

# Catatonia in Neurologic and Psychiatric Patients at a Tertiary Neurological Center

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This study describes the prevalence, phenomenology, treatment, and outcome of neurological patients and psychiatric patients with catatonia at a tertiary neurological center. Clinical variables included nosological diagnoses and complications. Admission length and days with catatonia were used as outcome measures. Of 2,044 patients who were evaluated prospectively, 68 (3.32%) had catatonia, 42 (61.7%) were neurological patients, 19 (27.9%) were psychiatric patients, and 7 (10.2%) had drug-related diagnoses. Of all patients, the ratio of neurological to psychiatric patients was 3:1. Encephalitis was the most common diagnosis (N=26 [38.2%]), followed by schizophrenia (N=12 [17.6%]). Psychiatric patients exhibited a stuporous type of catatonia (15 [83.3%] versus 14 [33.3%],  $p>0.001$ ), whereas neurological patients exhibited a mixed form of catatonia (25 [59.5%] versus 1 [5.6],  $p<0.001$ ). Neurological patients had more complications, longer hospitalizations, and more days with catatonia. A total of 56 patients (82.3%) received lorazepam, and 14 patients (20.5%) underwent ECT. Second- and third-line treatments included amantadine, bromocriptine, and levodopa. Catatonia is a prevalent syndrome that can remit with proper and opportune treatment.

*J Neuropsychiatry Clin Neurosci* 2016; 28:124–130; doi: 10.1176/appi.neuropsych.15090218

Catatonia was first described in 1874 by Karl Kahlbaum as a unique nosological entity. Emil Kraepelin included catatonia as a presentation of dementia praecox. Eugen Bleuler promoted catatonia as a subtype of schizophrenia.<sup>1</sup> Catatonia has been included as a subtype of schizophrenia since the first *DSM* in 1952, as well as in all ICD editions. Despite the recommendations of several researchers, catatonia was not delineated as an independent disorder in the 2013 introduction of *DSM-5*. However, a beneficial element was the deletion of catatonia as a type of schizophrenia and the support and addition of the *catatonia* diagnosis associated with another mental disorder together with *catatonic disorder* due to another medical condition, which was introduced in *DSM-IV*.<sup>2</sup>

This unfortunate, long-lasting nosological confusion<sup>3</sup> can help explain the underdiagnosis and mismanagement of catatonia. Without recognition and treatment, catatonia may persist and worsen. With the erroneous yet persistent past association of catatonia as synonymous with schizophrenia, clinicians have been more prone to use neuroleptics without further investigation of the illness and sometimes inadvertently convert the episode to neuroleptic malignant syndrome, a malignant form of catatonia.<sup>4</sup> It remains to be seen whether the less-than-optimal nosological changes made in *DSM-5* will do enough to mitigate this reflexive treatment mistake.

In recent years, recognition of catatonia associated with general medical illnesses has increased<sup>5</sup> and associations of

catatonia with a variety of psychiatric disorders in addition to schizophrenia have been expanded. Indeed, primary psychiatric catatonia is most often seen with affective disorders such as bipolar disorder.<sup>6</sup> In childhood and adolescence, autism is increasingly recognized as an associated condition.<sup>7</sup>

This study aimed to show the prevalence, phenomenological presentation, and clinical outcome of catatonia among psychiatric and neurological patients seen at a third-level neurological referral center.

## METHODS

The sample included all patients admitted to the National Institute of Neurology and Neurosurgery of Mexico (NINN) neurologic and psychiatric wards between January 2013 and December 2014, who fulfilled *DSM-5* criteria of catatonia associated with another mental disorder and/or catatonic disorder due to another medical condition and who had the presence of four or more catatonic symptoms according to the Bush Francis Catatonia Screening Instrument (BFCSI) and the Bush Francis Catatonia Rating Scale (BFCRS).<sup>8,9</sup> On admission, all patients were systematically assessed with a standard mental status examination and a neurological examination (performed by M.E.-N., M.C.O.-L., J.R.-B., and A.F.P.-G.). To determine the presence and severity of the syndrome, clinicians (M.E.-N. and A.F.P.-G.) administered

