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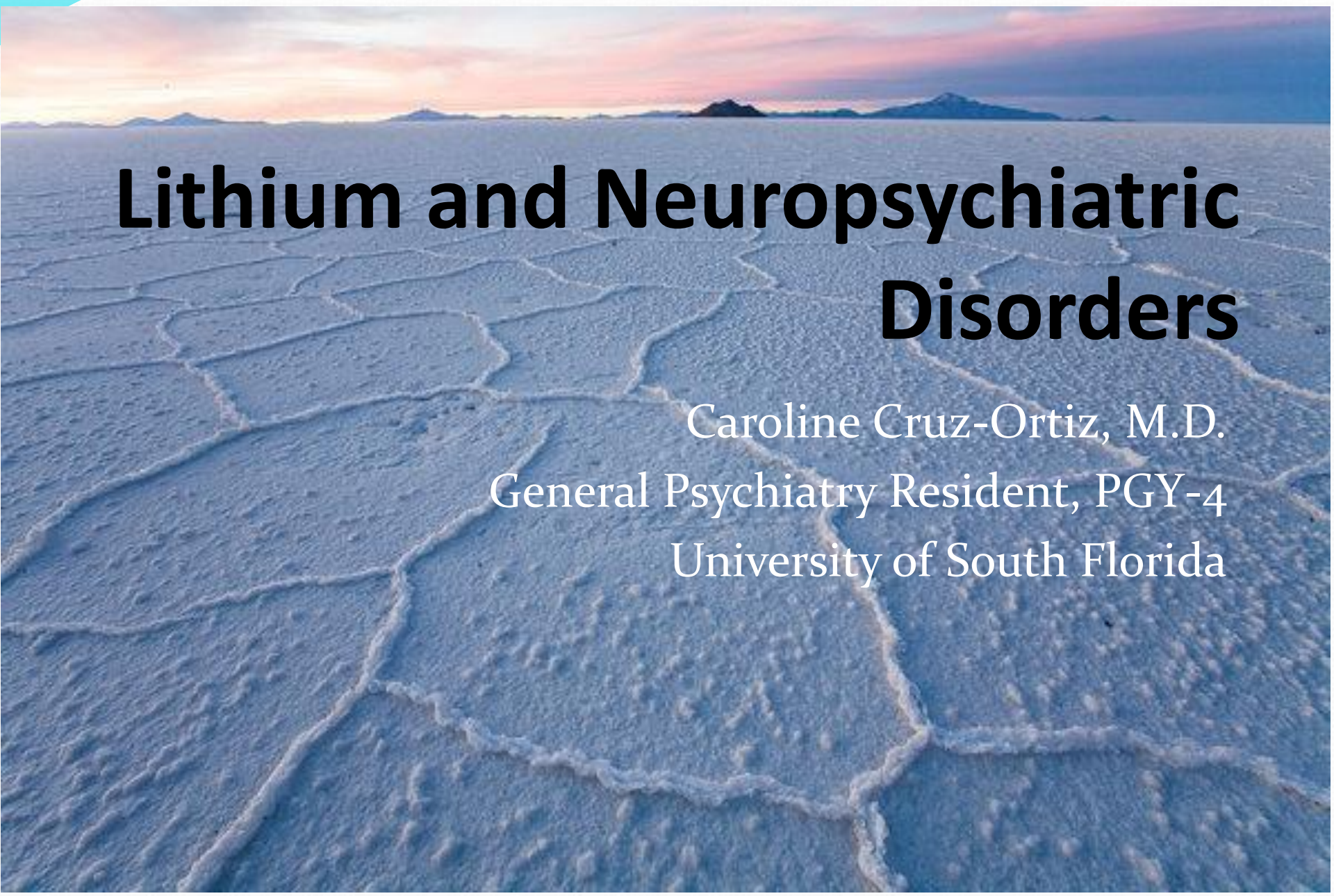

Lithium and Neuropsychiatric Disorders

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- none

Objectives

- Review the case of a patient with a traumatic brain injury (TBI)
- Understand the FDA approved indications of lithium
- Review the existing literature on lithium use in neuropsychiatric disorders

Case

- 60 yo who had a severe head injury in an MVA at 32 years of age. No information about the injury is available but CT head scan shows extensive left frontal, parietal and temporal encephalomalacia and he was left with dense right hemiparesis, a seizure disorder and severe cognitive impairment. Following the injury, he had failed placement in 5 different SNFs due to behavioral problems and he was ultimately admitted to the CLC.

