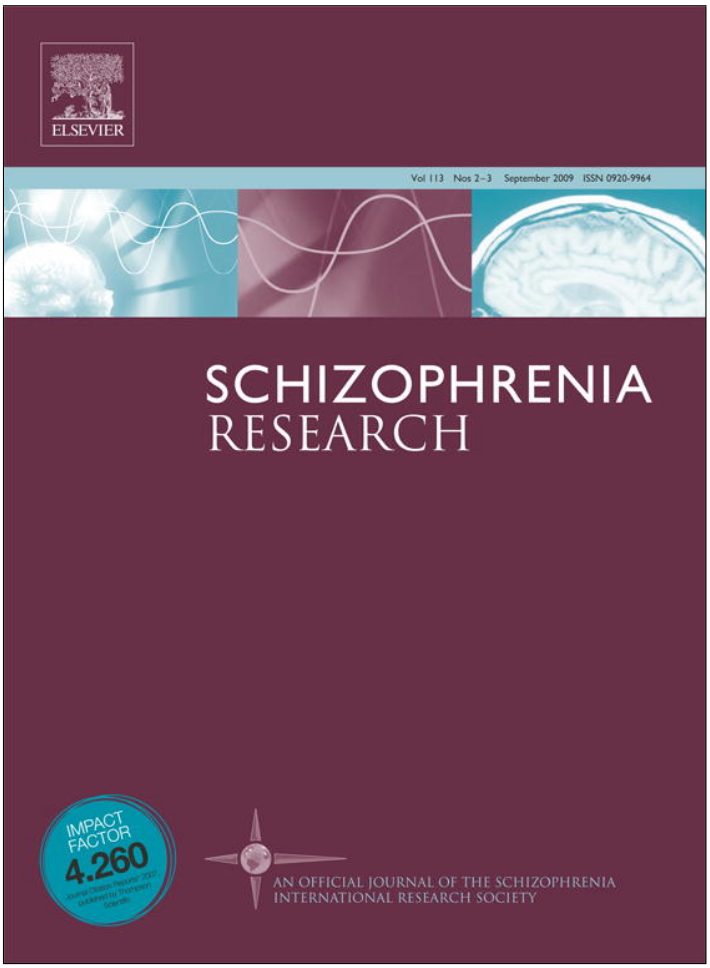

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Association of adolescent catatonia with increased mortality and morbidity: Evidence from a prospective follow-up study

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ABSTRACT

This paper examined outcomes among youth with catatonic syndrome and determined whether the characteristics suggesting the relevance of chronic catatonic schizophrenia (CCS) at index episode remained stable at follow-up. From 1993 to 2004, 35 individuals aged 12 to 18 years were prospectively admitted for management of catatonic syndrome and followed up after discharge. Mean duration from discharge to follow-up was 3.9 years (range 1–10). Four patients were lost to follow-up. Among the remaining 31 subjects (mean age = 19.5 years, range 15–26), life-time diagnosis using the Diagnostic Interview for Genetic Studies was unchanged in 28 patients, and included schizophrenia (all subtypes; $N=20$), major depressive episode ($N=5$), bipolar disorder type I ($N=4$) and brief psychotic episode ($N=2$). Mortality (all-cause Standardized Mortality Ratio = 6266; 95% CI = 1181–18,547) and morbidity were severe, with 3 deaths (including 2 suicides), 6 patients presenting with a causal organic condition and 14 subjects needing continuous psychiatric care. All males in the study ($N=8$) who had chronic catatonic schizophrenia at the index episode still had chronic catatonic signs at follow-up.
Catatonia is one of the most severe psychiatric syndromes in adolescents. It is associated with a 60-fold increased risk of premature death, including suicide, when compared to the general population of same sex and age. This increased risk of premature death remains higher than the one measured in former adolescent psychiatric patients (all-cause SMR = 221; 95% CI = 156–303; Engqvist and Rydelius, 2006), or in schizophrenia irrespective to age and subtype (all-cause SMR = 157; 95% CI = 153–160; Harris and Barraclough, 1998).

Catatonia is a syndrome characterized by the coexistence of psychic and motor symptoms (Table 1) (Cohen et al., 2005). It occurs in various psychiatric disorders and organic conditions and is generally associated with a normal neurological examination (Cohen et al., 1999a,b; Taylor and Fink, 2003). As a result, catatonic symptoms are often regarded as functional and must be understood at the level of the subjects' experience, which results in catatonic motor dysfunction (Cohen, 2006). Regardless of the underlying disease, catatonic signs are a consequence of (i) differential motor responses to hallucinations and/or delusions leading to a dysfunction of intentionality (e.g., when a patient resists hallucinatory orders to commit suicide), or to a dysfunction of behavioural pattern planning (e.g., when a patient strictly adheres to voices or hallucinations that order movements, so called "De Clérambault's psychomotor automatism") (De Clérambault, 1927), or (ii) a dysfunction of emotional regulation marked by extreme emotional involvement that some authors have related to the immobilization reflex of

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Table 1
Catatonia symptom list.

Motor symptoms	Other symptoms
Catalepsy	Social withdrawal
Stupor	Mutism
Posturing	Mannerism
Waxy flexibility	Echolaly
Staring	Incontinence
Negativism	Verbigeration [b]
Stereotypies	Schizophasia [c]
Psychomotor excitement	Acrocyanosis [d]
Automatic compulsive movements [a]	Refusal to eat
Echopraxy	
Muscular rigidity	

[a] Including grimacing.
[b] Meaningless and stereotyped repetition of words.
[c] Scrambled speech.
[d] Cyanosis of the extremities.

many animals (e.g., in stuporous anxious states). Although direct correlation is not possible, these various dysfunctions in motor control may explain the variation in catatonic motor signs (i.e., catatonic stupor, psychomotor automatism, excited catatonia; Cohen, 2006).

