

Treatment Plan



Injury → Correlating neurotransmitter(s) → Symptom(s)

Acute

Subacute

Chronic

Changes
by phase

Re-evaluate

- Start low, go slow
- One intervention at a time

Brain Injury Sequelae



- Cognitive deficiencies
 - Attention/concentration and speed of processing
 - Memory
 - Executive functions
- Behavioral
- Emotional
- Other
 - Fatigue
 - Insomnia
 - Aphasia
 - Pseudobulbar affect (PBA)

Treatment of Cognitive Deficiencies



- Dopamine, acetylcholine, serotonin, norepinephrine
- No “standards”, just guidelines and options
- Dopamine enhancers
 - Bromocriptine (Parlodel®)
 - Guideline-level recommendation
 - Executive functioning
 - Divided attention
 - Initiation
 - Mental flexibility

Treatment of Cognitive Deficiencies



■ Dopamine enhancers

□ Amantadine (Symmetrel®)

- NMDA antagonist
- General cognitive functions
- Attention/concentration and speed of processing
- Apathy/poor initiation
- Motivation
- Perseveration

Treatment of Cognitive Deficiencies

- Dopamine enhancers
 - Carbidopa/levodopa (Sinemet®), pramipexole (Mirapex®), selegiline (Eldepryl®)
 - Initiation
 - Alertness
 - Wakefulness



Treatment of Cognitive Deficiencies



■ Stimulants

- Methylphenidate (Ritalin®)
 - Dopamine and norepinephrine
 - Guideline- and option-level recommendations
 - Memory
 - Attention/concentration and speed of processing
 - Mental processing
 - Learning
 - Arousal
 - Apathy/poor initiation
 - General cognitive functions

Treatment of Cognitive Deficiencies



■ Stimulants

- Dextroamphetamine (Dexedrine®)
 - Dopamine and norepinephrine
 - Attention
 - Working memory
- Modafinil (Provigil®)
 - Dopamine, histamine, alpha-1 agonist, inhibits GABA
 - Attention
 - Apathy/poor initiation
 - Memory
 - Speed of processing

Treatment of Cognitive Deficiencies



- Acetylcholinesterase inhibitors
 - Donepezil (Aricept®)
 - Guideline-level recommendation
 - Better general functioning
 - Attention/concentration and speed of processing
 - Learning
 - Memory
 - Apathy/poor initiation

Treatment of Cognitive Deficiencies



- Acetylcholinesterase inhibitors
 - Other acetylcholinesterase inhibitors
 - Galantamine (Razadyne®)
 - Rivastigmine (Exelon®)
 - Physostigmine

Treatment of Cognitive Deficiencies



■ Other options

□ Memantine (Namenda®)

- NMDA receptor antagonist
- Cognitive function
- Memory

□ Bupropion (Wellbutrin®)

- Dopamine and norepinephrine reuptake inhibitor
- Cognitive function

Treatment of Cognitive Deficiencies

■ Other options

□ Atomoxetine (Strattera®)

- Selective norepinephrine reuptake inhibitor
- Attention (lower doses)
- Memory
- Arousal (higher doses)
- Apathy/poor initiation
- Speed of processing



Self-Assessment Question



- A 51 y/o female involved in a MVA resulting in diffuse axonal injury is experiencing deficits in wakefulness, arousal, purpose, and initiation. An appropriate neurotransmitter target for pharmacotherapy includes:
 - ❑ A. Glutamate agonist
 - ❑ B. GABA agonist
 - ❑ C. Dopamine agonist
 - ❑ D. Dopamine antagonist

Treatment of Aggression

- Disruption to dopamine, norepinephrine, acetylcholine, serotonin
- No standards
- Guideline-level recommendations
 - Propranolol (Inderal®)
 - Pindolol



Treatment of Aggression



■ Options

□ Antihypertensives

- Metoprolol (Lopressor®)
- Clonidine (Catapres®)

