Catatonia in Medically Ill: Trends and Novel Approaches
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Disclosure: Kamalika Roy, MD

With respect to the following presentation, there has been no relevant (direct or indirect) financial relationship between the party listed above (and/or spouse/partner) and any for-profit company which could be considered a conflict of interest.
Outline of discussion

- Medical catatonia: evolution
- Medical catatonia: distribution
- Medical catatonia: work up
- Current evidence for treatment with benzodiazepines
- Review of all alternative treatment agents
- Proposal for a modified algorithm
You diagnose catatonia in an ICU patient. What is the probability that this case of catatonia has a medical cause?

A. < 5%
B. 20%
C. 33%
D. > 50%
Name the underlying diagnosis of catatonia least responsive to lorazepam treatment

A. Major depressive disorder
B. Schizophrenia
C. Bipolar disorder
D. Medical/ neurological disorders
Which blood test might be helpful in predicting development of malignant catatonia?

- Serum CPK
- Serum calcium
- Serum iron
- CSF NMDA receptor antibody
Medical catatonia: evolution
Evolution

- Initially described by Karl Kahlbaum: 26 cases where patients had the following symptoms
  
  “…remains entirely motionless, without speaking, and with a rigid, masklike facies, the eyes focused at a distance… seems to devoid of any will to move or react to any stimuli… waxen flexibility. The general impression conveyed by such patients is one of profound mental anguish”

- In 20th century, with Dr. Bleuler and Dr. Kraeplin’s important contributions, catatonia became strongly linked with schizophrenia or *dementia praecox* and *hebephrenia*

- In DSM III catatonia was only a subtype of schizophrenia
Diagnostic and Statistical Manual-5 : Catatonia due to another medical condition (CD-AMC)

-Catatonic type of schizophrenia removed
-Catatonia is a specifier to 10 psychiatric disorders (293.89)
-Catatonia due to another medical disorder (293.89)
-Unspecified catatonia (code 781.99 or “other symptoms involving nervous and musculoskeletal systems”): when not meeting full criteria

-Areas not addressed:
1. Catatonia due to AMC cannot be diagnosed exclusively in presence of delirium
2. Catatonia is still classified under psychosis disorders section
3. Many well recognized signs of catatonia are not included in DSM-5 diagnostic criteria
4. There are similar physical signs listed as criteria
Medical Catatonia: Distribution
Prevalence: Not well defined

- Retrospective review of 95 diagnosed cases\(^1\): Catatonia due to GMC in 21%
- Retrospective review of 148 cases\(^2\): Catatonia due to GMC in 20%
- Prospective study of older adults\(^3\): Catatonia due to GMC in 8.9%, by consult service
- Retrospective review in a tertiary neurological center\(^4\): Catatonia due to GMC in 72%
Prevalence of medical cause in catatonia

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>n</th>
<th>Setting</th>
<th>Reference</th>
<th>Institution (country)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16%</td>
<td>55</td>
<td>General hospital</td>
<td>Abrams 1974</td>
<td>State U of NY at Stony Brook (US)</td>
</tr>
<tr>
<td>20%</td>
<td>148</td>
<td>CL &amp; psych hospital</td>
<td>Rosebush 2009</td>
<td>McMaster University (Canada)</td>
</tr>
<tr>
<td>20%</td>
<td>25</td>
<td>Neuro department</td>
<td>Barnes 1986</td>
<td>Middlesbrough General (UK)</td>
</tr>
<tr>
<td>21%</td>
<td>95</td>
<td>EMR (system-wide)</td>
<td>Smith 2012</td>
<td>Mayo Clinic (US)</td>
</tr>
<tr>
<td>33%</td>
<td>22</td>
<td>Neurobehavioral unit</td>
<td>Altshuler 1986</td>
<td>UCLA (US)</td>
</tr>
<tr>
<td>54%</td>
<td>54</td>
<td>EMR (medicine)</td>
<td>Llesuy 2017</td>
<td>University of Chicago (US)</td>
</tr>
<tr>
<td>55%*</td>
<td>11</td>
<td>CL service</td>
<td>Carroll 1992 &amp; 1993</td>
<td>Ohio State University (US)</td>
</tr>
<tr>
<td>65%</td>
<td>34</td>
<td>ER series</td>
<td>Huang 2007</td>
<td>Chang Gung Memorial Hosp (China)</td>
</tr>
<tr>
<td>72%</td>
<td>68</td>
<td>3° neurologic. center</td>
<td>Espinola-Nadurille 2016</td>
<td>Nat’l Inst Neuro &amp; Neurosurg (Mexico)</td>
</tr>
<tr>
<td>80%*</td>
<td>5</td>
<td>ICU series</td>
<td>Saddawi-Konefka 2014</td>
<td>Mass General Hosp (US)</td>
</tr>
<tr>
<td>83%*</td>
<td>6</td>
<td>Elders on CL service</td>
<td>Kaelle 2016</td>
<td>Wollongong Hosp (Australia)</td>
</tr>
</tbody>
</table>
Proportion of causes with direct CNS involvement