the BFCSI and BFCRS when catatonic signs were detected, with the standard protocol proposed by Bush et al.<sup>8</sup> in 1996. The BFCRS has been considered the preferred catatonia screening and rating instrument because of its validity, reliability, and ease of administration.<sup>10</sup> The BFCSI and BFCRS were administered as soon as the catatonic signs were exhibited during the hospitalization and always before the therapeutic interventions were initiated. We collected sociodemographic data on age, gender, marital status, and years of education. Clinical variables included nosological diagnoses and concomitant complications. The presence of each catatonic symptom included in the BFCRS was recorded in every case. The type of catatonia was classified as excited, stuporous, or mixed if the catatonia alternated periods of predominantly stuporous catatonic symptoms with excited symptoms. For all patients, general laboratory investigations were carried out and EEGs were obtained. All patients with encephalitis had viral serology testing including polymerase chain reaction for herpes simplex 1, herpes simplex 2, cytomegalovirus, Epstein-Barr virus, varicella zoster, human herpes virus (HHV) 8, HHV6, HHV7, enterovirus, toxoplasmosis, parvovirus B19, hepatitis C virus, and lymphocytic choriomeningitis virus. CSF adenosine deaminase and cultures for *Mycobacterium tuberculosis* and *Cryptococcus neoformans* were examined. N-methyl-D-aspartate receptor autoantibodies (anti-NMDAR) were studied for patients in whom autoimmune limbic encephalitis was suspected because of the predominance of symptoms of limbic dysfunction. These symptoms include confusion, seizures, orolingual and limb dyskinesias, short-term memory loss, and neuropsychiatric symptoms associated with neuroimaging (MRI or positron emission tomography) evidence of temporal lobe involvement and/or CSF inflammatory abnormalities (lymphocytic pleocytosis).<sup>11</sup> Among patients with negative anti-NMDAR antibodies, other causes of autoimmune encephalitis were studied (e.g., autoimmune systemic diseases and other antineuronal antibodies according to paraclinical findings). Remission rates, days of hospitalization, and days with catatonia were included as outcome measures. Therapeutic interventions are described.

We used descriptive statistics in terms of central tendency and dispersion measures in the case of numerical variables, and we used proportions in relationship to nominal variables. Inferential statistical analyses (represented by chi-square tests, Mann-Whitney tests, and t tests) were performed. Data were analyzed using SPSS software (version 20; SPSS, Chicago). The study protocol was revised and approved by the NINN Ethics Committee and conforms to the provisions of the Declaration of Helsinki.

## RESULTS

Over the 2-year study period, 2,044 patients were admitted to the NINN neurologic (N=1,122) and neuropsychiatric (N=922) wards. A total of 68 patients (3.32%) exhibited catatonia. Of these patients, 42 (61.7%) had a neurological

**TABLE 1. Neurological and Psychiatric Conditions Associated With Catatonia**

Type of Diagnosis	N	%
Neurological—total	42	61.7
Venous thrombosis	1	1.4
Acute disseminated encephalomyelitis	3	4.4
Epilepsy plus postictal psychosis	7	10.2
Epilepsy plus status epilepticus	1	1.4
Encephalitis	26	38.2
Tuberculous meningoencephalitis	3	4.4
Postsurgical panhypopituitarism	1	1.4
Psychiatric—total	19	27.9
Intellectual disability plus major depressive disorder	4	5.8
Bipolar I disorder manic episode with mixed features	1	1.4
Major depressive disorder with psychotic features	2	2.9
Schizophrenia	12	17.6
Drug-related—total	7	10.29
Neuroleptic malignant syndrome	3	4.4
Inhalant dependence/abstinence	2	2.9
Epilepsy plus levetiracetam	1	1.4
Epilepsy plus hyperammonemia due to valproate	1	1.4

disorder, 19 (27.9%) had a psychiatric diagnosis, and 7 (10.2%) had a drug-related diagnosis. The mean age of all patients was  $29 \pm 13.1$  years; 28 patients (40.6%) were women, 46 (66.7%) were single, 20 (28.9%) were married or in a common-law relationship, and 2 (2.9%) were divorced. Patients had a mean  $9.2 \pm 3.5$  years of education.