■ Options

□ Mood stabilizers

- Carbamazepine (Tegretol®)
- Valproic acid (Depakote®)
- Lithium (Lithobid®)

Treatment of Aggression



■ Options

□ Antidepressants

- Sertraline (Zoloft®)
- Paroxetine (Paxil®)
- Fluoxetine (Prozac®)
- Citalopram (Celexa®)

■ Options

□ Antidepressants

- Trazodone (Desyrel®)
- Amitriptyline (Elavil®)
- Desipramine (Norpramin®)
- Protriptyline (Vivactil®)

Treatment of Aggression



■ Options

□ Atypical antipsychotics

- Risperidone (Risperdal®)
- Clozapine (Clozaril®)
- Olanzapine (Zyprexa®)
- Quetiapine (Seroquel®)
- Ziprasidone (Geodon®)

□ Stimulants

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

■ Options

□ Hormones

- Estrogens
- Medroxy-progesterone (DepoProvera®)

□ Others

- Amantadine (Symmetrel®)
- Buspirone (Buspar®)

Self-Assessment Question



- A patient's brain CT scan shows bilateral frontal and diffuse axonal injury. He is impulsive and agitated. The best option for pharmacologic treatment of his agitation is:
 - ❑ A. Haloperidol
 - ❑ B. Diazepam
 - ❑ C. Diphenhydramine
 - ❑ D. Propranolol

Treatment of Psychiatric Disorders



- Serotonin, norepinephrine, dopamine
- Depression/emotional deficits
 - Antidepressants (TCA and selective serotonin reuptake inhibitors)
 - Nortriptyline (Pamelor®)
 - Amitriptyline (Elavil®)
 - Desipramine (Norpramin®)
 - Citalopram (Celexa®)
 - Escitalopram (Lexapro®)
 - Paroxetine (Paxil®)
 - Sertraline (Zoloft®)

Treatment of Psychiatric Disorders



- Depression/emotional deficits
 - Venlafaxine (Effexor®), serotonin/norepinephrine
 - Atomoxetine (Strattera®), norepinephrine
 - Modafinil (Provigil®), ↓ GABA
- Bipolar disorder
 - Valproic acid (Depakote®)
 - Carbamazepine (Tegretol®)
 - Lithium
- Psychosis
 - Olanzapine (Zyprexa®)
 - Clozapine (Clozaril®)

Treatment of Psychiatric Disorders

■ Anxiety

- Tricyclic antidepressants (TCA)
- Selective serotonin reuptake inhibitors (SSRI)
- Benzodiazepines
 - Lorazepam (Ativan®)
 - Clonazepam (Klonopin®)
 - May interfere with cognition



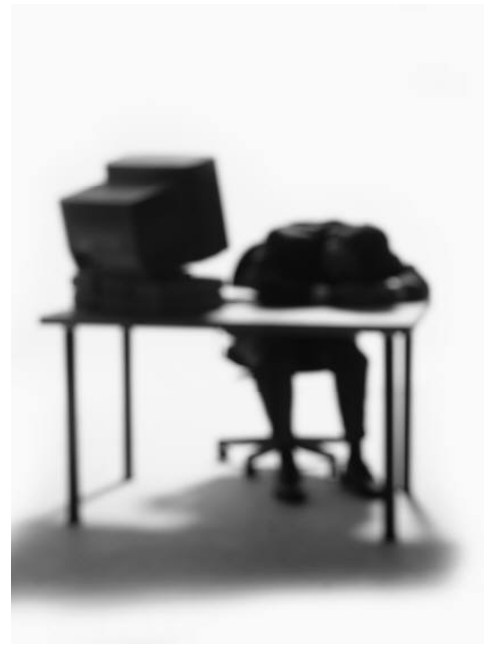
Self-Assessment Question



- An obstacle to treating a TBI patient with depression includes:
 - ❑ A. The patient may be more sensitive or less responsive to medication
 - ❑ B. The patient's previous history does not contribute to current symptoms
 - ❑ C. Depression in TBI patients is not affected by neurotransmitters
 - ❑ D. Two medications should be started simultaneously