<table>
<thead>
<tr>
<th>Cause</th>
<th>Carroll 1994</th>
<th>Frequency</th>
<th>Case series</th>
<th>Case reports</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miscellany</td>
<td>60*</td>
<td>23%</td>
<td>24</td>
<td>6</td>
<td>13%</td>
</tr>
<tr>
<td>Inflammation (CNS)</td>
<td>75**</td>
<td>29%</td>
<td>56</td>
<td>23</td>
<td>33%</td>
</tr>
<tr>
<td>Neural injury</td>
<td>80</td>
<td>31%</td>
<td>28</td>
<td>12</td>
<td>17%</td>
</tr>
<tr>
<td>Developmental</td>
<td>5</td>
<td>0%</td>
<td>5</td>
<td>0</td>
<td>2%</td>
</tr>
<tr>
<td>Structural</td>
<td>14</td>
<td>21%</td>
<td>14</td>
<td>9</td>
<td>10%</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>25</td>
<td>10%</td>
<td>14</td>
<td>9</td>
<td>10%</td>
</tr>
<tr>
<td>Toxins &amp; medications</td>
<td>18</td>
<td>7%</td>
<td>17</td>
<td>8</td>
<td>11%</td>
</tr>
<tr>
<td><strong>TOTALS</strong></td>
<td><strong>258</strong></td>
<td><strong>100%</strong></td>
<td><strong>160</strong></td>
<td><strong>79</strong></td>
<td><strong>100%</strong></td>
</tr>
<tr>
<td>CNS involvement</td>
<td></td>
<td><strong>70%</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Includes metabolic disturbances and “other”
**Infectious and autoimmune
A systematic retrospective review by Llesuy and colleagues\(^5\), 2017

Chart review of all adult patients in University of Chicago Medical Center, general hospital for 3 years.

- Total 170 charts with 3 key words about catatonia
- 133 met diagnostic criteria for DMS-5 catatonia
  - Diagnosed as catatonia: 54 cases
  - Undiagnosed: 79 cases (60%)
- Past psychiatric history in 42%
- Diagnosis of delirium in 53%
- Preceding D2 antagonist in 60%
Medical catatonia: work up
Limitations in evaluation of catatonia due to AMC

- An evidence based work up recommendation is difficult to suggest
- Pre-test probability of the abnormal findings are not well defined: goes up with age, acuity and medical comorbidities
- Lack of systematic data on rates of medical etiologies makes it hard to delineate a practice guideline for laboratory tests
- Currently there is no standardized practice guideline for ruling out AMC as a cause of catatonia or ruling in psychiatric causes.
# Catatonia due to medical conditions: causes and work up

