Review article

Catatonia

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Summary

Catatonia was first described by Karlbaum in 1874. It was subsequently catogorised as a subtype of schizophrenia. With the recognition of NMS as a form of catatonia and awareness that catatonia could occur in a number of psychiatric and medical illnesses, catatonia is now increasingly identified in clinical practice. Irrespective of the cause, the treatment of catatonia is the same as that of NMS. Benzodiazepine such as lorazepam in high dose are effective in the treatment of catatonia and ECT should be used in patients who do not respond adequately to benzodiazepines. In addition the underlying condition should be treated and in NMS antipsychotics should be withdrawn.

SL J Psychiatry 2013; 4 (1) 3-6

Introduction

If one were to ask a psychiatrist, what catatonia is, the answer might be, "it is a type of schizophrenia". Karl Karlbaum in 1874 described catatonia in 26 patients who were inmates of the asylum where he worked. The patients described by Karlbaum were a heterogeneous group with multiple aetiologies. Among his patients were some with neurological disorders, epileptic seizures and medical conditions such as tuberculosis. Two decades later, Emil Kraepelin, an influential figure in psychiatry, grouped together catatonia, hebephrenia and paranoid psychosis as dementia praecox (1). He described catatonia as a "secondary accompanying phenomena" rather than a fundamental clinical sign of dementia praecox. Due to his influence and extensive writing, the view that catatonia is synonymous with schizophrenia has persisted to this day. In the 1980s it was thought that catatonia had become rare. This apparent decline was probably due to change of treatment setting from asylum to modern day-care units. Not conducting detailed physical examinations and lack of awareness about catatonia in mood disorders also contributed to the decline in the number diagnosed with catatonia (2).

Because catatonia is considered a subtype of schizophrenia, clinicians automatically assume that patients with catatonia have schizophrenia. This could result in antipsychotic treatment which can harm the patient if the catatonia is due to neuroleptic malignant syndrome. Associating catatonia with schizophrenia can also prevent the clinician from looking for other causes of catatonia. It is therefore important that psychiatrists are knowledgable about catatonia.

Pathophysiology

The early writers, Karlbaum, Kraepelin and others thought that catatonia was a problem of volition or will. This was based on the tripartite model of mind function. The mind or brain was thought to have three main functions; emotion, will or volition and thinking. Kraepelin described deficits in all three areas in dementia praecox (3). In manic depressive psychosis he described that the primary deficit was of emotions. He thought in catatonia, the primary deficit was in will or volition. A patient with catatonia remained fixed in a posture because he could not will himself from that posture. He was also not able to resist the manipulations of the examiner because he lacked will. This was described as the cause of the phenomenon known as waxy flexibility. This model of catatonia is now considered outmoded, but the exact mechanism which causes catatonia has remained elusive. Though the symptom complex is distinctive, the aetiology is varied and it is likely that the syndrome has a final common pathway. However it is puzzling as to why only a percentage of patients with conditions know to predispose to catatonia develop the disorder. For example, although mood disorder is implicated in the aetiology in about 50% of patients with catatonia, only 10-20% with mania develop catatonia.

The pathophysiology of catatonia is most likely linked to a dysfunction of the motor system (3). Early studies focused on the basal ganglia because subcortical structures are involved in initiating movement. Early postmortem studies of patients with catatonic schizophrenia showed lesions in the basal ganglia. It is uncertain whether these changes were due to catatonia or schizophrenia. Functional imaging which allows the study of cortical functioning during motor activity, shows involvement of the parietal cortex with additional changes in the orbitofrontal cortex (4).

It is important to explore the relationship between catatonia and neuroleptic malignant syndrome (NMS) as these syndromes may have the same pathophysiological basis. In both catatonia and NMS, rigidity and akinesia is present but tremor is prominent in NMS (5). Waxy flexibility, motor anosognosia and affective and behavioural changes are more likely in catatonia.

The role of dopamine has been of primary interest in catatonia. In early studies, increased levels of metabolites of catecholamines have been found in the urine of patients with catatonia. This suggests that the

dopamine system is overactive in catatonia. However this contradicts the observation that neuroleptics which block dopamine can cause catatonia.

The evidence for implicating dopamine in the aetiology of the related condition NMS, is more definite. Typical antipsychotics with a high affinity for D2 receptors are more likely to cause NMS than atypical antipsychotics. Also studies have shown significantly low levels of homovanillic acid (HVA) in patients with NMS. It is also known that dopamine agonist drugs are beneficial in the treatment of NMS (3).

The benzodiapine receptors, GABA-A has also come to attention as lorazepam is an effective treatment in the majority of catatonic patients. In NMS too GABA may be implicated in the aetiology, as lorazepam is effective in the treatment, though with less dramatic effect than in catatonia. The glutamate systems in particular the NMDA receptors may be of importance as some patients with catatonia have responded to the NMDA antagonist amantadine. The response is slower than with lorazepam and may be mediated by secondary mechanisms (3).

