Neuropsychiatry of TBI

Part 2

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Disclosures

- I have nothing to disclose
- I will talk about off-label uses of medications (because no medication has FDA approval for neuropsychiatric symptoms of TBI)

Learning objectives

- Describe the bidirectional relationship between TBI and psychiatric disorders
- Identify risk factors for psychiatric disorders in TBI
- Recognize that TBI can cause catatonia

TBI and Psychiatric Disorders: a Bidirectional Relationship

- Psychiatric disorders may increase the risk for TBI by 70%
  - May place individuals in situations where TBIs occur
    - Intoxication due to alcohol and substance use disorders
    - Impaired judgment and acting in response to hallucinations and delusions due to mania or psychosis
    - Can lead to TBI-producing situations like car accidents, falls, and fights

- ADHD increases the risk of TBI
  - Possibly due to inattention and impulsivity
  - Treating ADHD may lower this risk
- 40% of gun-related TBIs are due to suicide / suicide attempts
- By treating these psychiatric disorders, we can help with primary prevention of TBI

TBI significantly increases the risk of psychiatric disorders

- Both in the immediate post-TBI period and later in life
- The direct effects of injury to the brain play a role in post-TBI psychiatric disorders
  - ie, NOT just the stress / pain of having significant accident
    - Rates of post–injury psychiatric disorders are much higher in TBI than in other types of injuries
- Biggest risk factor for post-TBI psychiatric disorders:
  - History of premorbid psychiatric disorder
  - Consistent with studies of non-TBI related disorders, which show that having one psychiatric disorder increases the risk for developing others
- TBI severity doesn't appear to significantly affect whether psychiatric disorder develops

Treating post-TBI psychiatric disorders

- Evidence base is VERY limited
  - Most things not studied
    - Neither specific disorders/symptoms nor specific medications/interventions

- What data exists, is often contradictory
  - Individual studies of the same interventions have different results
  - Very similar meta-analyses of the same interventions have different results
  - Very similar systematic reviews of the same meta-analyses have different conclusions

- Treatment generally follows the same biopsychosocial approach used for idiopathic psychiatric disorders
    - Since evidence base for post-TBI psychiatric disorders remains preliminary
  - Individuals with TBI may be more sensitive to medication side effects
    - May benefit from a start-low-go slow approach to dosing
      - Though more consensus opinion than actual data
    - But still need adequate treatment duration at clinically effective doses before concluding that a medication didn't help
- Whatever you do, is going to be a N of 1 treatment trial

- Psychotherapy
  - Can be useful in patients cognitively able to participate
- Psychosocial interventions
  - TBIs can lead to relationship problems and impaired occupational functioning
  - Not much data on marital and family therapy or vocational rehab in TBI, but reasonable to try

Specific post-TBI psychiatric disorders

Depression

- Possibly the most common post-TBI psychiatric disorder
  - Occurs in 1 out 6 of individuals during the first year after TBI
  - Another 25% develop it in the second year
  - Risk of new-onset depression remains elevated for a long time
    - Possibly decades
  - Can last for one year or longer
  - May be recurrent

- Differentiating from physical disability and cognitive impairment
  - Fatigue, psychomotor changes, and problems with attention and concentration can occur with both physical/cognitive disability and depression
  - Affective symptoms like hopelessness, feelings of worthlessness, and anhedonia are much more specific to depression than to other post-TBI problems

- Depression worsens TBI outcomes
  - Independent of other injury-related factors
  - Individuals with depression have:
    - Higher levels of disability
    - Worse functional outcomes
    - Lower employment
    - Less independence in ADLs
- TBI DOUBLES the risk of death by suicide
  - So essential to screen for suicidality
    - Though we should always do that for all our patients!

- Depression has the largest evidence basis for treatment of any post-TBI psychiatric disorder
  - But still preliminary
- Best-studied pharmacotherapy for depression in TBI
  - Sertraline
    - Multiple RCTs: some found benefit, others didn't.
    - Balance of evidence indicates it's effective, safe, and well-tolerated
- Other SSRIs/antidepressants not much studied; RCTs that exist also have mixed results but lean towards effective and safe
- In the general population:
  - Evidence for venlafaxine and duloxetine for migraine prophylaxis and chronic pain
  - Not studied in post-TBI depression, but may be reasonable options in individuals with these comorbidities
- Stiumlants (especially methylphenidate) may help with depression in TBI, as well as with fatigue and cognition; but less studied than SSRIs

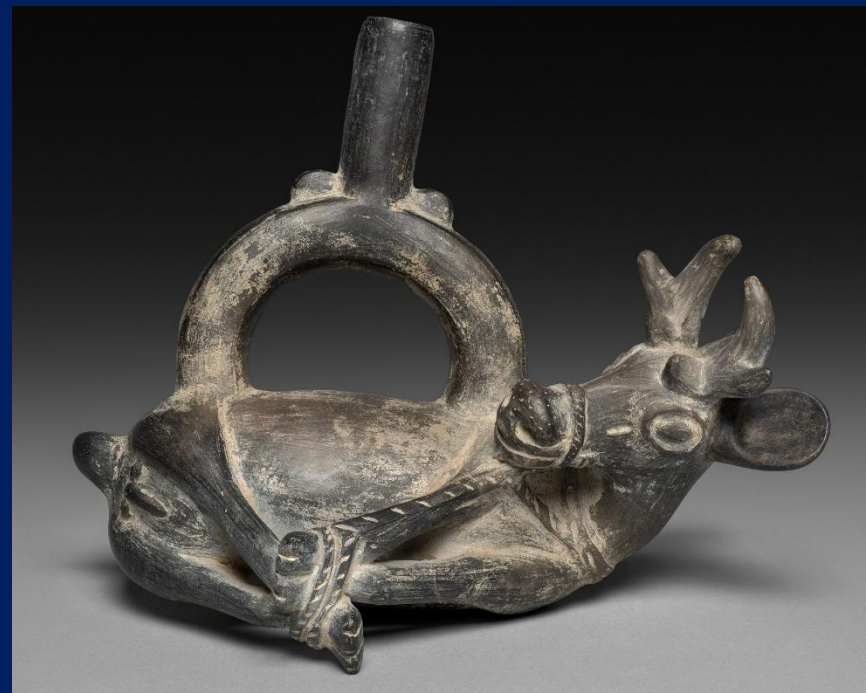
- Antidepressants to avoid in TBI
  - AVOID paroxetine
    - Paroxetine is fairly anticholinergic
    - The only SSRI that may increase risk for dementia
  - AVOID TCAs
    - Also anticholinergic
    - The limited available evidence suggests they do NOT work in post-TBI depression
  - Bupropion
    - Lowers the seizure threshold and should be avoided in patients with or at significant risk for posttraumatic epilepsy

