Wait, where’s my man?
Cognitive testing for the bipolar patient

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Overview

- Case: Mrs. T

- Bipolar disorder (BPD) in geriatric population

- Are there evidence based cognitive testing of elderly patients with bipolar disorder?
  - MCCB

- Pharmacological management

- Case conclusion
New Patient: Mrs. T.

- 86F longstanding bipolar disorder presents with cognitive decline

PMHx:
- Bipolar disorder I with prior hospitalizations for manic episodes (last 2011)
- Stage 4 CKD secondary to DM and Li toxicity (dialysis Feb 2012)
- Longstanding Li toxicity – false dx movement disorder
- Hypothyroidism – recently controlled
- L IJ thrombosis 2dary dialysis fistula March 2012
- DM2 x decades
- CAD, HTN
  - Pacemaker failure and subdural hematoma Feb 2012
  - CABG 2000
- Diverticulosis
- Macular degeneration
- Chronic pain for degenerative disc disease
Case: Medications

- Divalproex 250mg daily since Nov 2011
- Quetiapine 25mg daily
- Metoprolol 25mg daily
- Repaglinide 1mg tid with meals
- Atorvastatin 40mg
- Furosemide 40mg daily
- Candesartan 8mg daily
- ASA 81mg daily
- Tylenol arthritis 650mg tid
- Synthyroid
- Calcitomin 200u spray
- Darbepoetin 40mcg/vial weekly

- Previously on lithium x several decades
Case: The Lost Referral

- Mostly manic 2010-2011
  - Inpatient psychiatry consult service
  - Li stopped (Cr 200->500s)
  - Epival initiated and doubled 2011
  - Referred to CGMH but referral lost after move home to DAL

- Still focused on finding a husband, rapid speech

- Patient: “I need a man.” Divorced previous husband

- Daughter: Word finding difficulties, worsening STM x 2 years. Pt has obsession with men during mania. Forgets about boyfriends even when in relationship and prior financial scams
She’s manic…but what about her cognitive decline?

- MOCA 23/30 (0/5 recall) 2011

In clinic:

- MMSE 27/30
- GDS 7/15
- FAB 15/15
Bipolar disorder aged 60+

- Prevalence 0.5-1% amongst >60 years old
- 50% cognitive deficits
- 66% memory complaints
- 6% geriatric psychiatry outpatient visits
- 8-10% geriatric inpatient admissions
- Cognitive deficits (processing speed, verbal learning/memory) independent predictors of functional recovery
- Improvement in neurocognitive status can predict changes in functional outcome

Lala and Sajatovic. “Medical and Psychiatric Comorbidities among Elderly Individuals with Bipolar Disorder: A Literature Review.”
Cognitive decline in BPD

- Cognitive impairment of BPD
  - 15 yrs:↓processing speed, verbal learning, social, global dysfunction
  - Mania early life ↑ risk late cognitive dysfunction

- BPD type 1
  - ↓Verbal and visual memory, semantic fluency
  - During mania: ↓Verbal memory, executive function
  - During depression: Above+↓visuospatial memory

Lopes and Fernandes. “Bipolar Disorder: Clinical Perspectives and Implications with Cognitive Dysfunction and Dementia.”
Are there evidence-based cognitive testing of elderly patients with bipolar disorder?
Neuropsychiatric assessment of cognitive dysfunction

- MMSE
- MATRICS Consensus Cognitive Battery (MCCB)
  - Processing speed, attention, working memory, verbal learning, visual learning, executive function, social cognition
- California Verbal Learning Test
  - More complex test of verbal learning
- Stroop Test, Trail Making part B, Wisconsin Card Sorting Test
  - More complex test of executive function, emotional processing, social cognition

Burdick et al. “MATRICS Consensus Cognitive Battery in Patients with Bipolar I Disorder.”
Yatham et al. “International Society for Bipolar Disorders- Battery for Assessment of Neurocognition.”
MATRICS Consensus Cognitive Battery (MCCB)

The MATRICS consensus cognitive battery in patients with bipolar I disorder.

Burdick KE, Goldberg TE, Cornblatt BA, Keefe RS, Gopin CB, Derosse P, Braga RJ, Malhotra AK.
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Abstract
The Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) initiative was devised to identify a neurocognitive battery to be used in clinical trials targeting cognition in schizophrenia, a process, which resulted in the MATRICS Consensus Cognitive Battery (MCCB). The MCCB has been selected by the United States Food and Drug Administration to be used as the primary outcome measure in registry trials for cognitive agents in schizophrenia. Given the clinical and cognitive overlap between schizophrenia and bipolar disorder (BPD), it is likely that any compound shown to have cognitive benefits in schizophrenia will subsequently be tested in BPD. Unlike the MCCB for schizophrenia, there remains no consensus regarding outcome measures if cognitive trials were to be undertaken in BPD. The utility of the MCCB in BPD has not yet been systematically investigated. We administered the MCCB to 80 bipolar I patients; 37 were strictly euthymic and 43 were symptomatic. We compared their performance with a demographically matched healthy sample (n=148) on seven MCCB domains, and the composite. BPD patients were statistically significantly impaired on five of seven MCCB domains at levels consistent with meta-analytic studies of cognition in BPD. In contrast, patients’ performance was less impaired on the Reasoning and Problem-solving and Social Cognition domains, differences that did not survive statistical correction for multiple testing. Symptomatic status only modestly influenced performance. These data suggest that the MCCB, devised for use in schizophrenia, may also represent a useful outcome measure in cognitive trials for BPD. Additional studies should address important psychometric features such as repeatability and potential practice and/or ceiling effects.

