

# Catatonia in Psychiatric Illnesses

Dirk M. Dhossche, M.D., Ph.D., Lee Elizabeth Wachtel, M.D., Michal Goetz, M.D., Ph.D.,  
and Pascal Sienaert, M.D., Ph.D.

**Abstract** Increased interest in the demarcation of catatonia from other conditions such as schizophrenia and autism is shown in the new DSM-5 category Catatonia Not Elsewhere Classified (NEC) encompassing catatonia of uncertain origin or associated with developmental conditions. Catatonia NEC is an imminently relevant diagnosis in patients who meet criteria for catatonia but without clearly defined associated psychotic, affective, or medical disorders. Catatonia NEC should be considered when catatonic symptoms present in patients with autism spectrum disorders, developmental disorders such as Prader-Willi Syndrome and Down Syndrome, tic disorders and Tourette Syndrome, Kleine-Levin Syndrome, aseptic encephalitis such as Anti-*N*-methyl-D-aspartate Receptor encephalitis, Pervasive Refusal Syndrome, or complex posttraumatic conditions.

Current experiences continue to support the use of benzodiazepines and ECT in catatonia as safe and effective treatments without the risk of worsening catatonia or precipitating Neuroleptic Malignant Syndrome as opposed to when antipsychotic medications are used as first-line or sole treatment

Historical and contemporary clinical and experimental catatonia models are available for future research, focusing on motor circuitry dysfunction, abnormal neurotransmitters, epileptic discharges, genetics, neuroendocrine and immune abnormalities, fear reactions akin to the animal defense strategy of tonic immobility, and developmental risk factors.

There have been advances in demarcating catatonia in a wide variety of patients as a treatable condition that requires prompt identification. Catatonia NEC in DSM-5 is likely to improve proper diagnosis and treatment of catatonia and to intensify research of this condition.

**Keywords** Catatonia • Malignant • Psychomotor abnormalities • Movement disorders • Schizophrenia • Mood disorder • Psychosis • Autism spectrum disorders • Developmental disorders • Tourette syndrome • Tics • Self-injury • Autism • Kleine-Levin Syndrome • Anti-*N*-methyl-D-aspartate Receptor encephalitis • Posttraumatic stress disorder • Neuroleptic Malignant Syndrome • Toxic Serotonergic Syndrome • Delirium • Children and adolescents • Benzodiazepines • Electroconvulsive treatment (ECT) • Autonomic symptoms • Vagal nerve

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D.M. Dhossche, M.D., Ph.D. (✉)

Professor, Department of Psychiatry, University of Mississippi Medical Center, Jackson, MS, USA  
e-mail: [dirkdhossche@gmail.com](mailto:dirkdhossche@gmail.com)

L.E. Wachtel, M.D.

Associate Professor, Department of Psychiatry, Johns Hopkins University, School of Medicine; Medical Director,  
Neurobehavioral Unit, Kennedy Krieger Institute, Baltimore, MD, USA  
e-mail: [wachtel@kennedykrieger.org](mailto:wachtel@kennedykrieger.org)

M. Goetz, M.D., Ph.D.

Assistant Professor, Department of Child Psychiatry, University Hospital Motol,  
Charles University, Prague, Czech Republic  
e-mail: [michal.goetz@lfmotol.cuni.cz](mailto:michal.goetz@lfmotol.cuni.cz)

P. Sienaert, M.D., Ph.D.

Assistant Professor, Department of Psychiatry, University Psychiatric Center – Catholic University of Leuven,  
campus Kortenberg, Kortenberg, Belgium  
e-mail: [pascal.sienaert@uc-kortenberg.be](mailto:pascal.sienaert@uc-kortenberg.be)

*And the more you really see mental patients and get to know their symptoms, the more you will be convinced that finally nothing else can be found and observed but movements and the whole pathology of mental patients consists of nothing else but the peculiarities of their motor behavior.*

Carl Wernicke, 1900 (1)

*It happens quite often that we fail to see something because it's too big.*

Multatuli (pseudonym of Eduard Douwes Dekker; Dutch writer; 1820–1887)

## 27.1. Introduction

Catatonia is a unique syndrome characterized by specific motor signs, at times life-threatening when aggravated by autonomic dysfunction and fever, but treatable with benzodiazepines and electroconvulsive therapy (ECT) if recognized early (2, 3). Identifiable motor signs are immobility sometimes alternating with excessive motor activity that is mostly purposeless and not influenced by external stimuli, extreme negativism, reduced speech or muteness, repetitive movements (stereotypy), echolalia, echopraxia, and other peculiarities of voluntary movement. Tics and other sudden and non-rhythmic movements, often with self-injury, occur commonly in catatonic patients and may qualify as additional catatonic symptoms (4, 5).

Since the publication of the first version of this chapter in 2008, catatonia has been further delineated across a wide range of disorders (6, 7). An update on symptoms, prevalence, evaluation, treatment, risk factors, and experimental models of catatonia is presented, through review of literature and case-reports since 2008, incorporating important changes in the classification of catatonia that have been made in DSM-5 (8) (Table 27.1).

TABLE 27.1 Definition of catatonic symptoms.

Excitement	Extreme hyperactivity, constant motor unrest which is apparently non-purposeful
Immobility/stupor	Extreme hypoactivity, immobility. Minimally responsive to stimuli
Mutism	Verbally unresponsive or minimally responsive
Staring	Fixed gaze, little or no visual scanning of environment, decreased blinking
Posturing/catalepsy	Maintains posture(s), including mundane (e.g., sitting or standing for hours without reacting)
Grimacing	Maintenance of odd facial expressions
Echopraxia/echolalia	Mimicking of examiner's movements/speech
Stereotypy	Repetitive, non-goal directed motor activity (e.g., finger-play, repeatedly touching, patting or rubbing self)
Mannerisms	Odd, purposeful movements (hopping or walking tiptoe, saluting passers-by, exaggerated caricatures of mundane movements)
Verbigeration	Repetition of phrases or sentences
Rigidity	Maintenance of a rigid position despite efforts to be moved
Negativism	Apparently motiveless resistance to instructions or to attempts to move/examine the patient. The patient does the opposite of the instruction
Waxy flexibility	During repositioning, patient offers initial resistance before allowing himself to be repositioned (similar to that of bending a warm candle)
Withdrawal	Refusal to eat, drink, and/or make eye contact
Impulsivity	Patient suddenly engages in inappropriate behavior (e.g., runs down the hallway, starts screaming, or takes off clothes) without provocation. Afterwards, cannot explain
Automatic obedience	Exaggerated cooperation with examiner's request, or repeated movements that are requested once
Passive obedience (mitgehen)	Raising arm in response to light pressure of finger, despite instructions to the contrary
Gegenhalten/Counterpull	Resistance to passive movement that is proportional to strength of the stimulus; response seems automatic rather than willful
Ambitendency	The patient appears stuck in indecisive, hesitant motor movements
Grasp reflex	Strike open palm of patient with two extended fingers of examiner's hand. Automatic closure of patient's hand
Perseveration	Repeatedly returns to the same topic or persists with same movements
Combativeness	Usually in an undirected manner, without explanation
Autonomic abnormality	Abnormality of temperature (fever), blood pressure, pulse rate, respiratory rate, inappropriate sweating

## 27.2. Catatonia NEC: A Dark Horse in DSM-5

Catatonia was originally described in 1874 by Kahlbaum as a separate brain disorder with a cyclic, alternating, and ultimately progressive course (9). Kraepelin viewed catatonia as an exclusive subtype of dementia praecox or schizophrenia. In contrast, recent studies show the preponderance of underlying affective symptoms and syndromes, particularly mania, in adult catatonic patients (10–13) and comorbidity with an expanding list of adult and pediatric conditions (Table 27.2). Examples of catatonia are provided in Figs. 27.1–27.4.

In DSM-IV (44), catatonia was a specifier of Schizophrenia, Primary Mood Disorder, and Mental Disorder due to a General Medical Condition. However, major changes have been made in DSM-5 (8) including the deletion of catatonia as a type of schizophrenia, the creation of a new class of Catatonia Not Elsewhere Classified (NEC), and the addition of a catatonia specifier for 10 primary diagnoses. A uniform list of catatonia signs was adopted across all categories. Catatonia Secondary to a general Medical Condition created in 1994 has been retained.

TABLE 27.2 Disorders in which catatonia can emerge.

Developmental disorders
Autistic disorder (14–17)
Childhood disintegrative disorder (18, 19)
Mental retardation (20) including Down syndrome (21)
Prader-Willi syndrome (22)
Medical and neurological disorders
Catatonia due to a general medical condition (brain structural damage, seizures, metabolic, endocrine, and autoimmune disorders) (23–27)
Psychiatric disorders
Psychotic disorders (28)
Mood disorders (28)
Substance-induced disorders (23)
Medication-induced movement disorder (NMS) (29, 30)
Tourette syndrome (4, 17, 31)
Miscellaneous conditions
Anti-NMDA ( <i>N</i> -methyl-D-aspartic acid) receptor encephalitis (32–36), PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections) (24, 26), encephalitis lethargica (37), and other aseptic encephalitides (38)
Kleine-Levin syndrome (19)
Psychogenic catalepsy (39)
Anaclitic depression (40, 41)
Pervasive refusal syndrome (42, 43)

FIGURE 27.1 Catatonic rigidity (from reference 155, p. 267).

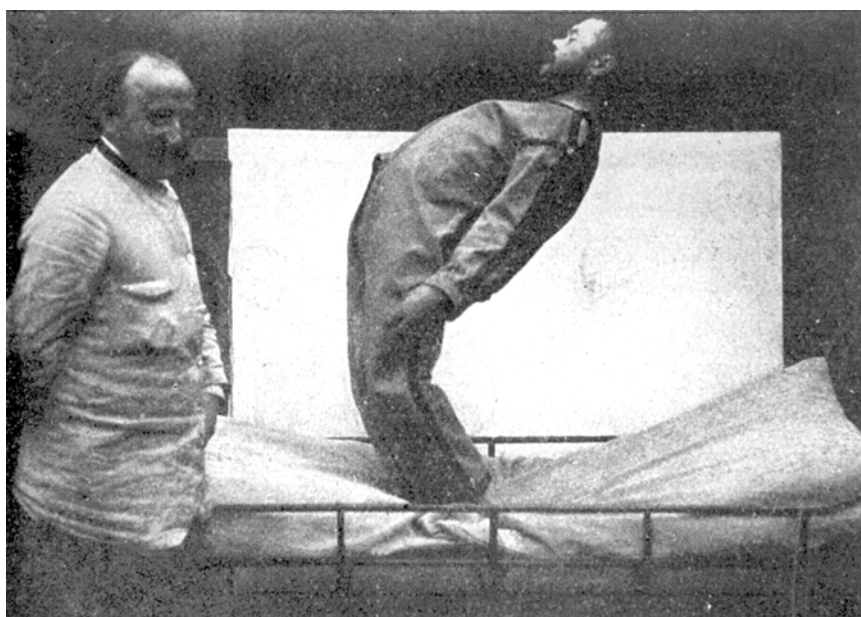


FIGURE 27.2 Catatonic rigidity ("pillow sign") (from reference 155, p. 269).