Apathy

- Affects anywhere from 1/5 to 3/4 of patients with TBI
- Tends to be persistent

- Apathy vs depression
  - Apathy is commonly confused with depression
  - May be comorbid with depression
  - But is a DISTINCT SYNDROME which may require different treatment
- Consequences of apathy
  - Negatively affects rehabilitation participation
  - Negatively affects interpersonal relationships

- Clinical manifestations of apathy
  - Loss of motivation
  - Social withdrawal
  - Emotional flattening
- Patients typically engage in few activities, and may not interact much with others.
  - But when directly asked about their mood, patients with isolated apathy generally say they feel fine and that nothing is wrong
  - Don't spontaneously initiate much activity, but often participate in and enjoy activities arranged and facilitated by others
  - One way to distinguish apathy from depression:
    - Look at who it bothers
      - Depression bothers the patient
      - Apathy bothers the family



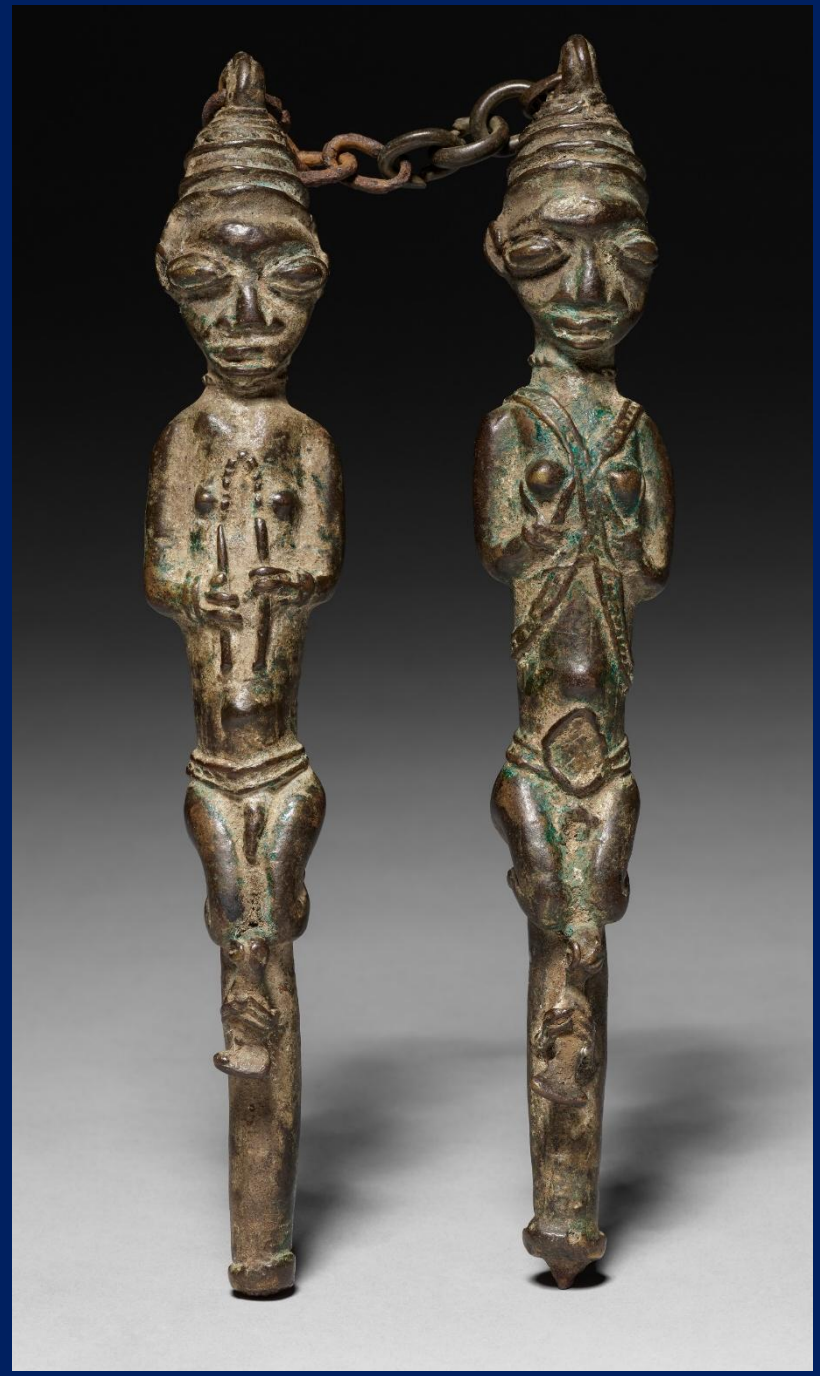
Treatment of apathy

- Provide a structured environment and encourage activities
  - Can help maximize functioning
- Psychoeducation
  - Sometimes families and caregivers worry that prompting the patient to do things just enables him or her to avoid responsibility
  - Can explain that apathy is a neuropsychiatric disorder caused by TBI, and NOT laziness or deliberate withdrawal of affection
    - Can help family members and friends not feel personally rejected by the individual with apathy
    - Can encourage them to help the patient participate in activities
- Pharmacotherapy
  - Nothing well-validated for apathy due to TBI
  - Limited available data for treatment of apathy due to other etiologies (ie dementia) suggests possible benefit from:
    - Cholinesterase inhibitors
    - Methylphenidate
    - Ginkgo biloba