In the field of child and adolescent psychiatry, catatonia has been poorly investigated. It is an infrequent but severe condition (Cohen et al., 1997), which may result in death (Ainsworth, 1987; Dimitri et al., 2006). While the symptomatology and associated disorders seen in young patients with catatonia are similar to those reported in the adult literature (Taylor and Fink, 2003), findings differ with regard to the female-to-male ratio (Cohen et al., 2005; Thakur et al., 2003) and the relative frequencies of the associated disorders (Cohen et al., 1999a,b; Takaoka and Takata, 2003). First, catatonia in children or adolescents occurs more frequently in boys than in girls. Second, regarding underlying psychiatric conditions, schizophrenia is the most frequent associated diagnosis, but mood disorders may also be encountered (Cohen et al., 1999a,b; Takaoka and Takata, 2003). Third, regardless of psychiatric presentation, organic conditions are associated with up to 20% of cases (Lahutte et al., 2008). Medical conditions associated with catatonia can be divided into four groups: (1) infectious diseases (e.g. encephalitis), (2) neurological conditions (e.g. neurolupus), (3) toxic induced states (e.g. ecstasy), and (4) genetic conditions (e.g. Pader-Willi syndrome). Fourth, catatonia can occur in children and adolescents with a history of Pervasive Developmental Disorder (PDD; Wing and Shah, 2000; Billstedt et al., 2005; Ohta et al., 2006; Wing and Shah, 2006; Kazooga-Mwesige et al., 2008). Despite these differences, the symptomatic treatment approach utilized in the young is similar to that used in adult catatonia and includes the use of high dosages of benzodiazepines, such as lorazepam, at doses of up to 16 mg/day, depending on adverse sedative effects, and electroconvulsive therapy (ECT), which is used as second line management (Taylor and Fink, 2003; Cornic et al., 2007). This management is utilized even in cases of autism (Wachtel et al., 2008). However, to date, no follow-up data are available.

In the only published report on catatonia in the context of youths with Childhood Onset Schizophrenia (COS), approximately one-third of the 38 COS patients studied also presented with catatonia and grossly disorganized behaviour (Green et al., 1992). Compared to adult-onset schizophrenia, COS is characterized by greater clinical morbidity, more severe negative symptoms (Rapoport and Inoff-Germain, 2000), and is often associated with a history of Pervasive Developmental Disorder (PDD; Sporn et al., 2004). However, catatonia has not been systematically assessed in most studies of COS. In previous works, we showed that non-motoric symptoms differ in catatonic COS vs. non-catatonic COS inpatients, with catatonic COS associated with more severe symptoms in nearly all clinical dimensions at both admission and discharge (Bonnot et al., 2008). Furthermore, in a consecutive sample of 30 youths with catatonia, we identified a subgroup of six males in whom catatonia appeared to be associated with an insidious onset COS that had a chronic course and was treatment resistant (Cohen et al., 2005).

The current study aimed to assess the naturalistic long-term outcome of catatonia among youth, in terms of lifetime diagnosis, morbidity and mortality, by following up a prospective sample of 35 inpatient youths with catatonia at least one year after discharge. Given that catatonia is a syndrome and that it may be (i) causally related, (ii) non-causally associated as a marker of severity with several psychiatric conditions, and (iii) chronic in some schizophrenic patients, we specifically utilized a multi-axial assessment focusing on catatonic symptoms, Axis I psychiatric diagnosis, morbidity, mortality, Axis I diagnostic changes between index episode and follow-up as well as organic conditions (Axis III) diagnosed during follow-up. Our hypotheses were as follows: (1) as catatonia at index episode was associated with COS, diagnosis at follow-up should be rather stable; (2) catatonia would be among the most severe psychiatric condition in terms of mortality and morbidity; (3) the characteristics of chronic catatonic schizophrenia would remain stable at follow-up, and the ratio of catatonia duration: follow-up duration would be close to one in these patients.

1. Methods

1.1. Patient selection

Between 1993 and 2004 in the Department of Child and Adolescent Psychiatry at La Pitié-Salpétrière Hospital, and between 1999 and 2003 in the Department of Child and Adolescent Psychiatry at Bicêtre Hospital, both located in Paris, all children who were admitted to either psychiatric unit were systematically assessed for catatonic signs. At entry or during the course of hospitalization, each patient with motor signs was examined by one of the three study-associated clinicians (DC, DP, MS). The diagnosis of catatonia was made based on the presence of at least two catatonic motor signs or one catatonic motor sign combined with a non-motor catatonic symptom indicative of severe impairment in behavioral and emotional functioning (Cohen et al., 2005; Table 1). Patients with pure extrapyramidal symptoms secondary to antipsychotic prescriptions were not eligible and excluded. Finally, 35 patients (30 from La Salpétrière and 5 from Bicêtre) met these criteria for catatonia and were prospectively enrolled. At the time of the index episode, the number of symptoms listed in Table 1 per patient ranged from 5 to 16 (mean = 10) (Cohen et al., 2005). The decision to engage in follow-up was decided when the sample of prospective

Table 2
Socio-demographic and clinical characteristics and diagnoses of young patients with catatonia at index episode and follow-up.

	Index episode		Follow-up
	$N=35$		$N=31$
Mean age (±SD), years	15.4 (±1.41)		19.5 (±3.16)
Female/male	13 F, 22 M		10 F, 21 M
High/middle/low SES	12/14/9		9/14/8
European/non European [a]	16/19		12/19
	Admission	Discharge	
GAF score, mean (±SD)	18.5 (±6.3)	54.3 (±17.1)	61 (±19.2)
CGI-S, mean score (±SD)	6.8 (±0.4)	4 (±1.38)	4 (±1.6)
Catatonia	$N=35$	$N=8$	$N=14$
Catatonia due to medical condition [b]	Lupus: $N=3$		Huntington Disease: $N=1$
	FFI: $N=1$		Storage disease: $N=1$
Primary diagnosis			
Schizophrenia	$N=19$		$N=20$
Major Depressive Episode	$N=8$		$N=5$
Bipolar Disorder, Type I	$N=5$		$N=4$
Brief Psychotic Episode	$N=3$		$N=2$
Secondary diagnosis			
OCS	$N=6$		$N=8$
General anxiety	$N=0$		$N=1$
Substance abuse	$N=0$		$N=1$
PDD	$N=5$		$N=5$
Mental retardation	$N=2$		$N=2$

SES = socio-economic status; CGI-S = Clinical Global Impression-Severity; GAF = Global Assessment Functioning; FFI = Fatal Familial Insomnia; OCS = Obsessive–Compulsive Symptoms; PDD = Pervasive Developmental Disorder.

[a] Mainly from North Africa and French Central Africa.

