

Catatonia and neuroleptic malignant syndrome : two sides of a coin ?

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Abstract

Catatonia was first described by Kahlbaum in 1874. Ever since, the concept of catatonia has been the focus of debate, a major point of discussion being its nosological status. The question rises whether it is to be considered a syndrome with a wide variety of causes and clinical signs or a distinct clinical entity. Since catatonia shares a number of symptoms with the neuroleptic malignant syndrome (NMS) and similar treatments can be used in both conditions, it has also been suggested that NMS and catatonia are two variants of the same disorder. In this article we describe five cases of catatonia and NMS in order to approach this nosological question. The clinical similarity between both syndromes is demonstrated in our cases. On the level of pathophysiology however, catatonia and NMS are quite different, with catatonia rather being a cortical psychomotor syndrome and NMS a subcortical motor disorder. Similarities can be explained by means of well-known models of basal ganglia function. The nosological problem, however, can only be resolved when the concept of catatonia is better defined.

Key words : Catatonia ; neuroleptic malignant syndrome ; neuroleptics ; benzodiazepines ; fronto-subcortical circuits.

Introduction

The concept of catatonia, literally meaning “to stretch tight”, goes back to the original description by Karl Ludwig Kahlbaum in 1874. In his monograph Kahlbaum characterized catatonia as a motor disorder representing a phase in an illness that progresses from mania, depression and psychosis to a final end stage of dementia (Kahlbaum, 1974 ; Fink and Taylor, 2001). Due to the ideas raised by Kraepelin and Bleuler, the concept of catatonia was embedded into the classification of schizophrenia (Pfulmann and Stöber, 2001). Although numerous authors raised arguments against this view, the idea of catatonia as a subtype of schizophrenia persisted throughout the 20th century and was adopted in all DSM versions, including DSM-IV. Nevertheless, apart from its association with psychotic disorders, catatonia has been described in general medical conditions (medical catatonia), and most frequently

in mood disorders (especially mania) (Taylor and Fink, 2001 ; Peralta *et al.*, 1997). A major point in the discussion is the nosological status of catatonia ; is it to be considered an aspecific syndrome with a panoply of possible clinical signs and symptoms (Table 1) or is it a separate entity for which proper diagnostic criteria should be developed, as suggested by Taylor and Fink (2003) (Table 2).

Since the introduction of neuroleptics, the incidence of catatonia has decreased significantly (Northoff, 1997). However, it became clear that administration of neuroleptics could eventually lead to catatonia-like symptoms (Bush *et al.*, 1996), as is the case in neuroleptic malignant syndrome (NMS). NMS shares with catatonia a number of symptoms e.g. immobility, rigidity and stupor (Koch *et al.*, 2000). Moreover, treatment strategies applied to catatonic patients may also be beneficial to NMS patients. Therefore, some have suggested that NMS and catatonia are variants of the same disorder (Fink and Taylor, 2001).

We will report on five cases of catatonia and NMS and discuss the issue of classification of both entities.

Case reports

CASE 1

This 55-year old man sustained a severe traumatic brain injury. He was in a coma for one week after which he was left with an organic brain syndrome. Due to a severe behavioral disorder treatment with multiple neuroleptics was necessary.

One year after his head injury he came to the emergency room for an erysipelas for which antibiotic treatment was started. At that moment he was treated with risperdone and pimozide. On admission he did not respond adequately, was extremely apathetic and his consciousness was found to be decreased. Generalised muscular rigidity was found, as well as elevated body temperature. Levels of creatin kinase were also raised, supporting a diagnosis of neuroleptic malignant syndrome. Neuro-imaging demonstrated aspecific and mild cortical-subcortical atrophy.

