Multidisciplinary approach of organic catatonia in children and adolescents may improve treatment decision making

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1. Introduction

Catatonia is a rare and severe psychiatric syndrome. It is defined by the association of motor abnormalities (stupor, excitement, posturing, catalepsy, negativism, waxy flexibility, and stereotyped movements) and psychic symptoms (mutism, social withdrawal, mannerism, echolaly, verbigeration, schizophrenia). Several variations can be distinguished (Cohen et al., 2005; Taylor and Fink, 2003): stuporous catatonia, excited catatonia, malignant catatonia and psychomotor automatism. 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, is usually associated with mood disorders (Taylor and Fink, 2003), and can occur in organic conditions (Cottencin et al., 2007). In the field of child and adolescent psychiatry, several studies suggested a prevalence range from 0.6% to 17.7% (Thakur et al., 2003; Cohen et al., 2005). While the symptomatology and associated disorders are similar to those reported in the adult literature, findings differ with regard to the female-to-male ratio and the relative frequencies of associated disorders. Catatonia in children or adolescents is more frequent in boys (Takaoka and Takata, 2003) and schizophrenia is the most frequent associated diagnosis (Cormic et al., 2007). When encountered in child and adolescent clinic, the disease must lead to specific investigations, because its etiology often reveals among psychiatric presentations, various organic diseases: neurologic diseases, intoxications and metabolic conditions (Cohen et al., 1999). The state for clinical practice resides in the potential display of a curative treatment of the underlying affection. It concerns the prognosis, by the perspective of the psychiatrist (to give the opportunity to treat the catatonic state with the treatment of the organic aetiology), but also by the perspective of the neurologist (by the recognition of psychiatric state ushering the neurologic symptoms and therefore highlighting the development of the organic condition). Besides, the diagnosis of the organic condition appears essential regarding the severity and the possible lethality of the underlying states in organic catatonia (Ainsworth, 1987; Dimitri et al., 2006).

The aims of the current study were (1) to list case reports of catatonia due to organic conditions in youth and to spot clinical characteristics and organic aetiology, and (2) to formulate recommendations and guidelines including which investigations and clinical manifestations may help determination of a cause and therefore treatment decision making.

2. Method

We conducted a literature search in the Medline database for all reports associated with the following key-words: catatonia and/or catatonic syndrome, and children and/or adolescent. Corresponding references were then studied to determine whether cases corresponded effectively to both catatonia and organic condition criteria, and therefore could be included in this study. During the period that extended from January 1969 to June 2007, a total of 90 references were collected, among which we selected reports including medical conditions. We also performed a manual search of reference lists of the selected papers and of all reviews on catatonia in youths. In total, 30 papers mostly single case report or series were selected. We also included three patients admitted and treated in our Department. Two were reported in a follow-up study presented at an international meeting (Cornic et al. 2006). This led to a total of 38 patients to be reviewed (Table 1). Data were extracted according to a screening collecting socio-demographic characteristics (sex, age), organic diagnosis, clinical characteristics of the catatonic syndrome according Taylor and Fink classification adapted for children and adolescent (Cohen et al., 2005), and treatment. Based on this literature review, a multidisciplinary group including experienced child psychiatrists (DC, OB, AC), one adult psychiatrist (FC), neurologists keen on epilepsy (IA) and neurometabolism (FS), and one internist (ZA), all involved in catatonic research formulated guidelines for investigation and recognition of potential organic causes in youth catatonia. These guidelines include all the cases found in the literature, but also other rare metabolic diseases that should be known by child and adolescent psychiatrists as they were identified as possible treatable causes of catatonia in youth.