Table 1 provides the neurological and psychiatric diagnoses of the catatonic patients. Encephalitis was the most common diagnosis (N=26 [38.2%]), followed by schizophrenia (N=12 [17.6%]). Of the 26 patients with encephalitis, serological investigation for a viral etiology was positive among only four patients; two patients had enterovirus and two patients had herpes simplex 1 isolated from the CSF. Treatment with acyclovir and dexamethasone was started for all patients with encephalitis. Of 13 patients who underwent investigation for anti-NMDAR, five female patients and one male patient had positive results. All patients with suspected autoimmune encephalitis were treated with corticosteroids, and plasma exchange was administered to patients with positive anti-NMDAR or partial response to corticosteroids.<sup>12</sup> In three patients, an ovarian teratoma was found and was surgically treated. Another patient was classified as having parainfectious autoimmune encephalitis because she had herpes simplex encephalitis before anti-NMDAR antibodies were detected. These were performed because of insidious cognitive decline and resistant catatonia starting 2 years after the initial viral encephalitis. The remaining two patients with positive anti-NMDAR encephalitis are undergoing yearly tumor surveillance.<sup>11</sup> Of the 26 patients with encephalitis, viral origin was presumed for 17 (65.3%) but remained without confirmed etiology, a situation that has been reported worldwide.<sup>13</sup> Other patients with suspected autoimmune encephalitis had a negative test result in the extended investigation.

**TABLE 2. Presence of Bush Francis Catatonia Rating Scale Catatonic Symptoms in Neurological and Psychiatric Patients**

Symptoms	Neurological Patients (N=42)		Psychiatric Patients (N=19)		p
	N	%	N	%	
Excitement	21	50	2	10.5	0.003
Immobility/stupor	38	90.5	18	94.7	0.57
Mutism	40	95.2	19	100	0.33
Staring	34	81	15	78.9	0.86
Posturing/catalepsy	31	73.8	16	84.2	0.37
Grimacing	19	45.2	5	26.3	0.16
Echopraxia/echolalia	20	47.65	5	26.3	0.12
Stereotypy	23	54.8	2	10.5	0.001
Mannerisms	5	11.9	4	21.1	0.35
Verbigeration	12	28.6	1	5.3	0.40
Rigidity	33	78.6	8	42.1	0.01
Negativism	32	72.2	12	63.2	0.29
Waxy flexibility	23	54.8	8	42.1	0.36
Withdrawal	28	66.7	14	73.7	0.58
Impulsivity	12	28.6	2	10.5	0.12
Automatic obedience	10	23.8	11	57.9	0.01
Mitgehen	12	28.6	10	52.6	0.07
Gegenhalten	25	59.5	8	42.1	0.21
Ambitendency	9	21.4	8	42.1	0.10
Grasp reflex	11	26.2	0	0	0.01
Perseveration	6	14.3	0	0	0.08
Combateness	10	23.8	0	0	0.02
Autonomic abnormality	16	38.1	1	5.3	0.01

Mean scores in the 14-item BFCRS were higher in neurological than in psychiatric disorders ( $8.5 \pm 2.1$  versus  $6.7 \pm 1.4$ ,  $p=0.001$ ). Of the 23 items that the BFCRS includes as catatonic symptoms, neurological patients presented more symptoms than psychiatric patients ( $11.45 \pm 2.8$  versus  $8.6 \pm 1.6$ ,  $p \leq 0.001$ ). Neurological patients also exhibited a more severe form of catatonia assessed by the BFCRS ( $24.4 \pm 7.4$  versus  $18.5 \pm 5.0$ ,  $p=0.003$ ). The presence of each symptom of the BFCRS is shown in Table 2.