<table>
<thead>
<tr>
<th>Medical conditions (MINDSET)</th>
<th>Work-up</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medications (direct effect and withdrawal)</strong></td>
<td>- Detailed work up should not delay treatment</td>
</tr>
<tr>
<td>Inflammatory</td>
<td>- Lorazepam challenge is therapeutic and diagnostic</td>
</tr>
<tr>
<td>- Infectious (encephalitis &gt;&gt; UTI, sepsis, PNA)</td>
<td>- Goal is to find contributing cause that inform treatment:</td>
</tr>
<tr>
<td>- Autoimmune encephalopathy</td>
<td>• CXR, UA, U tox</td>
</tr>
<tr>
<td>- Paraneoplastic syndrome</td>
<td>• Blood: CMP, CBC, iron</td>
</tr>
<tr>
<td>Neural injury</td>
<td>• Brain MRI: encephalitis, stroke, neurodegenerative disease, SOL</td>
</tr>
<tr>
<td>- Neurodegenerative</td>
<td>• Lumbar puncture: autoimmune and paraneoplastic panels</td>
</tr>
<tr>
<td>- Traumatic</td>
<td></td>
</tr>
<tr>
<td>- Vascular/hemorrhage (CVA)</td>
<td></td>
</tr>
<tr>
<td>- PRES</td>
<td></td>
</tr>
<tr>
<td>Developmental</td>
<td></td>
</tr>
<tr>
<td>- Inborn errors of metabolism (esp. porphyrias)</td>
<td></td>
</tr>
<tr>
<td>- Autism spectrum disorder</td>
<td></td>
</tr>
<tr>
<td>Space-occupying or other structural change</td>
<td></td>
</tr>
<tr>
<td>Epilepsy</td>
<td></td>
</tr>
<tr>
<td>Toxins (PCP, ketamine, cannabinoids)</td>
<td></td>
</tr>
</tbody>
</table>
## Differential diagnoses

<table>
<thead>
<tr>
<th>Hypo or hyperkinetic states with rigidity</th>
<th>Behavioral/psychological problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Akinetic mutism (prion and tacrolimus can cause both)</td>
<td>- Selective mutism</td>
</tr>
<tr>
<td>- Parkinson’s disease</td>
<td>- Volitional uncooperativeness</td>
</tr>
<tr>
<td>- Stiff person’s syndrome</td>
<td></td>
</tr>
<tr>
<td>- Locked in syndrome</td>
<td></td>
</tr>
<tr>
<td>- Non convulsive status epilepticus</td>
<td></td>
</tr>
</tbody>
</table>
Importance of prompt diagnosis

- Informs appropriate and timely treatment
- Delayed recognition of catatonia may lead to:
  - Dehydration
  - Acute renal failure
  - Electrolyte imbalance
  - Malnutrition
  - Deconditioning in chronic, periodic cases
  - Contracture
  - Deep vein thrombosis
  - Infection, sepsis: aspiration pneumonia, impetigo
  - Pressure ulcer
Delirium and Catatonia (DeCat) in Critically Ill Patients
Prospective Cohort Investigation

- **Objective:**
  - Describe relationship between delirium and catatonia in ICU patients
  - Determine diagnostic thresholds for commonly used catatonia screening instrument (Bush Francis Catatonia Rating Scale; BFCRS) in the ICU

- **Design:**
  - Single Center
  - Nested Prospective (convenient sample) Cohort Study
  - Delirium (CAM-ICU) and Catatonia (BFCRS) raters remained blinded
Distribution of Acute Brain Dysfunction

- Delirium: N=58 (42.7%)
- Delirium and Catatonia: N=42 (30.9%)
- Catatonia: N=4 (2.9%)
- Neither: N=32 (23.5%)
Prevalence of Catatonia Signs

Percentage of Time Catatonia Sign Present in Delirious / Non-Delirious Patient Assessments (%)
<table>
<thead>
<tr>
<th>BFCSI Cut-Off Point</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 2 signs</td>
<td>1 (0.958 – 1)</td>
<td>0.468 (0.423 – 0.514)</td>
</tr>
<tr>
<td>≥ 3 signs</td>
<td>1 (0.958 – 1)</td>
<td>0.65 (0.605 – 0.692)</td>
</tr>
<tr>
<td>≥ 4 signs</td>
<td>0.908 (0.829 – 0.953)</td>
<td>0.906 (0.876 – 0.929)</td>
</tr>
<tr>
<td>≥ 5 signs</td>
<td>0.586 (0.481 – 0.684)</td>
<td>0.989 (0.975 – 0.995)</td>
</tr>
</tbody>
</table>
Medical Catatonia: treatment: standard and current trends
Traditional Treatments

- Benzodiazepine is the first line agent
- *Intravenous lorazepam* is preferred over other routes
- Response: No randomized trial
  - Lorazepam is preferred, but variable response rate
  - In one small study\(^7\) (n=30, total 68 episodes of catatonia) a total of 79.4% had full response for all catatonic episodes
  - Partial response in 14.7%
  - No response in 5.9%
  - Schizophrenia (63.3% of all subjects) had a lower response rate: 47.4% had a full response for all of the catatonic episodes versus another 47.3% had variable response for different episodes
  - MDD: All subjects had full response for all episodes
  - Catatonia due to another medical condition: 3 out of 4 people had variable response, with relapses
Variation in responses with lorazepam