3. Results

3.1. Characteristics of patients

The literature review collected 38 cases of children and adolescents with catatonia due to an organic condition reported from January 1969 to September 2007. The catatonic syndrome occurred in 21 (57%) females and 16 (43%) males. The mean age of patients was 14.5 years (range=7–18 years) and only six patients were younger than 11. Three patients died from their condition: the first had encephalitis (Ainsworth, 1987), the second had venous cortical thrombosis (Gangadhara et al., 1983) and the third had Fatal Familial Insomnia that is a rare autosomal dominant condition belonging to the prion disease group (Dimitri et al., 2006). All organic conditions encountered are listed in Table 1. They were classified as follow: infectious diseases (N=10), mainly typhoid and viral encephalitis; neurologic conditions (N=10) with complex seizures and auto-immune conditions with cerebral tropism being the most frequent; toxic induced states (N=12) that may be either secondary effects of treatments (e.g., closporin) or consequences of prohibited drugs (e.g., ecstasy); and finally, genetic conditions (N=6) including inborn errors of metabolism.

3.2. Clinical characteristics

Apart from few specific symptoms of the underlying organic condition (see details in Table 1), clinical characteristics of the catatonic syndrome were as follow: (1) onset was dominantly acute (96%); (2) using Taylor and Fink modified classification of catatonia, we distinguished 27 (73%) stuporous catatonia, 7 (19%) excited catatonia, 2 (5%) malignant catatonia and one case of psychomotor automatism with a progressive onset.

Regarding associated psychiatric diagnosis, in 19 cases, the only psychiatric diagnosis reported was catatonia. In the remaining 18 cases, 6 received a diagnosis of psychosis or brief psychotic disorder, 6 of psychotic depression, 3 of schizophrenia and 2 of delirium. The last 16 patient had Attention Deficit Hyperactivity Disorder associated with Obsessive–Compulsive symptoms due to a PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections).
### Table 1

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>N</th>
<th>Sex</th>
<th>Age</th>
<th>Clinical characteristics</th>
<th>Authors, year</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infectious diseases (N=10)</strong></td>
<td></td>
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<tr>
<td>Typhoid</td>
<td>4</td>
<td>2M</td>
<td>2F 7-17-</td>
<td>Acute onset (N=4) Stuporous catatonia (N=2)</td>
<td>Breakkey &amp; Kala (1977)</td>
</tr>
<tr>
<td>Viral encephalitis</td>
<td>4</td>
<td>1M</td>
<td>14-13-</td>
<td>Acute onset (N=4) Stuporous catatonia (N=4)</td>
<td>Ainsworth, 1987</td>
</tr>
<tr>
<td><strong>Neurological conditions (N=10)</strong></td>
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<tr>
<td><strong>Toxic induced states (N=12)</strong></td>
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</tr>
<tr>
<td>Corticotherapy</td>
<td>2</td>
<td>2M</td>
<td>17-11</td>
<td>Acute onset (N=2) Stuporous catatonia (N=2)</td>
<td>Sullivan &amp; Dickerman (1979), Doherty &amp; Doherty (1991)</td>
</tr>
<tr>
<td>Chlorphenamine maleate</td>
<td>1</td>
<td>1M</td>
<td>17</td>
<td>Acute onset Stuporous catatonia (N=2)</td>
<td>Johnson &amp; Lucey (1987)</td>
</tr>
<tr>
<td>Ciclosporin</td>
<td>1</td>
<td>1F</td>
<td>14</td>
<td>Acute onset Stuporous catatonia (N=2)</td>
<td>Unpublished</td>
</tr>
<tr>
<td>Ecstasy</td>
<td>3</td>
<td>1M</td>
<td>17-17-2F 16</td>
<td>Acute onset (N=3) Stuporous catatonia (N=3)</td>
<td>Maxwell et al. (1993), Masi et al. (2002)</td>
</tr>
<tr>
<td>Phencyclidine</td>
<td>1</td>
<td>NR</td>
<td>NR</td>
<td>Non Specified Stuporous catatonia (N=2)</td>
<td>Unpublished</td>
</tr>
<tr>
<td>Lithium</td>
<td>1</td>
<td>1F</td>
<td>16</td>
<td>Acute onset Stuporous catatonia (N=1)</td>
<td>Unpublished</td>
</tr>
<tr>
<td>Other toxic</td>
<td>2</td>
<td>1M</td>
<td>16-17</td>
<td>Acute onset Stuporous catatonia, acute onset (N=2) Drug inhaled induced delirium (N=2)</td>
<td>Lee (1998), Lee &amp; Masi et al. (2000)</td>
</tr>
<tr>
<td>Anaphylactic shock</td>
<td>1</td>
<td>1F</td>
<td>12</td>
<td>Acute onset Stuporous catatonia Neurologic signs</td>
<td>Pranzatelli et al. (1994)</td>
</tr>
</tbody>
</table>

