any catatonia cases respond to benzodia-
zepines—especially lorazepam—but up
to 30% do not. Electroconvulsive therapy (ECT)
can be effective, but what’s the next step when
ECT is unavailable or inappropriate for your
patient?

To help you solve this dilemma, we describe
our diagnosis and treatment decisions for a patient
we call Mr. C. We explain how our process was
guided by recent understandings of an abnormal
neural circuit that appears to cause catatonia’s
complex motor and behavioral symptoms.
This article describes that neurologic pathology and answers common questions about the clinical workup and treatment of catatonia.

**CASE: TROUBLE IN TV LAND**
Mr. C, age 69, caused a disturbance at a local TV station, demanding that they broadcast a manuscript he had written. Police took him to a local hospital, where he was stabilized and then transferred to a neuropsychiatric hospital for evaluation.

The psychiatric interview revealed that he had developed insomnia, excessive activity, and delusional thinking 2 weeks before admission. His medical history included coronary artery disease (CAD), hypertension, and hypothyroidism. Medications included thyroid hormone replacement therapy, furosemide, potassium, ranitidine, simvastatin, metoprolol, and lisinopril. CAD treatment included stent placement and nitroglycerin as needed.

He had been hospitalized in his 30s and treated with ECT for what he called “bad thoughts.” He said he improved after 1 month and had no subsequent psychiatric history. He denied drug or alcohol abuse.

Shortly after admission, he refused to eat or drink and after 1 week became dehydrated. He also showed mutism, immobility, and stupor. He was transferred to the medical service for IV rehydration.

**MANY SCENARIOS AND SIGNS**
Mr. C’s symptoms suggest possible catatonia, a neuropsychiatric syndrome of motor dysregulation found in up to 10% of acutely ill psychiatric inpatients. A movement disorder, catatonia occurs with general medical conditions and psychiatric disorders (Table 1).

**Pathophysiology.** Catatonic signs develop when aberrant signals from neurochemical abnormalities trigger a neural circuit that affects the medial gyrus of the orbital frontal lobe, the lateral gyrus, caudate nucleus, globus pallidus, and thalamus (Box, page 58).

**Presentation.** A focused exam is required because patients with catatonia often do not provide a comprehensive or reliable history. They show mutism, characteristic postures, rigidity, aberrant speech, negativism, and stereotyped behaviors. They may present in an excited or retarded state:
- Excited patients may injure themselves or others and develop hyperthermia, tachycardia, and elevated blood pressure from excessive motor activity.
- Patients in a retarded state may present with bradykinesia and poor self-care. They may be unresponsive to external stimuli, develop cataleptic stupor, and refuse to eat or drink.

Mr. C’s earlier insomnia, excessive activity, and delusional thinking (such as the TV station incident) may have signaled an excited catatonia. On admission to the medical service, however, he presented in a retarded state.

**Signs.** Part of the challenge with detecting catatonia’s signs is that there are so many; some rating scales list more than 20. Not all signs need to be present to make the diagnosis, however, and if you find one, others usually turn up in the examination.

A mnemonic from the Bush-Francis Catatonia Screening Instrument (Table 2, page 59) represents diagnostic signs in patients with the excited or

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**Table 1**

<table>
<thead>
<tr>
<th>Common diagnoses of patients with catatonia</th>
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<tr>
<td><strong>Psychiatric</strong></td>
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<tr>
<td>Mood disorder (depression, bipolar disorder [manic, mixed, depressed])</td>
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<tr>
<td>Other psychoses</td>
</tr>
<tr>
<td>Personality or conversion (somatoform) disorders</td>
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<tr>
<td>Developmental disorders (autism)</td>
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<tr>
<td><strong>Organic</strong></td>
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<tr>
<td>Drug-induced</td>
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<tr>
<td>Idiopathic</td>
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Catatonia is caused by neurochemical abnormalities including low GABA activity in the frontal cortex, low dopamine (D2) activity in the basal ganglia, high glutamate—N-methyl-D-aspartate (NMDA)—activity in the parietal cortex, or a combination of these. Catatonic signs occur when these neurochemical changes cause aberrant signals and trigger a neural circuit affecting the medial gyrus of the orbital frontal lobe, the lateral gyrus, caudate nucleus, globus pallidus, and thalamus (Figure).

Posturing occurs when the aberrant signal reaches the posterior parietal lobe. Patients’ bizarre and mundane postures in catatonia are maintained by “anosognosia of position.” For example, an individual does not know the position of rest for his arm, and it remains in an unusual position as if at rest.

