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ORIGINAL CONTRIBUTION

The multiple faces of catatonia in autism spectrum disorders: descriptive clinical experience of 22 patients over 12 years

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Abstract
A retrospective review was conducted from the inpatient and outpatient records of twenty-two autistic youth presenting to a neurobehavioral service over a twelve-year period for combined psychiatric and behavioral pathology who also met DSM5 criteria for catatonia. Six autistic girls and 16 autistic boys ranging from ages eight to 26 years old were identified, and their variegated symptoms evaluated. Stereotypy, posturing, negativism, mutism and stupor were the most common catatonic symptoms, each present in more than half of the study patients. One patient had abnormal vital signs indicative of malignant catatonia. Twenty patients had concomitant repetitive self-injurious behaviors that had led to significant tissue injury and were refractory to psychotropic and behavioral interventions. The sample was weighted towards patients with severe self-injurious behavior, which often was the reason for admission. The many "faces" of catatonia in autism spectrum disorders are seen in this sample, and the novel recognition of repetitive self-injury as an under-recognized motor symptom of catatonia is highlighted. The preliminary findings in this study open many important future vistas for ongoing research regarding catatonia in ASDs.

Keywords Catatonia · Autism · Self-injury · Benzodiazepines · Electroconvulsive therapy

Introduction

Catatonia is a unique entity whose classic motor, vocal and behavioral symptoms were initially delineated by Karl Kahlbaum in 1874 [1]. Catatonia was subsequently erroneously subsumed in the diagnosis of schizophrenia for well over a century until such *de rigueur* linkage was removed by the DSM5 [2]. A malignant form of catatonia was recognized in the 1930s, and in the late 1970s, rekindled interest in the prevalence of catatonia amongst psychiatric inpatients led to the discovery that the syndrome actually occurs most commonly in affective illness [3]. The modern catatonic syndrome, including efficacious treatment with benzodiazepines and electroconvulsive therapy, was presented in two sentinel papers by Bush et al. in 1996, and subsequently further solidified to include symptom range and myriad systemic etiologies, assessment and treatment, and unfolding recognition as an independent medical syndrome [4–7].

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Autism is a childhood-onset neurodevelopmental disability currently recognized by the Center for Disease Control to afflict one in 59 American children. Over the past 17 years, catatonia has been found to occur in 12–20% of individuals with autism spectrum disorders (ASDs) in four international studies [8–11]. Multiple case reports have presented the range of psychomotor retarded, agitated and mixed catatonic presentations in autism spectrum disorders (ASDs), with swift, safe and efficacious treatment with electroconvulsive therapy. Illness severity and ready response to anti-catatonic treatment paradigms make the prompt diagnosis and treatment of all forms of catatonia in ASDs of paramount importance [12–17].

Within the neurobehavioral services of a pediatric rehabilitation hospital in the eastern seaboard of the United States, youth with autism and intellectual disability are routinely evaluated for psychiatric and behavioral disturbance, including self-injurious behavior (SIB). SIB in ASDs encompasses a wide variety of self-damaging behavior, including hitting, banging, slapping, biting and scratching of the self, and can encompass all body surfaces. Some of the most devastating topographies of self-injury are aimed at the head, with inherent risk for severe damage to the brain

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and eyes, including the development of traumatic cataracts, retinal detachment, and associated vision loss [18]. Global estimates of SIB prevalence in ASDs vary, but a recent study of 8065 children within the United States' Autism and Developmental Disability Monitoring (ADDM) Network documents a 27.7% prevalence across time and site [19]. A 2018 study of adults with autism and intellectual developmental disorders found that SIB occurred in 37.7% of individuals with both diagnoses, yet only 11.4% of those without autism [20]. Self-injurious behavior in autism is a crippling condition with high medical and psychosocial morbidity, wreaking havoc on the lives of patients and their families. Preliminary case reports have demonstrated reduction of SIB in ASDs with electroconvulsive therapy (ECT), and proposed a link between repetitive self-injury and catatonia [13, 16, 21].

In the current study, a subset of 22 autistic patients from the neurobehavioral services has been diagnosed over the past decade with multiple classically recognized catatonic symptoms, of which 20 patients additionally displayed repetitive self-injury. Indeed, severe, treatment-refractory self-injury was often the reason for their admission. These patients had failed to respond to myriad pharmacological and behavioral interventions over the course of months–years, with accrual of profound bodily injury and global psychosocial incapacitation, often leading to urgent inpatient admission under highly restrictive conditions. The recognition of the catatonia syndrome within this subset of patients, and the implementation of the anti-catatonia paradigms including electroconvulsive therapy, resulted in life-saving and life-altering improvement for these children. This descriptive report is their story, and is a further development in the history of catatonia as a medical syndrome that is readily diagnosable and, most importantly, readily treatable.