**NR** = Not reported; *Acute defined as ≤15 days; chronic as ≥16 days; subtypes of catatonia were as follow: stuporous – excited – malignant – psychomotor automatism defined as automatic movements secondary to hallucinations being the most prevalent symptom (Cohen et al., 2005).

As for the organic examination, symptoms could be observed in 19 patients, such as fever (N=5), neurological symptoms (N=7), confusional states (N=4), hyponatremia (N=2) and hepatomegaly (N=1).

### Table 1 (continued)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>N</th>
<th>Sex</th>
<th>Age</th>
<th>Clinical characteristics</th>
<th>Authors, year</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Genetic conditions (N=6)</strong></td>
<td></td>
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</tr>
<tr>
<td>Prader-Willi syndrome</td>
<td>1</td>
<td>1M</td>
<td>17</td>
<td>Acute onset Stuporous catatonia (N=2)</td>
<td>Dhosiche &amp; Bounam (1997)</td>
</tr>
<tr>
<td>Fatal familial Insomnia</td>
<td>1</td>
<td>1M</td>
<td>18</td>
<td>Acute onset Stuporous/excited catatonia</td>
<td>Dimitri et al. (2006)</td>
</tr>
<tr>
<td>Huntington disease</td>
<td>1</td>
<td>1M</td>
<td>17</td>
<td>Progressive onset Psychomotor automatism</td>
<td>Unpublished, Corn (et al, 2006)</td>
</tr>
<tr>
<td>Tay-Sachs disease</td>
<td>1</td>
<td>1M</td>
<td>17</td>
<td>Progressive onset Stuporous catatonia</td>
<td>Rosebush et al. (1995)</td>
</tr>
<tr>
<td>Wilson disease</td>
<td>1</td>
<td>1M</td>
<td>12</td>
<td>Acute onset Stuporous catatonia</td>
<td>Davis &amp; Borde (1993)</td>
</tr>
<tr>
<td>Storage disease</td>
<td>1</td>
<td>1M</td>
<td>16</td>
<td>Acute onset Excited catatonia</td>
<td>Unpublished, Corn (et al, 2006)</td>
</tr>
</tbody>
</table>

4. Discussion

4.1. Summary of the current review

The current review demonstrates that organic conditions can occur in children and adolescents catatonia and may lead to death. Although...
catatonia is rare in children and adolescents, the proportion of organic causes is high for a psychiatric condition. First, Cornic et al. (2006) reported 6 organic conditions among a consecutive series of 35 patients, leading to a rate of 16%. Second, the largest review of literature of youth catatonia (Takaoka and Takata, 2003) listed 73 cases published during the period 1982–2002 including 17 cases due to an organic condition leading to a rate of 23%. Given that there is probably a bias in reporting organic cases, an estimation of the proportion of organic condition in catatonic syndromes in youth could be 15–20%. Furthermore, the review highlights that organic catatonia is not just a subtype of catatonia. Sex ratio and associated psychiatric diagnosis differs from children and adolescents non-organic catatonia, with more female than male and more acute psychosis and psychotic depression than schizophrenia in the organic group, whereas a reversal pattern is found in the non-organic group (Takaoka and Takata, 2003; Cornic et al., 2007). However, whether organic catatonia differs from non-organic ones in terms of physiopathology, response to symptomatic treatment of catatonia, prognosis and course, need to be explored although prognosis and course is linked to the accessibility of an efficient treatment towards the organic cause.