FIGURE 27.3 Flexibilitas cerea (from reference 155, p. 270).



FIGURE 27.4 Flexibilitas cerea (from reference 155, p. 272).



TABLE 27.3 Comparison between (malignant) catatonia and anti-NMDAR encephalitis.

	Catatonia	Anti-NMDAR encephalitis
First described by	Kahlbaum in 1874 (9) (catatonia) and Stauder in 1934 (50) (lethal or malignant catatonia)	Dalmau in 2007 (47)
Symptoms		
Abnormal movements	++	++
Autonomic dysfunction	++	++
Seizures	+	++
Risk factors		
Teratomata (ovarian)	-	++
Neoplasms	+	+
Viral infections	+	+
Antipsychotics	++	?
Treatment		
Benzo's/ECT	++	?
Immune treatments	?	++

The recommendation for catatonia as an independent syndrome in the form of a separate category Catatonia NEC is profound and finalizes the divorce between catatonia and schizophrenia, in order to allow experience to refine the place of catatonia in clinical care and to offer the recommended treatments for catatonia to a wider range of patients. The known experience finds about 80% of the patients with catatonia respond to the benzodiazepines, and almost universal response to ECT in those who fail benzodiazepines. Prompt recognition of catatonia and in some cases treatment with ECT is likely to prevent medical complications, such as deep vein thrombosis, pulmonary emboli (45, 46), dehydration, malnutrition, and physical exhaustion.

The designation of catatonia specifiers for 10 primary diagnoses and the retention of a Catatonia Secondary to a Medical Disorder sustain the secondary position of catatonia in the prior classifications and do not encourage the first-line use of benzodiazepines in patients who meet the criteria for catatonia thereby continuing to create treatment dilemmas.

For example, the distinction between Catatonia Secondary to a Medical Disorder and Catatonia NEC is unclear. A case-in-point is the patient who meets criteria for (malignant) catatonia and tests positive for anti-NMDA receptor antibodies. Is the patient suffering from the newly coined anti-NMDAR encephalitis (47) that should be treated with immune treatments? Or is the patient suffering from malignant catatonia that should be treated swiftly with benzodiazepines and ECT? The enthusiasm for the newly defined disorder of anti-NMDA receptor encephalitis should not be a barrier for treating the recognized catatonia vigorously (32). The immune treatments that are recommended for the newly proposed form of synaptic autoimmune encephalitis often yield equivocal results, especially in pediatric cases. The sharp increase in the number of reports of pediatric cases of anti-NMDA receptor encephalitis highlights that catatonia is common yet often unacknowledged in children and adolescents (6, 19). There are now a few reports that show the efficacy of treatment with high-dose benzodiazepine and ECT in anti-NMDA receptor encephalitis (36, 48, 49). Studies comparing benzodiazepines or ECT with immune therapies in children, adolescents, and adults who meet criteria for catatonia and who test positive for the anti-NMDA receptor antibody are warranted (Table 27.3).

### 27.3. Evaluation, Differential Diagnosis, and Treatment

Catatonia should be considered in any patient when there is a marked deterioration in psychomotor function and overall responsiveness. Observation and psychiatric interview will not suffice to detect the catatonic syndrome, since the most striking symptoms such as posturing, are present only in a minority of the cases. It is of importance to elicit specific catatonic signs (such as negativism, automatic obedience, passive obedience, gegenhalten, or grasp reflex) during a neuropsychiatric examination. A rating scale or checklist may aid the detection and quantification of catatonia. Up to date, 6 different catatonia rating scales have been published: the Rogers Catatonia Scale (51), the Bush-Francis Catatonia Rating Scale (52), the Northoff Catatonia Rating Scale (53), the Braunig Catatonia Rating Scale (54), the Bush-Francis Catatonia Rating Scale Revised Version (55) and the Kanner Scale (56). Characteristics of these scales are presented in Table 27.4.

Reflecting different underlying diagnostic concepts, current diagnostic rating scales differ substantially in the nature and number of the items included. The total number of items ranges from 18 to 40. Both sensitivity and specificity of current rating scales is high. With the exception of the MRS-C, all rating scales provide a threshold score for the diagnosis of catatonia, based on the total score of the scale or on the score of a screening instrument, as in the BFCRS and the Kanner scale. Probably, not all scales are suited for use in the divergent patient groups in which catatonia can be encountered: the RCS is designed to detect catatonia in depression, whereas the MRC may be better suited in schizophrenia. None of the scales have been applied to autis-

TABLE 27.4 Overview of catatonia rating scales.

Dimension	MRS-C	RCS	BFCRS	NCRS	BCRS	Kanner
Screening instrument	No	No	First 14 items	No	No	11 items
Catatonia definition	?	>7	≥2 items of the screening instrument	1 item of each category and total score >7	4 criteria with score ≥2	≥2 items of the screening instrument
Number of items	18	22	23	40 (13 motor, 12 affective, 15 behavioral)	21 (16 motor, 5 behavioral)	18
Range of item scores	0–2	0–2	0–3	0–2	0–4	0–8
Total scores	0–36	0–44	0–69	0–80	0–84	0–144
Procedure	Standard motor examination	Standard motor examination	Standard procedure	?	Semistructured examination	Semistructured examination
Inter-rater reliability (Correlation coefficient)	?	0.81	0,93 (0,95 BFCSI)	0.80–0.96	>0.83	?
Inter-rater reliability (Cohen's Kappa)	0.87	?	0.73 (0.83 BFCSI)	0.81	?	?
Test-retest reliability	0.67	0.89	?	0.80–0.95	?	?
Validity	?	Sens. and spec. 100% to DSM-IV in depressive subgroup	Sens. 100%, spec. 75–100% to older criteria	Sens. and spec. 100% to older scales and criteria	?	?

MRS-C=Modified Rogers Scale, Catatonia Subscale; RCS=Rogers Catatonia Scale; BFCSI=Bush-Francis Catatonia Screening Instrument; BFCRS=Bush-Francis Catatonia Rating Scale; NCRS=Northoff Catatonia Rating Scale; BCRS=Braunig Catatonia Rating Scale; Kanner=Kanner scale.

Adapted from (57), copyright (2011) with permission from Elsevier.

TABLE 27.5 Diagnostic criteria for catatonia as per Fink &amp; Taylor (3).

Criterion A	Immobility, mutism, or stupor of at least one hour duration, associated with at least one of the following: catalepsy, automatic obedience, or posturing, observed or elicited on two or more occasions.
Criterion B	Two or more of the following, which can be observed or elicited on two or more occasions: stereotypy, episodes of frenzied agitation, echolalia/echopraxia, waxy flexibility, automatic obedience, posturing, negativism, or ambitendency.

tic populations. The BFCRS, the BCRS and the Kanner scale are completed during a semi-structured interview. A correct BCRS examination is time consuming, whereas completing the BFCRS is easily integrated in a psychiatric evaluation, making the BFCRS a practical screening tool for routine clinical practice. Current rating scales seem best suited for screening, offering the clinician a scheme to perform a neuropsychiatric examination and improving the detection of catatonic symptoms. These scales are less well suited for assessing severity and change, since they lack the sensitivity necessary to measure change (58).

Although different criteria for a diagnosis of catatonia are used, we find the criteria proposed by Fink & Taylor (3) relevant and practical (Table 27.5). In DSM-5, catatonia is diagnosed when three or more of a list of 12 catatonic symptoms are present (8). The 12 catatonic symptoms are: stupor, catalepsy, waxy flexibility, mutism, negativism, posturing, mannerism, stereotypy, agitation (non-influenced by external activity), grimacing, echolalia, and echopraxia.

### 27.3.1. Differential Diagnosis

A detailed history, clinical examination, and application of diagnostic criteria must be used to differentiate catatonia from other well-recognized conditions, syndromes, or disorders featuring psychomotor abnormalities that may overlap with the manifestations of catatonia. Making an adequate differential diagnosis of catatonia is complicated by the fact that there is no biologic marker diagnostic of catatonia. The differential diagnosis of catatonia when motor activity is increased or reduced is shown in Table 27.6.

Some motor manifestations of catatonia such as catatonic excitement, psychomotor retardation, or negativism may be mistaken for purposeful, oppositional and attention-seeking behaviors that are under full control of the patient and for secondary gain. Decreased speech, muteness, or posturing may be mistaken as indicative of conversion disorder especially when following stressful events or trauma. It may be very difficult in some instances to determine the origin of these behaviors and



TABLE 27.6 Differential diagnosis of catatonia.

Differential diagnosis; when increased motor activity
Acute dystonia
Tardive dyskinesia
Akathisia
Withdrawal-emergent dyskinesias
Tics/Gilles de la Tourette
Purposeful, oppositional, or attention-seeking behaviors
Conversion disorder
Compulsions (in obsessive-compulsive disorder)
Epilepsy
Delirium
Differential Diagnosis; when reduced motor activity
Parkinsonism and Parkinson's disease
Malignant hyperthermia
Neuroleptic malignant syndrome
Toxic serotonergic syndrome
Epilepsy
Selective mutism
Conversion disorder
Purposeful, oppositional, or attention-seeking behaviors
Status epilepticus
Delirium
Coma

FIGURE 27.5 Portrait of Karl Ludwig Kahlbaum, M.D., (1828–1899).



*Kahlbaum*

degree of control that the patient has on these behaviors, even during longer periods of observation. The catatonia benzodiazepine challenge test that will be discussed in the treatment section may be useful in such situations. A profoundly positive response would support a diagnosis of catatonia, although the therapeutic effects of anxiolytics including amytal and benzodiazepines as diagnostic tools and treatment are also known in conversion disorders (59–63). A negative challenge test is expected when motor abnormalities represent voluntary behaviors for secondary gain although there may be mild improvement due to specific sedative effects.