Personality change

- TBI can cause significant personality changes
  - Often related to executive function deficits
    - Can cause patients to act without thinking through the consequences
    - Disinhibited and socially maladaptive behavior
    - Emotional lability
    - Aggression

- Nonpharmacologic options:
  - Preliminary data psychotherapy is effective (few small studies, not RCTs)
  - Psychoeducation
    - Prevent misinterpretation of these behaviors as a deliberate choice



Pharmacologic treatment of irritability / aggression

- SSRIs/SNRIs: in practice, used first-line (especially as irritability often overlaps significantly with depression, anxiety, PTSD)
    - RCT evidence they are effective and safe for irritability in the general population
        - Independent from effect on depression
    - However no RCTs in TBI specifically looking at irritability / aggression
    - Evidence of benefit in case series—someone needs to do a RCT with this as the primary outcome measure!
- Amantadine: beneficial in some RCTs, not others; overall evidence leans towards efficacy
- Beta-blockers (propranolol, pindolol): beneficial in some RCTs, not others; overall evidence leans towards efficacy
- Antipsychotics: unclear if effective, atypicals may be preferable to typicals
- Stimulants: some RCTs found helpful, others not helpful, others found worsened irritability / aggression

- AEDs: few small RCTs: limited data found benefit for divalproex but not carbamazepine
- Cognitively high-risk options?
  - Divalproex and carbamazepine cognitively harmful in non-TBI population (epilepsy, bipolar disorder)
    - Divalproex and carbamazepine associated with cognitive side effects during use
    - Divalproex and carbamazepine associated with increased risk of irreversible dementia in observational studies
    - Individuals with TBI already at increased risk for cognitive impairment and dementia
    - RCT in Alzheimer disease found that divalproex accelerates brain volume loss
  - Also…multiple RCTs showing divalproex is INEFFECTIVE and HARMFUL for agitation in dementia
    - Unclear whether/how this extrapolates to TBI

Post-TBI mania

- Develops up to 1 in 10 individuals shortly after TBI
- Generally resolves quickly without treatment
- Little-to-no evidence base for any specific treatment option

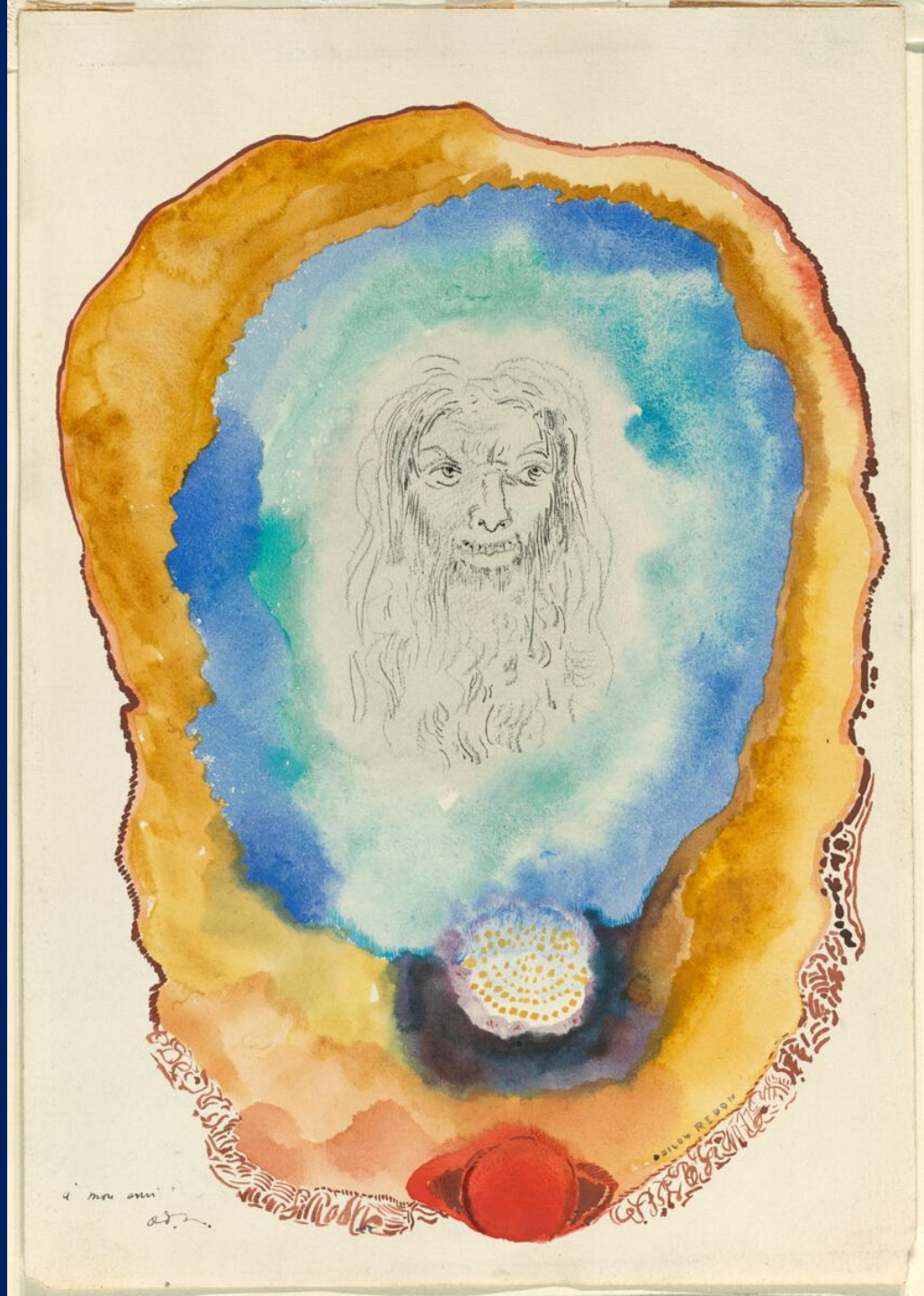
- TBI may be a risk factor for future bipolar disorder
  - Individuals with TBI have a 30% increased lifetime risk of developing classic bipolar disorder