Benzodiazepines (e.g., lorazepam) or other sedative drugs and antiparkinsonism drugs (e.g., amantadine) may prove useful on catatonic manifestations and should be the first treatment option. In adult, these treatments have been shown to be helpful (Taylor and Fink, 2003). However, in the current review the poor reporting of benzodiazepine prescription highlights that the indication of these drugs in catatonia is not well known in child and adolescent psychiatric practice. In case of resistance, ECT is usually efficient on catatonia (Taylor and Fink, 2003). Finally, treatment of the underlying organic affection, when available, may be efficient as well but a rapid diagnosis is needed given the severity of most catatonic states.

4.2. Clinical contribution of a multidisciplinary approach for recognition of organic underlying condition

Fig. 1 states the general guidelines (Cornic et al., 2007) for aetiological diagnosis and treatment orientation in catatonia formulated by a multidisciplinary group of physicians all involved in treatment and research in the field of catatonia.

(1) To address organic conditions, both careful medical examination, including accurate neurological examination, and psychiatric examination are warranted to identify and rule out treatable medical disorders.

(2) Regarding psychiatric investigations, some psychiatric manifestations are useful items for clinical orientation: type of onset, acute or insidious, mood symptoms, hallucinations, and delusions. Confusion and subtype of catatonia – stupor – should be considered, as they are the most common features in organic catatonia (Table 1). The psychiatric and medical history of the family and the patient should be collected as well as the medications used or the drug consumption. The use of catatonia rating scales to monitor symptoms should be recommended. Five validated rating scales are available in adults (Bush et al, 1996; Kruger et al, 2003; Northoff et al, 1999; Cuesta and Peralta, 2001; Lund et al, 1991) but can be used in adolescents, as well (Cohen et al, 2008).

(3) Regarding somatic manifestations, some symptoms should be actively searched in the development of the catatonic somatopathology, or in the amenity of the patients, as they may orient diagnosis, through the identification of actual clinical manifestations (e.g., seizures, fever or encephalopathy), or through the existence or discovery of an evolutive organic condition (e.g., lupus erythematosus symptoms; Keiser–Fleisher corneal ring; dysmorphism; mental retardation). In summary, somatic survey will consider general examination and issuing, neurologic and ophthalmologic examination.

(4) Paraclinical investigations should be led by clinical data. First line tests will complete or precise the clinical approach (see below).

Determination of organic condition type from somatic and psychiatric examination is not immediate, as pathognomonic symptoms are rare. Neurologic manifestations are omnipresent, and it should be distinguished whether they rely on neurological specific condition, or are

**Fig. 1.** Catatonia in children and adolescents: a multimodal framework for evaluation and treatment (PDD = pervasive developmental disorder; NLP = neuroleptic drug; SCZ = schizophrenia; ECT = electro-convulsive therapy) (adapted from Cornic et al., 2007).

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Inborn errors of metabolism that may present as catatonic states in children and adolescents: clinical characteristics and screening tests (adapted from Sedel et al, 2007)