Epilepsy and status epilepticus are important differential diagnoses given the overlap of symptoms between psychomotor seizures and catatonia and the increased prevalence of seizures in catatonic patients (3). In his original description, Kahlbaum (Fig. 27.5) reported seizure-like symptoms in catatonia (9). Seizures are also frequent in children and adolescents with autism (64, 65) and catatonia (7, 20). Seizures and catatonia are not mutually exclusive in this population. However, frank epileptic activity is usually absent in EEG recordings in catatonic patients. Typical findings in catatonia include diffuse slowing in patients in catatonic stupor and a dysrhythmic EEG in catatonia. These findings are consistent with non-convulsive status epilepticus that

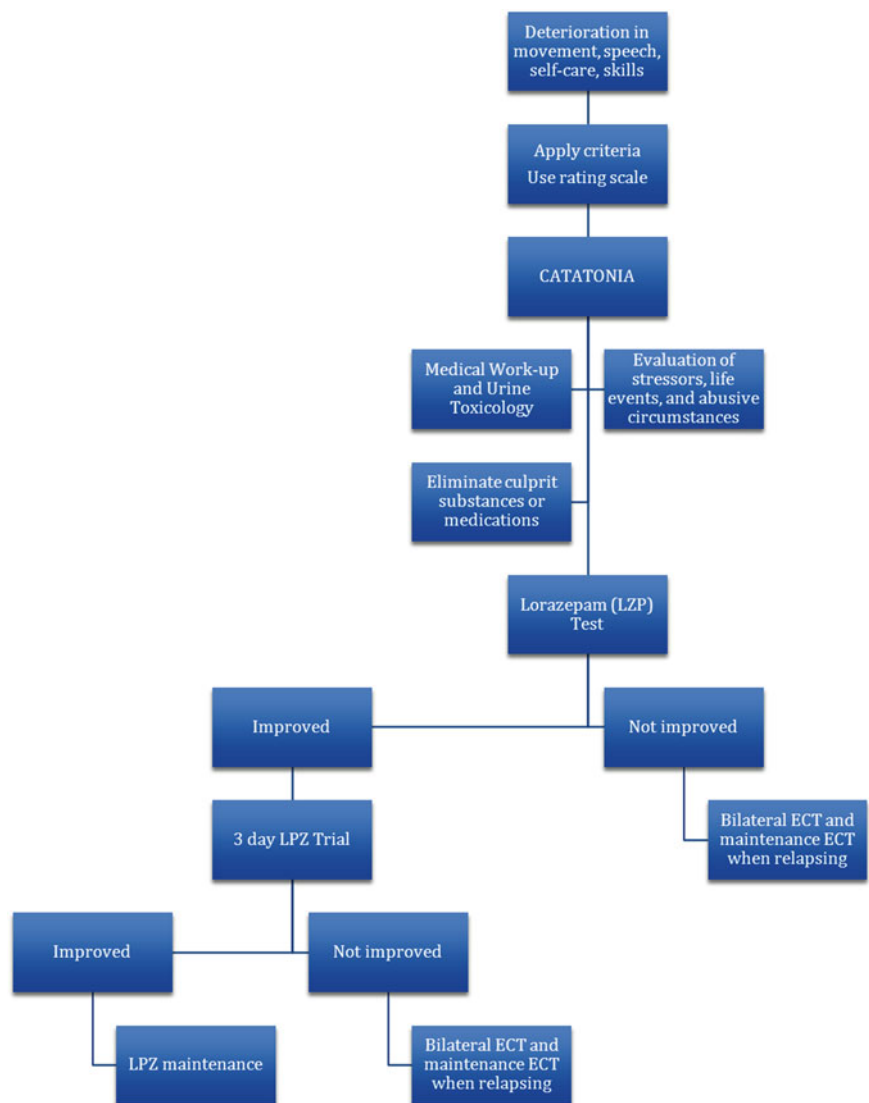
resolves when catatonia remits and is consistent with the underlying theory (66, 67) of this disorder, that there is localized brain excitation in catatonic patients in specific deep brain structures that are not detected by current EEG techniques, which improves with anticonvulsant medications but especially with benzodiazepines and ECT.

### 27.3.2. Laboratory and Other Investigations

Various infectious, metabolic, endocrine, neurological, toxic and autoimmune conditions have been associated with catatonia and must therefore be assessed. Proposed basic investigations include a complete blood count and metabolic panel, erythrocyte sedimentation rate, magnetic resonance imaging, electroencephalogram, cerebrospinal fluid analysis, antinuclear antibodies, and urine and organic metabolic testing, with further testing based upon clinical findings (68) (Fig. 27.6).

A drug screen to detect common illicit and prescribed substances is necessary. Recreational drugs (phencyclidine, mescaline, psilocybin, cocaine, ecstasy, opiates and opioids), disulfiram, steroids, antibiotic agents (ciprofloxacin), baclofen and bupropion have been associated with the emergence of catatonia. Withdrawal of benzodiazepines, gabapentin and dopaminergic drugs, especially if done rapidly, has precipitated catatonia in some patients (3).

FIGURE 27.6 Assessment and treatment algorithm for catatonia.





### 27.3.3. Medication Management

All prescribed medications should be evaluated for their potential to induce catatonic symptoms, since many medications can cause catatonia or catatonia-like conditions. Antipsychotic agents, especially of the first generation, should be discontinued as they are contraindicated in patients who exhibit the signs of catatonia because of the reported increased incidence of malignant catatonia or neuroleptic malignant syndrome (NMS) in patients with incipient signs of catatonia (69, 70). The symptoms of malignant catatonia or NMS are essentially the motor symptoms of catatonia compounded with autonomic symptoms (fever, blood pressure abnormalities, hypoventilation, excessive sweating). NMS is considered a toxic reaction to psychotropic medications, particularly antipsychotics.

Once catatonia is resolved, second generation antipsychotics with low D2 blockade (quetiapine, olanzapine) or with D2 partial agonism (aripiprazole) should be preferred for treatment of residual psychotic symptoms, if any (71).

### 27.3.4. Medical Management

Simultaneous treatment of catatonia and a drug-induced or medical condition, if any is detected, is generally recommended in addition to supportive measures. For instance, despite the withdrawal of the offending agent, treatment of an underlying infection or metabolic disease, or the removal of a malignancy, as the case may be, catatonia often persists and requires urgent intervention that should not be postponed for elaborate searches for ill-defined or poorly treatable medical conditions. This may be particularly relevant in recent cases of presumed autoimmune entities such as Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections (PANDAS) and anti-NMDA-receptor encephalitis where catatonic symptoms are evident, yet well documented anti-catatonic treatments are rejected in favor of novel immunological interventions of questionable benefit and possible danger (32, 72).

### 27.3.5. Lorazepam Test Validates Catatonia

As a first step, a benzodiazepine challenge test of 1 or 2 mg of lorazepam that can be administered per os, intramuscularly, or intravenously, should be used to verify the catatonia diagnosis (Fig. 27.6) (2, 3, 73). If intravenous lorazepam is used, any changes in the next two to five minutes are noted. If no change is observed, the second 1 or 2 mg lorazepam is injected, and the assessment is repeated. The interval for the repeat dose is longer for intramuscular (15') and peroral (30') administration. The use of the gamma-aminobutyric acid-A (GABA) receptor modulator zolpidem has also been developed as an alternative catatonia challenge test and implemented, particularly in Europe (74). Zolpidem is only available in oral form.

When a single dose of lorazepam improves catatonia, lorazepam can be prescribed at regular intervals to maintain improvement. Many catatonic patients require relatively high dosages of lorazepam, occasionally up to 24 mg daily, for symptom resolution. Our experience shows that in some patients with catatonia doses up to 24 mg daily are tolerated without ensuing sedation, especially when instituted using daily incremental dosages, and result in marked reduction of catatonic symptoms. This suggests that in some cases, catatonia may be associated with high tolerance to benzodiazepines. Careful monitoring in a medical setting for excessive sedation, respiratory compromise, and other side effects is required.

### 27.3.6. Pre-ECT Laboratory and Other Investigations

Routine laboratory tests and an anesthesia consult are required during the pre-ECT work-up. Routine brain imaging studies is not generally recommended prior to ECT, however, in some hospitals, pre-ECT brain CT or MRI is mandatory. Additional consultation may be required in selected cases to stabilize general medical issues such as risk of dehydration and hemodynamic abnormalities in catatonic patients before starting ECT (Fig. 27.6).

### 27.3.7. ECT Parameters

The relief of catatonia often seems to require more frequent seizures than those necessary for the relief of major depression. The UK standard practice of two seizures a week, although effective for major depression, may not be so for catatonia. In severe or malignant catatonia, daily ("en bloc") treatment for three to five days may be necessary. Second, the efficacy of bilateral (bitemporal or bifrontal) electrode placement is better documented than is unilateral placement. Therefore, based on practical experience, the authors recommend bilateral electrode placement for catatonia. Furthermore, in our experience the number of treatments, before substantial and sustained improvement becomes obvious, cannot be predicted. Therefore, ECT treatment must be individually tailored and the duration and the frequency of treatment should be based on regular assessments, possibly after every 6–12 treatments.

### 27.3.8. ECT and Concurrent Medications

All psychiatric medications should be stopped prior to initiation of ECT, as well as any other non-psychiatric medications, if possible. An exception is when there was a partial response with benzodiazepine treatment, often administered in a high dose; in these instances, ECT and a benzodiazepine may be administered concurrently. Discontinuation or rapid taper of the benzodiazepine may not be advisable at the start of the ECT course, because of a risk of altering the seizure threshold. Concurrent use of lorazepam (or another benzodiazepine) and ECT is then a useful treatment variant. Intravenous administration of flumazenil, a benzodiazepine antagonist, can be used if lorazepam interferes with eliciting seizures during ECT and may be beneficial even if seizures outwardly appear adequate; indeed, use of flumazenil has also been proposed in benzodiazepine-naïve patients for augmentation of ECT effect (75).

### 27.3.9. Maintenance ECT in Catatonia

Maintenance-ECT (M-ECT) may be useful for sustained symptom-remission (76, 77). There are no studies which suggest evidence for structural or histopathological changes during M-ECT (78, 79). Studies of various cognitive functions also demonstrate a stability of various longitudinal cognitive measures (80–82).