Patients with catatonia show ansognosia or lack of self awareness regarding posturing (3). Unlike patients with NMS and Parkinson's disease these patients are unaware of their difficulties in initiation of movements. Therefore it is likely that in catatonia there are primary cortical deficits with secondary effects on striatal areas, whereas in NMS and Parkinson's disease the motor deficits are mainly of subcortical origin.

Symptoms and signs

The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) describes catatonia as a syndrome with marked psychomotor disturbance that may involve motor immobility, excessive motor activity, extreme negativism, mutism, peculiarities of voluntary movement, echolalia or echopraxia (6).

Mutism and stupor are considered core features of catatonia. Though these are characteristic, they are not pathognomonic, and other motor signs should be present for diagnosis. Mutism is often but not always associated with immobility. In stupor the patient is unresponsive to commands and when severe, even to painful stimuli (3).

Abnormalities in posture are seen in catatonia. In catalepsy the patient maintains awkward or uncomfortable postures for long periods of time. These include facial postures such as grimacing or Schnauzkrampf and body postures like psychological pillow. In psychological pillow, the patient keeps the head a few inches above the pillow for extended periods of time. In waxy flexibility there is initial resistance to attempts to move the limbs but the limbs are maintained in whatever position put in by the examiner. This has been likened to the bending of a soft candle (3, 7).

Mannerisms and sterotypy are abnormal movements which occur in catatonia. Stereotypy are non-goal directed repetitive motor movements. Mannerisms in contrast, are semi purposive movements which are exaggerated or inappropriate to the situation. These may be simple or complex and may include self-mutilation. The meaningless repetition of phrases and sentences in a repetitive manner verbigeration is verbal stereotypy (7).

In catatonia there are abnormalities in the execution of movements. In automatic obedience there is exaggerated cooperation to an examiners request. Mitmachen and Mitgehen are forms of automatic obedience. In mitmachen the patient allows the examiner to move his limbs into any position in spite of instructions to the contrary. Mitgehen is an extreme form of cooperation because the patient moves the body in response to the slightest pressure by the examiner (7). Some catatonic patients oppose all passive movements with the same degree of force applied by the examiner (7). This is known as Gegenhalten or opposition. Negativism can be considered an exaggerated form of opposition. In negativism, the patient resists attempts at manipulation of limbs by the examiner. Ambitendency is a mild variety of negativism. In ambitendency the patient appears hesitant and indecisive in his movements. He may be unable to pass through a doorway, repeatedly going backwards and forwards(7).

Speech abnormalities in catatonia include mutism, perseveration and echolalia where the patient repeats what is said by the examiner. In echopraxia patient imitates the motor movements of the examiner.

There is no consensus regarding the diagnostic criteria for catatonia. The existing diagnostic criteria differ in the number of signs and the duration necessary for diagnosis of catatonia. The DSM-IV lists five and the International Classification of Diseases Tenth Revision (ICD-10) seven categories of signs for catatonia (6,8). The DSM IV requires signs from at least two categories and the ICD-10 signs from one category to be present, in addition to fulfilling the criteria for schizophrenia.

The DSM II and DSM III classified catatonia only as a subtype of schizophrenia. The DSM IV added a category "Catatonic disorder due to . . . general medical condition or side-effect of a medication". It also included a specifier within the diagnoses of mania and depression, but without a numeric category designation. According to the ICD-10, the subcategory of "organic catatonic disorder" can be used when the patient has a cerebral disease or dysfunction with catatonic symptoms. Taking into consideration the current scientific evidence, Fink and others have argued strongly for a separate category of catatonia. Fink has proposed three subtypes of catatonia, non-malignant catatonia, delirious or excited catatonia associated with mania or excitement and malignant catatonia associated with fever and autonomic instability (2). The DSM-5 made several changes in the classification of catatonia (9). Schizophrenia, catatonic type has been eliminated. Catatonia is included as a specifier across

the 10 principal primary diagnoses. The sub category "catatonia associated with another mental disorder" is retained and a new subcategory of "catatonia not elsewhere classified" has been included.

Differential Diagnosis

Catatonia is a condition with varied presentations and can occur in several psychiatric disorders. It is possible that there is no primary catatonia and that it is always secondary to an underlying disorder. Clinically it is important to identify catatonia and its aetiology. The most likely cause of catatonia is a mood disorder and not schizophrenia. Other causes include drug intoxication and withdrawal, sudden withdrawal of antipsychotics or antiparkinsonian drugs, neurological conditions such as Parkinson's disease and epilepsy, metabolic disorders and pervasive developmental disorder (5,10).

Catatonia occurs in about 15% of manic episodes in bipolar disorder. Conversely 50% of catatonic patients suffer from bipolar disorder. When the classic signs of mania coexist with catatonia the diagnosis is not difficult. However catatonia in irritable mania or mixed affective states may be mistaken for schizophrenia.

Sometimes mutism, negativism and slow movements of catatonia may be attributed to blunting of mood which is seen in schizophrenia. This mistake is even more likely as catatonia is firmly linked in the minds of most clinicians with schizophrenia (3).