Table 1
Clinical signs in catatonia

<i>Motor signs</i>	<i>Cognitive-behavioral signs</i>
akinesia, bradykinesia, hypokinesie, hyperkinesias, rigidity, catalepsy, gegenhalten, paratonia, primitive reflexes, perseverations, impulsivity, tics	Negativism, posturing, grimacing, stereotypies, psychosis, manic behaviour, agitation, withdrawal, regression, mannerisms, rituals, utilization behaviour, imitation behaviour, echopraxia, automatic obedience

Table 2
Proposed diagnostic criteria for catatonia, as proposed by Fink and Taylor (2003)

<p>A. Immobility, mutism, or stupor of at least 1 hour's duration, associated with at least one of the following :</p> <ul style="list-style-type: none"> - catalepsy - automatic obedience - posturing <p>observed or elicited on two or more occasions.</p>	<p>B. In the absence of immobility, mutism, or stupor, at least two of the following :</p> <ul style="list-style-type: none"> - stereotypy - echophenomena - catalepsy - automatic obedience - posturing - negativism - gegenhalten - ambitendency <p>observed or elicited on two or more occasions</p>
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Neuroleptic treatment was stopped and a treatment regimen with 10 mg t.i.d. bromocriptine, 100 mg t.i.d. dantrolene and 2 mg clonazepam IV was started. The creatin kinase level normalized and the clinical image improved gradually over a period of two of weeks. The patient was transferred to a psychiatric ward. The ultimate diagnosis was neuroleptic malignant syndrome in a patient with an organic brain syndrome.

CASE 2

A 35-year-old man with known bipolar disorder was admitted to the intensive care unit for auto-intoxication with alprazolam, paroxetine and lithium. The episode was complicated by renal insufficiency, aspiration pneumonia, development of pressure wounds, bruises and rib fractures. After recovery he was admitted to the psychiatric ward where an episode of psychotic depression was diagnosed. He was treated with haloperidol, which was switched to risperidone later on.

One month after his suicide attempt he was admitted to the neurological ward with progressive dyspnoea, a slight cough, swallowing problems and apathy. On clinical examination a bilateral marked cogwheel rigidity, especially at the upper limbs, was found as well as additional axial rigidity. He also had little facial expression, a bulbar dysarthria with marked salivation and swallowing problems. Imaging of the brain was normal. Levels of creatin kinase were elevated (1100 U/L). The diagnosis of neuroleptic malignant syndrome was made. His neuroleptic treatment was stopped and 10 mg t.i.d. bromocriptine, 100 mg t.i.d. dantrolen and 1 mg t.i.d. lorazepam were started, along with antibiotic

treatment by means of doxycyclin. The patient recovered over a period of three weeks.

CASE 3

A 49-year old woman with a previous history of alcohol abuse and depressive episodes was admitted for investigation of subacute dementia.

The clinical picture consisted of bradyphrenia and hypokinesia, a fine tremor of the upper limbs, decreased facial expression, disinhibited primitive reflexes, diminished attention and memory. Perseverations, neologisms, stereotypies and echoing were notably present. Comprehension could not be evaluated.

Serum tests did not show any abnormality. Investigation for infectious and auto-immune causes remained negative. The CSF did not show signs of central nervous system inflammation. Magnetic resonance imaging of the brain was normal, as well as the evaluation of cerebral blood flow by means of SPECT-scan. The EEG showed an increase of slow wave activity. Screening for paraneoplastic disorders also remained negative, except for some aspecific sequellar micronodules in the lungs and 2 biliar cysts in the liver, as seen on CT.

In the absence of any clear organic cause this picture was diagnosed as a catatonic episode probably due to an underlying psychotic depression. A treatment with 4 mg q.i.d. intravenously lorazepam was rapidly successful and the patient was transferred to the psychiatric ward. The diagnosis of psychotic depression was confirmed. She was treated with an SSRI and is doing well since. The original hypothesis of dementia was not retained.

CASE 4

This 66-year old woman had a previous history of recurrent depressive episodes and psychosis, for which she had been treated with electro-convulsive therapy. She was admitted to a psychiatric ward because of paranoid delusions, and a treatment with neuroleptics was started. She developed swallowing problems and shortly thereafter a pneumonia was diagnosed. As her consciousness deteriorated and respiratory parameters worsened she was temporarily admitted to the intensive care ward. At that time a generalised increase of muscle tone with cogwheel rigidity and hypokinesia was noted.