Less information is available regarding M-ECT in patients with catatonia and autism. One case series (83) presents the M-ECT courses of three autistic catatonic patients who received up to 286 maintenance treatments with sustained remission of catatonia and without subjective evidence of decline in cognitive or adaptive skills. One patient was unable to access M-ECT for legal reasons and promptly relapsed into catatonia. While the number of M-ECT delivered to these patients appears high, this finding is considered within the context of a special patient population who are known to have a relatively poor response to psychotropic agents, and possibly a higher overall propensity for treatment resistance.

## 27.4. Malignant Catatonia and Related Conditions

Malignant catatonia is a severe form of catatonia, coined as “lethal catatonia” by Stauder (50) in 1934, that includes the constellation of catatonic signs, motoric excitement, stuporous exhaustion, autonomic instability, respiratory failure, collapse, coma and ultimately death. This malignant form of catatonia is of acute onset and systemically devastating requiring intensive medical care. Patients appear to have an acute infectious process leading to exhaustive but negative evaluations. Patients with malignant catatonia may present in both agitated and stuporous states (3). Untreated malignant catatonia is fatal in 10–20% of cases, with death ensuing within mere days of onset. Malignant catatonia also occurs in children and adolescents (84–87). Malignant catatonia should feature prominently in the differential diagnosis of the acute encephalopathies as a treatable syndrome with acute onset of unresponsiveness, muteness, echolalia, echopraxia, and other psychomotor abnormalities, along with fever and signs of autonomic instability.

Neuroleptic Malignant Syndrome (NMS) is a similar syndrome caused by typical as well as atypical antipsychotics and other psychotropic medications, and characterized by motor rigidity, lowered consciousness, autonomic instability, and fever. NMS is best considered malignant catatonia caused by administration of antipsychotic and other psychotropic agents; indeed, the physical and physiological symptoms as well as the laboratory indices, such as leukocytosis, elevated creatine phosphokinase, and decreased serum iron, show prominent correlation (2, 3). NMS responds to classic anti-catatonic treatments, i.e., benzodiazepines and ECT (2, 3, 69).

Toxic serotonin syndrome, malignant hyperthermia, and delirium constitute another group of disorders that are characterized by varying levels of hypokinesia and muscle stiffness, in combination with altered levels of consciousness and autonomic dysfunction. For example, there is discussion in the literature if toxic serotonin syndrome truly differs in key aspects with catatonia, or alternatively, if toxic serotonin syndrome should be regarded as another medication-induced form of catatonia (69, 88). Response of toxic serotonin syndrome to the same treatments as catatonia would strengthen the argument of relatedness. Malignant catatonia is similar to malignant hyperthermia in that both share muscular rigidity, hypermetabolic and hyperthermic states, yet the latter is uniquely associated with either succinylcholine usage or a genetic response to inhaled anesthetics (2, 3). A genetic model of hyperthermia is the Porcine Stress Syndrome, a congenital, autosomal recessive disorder which affects pigs, dogs, cats, and horses and is caused by a fundamental intolerance of stress due to a defective ryanodine receptor which affects closure of calcium channels in the sarcoplasmic reticulum and causing a sudden, sustained rise in intracellular calcium and consequent muscle contracture and up-regulation of metabolism (89).

Some patients diagnosed with delirium meet criteria for malignant catatonia (90, 91). Classifying these patients is difficult because DSM diagnostic rules state that catatonia should not be diagnosed if occurring exclusively during the course of a delirium while acknowledging that similar medical conditions of infectious, metabolic, endocrine and neurological etiologies

are associated with both catatonia and delirium (44). The validity of this DSM provision is uncertain given the lack of studies in the literature that have assessed the importance of catatonia during delirium. The issue is important because treatments for catatonia and delirium are different, albeit with overlap. While delirium is typically treated with (typical or atypical) antipsychotics, the emergence of catatonia in delirium may caution against the use of antipsychotic medications due to the aforementioned risk of worsening catatonia with antipsychotic medications (69, 70). There are no new guidelines regarding this issue in DSM-5, probably due to the lack of studies.

Another unresolved classification issue is whether catatonia should be included in the differential diagnosis in patients with coma (complete unresponsiveness) (92), and, in a similar vein, if stupor or profound unresponsiveness can be the sole presenting symptom of catatonia (92–94). Recent case-reports have shown that patients with levels of unresponsiveness similar as in coma, and without other catatonic symptoms (except resistance to eye-opening) responded to electroconvulsive therapy (95) and intravenous benzodiazepines (94).

## 27.5. Pediatric Catatonia

A previous literature review from 1966–1996 (20, 22) found 30 cases of catatonia in patients younger than 18 years of age. Several children and adolescents had underlying mental retardation or autism spectrum disorder. Benzodiazepines and ECT were the most reliable treatments, similar as reported in adult catatonia. Table 27.7 shows the frequencies of the most common catatonic symptoms in children and adolescents reported by Dhossche & Bouman (20, 22).

Since then, other cases have been published confirming that catatonia occurs in children and adolescents with associated psychotic, affective, drug-induced, or medical disorders, but also in patients with autistic, developmental, and tic disorders, and occasionally in children with no clearly identifiable medical or psychiatric conditions (4, 19).

Table 27.8 lists pediatric studies showing a wide variability of prevalence rates of catatonia in selected patient groups and settings, suggesting that catatonia may not be rare. Adolescents with catatonia comorbid with schizophrenia and affective dis-

TABLE 27.7 Catatonic symptoms in children and adults.

	Children	Adults
	%	%
Mutism	87	78
Posturing/grimacing	52	66
Stupor	80	66
Staring	49	57
Waxy flexibility	62	35

Adapted from (22), copyright (1997) with permission from Springer Science + Business Media.

TABLE 27.8 Prevalence of pediatric catatonia: review of the literature since 1992.

Authors (year)	Sample size	Design sample population	% with catatonia
Green et al. (1992) (97)	38	Prospective Childhood schizophrenia	32
Moise & Petrides (1996) (98)	13	Retrospective ECT	46
Wing & Shah. (2000) (99)	506	Prospective Autism	17
Thakur et al. (2003) (28)	198	Prospective Psychiatric clinics	18
Cohen et al. (2005) (100)	4976	Prospective Psychiatric clinics	0.6
Billstedt et al. (2005) (101)	120	Prospective Autism	12
Ohta et al. (2006) (102)	69	Prospective Autism	12
Consoli et al. (2009) (103)	199	Meta-analysis ECT	6
Ghaziuddin et al. (2012) (104)	101	Retrospective At-risk inpatients	18
Goetz et al. (unpublished)	92	Retrospective First-break adolescent psychosis	33

orders have a 60-fold increased risk of premature death, including suicide, when compared to the general population of same sex and age (96).

## 27.6. Catatonia in Autism Spectrum Disorders

Catatonia has been increasingly recognized as a comorbid syndrome of autism spectrum disorders, identified at a rate of 12–17% in adolescents and young adults with autism spectrum disorders (99, 101) and with other intellectual disabilities (22, 105). Catatonic symptoms, such as mutism, stereotypic speech, echolalia, stereotypic or repetitive behaviors, posturing, grimacing, rigidity, mannerisms and purposeless agitation feature prominently in autism. Therefore, only a sharp and marked increase in these symptoms, often in adolescence, qualifies for a diagnosis of catatonia (99, 106, 107).

In some cases, catatonia may be a feature of another major psychiatric syndrome such as depression (108), bipolar illness (109) or schizophrenia (110), yet many patients do not qualify for a clear diagnosis of mood or a psychotic disorder, often due to the fact that patients are nonverbal and have severe cognitive impairments. Case-reports also describe catatonia in pediatric patients with genetic disorders which are characterized by varying degrees of developmental impairment but the autistic features often do not amount to a full diagnosis of autism; catatonia has been reported in patients with Prader-Willi Syndrome (22) and Down Syndrome (111).

Most cases of catatonia in children and adolescents with autism spectrum disorders are not associated with underlying medical or psychiatric conditions. For example, in a sample of 58 children and adolescents with catatonia, 18 (31%) had a history of developmental disorder, i.e., autism spectrum disorder, intellectual disability or neurodevelopmental malformation (112). Only two of those had an identifiable underlying medical or psychiatric condition.

Two systematic studies show catatonia to occur in 12% to 17% of adolescents and young adults with autism spectrum disorders (99, 101). Wing & Shah report that 17% of a large referred sample of adolescents and young adults with autism spectrum disorders satisfied modern criteria for catatonia (99). Thirty individuals with autism spectrum disorders aged 15 years or older met criteria for catatonia, with classic Autistic Disorder diagnosed in 11 (37%), atypical autism in 5 (17%), and Asperger Disorder in 14 (47%). Under age 15, no child demonstrated the full syndrome although isolated catatonic symptoms were often observed. In the majority of cases, catatonic symptoms started between 10 and 19 years of age. Five individuals had brief episodes of slowness and freezing during childhood before age 10. Obsessive-compulsive and aggressive behaviors preceded catatonia in some. Visual hallucinations or paranoid ideas were occasionally reported, but no diagnosis of schizophrenia could be made. This study also emphasized additional symptoms of catatonia that may be particularly characteristic of catatonia in autism spectrum disorders, including amotivation, global slowness, and prolonged time to complete previously mastered tasks. It is important to recognize these additional symptoms along the catatonic spectrum, because they may otherwise be erroneously attributed to as oppositional or “stubborn” behavior.

In the second study, 13 (12%) of 120 autistic individuals, between ages 17–40 years, had clinically diagnosed catatonia with severe motor initiation problems (101). Another four individuals had several catatonic symptoms, but did not meet criteria for the full syndrome. Eight of the 13 individuals with catatonia suffered from classic Autistic Disorder; the remaining five were diagnosed with atypical autism. The proportion of those with Autistic Disorder that were diagnosed with catatonia was 11% (8/73). Fourteen percent (5/35) of those with atypical autism had catatonia.

A recent hospital-based study (104) of 101 child and adolescent psychiatric inpatients with “at risk” diagnoses including any autism spectrum disorder, psychotic disorder not otherwise specified, intermittent explosive disorder, mental retardation, neuroleptic malignant syndrome or previously diagnosed catatonia found that 18% of patients met criteria for catatonia, based upon three or more symptoms, including unexplained agitation or excitement, disturbed or unusual movements, reduction in movement, reduction or loss of speech and repetitive/stereotyped movements. The authors emphasized poor recognition of catatonia in these pediatric conditions, including, but not limited to, pervasive development disorders.

