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MEDICATION MANAGEMENT OF BRAIN INJURED PATIENTS

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DISCLOSURE

- Dr. Collins has no financial or non-financial conflicts of interest related to this activity.
- Non-FDA approved products and indications will be discussed during this presentation.

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OBJECTIVES

- Describe the obstacles for standardizing medication treatments in brain injured patients.
- Identify at least 3 neurotransmitter targets for pharmacotherapy.
- Discuss factors that should be considered in choosing medication treatment in a brain injured patient.
- List 2 medications that should be used with caution in a brain injured patient.

PUZZLE TIME

Spot 10 differences

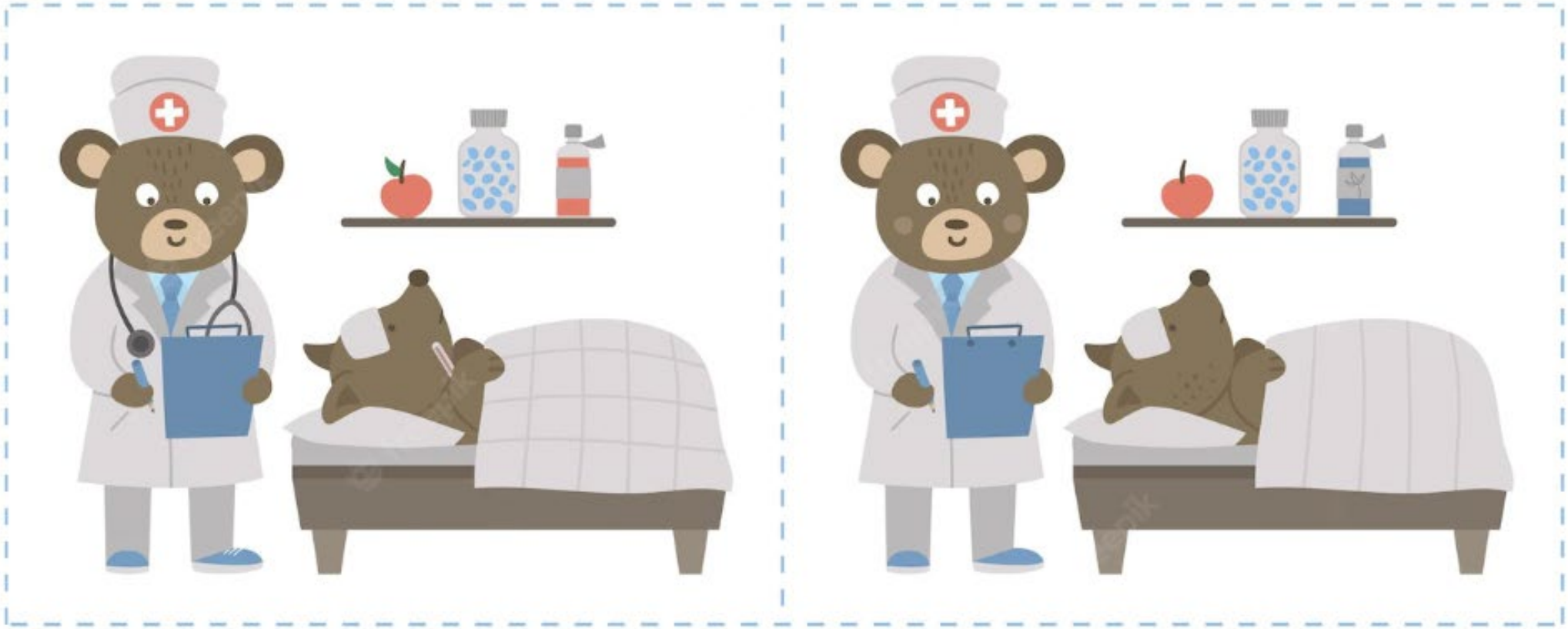
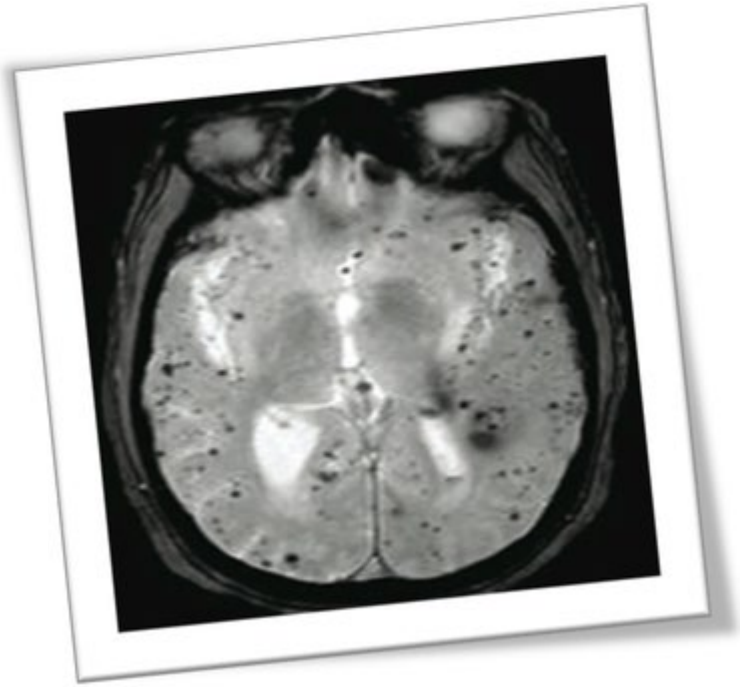