Methods

IRB approval was granted for the retrospective review of catatonic symptomology within inpatient and outpatient psychiatry, behavioral psychology and ECT clinical records from the Kennedy Krieger Institute and Johns Hopkins School of Medicine for 22 patients diagnosed with autism in early childhood and prior to admission, who presented with DSM5 catatonia criteria between the years of 2005 and January 31, 2017. All patients underwent comprehensive psychiatric evaluation by the author, who subsequently followed their course of treatment over time periods ranging from months to years.

Results

Twenty-two patients were identified, including six girls and 16 boys ranging in age from 8- to 26-years-old. Nineteen patients were Caucasian, one was African-American, and two were biracial, namely Caucasian-Hispanic and African-American-Hispanic. All patients had been diagnosed with an autism spectrum disorder in early childhood; they were admitted for evaluation of possible behavioral and catatonic disturbances. All patients underwent comprehensive multidisciplinary evaluation including psychiatric assessment, formal, functional behavioral analysis, medical, speech and language and educational assessments and investigations. Functional behavioral analytic work aimed to identify operant, or environmental functions to a patient's behavior, and to accordingly develop behavioral treatment interventions. The results of the myriad prior assessments and treatment initiatives are beyond the scope of this paper, but a commonality amongst all patients was global lack of response despite months–years of such evaluations and therapies.

In Fig. 1, the 22 patients are listed in the chronological order in which they were treated, with the presence or absence noted of each of the DSM5 catatonia criteria, including stupor, catalepsy, waxy flexibility, mutism, negativism, posturing, mannerism, stereotypy, agitation, grimacing, echolalia, and echopraxia.

Figure 2 presents this data based on the frequency of each DSM catatonia symptom across the entire patient sample. The most common identified catatonic symptom was agitation ($N=21$), followed by stereotypy ($N=20$), posturing ($N=18$), negativism ($N=17$), mutism ($N=14$), stupor ($N=13$) and grimacing ($N=7$). Catalepsy, mannerism, echolalia and echopraxia were each found in two patients and waxy flexibility in one. This is roughly congruent with the presentation of catatonia in other pediatric and adult populations, where stupor, mutism, food refusal, and negativism often go together.

Of special interest is the presence or absence of self-injurious behavior (SIB) and vital sign abnormalities, with 20 of 22 (90.9%) patients displaying self-injury, and one of 22 (4.5%) patients displaying abnormal vital signs.

Figure 3 shows the number of catatonic symptoms each patient presented, ranging from two to eight. Five patients (22.7%) displayed six catatonic symptoms, four patients (18.2%) displayed eight catatonic symptoms, three patients (13.6%) displayed seven, five, four or two catatonic symptoms, and one patient (4.5%) displayed three catatonic symptoms.

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
1	Patient #	Stupor	Catalepsy	Waxy Flexibility	Mutism	Negativism	Posturing	Mannerism	Stereotypy	Agitation	Grimacing	Echolalia	Echopraxia	SIB	VS Abnormality
2	1	Y	Y	N	Y	Y	Y	N	Y	Y	Y	N	N	Y	N
3	2	Y	Y	Y	Y	Y	Y	N	N	Y	N	N	N	Y	Y
4	3	Y	N	N	Y	Y	Y	N	N	Y	Y	N	N	Y	N
5	4	N	N	N	N	N	N	N	Y	Y	N	N	N	Y	N
6	5	N	N	N	N	Y	Y	N	Y	Y	N	N	N	Y	N
7	6	N	N	N	N	N	N	N	Y	Y	N	N	N	Y	N
8	7	Y	N	N	Y	Y	Y	N	Y	Y	N	N	N	Y	N
9	8	N	N	N	N	Y	Y	N	Y	Y	N	N	N	Y	N
10	9	N	N	N	N	N	Y	N	Y	Y	Y	N	N	Y	N
11	10	N	N	N	N	N	N	N	Y	Y	N	N	N	Y	N
12	11	Y	N	N	N	Y	Y	Y	Y	Y	Y	N	Y	Y	N
13	12	Y	N	N	Y	Y	Y	N	Y	Y	N	Y	Y	Y	N
14	13	N	N	N	Y	Y	Y	N	Y	Y	N	N	N	Y	N
15	14	Y	N	N	Y	Y	Y	N	Y	Y	N	N	N	Y	N
16	15	Y	N	N	Y	Y	Y	N	Y	Y	N	N	N	Y	N
17	16	N	N	N	Y	Y	N	N	Y	Y	N	Y	N	Y	N
18	17	N	N	N	N	N	Y	N	Y	Y	N	N	N	Y	N
19	18	Y	N	N	Y	Y	Y	N	Y	Y	Y	N	N	Y	N
20	19	Y	N	N	Y	Y	Y	Y	Y	Y	Y	N	N	N	N
21	20	Y	N	N	Y	Y	Y	N	Y	N	N	N	N	N	N
22	21	Y	N	N	Y	Y	Y	N	Y	Y	N	N	N	Y	N
23	22	Y	N	N	Y	Y	Y	N	Y	Y	Y	N	N	Y	N