[b] Diagnoses indicated at follow-up that molecular diagnosis or certainty of an organic condition occurred during the consecutive years following discharge from index episode.

patients reached 35 subjects. At least one year after enrollment, subjects were approached for a follow-up clinical evaluation. Of the sample, 4 (3 females and 1 male) could not be reached due to change of address and telephone number and were thus considered to be lost to follow-up. Two had catatonia associated with major depression with psychotic features and two had catatonia associated with schizophrenia. Follow-up data were available for 31 patients (88.5%). Clinical characteristics of all patients at index episode are summarized in Table 2 (see details for 30 subjects in Cohen et al., 2005). We obtained written informed consent from all participants (and/or their parents) at the time of the index episode. In 2004, patients were contacted for a follow-up evaluation. A second written informed consent was obtained at this time. The study was conducted in accordance with the guidelines provided by the ethical committee at La Salpêtrière University Hospital.

1.2. Patient assessment and procedure

At follow-up, after informed consent was obtained (including parents' consent for minors), all subjects were personally interviewed by one of the authors (FC) who was blind to the diagnosis given at index episode; subjects were also given a battery of clinical evaluations. General socio-demographic information included age, sex, origin, socio-economic status of the family, and current school or professional level. Lifetime and current psychiatric diagnoses were assessed using the Diagnostic Interview for Genetic Studies (DIGS), version 2.0, a semi-structured diagnostic interview developed by the Human Genetics Initiative of the National Institute of Mental Health (Nurnberger et al., 1994; www.nimhgenetics.org; French translation by CL). The DIGS elicits information necessary to diagnose psychotic, mood, anxiety, substance use and eating disorders by DSM-IV criteria, as well as suicidal behaviors. Current clinical state was assessed using the following instruments: the Montgomery-Asberg Depression Rating Scale (MADRS) to evaluate depressive symptoms (Montgomery and Asberg 1979), the Brief Psychiatric Rating Scale (BPRS) to index global psychopathology (Overall and Gorham, 1962), the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1981) and the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1983) to score negative and positive symptoms of schizophrenia. To delineate catatonic signs, we used the 14-item Bush–Francis catatonia rating scale (Bush et al., 1996), to which we added items for the following six symptoms taken from Ey's earlier description (1950): catalepsy, refusal to eat, incontinence, cyanosis of hands and feet (acrocyanosis), word salad (schizophasia) and automatic compulsive movements (Cohen et al., 2005). Current functioning and disease severity were scored on the Clinical Global Impression-Severity (CGI-S; Guy, 1976) and the Global Assessment of Functioning (GAF) scales. The work/school, leisure, and peer relationships sections of the Social Adjustment Scale (SAS self report or hetero-questionnaire when clinical status did not allow for use of self report) were administered to evaluate quality of recent social functioning (Weissman and Bothwell, 1976), and this information was used to rate a global adaptation score, which we modeled on the CGI scales, ranging from one (poorly adapted) to seven (highly adapted). This score, referred to as the SAS score below, took into account current work or school achievement, leisure activities, peer relationships, and dependency on family according to age.

To maximize the accuracy of psychiatric and medical diagnoses, every effort was made to obtain clinical information from each patient's regular psychiatrist and/or medical physician. At the index episode of catatonia, subjects received systematic assessment with an internist and a neurologist, as well as a systemic screening with Magnetic Resonance Imaging, Electro-Encephalography, and blood tests (see details in Cohen et al., 2005). In addition to this, an additional examination was performed at follow up under conditions of clinical worsening, dementia, and new physical symptoms. Best estimate DSM-IV psychiatric diagnoses, based on all available information, were assigned by a consensus of the patient's treating clinician, the DIGS interviewer (FC) and one additional child/adolescent psychiatrist (DC, DP, AC). Given the naturalistic design of the follow-up study, treatment was at the discretion of the treating psychiatrist, who was not a member of the University staff, in most cases. All treatments and other interventions during follow-up were systematically recorded and presented by therapeutic class. Antipsychotic dosages were transformed into chlorpromazine equivalency units.

1.3. Statistical analysis

Statistical analysis was performed using SAS software. Descriptive statistics were computed for sociodemographic

variables (i.e., sex, age, economic status, European vs. non-European parents (meaning at least one), SAS score, academic delay, need for institution) and clinical characteristics (i.e., catatonia score, CGI-S, GAF, MADRS score, BPRS score, SANS and SAPS scores, the ratio of catatonia duration to follow-up duration and Axis I and Axis III diagnoses). Patients were then classified into two diagnostic categories: schizophrenia vs. other diagnoses. Due to the small sample size, initial comparisons between the two groups were made using nonparametric univariate tests. Stepwise regression analyses were then conducted. The first analysis was run in order to determine which clinical variables could predict a better prognosis and used the SAS-score at follow-up as the dependent variable. The second analysis was run to determine whether catatonia would have a more chronic course in patients with COS and used the ratio of catatonia duration to follow-up duration as the dependent variable. Explicative variables included sex, age, economic status, European vs. non-European parents, catatonia score at index episode, CGI-S and GAF scores at discharge of the index episode, and Axis I and Axis III diagnoses. Regression analyses were conducted on the whole sample ($N=31$) and in the subgroup of patients with schizophrenia ($N=20$).

The standardized mortality ratio (SMR) ([number of observed death/number of expected death]$\times$100) and the 95% Confidence Interval (95% CI) were calculated using the method of Harris and Barralclough (1998). Using the mortality rates for boys and girls aged 15–20 years in the Île de France (Paris area) per 100,000 people (47 and 21, respectively), we estimated the number of expected deaths in our sample for all causes, including the number of expected completed suicides given that, in this age group, suicide accounts for 7% and 10% of deaths in boys and girls, respectively (Pépin and Grémy, 2000). All-cause SMR and suicide SMR were calculated. The difference between observed and expected numbers of the deceased was tested by using the z test variable: $z=[OD-ED]/\sqrt{ED}$, where OD denotes number of observed dead and ED denotes expected number dead (Engqvist and Rydélius, 2006). The SMR, which gives the risk of death compared with a general population of similar age, gender and area of living, is considered to be raised significantly when the lower range of the 95% CI is greater than 100; is considered not to differ from the general population when the 95% CI includes the conventional mean value in the general population, that is 100 (like for Intellectual Quotient); and is considered to be significantly reduced when the upper range of the 95% CI is less than 100. E.g: if SMR is 250 for a specific disease, that means that the disease is associated to an increase of 250% of observed deaths compared with the expected deaths in the general population, or that all cause of death risk is 2.5 times that expected.

