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neuroscience CME

Master Class for Neuroscience Professional Development

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Psychiatric Comorbidities in Patients with Neurologic Conditions

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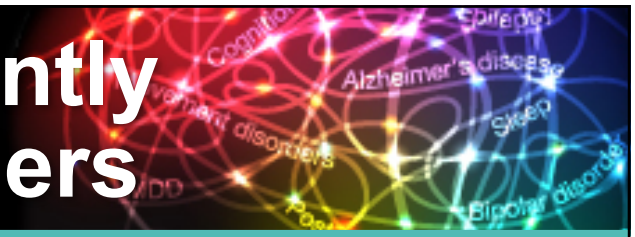
Learning Objective 1

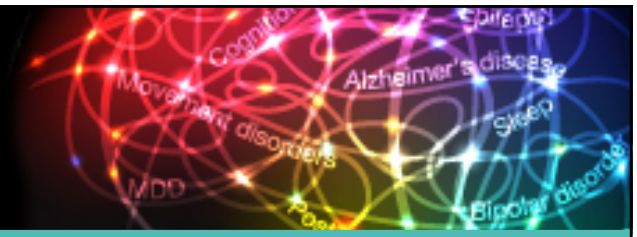
Integrate evidence-based strategies to optimize treatment selection for psychiatric patients with comorbid neurologic conditions

Neurologic Conditions Frequently Accompanied by Mood Disorders



- Epilepsy
- Migraine
- Stroke
- Parkinson's disease
- Multiple sclerosis
- Pseudobulbar affect

Case: Mr. B



- 57-year-old divorced Wisconsin farmer presents with sister for TRD evaluation (index episode< 6 mos)
  - 1 prior psychiatric hospitalization in 2012
  - 5 admissions in 2017 (31 days over 11-weeks)
  - Sister as main historian (living in patient's home)
    - reporting cognitive difficulties
    - tremor in his left hand /head

TRD = treatment resistant depression.

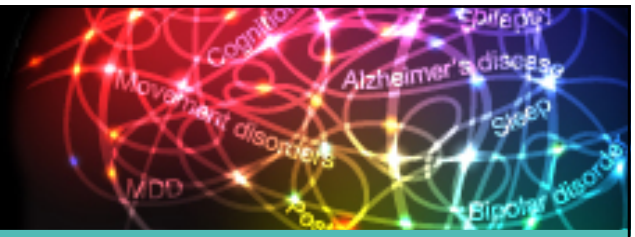
Case: Chief Complaint

- Rating scale data PHQ-9 = 15 (Q-9 = 1), GAD-7 = 4, AUDIT = 1
- Depressed mood and cognitive decline
- Not able to work this planting season
- Temazepam /clonidine helpful (↓ nightmares & nocturnal anxiety)
  - 6-7 hours, but still early morning awakening
- Suicidal ideation 2-3 weeks ago at height of insomnia (no prior attempts)
- Desvenlafaxine 50 mg po qhd (x 3 weeks)
- Fluoxetine 20 mg capsule and Olanzapine 5 mg po qhs (x 3 months)
- Clonidine 0.1 mg tablet po qhs for anxiety (x 10 days)
- Temazepam 30 mg po qhs (x 3 days)

Case: Current Presentation (cont'd)

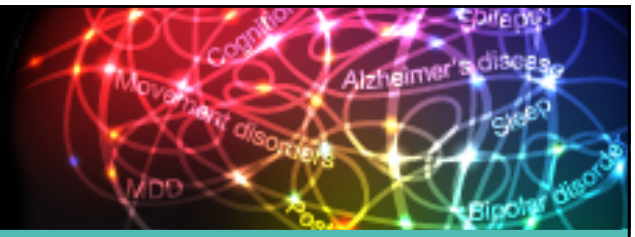
- Mental Status Examination
  - Alert and oriented to person, place, date, and situation
  - Speech is slowed not dysarthric
  - Mood is depressed - Affect is flat - hypomimia
  - Thought processing logical, goal-directed.
  - Negative for acute suicidality. No psychosis
  - Insight and judgment are intact.
- Physical Exam Findings:
  - Bradykinetic
  - Mild rigidity of the lower / upper rigidity extremities
  - Arm swing moderately reduced bilaterally

Neurocognitive Testing



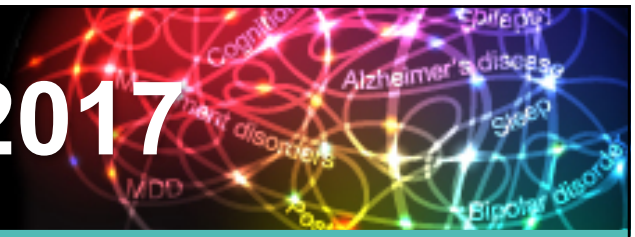
- In comparison to outside study 1 year prior
- Deficits in learning & memory for novel verbal & visual information
- Visuospatial/constructional skill and language functioning improved
- Attention impaired
- RBANS is comparable (77 standard score current exam, vs. 73)
- Variability in performance
  - unlikely to be neurologically-based cognitive decline
- Reassessment 3-6 months