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Psychiatric signs</th>
<th>Neurological signs</th>
<th>Systemic signs</th>
<th>Screening tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatable diseases</strong></td>
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<tr>
<td>Urea cycle disorders</td>
<td>Attacks of confusion, bizarre behaviour, delusion triggered by high protein intake or situations of protein catabolism</td>
<td>Stroke like episodes (diplopia, hemiparesis), pyramidal signs, epilepsy, coma.</td>
<td>Nausea, vomiting, cephalalgia</td>
<td>Ammoniemia</td>
</tr>
<tr>
<td>MTHFR deficiency</td>
<td>Mild mental retardation, confusion, depression, psychosis</td>
<td>Coma, pyramidal syndrome (subacute degeneration of the cord), peripheral neuropathy, strokes.</td>
<td>Thromboembolic events</td>
<td>Homocysteinemia</td>
</tr>
<tr>
<td>Chls</td>
<td>Mild mental retardation, confusion, depression, psychosis</td>
<td>Pyramidal signs (subacute degeneration of the cord), peripheral neuropathy, optic atrophy.</td>
<td>Retinitis pigmentosa, glomerular nephritis, thromboembolic events.</td>
<td>Homocysteinemia</td>
</tr>
<tr>
<td>Acute porphyrias</td>
<td>Episodes of confusion, psychosis, depression</td>
<td>Acute peripheral neuropathy, epilepsy</td>
<td>Intestinal problems (pain, constipation), dysautonmia, dark urines, cutaneous signs (coproporphiria and porphyria variegata)</td>
<td>Urinary porphobiligen</td>
</tr>
<tr>
<td>Wilson’s disease</td>
<td>Disorders of behaviour and personality, depression. Rare cases of psychosis</td>
<td>Movement disorders, dysartria</td>
<td>Corneal Kayser–Fleischer ring, chronic liver disease</td>
<td>Ceruleoplasmine, cupremia, cupuria Sterol HPLC</td>
</tr>
<tr>
<td>Cerebrotendinous xanthomatisis</td>
<td>Rare cases of psychosis</td>
<td>Cerebellar ataxia, spastic paraparesis, dementia, peripheral neuropathy, parkinsonism</td>
<td>Juvenile cataract, xanthomas, chronic diarrhoea</td>
<td></td>
</tr>
<tr>
<td><strong>Non treatable diseases</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metachromatic leukodystrophy</td>
<td>Psychosis like features (mimicks schizophrenia)</td>
<td>Cognitive troubles, spastic paraparesis, cerebellar ataxia, demyelinating polyneuropathy.</td>
<td>None</td>
<td>Arylsulfatase A</td>
</tr>
<tr>
<td>GM2 gangliosidosis</td>
<td>Episodes of psychosis, depression, mania</td>
<td>Lower motoneuron disease, cerebellar ataxia, pyramidal signs, dystonia, sensitive polyneuropathy.</td>
<td>Dysautonmia</td>
<td>Hexosaminidases</td>
</tr>
<tr>
<td>Niemann Pick disease type C</td>
<td>Psychosis, depression, mania</td>
<td>Cognitive troubles, cerebellar ataxia, vertical oculonmotor apraxia, movement disorders (dystonia, myoclonus)</td>
<td>Splenomegaly, hemotegaly</td>
<td>Filipin staining</td>
</tr>
</tbody>
</table>

We consider that a systematic search of the treatable diseases is necessary even if most of these conditions are rare. Indeed, treatment at the “psychiatric stage” before the occurrence of neurological symptoms, can lead to higher frequency of reversal of symptoms (Sedel et al, 2007).
4.3. Summary of paraclinical investigations to screen organic conditions in isolated youth catatonia

As a consequence of these organic implications, the clinical encounter with a catatonic syndrome should lead to clinical and paraclinical investigations. Accurate organic diagnosis and treatment indication relies upon internists and neurologists. Unless examination is positive and suggest specific paraclinical investigations, first line ones should be sufficient to determine whether the hypothetical medical condition consists in an acute or a chronic situation, and so adapt treatment decision making. Taking into account the contribution developed above, our recommendations to screen organic conditions associated with catatonia are presented in Table 3.

5. Conclusion

This review stresses upon the fact that catatonic syndromes can be observed in children and adolescents in association with organic diseases. These are rare but severe and potentially lead to lethal conditions. Set aside the interest of orienting the aetiologic diagnosis, this fact implies necessary inquiries for the clinician, in order not to neglect the perspective of treatment of the organic causal disease. The stakes are important, relying upon psychiatric symptoms reduction, but also hindering the course of metabolic or neurological diseases. Several basic investigations should be realised, lead by anamnesis, neurological and systemic symptoms, and may assist the clinician enlightened by these considerations.

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