The majority of psychiatric patients manifested a stuporous type of catatonia, in contrast with the neurological patients ( $N=15$  [83.3%] versus  $N=14$  [33.3%],  $p>0.001$ ). Neurological patients mainly exhibited a mixed type of catatonia ( $N=25$  [59.5%] versus  $N=1$  [5.6%],  $p<0.001$ ), and both groups presented few cases of pure excited-type catatonia ( $N=3$  [7.1%] versus  $N=2$  [11.1%] for neurological patients versus psychiatric patients, respectively,  $p=0.23$ ).

Concomitant complications developed in 36 patients (85.7%), and all of these individuals had neurological diagnoses (Table 3). The most common complications were delirium ( $N=34$  [81%]) followed by urinary tract infection ( $N=31$  [73.8%]), pneumonia ( $N=24$  [57.1%]), and epileptic seizures ( $N=20$  [47.6%]). A patient with acute disseminated encephalomyelitis died, as did a patient with encephalitis (Table 3).

Laboratory findings that increased in severe forms of catatonia, such as creatine phosphokinase ( $2,236 \pm 4,019$  versus  $370 \pm 591$ ,  $p=0.01$ ) and white cell blood count ( $12,053 \pm 416$  versus  $8,700 \pm 237$ ,  $p=0.002$ ), were higher in neurological patients.<sup>14</sup> Thirty-two neurological patients and one psychiatric

patient (with intellectual disability) had an abnormal EEG result (32 [78%] versus 1 [0%],  $p<0.001$ ).

Neurological patients had a longer hospital stay (34 [12–92] versus 16.5 [12–37] days,  $p<0.004$ ) as well as more days with catatonia (23.5 [7–75] versus 13 [7–28] days, 0.02) than psychiatric patients. All patients showed remission of catatonia at discharge except for the two patients who died. Almost all neurological patients as well as psychiatric patients ( $N=63$  [92.6%]) received oral lorazepam as a first-line treatment (mean dosage= $7.3 \pm 2.8$  mg/day). Eleven psychiatric patients (57.9%) who did not respond to lorazepam after 2 days underwent ECT with a successful outcome. The three patients with neuroleptic malignant syndrome were immediately treated with lorazepam, bromocriptine, and ECT with a successful outcome. Only three neurological patients underwent ECT (one with encephalitis, another with postictal psychosis with remission of catatonia, and a neurological patient with acute disseminated encephalomyelitis) as a last-option rescue measure, without success. In neurological patients who had concomitant epileptic seizures, status epilepticus, or an EEG result with epileptic activity, we withheld ECT because of the risk for prolonged seizures or progression to status epilepticus.<sup>15</sup> In these patients, we used adjunctive anticatatonic medications in addition to lorazepam. Amantadine (mean dosage= $243 \pm 57$  mg/day) was selected as a second-line treatment, and bromocriptine (mean dosage= $5 \pm 2.5$  mg/day) and levodopa (mean dosage= $678 \pm 221$  mg/day) were used as third-line treatments. The mean number of anticatatonic medications in neurological patients was  $1.8 \pm 0.9$  versus  $0.7 \pm 0.4$  in psychiatric patients ( $p<0.001$ ). Atypical antipsychotic medication was administered to 48 patients (70.5%) at some point while these patients were in a catatonic state. These patients were previously receiving lorazepam as buffers against neuroleptic worsening of catatonia. Antipsychotic medications were not given to patients who had increased creatine phosphokinase levels. Atypical antipsychotics were mainly used in neurological patients for the management of symptoms of excited catatonia, specifically quetiapine (mean dosage= $291 \pm 178$  mg/day). In psychiatric patients, the main indication was treatment of psychotic symptoms, which persisted among many patients after remission of catatonia and were related to the underlying diagnosis (i.e., schizophrenia). Olanzapine was preferred for these patients (mean dosage= $13.7 \pm 5.6$  mg/day) (Table 4).