In another retrospective study with n= 107\(^8\)

- Lorazepam 3-6 mg daily intravenous was used for a period of 3- 7 days
- Two thirds had symptom improvement
- One third had full response (did not meet diagnosis of catatonia any more)
- Lower response rate was attributed to longer duration of illness (83.8±22.1 days)

In most of the studies poor response is proposed to be associated with\(^3\):

- Diagnosis of schizophrenia
- Catatonia due to medical condition
- Longer duration of catatonia before treatment
Lorazepam in catatonia due to another medical condition (CDAMC)

A small retrospective study looked into 21 subjects with catatonia due to another medical condition\(^{10}\)

- No psychiatric diagnosis
- Response was measured as not meeting DSM-IV diagnostic criteria
- Full response in 66.7% cases with lorazepam initial dose
- A total of 85.7% responded with subsequent diazepam treatment
- A total of 14.3% did not respond
- Five died: 2 of them did not respond to treatment
- Initial response was lower than that of catatonia in schizophrenia and mood disorder patients
Treatment response in medically complex patients

In a retrospective study of 34 catatonic patients\textsuperscript{11}

- Neurological and medical disorders in half of the cases
- Direct ECT in 12\%, medication in 88\%, ultimately 88\% had ECT
- Mean dose of lorazepam was 6.7±4.6 mg daily
- Only 58\% had complete remission, 18\% had partial remission, a total of 76\% had improvement of symptoms
- A total of 24\% did not improve with treatment
- Only 4 patients responded to only medication (did not require ECT)
- Six patients relapsed one or more times after discontinuation of treatment
Llesuy et al. : Retrospective study of predicting thoroughness of catatonia evaluation, 2017

Response to lorazepam in retrospective observation: n= 54
Psychiatric population:100.00% response
GMC: 82% response
No statistical significance
Limitations of available evidences

- No prospective study
- Very small sample size (all published reports)
- No randomization, no control group to compare
- Standardized rating scales often not used for monitoring treatment response
- Variable doses of lorazepam were used for variable duration of time
- No study looked into differences in responses in medically ill population and psychiatric population
- No study looked into variations in treatment response between stuporous and excited catatonia
Prognosis of catatonia

- Long term prognosis is not studied methodically
- Most cases resolve with treatment of the contributing causes
- Relapses and resurgences are not well defined in medically ill population as many drugs contribute to catatonia either directly or through withdrawal
- Short term prognosis: response to high dose lorazepam at the end of day 1 can predict the final outcome of a 5 day protocol (Francis et al.)
- In one study with small sample size 66.7% were maintained on lorazepam at discharge
- Resurgence of catatonia is known to happen after complete resolution of symptoms even with slow tapering of lorazepam over weeks
Medical catatonia: treatment with alternative agents
Proposed neurobiology of catatonia

- Hypo-activity of GABA\textsubscript{A}
- Dysregulation of GABA\textsubscript{A} and GABA\textsubscript{B}
- Glutamate hyper-toxicity in certain brain areas: NMDA hyperactivity, driven by or resulting in acute phase reaction (low serum iron level)
Dr. Carroll reviewed the role of NMDA-A: published in 2007\textsuperscript{13}

Dr. Beach and colleagues reviewed available evidences of use of alternative agents\textsuperscript{14}: Review was done in August 2016

Additional four cases treated with NMDA-A (3 published in November 2016 and one unpublished)\textsuperscript{15}: not reviewed in Dr. Beach’s work
### Systematic review by SR Beach et al. \(^{14}\): NMDA-A

- A total of 72 articles reporting 98 individual cases were reviewed (1983-August 2016)

<table>
<thead>
<tr>
<th>Number of cases</th>
<th>Presumed cause</th>
<th>Excited features</th>
<th>Benzodiazepine use</th>
<th>Alternative agent</th>
<th>Most common dose</th>
<th>Time for symptom resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>SZ 11 SZA 2 MDD with psychosis 1 BPAD 2 Autism 2</td>
<td>no</td>
<td>In 6 cases, stopped for different reasons/inadequate response</td>
<td>Amantadine</td>
<td>200 mg daily (100-600 mg)</td>
<td>Most common 1-2 days (few hours-few weeks)</td>
</tr>
<tr>
<td>9</td>
<td>SZ 4 MDD2 BPAD 1 Cannabis 1 Delirium 1</td>
<td>In one case</td>
<td>In 5 cases: Stopped due to partial response or side effect in 4 cases</td>
<td>Memantine</td>
<td>20 mg daily (5-20 mg)</td>
<td>Most common 1-2 days (days to weeks)</td>
</tr>
</tbody>
</table>

