

# Neurostimulants in Stroke Recovery

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Stroke Update 2018

# Objectives

- Review principles of stroke recovery
- Understand considerations for use of medications to enhance recovery after stroke
- Identify commonly used neurostimulant medications for post-stroke recovery
- Use clinical cases to highlight possible indications for neurostimulant medication use post-stroke
- Understand considerations for choice of medication based on clinical experiences and current literature

# Cognitive Changes after Stroke

- Arousal
- Attention
- Concentration
- Memory
- Executive functions

# Stroke Recovery/Neuroplasticity

- Early onset of rehabilitation program improves functional recovery
  - focus on facilitating, directing or promoting plasticity of nerve tissue
- Neurotransmitters such as glutamate, dopamine, acetylcholine, norepinephrine, serotonin thought to be involved in plasticity process
- Stimulation and modulation of these neurotransmitter systems may increase recovery after acquired brain injury

# General Considerations for Neurostimulant Use

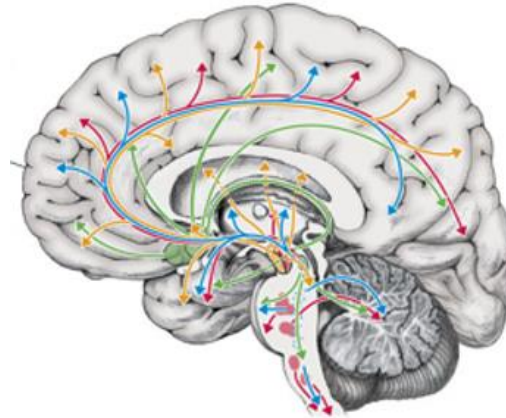
- Goals of therapy
- Location of infarct/lesion
- Medical comorbidities
- Sedating medications
- Sleep
- Measures of efficacy

# Clinical Cases

1. 69 yo M, large R MCA/ACA infarcts, lethargy/poor arousal, L hemiplegia, L neglect
2. 25 yo F, pontine hemorrhage, poor arousal and command-following
3. 62 yo F, L MCA infarct, moderate Broca's aphasia, R hemiparesis, impaired attention
4. 46 yo M, anoxic BI, poor arousal, bradykinesia

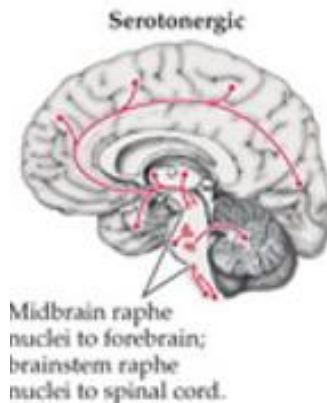
# Neurostimulant Medications

- Fluoxetine/SSRIs
- Donepezil
- Methylphenidate
- Modafinil
- Bromocriptine
- Levodopa
- Amantadine
- Memantine
- Zolpidem



# SSRI

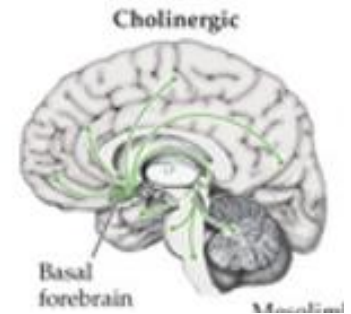
- Fluoxetine
  - FLAME study
  - Immediate administration > delayed
  - Possible clopidogrel interaction
  - Dosing: 20mg daily
- Other SSRIs
  - Less evidence for motor recovery
  - Positive effects on mood, dependency, disability





# Donepezil

- Acetylcholinesterase inhibitor
- Associated with improvements in:
  - Cognitive function
  - Aphasia
  - Motor function
- Relatively good tolerability/safety profile
- Dosing: 5-10mg daily



# Amantadine

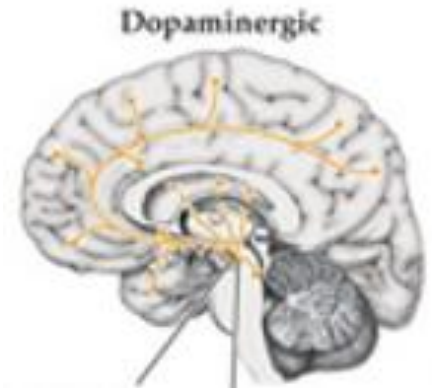
- NMDA receptor antagonist, dopaminergic
- Most data in TBI
- Associated with:
  - Faster recovery in disorders of consciousness
  - Improved irritability/agitation
  - Improved memory and reaction time in subjects with concussion
- Fair tolerability
- Dosing: 100-200mg bid