2. Results

2.1. Socio-demographic characteristics and diagnosis at follow-up

Duration of follow-up was 3.9 years (range 1–10 years). Data were available for 31 patients, including 21 males and 10 females. Mean age at follow-up evaluation was 19.5 ($\pm$3) years (range: 15–26). Socio-demographic and clinical characteristics and diagnoses of patients at index episode and follow-up are presented in Table 2. Of note, most of the patients (90%) had the same primary diagnosis at the index and follow-up assessments. The three changes in diagnosis were all from other diagnoses at index assessment to schizophrenia at follow-up (undifferentiated ($N=2$) and paranoid ($N=1$) subtypes). Schizophrenia was the most frequent final best estimate diagnosis ($N=20$, 65%). Psychiatric comorbid symptomatology included general anxiety ($N=1$), obsessive–compulsive symptoms (OCS) ($N=8$), substance abuse ($N=1$), a history of pervasive developmental disorder ($N=5$) and mental retardation ($N=2$). There were nine patients (30%) with a chronic organic comorbid condition and in six of these cases (19%), the condition was judged to be a likely etiologic factor in the catatonia (whether acute or chronic). Three of the organic cases had lupus erythematosus diagnosed at index episode. Three had one of the following genetic diseases: Huntington's disease, Fatal Familial Insomnia (FFI), and a storage disease of unknown origin. Only one patient (FFI) was diagnosed at index episode. The last two cases were associated with chronic catatonic COS and were diagnosed at follow-up. For the patient with storage disease, Niemann–Pick disease type C was ruled out by a skin biopsy, but the family decided to discontinue the genetic investigation given the poor prognosis. However, the clinical outcome was consistent with a metabolic disease, with subcortical dementia and hepato-splenomegaly in addition to psychotic symptoms at follow-up.

Of the 28 patients alive at the follow-up evaluation, only one patient took no medication and two others were untreated due to poor compliance. The remaining 25 patients took one ($N=5$) or a combination of medications ($N=20$) that included *atypical antipsychotics* ($N=20$; mean dose = 301 mg of chlorpromazine equivalent; range: 25 to 700 mg; amisulpride: $N=4$; olanzapine: $N=6$; risperidone: $N=8$; clozapine: $N=2$), *typical antipsychotics* (mainly phenothiazines: $N=4$), *benzodiazepines* ($N=5$; lorazepam: $N=2$; clorazepate: $N=1$; alprazolam: $N=1$; diazepam: $N=1$), *antidepressants* ($N=8$; fluoxetine: $N=2$; paroxetine: $N=2$; citalopram: $N=1$; clomipramine: $N=1$; sertraline: $N=1$; mianserine: $N=1$), or *mood stabilizers* ($N=8$; valproate: $N=6$; lithium: $N=1$; cabamazepine: $N=1$). Notably, careful recording of psychotropic treatments evidenced that many changes and therapeutic proposals were made during the follow-up period. Not including dose adjustments, we found more than 60 changes or additions to psychotropic compounds. Finally, two subjects underwent ECT during the follow-up period, including one who was undergoing maintenance ECT (Consoli et al., 2009).

2.2. Mortality and morbidity

At follow-up, three patients were deceased. Two patients with schizophrenia and without a history of organic comorbidity or PDD, had died from suicide. The third patient died of Fatal Familial Insomnia at index episode (FFI; Dimitri et al., 2006). Furthermore, premature death is highly probable for the two patients with Huntington's disease and the storage disease since these conditions are life-threatening (e.g., mean survival after molecular diagnosis of Huntington disease is 15 years on average; Gargiulo et al., 2009). All-cause SMR and suicide SMR are given in Table 3A, along with a 95% CI and z

Table 3A
Standardized mortality ratio (SMR) with 95% confidence intervals (CIs) for adolescents who exhibited catatonia: all causes and completed suicide.

Youth catatonia						
	N	OD	ED	Z	SMR	95%CI
All causes	31	3	0.048	13.2	6265	1181–18,547
Suicide	31	2	0.00364	33.1	54,945	5180–202,066

OD = number of observed dead; ED = expected number of dead; $z = [OD–ED]/\sqrt{ED}$.
The z value represents a description of how far a sample or a point is away from its mean expressed in standard deviation ($p<0.001$ when $z>3.29$).

value; these data show a high increase in premature death in adolescent catatonia.

Despite systematic use of benzodiazepine trials at index episode, morbidity was severe with (a) 14 (45%) subjects needing continuous psychiatric care including seven (23%) in full-time institutional care, (b) a mean academic delay of 3.1 (±2.4) years, and (c) a moderate to severe impact on social functioning (SAS score mean = 4.11 ±1.77). Furthermore, during follow-up, four patients, one with schizophrenia and three with mood disorders, attempted suicide and, among the 24 who were not chronically hospitalized, 12 required re-hospitalization for psychiatric treatment. Overall, the cumulative duration of hospitalization was 3.6 ± 7.7 months. Two patients were hospitalized throughout the follow-up period: one patient with chronic catatonic COS required maintenance ECT to maintain moderate improvement (Consoli et al., 2009) and the second developed sub-cortical dementia due to a metabolic disease and thus could not be discharged. Notably, all patients who had acute catatonia due to lupus erythematosus were symptom-free at follow-up under specific treatment.

Table 3B
Most elevated SMR with 95% CIs for adult and adolescent psychiatric conditions: all-cause and completed suicide (data extracted from Harris and Barraclough meta-analysis, 1998; Engqvist and Rydelius, 2006).

Adult		
Eating disorder		
All causes	538	389–725
Suicide	3333	1822–5593
Opioid abuse		
All causes	638	599–680
Suicide	1003	783–1265
Schizophrenia*		
All causes	157	153–160
Suicide	900	842–962
Major depression		
All causes	136	126–145
Suicide	2124	1789–2504
Child and adolescent		
Psychiatric inpatients**		
All causes	221	156–303
Suicide	NR	NR
Who attended probationary school		
All causes	599	501–711
Suicide	521	346–754
Who were referred for self-poisoning		
All causes	400	192–736
Suicide	333	8–1857

NR = not reported in Engqvist and Rydelius (29). *SMR according to subtypes of schizophrenia is not available in adult literature; **Psychiatric inpatients whatever the psychiatric diagnosis, so it includes all subtypes of schizophrenia, mood disorders and other psychiatric conditions.

Table 4
Socio-demographic and clinical characteristics of young patients with catatonia at 4-year follow-up according to diagnosis.