## DISCUSSION

Studies on the prevalence of catatonia and nosological conditions associated with this disorder remain scarce and show diverse results depending on the clinical settings where they are performed. Recent retrospective studies have provided some data. Dutt et al.<sup>16</sup> reported a 4.8% prevalence of catatonia in a psychiatric ward in which 78.8% of patients had a primary psychotic disorder. In a 20-year retrospective cohort analysis of the Mayo Clinic registries, Smith et al.<sup>5</sup> reported 95 cases of catatonia. Of these cases, 75 were

associated with a primary psychiatric disorder (53 patients [75%] had an affective disorder and 22 patients [25%] had a primary psychotic disorder), and 20 cases were due to a general medical condition. Of the latter, all patients had a neurologic disorder and encephalitis was the main etiology, as in our neurologic cases.<sup>5</sup> A 5-month prospective study reports a frequency of 8.9% multifactorial catatonia in older adults seen by a liaison psychiatry service in a general hospital. In this population, death was reported in 20% of patients.<sup>17</sup> In our 2-year prospective study, the overall prevalence was 3.327% and neurological disorders (42 [61.7%]) stood out as the predominant conditions associated with catatonia. This finding can be explained by our sample obtained from a national neurological referral center, which receives a variety of patients with neurological and psychiatric disorders; however, these patients are referred from general hospitals and psychiatric hospitals. The most important pathologies attended to at NINN include epilepsy, cerebrovascular disease, degenerative disorders, brain tumors, spinal diseases, and brain infections. This must be taken into account when comparing the clinical epidemiology of this institution with others, considering that studies focusing on the prevalence of catatonia in general hospitals have a different clinical profile. Primary psychiatric disorders are treated in the NINN neuropsychiatric unit; however, of the total sample, the ratio of neurological patients to psychiatric patients is 3:1. Yet the findings of our study, which exposes a large distribution of diagnoses associated with catatonia (Table 1), support the notion of non-specificity of the syndrome, which Caroff et al.<sup>18</sup> broadly described in a review of the epidemiology of catatonia.

In our study, encephalitis was the main diagnosis, accounting for 38.2% of the entire sample. It is noteworthy that apart from the report from Smith et al.<sup>5</sup> mentioned previously, the association of viral encephalitis with catatonia can be traced only in case reports in the literature.<sup>19</sup> On the other hand, the recent discovery that several forms of encephalitis result from antibodies against the neuronal cell membrane has led to a paradigm shift in the diagnostic approach to autoimmune encephalitis.<sup>20</sup> Recent studies have reported that up to 21% of encephalitides are immune mediated and are potentially treatable.<sup>21</sup> Catatonia is being recognized as one of the most noticeable hallmarks of anti-NMDAR encephalitis, a life-threatening autoimmune condition that is increasingly being reported worldwide.<sup>22</sup> As in our cases, prompt diagnosis, initiation of immunosuppressive therapies, tumor search, and tumor resection are decisive for better prognosis among these patients. Besides encephalitis, our study is in agreement with previous reports that many neurological diseases, such as acute disseminated encephalomyelitis and brain tumors, can present with catatonia.<sup>23</sup> Schizophrenia is the

**TABLE 3. Complications in Neurological and Psychiatric Patients With Catatonia**

Complications	Neurological Patients (N=42)		Psychiatric Patients (N=19)		p
	N	%	N	%	
Total	36	85.7	0	0	<0.001
Delirium	34	81	0	0	<0.001
Epileptic seizures	20	47.6	0	0	0.002
Status epilepticus	3	7.1	0	0	0.23
Hepatic failure	1	2.4	0	0	0.50
Renal failure	2	4.8	0	0	0.33
Pneumonia	24	57.1	0	0	0.001
Urinary tract infection	31	73.8	0	0	0.06
Malnutrition	8	19	0	0	0.04
Hydroelectrolytic imbalance	11	26.2	0	0	0.01
Glycemic imbalance	1	2.4	0	0	0.50
Decubitus ulcers	2	4.8	0	0	0.33
Rhabdomyolysis	1	2.4	0	0	0.50
Intravascular disseminated coagulation	1	2.4	0	0	0.50
Sepsis	4	9.5	0	0	0.16
Death	2	4.8	0	0	0.33

second nosological condition associated with catatonia (N=12 [17.6%]); however, the relatively low frequency of primary psychotic and affective patients with catatonia can be explained by the 3:1 ratio of neurological patients to psychiatric patients in our study sample.