Medications for Fatigue

- Acetylcholinesterase inhibitors
- Methylphenidate (Ritalin®)
- Modafinil (Provigil®)
- Atomoxetine (Strattera®)



Medications for Insomnia

- Trazodone (Desyrel®)
- Imipramine (Tofranil®)
- Nortriptyline (Pamelor®)
- Mirtazapine (Remeron®)
- Ramelteon (Rozerem®)



Medications for Aphasia



- Tricyclic antidepressants
 - Nortriptyline (Pamelor®)
 - Desipramine (Norpramin®)
- Increase serotonin and norepinephrine

Pseudobulbar Affect



- Uncontrollable, inappropriate affect
- Some success
 - Antidepressants (TCA, SSRI)
 - Dopaminergic agents

Pseudobulbar Affect



- Dextromethorphan/quinidine (Nuedexta®)
 - Discovered while studying different use for ALS
 - Dextromethorphan
 - Cough suppressant
 - NMDA antagonist
 - Quinidine
 - Antiarrhythmic agent
 - Slow metabolism of dextromethorphan

Side Effects



- Are sometimes “therapeutic”
- Vary among medications in each class
- Guide medication selection
- Make some medications inappropriate for brain injury patients

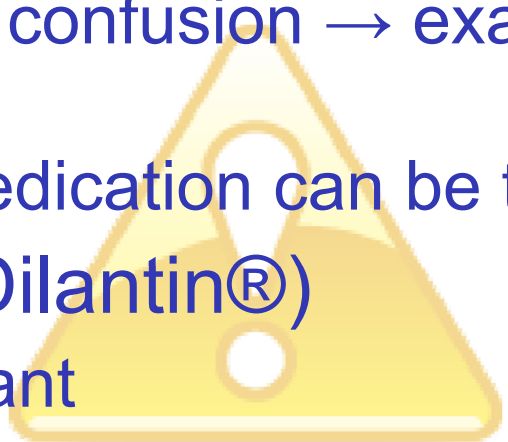
Medications to Use with Caution in TBI

■ Benzodiazepines

- ❑ Exacerbate confusion (“benzodiazepine psychosis”)
- ❑ Impairs memory
- ❑ Common for insomnia and agitation
- ❑ Stopping the medication may be the “therapeutic event”



Medications to Use with Caution in TBI

- First generation antipsychotics (Haldol®)
 - ❑ Block dopamine → interferes with recovery
 - ❑ Sedation → confusion → exacerbate aggression
 - ❑ Stopping medication can be therapeutic
 - Phenytoin (Dilantin®)
 - ❑ Anticonvulsant
 - ❑ Impairs cognitive function recovery initially
 - ❑ Better alternatives for seizure prophylaxis
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Self-Assessment Question



- A TBI patient recently transferred from the ICU has been receiving haloperidol for aggressive behavior. He continues to be assaultive toward caregivers, especially at night. The best intervention would be:
 - ❑ A. Adding lorazepam PRN
 - ❑ B. Adding amantadine PRN
 - ❑ C. Increasing the haloperidol dose
 - ❑ D. Stopping the haloperidol

Self-Assessment Question



- A TBI patient with a pre-morbid history of seizure disorder is currently receiving levetiracetam and phenytoin. An intervention to facilitate cognitive recovery would be:
 - ❑ A. Stop levetiracetam and increase phenytoin dose
 - ❑ B. Stop phenytoin and add lacosamide
 - ❑ C. Add phenobarbital
 - ❑ D. Avoid making any changes to current regimen