Based on this clinical picture and the elevated serum levels of creatin kinase a diagnosis of neuroleptic malignant syndrome was suspected.

She was also treated with 4 mg q.i.d. intravenously lorazepam and the clinical picture cleared in three weeks. The patient remained emotionally unstable, with crying fits, and showed a very negativistic attitude as well as bizarre somatoform delusions. She was transferred to the psychiatric ward for further treatment. The final diagnosis was NMS and catatonia due to psychotic depression.

CASE 5

A 67-year old woman, known with a history of psychosis and alcohol and benzodiazepine abuse, was admitted to the neurology department because of motor and cognitive deterioration. On clinical testing generalized muscle rigidity, diminished reflexes, mutism and negativistic behaviour were found.

Imaging studies showed no abnormalities, except for a cortico-subcortical atrophy and some aspecific white matter changes. Based on the history taking a diagnosis of progressive dementia was suspected and the hypothesis of dementia with lewy bodies was raised.

After a ten days treatment with diazepam, risperidone and rivastigmine the patient's situation improved substantially with increase of verbal output and better cooperation. A brief episode of pulmonary infection induced a recurrence of the same symptomatology and the diagnosis of catatonia was made based on the presence of negativism, mutism, rigidity, hypokinesia and oppositional behaviour. Because of this catatonic picture, she was treated with lorazepam IV and additionally with amtryptiline, levodopa. The clinical signs improved gradually although episodes of oppositional behaviour persisted and stereotypic movements occurred.

The final diagnosis was a primary degenerative dementia, most probably dementia with lewy bodies, accompanied by catatonia, which could be considered inherent to the clinical picture although a mood disorder cannot be excluded.

Discussion

Three out of our 5 presented patients suffered from NMS, while two were diagnosed as catatonic, in one patient there were arguments for both albeit in a sequence of events. As is clear from these cases, there are many similarities between NMS and catatonia. On a symptomatic level, both conditions share the occurrence of specific symptoms like akinesia, muscle rigidity, stupor and mutism. Clinical similarities between catatonia and NMS have also been confirmed by Koch *et al.* (2000), who found that most of their patients meeting criteria for NMS, simultaneously met clinical and research criteria for catatonia. On the other hand, there are also clear differences. Behavioral symptoms are more prominent in catatonia, but symptoms of autonomic dysfunction are characteristic of NMS.

NMS and catatonia also share similarities in treatment strategies. As was demonstrated in our case reports, benzodiazepines are considered standard therapy in both conditions. In the NMS, dantrolene and dopamine receptor agonists are also useful. In resistant cases, electroconvulsive therapy is shown to be effective in both conditions (Koch *et al.*, 2000). Most cases of NMS and catatonia are now readily treatable, if adequately recognized.

In an excellent review on the subject of NMS and catatonia, Northoff (2002) proposes an interesting hypothesis explaining both the similarities and the differences between both entities. The presented evidence from functional neuro-imaging, neurophysiology, neurochemical and neuropharmacological data, converges to a model of predominant cortical dysfunction in catatonia, which is thus to be regarded as a cortical "psychomotor syndrome", while NMS is to be considered a subcortical "motor disorder". The predominant areas of functional disturbance in catatonia are supposed to be the medial orbitofrontal cortex and the posterior parietal cortex. The former is specifically involved in affective and behavioral symptoms, while the latter is involved in spatial characteristics of movement, and hence perhaps in adequate termination of ongoing movements. The focus of dysfunction in NMS is supposed to be the striatum, especially the posterior part, involved in initiation of movements, and to a lesser extent the ventral and anterior parts of the striatum, involved in cognitive and behavioral control. Moreover, in catatonia a functional down-regulation of the cortical GABA system was found, especially in the right posterior parietal cortex, and the right lateral orbitofrontal cortex (Northoff *et al.*, 1999), while in NMS a predominance of dopaminergic dysfunction in the striatum is suspected. This is reflected in the treatment strategies used in both conditions.