Fig. 1 DSM-5 Catatonia Symptom Chart

Discussion and demonstrative case examples

The patient data presented in this report represent a decade's experience in working with 22 autistic children, adolescents and young adults presenting with various catatonic symptoms. Symptom severity and acute medical morbidity were high, prompting evaluation in a tertiary care center where most patients were initially hospitalized. The early lessons learned from this catatonia cohort were many. Comprehensive treatment experiences are presented separately.

The diagnosis of catatonia does not require the presence of any single symptom. In the DSM5, patients simply must display three of 12 listed criteria. Similarly, no one symptom is pathognomonic for catatonia and symptoms may vary widely across patients and time [2, 4, 6]. In a chart review of 250 typically developing adult psychiatric inpatients with catatonia, Morrison found that 110 were of the predominantly psychomotor retarded type, and 67 predominantly psychomotor excited, but no single catatonia symptom was found exclusively in either type. The most common symptoms of the psychomotor retarded group were mutism, negativism, rigidity, catalepsy and staring, whereas in the psychomotor agitated group, the most frequent symptoms were impulsivity, combativeness and disrobing [3]. It is currently believed that alternating stupor and agitation is virtually pathognomonic for catatonia [22].

Catatonic symptomology in ASDs

In this study of 22 autistic youth, the most common catatonic symptoms were agitation (21/22), stereotypy (20/22), posturing (18/22), negativism (17/22), mutism (14/22), stupor (13/22) and grimacing (7/22). An additional 20/22 patients engaged in repetitive self-injury. Significantly, all patients displayed multiple topographies of head and body directed SIB, and all patients had experienced associated tissue injury

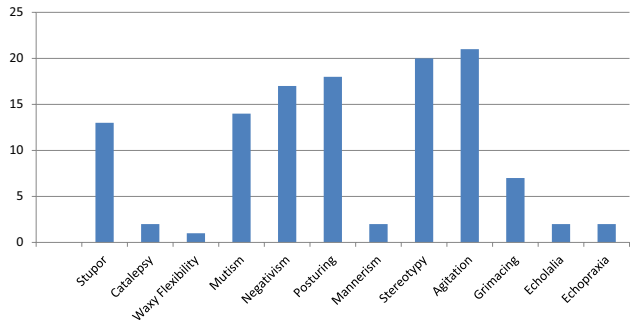

Fig. 2 Frequency of DSM-5 catatonia symptoms

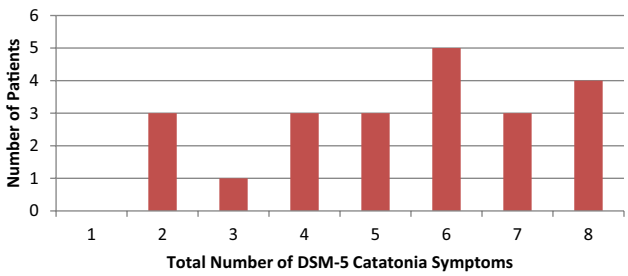

Fig. 3 Frequency of total number of catatonia symptoms

severe enough to warrant hospital care. These data suggest that there is a core group of catatonic symptoms, with a mixture of retarded and agitated signs, including self-injury, amongst autistic individuals.