Behavioral problems

- Since 38 years of age, and likely beforehand, he had problems with frequent outbursts of angry screaming (without any discernible words) directed toward people in his immediate area, also sometimes pounding his chest or fleeing the area in his wheelchair. He was never combative. The episodes were brief, usually no more than 5–10 seconds, but were quite disruptive, occurring perhaps 8-10 times per hour. They were sometimes precipitated by nursing care or phlebotomy, but more often by staff or patients (especially men) approaching him from the front or inadvertently cornering him. Remarkably, his disposition between episodes was invariably pleasant and smiling, returning immediately after the several seconds of screaming.

PMHx

- HTN
- DM
- Seizure disorder
- No known pre-morbid history of psychiatric illness or substance abuse.

Medications

- Risperidone 2mg/d
- Buspirone 60mg/d
- Trazodone 100mg/d
- Levetiracetam 1500 mg/d
- Lisinopril
- Simvastatin
- Metformin
- Aspirin

Previous medication trials

- Valproic acid
- Tegretol
- Risperidone up to 4mg/d
- Haloperidol up to 22.5mg/d
- Optimization of staff approach was minimally effective.

Our approach

- Lithium carbonate was started with a maximum dose of 900mg at bedtime
- Lithium level was 0.77 mEq/L
- Trazodone was d/c
- Risperidone was tapered and d/c after 6 weeks
- Buspirone was tapered and d/c 2 weeks after risperidone was d/c

Today

- Over the subsequent 6 months, the outbursts continued to decrease in frequency. Now, they are occurring no more than 4-5 times per week, and usually in the context of phlebotomy or other uncomfortable procedures.

History of Lithium

- Lithium use documented as far back as 1859 for gout by London internist, Alfred Baring Garrod.[1]
- In 1870, Dr. Silas Weir Mitchell recommended lithium bromide as an anticonvulsant and hypnotic.
- In 1871, William Hammond from Bellevue Hospital became the first to prescribe lithium for mania.
- Then in 1894, in Denmark, psychiatrist Frederik Lange made explicit reference to lithium in treatment of melancholic depression.
- Found to be effective for mania by John Cade in 1949.
- That same year,, an article in JAMA appeared in the U.S> resulted in multiple deaths when used as a salt substitute for CHF[2]

FDA-approved indications

- Manic episodes of manic-depressive illness
- Maintenance treatment for manic-depressive patients with a history of mania

Common uses of Lithium

- Bipolar depression
- Major depressive disorder (adjunctive)
- Schizoaffective disorder, bipolar type

Review of the literature

Lithium and Suicide

- Cipriani et al conducted a meta-analysis that showed patients with mood disorders treated with lithium had a lower rate of suicide.[3]
- Another meta-analysis by Baldessari et al. in 2006 found even lower rates of suicide- six fold reduction of risk in suicidal acts in patients treated with lithium.[4]
- Review of studies of lithium in drinking water by Vito et al. discussed water study in Texas, Japan, Austria, East England and Greece.[5]

Lithium in TBI

- Cohn et al first reported a case study in 1977 of an adolescent with a TBI with aggression, disinhibited behavior and volatility. Lithium was started two weeks after the injury and behavior improved. [6]
- Haas and Cope also published a case report of a single patient with cognitive impairment and disinhibition after a TBI.[7]
- Haas and Donaldson reported a case series of 5 patients with various conditions including 2 with TBI, who responded to lithium.[8]
- Glenn et al. reported on 10 brain-injured patients treated with lithium for aggression, combativeness or self injurious behaviors.[9]
- Bellus et al reported on two aggressive patients with TBI who had resided in a state hospital. Both improved with lithium but both were taking neuroleptics as well. [10]

Neuroprotective effects of Lithium

- Case registry studies found a lower risk for incident dementia, in particular of AD, in bipolar patients after long-term lithium use.[11, 12]
- In a retrospective study, Terao et al found that patients on chronic lithium treatment showed lower rates of cognitive decline as measured by the Mini-Mental State Examination.[13]
- A prospective observational study showed that older bipolar patients on chronic lithium treatment had a significantly lower incidence of AD compared to those with no lithium exposure.[14]

Lithium and Schizophrenia

- Although earlier papers showed benefit from lithium use as an adjunctive, later better designed studies did not.[15]
- Cochrane meta analysis from 2015.[16]
  - Lithium had a significant improvement in sx but not when patients with schizoaffective disorder were excluded.
- Another meta-analysis (Lecht et al.) showed treatment of schizophrenia with lithium alone is not effective. Results of lithium augmentation are inconclusive.[17]
- One review by Citrome noted that lithium has been helpful as an adjunctive to clozapine to prevent neutropenia.[18]

Pop Quiz
(Get it?)