- Schizophrenia clinical trial (risperidone, lurasidone)
- N=80 bipolar I (37 euthymic, 43 symptomatic) matched N=148
- Age 39.8 +/- 11.2 years, gender controlled
MCCB Subtests

1. Trail Making Part A
2. Brief Assessment of Cognition in Schizophrenia: Symbol Coding
3. Hopkins Verbal Learning Test
4. Wechsler Memory Scale: Spatial Span
5. Wechsler Memory Scale: Letter-Number Span
6. Neuropsychological Assessment Battery: Mazes
7. Brief Visuospatial Memory Test
8. Category Fluency: Animal Naming
9. Mayer-Salovey-Caruso Emotional Intelligence Test
10. Continuous Performance Test

- 7 domains tested:
  - Processing speed
  - Attention/vigilance
  - Working memory
  - Verbal learning
  - Visual learning
  - Reasoning/Problem-solving
  - Social Cognition
Evaluation MCCB for BPD 1

Objective

**OBJECTIVES:** Although cognitive impairment is recognized as an important clinical feature of bipolar disorder, there is no standard cognitive battery that has been developed for use in bipolar disorder research. The aims of this paper were to identify the cognitive measures from the literature that show the greatest magnitude of impairment in bipolar disorder, to use this information to determine whether the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery (MCCB), developed for use in schizophrenia, might be suitable for bipolar disorder research, and to propose a preliminary battery of cognitive tests for use in bipolar disorder research.

**METHODS:** The project was conducted under the auspices of the International Society for Bipolar Disorders and involved a committee that comprised researchers with international expertise in the cognitive aspects of bipolar disorder. In order to identify cognitive tasks that show the largest magnitude of impairment in bipolar disorder, we reviewed the literature on studies assessing cognitive functioning (including social cognition) in bipolar disorder. We further provided a brief review of the cognitive overlap between schizophrenia and bipolar disorder and evaluated the degree to which tasks included in the MCCB (or other identified tasks) might be suitable for use in bipolar disorder.

**RESULTS:** Based on evidence that cognitive deficits in bipolar disorder are similar in pattern but less severe than in schizophrenia, it was judged that most subtests comprising the MCCB appear appropriate for use in bipolar disorder. In addition to MCCB tests, other specific measures of more complex verbal learning (e.g., the California Verbal Learning Test) or executive function (Stroop Test, Trail Making Test-part B, Wisconsin Card Sorting Test) also show substantial impairment in bipolar disorder.

**CONCLUSIONS:** Our analysis reveals that the MCCB represents a good starting point for assessing cognitive deficits in research studies of bipolar disorder, but that other tasks including more complex verbal learning measures and tests of executive function should also be considered in assessing cognitive compromise in bipolar disorder. Several promising cognitive tasks that require further study in bipolar disorder are also presented.

- **Pro:** Standardized test n=300, no other recommended starting point yet
- **Con:** 70 min in 1 visit. Designed for schizophrenia, unclear sensitivity
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<th>Cognitive domain</th>
<th>Test</th>
<th>Additional Information</th>
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<td>Processing speed</td>
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<td><strong>Category Fluency: Animals</strong></td>
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<td><strong>Trail Making Part A</strong></td>
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<td>Working memory</td>
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<td><strong>WM3: Spatial Span</strong></td>
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<tr>
<td>Verbal learning/memory</td>
<td><strong>Hopkins Verbal Learning Test</strong></td>
<td><strong>California Verbal Learning Test</strong></td>
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<td>more sensitive but HVLT alternate versions</td>
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<td>Visual learning</td>
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<td>Executive Function</td>
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<td></td>
<td><strong>Trail Making Part B</strong></td>
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<td></td>
<td><strong>Wisconsin Card Sorting Test</strong></td>
<td><strong>More sensitive than Neuropsych Ax Battery Mazes (N when euthymic)</strong></td>
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**MCCB Subtests:** NAB (Mazes), MSCEIT – unclear evidence
Medications: Bipolar Disorder I

- Mood stabilizer, not antidepressants alone (hypomania/mania)
  - Sodium valproate - first line in elderly
    - 125-250mg/day to max 500-1000mg/day
  - Target level 400-700 mmol/L
  - Check 3-5 days after dose titration
  - Trough level (12 h post-dose)

- Carbamazepine – less well-tolerated
- Lithium – neurotoxicity and side effects
  - S/e: decreased STM, motor function, verbal fluency, attention

- Antipsychotics
  - Only if agitation despite being on mood stabilizer
Medications: Alzheimer’s Dementia

- Cholinesterase inhibitors
  - Donepezil
    - N=58 in private practice, temporary improvement
    - Can destabilize BPD 1 (57% switch to mania, no benefit)
  - Galantamine – possible improvement
    - Case reports

- NMDA
  - Memantine no benefit over placebo

Kelly. “Is donepezil useful for improving cognitive dysfunction in bipolar disorder?”
Lopes et al. “Bipolar Disorder: Clinical Perspectives and implications with Cognitive Dysfunction and Dementia”
Theoretical future directions

- ? Glucocorticoid receptor antagonists (research phase)
  - Mifepristone 600mg/day

- ? Psychostimulants (amphetamine, methylphenidate)
  - Scarce data

- ? Modafinil

- ? Antiparkinsonian drugs

- ? Antioxidants
Conclusions

- Coexisting BPD and cognitive dysfunction is little studied.
- Ongoing research on evidence of tailoring MCCB for BPD:
  - Available in German, Spanish, Chinese, Russian, Hindi, Norwegian, Japanese
  - [www.matrics.ucla.edu](http://www.matrics.ucla.edu)
- Stabilize BPD first then cognitive testing.
Case conclusion: Mrs. T

- On dialysis, switched evening daily dosing
- If still manic, consider Epival levels to titrate dose
- Connect with CGMH
- May consider neuropsychiatric assessment but not at this time
References

Thank you!

Questions?