IMAGE: FREEPIK.COM

OBSTACLES TO DEVELOPING STANDARD OF CARE



Differences among patient population

- Individual injury
  - Neuroanatomy
  - Neurophysiology
  - Neurochemistry
- Individual pre-morbid function
- Individual post-injury sequela

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OBSTACLES TO DEVELOPING STANDARD OF CARE

- Variable responses to medications
  - Some patients benefit
  - Some patients get worse
  - Some patients more sensitive
  - Some patients resistant or need extreme doses
- Compliance issues
  - Memory
  - Adverse effects and interactions
- Measuring cognition and behavior
  - Patient may test well, but function poorly
  - Patient may test poorly, but function well
- Variations in biochemistry balance

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OBSTACLES TO DEVELOPING STANDARD OF CARE

Standards	Guidelines	**Options**
Based on at least 1, well-designed class I study with adequate sample OR overwhelming class II evidence	Based on well-designed class II studies	**Based on class II or class III studies with additional grounds to support a recommendation**

*** Lack of evidence ≠ lack of efficacy ***

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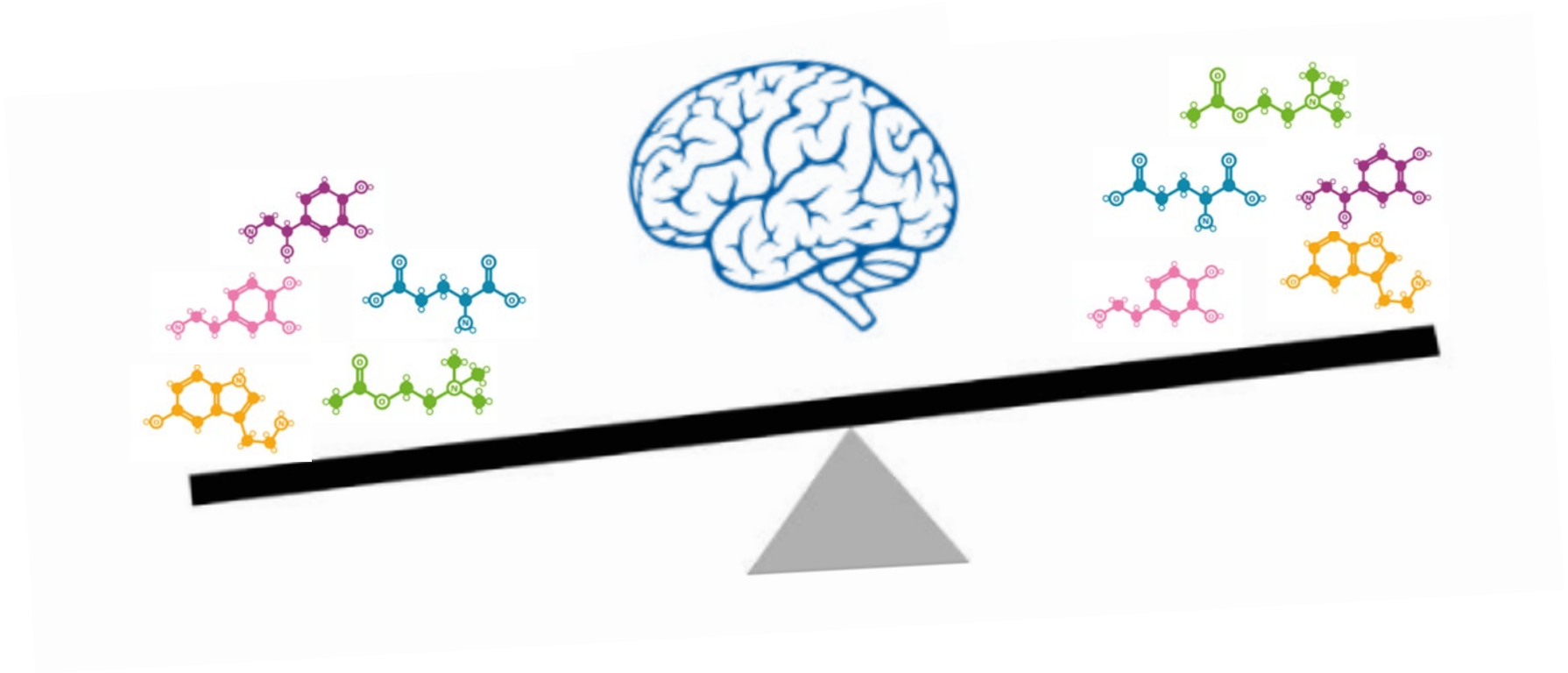
NEUROCHEMICAL APPROACH TO TREATMENT



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NEUROCHEMICAL APPROACH TO TREATMENT

Serotonin

- Memory
- Emotion
- Sleep/wake

Side effects

- Nausea
- Sexual side effects

Selective serotonin reuptake inhibitors (SSRIs)	• Sertraline (Zoloft®) • Citalopram (Celexa®)
Serotonin/norepinephrine reuptake inhibitors (SNRIs)	• Duloxetine (Cymbalta®) • Venlafaxine (Effexor®)