Example: classic catatonia

The patient was a 15-year-old Caucasian male with prior diagnoses of ASD and mild ID who functioned pre-morbidly at a kindergarten academic level, able to independently complete personal hygiene, dressing and self-feeding, as well as perform simple chores such as vacuuming carpet and unloading the dishwasher. He spoke in full, albeit simple, sentences and engaged in spontaneous conversation. Over the course of a few weeks, he lost all verbal and functional communication skills, completely stopped eating and developed insomnia of several days' duration. He displayed waxy flexibility, postured rigidly in the mudroom for hours at a time on one foot with his hips flexed forwards or lay unresponsive in a ball on the floor. He demonstrated a partial response to lorazepam up to 19 mg daily in four divided dosages, although he still required extensive physical prompting to move and eat, and spoke only one to three words every few days. He demonstrated an excellent response to ECT in terms of resolution of motor and vocal catatonic symptoms, although his parents reported that his academic skills did not return to his premorbid baseline. The patient relapsed briefly when insurance denied ongoing coverage for ECT, but recovered promptly when ECT services were resumed.

In Wing & Shah's seminal study (2000), 30 patients from a cohort of 506 autistic individuals were diagnosed with catatonia according to their "essential" criteria of slowness, passivity, difficulty initiating movement and prompt dependence. Wing and Shah also noted frequent behavioral abnormalities including day–night reversal, Parkinsonian features, excitement and agitation, and increase in repetitive, ritualistic behaviors; these last two criteria most commonly seen in this study [9]. Of course, agitation and stereotypy are symptoms that may be readily found in children with autism, and stereotypy figures within the DSM5 diagnostic criteria for autism spectrum disorders [2]. Within this patient cohort, stereotypy and related repetitive behaviors were only rated as a catatonic symptom when they exceeded baseline stereotypical behaviors as reported in the developmental history by their parents. In the case of agitation, all the children had undergone months, and in many cases years, of exhaustive behavioral assessments and treatment initiatives targeting environmental causes of behavioral agitation. Agitation was only ranked as a symptom of catatonia if it had been found via functional behavioral assessment to have no operant function.

Wing & Shah further reported on classic catatonic symptoms amongst the 30 identified patients, including one odd gait (90%), odd, stiff postures (63.3%), freezing (56.7%), impulsivity (53.3%), inability to stop actions (23.3%) and excited behavior (23.3%). The high rate of motor abnormalities was similar to that found in this study, although excitement was much lower in the British study than the current one. The UK study did not comment upon self-injury or aggression other than to indicate that some patients were referred for behavioral concerns. Interestingly, only four of the 30 patients in the UK study were identified as "severely affected," in that catatonic symptoms completely disrupted their lives, whereas such was the case for all patients in this study [9]. Clearly, the Wing-Shah population is not identical to study cohort.

Billstedt et al. (2005) evaluated the outcomes of autism after adolescence in 120 patients, reporting that 12% demonstrated "clinically diagnosed catatonia with severe motor initiation problems". Most of the identified patients were reported to have "very awkward gait movements," a finding in line with the high rate of posturing in this sample. Interestingly, within the entire cohort, 50% of cases were additionally diagnosed with self-injury, although no connection was made to catatonia [10]. Again, this was a milder treatment group than the seriously affected patients presented here.

Ghaziuddin et al. (2012) conducted a retrospective review of 101 patients with multiple at-risk diagnoses for catatonia, and found that fully 17.8% met criteria for catatonia based on having three or more of the following symptoms: (1) unexplained agitation/excitement (75.2%), (2) disturbed or unusual movements (33%), (3) reduced or loss of speech (29%), (4) reduced movements (15%), and (5) repetitive or stereotyped movements. 81% of the patients diagnosed with catatonia also had a pervasive developmental disorder. Their findings demonstrated high rates of agitation similar to those in our study. Significantly, only two patients had been diagnosed with catatonia at the time of clinical presentation; indeed, the authors emphasize the delayed and often missed catatonia diagnosis and implementation of appropriate treatment. This same 2012 US study further documented that 32% of catatonic patients had reduced solid intake, and 13% reduced liquid intake; these figures are somewhat lower than the high rate of negativism (77.3%) in this sample [8]. While weights and caloric intake were not tracked in the study patients, it is an important anecdotal observation that many of these children experienced extended periods with compromised nutrition, often requiring coaxing and/or force-feeding, and calorie-dense medical juices and formulas. Many of the patients were at risk for aspiration, with some experiencing such, due to the necessary manner of feeding and their reduced movements and posturing.