The PP goes on to influence the supplemental motor area (SMA), causing bradykinesia, rigidity, and other motor phenomena that catatonia shares with Parkinson’s disease. The SMA feeds back to the medial orbital gyrus, completing the neural circuit.

Regions such as the anterior cingulate area (ACA) and amygdala (AMG) may be recruited into the expanded circuit. ACA recruitment may cause akinetic mutism, and fear is a symptom of AMG recruitment. If the anterior hypothalamus is affected, malignant catatonia or neuroleptic malignant syndrome may occur.

This neural loop demonstrates an integrated model of psychosis. It may help explain why catatonia responds to treatment with lorazepam, ECT, and other agents such as antipsychotics and NMDA antagonists.

Illustration for CURRENT PSYCHIATRY by Marcia Hartsock, CMI

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**Neural loop may explain catatonia’s symptoms and treatment response**

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Illustration for CURRENT PSYCHIATRY by Marcia Hartsock, CMI
hydration. Because of Mr. C’s earlier excited symptoms and delusional thinking, we considered a diagnosis of bipolar disorder with catatonia. However, his symptoms did not improve with a trial of valproic acid (serum level 64 mcg/mL).

Head CT showed generalized atrophy and EEG showed delta slowing. Single-photo emission computer tomography (SPECT) showed areas of decreased perfusion in the cortex, with no perfusion in the left posterior parietal area (PP).

Mental status exam found Mr. C disoriented with poor short-term memory and unable to complete the Mini Mental State Examination (MMSE). His Bush-Francis Catatonia Rating Scale score was 28 and included many catatonic signs that would not be seen in a patient with simple dehydration.

The workup supported a diagnosis of catatonia due to general medical condition (vascular dementia) and ruled out schizophrenia with catatonic features, bipolar disorder, or major depression with catatonia.

**EVALUATION AND DIAGNOSIS**

**Medical causes.** A careful history and thorough physical examination are essential for making an accurate diagnosis and ruling out medical conditions that could present with or mimic catatonia (Table 3, page 60). Medications that can induce catatonia include antipsychotics, corticosteroids, and disulfiram at therapeutic doses. Drug abuse (such as with phencyclidine), use of the general anesthetic ketamine, and benzodiazepine withdrawal may also lead to catatonia.

Head CT or MRI is indicated for patients being considered for ECT or for localizing neurologic findings. EEG can be useful when patients present with features of seizure activity—such as tongue biting, incontinence, or stupor—or with catatonia as a manifestation of delirium or dementia.

A history of head injury or neurologic disease warrants further neurologic investigation. Also consider a neurology consult when the patient has prolonged stupor or does not respond to initial drug therapy.

**Psychiatric causes.** The clinical setting may suggest the most likely primary psychiatric disorders to consider, such as:

- bipolar or major depression in acute inpatient psychiatric units
- autism and pervasive developmental disorders (PDD) in pediatric or PDD units
- catatonic schizophrenia in chronic psychotic patients
- somatoform or factitious disorders in forensic settings.

These generalizations are not clinically exclusive, of course, but may provide a starting point for the treatment team confronted with limited history and exam information.

**Initial treatment.** Catatonia related to medical and psychiatric causes has been shown to respond to lorazepam and to ECT. Lorazepam is preferred because of its specificity for the GABAA receptor and ease of administration (oral, IM, or IV). Other agents that act on GABA—including amobarbital and zolpidem—have also been used. Catatonia’s hallmark features such as mutism

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**Table 2**

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<thead>
<tr>
<th>WIRED ‘N MIRED: Mnemonic for detecting catatonia</th>
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<tr>
<td><strong>W</strong>axy flexibility/catalepsy</td>
</tr>
<tr>
<td><strong>I</strong>mmobility/stupor</td>
</tr>
<tr>
<td><strong>R</strong>efusal to eat or drink</td>
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<tr>
<td><strong>E</strong>xcitement</td>
</tr>
<tr>
<td><strong>D</strong>eadpan staring</td>
</tr>
<tr>
<td><strong>N</strong>egativism/negative symptoms</td>
</tr>
<tr>
<td><strong>M</strong>utism</td>
</tr>
<tr>
<td><strong>I</strong>mpulsivity</td>
</tr>
<tr>
<td><strong>R</strong>igidity</td>
</tr>
<tr>
<td><strong>E</strong>cholalia/echopraxia</td>
</tr>
<tr>
<td><strong>D</strong>irect observation</td>
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</table>
ECT. An ECT workup can begin as soon as a patient presents with catatonia. If lorazepam produces no response within 24 hours, consider ECT.