Treatment options

- Again, no real evidence for post-TBI mania/bipolar disorder treatment: so probably preferable to start with medications with a safer cognitive profile
- Lithium, lamotrigine, nonanticholinergic antipsychotics may be best options cognitively
  - Lamotrigine not associated with cognitive side effects nor increased dementia risk
  - Lithium may actually be cognitively beneficial in the long run!
    - Lithium associated with REDUCED risk of dementia in idiopathic bipolar disorder (observational studies, not RCTs)
    - RCT of lithium in mild cognitive impairment found that lithium DECREASED cognitive decline and improved CSF AD biomarkers
    - Some (not all) epidemiologic studies have found that places with higher levels of lithium in the water have lower rates of dementia
- Divalproex and carbamazepine are associated with adverse cognitive effects and increased risk for dementia in the non-TBI population (individuals with idiopathic bipolar disorder and idiopathic epilepsy)
  - Divalproex caused accelerated brain shrinking in a RCT in AD
- Avoid anticholinergic antipsychotics
- Psychotherapy clearly effective (in ADDITION to medications) in idiopathic bipolar disorder
  - Not generally feasible in acute mania; not studied in post-TBI bipolar disorder, but likely worth a try

Psychosis

- Rates of hallucinations and delusions shortly following a brain injury range from 1/7 to 2/3
  - Higher risk in moderate or severe TBI and in individuals with posttraumatic epilepsy
- Often resolves on its own without treatment, but can persist in some cases
- Symptoms can resemble schizophrenia-like hallucinations and delusions
- Can also see unusual hallucinations and delusions that likely reflect a combination of psychosis and cognitive deficits



Unilateral Capgras syndrome and phantom vest

- Patient with R hemisphere injury and L hemineglect
- L unilateral Capgras syndrome: had recurrent spells of thinking his wife had been replaced by an impostor, triggered by seeing her in his L hemispace
- Tactile hallucination of wearing a tightly fitted vest
  - NOT associated with any primary sensory deficits or changes in the area of the vest, occurred even when not wearing any clothing

Capgras Syndrome and Phantom Vest Following Traumatic Brain Injury

To the Editor: Delusional misidentification syndromes, including Capgras delusion, are uncommon but potentially disabling consequences of traumatic brain injury (TBI).[1] Tactile hallucinations have classically been described in delirium tremens, stimulant intoxication, and schizophrenia[2] but are not usually associated with TBI.[3] We present a case of severe TBI with episodic Capgras delusions and tactile hallucination of clothing (i.e., a "phantom vest"), the latter of which, to our knowledge, has not been reported previously.

Case Report

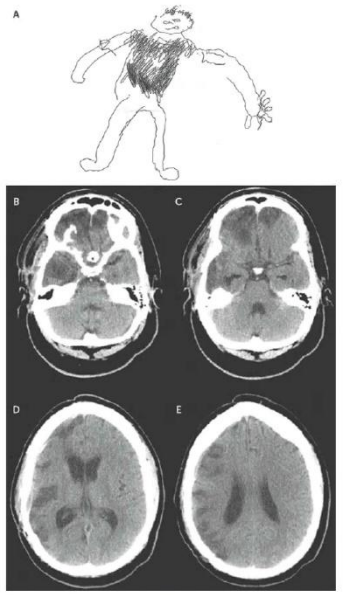
A left-handed man in his 30s experienced a severe TBI in a motor vehicle accident. His past medical history included hypertension and moderate alcohol use disorder but no other psychiatric problems. His initial injury presentation included a right subdural hematoma, producing right to left midline shift and necessitating a hemicraniectomy and external ventricular drain (EVD) placement. The patient developed seizures 4 weeks postinjury in the context of EVD malfunction. After correction of that malfunction and transitioning from levetiracetam to phenytoin, he remained free of clinically apparent seizures. The patient underwent a cranioplasty 5 weeks postinjury; his family reported that during this period, he was oriented consistently to time, place, and the etiology of his deficits.

On examination in the inpatient rehabilitation setting 6 weeks after the injury, the patient and his wife reported daily episodes (of approximately 1-hour duration) during which the patient stated that his wife had been replaced by an impostor. The episodes began a few days after he developed clinically apparent seizures and appeared to be triggered by his wife standing in his left hemispace. By contrast, the patient did not experience his wife as an impostor when he spoke to her over the phone. He also endorsed a constant sensation of wearing a vest, which he described as tightly covering his torso and extending onto his upper arms. This sensation began a few days after the cranioplasty and was not linked to his episodes of delusional misidentification. The "vest" sensation was consistent in character and intensity on the front, back, and sides of his torso and did not vary in relation to the presence or absence of clothing (i.e., it was not an illusion triggered by actual clothing). Three weeks into his rehabilitation hospitalization, the patient reported momentary relief from the vest sensation while showering with hot water and when his wife kissed his chest; the sensation otherwise persisted.

A neurological examination demonstrated motor aprosodia, normal visual fields, mild left lower facial and extremity hemiparesis, normal elementary sensory function, and left-sided extinction to double simultaneous stimuli. The patient scored 28 of 30 points on the Orientation Log,[4] reflecting recovery of orientation; he scored 17 of 18 (z score = −1.2) on the Frontal Assessment Battery,[5] reflecting mild executive dysfunction.[6] Line bisection and circle cancellation tests were consistent with left egocentric neglect. The patient drew a picture of himself using his nondominant hand and demarcated the location of the vest (Figure 1A). He correctly identified which side of the drawing was his left and right sides, suggesting relative preservation of left- and right-sided body representation. The patient was able to correctly identify pictures of familiar and unfamiliar faces. When presented with famous faces (from a set customized to his general knowledge and interests), he correctly matched 83% of faces and names.