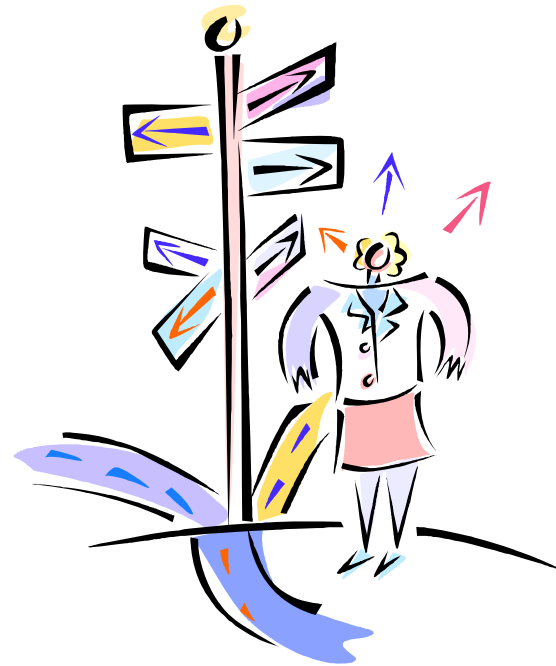
Summary

- Obstacles to good evidence
 - Heterogeneity of patient population
 - Variable responses to medications
 - Compliance issues
 - Measuring cognition and behavior
 - Variations in biochemistry balance



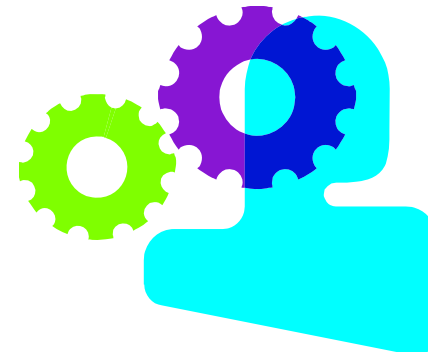
Summary

- Limited evidence
 - Few standards
 - Few guidelines
 - Lots of options



Summary

- Treatment of cognitive deficiencies
 - Dopamine enhancers
 - Stimulants
 - Acetylcholinesterase inhibitors
 - Norepinephrine reuptake inhibitor
 - NMDA antagonist



Summary

■ Treatment of aggression



- ❑ Beta blockers
- ❑ Alpha adrenergic agonist
- ❑ Mood stabilizers
- ❑ Antidepressants
- ❑ Atypical antipsychotics
- ❑ Stimulants
- ❑ Dopamine enhancers

Summary

■ Psychiatric disorders

- Depression
- Bipolar disorder
- Psychosis
- Anxiety



■ Treatment

- TCA, SSRI
- Mood stabilizers
- Atypical antipsychotics
- TCA, SSRI

■ Try to Avoid

- First generation antipsychotics
- Benzodiazepines

Summary



- Treatment of fatigue
 - Acetylcholinesterase inhibitors
 - Methylphenidate (Ritalin®)
 - Modafinil (Provigil®)
 - Atomoxetine (Strattera®)

Summary

- Treatment of sleep disorders
 - ❑ Trazodone (Desyrel®)
 - ❑ Imipramine (Tofranil®)
 - ❑ Nortriptyline (Pamelor®)
 - ❑ Mirtazapine (Remeron®)
 - ❑ Ramelteon (Rozerem®)



Summary



- Treatment of aphasia
 - Nortriptyline (Pamelor®)
 - Desipramine (Norpramin®)
- Treatment of pseudobulbar affect
 - Dextromethorphan/quinidine (Nuedexta®)
 - Antidepressants (TCA, SSRI)
 - Dopaminergic agents

Summary

- Side effects to monitor
 - ❑ Sexual side effects
 - ❑ Headache, GI
 - ❑ Dizziness
 - ❑ Insomnia
 - ❑ Sedation
 - ❑ Weight gain
 - ❑ Extrapyrasidal symptoms



Summary



- Medications to try to avoid
 - Benzodiazepines
 - First generation antipsychotics
 - Phenytoin (Dilantin®)

Thank you for your attention.



Selected References



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