Tricyclic antidepressants (TCAs)	• Amitriptyline (Elavil®) • Nortriptyline (Pamelor®)

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NEUROCHEMICAL APPROACH TO TREATMENT

Dopamine

- Voluntary movement
- Motivation/initiation
- Memory

Side effects

- Nausea
- Headache
- Impulsivity

Parkinson's disease medications (↑dopamine)	• Bromocriptine (Parlodel®) • Levodopa/carbidopa (Sinemet®)
NMDA antagonists (↑dopamine/↓glutamate)	• Amantadine (Symmetrel®) • Memantine (Namenda®)
Atypical antipsychotics (↑serotonin/dopamine)	• Risperidone (Risperdal®) • Aripiprazole (Abilify®) • Quetiapine (Seroquel®)

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NEUROCHEMICAL APPROACH TO TREATMENT

Norepinephrine

- Arousal
- Attention
- Improve cognitive function

Side effects

- Agitation
- Insomnia
- Decrease appetite

Stimulants (↑ norepinephrine/dopamine)

- Methylphenidate (Ritalin®)
- Dextroamphetamine (Dexedrine®)
- Atomoxetine (Strattera®)

β-blockers (↓norepinephrine)

- Propranolol (Inderal®)

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NEUROCHEMICAL APPROACH TO TREATMENT

Acetylcholine

- Memory
- Improve fatigue

Side effects

- Nausea
- Insomnia
- Impulsivity

Acetylcholinesterase inhibitors (↑ acetylcholine)

- Donepezil (Aricept®)
- Galantamine (Razadyne®)
- Rivastigmine (Exelon®)

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NEUROCHEMICAL APPROACH TO TREATMENT

Glutamate

- Excitatory transmitter
- Overstimulation → cell death
- Affects cognition

Side effects
- Headache
- Insomnia

NMDA antagonists
(↑dopamine/↓glutamate)