# Memantine

- NMDA receptor antagonist
- Possible neuroprotective effects
- Improvements in aphasia
- Good safety/tolerability
- Dosing: 10-20mg daily

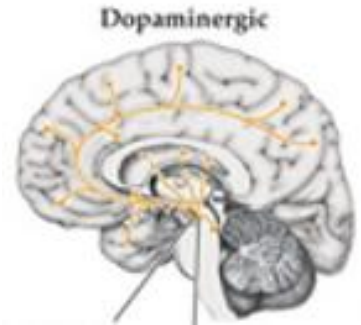
# Levodopa

- Dopaminergic
- Associated with improvements in:
  - motor function/motor learning
  - ?aphasia
  - ?mood
  - ?neglect
- Relatively good tolerability
- Dosing: 100-200mg daily to TID



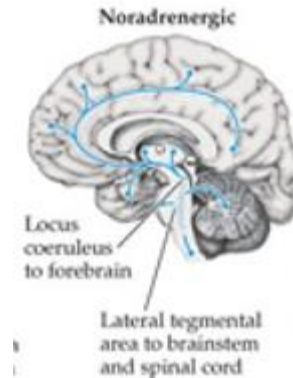
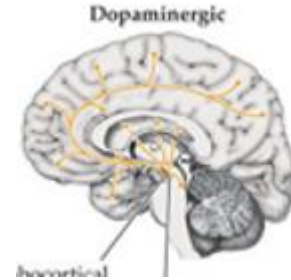
# Bromocriptine

- Dopaminergic
- Associated with improvements in:
  - aphasia
  - Cognition/memory/executive functioning
  - Neglect/inattention
- Variable tolerability
- Dosing: 2.5-10mg daily



# Methylphenidate

- Dopamine, norepinephrine, serotonin
- Associated with improvements in:
  - arousal
  - ?motor function
  - Mood (post-stroke depression)
  - Cognitive function
  - ?aphasia
- Fair tolerability at low doses
- Dosing: 2.5-5mg daily-bid



# Modafinil

- CNS stimulant; monoaminergic
- Improvements in:
  - Arousal
  - Fatigue
  - Quality of life
- Good tolerability
- Cost/coverage possibly prohibitive
- Dosing: 100-200mg daily-bid

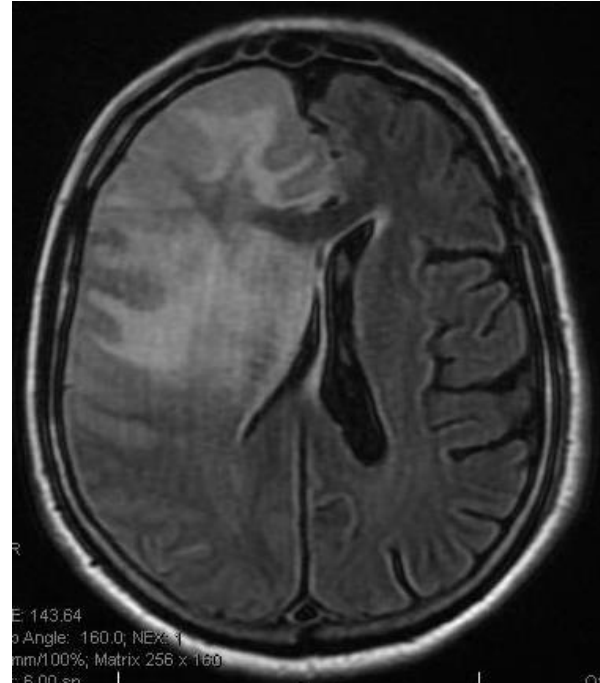
# Zolpidem

- Non-benzodiazepine hypnotic
- Emerging data for use in disorders of consciousness
- Associated with:
  - Improved arousal in vegetative and minimally conscious states
  - Improved cerebral perfusion, metabolic activity in studies using functional neuroimaging
  - Improved verbal communication
- Low percentage of responders
- Good tolerability
- Dosing: 10-15mg, daily+



# Case 1

- 69 yo M, no PMH
- R MCA, ACA infarcts, hemorrhagic conversion
- R hemicraniectomy
- Medical complications
- L hemiplegia, neglect
- Decreased arousal
- 50% command-following