Functional regression in daily self-care, social and educational activities may also be a prominent feature of the catatonic presentation in autism. In many cases, the ability to self-feed, dress and bathe, or participate in previously mastered leisure and educational activities may be sharply compromised. Additionally, continence may be lost (22).

## 27.7. Post-traumatic Catatonia: The Ultimate Motor Response to Fear

Catatonia has been called “*the ultimate response to fear*” (113), representing a common final pathway in the response to impending doom, analogous to the animal defense strategy of tonic immobility or freezing (114). Tonic immobility is a last-ditch animal defense strategy against entrapment by a predator within a sequence of freezing-flight-fight-tonic immobility.

This notion is supported by observations that catatonia can develop after severe traumatic events in children and adolescents (115–117). For example, a recent case was reported of a 14-year-old-girl with severe catatonia precipitated by emotional turmoil due to cyber-bullying who was successfully treated with ECT and amantadine (118). In an epidemiologic study of 1098 adolescents, those who experienced bullying three or more times a month were 3.43 times as likely to report increasing psychotic experiences (119). The case-report extends findings that adolescent bullying increases the risk for psychotic experiences by linking cyber-bullying, an intrusive form of bullying, to onset of catatonia.

Shah & Wing (120) found that ongoing stressful experiences often precede the development of catatonia in autistic young adults. Life events, the loss of routine and structure, experiences of loss, conflicts with parents, caregivers, or peers, and discrepancies between the higher functioning autistic individual's capabilities and the expectations of parents, can precipitate catatonia.

Observations that catatonia follows overwhelming anxiety due to trauma or perceived danger, the positive response of catatonia to anxiolytics such as benzodiazepines or barbiturates, and psychogenic theories of catatonia (121) are particularly applicable to people with psychosis or autism spectrum disorders due to their increased social, cognitive, and sensory vulnerabilities (115, 122). It is recommended that patients with catatonia are assessed for traumatic and abusive events in family and broader environments in addition to medical causes for catatonia.

## 27.8. Mechanism of Catatonia

Although the etiology and pathophysiology of catatonia are unknown, findings about the occurrence of catatonia in a wide variety of conditions, including autism, suggests that the available models (66, 123) to study catatonia should be broadened to include models of developmental impairment.

Historically, the study of experimental catatonia in animals induced by bulbo-capnine injections was introduced in 1928 by de Jong and Baruk (124). Bulbo-capnine is an alkaloid resembling apomorphine, a dopamine agonist. Later mescaline was found to produce similar effects in animals, along with reserpine, adrenocorticotrophic hormone (ACTH), and chlorpromazine. Baruk also described hypopituitary, hepatic, and asphyxia models of catatonia. Table 27.9 shows an overview of tentative clinical (66) and corresponding experimental models.

An appropriate focus is the area of stereotypic or repetitive movement abnormalities which are considered cardinal symptoms of several disorders including catatonia, autism, stereotypic movement disorder, and tic disorders (when tics are viewed as sudden and non-rhythmic variants of stereotypy) (4, 130). Motor stereotypy constitutes a separate domain with increasing evidence of a neurobiological mechanism involving neuroadaptations in cortico-basal ganglia pathways arising from the interplay of genetic and experiential factors (125, 131).

Catatonia has been associated with Prader-Willi Syndrome (PWS), a genetic disorder arising from the lack of expression of genes on the paternally derived chromosome 15q11-q13 (22, 105). The behavioral phenotype of PWS consists of catatonic symptoms, stereotypies, compulsive self-injury, excessive sleepiness or unresponsiveness, and psychosis. The abnormal pattern of expression of sex-specific imprinted genes on 15q11-13 (containing a cluster of GABA<sub>A</sub> receptor subunit genes) may increase risk for catatonia in PWS.

Several lines of evidence suggest the importance of neuroendocrine abnormalities in catatonia. A clinical endocrine model is provided by the Kleine-Levin Syndrome (KLS), a poorly understood syndrome, occurring mostly in male adolescents, that is characterized by recurrent episodes of excessive sleep, and behavioral abnormalities such as hyperphagia or hypersexuality, in which altered diencephalic function is considered a central feature. KLS has been proposed as a type of episodic adolescent-

TABLE 27.9 Clinical and animal models for catatonia, immobility, catalepsy, and stereotypy.

Catatonia model	Clinical model	Animal model
Motor circuitry dysfunction	Stereotypical movement disorders	Dopamine agonists (e.g., apomorphine) injections in rat striatum (125)
Epilepsy	Nonconvulsive status epilepticus	Pentylenetetrazol injections in rats (126)
Genetic	Prader-Willi syndrome	Mutant mouse model for human 15q11-13 duplication (127) and porcine stress syndrome (89)
Neurotransmitter	Neuroleptic malignant syndrome	Drug-induced catalepsy induced by bulbo-capnine (124), reserpine, ketamine, or typical antipsychotics
Endocrine	Kleine-Levin syndrome Prader-Willi syndrome	Hormonal induction of catatonia by adrenaline, acetylcholine, and ACTH (124)
Immune	Autoimmune (limbic) encephalitis	Lipopolysaccharide-induced chronic inflammation in rats (128)
Fear reaction	Reactive catatonia	Tonic immobility in various animals (114)
Developmental	Autistic regression	Prenatal exposure to valproic acid in rats (129)



onset catatonia based on the symptom overlap between KLS and catatonia and on the profound response of all symptoms, including “hypersomnia”, to lorazepam (19).

The overlap between catatonia and pediatric autoimmune (limbic) encephalitis (32, 36) suggests involvement of autoimmunity and cerebral antibodies. There are now a few reports that show the efficacy of treatment with high-dose benzodiazepine and ECT in the recently coined and purportedly autoimmune anti-NMDA receptor encephalitis (36, 48, 49).

The finding that severe trauma may precipitate catatonia raises questions about mechanisms by which trauma leads to catatonia or other disorders. The biological pathways of early trauma leading to psychiatric and medical disorders are thought to encompass endocrine, immune, electrophysiological, and neuropsychological factors as well structural changes in the developing brain (132–136). The likely involvement in catatonia of central GABA function and its major role in central integration of hypothalamic-pituitary-adrenal stress responses in the basal forebrain and hypothalamus (137) is an important lead for future clinical and experimental studies assessing early trauma as contributing to the development of catatonia.

A speculative model concerns developmental catatonia, i.e., the occurrence of catatonia in young children causing over time irreversible psychopathology similar to autistic impairment (138, 139). Prenatal exposure to valproic acid (VPA) is a promising animal model of early-onset catatonia that has also been studied as a model for autism (129). Offspring of female rats injected with VPA on day 12.5 of gestation show brain abnormalities including smaller cerebella with fewer Purkinje cells. The rats exhibit catatonic-like behaviors appearing before puberty that include lower sensitivity to pain, diminished acoustic prepulse inhibition, repetitive hyperactivity, unresponsiveness and withdrawal.

## 27.9. Novel Vagal Theory of Catatonia

Although catatonia is considered primarily a motor syndrome, forty percent of catatonic patients show autonomic symptoms including abnormalities of temperature, blood pressure, pulse rate, respiratory rate, and perspiration (3, 22). Forty-five percent of pediatric cases show urinary-fecal incontinence (22), another feature of autonomous dysfunction. Some cases show bradycardia (94, 140) and bronchorrhea (141), indicative of strong vagal activity. Autonomic dysfunction is the hallmark of malignant catatonia (2, 3), its drug-induced variant Neuroleptic Malignant Syndrome (142), and aseptic encephalitis with catatonic symptoms, including the recently coined anti-NMDAR encephalitis (19, 32, 47). Early studies also support that there is autonomic dysfunction in catatonia (143, 144).

Autonomic abnormalities in catatonia support the image that catatonia represents a common end state response to feelings of impending doom across a wide range of medical and psychiatric disorders, finding its evolutionary counterpart in tonic immobility (114). Volchan et al. (145) found signs of tonic immobility, such as reduced body sway, increased heart rate, and diminished heart rate variability, in trauma-exposed patients with PTSD while listening to their autobiographical trauma, implying that tonic immobility is preserved in humans as an involuntary defensive strategy.

Autonomic dysfunction in catatonia implies involvement of the autonomic nervous system that consists of the parasympathetic subsystem, mediated by the vagus nerve, and the sympathetic subsystem, mediated by sympathetio-adrenal circuits in the spinal cord. A useful framework is the Polyvagal Theory that was first formulated by Porges in 1995 (146, 147).

The Polyvagal Theory poses that two different vagal branches control different behavioral responses to threat, and that a human immobility response with behavioral (stupor) and metabolic shutdown (increased sweating, hypoventilation, decreased peristalsis, urinary and fecal incontinence, and vasovagal responses) represents the most primitive response to perceived imminent danger when fight-flight reactions fail or are not available.

A separate set of unmyelinated vagal fibers projecting to the nucleus dorsalis of the vagal nerve is thought to mediate this response through efferent fibers to the diaphragm, heart, gastrointestinal tract, lungs, pancreas, and other visceral organs. This reflex is adaptive in reptiles but potentially lethal in humans. Catatonia resonates clearly in the description of the immobility response and yet is not recognized or acknowledged in the Polyvagal Theory as its clinical manifestation.

A *vagal theory of catatonia* (148) supports abnormalities in a wide range of functions, regulated by the efferent vagal nerve and associated with catatonia, encompassing brain electrical and motor circuitry function, neurotransmitters, neuroendocrine and immune function. Toxic and medical factors may also trigger catatonia through afferent vagal activation. It is an intriguing thought that the vagal nerve, whose fibers are eighty percent afferent, may also be involved in signaling, through its afferent pathways, information to the brain about “internal” (toxic, immune, infectious, metabolic) precipitants of catatonia. Studies support effects on vagal tone by benzodiazepines (149–151), zolpidem (152) (a non-benzodiazepine sedative that has been effectively used in catatonia) and ECT (153), as predicted and required by a vagal theory.

Studies are warranted into various aspect of autonomic dysfunction of catatonia. There is evidence that increased anxiety and arousal accompany the development of catatonia (115). These observations beg for more scrutiny, using modern techniques, along the lines of earlier studies (143, 144). A vagal theory intimates use of vagal nerve stimulatory techniques as novel treatments for catatonia. The Food and Drug Administration (FDA) approved intermittent stimulation of the left vagal nerve (Vagal



Nerve Stimulation; VNS) as adjunctive therapy for partial-onset epilepsy in July 1997 and for treatment-resistant depression in 2005. Improvement in the control of seizures has been well documented with VNS. The effects in treatment-resistant depression remain controversial. Non-epileptic benefits in the quality of life and changes in behavior have not been as well documented, except for the enhancement of short-term memory (154). Further studies need to assess if vagal nerve stimulation has any role in the treatment and relapse prevention of catatonia. Several patients require maintenance ECT for months and even years to avoid relapses into catatonia. Although maintenance ECT is safe and without neuropsychological sequelae in such patients, finding adjuvant or alternative preventive treatments would be very valuable.

