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## Does catatonia influence the phenomenology of childhood onset schizophrenia beyond motor symptoms?

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### Abstract

Childhood onset schizophrenia (COS) and catatonia (C) are rare and severe psychiatric disorders. The aim of this study was to compare the phenomenology of COS with and without catatonia. We examined 33 cases consecutively referred to two major public university hospitals in Paris. There were 18 cases of COS (age=15.9±0.8 years) and 15 of COS+C (age=15.4±1.4 years). Patients were referred over the course of 3 and 9 years, respectively. Psychiatric assessment included socio-demographic, clinical and psychometric variables: the Brief Psychiatric Rating Scale (BPRS), the Scales for the Assessment of Positive (SAPS) and Negative Symptoms (SANS), and a catatonia rating scale. Patients with COS+C appeared to be more severely ill at admission and discharge compared with COS in nearly all clinical scores. They also exhibited significantly longer episode duration (50.8 weeks±4.8 vs 20.6±19.5). On the basis of multivariate logistic regression, the only clinical measure which significantly predicted group membership was the SANS Affective Flattening score (odds ratio=1.24; 95% CI=1.06–1.43). Our findings strongly suggest that catatonic COS differs from COS in ways that extend beyond motor symptoms. The SANS and SAPS scales, commonly used in schizophrenia, are not detailed enough to accurately describe catatonia in COS. The use of a catatonia rating scale is recommended to enhance recognition of and research into COS with catatonia.

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### 1. Introduction

Childhood onset schizophrenia (COS), defined as onset of schizophrenia before 18 years of age (AACAP,

2001), is rare, but its incidence increases remarkably during adolescence. One percent of schizophrenic disorders manifest themselves before age 10, 4% before age 15 and 20% before age 19 (Loranger, 1990; Remschmidt et al., 1994; Rapoport and Inoff-Germain, 2000). Compared with its adult counterpart, COS is characterized by a greater clinical morbidity, a greater number of negative dimension symptoms (Rapoport and Inoff-Germain, 2000), and often an associated history of pervasive

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developmental disorder (PDD) (Sporn et al., 2004). However, catatonia is not systematically assessed in most studies of COS. We only found one clinical report (Green et al., 1992) which reported that one-third of a sample of 38 patients with COS also presented catatonic and grossly disorganized behavioral symptoms.

Catatonia is a neuropsychiatric syndrome occurring in various psychiatric disorders, neurological diseases, intoxications and metabolic conditions (Cohen et al., 1999). It is defined by the association of motor abnormalities and psychic symptoms. In adults, epidemiological studies using catatonia rating scales found that the prevalence of catatonia ranges from 7.6% to 38% among psychiatric inpatients. The syndrome is more frequent in female patients, and it is usually associated with mood disorders (Taylor and Fink, 2003). Although catatonic schizophrenia is rare, a recent study among 225 adult chronic patients with schizophrenia showed that 32% meet full criteria for catatonia (Ungvari et al., 2005). Subjects in the catatonia group had an earlier age of onset and more negative symptoms. Furthermore, in a multiple linear regression model, the Bush–Francis Catatonia Rating Scale total score was best predicted by the SANS total score and age of onset.

There are few studies on catatonia in the field of child and adolescent psychiatry. Catatonia is an infrequent but severe condition in young people. The prevalence of catatonia ranges from 0.6 to 17.7% in psychiatric inpatients (Cohen et al., 1999; Wing and Shah, 2000; Takaoka and Takata, 2003; Thakur et al., 2003; Cohen et al., 2005). A personal history of PDD is sometimes found in patients with catatonia (Hare and Malone, 2004; Cohen, 2006; Ohta et al., 2006). In the largest prospective series of youths with catatonia, all patients ( $n=5$ ) with a history of PDD exhibited catatonic schizophrenia (Cohen et al., 2005). However, the literature indicates that mood disorders can also be associated with catatonia in young patients with a history of PDD (Ghaziuddin et al., 2005). In contrast to findings in adults, catatonia in children or adolescents is more frequent in boys and, except for one study conducted in Ranchi, India (Thakur et al., 2003), schizophrenia was the most frequent diagnosis associated with catatonia.

In previous work, we have shown that catatonic schizophrenia in adolescence appears to be a clinically relevant but understudied subgroup. We isolated a subgroup of males with schizophrenia in a sample of 30 youths with catatonia who were consecutively referred. In this subgroup, catatonia appeared to be chronic and resistant, with an insidious onset (Cohen et al., 2005). The aim of the current study was to compare the phenomenology of COS with and without catatonia.