	Schizophrenia	Other	*P* value*
	N = 20	*N* = 11	
Mean age (±SD), years	20 (±3.2)	18.3 (±2.8)	0.6
Female/male	2 F, 18M	8 F, 3M	0.001
Good/middle/poor SES	6/9/5	3/5/3	0.5
European/non European	8/12	4/7	0.34
GAF score, mean (±SD)	47 (±22.3)	70 (±26.2)	0.008
CGI-S score, mean (±SD)	4.8 (±1.2)	2.4 (±1.2)	0.001
SAS score, mean (±SD)	3.5 (±1.6)	5.1 (±1.7)	0.04
Academic delay, mean (±SD)	3.9 (±2.7)	1.7 (±1.9)	0.004
Need for institution, mean (±SD)	0.55 (±0.49)	0.05 (±0.15)	0.007
Catatonia score, mean (±SD)	9.12 (±9.2)	0.6 (±1.8)	0.001
MADRS score, mean (±SD)	13.56 (±7.2)	6.9 (±8.3)	0.7
BPRS score, mean (±SD)	58.5 (±16.1)	24.3 (±7.5)	0.004
SANS score, mean (±SD)	75.5 (±33.7)	9 (±17)	0.07
SAPS score, mean (±SD)	55.1 (±29.5)	1.3 (±2.16)	0.005
Catatonia duration/follow-up duration, mean (±SD)	0.47 (±.046)	0.07 (±0.12)	0.01

SAS = Social-Adjustment Scale; MADRS = Montgomery-Asberg Depression Scale; SES = : socio-economic status; CGI-S = Clinical Global Impression-Severity; GAF = Global Assessment Functioning; BPRS = Brief Psychiatric Rating Scale; SAPS = Scale for the Assessment of Positive Symptoms; SANS = Scale for the Assessment of Negative Symptoms.
*Comparisons were performed by a Fisher exact test for dichotomous variables and by a Wilcoxon sign rank test for continuous variables.

2.3. Chronic catatonia in males with childhood onset schizophrenia

Table 4 summarizes the analyses of the clinical differences between the schizophrenia and non-schizophrenia groups. Patients with schizophrenia were more impaired at follow-up in essentially all domains. Of the 14 subjects with catatonic signs at follow-up, all had diagnoses of schizophrenia.

Variables entered into the multiple regression analyses included sex, age, economic status, European vs. non-European parents, index episode catatonia score, CGI-S and GAF scores at discharge after the index episode, as well as Axis I and Axis III diagnoses. The only predictor of SAS score at follow-up was Axis I diagnosis, with schizophrenia patients showing more impairment ($p = 0.04$). Longer catatonia duration (the ratio of catatonia duration to follow-up duration) was predicted by European origin of parents ($p = 0.006$), male sex ($p = 0.009$), severity of catatonia at index episode ($p = 0.044$) and CGI-S score at discharge after the index episode ($p = 0.001$). When the analysis was restricted to patients with schizophrenia, only origin and sex predicted longer catatonia duration.

Of the eight males who had chronic catatonic COS at index episode, all still had chronic catatonic signs at follow-up. This group included the two patients with genetic disease. Distribution of the ratio [catatonia duration/follow-up duration] clearly distinguished them from other adolescents who had catatonia at index episode. For subjects with non-chronic catatonia ($N = 22$), the mean ratio is 0.1 (SD = 0.15; median = 0.039). For subjects with chronic catatonia ($N = 8$), the ratio is equal to 1. In addition, all had European parents, suggesting that this subgroup was primarily responsible for the prediction of catatonia outcome in the multiple regression

analysis. Of note, all of these patients met criteria for OCD at follow-up. The most frequent catatonic signs were mannerisms ($N=8$), stereotypies ($N=7$), negativism ($N=7$), social withdrawal ($N=7$), staring ($N=5$), and automatic movements ($N=5$).

3. Discussion

3.1. Mortality, morbidity and associated organic conditions

The most striking result of this follow-up study is the high mortality and morbidity level associated with young patients presenting with catatonia. Although we found anecdotal reports in the literature of death in youths with catatonia (Ainsworth, 1987; Dimitri et al., 2006), the 10% rate of mortality found at 4-year follow-up, on average, classifies catatonia among the most severe syndromes in adolescent psychiatry. To our knowledge, no single psychopathology is associated with such a high rate of mortality and suicide. Given that the SMR is the gold standard for assessing the risk of premature death due to a specific condition and allows for comparisons between diseases and causes of death controlling for gender, age, and area of recruitment, we summarized the main SMR data available for psychiatric conditions in Table 3B. Most of the available data about mortality among former psychiatric patients comes from Scandinavian follow-up studies (Harris and Barralclough, 1997; Engqvist and Rydélius, 2006). In adults, the highest risks of premature death from both natural and unnatural causes are found in patients presenting with eating disorders and opioid abuse. In these disorders, suicide accounts for 40 and 60% of the observed deaths, respectively. Risk of suicide is especially high for schizophrenia and major depression (Harris and Barralclough, 1998). In the majority of child and adolescent psychiatric patients, there is a clear increase in early mortality, although reported SMR values are usually below or around 300 and deaths are due mainly to unnatural causes including suicide, drug overdose and traffic accidents (Engqvist and Rydélius, 2006), with the exception being child and adolescent psychiatric patients who attended probationary school or who were referred for self-poisoning (Harris and Barralclough, 1998). In sum, the estimated all-cause SMR for catatonia in adolescents corresponds to a 60-fold increased risk of premature death when compared to the general population of same sex and age. This SMR remains higher than the one measured in former adolescent psychiatric patients (all cause of death risk is 2.2 times that expected) and in schizophrenia irrespective to age and subtype (all cause of death risk is 1.5 times that expected) (see Table 3B). Similarly, the estimated suicide SMR for catatonia in adolescents corresponds to a 500-fold increased risk of suicide when compared to the general population of same sex and age. This suicide SMR remains higher than the one measured in schizophrenia irrespective to age and subtype (suicide risk is 9 times that expected) (see Table 3B). Given that two other patients would have premature death because of life threatening genetic conditions; this increased risk might be underestimated.