- Amantadine (Symmetrel®)
- Memantine (Namenda®)
- Dextromethorphan (Neudexta®)

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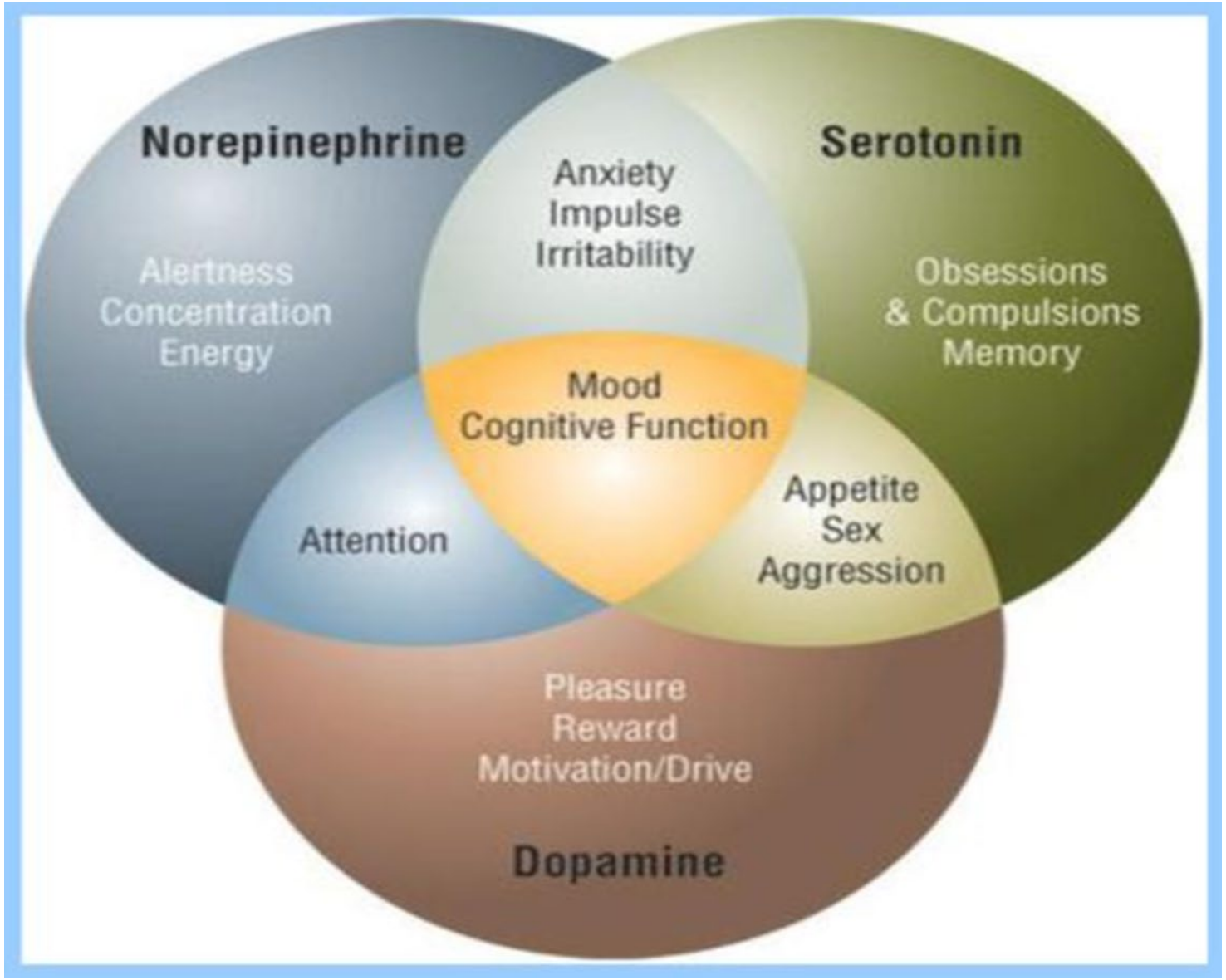
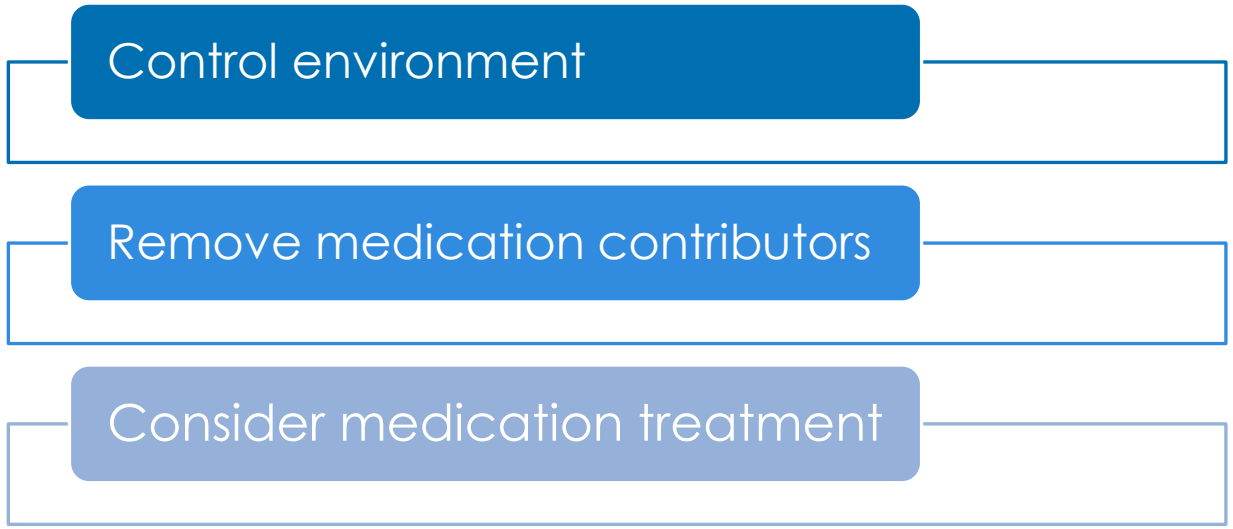