**SZ**: schizophrenia, **SZA**: schizoaffective disorder, **BPAD**: bipolar disorder, **MDD**: major depressive disorder
### Systematic review by SR Beach et al: Antiepileptic drugs

<table>
<thead>
<tr>
<th>Number of cases</th>
<th>Presumed cause</th>
<th>Excited features</th>
<th>Benzodiazepine use</th>
<th>Alternative agent</th>
<th>Most common dose</th>
<th>Time for symptom resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>MD 4, BPAD 1, HIV dementia 1, unknown 1</td>
<td>none</td>
<td>In 4 cases, inadequate response</td>
<td>Carbamazepine</td>
<td>600mg daily (100-1000 mg)</td>
<td>Most common 3-5 days (weeks)</td>
</tr>
<tr>
<td>5</td>
<td>SZ 3, BPAD 1,</td>
<td>In 3 cases</td>
<td>In one cases: inadequate response</td>
<td>Valproic acid</td>
<td>600-2500 mg daily</td>
<td>4-20 days</td>
</tr>
<tr>
<td>4</td>
<td>SZ3, BPAD 1</td>
<td>In one case</td>
<td>Used in combination in all cases</td>
<td>Topiramate</td>
<td>200 mg daily in all cases</td>
<td>Time frame unclear</td>
</tr>
</tbody>
</table>

SZ: schizophrenia, SZA: schizoaffective disorder, BPAD: bipolar disorder, MDD: major depressive disorder
TBI: traumatic brain injury
### Systematic review by SR Beach et al\(^{14}\): Atypical antipsychotics

<table>
<thead>
<tr>
<th>Number of cases</th>
<th>Presumed cause</th>
<th>Excited features</th>
<th>Benzodiazepine use</th>
<th>Alternative agent</th>
<th>Most common dose</th>
<th>Time for symptom resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>SZ 5, Brief psychosis 1, MDD 1, Cannabis 1</td>
<td>In one case</td>
<td>In 5 cases, stopped for inadequate response</td>
<td>Aripiprazole</td>
<td>15mg daily (3-30 mg)</td>
<td>Most common 3-5 days</td>
</tr>
<tr>
<td>8</td>
<td>SZ 4, Cannabis 1, BPAD 1, TBI1 Unknown 1</td>
<td>In 3 cases</td>
<td>In 5 cases: inadequate response</td>
<td>Clozapine</td>
<td>300 mg daily (150-800 mg)</td>
<td>Most common days to weeks</td>
</tr>
<tr>
<td>6</td>
<td>SZ2, BPAD 1, PRES 1, MCA stroke 1, delirium 1</td>
<td>none</td>
<td>In 3 cases: inadequate response</td>
<td>Olanzapine</td>
<td>5 mg daily (2.5-20 mg)</td>
<td>Most common days to weeks</td>
</tr>
<tr>
<td>7</td>
<td>SZ 6, unknown 1</td>
<td>In one case</td>
<td>Continued in 4 cases</td>
<td>Risperidone</td>
<td>4 mg daily (0.5-8 mg)</td>
<td>Days to weeks</td>
</tr>
</tbody>
</table>
Systematic review by SR Beach et al\textsuperscript{14}. :Other agents

- Levodopa/carbidopa in 6 cases, monotherapy, dose range 25-100 mg daily: all cases developed worsening psychosis
- Methylphenidate in 5 cases: psychosis worsened in one case
- TMS in 4 cases
- TDCS (transcranial direct current stimulation) in one case
- Minocycline in 2 cases
- Zolpidem in one case
- Dextromethorphan/quinidine in one case
- Fluoxetine in one case
- Fluvoxamine in one case
- Lithium in one case
### Alternative treatment: NMDA antagonists\(^{15}\) in four additional cases