Breen and Hare (2017) proposed that catatonic symptoms in autism may be considered "attenuated behaviors," and sought to evaluate their presence, frequency and severity

using an original measure that they termed the Attenuated Behavior Questionnaire. Within their sample of 87 informants, they identified six core attenuated behaviors wholly similar to Wing & Shah's "essential" criteria for catatonia in autism spectrum disorders, including (1) freezing or remaining still, (2) difficulty initiating actions, (3) difficulty stopping actions already started, (4) difficulty initiating movement, (5) slowed movements, and (6) prompt dependence to complete actions. Significantly, 20.2% of their subjects were reported by the informants to have a prior catatonia diagnosis, and 48.3% were reported to display three or more of the core attenuated behaviors, the questionnaire diagnostic cut-off. The authors emphasized the wide variability of the catatonia presentation in ASDs, and further noted the association between ABQ scores and those of measures for both depression and repetitive/restrictive behaviors [11]. The demonstrated link between attenuated and repetitive behaviors is salient in the context of the 90.9% rate of repetitive self-injurious behaviors found in the current study. However, once again the patients reviewed were overall markedly less ill than the youth in this study.

Several other case reports and series have reported the presence of catatonia in autism spectrum disorders, including the initial presentation and acute treatment course of eight of the 22 cohort patients [13, 15, 23–33]. In 2006, Dhossche et al. published a multi-authored textbook on catatonia in autism spectrum disorders, including treatment blueprints akin to anti-catatonic treatment paradigms in general psychiatry, namely discontinuation of offending agents, introduction of benzodiazepine therapy with upwards titration until symptoms remit, and electroconvulsive therapy (ECT) when benzodiazepines are insufficient and/or patient morbidity demands swift symptom remission [34, 35].

While our cases demonstrate a clear catatonic deterioration from baseline, there is nevertheless a likely symptom overlap between autism spectrum disorders and catatonia, a phenomenon first noted by Dhossche who proposed that in some cases, childhood autism may actually be a *forme fruste* of catatonia, with theoretical treatment implications for ECT [36, 37]. There are also likely common genetic loci for autism and catatonia, such as those found in the 15q11–13 region where the gamma amino-butyric acid (GABA) receptors are encoded as well as 22q11 [38]. Indeed, individuals with Prader-Willi and velo-cardio-facial syndrome often exhibit symptoms of autism, catatonia as well as psychosis [39, 40]. The same triad of symptoms has been further noted to occur in premutation carriers for Fragile X mental retardation, where patients display lower GABA and elevated glutamate levels, the latter related to the deficit in Fragile X mental retardation protein (FMRP) levels [41]. The co-occurrence of catatonia, psychosis and autism has been previously characterized as an Iron Triangle of symptoms that create a unique clinical presentation, with direct implication for ECT [42].

Only one patient in this series presented with the thermoregulatory and hemodynamic instability characteristic of malignant catatonia. Originally described in 1934 by Stauder as "fatal catatonia," this form of catatonia includes marked vital sign instability, rendering the condition lethal in 10–20% of untreated cases [6, 43]. While most of the malignant catatonia literature describes patients with tachycardia, hypertension and hyperthermia, it is also quite possible to find bradycardia, hypotension and hypothermia, as is demonstrated by the patient in this series.

Example: malignant catatonia

In malignant catatonia, a fatal outcome threatens. A 14-year-old Caucasian male diagnosed with autism and mild mental retardation at baseline functioned academically at a second–third grade level, was nearly independent for self-care, participated fully in a range of family and community activities, and had even completed his bar mitzvah including abbreviated reading in the original Hebrew. At age 14, he began to demonstrate marked slowness and prompt dependence, followed shortly by episodes of freezing and unresponsiveness, rigidity and waxy flexibility, echolalia and then complete mutism. Oral intake was profoundly affected, with a 35 lb weight loss over 6 months, and maintenance of a bare minimum of hydration and nutrition by force-feeding, jaw massage and cajoling to swallow by his parents. Exhaustive laboratory and imaging studies were all within normal limits, although vital signs were significant for pulse in the low 40 s beats per minute. 48-h video EEG was completed with over 40 push-button events of posturing indicated by the mother, none of which correlated with any seizure activity. The patient demonstrated fleeting response to lorazepam therapy, initiated at 1 mg TID and titrated up to 9 mg TID by 0.5 mg TID increments every few days, at which point the patient was hospitalized after requiring multiple emergency department visits for IV rehydration. Admission vital signs were remarkable for hypothermia of 34C and bradycardia at 24–40 beats/min. He remained under cardiorespiratory monitoring until ECT was initiated. Lorazepam was weaned, and ten right unilateral (RUL) treatments were administered at a thrice weekly schedule without benefit; in fact, the patient began to display new forms of posturing. The patient then received 12 bilateral (BL) ECT treatments, yet continued to show waxing and waning of his catatonic symptoms without consistent vital sign stability. Lorazepam was restarted at 1 mg TID and titrated up to 2.5 mg TID while thrice weekly BL ECT continued with flumazenil pre-treatment prior to stimulus application. All symptoms of malignant catatonia resolved, including hypothermia, bradycardia, hypotension and acrocyanosis, and the patient continued to show

