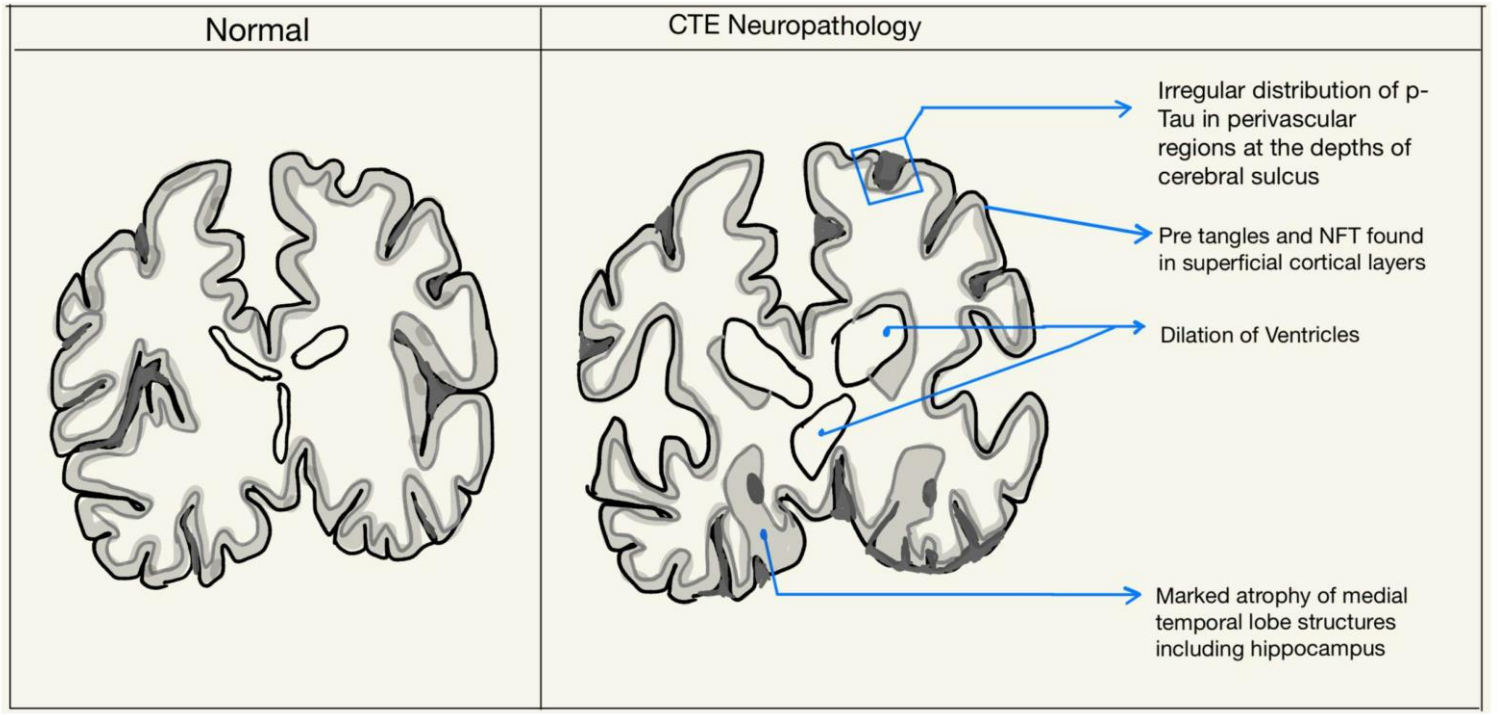
Brief History

- Early 1900s: traumatic insanity, post-traumatic psychosis, multiple traumatic cerebral hemorrhages, post-concussion neurosis-traumatic encephalitis, dementia pugilistica
- Martlands 1928 case study: “punch drunk syndrome” in boxers
- Bowman and Blau 1940: “chronic traumatic encephalopathy” in boxer
- Omalu 2005: CTE in American football

Definitions



- CTE is a neuropathological diagnosis made at autopsy
  - It is 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)
  - Staging scheme is used to determine prevalence and draw associations with number and severity of TBI
- Traumatic Encephalopathy Syndrome (TES) has been proposed as the clinical syndrome which results from the pathological state of CTE