## 2. Methods

### 2.1. Patient selection

Patients were selected from the departments of two public university hospitals in Paris, the Department of Child and Adolescent Psychiatry at the Pitié-Salpêtrière Hospital (during the period of 1995–2003), and the Department of Child and Adolescent Psychiatry at the Bicêtre Hospital (during the period of 1999–2003). Every child or adolescent admitted as an inpatient was systematically assessed for catatonic symptoms. At admission or during the course of hospitalization, each patient with COS who presented a motor symptom (Table 1) was examined by one of the four psychiatrists in charge of the study (AC, DC, FC and OB). A diagnosis of COS according to DSM-IV criteria was agreed on by the psychiatrist in charge of the patient and by one other psychiatrist, using a classic consensus diagnostic procedure. Criteria for the diagnosis of catatonia were the presence of at least two catatonic motor symptoms, or one catatonic motor symptom combined with a non-motor catatonic symptom indicative of severe impairment in behavioral and emotional functioning. Patients with COS were recruited consecutively in the same setting but during a shorter time (2000–2003) due to the rarity of COS with catatonia (COS+C) compared with COS. Written informed consent was obtained from the patient and/or the patient's parents before the study.

Table 1  
Catatonia symptom list and symptom frequency in adolescents with childhood onset schizophrenia (COS) without and with catatonia (COS+C)

Motor symptoms		Other symptoms	
Catalepsy	9 (60%)	Social withdrawal	13 (87%)
Stupor	6 (40%)	Mutism	7 (47%)
Posturing	11 (73%)	Mannerism	3 (20%)
Waxy flexibility	9 (60%)	Echolaly	1 (7%)
Staring	9 (60%)	Incontinence	9(60%)
		verbigeration <sup>a</sup>	
Negativism	12 (80%)	Schizophasia <sup>b</sup>	4 (27%)
Stereotypes	10 (67%)	Acrocyanosis <sup>c</sup>	2 (13%)
Psychomotor excitement	9 (60%)	Refusal to eat	10 (67%)
Automatic compulsive movements <sup>d</sup>	11 (73%)		
Echopraxy	1(7%)		
Muscular rigidity	9 (60%)		

<sup>a</sup> Meaningless and stereotyped repetition of words.

<sup>b</sup> Scrambled speech.

<sup>c</sup> Cyanosis of the extremities.

<sup>d</sup> Including grimacing.

Table 2  
Socio-demographic and clinical characteristics of 33 adolescents with Childhood Onset Schizophrenia (COS) without and with Catatonia (COS+C) by diagnosis