Case: Psychiatric History



- 2012
  - Hospitalization for non-psychotic major depression (age 52) in context of 2nd marital separation and divorce
  - good response to ECT in 2012
  - maintenance fluoxetine 20 mg 4 years
  - D/C'd for 1 year prior to 2nd episode recurrence
- 2017
  - 5 hospitalizations, 31 hospital days over an 11-weeks.
  - Prior treatments: nortriptyline 50 mg, lithium 450 mg
  - 13 ECT treatments- improvement in affect and mood, but anxiety and confusion prompted DC

Psychological Evaluation 2017



- Millon Clinical Multiaxial Inventory
  - dependent and melancholic personality patterns
  - consistent with major depression and anxiety
- Malingering Probability Scale
  - very low likelihood of malingering
  - reliable claim of psychological discomfort and distress

Case: Medical History and Other History

- Medical History:
  - No loss of consciousness, seizures, surgeries. No known drug allergies
  - Mild hand tremor, head-nodding tremor exacerbated by neuroleptics.
- Social History:
  - Divorced and lives on a farm that has been in his family since 1926.
  - Two daughters, both supportive and doing well.
- Family Medical History:
  - Father died at age 85 with hypertension and dementia
  - Mother dementia, recurrent depression through her 40's
  - Sister age 47, episode of depression late 20s, (+) response
  - No family history of Parkinson's disease

Case: Test Results

- MRI Brain
  - Few nonspecific foci of increased T2 signal within white matter of both cerebral hemispheres, consistent with minimal leukoaraiosis.
  - Nonspecific foci of increased T2 signal within the pons.
  - Grossly normal brain morphology
- Laboratory Exam
  - All labs unremarkable
- Genotyping
  - SS genotype serotonin transporter (SLC6A4)
  - *4/*9 Cytochrome p450 2D6 poor metabolizer phenotype

Case: Diagnosis

- Major depressive disorder, recurrent, severe
- Parkinsonism
- Cognitive decline

Parkinson's Disease & Depression

- Spectrum of Depression
  - Depressive symptoms (50-70%)
  - Clinically significant symptoms (35%)
  - Major depressive disorder (17%)
  - "Off" only (%?)
- Meta-analysis (n = 13 studies)
  - Both SSRI's aggregate & CBT > placebo
- Bupropion* improves depression & motor symptoms
- Pramipexole* controlled evidence
  - Depressive symptoms + PD
  - Major depressive disorder
  - Bipolar I/II depression

* = Not FDA approved for Parkinson's disease

Corrigan MH, et al. *Depress Anxiety.* 2000;11(2):58-65; Bomasang-Layno E, et al. *Parkinson Rel Dis*. 2015 ;21(8):833-842; Goetz CG, et al. *Neurology*. 1989;39(11 Suppl 2):63-66; Cooney JW, et al. *Curr Neurol Neurosci Rep*. 2016;16(5):49; Goldberg, et al. *Am J Psych.* 2004, Zarate CA, et al. *Biol Psychiatry.* 2004;56(1):54-60.

Parkinson's Disease Psychosis Treatment

	Pimavanserin	Clozapine	Quetiapine
FDA approved for PDP	Yes	No	No
Titration	None	Cautious titration	Slow
Strength of evidence	RDBPC	RDBPC, mean dose = 25mg	1 (+), 3(-)
Drug interactions	Strong CYP3A4 inhibitors and inducers	Use caution with CYP1A2, CYP3A4, and CYP2D6 inducers or inhibitors	May antagonize effects of levodopa and dopamine agonists
Geriatric use	No titration required	May be more susceptible to anticholinergic effects, rates of TD higher in elderly women	Start low, go slow

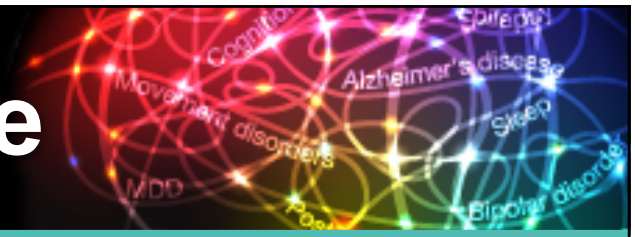
RDBPC = randomized double blind placebo controlled

Cooney & Stacy. *Curr Neurol.* 2016.; Cummings, et al. *Lancet* 2014, Pimavanserin PI.

Case: Plan

- Recommendations?
  - Start carbidopa/levodopa?
  - Start pramipexole?
  - Tapering olanzapine?
  - Taper desvenlafaxine?
  - Taper fluoxetine?

Outpatient Inpatient Course



- Discontinued SSSRI, SNRI, and olanzapine
- Mirtazapine at bedtime 30 mg po qhs
- Carbidopa/levodopa 25/100 immediate release TID some improvement in motor but not mood
- Carbidopa / levodopa DC and pramipexole titrated to 1 mg po qhs
- Sister says he is 90% better toward baseline.
- Slight tremor is noted, left upper extremity/neck.
- Repeat Neuropsychology Testing
  - Despite his many cognitive complaints
  - Language, visuospatial, and executive functioning broadly intact
  - Profile is most compatible with a subcortical process

Call to Action

- Screening for psychiatric disorders in patients with neurological disorders
- Collaborate with your colleagues in neurology and psychiatry to improve the lives of people affected by neurologic disorders and comorbid psychiatric disorders

Questions & Answers

Don’t forget to fill out your evaluations to collect your credit.