CASE CONTINUED: PERSISTENT SYMPTOMS

After three 1-mg doses of lorazepam, Mr. C became more alert and oriented but his catatonia symptoms persisted, as indicated by a Bush-Francis score of 23, significant grasp reflex, and gegenhalten (automatic rather than willful resistance to passive limb movement in proportion to the strength of the stimulus). An attempt to gradually increase lorazepam to 2 mg tid produced delirium. He remained confused even when lorazepam was reduced to 0.5 mg tid, so the drug was discontinued.

Mr. C’s neurologist added amantadine, 100 mg tid, and carbidopa/levodopa, 10/100 mg tid, to treat his parkinsonian rigidity.

WHAT NEXT? OTHER OPTIONS

Antipsychotics have been investigated as a possible treatment for catatonia. The literature suggests that conventional antipsychotics may cause catatonia and atypical antipsychotics may improve it. Conventional antipsychotics are best avoided in catatonia because they:

• appear less effective than other treatments in resolving catatonic symptoms
• are associated with catatonic-like side effects, such as rigidity, akinesia, and staring
• appear to increase NMS risk in patients with catatonic symptoms

Atypicals appear more effective in treating catatonia and less likely to cause NMS. Case reports indicate many of these agents can be effective and well tolerated in treating catatonic symptoms, although this was not the case for Mr. C.
Anticonvulsants such as valproate and carbamazepine, 600 to 1200 mg/d, may take longer to work than lorazepam but may be options for patients who do not respond to benzodiazepines.

Amantadine, an N-methyl-D-aspartate (NMDA) antagonist, has been used with some success for catatonia that does not unrespond to lorazepam. However, amantidine’s dopamine agonist activity could worsen underlying psychosis.

Memantine—another NMDA antagonist—differs from amantadine despite having a similar chemical structure. Memantine is a noncompetitive antagonist at the NMDA receptor, without affinity for dopamine, norepinephrine, serotonin, or muscarinic receptors.

Although no published data support using memantine in patients with catatonia, it might be considered for those who are not candidates for lorazepam or ECT. For instance, a double-blind, placebo-controlled study found that lorazepam was not effective for catatonic schizophrenia. We have found memantine to help in some patients with catatonic schizophrenia.

CASE CONTINUED: TRIAL OF MEMANTINE

Mr. C remained in a catatonic stupor, but we decided against ECT because he resumed eating and drinking and was not medically at risk. Quetiapine, 100 to 300 mg/d, was tried to address his dementia symptoms, confusion, and poor mentation. This trial was discontinued after Mr. C fell and was readmitted to the medical unit. We then added memantine, 5 mg bid.

In the first week after beginning memantine, Mr. C’s MMSE score was 21, consistent with vascular dementia, but he remained immobile and staring. Motor signs also persisted, including automatic obedience, ambitendency, and a grasp reflex.

The next week, we increased memantine to 10 mg bid. Mr. C was oriented to person, place, and time, and his affect was blunted. His MMSE score increased to 25, showing improved cognition and memory. His Bush-Francis scale score was 6, showing reduced catatonic signs, with remaining mild immobility, bradykinesia, speech-prompt mutism, staring, and grasp reflex.

He maintained this improvement on carbidopa/levodopa, 10/100 tid; amantadine, 100 mg tid; and memantine, 10 mg bid, and was discharged from the nursing home unit.

IMPROVEMENT WITH MEMANTINE

Memantine may reduce excess glutamate at the NMDA receptor in the parietal-SMA-frontal cortical circuit. It may help to increase GABA and dopamine, which are deficient in catatonia. Our patient with vascular dementia had a severe ischemic deficit in the posterior parietal area, as seen on SPECT.

Amantadine, another NMDA receptor antagonist, acts on dopamine neurons and may have anticholinergic-like side effects, whereas memantine does not. Although both drugs share antagonism at the NMDA glutamate receptor, noncompetitive binding is weak for amantadine and moderate for memantine. Memantine has some serotonin (5-HT3) antagonism, but neither agent has direct GABA activity.

Memantine can improve function in vascular dementia. Thus, Mr. C’s improvement may...
agent asking him about serious tax problems. Upon reflection, he said he no longer believes this.

References

have been caused by the drug’s effect on his vascular dementia, the primary neuropsychiatric illness. However, his catatonic signs improved without antipsychotics, cholinesterase inhibitors, benzodiazepines, or ECT. No anticoagulation treatment or cerebral perfusion procedures account for his improved mental status.

CASE CONCLUSION
Mr. C went to live with his son’s family. Although he has problems with calculation, he shows good self-care. When asked why he did not respond during his catatonic stupor, Mr. C stated that he believed the physician was an Internal Revenue Service

References