Cognitive “Profile” - TES

- Challenges:
  - No in-vivo disease biomarker
  - Frequent co-pathology
  - Lack of comprehensive work-up prior to brain donation
- Traumatic Encephalopathy Syndrome
  - Substantial repetitive head injury equal or commensurate to at least 5 years of American football (at least 2 years at high school or above)
  - 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)
- Level of certainty: Suggestive, Possible, Probable, Definite
  - Cognitive decline necessary for greater than Suggestive
  - Definite requires autopsy

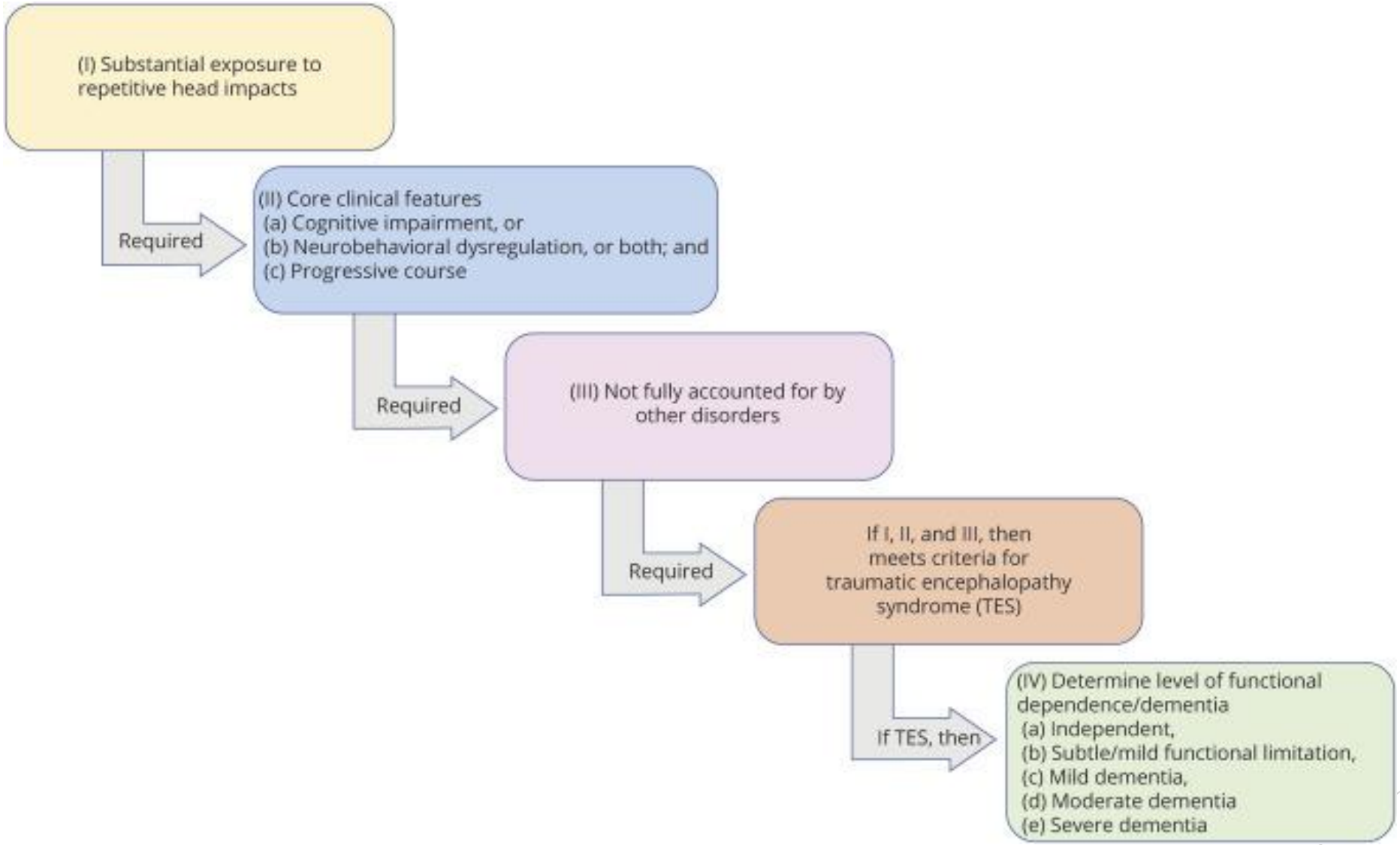
What sort of head injuries?