Aside from supporting that catatonia is frequently present in neurological diseases, our study reveals very important clinical features that can be relevant for proper identification of the syndrome. Core symptoms of catatonia that were present in both groups included immobility/stupor, mutism, staring, catalepsy, negativism, and withdrawal. Neurological patients exhibited more excitement, grimacing, echophenomena, stereotypies, verbigeration, rigidity, impulsivity, grasp reflex, combativeness, and autonomic abnormalities. Automatic obedience and ambitendency

**TABLE 4. Outcome Measures and Treatments Used in Neurological and Psychiatric Patients With Catatonia<sup>a</sup>**

Outcome Measures and Treatments	Neurological Diagnosis (N=42)	Psychiatric Diagnosis (N=19)	p
Days of admission	36.4±19.4	18±0.6.6	<0.001
Days with catatonia	22.9±17.4	12.05±6.1	0.01
Treatment			
Lorazepam	40 (97.6)	16 (84.2)	0.09
Amantadine	23 (56.1)	0	<0.001
Bromocriptine	8 (19.5)	0	0.04
Levodopa	7 (17.1)	0	0.09
ECT	3 (7.3)	11 (57.9)	<0.001
Number of antiepileptic medications	1.8±0.9	0.7±0.4	<0.001
Antipsychotic medication	33 (80.5)	15 (78.9)	0.89
For treatment of agitation	31 (75.6)	1 (5.3)	<0.001
For treatment of psychosis	4 (9.8)	14 (73.7)	<0.001

<sup>a</sup> Data are presented as the mean ± standard deviation or number (percentage).



were more frequent in psychiatric patients (Table 2). Catatonia in psychiatric patients may be easier to recognize because such patients may show stuporous or retarded catatonia (the classic type of the syndrome) with few fluctuations.<sup>24</sup> On the other hand, neurological patients in our sample exhibited more periods of the excited type of catatonia with more diversity of “nonclassic” symptoms of the syndrome and prominent fluctuations. In this regard, our group and other authors recently suggested that a subtype of delirium exists, which we refer to as “catatonic delirium” or “catatonia with delirium symptomatology.”<sup>25</sup>

Our findings of the nonclassic phenomenological presentation of catatonia in neurological patients can alert clinicians to the presence of catatonia. If these findings are replicated, presentation of catatonia with nonclassic diverse symptomatology could help differentiate between neurological and psychiatric causes, which could become critical for proper prognostication and therapeutic management. Likewise, in this study, all but one patient with a psychiatric diagnosis had a normal EEG result, suggesting that all catatonic patients with an abnormal EEG finding would benefit from a full neurological evaluation including lumbar puncture.

The higher screening and severity BFCRS scores in neurological patients suggest that catatonia per se is more severe in this group than in psychiatric patients. The greater number and type of complications and the worse outcomes (e.g., more hospital days, more days with catatonia, and larger number of anticatatonic pharmacological medications needed for the remission of catatonia) can be understood in two ways. First, neurological patients may have greater functional disruption of the circuits and networks associated with catatonia, making these patients more susceptible to other comorbid complications. Second, catatonia is a complication that makes neurological patients more vulnerable to further complications.<sup>26</sup> Either way, we believe that catatonia makes the patient more vulnerable to other complications such as delirium and pneumonia and these conditions, in turn, can perpetuate catatonia. Accordingly, expeditious diagnosis and treatment of catatonia in neurological diseases is imperative. None of the psychiatric patients with catatonia had complications. ECT was promptly started in these patients, preventing further complications of prolonged catatonia.

