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Catatonia is not schizophrenia and it is treatable

Francisco J. Appiani [a,*], Gonzalo S. Castro [b]

[a] Program of Pharmacology, Direction of Teaching and Research, Hospital de Clínicas José de San Martín, Universidad de Buenos Aires, Buenos Aires, Argentina
[b] Fellowship in abnormal movements, Program of Abnormal Movements and Parkinson disease, Neurology Division, Hospital de Clínicas José de San Martín, Universidad de Buenos Aires, Buenos Aires, Argentina

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ABSTRACT

Catatonia is a cluster of motor features that appears in many recognized psychiatric illnesses, that according to the DSM-5 it is not linked as a subtype to schizophrenia anymore. The classic signs are mutism, a rigid posture, fixed staring, stereotypic movements, and stupor, which are all part of a broad psychopathology that may be found in affective, thought, neurological, toxic, metabolic and immunological disorders. Despite the many etiologies, catatonia may be a life-threatening condition with a specific treatment. Benzodiazepines are the first line therapeutic option for catatonia, being lorazepam the first-choice drug. Eighty percent of the patients are relieved by the use of barbiturates or benzodiazepines, while in those who fail, an improvement is achieved by electroconvulsive therapy (ECT). With more than 60 years of use in catatonic patients, ECT has proven to be an effective and safe tool for the treatment of this frequent and sometimes forgotten syndrome.

1. Introduction

Psychomotor symptoms in psychiatric disorders have been a controversial issue in modern psychiatry. Karl Ludwig Kahlbaum (1828–1899) was the first psychiatrist to clearly associate psychomotor symptoms to psychiatric disorders.

Since Kahlbaum's first description of catatonia there were many different positions about this entity (Caroff et al., 2004). Kahlbaum syndrome refers to the most common presentation of retarded catatonia, generally with a favorable outcome, named "Atonic melancholia". According to his descriptions, the patient has a melancholic prodromal state, followed by impairment of thought, associated to choreiform movements that limit his ability to carry out voluntary movements (Fink and Taylor, 2003).

Emil Kraepelin inserted catatonia as a subtype of his Dementia praecox classification. Despite the clinical reality of Catatonia syndrome, the inclusion in Dementia Praecox and then in Schizophrenia nearly erased the original concept of Kahlbaum's catatonia and remained associated to schizophrenia during many decades. As presented below, this situation was not only a nosography dilemma but it has therapeutic implications.

Other authors like Karl Wernicke put Catatonia closer to neurology nosology. He was convinced that the whole pathology of mental patients consists of nothing else but the peculiarities of their motor behavior. He coined the term psychomotor disturbances referring to abnormalities of motion and speech which were independent from thought and will (Pfuhlmann and Stüber, 2001).

Karl Leonhard and Karl Kleist were clinicians who continued and delineated Wernicke's ideas. They established a new nosology of what they called "endogenous psychosis" with emphasis in catatonic symptoms as "motility symptoms". K. Leonhard described acute (and benign) catatonia (Cycloid Psychosis) separated from those chronic and refractory to treatment (systematic schizophrenias) (Teichmann, 1990). This clinical observation is relevant, because there are descriptions of treatment refractory patients in those with chronic catatonia presentations (Ungvari et al., 1999).

Nowadays a group of scholars led by Fink et al. had been working in the recognition of catatonia syndrome as a different clinical entity. According to clinical and basic research, catatonia is a cluster of motor features that appears in many recognized psychiatric illnesses. The classic signs are mutism, a rigid posture, fixed staring, stereotypic movements, and stupor, which are all part of a broad psychopathology that includes most of the major diagnostic classes (Bleckwenn, 1930). Psychomotor symptoms may be found in affective, thought, neurological, toxic, metabolic and immunological disorders. Clinical forms may be transient or "benign", with a good response to specific treatment, and it can also have a malignant course like in Stauder's catatonia, neuroleptic malignant syndrome and toxic serotonin syndrome (Fink and Taylor, 2003). It is necessary to highlight that the fifth version of the Diagnostic and Statistical Manual of Mental Disorders (DSM 5), published by the American Psychiatric Association, removed the diagnosis of catatonic schizophrenia. Instead catatonia is a specifier for schizophrenia as it is for mood disorders.

* Corresponding author.
E-mail address: Franciscoappiani@live.com.ar (F.J. Appiani).

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DSM 5 also added catatonia as a specifier for brief psychotic disorder, schizophreniform disorder, schizoaffective disorder and in substance-induced psychotic disorder.

Before DSM-5, Catatonia was restricted to sections of the psychotic, affective, or medical disorders in adult patients. During the last few years, progress has been made in delineating this syndrome in children and adolescents across a wide range of disorders. Dirk Dhossche and his group have showed that catatonia may be present in children and adolescents with autistic, developmental, and tic disorders, and in its idiopathic form, with a similar response to treatment like in adult patients. Finally DSM-5 included catatonia as a specifier in autistic spectrum disorders.

The study of pediatric catatonia supports a home of its own for catatonia in DSM-5. (Dhossche et al., 2010a). (Dhossche et al., 2010b).

Catatonia can also be diagnosed as a consequence of medical condition and as catatonia not otherwise specified NOS (American Psychiatric Association, 2013).

In summary, catatonia is a treatable syndrome secondary to many etiologies that it is not linked as a subtype to schizophrenia anymore.