## 27.10. Conclusions

There have been advances in demarcating catatonia in a wide variety of patients as a treatable condition that requires prompt identification. Benzodiazepines and electroconvulsive therapy remain first-line interventions. The new DSM-5 Catatonia NEC purports to improve proper diagnosis and early treatment and to intensify research of this condition.

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## References

1. Wernicke C. Grundriss der Psychiatrie in klinischen Vorlesungen (Parts I-III). Leipzig: Thieme; 1900.
2. Caroff S, Mann S, Francis A, Fricchione G. Catatonia. From Psychopathology to Neurobiology. Arlington, VA: American Psychiatric Association Publishing; 2004.
3. Fink M, Taylor M. Catatonia. A clinician's guide to diagnosis and treatment. Cambridge: University Press; 2003.
4. Dhossche DM, Reti IM, Shettar SM, Wachtel LE. Tics as signs of catatonia: electroconvulsive therapy response in 2 men. *J ECT* 2010;26:266–269.
5. Wachtel LE, Dhossche DM. Self-injury in autism as an alternate sign of catatonia: implications for electroconvulsive therapy. *Med Hypotheses* 2010;75:111–114.
6. Dhossche D, Cohen D, Ghaziuddin N, Wilson C, Wachtel LE. The study of pediatric catatonia supports a home of its own for catatonia in DSM-5. *Med Hypotheses* 2010;75:558–560.
7. Dhossche D, Wilson C, Wachtel L. Catatonia in childhood and adolescence: implications for the DSM-5. *Primary Psychiatry* 2010;17:35–39.
8. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, (5th Edition) (DSM-5). Arlington, VA: American Psychiatric Association Publishing 2013.
9. Kahlbaum K. Die Katatonie oder das Spannungsirresein. Berlin: Verlag August Hirshwald; 1874.
10. Morrison J. Catatonia: retarded and excited types. *Arch Gen Psychiatry* 1973;28:39–41.
11. Abrams R, Taylor M. Catatonia: a prospective clinical study. *Arch Gen Psychiatry* 1976;33:579–581.
12. Gelenberg A. The catatonic syndrome. *Lancet* 1976;1:1339–1341.
13. Braunig P, Kruger S, Shugar G. Prevalence and clinical significance of catatonic symptoms in mania. *Compr Psychiatry* 1998;39:35–46.
14. Wing L, Attwood A. Syndromes of autism and atypical development. In: Cohen D, Donnellan A, eds. *Handbook of autism and pervasive developmental disorders*. New York: Wiley-Interscience; 1987:3–19.
15. Realmuto G, August G. Catatonia in autistic disorder: a sign of comorbidity or variable expression. *J Autism Dev Disorder* 1991;21:517–528.
16. Dhossche D, Wing L, Ohta M, Neumarker K-J, eds. *Catatonia in Autism Spectrum Disorders*. San Diego, California and London, UK: Elsevier Academic Press; 2006.
17. Wachtel L, Kahng S, Dhossche D, Cascella N, Reti I. Electroconvulsive Therapy for catatonia in an autistic girl. *Am J Psychiatry* 2008;165:329–333.
18. Creten C, van der Zwaan S, Blankespoor RJ, Maatkamp A, Nicolai J, van Os J, Schieveld JN. Late onset autism and anti-NMDA-receptor encephalitis. *Lancet* 2011;378:98.
19. Dhossche DM, Wachtel LE. Catatonia is hidden in plain sight among different pediatric disorders: a review article. *Pediatr Neurol* 2010;43:307–315.
20. Dhossche D, Bouman N. Catatonia in children and adolescents (letter). *J Am Acad Child Adolesc Psychiatry* 1997;36:870–871.
21. Jap SN, Ghaziuddin N. Catatonia Among Adolescents With Down Syndrome: A Review and 2 Case Reports. *J ECT* 2011;27:334–337.
22. Dhossche D, Bouman N. Catatonia in an adolescent with Prader-Willi Syndrome. *Ann Clin Psychiatry* 1997;4:247–253.
23. Sullivan B, Dickerman J. Steroid-associated catatonia: report of a case. *Pediatrics* 1979;63:677–679.
24. Elia J, Dell M, Friedman D, Zimmerman RA, Balamuth N, Ahmed AA, Pati S. PANDAS with catatonia: a case-report. Therapeutic response to lorazepam and plasmapheresis. *J Am Acad Child Adolesc Psychiatry* 2005;44:1145–1150.

25. Davis E, Borde M. Wilson's disease and catatonia. *Br J Psychiatry* 1993;162:256–259.
26. Perisse D, Amoura Z, Cohen D, Saintigny P, Mekhloufi F, Mazet P, Piette JC. Case study: effectiveness of plasma exchange in an adolescent with systemic lupus erythematosus and catatonia. *J Am Acad Child Adolesc Psychiatry* 2003;42:497–499.
27. Wang H-Y, Huang T-L. Benzodiazepines in catatonia associated with systemic lupus erythematosus. *Psychiatry Clin Neurosci* 2006;60:768–770.
28. Thakur A, Jagadheesan K, Dutta S, Sinha V. Incidence of catatonia in children and adolescents in a pediatric psychiatric clinic. *Aust NZ J Psychiatry* 2003;37:200–203.
29. Woodbury M, Woodbury M. Neuroleptic-induced catatonia as a stage in the progression toward neuroleptic malignant syndrome. *J Am Acad Child Adolesc Psychiatry* 1992;31:1161–1164.
30. Revuelta E, Bordet R, Piquet T, Ghawche F, Destee A, Goudemand M. Acute catatonia and neuroleptic malignant syndrome. A case of infantile psychosis. *Encephale* 1999;20:351–354.
31. Cavanna A, Robertson M, Critchley H. Catatonic signs in Gilles de la Tourette syndrome. *Cogn Behav Neurol* 2008;21:34–37.
32. Dhossche D, Fink M, Shorter E, Wachtel LE. Anti-NMDA receptor encephalitis versus pediatric catatonia (letter to the editor). *Am J Psychiatry* 2011;168:749–750.
33. Consoli A, Ronen K, An-Gourfinkel I, Barbeau M, Marra D, Costedoat-Chalumeau N, Montefiore D, Maksud P, Bonnot O, Didelot A, Amoura Z, Vidailhet M, Cohen D. Malignant catatonia due to anti-NMDA-receptor encephalitis in a 17-year-old girl: case report. *Child Adolesc Psychiatry Ment Health* 2011;5:15.
34. Lee A, Glick D, Dinwiddie S. Electroconvulsive therapy in a pediatric patient with malignant catatonia and paraneoplastic limbic encephalitis. *J ECT* 2006;22:267–270.
35. Schimmel M, Bien C, Vincent A, Schenk W, Penzien J. Successful treatment of anti-N-methyl-D-aspartate receptor encephalitis presenting with catatonia. *Arch Dis Child* 2009;94:314–316.
36. Agarwala P. Catatonia in an adolescent with anti-N-Methyl-D-Aspartate receptor encephalitis: successful treatment with high-dose lorazepam. *Resident J* 2011:10–11.
37. Ono Y, Manabe Y, Hamakawa Y, Omori N, Abe K. Steroid-responsive encephalitis lethargica syndrome with malignant catatonia. *Intern Med* 2007;46:307–310.
38. Ali S, Welch C, Park L, Pliakas AM, Wilson A, Nicolson S, Huffman J, Fricchione GL. Encephalitis and catatonia treated with ECT. *Cogn Behav Neurol* 2008;21:46–51.
39. Kanner L. The occurrence of cataleptic phenomena in children. *J Pediatrics* 1934;5:330–340.
40. Spitz RA. Hospitalism. An inquiry into the genesis of psychiatric conditions in early childhood. *Psychoanalytical Study Child* 1945;1:53–74.
41. Spitz RA. Hospitalism. A follow-up report on investigation described in volume 1 1945. *Psychoanalytical Study Child* 1946;2:113–117.
42. Bodegard G. Pervasive loss of function in asylum-seeking children in Sweden. *Acta Paediatr* 2005;94:1706–1707.
43. Bodegard G. Depression-withdrawal reaction in refugee children. An epidemic of a cultural-bound syndrome or an endemic of re-traumatized refugees? *Acta Paediatr* 2010;99:959.
44. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders (4th ed.)*. Arlington, VA: American Psychiatric Association Publishing; 1994.
45. McCall W, Mann S, Shelp F, Caroff S. Fatal pulmonary embolism in the catatonic syndrome: Two case reports and a literature review. *J Clin Psychiatry* 1995;56:21–25.
46. Lachner C, Sandson N. A case of catatonia-induced deep venous thrombosis. *Psychosomatics* 2003;44:512–514.
47. Dalmau J, Gleichman AJ, Hughes EG, Rossi JE, Peng X, Lai M, Dessain SK, Rosenfeld MR, Balice-Gordon R, Lynch DR. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. *Lancet Neurol* 2008;7:1091–1098.
48. Braakman HM, Moers-Hornikx VM, Arts BM, Hupperts RM, Nicolai J. Pearls & Oy-sters: electroconvulsive therapy in anti-NMDA receptor encephalitis. *Neurol* 2010;75:e44–6.
49. Matsumoto T, Matsumoto K, Kobayashi T, Kato S. Electroconvulsive therapy can improve psychotic symptoms in anti-NMDA-receptor encephalitis. *Psychiatry Clin Neurosci* 2012;66:242–243.
50. Stauder K. Die todliche Katatonie. *Arch Psychiatr Nervenkrank* 1934;102:614–634.
51. Starkstein S, Petracca G, Teson A, Chemerinski E, Merello M, Migliorelli R, Leiguarda R. Catatonia in depression: prevalence, clinical correlates, and validation of a scale. *J Neurol Neurosurg Psychiatry* 1996;60:326–332.
52. Bush G, Fink M, Petrides G, Dowling F, Francis A. Catatonia: I: Rating scale and standardized examination. *Acta Psychiatr Scand* 1996;93:129–136.
53. Northoff G, Koch A, Wenke J, Eckert J, Böker H, Pflug B, Bogerts B. Catatonia as a psychomotor syndrome: a rating scale and extrapyramidal motor symptoms. *Mov Disord* 1999;14:404–416.
54. Braunig P, Kruger S, Shugar G, Hoffer J, Borner I. The catatonia rating scale I — development, reliability, and use. *Compr Psychiatry* 2000;41:147–158.
55. Wong E, Ungvari G, Leung S, Tang W. Rating catatonia in patients with chronic schizophrenia: Rasch analysis of the Bush–Francis Catatonia Rating Scale. *Int J Methods Psychiatr Res* 2007;16:161–170.
56. Carroll BT, Kirkhart R, Ahuja N, Soovere I, Lauterbach EC, Dhossche D, Talbert R. Katatonia: a new conceptual understanding of catatonia and a new rating scale. *Psychiatry* 2008;5:42–50.
57. Sienaert P, Rooseleer J, De Fruyt J. Measuring catatonia: a systematic review of rating scales. *J Affect Disord* 2011;135:1–9.