LANNI . CELLULAR AND MOLECULAR LIFE SCIENCES. 2009

APPROACH TO TREATMENT



Medication considerations

- Age
- Comorbidities
- Drug interactions
- Sensitivities
- Adherence
- Costs

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PATIENT CASE

- MF is a 58 year old male who sustained a traumatic brain injury (TBI) due to a un-helmeted motorcycle accident approximately 2 months ago. Toxicology screen was positive for alcohol, marijuana, and cocaine.
- Past medical history is significant for asthma, hypertension, 20 pack year smoker.
- His course has been complicated by bilateral deep vein thrombosis (DVTs), occurrence of seizure, urinary retention, need for enteral feeding, and significant shoulder pain.

PATIENT CASE

Today's presentation

- Patient is agitated, un-oriented with reports of striking nursing staff and verbal outbursts that are un-intelligible.
- His blood pressures are labile.
- He is holding his head and moaning.
- Nursing reports poor sleep.

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MEDICATION TREATMENT TARGETS

Post Traumatic Headache

Hyper arousal/ aggression

Sleep

Cognition/Memory

Aphasia

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IMAGE: BY MEDOC FOUND AT HTTPS://OPENCLIPART.ORG/DETAIL/311706/BRAIN-PILLS

POST TRAUMATIC HEADACHE

- Occurring in 25-78 % of individuals with mild TBI
- More frequent in individuals with mild versus moderate of severe TBI
- Exacerbated by very mild physical or mental exertion
- Can be episodic or continuous

Presentation Types

- Migraine headache
- Tension headache
- Medication overuse headache

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VA/DOD CLINICAL PRACTICE GUIDELINES. MANAGEMENT OF CONCUSSION-MILD TRAUMATIC BRAIN INJURY (MTBI). 2016.

