Catatonia 2: diagnosis, management and prognosis

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This is the second of two articles reviewing catatonia. In the first, catatonia was described as an under-recognized syndrome with a potentially fatal outcome. It was suggested that treatment with neuroleptics may exacerbate the syndrome. The differential diagnosis, management and prognosis of catatonia are reviewed below.

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Catatonia may be classified as primary (or idiopathic) or secondary. The list of reported physical and psychiatric associations is lengthy and has been provided by Philbrick and Rummans (1994). As *Table 1* shows, catatonia may occur as a feature of neurological, systemic or psychiatric illness or as a side-effect of medication. The most well known example of the latter is neuroleptic malignant syndrome (NMS).

DIFFERENTIAL DIAGNOSIS

Descriptions of series of catatonic patients consistently show that secondary catatonia occurs in association with affective disorder more frequently than with schizophrenia (Abrams and Taylor, 1976; Ries, 1985; Barnes et al, 1986), as was suggested by Kahlbaum (1874). Samples of patients taken from psychiatric populations show a large preponderance of catatonia in the absence of any other diagnosable medical or psychiatric illness.

TABLE 1.
Some reported associations with catatonia

Category	Association
Idiopathic	Perhaps nearly 50% of patients
Psychiatric	Affective disorders, dissociative disorders, schizophrenia, drug-induced and other psychoses, obsessive compulsive disorder, personality disorder
Neurological	Cerebral tumours, subarachnoid haemorrhage, subdural haemorrhage, haemorrhagic infarcts, closed head injury, multiple sclerosis, narcolepsy, tuberous sclerosis, epilepsy, Wernicke's encephalopathy, parkinsonism, systemic lupus erythematosis
Metabolic	Addison's disease, Cushing's disease, diabetic ketoacidosis, hypercalcaemia, acute intermittent porphyria, Wilson's disease
Drugs and toxins	Alcohol, anticonvulsants, disulphiram, neuroleptics, amphetamines, mescalin, phenylcyclidine, aspirin, L-dopa, steroids
Infections	Encephalitis (especially herpes), malaria, syphilis, tuberculosis, typhoid, acquired immunodeficiency, mononucleosis, viral hepatitis

From Philbrick and Rummans (1994)

Benegal et al (1993) prospectively identified 65 patients admitted to a single psychiatric unit over 1 year who displayed one or more catatonic signs in the absence of physical illness. The primary *International Classification of Diseases* (ICD-9) diagnosis was bipolar affective disorder in 23%, paranoid schizophrenia in 17%, catatonic schizophrenia in 3%, other forms of schizophrenia in 9% and reactive psychosis in 1.5%. The remaining 46% of patients had presented with a catatonic syndrome in the absence of any underlying physical or psychiatric disorder. The authors commented on the 'marked tendency to recurrence' in 38% of those with primary catatonia.

Neuroleptic malignant syndrome

The clinical picture of NMS is identical to that of malignant catatonia. Attempts to differentiate the two syndromes on clinical grounds are unconvincing (Fleischhacker et al, 1990). NMS has a definite but undetermined mortality, with figures quoted in the literature ranging from 4% to 20%. Prospective studies suggest that it occurs in 0.05–0.2% of patients prescribed neuroleptics (Bertorini, 1997). Although it is considered more likely with long-acting neuroleptics of high potency, it has been reported with antidepressants, carbamazepine and lithium (Kellam, 1990).

NMS may be considered a particular form of iatrogenic malignant catatonia that has been induced by neuroleptics (Mann et al, 1986). It may be that the decline in incidence of malignant catatonia since the introduction of neuroleptics is because of reclassification of cases as NMS with an automatic assumption of neuroleptic causation. NMS is frequently preceded by catatonic symptoms (White and

Robbins, 1991), which are mistakenly treated with neuroleptics, which in turn precipitate a deterioration and the malignant syndrome (Singerman and Raheja, 1994; Fink, 1996). Treatment involves withdrawal of antipsychotic medication, hydration and temperature control. Electroconvulsive therapy (ECT) has been reported as effective; medical treatments include the combination of the dopamine agonist bromocriptine with a muscle relaxant such as dantrolene.

Serotonin syndrome

This is another iatrogenic syndrome that may present with catatonia. Other features are agitation, confusion, diaphoresis, mydriasis, hyperthermia, fluctuating blood pressure, tachycardia, tremor, myoclonus and seizures. Laboratory investigations show leucocytosis, acidosis and raised creatine phosphokinase (CPK), and it may be complicated by rhabdomyolysis and myoglobinuria. It may be precipitated by a variety of serotonergic drugs, including tryptophan, buspirone, selective serotonin reuptake inhibitors and monoamine oxidase inhibitors, particularly when used in combination (Sternbach, 1991).

Features that distinguish it from NMS are a history of exposure to serotonergic drugs (rather than neuroleptics), myoclonus and hyperreflexia (rather than lead pipe rigidity), and the presence of mydriasis (Martin, 1996). Treatment is the withdrawal of the precipitating serotonergic agents. Most cases resolve over 24–36 hours with supportive care. There is conflicting evidence over the use of benzodiazepines, dantrolene, dopamine antagonists and non-specific serotonin antagonists (chlorpromazine, methysergide, propranolol). Bromocriptine increases brain serotonin levels and may precipitate the syndrome (Martin, 1996).