The second most common cause of catatonia is severe depression (11). Often there is severe psychomotor retardation or stupor. Unlike manic patients with catatonia, they appear unaware of the environment. They are likely to stop eating and drinking leading to dehydration and weight loss. If mistakenly treated with antipsychotics, there is a risk of developing NMS. Younger patients with depressive catatonia are likely to be diagnosed with schizophrenia whereas elderly patients due to apparent cognitive impairment are more likely to be diagnosed as having dementia.

Around 10% of patients with catatonia have schizophrenia. Waxy flexibility and posturing are catatonic symptoms traditionally associated with schizophrenia. Emotional expression is reduced and the prognosis is poorer than for catatonia due to mood disorder. Treatment with antipsychotics increase risk of neurological adverse effects and worsen the prognosis.

General medical conditions that cause delirium are also associated with catatonia. Metabolic conditions, endocrine disorders, autoimmune conditions, infections, burns and neurological disorders are known to cause catatonia. Acute medically ill patients show excitement or stupor with motor signs of catatonia.

Antipsychotic drugs can cause a malignant variety of catatonia like NMS.The risk is higher with potent or depot antipsychotic drugs. Benzodiazepine withdrawal, if rapid could lead to catatonia. The patient is delirious with fluctuating catatonic signs. The withdrawal of dopaminergic drugs such as L-dopa or amantadine could also lead to catatonia. Overdose of opiates could cause a catatonia like syndrome with rigidity, posturing and signs of opiate intoxication such pin point pupils.

Catatonia could occur in partial complex seizures and postictal states following partial complex and generalised seizures. Compared to catatonia due to mood disorders and schizophrenia it is likely to be of shorter duration with more frequent recurrence.

Catatonia also occurs in neurological disorders that affect the motor system. These include encephalitis, subdural haematoma, focal lesions of the frontal, parietal and temporal lobes and multiple sclerosis. These causes should be considered when an older person develops catatonia but has no history of mood disorder. A number of metabolic disorders such diabetic ketoacidosis, hyperthyroidism and hepatic encephalopathy can cause catatonia.

There are several conditions that could be mistaken for catatonia. They include elective mutism, Parkinson disease, metabolic stupor, obsessive compulsive disorder, malignant hyperthermia and acute lesions in the ventral pons causing the locked-in syndrome. The presence of mutism alone is not adequate to diagnose catatonia and requires the presence of motor and other symptoms. In Parkinson disease severe bradykinesia may resemble catatonia. Mannerisms and stereotypes may be mistaken for obsessive compulsive disorder (OCD). The compulsions of OCD however are persistent and long lasting rather than episodic. Malignant hyperthermia is an autosomal dominant genetic disorder where inhalation anaesthetics such as halothane and muscle relaxants such as succinylcholine cause rigidity and tremor accompanied by fever and elevated CPK levels.

Treatment

Treatment of catatonia is as varied as its names. The treatment of catatonia is closely related to the evolution of treatment for NMS. With the advent of antipsychotics it was recognised that these drugs could cause a febrile type of acute catatonia. It was thought that dopamine blockade was the cause and therefore dopamine agonists bromocriptine and amantadine were advocated as treatment (11). Clinicians continued to use antipsychotics to treat the underlying psychosis. Only later was it realised that stopping the causal medication was important in its management. Around this time, another somewhat similar syndrome, malignant hyperthermia (MH) precipitated by inhalation anaesthetics was identified. Dantrolene a muscle relaxant was prescribed for this condition. As a result of this association, most guidelines now advocate bromocriptine and dantrolene as standard treatment for NMS. The non-febrile form of catatonia was first successfully treated with barbiturates and later with the safer benzodiazepines. Electroconvulsive therapy was also recognised as an effective treatment. When NMS was recognised as a form of catatonia, benzodiazepines and ECT were found to be effective for NMS. It can be argued now that in both NMS and catatonia the mainstay of treatment should be benzodiazepines and ECT. Even

so textbooks still continue to advocate dantrolene and bromocriptine as the standard treatment for NMS. Several studies have established the effectiveness of high dose lorazepam in 80% of patients with catatonia, with ECT being effective in the rest. Lorazepam is initially prescribed at 3–4 mg a day. If well tolerated, and catatonia does not resolve in two days, the dosage may increased progressively upto 8–24 mg a day. If, catatonia does not respond to lorazepam after a few days, ECT is recommended (12,13).

The same treatment is effective in NMS though the response time is longer. The medical aspects need more intensive management in NMS. If rigorously followed, such treatment can be lifesaving especially in NMS.

Increased awareness of the range of clinical features and the number of conditions which cause catatonia, will lead to better management of this interesting and historic condition.

Conclusions

Catatonia was first described by Karlbaum in 1874. It was subsequently catogorised as a subtype of schizophrenia. With the recognition of NMS as a form of catatonia and awareness that catatonia could occur in a number of psychiatric and medical illnesses, catatonia is now increasingly identified in clinical practice. Irrespective of the cause, the treatment of catatonia is the same as that of NMS. Benzodiazepine such as lorazepam in high dose are effective in the treatment of catatonia and ECT should be used in patients who do not respond adequately to benzodiazepines. In addition the underlying condition should be treated and in NMS antipsychotics should be withdrawn.

Declaration of interest

None declared

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