# Case 1

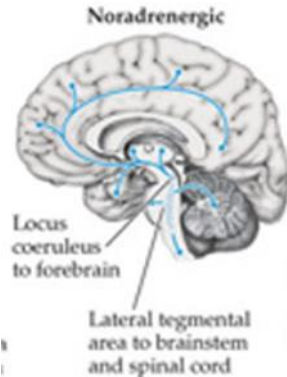
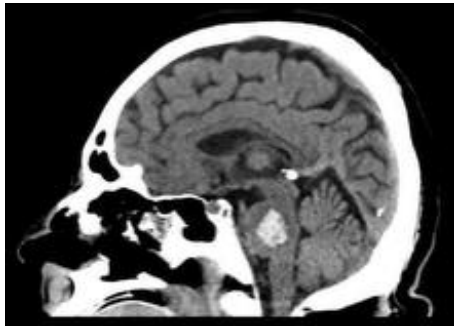
- Primary issues:
  - Arousal
  - Cognition
  - Hemiplegia
- Fluoxetine 20mg daily
- Modafinil
  - 100mg daily, initiated day 2 of IPR
  - Increased to 200mg daily week 2

# Case 2

- 25 year-old female
- No PMH
- Pontine hemorrhage
- Poor arousal
- <30% command-following

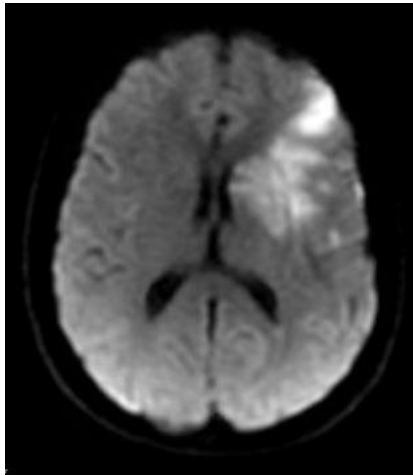
## Case 2

- Primary issue:
  - arousal
- Methylphenidate
  - 5mg bid
- Markedly improved arousal
- >75% command-following
- Improved therapy participation



## Case 3

- 62 year-old female
- Left frontal and basal ganglia infarcts
- Mild R hemiparesis
- History depression
- Expressive, Broca's type aphasia
- Oral motor apraxia
- Decreased initiation
- Impaired attention



# Case 3

- Primary issues:
  - Aphasia
  - Initiation
  - attention
- Donepezil 5mg daily
- Escitalopram 20mg daily

# Case 4

- 46 year-old male
- Hypoxic ischemic brain injury
- CKD, HTN, DM1
- Bradykinesia on exam, R side > L side
- Shuffling gait
- Slowed processing

# Case 4

- Primary Issues:
  - Arousal/attention
  - Bradykinesia
- Carbidopa/Levodopa
  - Initiated 25/100mg TID
  - Titrated up to 50/200mg TID



Medication	Dosing	Targeted neurotransmitter	Indications	Adverse Effects
Fluoxetine	20mg daily (x3 months)	Serotonin	Motor recovery	Plavix interaction QTc prolong. Serotonin syndrome
Donepezil	5-10mg daily	Acetylcholine	Cognition Arousal Aphasia Motor fnc	Nausea Irritability Muscle cramps seizure
Memantine	10-20mg daily	NMDA antagonist/ glutamate	Cognition Aphasia Arousal	Dizziness, nausea Headache SJS
Levodopa	100-200mg daily - TID	Dopamine	Motor fnc Aphasia Neglect mood	Anxiety Hallucinations Nausea/emesis Orthostasis

Medication	Dosing	Targeted neurotransmitter	Indications	Adverse Effects
Bromocriptine	2.5-10mg daily	Dopamine	Aphasia Cognition Neglect	Hypotension Lightheadedness Nausea/emesis Agitation
Methylphenidate	2.5 – 5mg bid (inc. as tol)	Dopamine norepinephrine	Cognition Arousal Mood	Tachycardia Paranoia/Irritability Decreased appetite
Amantadine	100mg-200mg bid	NMDA antag./ glutamate	Arousal Agitation	Orthostasis Seizure Livedo reticularis
Zolpidem	5-10mg daily	GABA A agonist	Arousal	Somnolence
Modafinil	200mg daily (100-400)	DA, NE, GABA Glutamate serotonin	Fatigue	Headache, nausea Insomnia, anorexia SJS

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