Question #1

- When was lithium approved by the FDA?
  a. 1950
  b. 1960
  c. 1970
  d. 1980

Question #2

- Who is credited for being the first to use lithium in psychiatric illness in the modern era?
  a. Carl Jung
  b. John Cade
  c. Emil Kraepelin
  d. Kurt Schneider

Question #3

- What country was the biggest producer of lithium in 2015?
  - a. Bolivia
  - b. China
  - c. Chile
  - d. Australia

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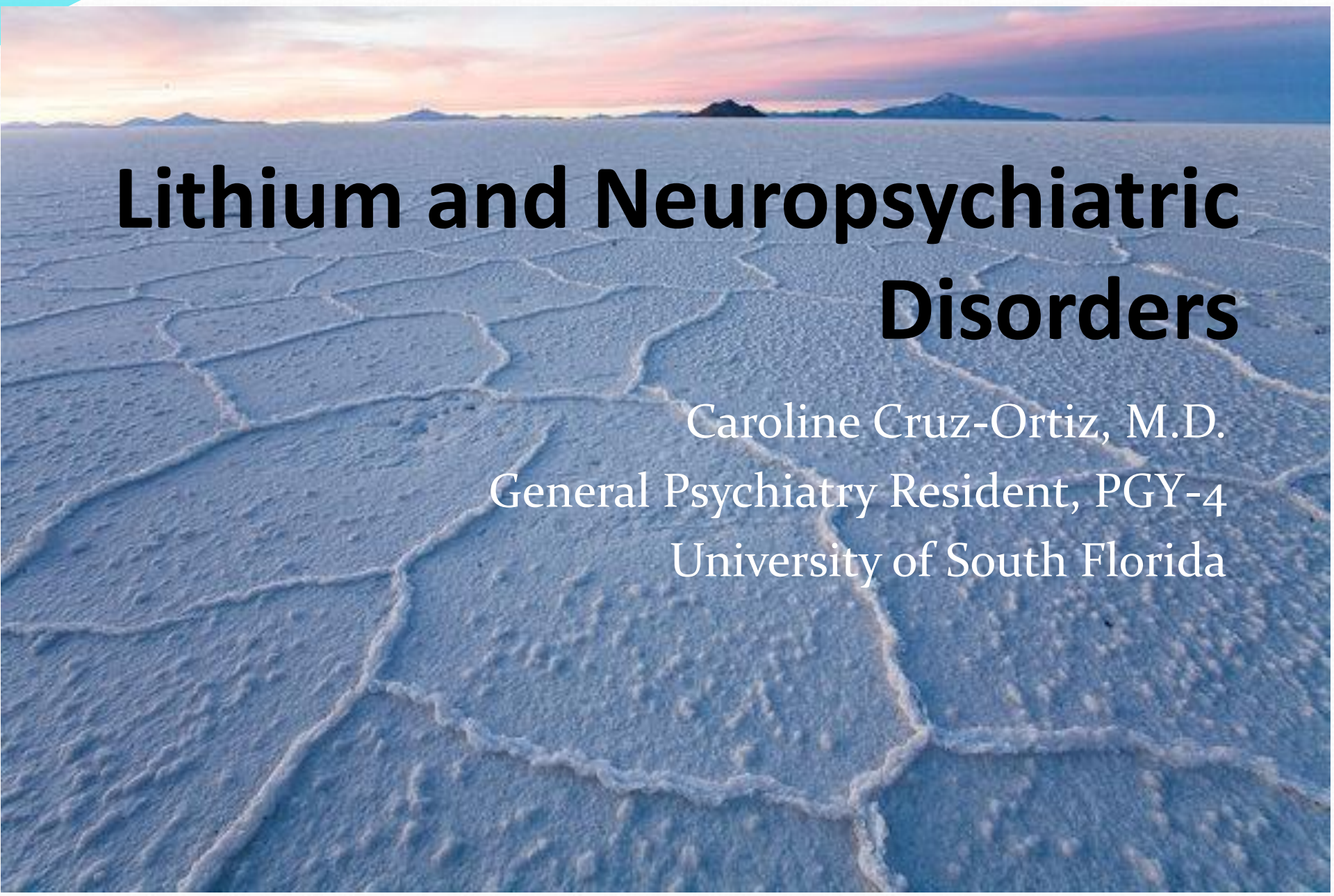

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