In terms of organic conditions, the impact of such conditions on morbidity depends on available therapeutic approaches. In genetic conditions, prognosis is poor due to the lack of available and successful treatment; however, in this series, the prognosis in lupus is much better due to the use of plasma exchange in association with immuno-suppressant drugs (Périsse et al., 2003; Marra et al., 2008). Regardless of comorbid organic conditions, morbidity was a major issue, as evidenced by the cumulative duration of hospitalization, number of suicide attempts, number of patients needing continuous psychiatric care, and patients presenting with academic delay and defects in social functioning. However, a better prognosis was associated with non-schizophrenic conditions (Table 4).

3.2. Stability of diagnosis and validity of chronic catatonic childhood onset schizophrenia

The high diagnostic stability (>85%) of patients presenting with catatonia is similar to that found in follow-up studies of adolescents with psychotic spectrum disorders (Jarbin and von Knorring, 2003). Notably, all changes in lifetime diagnosis occurred in favor of schizophrenia, confirming that it is the most frequent associated psychiatric condition in youth with catatonia (Cohen et al., 1999a,b). The second striking observation is that the subgroup of chronic catatonic schizophrenia was confirmed at follow-up and could be distinguished by other characteristics, such as comorbid symptomatology, sex, origin, high rate of suicide and obsessive–compulsive symptomatology. Children and adolescents with severe OCD can act in bizarre ways and show nearly delusional conviction, which might resemble the erroneous belief systems of schizophrenic patients (Flament and Cohen, 2000). However, in OCD, the absence of thought disorder and hallucinations, as well as the preservation of reality testing outside the area of the obsessional concern may help in distinguishing it from schizophrenia. On the other hand, the psychomotor symptoms of catatonic schizophrenia may mimic OC rituals when patients are not able to express their hallucinatory phenomena (Fenton and Mc Glashan, 1986) or may be found in adult patients with schizophrenia that is comorbid with OCD (Krüger et al., 2000). In this series, we previously pointed out how difficult it was to distinguish severe OCD with the beginnings of a catatonic schizophrenia when the patient was not able to express his actual intrapsychic experience (see detailed case description in Cohen et al., 1999a,b). In the subgroup of patients with chronic catatonic schizophrenia, the most frequent catatonic signs were those that have been classically described as psychomotor automatism by De Clérambault (1927). Although it has been studied poorly in both adults and young people because of the low incidence rate of catatonia (Ungvari et al., 2007), the validity of this rare subgroup of schizophrenia has been supported by several lines of evidence and suggested by Kraepelin (1913), who discussed the difference between the poor outcome of chronic catatonia and the better outcome of acute catatonia (see Braünig et al. (2001) for an in-depth review with a historical perspective).

There is some evidence that acute and chronic forms of catatonia may reflect different clinical entities. First, in our study, severity at discharge of the index episode, sex and origin predicted longer catatonia duration. Second, consistent factor-analytic results have been obtained in studies of catatonia rating scales. These include five validated rating

scales (Bush et al., 1996; Northoff et al., 1999; Lund et al., 1999; Krüger et al., 2003; Cuesta and Peralta, 2001) and numerous checklists, ranging from an original description of 17 symptoms (by Ludwig Kahlbaum in 1874) to more than 40 symptoms (Caroff et al., 2001). Symptoms usually aggregate along two to four dimensions that always include a factor resembling psychomotor automatism (Krüger et al., 2003). Third, two studies, the first an open trial, the second a double-blind placebo-controlled trial showed no effect of lorazepam on chronic catatonia (Ungvari et al., 1994; Lee et al., 2000), whereas the efficacy of sedative drugs has been well documented in acute catatonia (Taylor and Fink, 2003; Rosebush et al., 1990). This suggests that acute and chronic catatonic syndromes might have a different neurobiological basis. Fourth, in the largest study assessing catatonia in a random sample of patients with chronic schizophrenia (Ungvari et al., 2007), younger age at onset was associated with the factor "repetitive/echo phenomena" including mannerisms, grimacing and stereotypy.

3.3. Limitations and strengths of the study

There are several limitations in the current study. The main limitation is its sample size ($N=31$), which is due to the low incidence rate of catatonia in adolescents. Other limitations are as follows: (1) Despite a clear increased risk in mortality, SMR 95% confidence intervals (CIs) remain large due to the even lower incidence of death during follow up. (2) No consensus exists in the definitions of catatonia and several instruments are available (Bush et al., 1996; Northoff et al., 1999; Lund et al., 1999; Krüger et al., 2003; Cuesta and Peralta, 2001). However, our criterion of at least two catatonic symptoms was counter-balanced by the fact that all patients had more than five catatonic signs at index episode. (3) Patients were recruited in tertiary referral centres, which would likely have an impact on severity and we had no comparison group to assess this issue. (4) The group of patients with chronic catatonic schizophrenia included two patients with genetic conditions that had a delayed molecular diagnosis. We cannot, in these cases, exclude that catatonia could be a marker of the severity of their genetic conditions. (5) The naturalistic design of the study did not allow for standardization of treatment and we cannot exclude that the low use of benzodiazepines during follow-up may have worsened the prognosis. Furthermore, given the sample size and the diversity of treatments given, we could not assess the influence of treatment on the course of catatonia. (6) We cannot exclude that the poor outcome in males reflects the low number of females in this sample. Similarly, given the fact that catatonia is a clinical entity noted in all parts of the world, the specific relationship to European origin in this sample may be biased and needs to be further explored.

Strengths of the study include the following: (1) the prospective design; (2) the recruitment of subjects over a period of more than ten years, which permitted us to accumulate a substantial number of patients given the low prevalence of catatonia in adolescents; (3) the free access to tertiary referral in France when necessary; (4) the use of a semi-structured research diagnostic interview schedule adapted for psychotic diagnoses (Nurnberger et al., 1994); (5) an attrition rate of <10%, which is unusually low for a study of adolescents, probably due to close relationships that hospital staff established with patients and families during the index episode; and (6) the formulation of an *a priori* hypothesis regarding the chronic catatonic schizophrenia subgroup that was based on observation at index episode of a subgroup of patients included in this follow-up series (Cohen et al., 2005).

4. Conclusion

Catatonia is one of the most severe psychiatric syndromes in young people and is associated with a high proportion of organic diseases that should always be ruled out, an increased morbidity and a 60-fold increased risk of premature death, including suicide, when compared to the general population of same sex and age. This increased risk of premature death remains higher than the one measured in former adolescent psychiatric inpatients (all cause of death risk is 2.2 times that expected), or in schizophrenia irrespective to age and subtype (all cause of death risk is 1.5 times that expected). There is a need for research in the field of chronic catatonic schizophrenia in adolescents, as it appears to be a rare, severe, and understudied, yet highly morbid, clinical entity.