	COS (n=18)	COS+C (n=15)	Test score	P	Total (n=33)
Male	15 (83%)	15 (100%)	–	0.23	30 (91%)
vs. Female	vs. 3 (17%)	vs. 0 (0%)			vs. 3 (9%)
Age (years) mean±SD	15.94 (±0.87)	15.46 (±1.46)	–0.64	0.52	15.43 (±1.5)
SES High	2 (11%)	4 (27%)	–	0.31	6 (18%)
vs. Medium	vs. 11 (61%)	vs. 8 (53%)			vs. 19 (58%)
vs. Low	vs. 5 (28%)	vs. 3 (20%)			vs. 8 (24%)
European	13 (72%)	10 (67%)	–	0.73	23 (70%)
vs. non-European origin	vs. 5 (28%)	vs. 5 (33%)			vs. 10 (30%)
Acute onset	4 (22%)	3 (20%)	–	0.88	7 (21%)
vs. Insidious onset	vs. 14 (78%)	vs. 12 (80%)			vs. 26 (79%)
History of PDD: yes	4 (22%)	6 (40%)	–	0.45	10 (30%)
vs. no	vs. 14 (78%)	vs. 9 (60%)			vs. 23 (70%)
Psychiatric family history: yes	6 (33%)	11 (73%)	–	0.04	17 (51%)
vs. no	vs. 12 (67%)	vs. 4 (27%)			vs. 16 (49%)
Episode duration (weeks) mean±SD	20.67 (±19.49)	50.82 (±4.85)	2.79	<0.01	34.37 (±12.8)
GAS score, entry mean±SD	27.22 (±8.04)	17.67 (±7.04)	–3.39	<0.01	22.88 (±8.93)
CGI-S score, entry mean±SD	6.89 (±0.58)	6.87 (±0.35)	0.62	0.66	6.88 (±0.48)
GAS score, discharge mean±SD	42.50 (±15.27)	45.67 (±11.78)	0.43	0.67	43.94 (±13.68)
CGI-S score, discharge mean ±SD	4.89 (±0.83)	5.13 (±1.06)	0.39	0.70	5.00 (±0.94)
BPRS mean±SD	67.11 (±11.40)	88.60 (±10.49)	4.13	<0.01	76.88 (±15.34)
SAPS total score mean±SD	59.94 (±26.06)	83.13 (±22.65)	2.3	0.03	70.48 (±26.89)
SAPS total subjective evaluations mean±SD	10.11 (±3.99)	16.80 (±3.41)	4.03	<0.01	13.15 (±4.99)
SAPS total of sub-scores mean±SD	49.83 (±23.02)	67.00 (±19.68)	2.04	0.50	57.64 (±22.95)
SAPS hallucinations mean±SD	9.33 (±8.42)	17.07 (±4.86)	2.63	0.01	12.85 (±7.95)
SAPS delusions mean±SD	18.50 (±12.52)	20.93 (±6.68)	1.38	0.18	19.91 (±10.22)
SAPS bizarre behavior mean±SD	6.44 (±4.05)	13.73 (±3.39)	4.1	<0.01	9.76 (±5.23)
SAPS positive formal thought disorder mean±SD	15.56 (±4.77)	15.27 (±10.87)	–0.67	0.51	15.42 (±7.98)
SANS total scores mean±SD	69.83 (±25.83)	96.33 (±16.93)	2.80	<0.01	81.88 (±25.68)
SANS total subjective evaluations mean±SD	15.17 (±5.04)	20.47 (±3.70)	2.88	<0.01	17.58 (±5.17)
SANS total of sub-scores mean±SD	54.67 (±21.22)	75.87 (±13.97)	2.84	<0.01	64.30 (±20.97)
SANS affective flattening mean±SD	17.28 (±7.79)	27.27 (±6.49)	3.12	<0.01	21.82 (±8.73)
SANS alogia mean±SD	11.11 (±5.26)	13.93 (±3.51)	1.62	0.12	12.39 (±4.70)
SANS avolition–apathy mean±SD	8.89 (±3.32)	12.87 (±2.39)	3.57	<0.01	10.70 (±3.52)
SANS anhedonia–associability mean±SD	13.17 (±5.47)	16.33 (±4.42)	1.85	0.07	14.61 (±5.20)
SANS attention	4.22 (±2.04)	7.07 (±2.81)	2.92	<0.01	5.52 (±2.79)

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 using Fisher exact tests for qualitative variables and Mann–Whitney tests for continuous variables.

Protocols were approved by the ethics committee of Bicêtre University Hospital.

## 2.2. Clinical and psychometric evaluation

Systematic evaluation carried out within the first week of admission included: (i) collection of socio-demographic data (age, sex, origin and socio-economic status of the family); (ii) semi-structured interview with parents to establish personal and family history of psychiatric and medical disorders (for details, see Taieb et al., 2002); (iii) assessment of COS using the Scale for the

Assessment of Negative Symptoms (Andreasen, 1981) (SANS), the Scale for the Assessment of Positive Symptoms (Andreasen, 1983) (SAPS), and the Brief Psychiatric Rating Scale (BPRS, 18-item version, Overall and Gorham, 1962); (iv) characterization of episode onset ( $\leq 10$  days=acute;  $> 10$  days=insidious) and duration of the episode; (v) description of catatonic signs, using a modified version of the Bush–Francis Catatonia Rating Scale (BFCRS, Bush et al., 1996), as described in a previous article (Cohen et al., 2005) (see Table 1); and (vi) assessment of episode severity using the Clinical Global Impression-Severity (CGI-S) and the Global Assessment

of Functioning (GAF) scales. At discharge each patient was again scored on these scales to evaluate improvement.

During hospitalization, every effort was made to obtain a psychiatric and/or a medical diagnosis. Psychiatric diagnoses were based on DSM-IV criteria and a best estimate procedure. Given the frequency of negativism, mutism or stupor, semi-structured interviews for diagnosis (such as the Kiddie-SADS) are not helpful in instances of these severe clinical presentations. A semi-structured interview with parents assessed developmental and family history (for details, see Taieb et al., 2002). Where there was suspicion of a history of PDD, the Autism Diagnostic Interview — Revised (ADI-R, Lord et al., 1994) was administered. Additional investigations for all patients included routine hematological tests, electroencephalography, and neuro-imaging. Depending on both psychiatric and medical examinations, or in cases of refractoriness to pharmacotherapy, cerebro-spinal fluid examination and appropriate screening tests for the known metabolic causes of the syndrome were performed.