58. Kirkhart R, Ahuja N, Lee JW, Ramirez J, Talbert R, Faiz K, Ungvari GS, Thomas C, Carroll BT. The detection and measurement of catatonia. *Psychiatry* 2007;4:52–56.
59. McCall WV, Shelp FE, McDonald WM. Controlled investigation of the amobarbital interview for catatonic mutism. *Am J Psychiatry* 1992;149:202–206.
60. Naples M, Hackett T. The amytal interview: history and current uses. *Psychosomatics* 1978;19:98–105.
61. Perry JC, Jacobs D. Overview: clinical applications of the Amytal interview in psychiatric emergency settings. *Am J Psychiatry* 1982;139:552–559.
62. Panzer M, Grunhaus L. The diazepam interview: an underutilized diagnostic procedure? *Ann Clin Psychiatry* 1991;3:73–78.
63. Bleckwenn W. The production of sleep and rest in psychotic cases. *Arch Neurol Psychiatry* 1930;24:365–372.
64. Bolton PF, Carcani-Rathwell I, Hutton J, Goode S, Howlin P, Rutter M. Epilepsy in autism: features and correlates. *Br J Psychiatry* 2011;198:289–294.
65. Tuchman R, Cuccaro M. Epilepsy and autism: neurodevelopmental perspective. *Current Neurol Neurosci Rep* 2011;11:428–434.
66. Dhossche DM, Stoppelbein L, Rout UK. Etiopathogenesis of catatonia: generalizations and working hypotheses. *J ECT* 2010;26:253–258.
67. Fink M. The intimate relationship between catatonia and convulsive therapy. *J ECT* 2010;26:243–245.
68. Lahutte B, Cornic F, Bonnot O, Consoli A, An-Gourfinkel I, Amoura Z, Sedel F, Cohen D. Multidisciplinary approach of organic catatonia in children and adolescents may improve treatment decision making. *Prog Neuropsychopharmacol Biol Psychiatry* 2008;32:1393–1398.
69. Fink M, Taylor M. Neuroleptic malignant syndrome is malignant catatonia, warranting treatments efficacious for catatonia. *Prog Neuropsychopharmacol Biol Psychiatry* 2006;30:1182–1183.
70. Seitz DP, Gill SS. Neuroleptic malignant syndrome complicating antipsychotic treatment of delirium or agitation in medical and surgical patients: case reports and a review of the literature. *Psychosomatics* 2009;50:8–15.
71. Carroll B, Lee JW, Appiani F, Thomas C. Pharmacotherapy of Catatonia. *Primary Psychiatry* 2010;17:41–47.
72. Wachtel LE, Dhossche DM. Challenges of electroconvulsive therapy for catatonia in youth with intellectual disabilities: another tomato effect? *J ECT* 2012;28:151–153.
73. Bush G, Fink M, Petrides G, Dowling F, Francis A. Catatonia. II. Treatment with lorazepam and electroconvulsive therapy. *Acta Psychiatrica Scand* 1996;93:137–143.
74. Thomas P, Rasclé C, Mastain B, Maron M, Vaiva G. Test for catatonia with zolpidem. *Lancet* 1997;349:702.
75. Yi J, Torres J, Azner Y, Vaidya P, Schiavi A, Reti IM. Flumazenil Pretreatment in Benzodiazepine-Free Patients: A Novel Method for Managing Declining ECT Seizure Quality. *J ECT* 2012;28:185–189.
76. Kellner CH, Knapp GR, Petrides G, Rummans TA, Husain MM, Rasmussen K, Mueller M, Bernstein HJ, O'Connor K, Smith G, Biggs M, Bailine SH, Malur C, Yim E, McClintock S, Sampson S, Fink M. Continuation electroconvulsive therapy vs pharmacotherapy for relapse prevention in major depression: a multisite study from the Consortium for Research in Electroconvulsive Therapy (CORE). *Arch Gen Psychiatry* 2006;63:1337–1344.
77. Petrides G, Dhossche D, Fink M, Francis A. Continuation ECT: relapse prevention in affective disorders. *Convol Ther* 1994;10:189–194.
78. Lippman S, Manshadi M, Wehry M, Byrd R, Past W, Keller W, Schuster J, Elam S, Meyer D, O'Daniel R. 1,250 electroconvulsive treatments without evidence of brain injury. *Br J Psychiatry* 1985;147:203–204.
79. Scalia J, Lisanby SH, Dwork AJ, Johnson JE, Bernhardt ER, Arango V, McCall WV. Neuropathologic examination after 91 ECT treatments in a 92-year-old woman with late-onset depression. *J ECT* 2007;23:96–98.
80. Devanand DP, Verma AK, Tirumalasetti F, Sackeim HA. Absence of cognitive impairment after more than 100 lifetime ECT treatments. *Am J Psychiatry* 1991;148:929–932.
81. Wijkstra J, Nolen WA. Successful maintenance electroconvulsive therapy for more than seven years. *J ECT* 2005;21:171–173.
82. Zisselman M, Rosenquist P, Curlik S. Long-term weekly continuation electroconvulsive therapy: a case-series. *J ECT* 2007;23:274–277.
83. Wachtel LE, Hermida A, Dhossche DM. Maintenance electroconvulsive therapy in autistic catatonia: a case series review. *Prog Neuropsychopharmacol Biol Psychiatry* 2010;34:581–587.
84. Dhossche D, Shettar S, Kumar T, Burt L. Electroconvulsive therapy for malignant catatonia in adolescence. *Southern Med J* 2009;102:1170–1172.
85. Wachtel LE, Griffin MM, Dhossche DM, Reti IM. Brief report: Electroconvulsive therapy for malignant catatonia in an autistic adolescent. *Autism* 2010;14:349–358.
86. Consoli A, Benmiloud M, Wachtel L, Dhossche D, Cohen D, Bonnot O. Electroconvulsive therapy in adolescents with the catatonia syndrome: efficacy and ethics. *J ECT* 2010;26:259–265.
87. Slooter A, Braun K, Balk F, van Nieuwenhuizen O, van der Hoeven J. Electroconvulsive therapy of malignant catatonia in childhood. *Pediatr Neurol* 2005;32:190–192.
88. Fink M. Recognizing NMS as a type of catatonia. *Neuropsychiatr Neuropsychol Behav Neurol* 1995;8:75–76.
89. Rempel WE, Lu M, el Kandelgy S, Kennedy CF, Irvin LR, Mickelson JR, Louis CF. Relative accuracy of the halothane challenge test and a molecular genetic test in detecting the gene for porcine stress syndrome. *J Animal Sci* 1993;71:1395–1399.
90. Francis A, Lopez-Canino A. Delirium with catatonic features. *Psychiatric Times* 2009;26:32–36.
91. Rizos DV, Peritogiannis V, Gkogkos C. Catatonia in the intensive care unit. *Gen Hosp Psychiatry* 2011;33:e1–e2.