Table 1 Primary Diagnostic Criteria for TES: I. Substantial Exposure to Repetitive Head Impacts

History of substantial exposure to repetitive impacts to the head is required. These impacts may or may not have been associated with clinical symptoms or signs of concussion or TBI. Individuals should be screened for multiple possible sources of exposure over a lifetime. Examples of sources of substantial exposure to RHIs include the following:
Involvement in high-exposure contact or collision sports such as (but not limited to) boxing, American (tackle) football, ice hockey, soccer, rugby, professional wrestling, mixed martial arts, and some other sports with high risk of exposure to RHIs (e.g., motocross and bull riding).
For American football, a minimum of 5 y of organized play is required. This minimum should include ≥2 y at the high school level or beyond. [The inclusion of level of play (i.e., high school) is based on clinical judgment, with limited evidence]. Nearly all of the participants in a published study establishing the 5-y threshold played at least high school level football[1]
Exposure risk thresholds for other contact or collision sports, or combinations of contact/collision sports, have not yet been established but should be a substantial number of years (e.g., ≥ 5 y) at a level of play involving routine RHIs.
Military service involving RHIs, including (but not limited to) combat exposure to multiple blast and other explosions, noncombat exposure to explosions (including breacher training—blasting and forced opening of locked doors), or multiple blows to the head over an extended period of time (e.g., pugil stick training—repeated blows with a padded military training weapon).
Exposure risk thresholds for military service have not yet been established.
Other sources involving multiple head impacts over an extended period of time, including (but not limited to) domestic violence (or intimate partner violence), head banging, and vocational activities such as breaching locked doors and other barriers by first responders.
Exposure risk thresholds for other sources have not yet been established.
Abbreviations: RHI = repetitive head impact; TBI = traumatic brain injury; TES = traumatic encephalopathy syndrome.

Risk

- Autopsy series including 34 American football players found that pathological stage of CTE was correlated with length of playing career
- Questionnaires given to retired NFL players found that frequency of diagnosed Mild Cognitive Impairment, memory problems, and depression is elevated particularly in those with 3 or more concussions.
- An issue with any study trying to ascertain relation between TBI and CTE is recall bias and incomplete information about timing and severity
- Longitudinal cohort studies eliminate the recall bias but TBI presence is determined by medical records/diagnostics codes. Milder injuries are likely missed (which study of American football players suggests is very important in CTE)
- Problem of “reverse causality” – an individual with PD may report a head injury that actually occurred in early stages of disease rather than being a cause of that disease
- TBI in children or adolescents may be particularly morbid – critical period?



Katz et al. National Institute of Neurological Disorders and Stroke Consensus Diagnostic Criteria for Traumatic Encephalopathy Syndrome. 2021.