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Conflict of interest

The authors report no competing interests during the last 12 months.

Contributors

Françoise Cornic: Did all FU interview, analyzed the data, wrote the draft.

Angèle Consoli: Recruited patients at index episode, contacted them for FU, contributed to consensus life time diagnosis and to collection of clinical data during FU, analyzed the data, wrote the draft.

Marie-Laure Tanguy: Did all statistical analysis at both index episode and FU, supervised the draft.

Olivier Bonnot, Didier Périsse, Sylvie Tordjman: Recruited patients at index episode, contacted them for FU, contributed to consensus life time diagnosis and to collection of clinical data during FU, supervised the draft.

Claudine Laurent: Designed the study, analyzed the data, directed the consensus life time diagnosis based on the DIGS, wrote the draft.

David Cohen: Designed the study at both index episode and FU, analyzed the data, contribute to data collection at FU, and wrote the first draft.

Disclosure

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References

Ainsworth, P., 1987. A case of lethal catatonia in a 14 year-old girl. Br. J. Psychiatry 150, 110–112.
Andreasen, N.C., 1981. Scale for the Assessment of Positive Symptoms (SAPS). University of Iowa Press, Iowa City. (French translation by Lecrubier Y. and Boyer P.).
Andreasen, N.C., 1983. Scale for the Assessment of Negative Symptoms (SANS). University of Iowa Press, Iowa City. (French translation by Lecrubier Y. and Boyer P.).
Billstedt, E., Gillberg, C., Gillberg, C., 2005. Autism after adolescence, population-based 13- to 22-year follow-up study of 120 individuals with autism diagnosed in childhood. J. Autism Dev. Disord. 35, 351–360.
Bonnot, O., Tanguy, M.L., Consoli, A., Tordjman, S., Cornic, F., Graindorge, C., Laurent, C., Cohen, D., 2008. Does catatonia influence the phenomenology of childhood onset schizophrenia outside motor symptoms? Psychiatry Res. 158, 356–362.
Braünig, P., Krüger, S., History, I.N., 2001. In: Caroff, S.N., Mann, S.C., Francis, A., Fricchione, G.L., Arlington, V.A. (Eds.), Catatonia. From psychopathology to neurobiology. American Psychiatric Publishing.
Bush, G., Fink, M., Petrides, G., Francis, A., 1996. Catatonia I. Rating scale and standardized examination. Acta Psychiatr. Scand. 93, 129–136.
Caroff, S.N., Mann, S.C., Francis, A., Fricchione, G.L., 2001. Catatonia. From Psychopathology to Neurobiology. American Psychiatric Publishing, Arlington, VA.
Clérambault, G. (Ed.), 1927. Psychose à base d'automatisme et syndrome d'automatisme. Ann Méd-Psychol, vol. 1, pp. 193–239.
Cohen, D., 2006. Towards a valid nosography and psychopathology of catatonia in children and adolescents. Int. Rev. Neurobiol. 72, 132–147.
Cohen, D., Cottias, C., Basquin, M., 1997. Cotard's syndrome in a 15 year old girl. Acta Psychiatr. Scand. 95, 164–165.
Cohen, D., Flament, M., Dubos, P.F., Basquin, M., 1999a. The catatonic syndrome in young people. J. Am. Acad. Child Adolesc. Psych. 38, 1040–1046.
Cohen, D., Flament, M., Dubos, P.F., Basquin, M., 1999b. The catatonic syndrome in young people. J. Am. Acad. Child Adolesc. Psych. 38, 1040–1106.
Cohen, D., Nicolas, J.D., Flament, M., Perisse, D., Dubos, P.F., Bonnot, O., Speranza, M., Graindorge, C., Tordjman, S., Mazet, P., 2005. Clinical relevance of chronic catatonic schizophrenia in children and adolescents: evidence from a prospective naturalistic study. Schizophr. Res. 76, 301–308.
Consoli, A., Boulicot, V., Cornic, F., Fossati, P., Barbeau, M., Cohen, D., 2009. Moderate clinical improvement with maintenance ECT in a 17-year-old boy with intractable catatonic schizophrenia. Eur. Child Adolesc. Psychiatry 18, 250–254.
Cornic, F., Consoli, A., Cohen, D., 2007. Catatonic syndrome in children and adolescents. Psychiatr. Ann. 37, 19–26.
Cuesta, M.J., Peralta, V., 2001. Integrating psychopathological dimensions in functional psychoses: a hierarchical approach. Schizophr. Res. 52, 215–229.
Dimitri, D., Jehel, L., Dürr, A., Levy-Soussan, M., Andreux, V., Laplanche, J.L., Fossati, P., Cohen, D., 2006. Psychiatric adolescent onset of fatal familial insomnia. Neurology 67, 363–364.
Engqvist, U., Rydélius, P.A., 2006. Death and suicide among former child and adolescent psychiatric patients. BMC Psychiatry 6, 51 online journal.
Ey, H., 1950. Etudes psychiatriques. Désclée de Brouwer & Cie, Paris.
Fenton, W., Mc Glashan, T.H., 1986. The prognostic significance of obsessive–compulsive symptoms in schizophrenia. Am. J. Psychiatry 143, 437–441.
Flament, M., Cohen, D., 2000. In: Maj, M., Sartorius, N. (Eds.), Childhood obsessive compulsive disorders, in " Obsessive–compulsive disorder : evidence and practice. Word Psychiatric Association, Genève, pp. 147–183.
Gargiulo, M., Lejeune, S., Tanguy, M.L., Lalhou, K., Faudet, A., Cohen, D., Feingold, J., Durr, A., 2009. Long term outcome of presymptomatic testing in Huntington disease. Eur. J. Hum. Genet. 17, 165–171.
Green, W.H., Padron-Gayol, M., Hardesty, A.S., Bassiri, M., 1992. Schizophrenia with childhood onset: a phenomenological study of 38 cases. J. Am. Acad. Child Adolesc. Psych. 31, 968–976.
Guy, W., 1976. ECDEU Assessment Manual for Psychopharmacology. National Institute of Mental Health, Bethesda.