### 2.3. Statistical analysis

Categorical variables are expressed as percentages and continuous variables as mean  $\pm$  1 SD. Comparisons between the two groups were performed using Mann–Whitney tests for continuous variables and Fisher Exact tests for categorical variables. The ability of SANS and SAPS scores to discriminate between the two groups was assessed using a multivariate stepwise logistic regression. All variables which showed significant group effects ( $P < 0.05$ ) in the univariate analysis were included in the model. Because of the small number of patients in the study, the association of the SANS sub-score for affective flattening with symptom scores on the catatonia rating scale was tested using the Jonckheere–Terpstra test. All analyses were performed using SAS software, version 8.2 (SAS Institute, Cary, NC).

## 3. Results

### 3.1. Socio-demographic and clinical characteristics

During the time period of the study (1995–2003 for inclusion of COS+C, and 2000–2003 for inclusion of COS), data from 33 patients were collected. Eighteen (15 male, 3 female) were diagnosed COS without catatonia (mean age =  $15.95 \pm 0.87$  years) and 15 males were diagnosed COS with catatonia (mean age =  $15.47 \pm 1.46$  years). We found no significant statistical dif-

ference for age, sex, ethnic origin, socio-economic status, personal history of PDD, or mode of onset, 79% being insidious. Interestingly, family history was significantly higher in patients with COS+C than patients with COS alone (73% vs. 33%, respectively,  $P = 0.04$ ). All data are presented in Table 2. Regarding COS+C patients, although they were selected by the occurrence of a least two catatonic symptoms including at least one motor symptom, the mean number of catatonic symptoms was  $7.7 \pm 3.7$  (range = 3 to 15). Regarding history of PDD, we found the same proportion of autistic disorders, Asperger syndrome and PDD not otherwise specified (PDD-NOS) in both groups. Of note, all PDD-NOS patients met the criteria for multiplex developmental disorder (MDD) (Klin et al., 1995; Tordjman et al., 1997). The 10 patients with a history of PDD were diagnosed as autistic disorder ( $n = 4$ ), Asperger syndrome ( $n = 1$ ), and TED-NOS ( $n = 5$ ).

Patients with COS+C showed significantly higher scores in all but three global severity indicators. Episode duration was longer for COS+C than COS ( $50.82$  weeks  $\pm 4.85$  vs.  $20.67 \pm 19.49$ ,  $P = 0.0002$ ). For scores on the SANS and SAPS scales, both total scores and most of the sub-scores (SAPS hallucinations, SAPS bizarre behavior, SANS affective flattening, SANS avolition, SANS attention) were significantly higher in the COS+C group compared with the COS group. Only CGI at admission and CGI and GAS at discharge did not show any difference between patients with COS and catatonia (COS+C) and those without catatonia (COS). All data are detailed in Table 2.

### 3.2. Prediction of catatonia using SANS and SAPS sub-scores

Because the SANS and the SAPS are the most commonly used scales for schizophrenia, we wanted to examine the feasibility of using these scales to identify COS+C. We evaluated whether SAPS and SANS sub-score rates predicted to which group (COS or COS+C) a patient belonged. This was done using a multivariate logistic regression analysis, with all sub-scores that showed significant differences between the two groups as independent variables. Only the SANS sub-score for affective flattening appeared to be strongly predictive (odds ratio = 1.24; 95% CI = [1.06–1.43],  $P = 0.0058$ ). The risk of being catatonic increased by a factor of 1.24 for each 1-point increase in the SANS sub-score for affective flattening. When we examined which catatonic symptoms were associated with affective flattening, we found only rigidity showed a significant association (Jonckheere–Terpstra test,  $P = 0.04$ ).

### 3.3. Treatment characteristics

Regarding treatment at discharge, all patients were given an antipsychotic, in the vast majority an atypical one. One patient in the COS group and two patients in the COS+C were given clozapine. The dosage of antipsychotic medication was similar in both groups ( $322 \pm 167$  mg [150–800] vs.  $313 \pm 185$  mg [100–700] in chlorpromazine equivalents in COS and COS+C, respectively;  $P=0.7$ ). Although subjects with catatonia had more additional medications,  $1.07 \pm 1.1$  vs.  $0.56 \pm 0.7$ , this trend did not reach significance ( $P=0.2$ ). In the COS+C patient group, the additional medication was more likely benzodiazepines than in the COS group ( $n=11$  vs.  $n=3$ ,  $P=0.04$ ). Of note, all patients with catatonia had a trial under benzodiazepines. We found no complete remission, but 11/15 subjects were moderately improved. Divalproate was used in four patients in the COS+C group compared with eight patients in the COS group. Furthermore, one patient in each group had ECT. They both were resistant to clozapine, used after lack of improvement with at least two other neuroleptics. In the catatonic group, we also proposed ECT to one 13-year-old boy resistant to chlorpromazine (300 mg/day) or haloperidol (15 mg/day) and lorazepam (5 mg/day) with complications including skin injury, but the parents refused the treatment. A combination of amisulpride (800 mg/day) and pack therapy (envelopment in damp sheets for 1-h sessions), twice a week for 2 months permitted clinical improvement and discharge (details are given in [Cohen, 2006](#)).