1.1. Treatment of catatonic syndrome

Despite the many etiologies, catatonia has a specific treatment. Today, benzodiazepines are among first line treatment options for catatonia. The effectiveness of these compounds in the treatment of catatonic syndrome was first reported in 1930. W. J. Bleckwenn found that intravenous administration of amobarbital sodium produced a transient response in three catatonic patients (Bleckwenn, 1930). Barbiturates, according to a study done in 1992 (McCall et al., 1992), have a response rate of 50% in patients with catatonia, but due to its narrow therapeutic index they are not used anymore. Today, benzodiazepines are considered as an alternative with higher safety margins and are the first line treatment for this clinical entity.

1.2. Benzodiazepines

Though several hypotheses have been proposed, the molecular mechanism of catatonia remains unknown. Given the efficacy of BZD (a GABA-A agonist), in relieving catatonia, hypoactivity at GABA-A receptors was one of the most discussed molecular mechanisms involved in the pathogenesis of catatonia (Northoff et al., 1999).

Lorazepam is used at doses between 8 and 24 mg daily (https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=lorazepam, 2017), and is generally well tolerated without causing sedation, especially when daily incremental doses are performed. In case a higher dosage is chosen, the patient should be monitored for excessive sedation, which tends to occur earlier than respiratory compromise (Sienaert et al., 2014). Most authors suggest starting lorazepam at 1–2 mg every 4 to 12 h so as to avoid sedation (Daniels, 2009), and response is usually seen within 3–7 days, although might be gradual and slow.

It appears certain benzodiazepines are more effective for catatonia, and thus lorazepam is accepted to be a first-choice drug, with highest frequency of use. Successful use of diazepam, oxazepam or clonazepam has also been reported (Dhossche et al., 2014) (Table 1).

1.3. Indications and efficacy

The dramatic experience that established lorazepam as an effective drug for catatonia took place in 1983, when Gregory Fricchione described the rapid relief of neuroleptic malignant syndrome (NMS) by intravenous lorazepam at Massachusetts General Hospital. After various treatment options failed to produce any improvement, intravenous lorazepam in 2-mg doses was administered. NMS tended to resolved within a day, with some symptoms resolving within hours.

By 1996, a systematic study established the lorazepam sedative test as a diagnostic verification of catatonia (Bush et al., 1996a).The patient should be first examined for catatonic sigs, and then 1 or 2 mg of lorazepam should be administered intravenously. After 5 min, a re-examination of the patient must be done, and a second dose should be given in case no changes were observed (Bush et al., 1996b). The authors suggested as a clinical guide that a positive response to treatment may be considered when a reduction of at least 50% of catatonic signs and symptoms are observed using the Bush Francis catatonia Rating Scale (BFCRS) standardize rating scale, which usually occurs within 10 min (Fink and Taylor, 2003) unless the administration is via intramuscularly or per os, when the interval should be around 150 and 300 min respectively (Bush et al., 1996b).

Nowadays treatment with lorazepam is considered highly effective, easy and safe, and more than 80% of the patients are relieved by the use of barbiturates or benzodiazepines, while in those who fail, an improvement is achieved by ECT (Bush et al., 1996b; Fink and Taylor, 2003). This was described using high doses of lorazepam (6–16 mg/day) for 3–5 days, but in some cases dosages up to 30 mg/day may be necessary (Fink and Taylor, 2009). Hung et al. reported remission rates as high as 79% in seven catatonic patients suffering from major depression (Hung and Huang, 2006), while in another major study (n:107) two thirds responded but only half of them remitted (Tibrewal et al., 2010). According to Lin Chin-Chuen, describing intramuscular lorazepam or intravenously diazepam response in 68 instances of relapses and recurrences of catatonia, a full recovery was shown in most instances (79.4%) (Lin et al., 2016).

There is no consensus on how long benzodiazepines should be continued, and generally they are maintained until the underlying illness has remitted. Relapse into a catatonic state can occur if benzodiazepines are discontinued before the underlying disorder is resolved (Rasmussen et al., 2016; Rosebush et al., 1994).

1.4. Poor outcome predictors

Several studies have shown that benzodiazepines are effective on acute catatonia and in those cases of retarded catatonia related to diverse psychiatric, neurologic or medical disorder, but less when associated with schizophrenia. In a 5-year follow-up study, Beckmann et al. found benzodiazepines ineffective in the treatment of chronic catatonic schizophrenia (Beckmann et al., 1992), and similar outcomes were published in a randomized double-blind, placebo-controlled trial in 18 patients with chronic catatonia in schizophrenia (Ungvari et al., 1999). The poorer prognosis in patients with schizophrenia under treatment with lorazepam may be related to the chronicity of symptomatology, or it may suggest a distinct underlying pathophysiology, perhaps reflecting the prominence of psychosis affecting their motor behavior, like in systematic schizophrenias described by Karl Leonhard (Beckmann et al., 1992; Leonhard, 1986; Rasmussen et al., 2016; Rosebush et al., 1994).

According to Fink, prognosis is particularly favorable when catatonic syndrome is dominated by hyperactivity, rapid and pressured speech, stupor and lability of mood, as well as the history of a previous episode with complete recovery, rapid onset of the catatonic state and good social functioning before the episode (Fink, 2001; Fink and Taylor, 2003).

Table 1
Rates to response to lorazepam treatment in catatonic patients with various underlying diagnoses[22].

Diagnosis	Patients responding (%)
Bipolar disorders ($n = 31$)	97
Unipolar depression ($n = 30$)	93
Other psychoses ($n = 24$)	92
Medical/neurological conditions ($n = 11$)	82
Schizophrenia ($n = 22$)	59

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