Harris, E.C., Barralclough, B., 1997. Suicide as an outcome for mental disorders – a meta-analysis. Br. J. Psychiatry 170, 205–228.
Harris, E.C., Barralclough, B., 1998. Excess mortality of mental disorder. Br. J. Psychiatry 173, 11–53.
Jarbin, H., von Knorring, A.L., 2003. Diagnostic stability in adolescent onset psychotic disorders. Eur. Child Adolesc. Psychiatry 12, 15–22.
Kazooga-Mwesige, A., Watchel, L., Dhossche, D., 2008. Catatonia in autism: implication across lifetime. Eur. Child Adolesc. Psychiatry 17, 327–335.
Kraepelin, E., 1913. Dementia praecox and paraphrenia. Barth, Leipzig. Germany.
Krüger, S., Bräunig, P., Höffler, J., Shugar, G., Börner, I., Langkrär, J., 2000. Prevalence of obsessive-compulsive disorder in schizophrenia and significance of motor symptoms. J. Neuropsychiatry Clin. Neurosci 12, 16–24.
Krüger, S., Bagby, R.M., Höffler, J., Braünig, P., 2003. Factor analysis of the catatonia rating scale and catatonic symptom distribution across four diagnostic groups. Compr. Psychiatry 44, 472–482.
Lahutte, B., Cornic, F., Bonnot, O., Soussan, N., Amoura, Z., Sedel, F., Cohen, D., 2008. Multidisciplinary approach of organic catatonia in children and adolescents may improve treatment decision making. Prog. Neuro-psychopharmacol. Biol. Psychiatry 32, 1393–1398.
Lee, J.W., Schwartz, D.L., Pharm, B., Hallmayer, J., 2000. Catatonia in a psychiatric intensive care facility: incidence and response to benzodiazepines. Ann. Clin. Psychiatry 12, 89–96.
Lund, C.E., Mortimer, A.M., Rogers, D., McKenna, P.J., 1999. Motor, volitional and behavioural disorders in schizophrenia. 1: Assessment using the modified Rogers scale. Br. J. Psychiatry 158, 323–326.
Marra, D., Amoura, Z., Soussan, N., Haroche, J., Consoli, A., Ghillami-Dalbin, P., Diemert, M.C., Musset, L., Piette, J.C., Cohen, D., 2008. Plasma exchange in patients with catatonia and systemic lupus erythematosus. Psychother. Psychosom. 77, 195–196.
Montgomery, S.A., Asberg, M., 1979. A new depression rating scale designed to be sensitive to change. Br. J. Psychiatry 134, 382–389.
Northoff, G., Koch, A., Wenke, J., Eckert, J., Böker, H., Pflug, B., Bogerts, B., 1999. Catatonia as a psychomotor syndrome: a rating scale and extrapyramidal motor symptoms. Mov. Disord. 14, 404–416.
Nurnberger Jr, J.I., Blehar, M.C., Kaufmann, C.A., York-Cooler, C., Simpson, S.G., Harkavy-Friedman, J., Severe, J.B., Malaspina, D., Reich, T., 1994. Diagnostic interview for genetic studies. Rationale, unique features, and training. NIMH Genetics Initiative. Arch. Gen. Psychiatry 51, 849–859.
Ohta, M., Kano, Y., Nagai, Y., 2006. Catatonia in individuals with autism spectrum disorders in adolescence and early adulthood: a long-term prospective study. Int. Rev. Neurobiol. 72, 41–54.
Overall, J.E., Gorham, D.R., 1962. The Brief Psychiatric Rating Scale. Psychol. Rep. 10, 799–812.
Pépin, P., Grémy, I., 2000. La mortalité des jeunes en Île de France. Actualité et Santé en Santé Publique, vol. 33, pp. 67–70.
Perisse, D., Amoura, Z., Cohen, D., Saintigny, P., Mekhloufi, F., Mazet, P.h., Piette, J.C., 2003. Effectiveness of plasma exchange in an adolescent with systemic lupus erythematosus and catatonia. J. Am. Acad. Child Adolesc. Psych. 42, 497–499.
Rapoport, J.L., Inoff-Germain, G., 2000. Update on childhood-onset schizophrenia. Curr. Psychiatry Rep. 2, 410–415.
Rosebush, P.I., Hildebrand, A.M., Furlong, B.G., Mazurek, M.F., 1990. Catatonic syndrome in a general psychiatric population: frequency, clinical presentation, and response to lorazepam. J. Clin. Psychiatry 51, 357–362.
Sporn, A.L., Addington, A.M., Gogtay, N., Ordonez, A.E., Gornick, M., Clasen, L., Greenstein, D., Tossell, J.W., Gochman, P., Lenane, M., Sharp, W.S., Straub, R.E., Rapoport, J.L., 2004. Pervasive developmental disorder and childhood-onset schizophrenia: comorbid disorder or a phenotypic variant of a very early onset illness? Biol. Psychiatry 55, 989–994.
Takaoka, K., Takata, T., 2003. Catatonia in childhood and adolescence. Psychiatry Clin. Neurosci. 57, 129–137.
Taylor, M.A., Fink, M., 2003. Catatonia in psychiatric classification: a home of its own. Am. J. Psychiatry 160, 1233–1241.
Thakur, A., Jagadsen, K., Dutta, S., Sinha, V.K., 2003. Incidence of catatonia in children and adolescents in a pediatric psychiatric clinic. Aus. NZ J. Psychiatry 37, 200–203.
Ungvari, G.S., Leung, C.M., Lee, T.S., 1994. Benzodiazepines and the psychopathology of catatonia. Pharmacopsychiatry 27, 242–245.
Ungvari, G.S., Goggins, W., Leung, S.K., Gerevich, J., 2007. Schizophrenia with prominent catatonic features ('catatonic schizophrenia'). II. Factor analysis of the catatonic syndrome. Prog. Neuro-psychopharmacol. Biol. Psychiatry 31, 462–468.
Wachtel, L., Kahng, S.W., Dhossche, D., Cascella, N., Reti, I.M., 2008. ECT for catatonia in an autistic girl. Am. J. Psychiatry 165, 329–333.
Weissman, M.M., Bothwell, S., 1976. Assessment of social adjustment by patient self-report. Arch. Gen. Psychiatry 33, 1111–1115.
Wing, L., Shah, A., 2000. Catatonia in autistic spectrum disorders. Br. J. Psychiatry 176, 357–362.
Wing, L., Shah, A., 2006. A systematic examination of catatonic like clinical pictures in autism spectrum disorder. Int. Rev. Neurobiol. 72, 22–39.