92. Hem E, Andreassen O, Robasse J-M, Vatnaland T, Opjodsoen S. Should catatonia be part of the differential diagnosis of coma? *Nord J Psychiatry* 2005;59:528–530.
93. Benegal V, Hingorani S, Khanna S. Idiopathic catatonia: validity of the concept. *Psychopathology* 1993;26:41–46.
94. Freudenreich O, McEvoy J, Goff D, Fricchione G. Catatonic coma with profound bradycardia. *Psychosomatics* 2007;48:74–78.
95. Bender K, Feutrill J. Comatoid catatonia. *Aust NZ J Psychiatry* 2000;34:169–170.
96. Cornic F, Consoli A, Tanguy M, Bonnot O, Périsset D, Tordjman S, Laurent C, Cohen D. Association of adolescent catatonia with increased mortality and morbidity: evidence from a prospective follow-up study. *Schizophr Res* 2009;113:233–240.
97. Green W, Campbell M, Hardesty A, Grega DM, Padron-Gayol M, Shell J, Erlenmeyer-Kimling L. A comparison of schizophrenic and autistic children. *J Am Acad Child Psychiatry* 1984;23:399–409.
98. Moise FN, Petrides G. Case study: electroconvulsive therapy in adolescents. *J Am Acad Child Adolesc Psychiatry* 1996;35:312–318.
99. Wing L, Shah A. Catatonia in autistic spectrum disorders. *Br J Psychiatry* 2000;176:357–362.
100. Cohen D, Nicolas J, Flament MF, Périsset D, Dubos PF, Bonnot O, Speranza M, Graindorge C, Tordjman S, Mazet P. Clinical relevance of chronic catatonic schizophrenia in children and adolescents: evidence from a prospective naturalistic study. *Schizophr Bull* 2005;15:301–308.
101. Billstedt E, Gillberg IC, Gillberg C. Autism after adolescence: population-based 13- to 22-year follow-up study of 120 individuals with autism diagnosed in childhood. *J Autism Dev Disord* 2005;35:351–360.
102. Ohta M, Kano Y, Nagai Y. Catatonia in individuals with autism spectrum disorders in adolescence and early adulthood: a long-term prospective study. *Int Rev Neurobiol* 2006;72:41–54.
103. Consoli A, Boulicot V, Cornic F, Fossati P, Barbeau M, Cohen D. Moderate clinical improvement with maintenance ECT in a 17-year-old boy with intractable catatonic schizophrenia. *Eur Child Adolesc Psychiatry* 2009;18:250–254.
104. Ghaziuddin N, Dhossche D, Marcotte K. Retrospective chart review of catatonia in child and adolescent psychiatric patients. *Acta Psychiatr Scand* 2012;125:33–38.
105. Verhoeven W, Tuinier S. Prader-Willi syndrome: atypical psychoses and motor dysfunctions. *Int Rev Neurobiol* 2006;72:119–130.
106. Kakooza-Mwesige A, Wachtel L, Dhossche D. Catatonia in autism: implications across the life span. *Eur Child Adolesc Psychiatry* 2008;17:327–335.
107. Dhossche D, Reti I, Wachtel L. Catatonia and Autism: A historical review, with implications for ECT. *J ECT* 2009;25:19–22.
108. Wachtel LE, Griffin M, Reti I. Electroconvulsive Therapy in a Man With Autism Experiencing Severe Depression, Catatonia, and Self-Injury. *J ECT* 2010;96:70–73.
109. Wachtel LE, Jaffe R, Kellner CH. Electroconvulsive therapy for psychotropic-refractory bipolar affective disorder and severe self-injury and aggression in an 11-year-old autistic boy. *Eur Child Adolesc Psychiatry* 2011;20:147–152.
110. Volkmar F, Cohen D. Comorbid association of autism and schizophrenia. *Am J Psychiatry* 1991;148:1705–1707.
111. Jap SN, Ghaziuddin N. Catatonia among adolescents with Down syndrome: a review and 2 case reports. *J ECT* 2011;27:334–337.
112. Consoli A, Raffin M, Laurent C, Bodeau N, Champion D, Amoura Z, Sedel F, An-Gourfinkel I, Bonnot O, Cohen D. Medical and developmental risk factors of catatonia in children and adolescents: a prospective case-control study. *Schizophr Res* 2012;137:151–158.
113. Perkins RJ. Catatonia: the ultimate response to fear? *Aust N Z J Psychiatry* 1982;16:282–287.
114. Gallup G, Maser J. Tonic immobility: Evolutionary underpinnings of human catalepsy and catatonia. In: Maser J, Seligman M, eds. *Psychopathology: Experimental Models*. San Francisco: Freeman; 1977:334–357.
115. Dhossche DM, Ross CA, Stoppelbein L. The role of deprivation, abuse, and trauma in pediatric catatonia without a clear medical cause. *Acta Psychiatr Scand* 2012;125:25–32.
116. Bozkurt H, Mukaddes NM. Catatonia in a child with autistic disorder. *Turk J Pediatr* 2010;52:435–438.
117. Saito S, Yamaga K, Kobayashi T, Kato S. A case of Asperger's disorder with catatonia originally suspected of being catatonic schizophrenia. *Seishin Shinkeigaku Zasshi* 2011;113:241–247.
118. Goetz M, Kitzlerova E, Hrdlicka M, Dhossche D. Combined use of ECT and amantadine in adolescent catatonia precipitated by cyberbullying. *J Child Adolesc Psychopharmacol* 2013;23:228–231.
119. Mackie CJ, O'Leary-Barrett M, Al-Khudairy N, Castellanos-Ryan N, Struve M, Topper L, Conrod P. Adolescent bullying, cannabis use and emerging psychotic experiences: a longitudinal general population study. *Psychol Med* 2012;1–12.
120. Shah A, Wing L. Psychological approaches to chronic catatonia-like deterioration in autism spectrum disorders. *Int Rev Neurobiol* 2006;72:245–264.
121. Moskowitz AK. "Scared stiff": catatonia as an evolutionary-based fear response. *Psychol Rev* 2004;111:984–1002.
122. Dhossche D. Catatonia: the ultimate yet treatable motor reaction to fear in autism. *Autism-Open Access* 2011;1:e103.
123. Kanis S. Animal models. In: Caroff S, Mann SC, Francis A, Fricchione GL, eds. *Catatonia From Psychopathology to Neurobiology*. Arlington, VA: American Psychiatric Association Publishing; 2004:189–200.
124. De Jong HH, Barruk H. A clinical and experimental study of the catatonic syndrome (Étude comparative expérimentale et clinique des manifestations du syndrome catatonique). *H Revue Neurol* 1929;21.
125. Lewis MH, Tanimura Y, Lee LW, Bodfish JW. Animal models of restricted repetitive behavior in autism. *Behav Brain Res* 2007;176:66–74.
126. Wong M, Wozniak DF, Yamada KA. An animal model of generalized nonconvulsive status epilepticus: immediate characteristics and long-term effects. *Exp Neurol* 2003;183:87–99.

127. Nakatani J, Tamada K, Hatanaka F, Ise S, Ohta H, Inoue K, Tomonaga S, Watanabe Y, Chung YJ, Banerjee R, Iwamoto K, Kato T, Okazawa M, Yamauchi K, Tanda K, Takao K, Miyakawa T, Bradley A, Takumi T. Abnormal behavior in a chromosome-engineered mouse model for human 15q11-13 duplication seen in autism. *Cell* 2009;137:1235–1246.
128. Jeong HK, Jou I, Joe EH. Systemic LPS administration induces brain inflammation but not dopaminergic neuronal death in the substantia nigra. *Exp Mol Med* 2010;42:823–832.
129. Wagner GC, Reuhl KR, Cheh M, McRae P, Halladay AK. A new neurobehavioral model of autism in mice: pre- and postnatal exposure to sodium valproate. *J Autism Dev Disord* 2006;36:779–793.
130. Trivedi H, Mendelowitz A, Fink M. Gilles de la Tourette form of catatonia: response to ECT. *J ECT* 2003;19:115–117.
131. Singer HS. Motor stereotypies. *Semin Pediatr Neurol* 2009;16:77–81.
132. Ali I, Salzberg MR, French C, Jones NC. Electrophysiological insights into the enduring effects of early life stress on the brain. *Psychopharmacology (Berl)* 2011;214:155–173.
133. Charmandari E, Kino T, Souvatzoglou E, Chrousos GP. Pediatric stress: hormonal mediators and human development. *Horm Res* 2003;59:161–179.
134. De Bellis MD, Baum AS, Birmaher B, Keshavan MS, Eccard CH, Boring AM, Jenkins FJ, Ryan ND. A.E. Bennett Research Award. Developmental traumatology. Part I: Biological stress systems. *Biol Psychiatry* 1999;45:1259–1270.
135. De Bellis MD, Keshavan MS, Clark DB, Casey BJ, Giedd JN, Boring AM, Frustaci K, Ryan ND. A.E. Bennett Research Award. Developmental traumatology. Part II: Brain development. *Biol Psychiatry* 1999;45:1271–1284.
136. Pechtel P, Pizzagalli DA. Effects of early life stress on cognitive and affective function: an integrated review of human literature. *Psychopharmacology (Berl)* 2011;214:55–70.
137. Herman J, Cullinan W. Neurocircuitry of stress: central control of the hypothalamo-pituitary-adrenocortical axis. *Trends Neurosci* 1997;20:78–84.
138. Dhossche D. Autism as early expression of catatonia. *Med Sci Monit* 2004;10:RA31–39.
139. Dhossche D, Rout U. Are autistic and catatonic regression related? A few working hypotheses involving GABA, Purkinje cell survival, neurogenesis, and ECT. *Int Rev Neurobiol* 2006;72:55–79.
140. Wachtel L, Griffin M, Dhossche D, Reti I. Electroconvulsive therapy for malignant catatonia in an autistic adolescent. *Autism* 2010;14:349–358.
141. Hayashi H, Aoshima T, Otani K. Malignant catatonia with severe bronchorrhea and its response to electroconvulsive therapy. *Prog Neuropsychopharmacol Biol Psychiatry* 2006;30:310–311.
142. Gurrera RJ, Caroff SN, Cohen A, Carroll BT, DeRoos F, Francis A, Frucht S, Gupta S, Levenson JL, Mahmood A, Mann SC, Policastro MA, Rosebush PI, Rosenbergh H, Sachdev PS, Trollor JN, Velamoor VR, Watson CB, Wilkinson JR. An international consensus study of neuroleptic malignant syndrome diagnostic criteria using the Delphi method. *J Clin Psychiatry* 2011;72:1222–1228.
143. Gjessing LR. A review of periodic catatonia. *Biol Psychiatry* 1974;8:23–45.
144. Venables PH, Wing JK. Level of arousal and the subclassification of schizophrenia. *Arch Gen Psychiatry* 1962;7:114–119.
145. Volchan E, Souza GG, Franklin CM, Norte CE, Rocha-Rego V, Oliveira JM, David IA, Mendlowicz MV, Coutinho ES, Fiszman A, Berger W, Marques-Portella C, Figueira I. Is there tonic immobility in humans? Biological evidence from victims of traumatic stress. *Biol Psychol* 2011;88:13–19.
146. Porges SW. Social engagement and attachment: a phylogenetic perspective. *Ann N Y Acad Sci* 2003;1008:31–47.
147. Porges SW. The Polyvagal Theory: phylogenetic contributions to social behavior. *Physiol Behav* 2003;79:503–513.
148. Dhossche D. Autonomic dysfunction in catatonia in autism: implications of a vagal theory. *Autism-Open Access* 2012;2:e114.
149. Adinoff B, Mefford I, Waxman R, Linnoila M. Vagal tone decreases following intravenous diazepam. *Psychiatry Res* 1992;41:89–97.
150. Farmer MR, Ross HF, Chowdhary S, Osman F, Townend JN, Cote JH. GABAergic mechanisms involved in the vagally mediated heart rate response to muscle contraction as revealed by studies with benzodiazepines. *Clin Auton Res* 2003;13:45–50.
151. Vogel LR, Muskin PR, Collins ED, Sloan RP. Lorazepam reduces cardiac vagal modulation in normal subjects. *J Clin Psychopharmacol* 1996;16:449–453.
152. Chen HY, Kuo TB, Shaw FZ, Lai CJ, Yang CC. Sleep-related vagotonic effect of zolpidem in rats. *Psychopharmacology (Berl)* 2005;181:270–279.
153. Bar KJ, Ebert A, Boettger MK, Merz S, Kiehnopf M, Jochum T, Juckel G, Agelink MW. Is successful electroconvulsive therapy related to stimulation of the vagal system? *J Affect Disord* 2010;125:323–329.
154. Clark KB, Naritoku DK, Smith DC, Browning RA, Jensen RA. Enhanced recognition memory following vagus nerve stimulation in human subjects. *Nat Neurosci* 1999;2:94–98.
155. Bumke O. *Lehrbuch der Geisteskrankheiten*. Second ed. Munich: Bergmann; 1924.