MANAGEMENT OF CATATONIA

There are no randomized controlled trials of treatment in catatonia. Because of the view that it is a subtype of schizophrenia, neuroleptics are often employed. However, there is little evidence of their efficacy. In fact neuroleptics are more likely to exacerbate the condition and may precipitate malignant catatonia, which is more likely in patients prone to catatonic symptoms. The earliest treatments for catatonia were ECT and sedative drugs, both of which have been in use since the 1930s and remain the most effective treatments today (Fink, 1997). It is important to note that these therapies represent a specific treatment of the syndrome. Efficacy is not predicted by underlying cause and they are an appropriate therapy for catatonia occurring both in the context of psychiatric and other medical illnesses (Barnes et al, 1986).

Sedatives

Barbiturates, previously used widely in the treatment of catatonia, have now largely been superseded by the benzodiazepines. Their efficacy has been documented in many case reports and small open series. For example, Bush et al (1996) described a series of 21 patients, 16 of whom responded completely to a 5-day trial of lorazepam. Typically patients respond within minutes to parenteral benzodiazepines and within 1–2 hours of an oral dose. This therapeutic response has been shown to be reversed by flumazenil (Pollack, 1993). Lorazepam is the drug most commonly used and often high doses are required — up to 16mg a day. The medication is given in divided doses at intervals short enough to prevent recurrence of the catatonic symptoms.

Electroconvulsive therapy

This remains a useful and effective treatment for catatonia and is often of benefit for patients who have failed to respond to benzodiazepines. In Bush et al's (1996) study, four of the five patients who had not responded to lorazepam were then treated effectively with ECT. The family of the final patient refused to give consent. There is good evidence of the efficacy of ECT in malignant catatonia (Singerman and Raheja, 1994), and case reports suggest that a delay of more than 5 days between onset of malignant catatonia and initiation of treatment is associated with an increased mortality (Philbrick and Rummans, 1994).

Other treatments

The use of bromocriptine (a dopamine agonist) and dantrolene (a muscle relaxant) is well accepted when malignant catatonia is deemed secondary to neuroleptic medication. There is less experience of these treatments in catatonia from other causes. L-dopa has been used effectively to treat catatonic schizophrenia by Rogers (1991), apparently without an exacerbation of psychotic symptoms, and Mahmood (1991) claimed efficacy for bromocryptine. Northoff et al (1997) described successful treatment of three patients with amantadine, an antagonist at the N-methyl-D-aspartic acid (NMDA) glutamate receptor. Other treatments that have been described include calcium-chan-

nel blockers, corticosteroids, anticholinergics and carbamazepine (Philbrick and Rummans, 1994).

Based on the available evidence, in our unit we have formulated the following treatment protocol:

1. Withhold neuroleptic medication. This may of course have a place in the subsequent and continuing treatment of an underlying psychotic disorder
2. Investigations to exclude treatable physical disorders. This will include at least a full history and physical and mental state examination. It will almost certainly include haematological and biochemical profiles, including CPK, urinary drugs screen, an electroencephalogram to exclude a partial epileptic status and a computed tomography or magnetic resonance imaging scan. The patient's autonomic function (blood pressure, heart rate, respiratory rate), temperature, fluid balance and renal function are closely monitored
3. Trial of lorazepam. This is a safe, non-invasive treatment that does not require written consent and therefore is our first-line treatment. We administer 1–2 mg as often as required to achieve satisfactory relief of symptoms. If effective the patient is maintained on lorazepam at a gradually reducing dosage titrated to avoid any recurrence of symptoms
4. If the patient fails to respond to lorazepam and their clinical state warrants it, we would refer for ECT
5. Onset of either autonomic instability or hyperthermia may herald malignant catatonia. In this situation we would consider the earlier use of ECT
6. Continued investigation and treatment of underlying cause if present.

KEY POINTS

- Catatonia may be a feature of a wide range of disorders, both psychiatric and physical. It may also be precipitated by medicinal and illicit drug use and may occur as a primary syndrome.
- It shows a specific treatment response that is not dependent upon type of symptom or underlying cause.
- The assumption of a schizophrenic aetiology may lead to treatment with neuroleptics. This will not be effective, may lead to a deterioration and potentially will precipitate malignant catatonia.
- Improved recognition of the syndrome and early, appropriate treatment may reduce the likelihood of severe deterioration and death.

PROGNOSIS

The studies that are available seem to suggest that simple catatonia responds well to appropriate treatment. A difficulty has often been that the appropriate treatment has not been implemented. The literature is littered with case reports and letters about catatonic patients who 'unexpectedly' improved after receiving incidental treatment with benzodiazepines for some other reason. The prognosis of malignant catatonia has improved (probably because a diagnosis of NMS, whether correct or incorrect, leads to the withdrawal of neuroleptics), but there remains an associated mortality that could almost certainly be further reduced by improved recognition and treatment.

There are no studies evaluating the long-term outcome of patients with catatonia. It is generally assumed to be that of the underlying cause. In patients with primary catatonia, Benegal et al (1993) emphasized the tendency to recurrence in 38% of their patients. HM

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