gradual resolution of posturing, immobility, mutism, food refusal and stupor, allowing him to be discharged home after 16 months of inpatient therapy when once weekly maintenance ECT allowed consistent symptom remission [30].

Malignant catatonia has been reported in other pediatric patients. Dhossche et al. (2009) report a 17-year-old African-American male with sickle cell anemia who developed hallucinations, paranoia, mutism, echopraxia, echolalia, reduced movements, grimacing, sudden bouts of agitation necessitating four-point restraints, flushing, diaphoresis, fever and hypertension, and was effectively and safely treated with ECT after failed antipsychotic, anticonvulsant, benzodiazepine, antibiotic, antiviral and steroid therapy [44]. Wachtel et al. report a 15-year-old Caucasian male with cerebellar dysgenesis and intellectual disability who developed profound flushing, diaphoresis, rigidity, posturing, stupor, food refusal and urinary retention whose symptoms remitted with acute ECT, and required ongoing maintenance ECT for sustained symptom remission [45]. Wachtel et al. (2015) also describe an 18-year-old Caucasian male with autism, intellectual disability and bipolar disorder who developed tachycardia, hypertension, elevated creatinine phosphokinase and white blood cell count as well as multiple motor signs of catatonia including agitation requiring combined usage of propofol, fentanyl and dexmetomidate in an intensive care setting for safety after a 3-day trial of clozapine [29]. This case underlined in ASDs the recognition of neuroleptic malignant syndrome as malignant catatonia caused by antipsychotic administration, as well as life-saving benefit of ECT. Ghaziuddin et al. (2017) further report five children who developed malignant catatonia/neuroleptic malignant syndrome and were all successfully treated with ECT; three of these children had comorbid ASD diagnoses, and one had a diagnosis of intellectual disability [46].

Malignant catatonia is a life-threatening emergency, with 10–20% estimated fatality rate when left untreated. Patients may die from cardiovascular collapse, respiratory, renal and other organ failure, as well as arrhythmias and sheer physical exhaustion. Some cases of malignant catatonia are fatal within a few days of onset, underlining again the need for prompt diagnosis and treatment implementation [6, 7].

Self-injurious behavior

Self-injurious behavior is not an uncommon finding in autism and intellectual disability, with prevalence estimates ranging widely from 15 to 50% [47], and more readily found in those individuals with lower cognitive functioning, impaired communication, concomitant psychiatric, genetic and medical conditions. The assessment and treatment of self-injurious behavior, and the understanding of its etiology, has historically remained the unchallenged "sandbox" of applied behavioral analysis (ABA). ABA seeks to identify operant, or environmental, functions to SIB, with common functions including access to edible and non-edible tangibles, attention, and escape from demands [48, 49]. Patients for whom an assessment demonstrates a discrete social function to their behaviors will benefit from the implementation of a targeted behavioral protocol. Some self-injuring children demonstrate concomitant psychopathology, and may respond to classic single or combined treatment interventions of applied behavioral analysis and psychopharmacology [50, 51].