Computed tomography (CT) performed during the patient's rehabilitation stay revealed hypodensities in the gray and white matter structures of the bilateral straight and orbitofrontal gyri (right greater than left); the frontal polar region bilaterally; the right dorsolateral prefrontal (DLPF) region; the right anterior temporal polar region and the anterior and midinferior, middle, and superior temporal gyri; and the right supramarginal and angular gyri and right inferior and superior parietal lobules (Figure 1 B–E). CT imaging of the patient's chest with contrast was negative for fracture or other pathology. Routine electroencephalography performed during the patient's rehabilitation stay did not reveal epileptiform abnormalities, and his serum free phenytoin level was within normal limits during treatment with this medication.

FIGURE 1. Pictorial Representation and Imaging Results for a Patient With Capgras Syndrome and Phantom Vest After Traumatic Brain Injury



(A) The patient's pictorial representation of his body and the location of the vest. The right and left sides of his body are indicated. (B–E) Axial computed tomography images of the brain in ascending order.

Discussion

The Capgras delusion is predicated on disconnection between the visual facial processing regions of the temporal lobe and emotional input from limbic structures[1,7,8] and aberrant, left-hemisphere-mediated interpretation of that disconnection.[7,8] With respect to this anatomy of Capgras delusion, our patient sustained CT-evident injury to the right temporal pole, right DLPF region, and bilateral frontal poles. The lateral aspect of the right temporal pole supports facial recognition.[9] Damage to this area and to the limbic-paralimbic connections therein disrupts integration of visual, emotional/visceral input (in our patient, the integration of the visual percept of his wife with its appropriate social-emotional affects, such as affection, familiarity, and acceptance). The combination of injury to the right DLPF region and bilateral frontal poles provides an anatomic basis for aberrant error detection and correction in relation to impaired right temporal polar integration of visual and emotional/visceral information.

Consistent with the argument offered by Devinsky,[8] injury to these (and related) right-hemisphere structures in the context of relative preservation of left hemispheric (especially language-related) structures "releases" the left hemisphere to create dual categories and accompanying narrative for that information (i.e., the invention of a duplicate or impostor to resolve conflicting information). In this particular case, injury to the frontal poles (Brodmann area 10p), supramodal structures involved in the processing of internal states, memory retrieval, and the coordination overall of information processing across multiple cognitive operations[10] may compound these integrative failures and contribute to impaired insight into the narrative of an "impostor wife" (i.e., the Capgras delusion).

The combination of right temporal polar, bilateral frontal polar, and right parietal injuries may also have contributed to the patient's sensory experience we characterized as a "phantom vest." The right parietal lobe is a critical node in body representation; damage to this area, combined with the sensory-limbic integrative deficits arising from damage to other right-hemisphere structures and impaired monitoring attendant to bilateral frontal polar injury, may underlie this unusual sensory perceptual/experiential phenomenon. The bilaterality of this phenomenon remains unexplained by this patient's anatomy of injury. Nonetheless, this novel clinical observation is presented here as a phenomenon in need of replication and further anatomic characterization.

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TBI and schizophrenia risk

- People with a history of TBI have a 60% higher chance of developing schizophrenia later in life
  - Risk is highest among individuals with a family history of schizophrenia
- Suggests a genetic predisposition to schizophrenia, requiring a second hit (e.g., TBI) to develop the illness

Treatment of post-TBI psychosis

- No RCTs for psychosis due to TBI
- Need to evaluate for delirium, depression, and cognitive impairment: treating these problems may resolve the psychosis
- Antipsychotics may be an option in some TBI patients with significant psychosis that doesn't resolve; but need to monitor closely for adverse effects

Antipsychotic selection

- Use antipsychotics with lower anticholinergic effects
  - Anticholinergic antipsychotics: quetiapine, olanzapine, clozapine, low-mid potency typical antipsychotics
    - Clozapine has unique benefits that may outweigh its anticholinergic risks in some individuals; despite what drug company reps may try to claim, no one's ever shown that non-clozapine antipsychotics differ in efficacy in schizophrenia
- If extrapyramidal symptoms develop, switching to another antipsychotic agent generally better than adding anticholinergics, as much safer from a cognitive perspective
  - RCT evidence amantadine is safe and effective for EPS in schizophrenia
  - Amantadine established as safe and effective for other indications in TBI—not studied for EPS in TBI but reasonable to try if switching antipsychotics isn't an option
- Individuals with TBI already at higher risk for cognitive impairment and future irreversible dementia; anticholinergic drugs directly increase these risks further in everyone
  - In schizophrenia, higher anticholinergic burden (anticholinergic antipsychotics and/or anticholinergic antiparkinson agents) is associated with significantly worse cognition

Antipsychotic selection

- Probably preferable to avoid typical / strongly antidopaminergic antipsychotics
  - Patients with TBI may be at higher risk for motor side effects
  - Theoretical concern that antidopaminergic drugs could worsen frontal/executive deficits (never studied in any RCT)
- Individuals with TBI face 2x increased lifetime risk of CVA: using more metabolically neutral antipsychotics may help avoid increasing this risk further

Data from dementia on antipsychotic choice:

- For overall neuropsychiatric symptoms (not looking at psychosis separately from other treatment targets):
  - Aripiprazole, brexpiprazole, and quetiapine may be most effective and safest antipsychotics
    - Studies didn't look at long-term effects on cognitive worsening—likely less salient concern in individuals who already have dementia with significant behavioral disturbance
  - Risperidone likely effective but significant risk of adverse events
  - Olanzapine neither effective nor safe
  - Newer agents like lurasidone and lumateperone not yet studied in dementia
- Whether/how this extrapolates to individuals with TBI and psychosis is not known

Other treatment options:

- Cholinesterase inhibitors?
  - Growing body of evidence in dementia (Alzheimer disease, PD-spectrum disease) that cholinesterase inhibitors can be effective for dementia-related psychosis, not just cognition
    - On the other hand, cholinesterase inhibitors clearly not effective for psychosis in schizophrenia
  - Not yet studied for psychosis in TBI
    - Likely worth a try, as evidence for cognitive benefit in TBI; and safe generally well-tolerated drugs
- Psychosocial treatments such as psychoeducation, vocational rehabilitation, psychotherapy, and assertive community treatment can help in schizophrenia and other idiopathic psychosis
  - May help and unlikely to hurt in psychosis due to TBI, though not much studied

PTSD

- TBI DOUBLES the risk for PTSD compared to injuries to other body parts
  - Affects 1/7 people with TBI overall
  - May be as much as 9/10 people with military-related TBI
  - The circumstances of the TBI affect the risk for subsequent PTSD
    - Trauma deliberately inflicted by other human beings (bombs, shootings, beatings) >> accidental traumas (falls, car crashes)
  - TBIs often require ICU care
    - ICU experience itself can cause PTSD
- But, by definition, TBI involves loss or alteration of consciousness
  - How can you have recurrent intrusive memories, nightmares, and flashbacks about an event you can’t even remember?

- Brief amnesia for the traumatic event actually increases the risk of PTSD
- PTSD can develop even with prolonged loss of consciousness
- How is this possible?
  - Posttraumatic amnesia = absence of explicit memories (memories consciously known to us and which we can explicitly think about)
- We also have implicit memories
  - Includes but not limited to procedural memories like how to ride a bike
  - We don't consciously recollect implicit memories
  - But they can play an important role in fear conditioning
    - Even when no explicit memory for the fear cue
    - Individuals with autonomic findings associated with fear conditioning shortly after TBI go on to have higher rates of PTSD

- Explicit memory and implicit memory rely on different brain systems
  - Can have preserved implicit memory even when explicit memory is damaged
- So, via implicit memory, trauma-related stimuli can cause fear and distress even if you can't consciously recall sustaining the TBI
- Confusion / mystery surrounding a trauma you know occurred but can’t remember make it harder to work through it emotionally and integrate it into your overall life story

- Treatment
  - A few studies have specifically examined PTSD due to TBI, but most data is preliminary
  - Treatment generally is the same as for non-TBI-related PTSD
    - SSRIs / SNRIs are effective in PTSD in general, and are safe and well tolerated
      - Likely best first line medication in TBI
    - Avoid benzodiazepines
      - Worsen the course of PTSD in the general population and impair cognition
      - CBT, cognitive processing therapy, and prolonged exposure therapy may improve TBI-associated PTSD

Catatonia

Catatonia: poorly understood psychomotor syndrome characterized by lack of purposeful movement and meaningful communication

- Signs/symptoms include:
  - Stupor, staring, waxy flexibility, catalepsy, mutism, posturing, negativism, stereotypy, mannerisms, grimacing, purposeless movements, echopraxia, echolalia, autonomic instability

Who gets catatonia?

Catatonia can occur in psychiatric disorders and also in neurologic disorders; as well as other medical conditions like endocrinopathies and electrolyte disturbances

- 20-25% of catatonia cases are due to nonpsychiatric medical conditions
  - Of these, more than 1/2 are due to neurologic disorders, including TBI
- Catatonia often goes unrecognized in patients with serious neurologic disorders: but important to look for and diagnose it—because it's treatable!

Challenges in diagnosing catatonia in neurologic disorders

- Cognitive disorders and disturbances of consciousness can make it hard to recognize catatonia
  - If a patient isn't speaking much, is that mutism or nonfluent aphasia?
  - Catatonic echolalia or mixed transcortical aphasia?
- Same problem with some motor symptoms:
  - Catatonic grasp reflex or frontal release sign due to damaged long white matter tracts?
  - Catatonic rigidity or parkinsonism?
- Some catatonia symptoms overlap with delirium symptoms
  - EEG typically normal in catatonia, usually shows generalized slowing in delirium
  - Absence of deliriogenic conditions points towards catatonia

How does TBI cause catatonia?

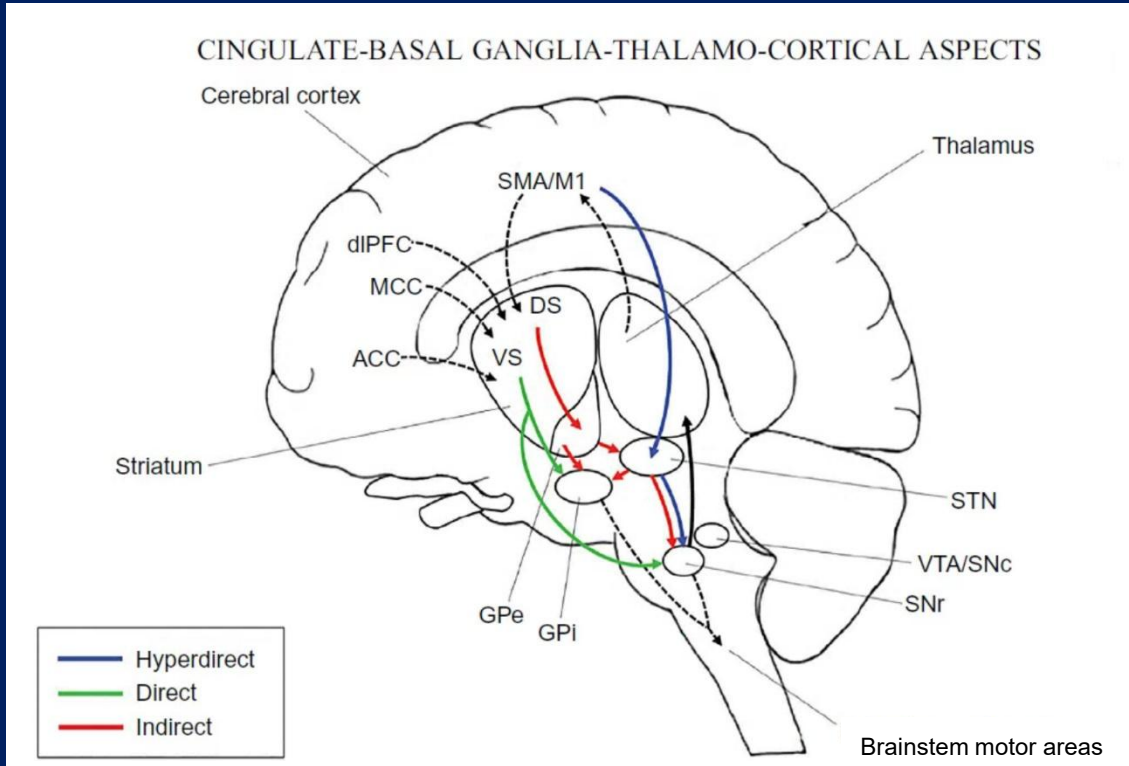
TBI can disrupt brain regions and networks needed to engage in purposeful goal-directed behavior and meaningful interaction with the environment