<table>
<thead>
<tr>
<th></th>
<th>Case one(^{15})</th>
<th>Case two(^{15})</th>
<th>Case three(^{15})</th>
<th>Case four</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associated psychiatric diagnoses</td>
<td>Schizophrenia</td>
<td>Unspecified depression</td>
<td>Schizoaffective</td>
<td>MDD</td>
</tr>
<tr>
<td>Delirium (reason)</td>
<td>+ dehydration (treated)</td>
<td>+ UTI (treated)</td>
<td>+ hyponatremia (corrected)</td>
<td>+ prolonged intubation, overdose (treated)</td>
</tr>
<tr>
<td>Initial BFRS</td>
<td>39</td>
<td>30</td>
<td>21</td>
<td>34</td>
</tr>
<tr>
<td>Lorazepam dose</td>
<td>2 mg Q4H PO &amp; IV x 8 days</td>
<td>2 mg Q6H x 8 days</td>
<td>2 mg Q6H Pox 2 days</td>
<td>2 mg IV once</td>
</tr>
<tr>
<td>Reason to stop lorazepam</td>
<td>Worsening confusion, lack of response</td>
<td>Worsening confusion, lack of response</td>
<td>Worsening confusion, lack of response</td>
<td>Hypotension, lack of response, aspiration</td>
</tr>
<tr>
<td>NMDAA start day</td>
<td>Day 8, Memantine 10 mg BID</td>
<td>Day 8, Memantine 10 mg BID</td>
<td>Day 3, Memantine 10 mg BID</td>
<td>Day 7, Amantadine 50 mg BID</td>
</tr>
<tr>
<td>BFRS 1 day after</td>
<td>15</td>
<td>12</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Other medications</td>
<td>None</td>
<td>PRN haloperidol</td>
<td>Valproate 500 BID</td>
<td>None</td>
</tr>
<tr>
<td>Discharge meds</td>
<td>Quetiapine 400 mg BID, Memantine 10 mg BID</td>
<td>Memantine 10 mg BID</td>
<td>Valproate 500 BID, Olanzapine 10 HS, Memantine 10 BID</td>
<td>Duloxetine 120 mg OD, Amantadine 50 mg BID</td>
</tr>
<tr>
<td>Reason to defer ECT</td>
<td>Lack of informed consent, difficult access</td>
<td>Family did not consent, difficult access</td>
<td>Lack of informed consent, difficult access</td>
<td>Lack of informed consent</td>
</tr>
</tbody>
</table>
Modified treatment algorithm: adopted from Carroll et al. and Beach et al.: based on safety and relative effectiveness

Step 1: Lorazepam challenge: 2 mg; maintain at 6-8 mg daily, for at least 3 days, PO not recommended in first 3 days. Work up for ECT

Step 2: ECT
10-20 treatments, at least 6→3 times weekly until symptom resolution→maintenance ECT for months to years

When step 2 is not available or not possible, move to step 3, 4, 5

Step 3: NMDAA
Amantadine 100 mg daily, titrate to 600 mg daily over 3-4 days
or
Memantine 10 mg daily, titrate to 20 mg daily over 3-4 days

Step 4:
Carbamazepine 300-600 mg daily
or Valproic acid 500-1500 mg daily

Step 5:
Aripiprazole 10-30 mg daily
or Olanzapine 2.5 -10 mg daily
or Clozapine 200-300 mg daily
Alternative treatments: current knowledge and future directions

- No study exclusively looked into alternative agents in cases of catatonia due to AMC
- Alternative agents might be considered early in cases of
  - Schizophrenia
  - medical causes, where benzodiazepine are less tolerated (worsening of delirium) and
  - prolonged untreated catatonia (less responsive to benzodiazepine)
- Lack of sufficient reports of negative data
- Heterogeneity of cases: schizophrenia spectrum disease is over represented, possibly indicating more refractoriness but might also indicate lack of research in catatonia in medically ill group
- Potential for future area of research:
  - Distribution of catatonia due to AMC should be more strongly based on systematic studies in different sub-population
  - Find out if catatonia due to AMC is different in clinical signs than psychiatric catatonia
  - Treatment as usual should be compared with alternative agent
References

2. Rosebush 2009
10. Lin CC, Hung YY, Tsai MC, Huang TL. The lorazepam an diazepam protocol for catatonia due to general medical condition and substance in liaison psychiatry. PLOS One 2017; 12 (1)
Thank you!
Question?