However, not all patients demonstrate social or psychiatric etiologies of their self-injury. These individuals are often labeled as having an "automatic" function to their self-injury that is maintained by an unclear form of internal positive reinforcement [18, 48] or driven by forces that are poorly understood. All of the SIB patients in this cohort fell into this category, as they had all undergone exhaustive functional behavioral assessments over the course of months–years which had failed to identify any distinct operant function. Such patients typically require extensive protective and restrictive equipment, including helmets, arm and leg restraints preventing flexion at the elbow or knee joints, limb and body padding, tethers, mats as well as ongoing caregiving blocking of self-injury. A highly limiting situation rapidly ensues, where a patient has nearly absent mobility for self-injury, yet also for daily functional activities. The child is essentially in a prison. It is not uncommon for these patients to engage in several thousand self-injurious behaviors daily. Some patients have been kept in four-point restraints for months–years, or even duct-taped to furniture. One parent offered an apt description of his son's self-injury, stating that whilst he had served as a fighter pilot in the US Air Force for over 26 years, never before had he witnessed a situation with such an immediate and urgent need for safe and effective resolution.

A novel and significant development of this study is the demonstration that many children with intractable self-injury devoid of operant function also meet classic catatonia criteria.

Examples: self-injurious behavior as a sign of catatonia

The patient was a 17-year-old Caucasian female diagnosed with autism and intellectual disability as a toddler. Premorbidly, she functioned very well with special education services, demonstrated excellent verbal skills, and was even able to travel the world with her parents and three siblings. At age 16, she presented to an inpatient neurobehavioral unit with a 3-year history of extensive self-injurious behavior of hitting her ears, temples, legs, sides and pelvis, and ripping out her hair, which had led to marked ecchymosis and edema throughout her body, as

well as two cauliflower ears requiring surgical drainage and suturing. She also displayed affective and behavioral instability, with discrete periods of dysphoria, crying, yelling, and moaning. When not engaged in SIB, she would lay immobile in a ball on the sofa, with her hands tucked between her legs. She had a history of slowed movements, echopraxia and echolalia, as well as remaining still, mute and negativistic for up to 16 h at a time, requiring forced feeding. Initial risperidone therapy at age 14 led to neck dystonia, which promptly recurred after a switch to haloperidol therapy. Clonazepam titrated up to 2 mg four times daily led to initial, but unsustained improvement at age 15. She experienced four spontaneous seizures attributed to rapid decrease in clonazepam dosage. After each seizure, family, school and mental health staff all noted a dramatic improvement and near return to baseline functioning. Such improvement, however, lasted only a few days. A valproic acid trial also led to unsustained benefit. Clonazepam was immediately rechallenged at 1 mg BID upon admission due to ongoing frenetic agitation and associated self-injury, yet it led to limited improvement with sedation at higher dosages. Behavioral assessments and interventions were pursued over the next several months while the patient demonstrated waxing and waning of catatonic symptoms along with evident dysphoria, tearfulness, loss of interest in activities, mutism, sleep and appetite disturbance. At her worst, the patient would lie under a weighted blanket on the sofa throughout the day, only rarely tolerating staff reading stories out loud. Bilateral ECT was initiated at a thrice weekly schedule, with flumazenil given prior to stimulus application due to concomitant clonazepam usage. The patient showed an astounding response after four treatments. Lithium was introduced when the ECT frequency was then decreased to twice weekly, and the patient was discharged home on a regimen of weekly maintenance ECT. The patient's behavior deteriorated when the ECT pulse width was changed from the original 1–0.25 ms as an outpatient. When ECT was restarted thrice weekly with a pulse width of 1 ms upon re-admission to the inpatient neurobehavioral service, the patient demonstrated prompt restabilization after three ECT. The patient was ultimately discharged to an adult residential treatment facility where she was able to benefit from comprehensive and meaningful adult programming, and also receive ongoing weekly m-ECT. She has been able to return home for holidays without incident, and was most recently photographed enjoying a group trip to a local basketball Hall of Fame.

Self-injurious behavior was first hypothesized as an alternate sign of catatonia in 2010, yet the earliest reference to the resolution of SIB with ECT was reported by Bates and Smeltzer (1982) in a 25 year-old male with intellectual disability [52], with a second report by Fink (1999) of a 14-year-old male with mental retardation [53]; neither case, however, drew the connection between SIB and catatonia.

Beginning nearly 30 years ago, literature regarding youth and adults without disability also documented benefit of ECT for SIB alongside affective, psychotic and catatonic symptomology. Carr et al. described a 12-year-old girl with bipolar illness and body slamming [54], Black et al. an 11-year-old boy with depression, headbanging and self-biting [55], Cizadlo and Wheaton an 8-year-old girl with catatonia, depression and hand-to-head self-injury [56], Chung and Varghese an 11-year-old girl with catatonia, psychosis, headbanging and self-scratching [57], and Arora et al. an adult man with psychotic depression and severe self-injury leading to various bodily wounds [58].