- This damage can give rise to catatonia

Motor circuit theory of catatonia

Cortico-striato-thalamo-cortical (CSTC) loop

- Balance of inhibitory and excitatory circuits
- Involved in planning, evaluating, selecting, initiating, and terminating movements
- Disruptions to this circuit can tip the balance excessively to inhibition or excitation: one potential mechanism for catatonia
  - Absence/severe limitation of purposeful, novel adaptive movements
  - Excess of purposeless repetitive movements
- This circuit involves voluntary self-initiated movements; even when the CSTC loop is damaged, individuals may be able to carry out meaningful activities when triggered by external cue
  - “Telephone sign” in catatonia



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Parietal lobes and catatonia

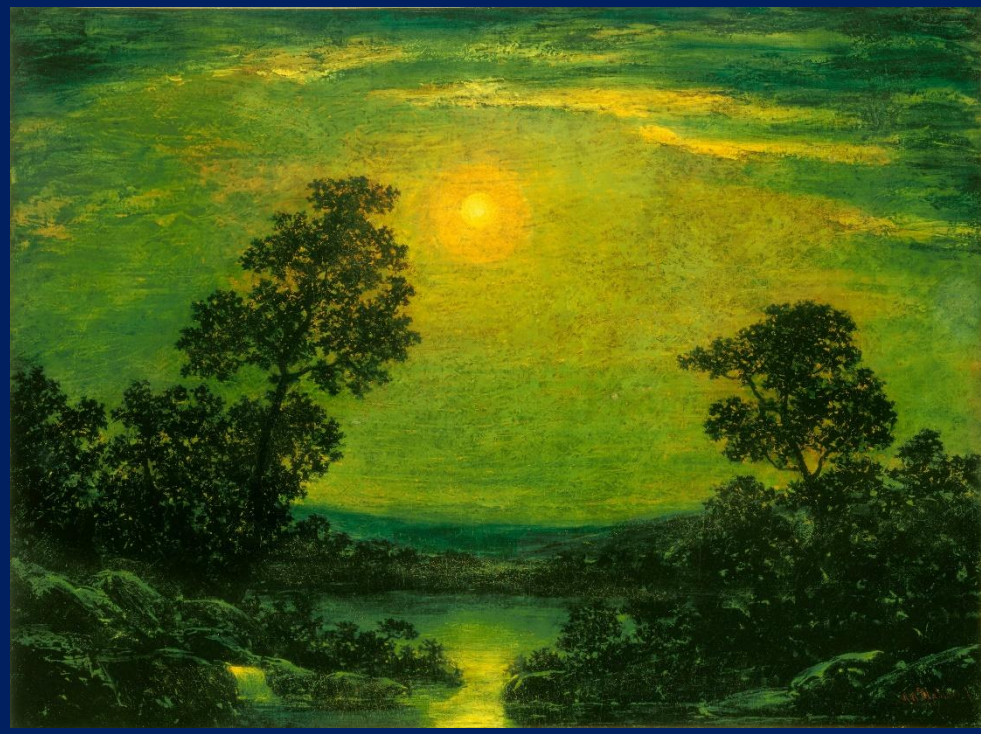
Parietal lobe involved in sensory integration, feedback/regulation of motor movements, spatial/environmental awareness/attention

- Damage/disruption may give rise to decreased attention to environment, impaired awareness of limb movement/position: leading to catatonia?
- Multiple case reports of catatonia due to parietal lobe lesions

Fear hypothesis of catatonia

Catatonia may represent an extreme manifestation of fear

- Freezing and tonic immobility: manifestation of the fight-flight-freeze response
- Individuals who have recovered from catatonia often report having felt extremely scared during the catatonia
- Cases of catatonia occurring from damage to limbic system (cingulate gyrus, amygdala) can produce catatonia
- Dysregulation of amygdala circuits can produce “freezing” and tonic immobility/waxy flexibility via projections to striatum and SMA
- Benzodiazepines clearly an effective treatment for catatonia



- Case report of catatonia occuring in the ER just after a mild TBI: authors felt that the fear produced by the accident may have triggered the catatonia

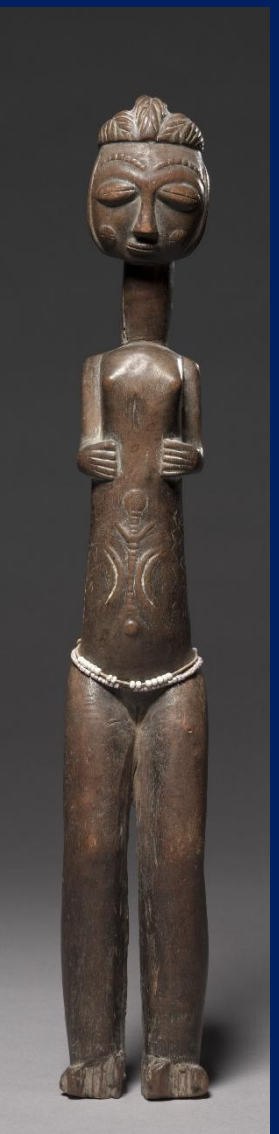
Treating catatonia in TBI

- Catatonia due to neurologic disease may respond to benzodiazepines and/or ECT. However, sometimes it doesn't.
- Data from case reports (mostly from non-TBI etiologies) suggests that:
  - Chronic catatonia due to chronic neurologic disorders may respond less to treatment
  - Response may improve when underlying neurologic/medical etiologies are treated (when possible)
  - Catatonia due to neurologic disorders may be more likely to respond to ECT when classic psychiatric features like depression, psychosis, or mania are also present
  - Catatonia due to neurologic disorders may require more intensive treatment to respond to ECT: higher stimulus thresholds, more ECT sessions, etc
- Remember: IF YOU DON'T LOOK FOR CATATONIA, YOU CAN'T TREAT CATATONIA