POST TRAUMATIC HEADACHE
ABORTIVE TREATMENT OPTIONS

Acetaminophen ± combinations	• APAP/ caffeine/ibuprofen
Anti-emetics	• Prochlorperazine • Promethazine
NSAIDS	• Ibuprofen • Ketorolac
Serotonin receptor agonists	• Sumatriptan • Rizatriptan
Calcitonin gene-related protein (CGRP) inhibitors	• Ubrogepant • Rimegepant

Patient considerations

- Consider scheduled dosing
- Caution for medication overuse
- Avoid sedating or activating agents
- Assess bleeding risk

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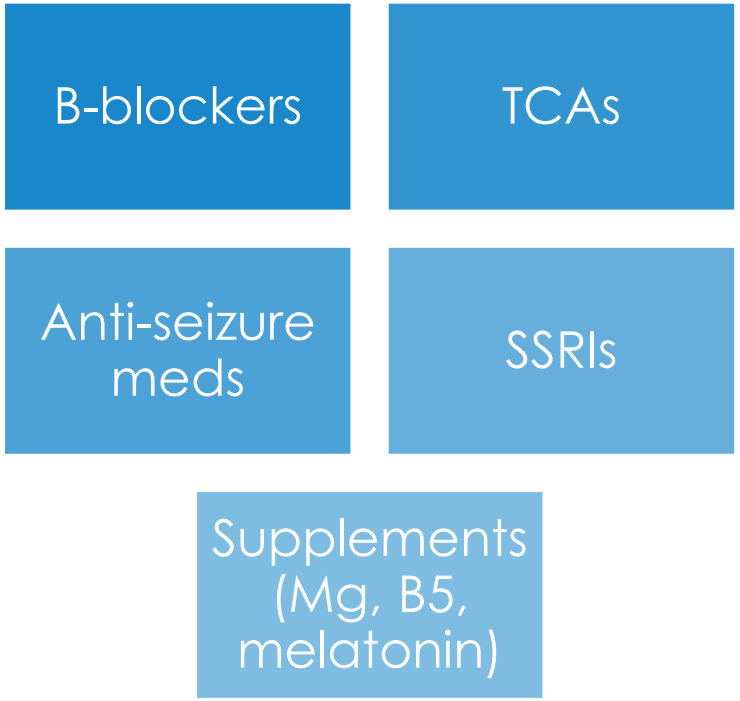
VA/DOD CLINICAL PRACTICE GUIDELINES. MANAGEMENT OF CONCUSSION-MILD TRAUMATIC BRAIN INJURY (MTBI). 2016.

POST TRAUMATIC HEADACHE
PROPHYLAXIS OPTIONS



Initiate headache prophylaxis if:

- migraine occurs >1/week or if tension headache occurs >3/week
- is disabling despite aggressive interventions
- affecting ADLs

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VA/DOD CLINICAL PRACTICE GUIDELINES. MANAGEMENT OF CONCUSSION-MILD TRAUMATIC BRAIN INJURY (MTBI). 2016.

HYPER-AROUSAL

Agitation/Aggression

- Common during post-traumatic amnesia
- Affects safety and adherence to treatment
- Most common in the acute phase, but can persist long term

Storming - dysautonomia

- Tachycardia
- Dystonia
- Diaphoresis
- Hypertension

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OBERHOLZER M, ETAL. NEUROREHABILITATION OF TRAUMATIC BRAIN INJURY (TBI): A CLINICAL REVIEW. MED SCI 2019;7:1-17