Wachtel and Dhossche formally presented self-injury in autism as part of the catatonia spectrum, reviewing historical descriptions of the phenomenon, and proposing self-injury as a stereotypy common to both catatonia and autism; this work further connected catatonia and autism with tic disorders, where self-injury may be found as a common denominator across the three conditions [21]. In a 2017 review, Wachtel et al. traced the recognition of self-injury as an agitated psychomotor symptom of catatonia as it unfolded over the course of acute treatment of seven of the children included in this longitudinal cohort [59]. The connection between catatonia and self-injury was first raised in a 2008 report of an 18-year-old autistic girl with posturing, rigidity, grimacing, mutism, stupor, massive skill regression and negativism requiring gastrostomy tube feedings who also displayed sudden bursts of severe self-injury that had led to bilateral traumatic cataract formation as well as bilateral retinal detachment. The patient was successfully treated for catatonia and self-injury with ECT, and able to successfully undergo retinal re-attachment surgery [16]. Subsequent reports included those of an 8-year-old autistic boy who presented with > 100 SIB/h after years of failed behavioral and psychotropic therapy, and demonstrated a reduction in SIB to 20/h with ECT [13], as well as two autistic youth with severe affective illness, catatonic symptomology and intractable SIB whose symptoms were markedly alleviated by ECT, allowing a return to home and community [15, 31]. Other cases of autistic individuals presented severe self-injurious behaviors in the context of combined catatonic and psychotic symptomology as well as malignant catatonia [29, 33]. The take-home messages of these reports were multifold, beginning with the recognition of repetitive self-injury along the catatonia spectrum, successful implementation of ECT, and the vast improvement conferred upon a child's life.

Indeed, it is catastrophic bodily harm and global psychosocial incapacitation of the child and family that anchors the recognition of intractable SIB along the catatonia spectrum. It is also one of the innovations of catatonia in autism spectrum disorders and a novel, significant contribution of

this study which further describes the most common catatonic symptoms and range of catatonic presentations in this severely afflicted ASD patient cohort. Classic catatonic symptoms, such as those delineated in the DSM5 and catatonia rating scales, are relatively easy to discern across age groups, regardless of disability [4, 6]. Treatment of catatonia with benzodiazepines and/or ECT is also straightforward, despite ECT-related stigma and resistance, and the recognized need for controlled trials of such in catatonia in ASDs [60]. But the shifting of treatment-refractory SIB from the realm of *behavior to biology* is a lesson of autism and the special children profiled here.

Most physicians do not work with individuals with autism. Even amongst child psychiatrists who serve youth with autism and neurodevelopmental disability, few manage cases with severe challenging behaviors, and even fewer have witnessed the degree of extreme bodily devastation wrought by self-injury in ASDs. These patients are also the *bête noire* of the modern autism world, where many professional and lay advocates argue that autism is just a form of diversity in need of nurturing, rather than disability in need of evidence-based treatment. This is a situation of uncontestable clinical devastation; a living nightmare for the child and his family. The recognition of SIB along the catatonia spectrum, and the subsequent implementation of efficacious ECT, is a viable option for these most severely afflicted patients who literally had run out of other options.

This study has important limitations, while also raising many questions for future investigation. First of all, as emphasized before, the cohort patients represent a small number of some of the most severely afflicted autistic individuals admitted to a sub-specialty tertiary care center in one country after having been unwell for months–years, and having failed multiple prior interventions. This may represent a selection bias. The information provided here is also a retrospective summary focusing solely on catatonic symptoms and self-injury, whereas a wider scope of investigation might have allowed for elucidation of further clinical components. The evaluation and care of these patients occurred during the early years of the catatonia in ASDs field, and was not driven by a research protocol. This descriptive case series does, however, lay the groundwork for important areas of current clinical consideration and future research, including (1) the relationship between specific topographies of SIB and catatonia, (2) risk factors for the development of SIB in ASD catatonia patients, (3) additional DSM-5 and medical pathology comorbid to catatonia in ASDs, (4) the routine evaluations of catatonia in ASD patients presenting with SIB, and of SIB in ASD patients presenting with catatonia, (5) the addition of SIB to catatonia rating scales, and, finally, (6) efficacious treatment options.

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Compliance with ethical standards

Conflict of interest The author hereby declares no conflicts of interest or necessary disclosures.

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