The hypothetic model raised by Northoff illustrates and underscores the problem of the

nosological status of catatonia. The well-known cortico-subcortical model of Alexander and DeLong (1986), with parallel loops mediating motor, cognitive and behavioral function allows the description of clinical syndromes with alike symptomatology due to dysfunctions in different parts of the system, be it cortical or subcortical, a suggestion already raised by Cummings (1993).

The issue of nosology can therefore only be resolved by either restricting the concept of catatonia or broadening it. In a restrictive way catatonia could be defined as a psychomotor disorder in the context of psychosis or affective disorder. A broader concept of catatonia would be defined as a psychomotor syndrome due to any condition, be it medical, pharmacological or psychiatric. As follows from the present discussion many of the symptoms of catatonia resemble symptoms encountered in frontal lobe dysfunction. However, it should be acknowledged that subcortical dysfunction, as in NMS, may also lead to similar clinical syndromes. In our view, the concept of catatonia and its relation to fronto-subcortical dysfunction deserves more attention. The restriction of catatonia to a subtype of schizophrenia is, in our opinion, obsolete.

REFERENCES

- ALEXANDER G. E., DELONG M. R., STRICK P. L. Parallel organization of functionally segregated circuits linking basal ganglia and cortex. *Annual Review of Neuroscience*, 1986, **9** : 357-381.
- BUSH G., FINK M., PETRIDES G., DOWLING F., FRANCIS A. Catatonia II: treatment with lorazepam and electroconvulsive therapy. *Acta Psychiatrica Scandinavica*, 1996, **93** : 137-143.
- CUMMINGS J. L. Frontal-subcortical circuits and human behaviour. *Archives of Neurology*, 1993, **50** (8) : 873-880.
- FINK M., TAYLOR M. A. The many varieties of catatonia. *European Archives of Psychiatry and Clinical Neuroscience*, 2001, **251** (suppl. 1) : I/8-I/13.
- KAHLBAUM K. L. Catatonia (Die katatonie oder das spannungsirresein). 1973, John Hopkins University Press, Baltimore.
- KOCH M., CHANDRAGIRI S., RIZVI S., PETRIDES G., FRANCIS A. Catatonic signs in neuroleptic malignant syndrome. *Comprehensive Psychiatry*, 2000, **41** (1) : 73-75.
- NORTHOFF G., ECKERT J., FRITZE J. Glutamatergic dysfunction in catatonia? Successful treatment of three acute akinetic catatonic patients with the NMDA-antagonist amantadine. *Journal of Neurology, Neurosurgery and Psychiatry*, 1997, **62** (4) : 404-406.
- NORTHOFF G., STEINKE R., CZCERVENKA C., KRAUSE R., ULRICH S., DANOS P., KROFF D., OTTO H., BOGERTS B. Decreased density of GABA-A receptors in the left sensorimotor cortex in akinetic catatonia: investigation of in vivo benzodiazepine receptor binding. *Journal of Neurology, Neurosurgery and Psychiatry*, 1999, **67** (4) : 445-450.
- NORTHOFF G. Catatonia and neuroleptic malignant syndrome: psychopathology and pathophysiology. *Journal of Neural Transmission*, 2002, **109** : 1453-1476.
- PERALTA V., CUESTA M. J., SERRANO J. F., MATA I. The Kahlbaum syndrome: a study of its clinical validity, nosological status, and relationship with schizophrenia and mood disorder. *Comprehensive Psychiatry*, 1997, **38** (1) : 61-67.
- PFUHLMANN B., STÖBER G. The different conceptions of catatonia: historical overview and critical discussion. *European Archives of Psychiatry and Clinical Neuroscience*, 2001, **251** (suppl. 1) : I/4-I/7.
- TAYLOR M. A., FINK M. Catatonia in psychiatric classification: a home of its own. *American Journal of Psychiatry*, 2003, **160** (7) : 1233-1241.

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