With regard to treatment, almost all patients initiated first-line treatment with oral lorazepam as soon as catatonia was diagnosed (Table 4). More than one-half of the psychiatric patients needed a second-line treatment (ECT) because of no or partial response to lorazepam. In our Mexican patients, we have not yet seen the dramatic response to lorazepam (total remission after first or second dosage) reported in the literature<sup>24</sup>; the likely reason is that intravenous or intramuscular lorazepam preparations are unavailable in our country. Other countries using oral lorazepam report a similar response as ours.<sup>27</sup> It has been known for some time that parenteral lorazepam behaves

pharmacodynamically quite differently from oral lorazepam, which has a short half-life. With parenteral administration of lorazepam, drug distribution is less rapid and less extensive, leading to prolonged clinical effects.<sup>28</sup> In this way, lorazepam given parenterally has an advantage over parenteral diazepam and oral lorazepam because it can remain as a GABA<sub>A</sub> receptor agonist for longer periods. It is a clinical reality that after intravenous lorazepam lyses catatonia, the transition to oral dosing is sometimes accompanied by a re-emergence of catatonia, reflecting the above-described difference. Therefore, we recommend that parenteral lorazepam be added to the formularies in countries where it is currently unavailable.

The treatment of catatonia in neurological patients with coexisting complications such as seizures, status epilepticus, or an EEG result with epileptic activity can be challenging. There are some case reports of successful use of ECT in patients with these conditions.<sup>19</sup> However, the use of ECT under conditions that manifest cerebral hyperexcitability and a low seizure threshold is associated with increased risks for prolonged seizures and status epilepticus, a condition with high morbidity and mortality risks.<sup>15</sup> Under circumstances in which ECT must be withheld or postponed, the use of amantadine in addition to lorazepam can be effective and safe.<sup>29</sup> Bromocriptine<sup>30</sup> and levodopa<sup>31</sup> may also be considered as adjunctive third-line treatments in patients with refractory catatonia.

Neurological patients, psychiatric patients, and neuroleptic malignant syndrome patients who underwent ECT had a prompt and robust response, with remission of symptoms after a mean of  $6 \pm 1.7$  sessions. There were no cases of nonneuroleptic-induced malignant catatonia in our series. Whenever malignant catatonia with fever and hyperautonomia is seen, early use of ECT is advised in order to reduce morbidity and mortality risks.<sup>32</sup>

One hypothesis of the etiopathogenesis of catatonia is dopamine dysfunction supported by the induction of neuroleptic malignant syndrome by antipsychotics that exert dopamine antagonism.<sup>4</sup> However, adjunctive therapy with atypical antipsychotic medication was used without complications among 48 patients (70.5%) in this sample at some point while these patients were catatonic. All of the patients who underwent antipsychotic medication while catatonic were first given lorazepam for treatment of catatonia, and they also continued with the benzodiazepine to buffer against worsening catatonia and neuroleptic malignant syndrome. In neurological patients, the main indication was treatment of agitation; quetiapine was preferred for its low affinity to dopamine D<sub>2</sub> receptors.<sup>33</sup> In psychiatric patients, the main indication was psychosis; olanzapine was preferred for its efficacy in the treatment of psychotic symptoms. Other studies have reported the use of antipsychotic medications in catatonia with undue risk for complications,<sup>24</sup> and there is literature suggesting that neuroleptic use in patients who are already catatonic increases the risk for neuroleptic malignant syndrome.<sup>34</sup> One way to mitigate this risk is to add

antipsychotic medications to psychotic and agitated patients with recent catatonia only when lorazepam is also administered to buffer against the recurrence or worsening of catatonia. It is also important to monitor for emergence of catatonia when benzodiazepines and antiparkinsonian medications are discontinued. In this regard, three of the patients with neuroleptic malignant syndrome in our sample were received with this condition from other hospitals where they were treated with haloperidol and without benzodiazepines or other anticatatonic treatment as buffer in our neuropsychiatric unit developed neuroleptic malignant syndrome.

Catatonia is an important syndrome with significant morbidity and mortality in patients with neurological, medical, and psychiatric conditions. With proper and opportune treatment, a satisfactory outcome with remission can be achieved. Efforts are needed to increase recognition of catatonia and to identify signs and symptoms early so that optimal treatment can be instituted.

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The authors report no financial relationships with commercial interests.

Received Sept. 7, 2015; revised Oct. 19, 2015; accepted Oct. 25, 2015; published online Dec. 16, 2015.

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