IMAGE: CC.EMOJIONE

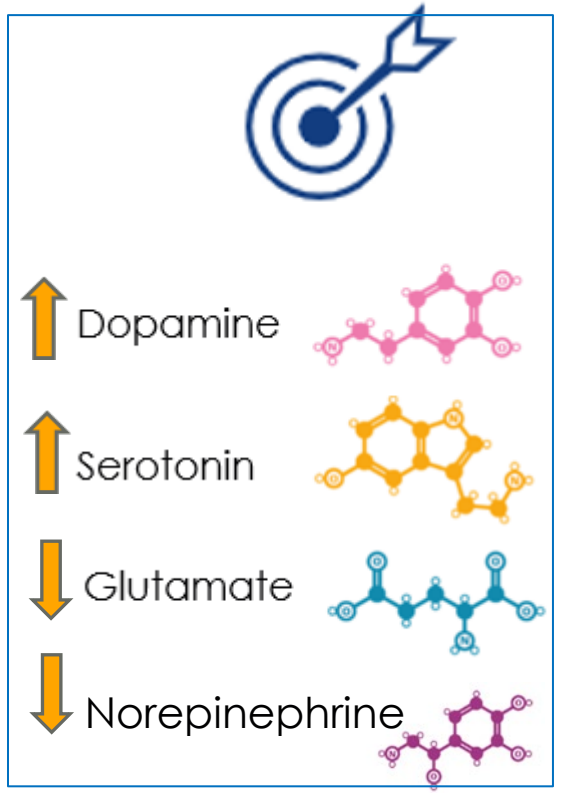
HYPER-AROUSAL

Atypical antipsychotics
- Aripiprazole
- Risperidone
- Quetiapine

SSRIs (↓
- Citalopram
- Sertraline

NMDA antagonists (↑dopamine/↓glutamate)
- Amantadine
- Memantine

β-blockers (↓ norepinephrine)
- Propranolol



Patient Considerations

- Prioritize safety
- Consider PMH of HTN
- Monitor closely for side effects

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SLEEP

Sleep disorders include

- Hyper somnolence
- Sleep related breathing disorders

Prevalent and persistent

- Present in 30-70% of patients with a history of brain injury
- Higher in the acute phase
- Usually decreases after a few years

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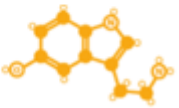
VIOLA-SALTZMAN NEURO CLIN 2012
IMAGE: OPENCLIPART

SLEEP

- Trazodone
- Melatonin
- Orexin inhibitors
- SSRIs
- "Z" meds (zolpidem)



Serotonin

Others:
histamine
orexin
melatonin

Patient Considerations

- Urinary retention
- Seizure history
- Goal is short term treatment

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COGNITION/MEMORY

- 40-60% of patients 1-3 months following TBI
- Correlates with injury severity
- Prolonged
- Removing or decreasing medications may be considered a "therapeutic event"

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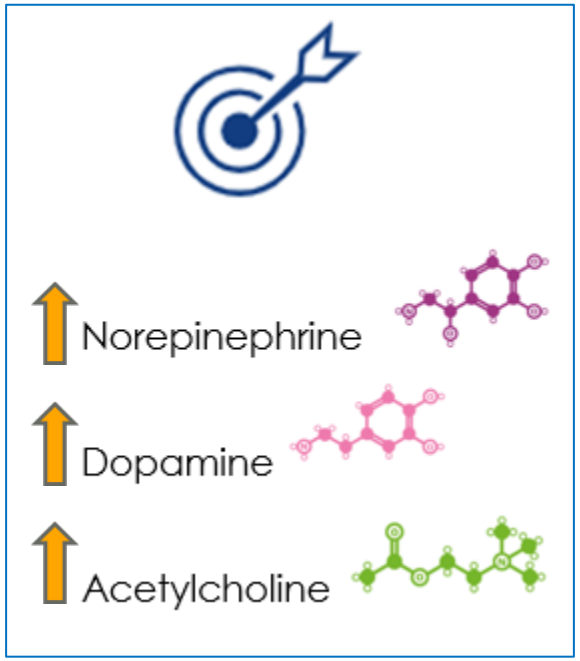
VA/DOD 2016; BHATNAGER 2016; ARCINIEGAS 2002

COGNITION/MEMORY

Stimulants (↑ norepinephrine)
- Methylphenidate
- Dextroamphetamine
- Atomoxetine