Substance use disorders and TBI: risk factors for each other

- Substance use disorders significantly increase risk for TBI
  - Especially alcohol use disorder
- In some epidemiologic studies, >50% of individuals with TBI were intoxicated at the time of their injury
- 1/3 of people with TBI met criteria for a substance use disorder prior to the TBI
- Substance use disorders (particularly alcohol) worsen TBI outcomes
  - Continued alcohol use following TBI:
    - Worsens rehabilitation and employment outcomes
    - Increases risk for seizures and repeat TBI

- TBI may increase risk for substance use disorders
  - Overall, substance use disorders may decrease following TBI
    - Disability may pose a barrier to use
    - Injury may serve as a wake-up call
  - But in some circumstances TBI may INCREASE the risk of subsequent substance use disorders.
    - Young children (ie, too little to be using substances) who experience TBI have HIGHER rates of substance use disorders later in life
      - May be in part mediated by genetic and environmental factors common to both TBI and substance use?
        - Child abuse
        - Parental substance use disorders
      - BUT: direct brain effects of TBI could also possibly lead to a greater propensity for subsequent substance misuse, and more difficulty controlling substance use
        - ie, if impairs ability to make good judgements, or if leads to self-medication with substances for other post-TBI psychiatric disorders



- US military personnel who sustain combat-related TBIs have INCREASED rates of substance use disorders after return home
  - Alcohol and other drugs are strictly prohibited in war zones
  - So association very unlikely due to different rates of substance use at the time of injury
  - It's possible direct brain effects of TBI are responsible for increase in substance use disorders once they have access to substances again

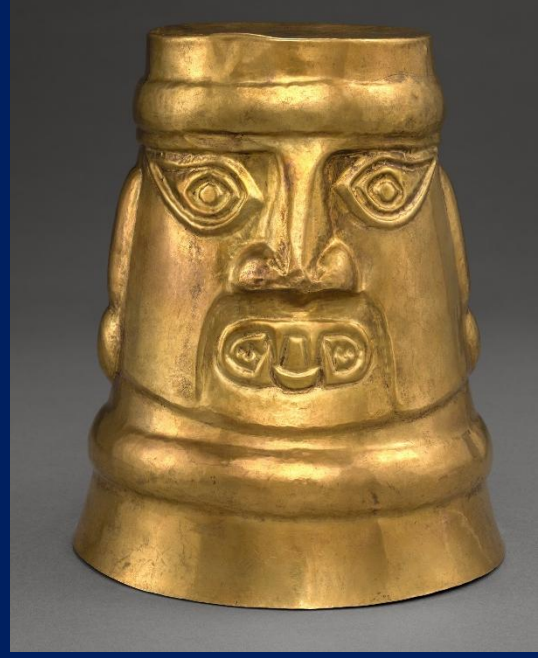
- Regardless of the direction of causality, TBI and substance use disorders are clearly highly comorbid
  - Patients with TBI need screening and treatment for substance use disorders
    - Amazingly, given the high comorbidity, treatment of substance use disorders in patients with TBI hasn’t been much studied

- In the general population, most effective treatment strategy for alcohol and opioid use disorders is medication-assisted treatment
  - Acamprosate and naltrexone for alcohol use disorders
  - Buprenorphine, methadone, and naltrexone for opioid use disorders
  - Not yet studied in TBI, but strong efficacy in the general population and no TBI-related contraindications
    - Likely very well worth trying
- Little to no data on effective psychotherapeutic interventions for substance use disorders in TBI
  - But reasonable to consider individual/group therapy, AA/NA, SMART Recovery, etc

Anxiety disorders

- TBI increases risk of GAD and agoraphobia
  - Post-TBI:
    - Agoraphobia: 1/10 patients
    - GAD: 1/7 patients
- Panic disorder, social phobia, and specific phobia same as in general population
  - ie NO increased risk with TBI
- Treatment
  - Not much evidence specifically in TBI; most treatment follows approach for general population
    - SSRIs/SNRIs: effective in general and lack cognitive side effects
      - Likely best 1st-line medication option
    - Buspirone also reasonable
    - CBT may help
- AVOID benzodiazepines and anticholinergic drugs
  - Worsen cognition and (clearly for anticholinergics, possibly for benzos) increase the risk of dementia

- TBI and sleep disorders
  - 50% of patients with TBI have sleep disorders
    - Insomnia
    - Hypersomnia
    - Excessive daytime sleepiness
    - Circadian rhythm disturbances
    - OSA
  - Sleep disorders are associated with worse functional status in TBI



- CBT for insomnia
  - Most effective treatment in the general population
    - Beats medications
  - One RCT found CBT-I improves insomnia in TBI as well
- Melatonin
  - Very safe, often effective in general population
  - Preliminary studies indicate melatonin improves sleep quality in TBI
- AVOID benzodiazepines, Z-drugs, and anticholinergic drugs
  - Cognitive side effects
  - Anticholinergic drugs increase risk of dementia
  - NOT actually all that effective (improve sleep by at most 9-30 min on the whole)
- TBI-associated excessive daytime sleepiness
  - May benefit from:
    - Modafinil
    - Armodafinil
    - Light therapy may improve

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Questions?