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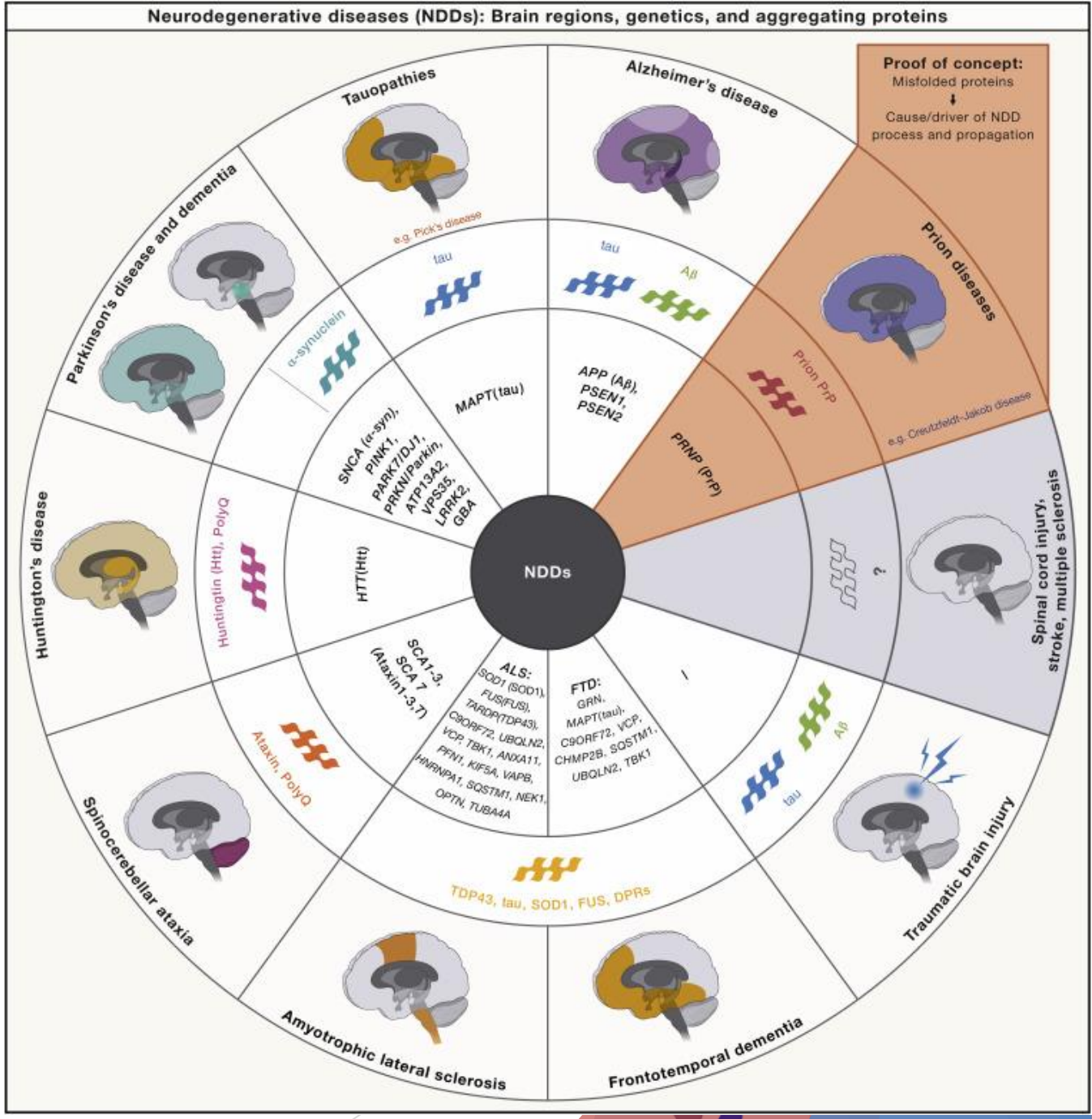
CTE in context

- CTE is a qualitatively different neuropathological state than other neurodegenerative diseases
- But CTE is not the only neurodegenerative disorder associated with repetitive head injury
  - AD, PD, ALS, FTD
- Most individuals with CTE at autopsy have other neuropathological findings (AD, LBD, LATE, vascular disease)
- In clinical practice, AD is the main differential diagnosis



Wilson et al. Hallmarks of neurodegenerative diseases. 2023.

Prevention

- CTE has a clear environmental trigger – TBI. This appears to be necessary but not always sufficient as a trigger
- 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 wearning

Summary

- TBI is common. It is typically mild with transient cognitive sequela.
- When cognitive and neuropsychiatric symptoms persistent a neurobiopsychosocial approach is helpful. History is key. Consider pre-disposing, precipitating, and perpetuating factors.
- Treatment of post-TBI cognitive/neuropsychiatric symptoms is “treatment by analogy”. Go low, slow, and hold the course as much as possible.
- Post-TBI psychosis happens. One must separate it from delirium, seizures, primary psychotic illness like schizophrenia, and neurodegenerative diseases.
- Post-TBI movement disorders are typically tremor or dystonia. They are rarely persistent.
- CTE is a neuropathological diagnosis. TES is the proposed clinical syndrome. Particularities of head injury risk for CTE are challenging to quantify.
- As with all neurodegenerative diseases co-pathology is common especially in elderly population. AD is the main differential diagnosis to consider first.
- Prevention is key. Lower risk of CTE and other neurodegenerative conditions.

References

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