NMDA antagonists (↑dopamine/↓glutamate)
- Amantadine
- Memantine

Acetylcholinesterase inhibitors
- Donepezil



Patient Considerations

- Avoid stimulants
- Monitor for side effects
- Set expectations for benefit

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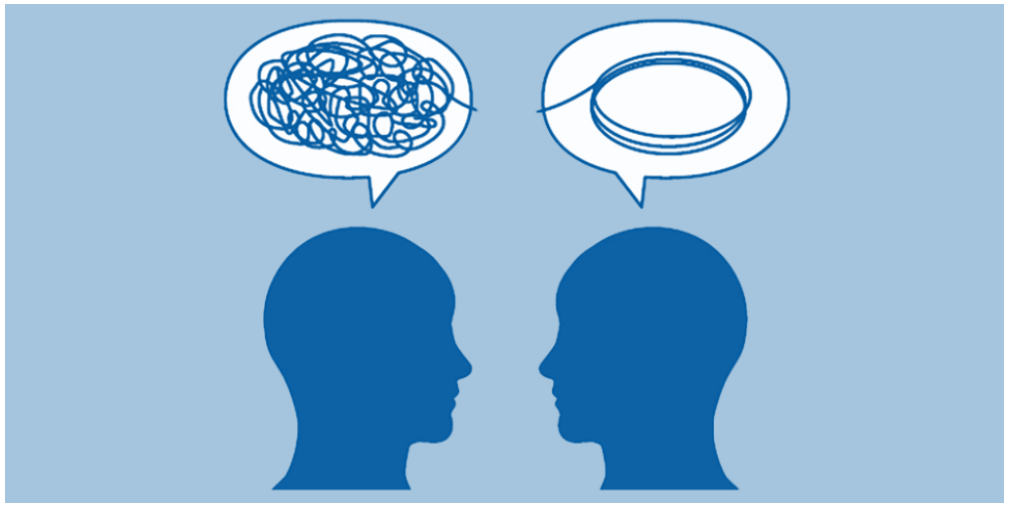
BHATNAGER 2016; MANKTELOW 2017

APHASIA

"Drug therapy might improve recovery from loss of language (aphasia)after stroke, but no drug has yet been proven to do more good than harm."

J Greener, Cochrane Stroke Group, Division of Clinical Neurosciences. 2010



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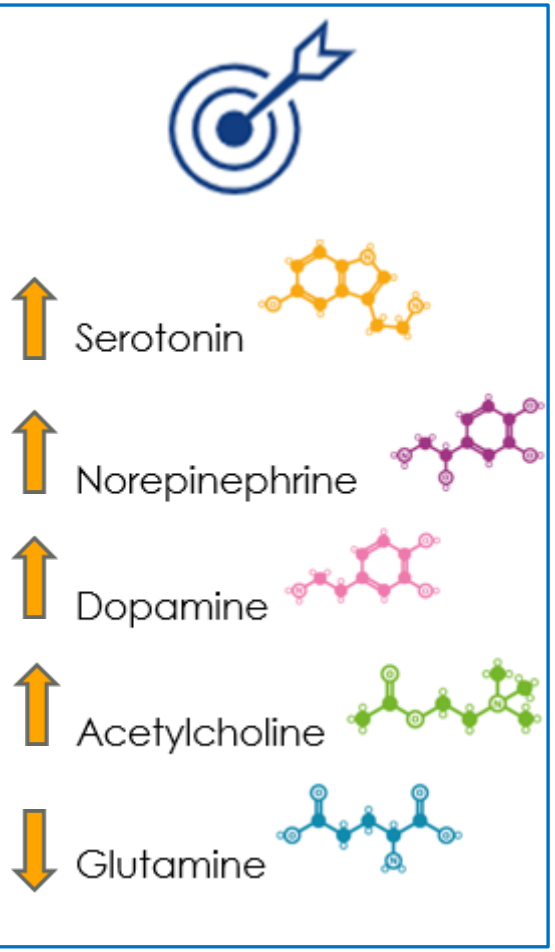
GREENER. COCHRANE DATABASE OF SYSTEMATIC REVIEWS 2001.
IMAGE: THE APHASIACENTER.COM;

APHASIA

TCAs	SSRIs
NMDA antagonists	Stimulants
Dopamine agonists	Acetylcholinesterase inhibitors

Patient considerations

- Consider medication if useful for other comorbidities



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GREENER. COCHRANE DATABASE OF SYSTEMATIC REVIEWS 2001.

MEDICATIONS TO USE WITH CAUTION

Benzodiazepines

- Common for insomnia and agitation
- Exacerbate confusion ("benzodiazepine psychosis")
- Impair memory
- Abuse potential
- Stopping the medication may be the "therapeutic event"

Typical antipsychotics (1st generation)

- Block dopamine
- May interfere with cognitive recovery
- Sedation->confusion-> aggression

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WARDEN . J NEURO TRAUMA 2006

PATIENT CASE

Treatment plan

- Initiate one intervention at a time
- Start low, go slow
- Monitor for response and side effects
- Trial lower doses with improvement or when stable
- Re-evaluate often

THANK YOU!

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