## 4. Discussion

### 4.1. Summary of the results and comparisons with previous studies

The current report contributes to a body of literature which confirms that catatonia is one of the most severe and challenging conditions in young people, whether catatonia is studied within patients with a history of pervasive developmental disorder ([Wing and Shah, 2000](#)), whether catatonic schizophrenia is compared with non-schizophrenic catatonia ([Cohen et al., 2005](#)) or whether catatonic schizophrenia is compared with non-catatonic COS (current report). Our results indicate that when catatonia was associated with COS, schizophrenia was more severe, associated with more impairment, and required a longer duration of inpatient care to attain sufficient improvement for discharge. Besides motor symptoms, patients with catatonic COS exhibited more impairment in several clinical dimensions assessed by the

SANS and the SAPS such as hallucinations, bizarre behaviors, affective flattening, avolition and attention. Although direct comparison with early works from Leonhard and his associates is not simple as they use their own classification of catatonic syndrome and schizophrenia, a male subgroup of adolescents with chronic and insidiously progressive schizophrenia was described, although the exact rate of catatonia was not reported ([Leonhard, 1979](#)). We support the view that this patient group should be subject to more specific research as their condition is very challenging for most clinicians.

Indeed, one major implication of our study relies on the fact that the SANS and the SAPS do not capture what catatonia refers to. In the 1980s when the SANS and the SAPS were devised, catatonia was in a dormant state as far as descriptive psychopathology was concerned. Therefore it is no surprise that it was considered beyond the scope of clinicians and researchers alike. In fact, only the SANS affective flattening sub-score predicted catatonia, and this was associated with only one catatonic symptom, rigidity. This means that the SANS scale only encompasses the immobility dimension of catatonia. In sum, the SANS and the SAPS are likely to be poorly predictive of whether patients with COS also present with a catatonic syndrome. Our results therefore argue for the adoption of specific scales to identify catatonic symptoms in patients with COS. It should be noted that this result is not surprising as the SANS and the SAPS were not designed for this purpose ([Andreasen, 1990](#)).

To assess catatonic symptoms, five validated rating scales ([Lund et al., 1991](#); [Bush et al., 1996](#); [Northoff et al., 1999](#); [Peralta and Cuesta, 2001](#); [Kruger et al., 2003](#)) and numerous checklists are available. A list of catatonia symptoms includes from 17 (original description by Ludwig [Kahlbaum, 1874](#); [Kahlbaum, 1973](#)) to more than 40 items ([Fink and Taylor, 2003](#)). Symptoms usually aggregate in two to four dimensions ([Kruger et al., 2003](#)): (1) catatonic excitement, (2) abnormal involuntary movements/mannerisms, also called psychomotor automatism ([Cohen et al., 2005](#)), (3) disturbance of volition/catalepsy, and (4) catatonic inhibition. However, validation is lacking in child and adolescent populations.

### 4.2. Strengths and limitations of current study

The major weakness of the current study is its sample size. This is due to the rarity of COS, especially its catatonic form. However, the design of the study with the inclusion of all consecutively referred cases during 9 years for COS+C and 3 years for COS, in two child and adolescent psychiatry departments, is a strong argument

for the representativeness of the sample. Sample size may be one reason for low statistical power.

Two other limitations may be noted: (i) our pooling procedure by junior psychiatrists combined with the duration of the entire study (9 years) may be responsible for missing cases; and (ii) the choice of a consensus diagnostic procedure excluded the possibility of calculation of inter-rater reliability statistics for diagnosis. However, we note that we have just finished a 5-year follow-up study of the catatonic group, and that for patients with COS at inclusion we found a 100% confirmation rate of the original diagnosis of schizophrenia, using the Diagnostic Interview for Genetic Studies for lifetime diagnosis (authors' unpublished data).

#### 4.3. Implications

In summary, our findings strongly suggest that (i) catatonic COS differs from COS in non-motor symptoms; (ii) the SANS and the SAPS, which are commonly used scales in schizophrenia, even though they are diagnostically non-specific, are not sufficiently precise to describe and assess catatonia in COS. The use of a catatonia rating scale is recommended to enhance recognition of COS+C and specific research should be conducted with this population.

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