The diagnosis and treatment of catatonia

Authors: Jonathan P Rogers, Michael S Zandi and Anthony S David

Catatonia is a severe neuropsychiatric syndrome that affects emotion, speech, movement and complex behaviour. It can occur in a wide range of psychiatric and neurological conditions, including depression, mania, schizophrenia, autism, autoimmune encephalitis (particularly NMDAR encephalitis), systemic lupus erythematosus, thyroid disease, epilepsy and medication-induced and -withdrawal states. This concise guideline highlights key recommendations from the British Association for Psychopharmacology (BAP) Catatonia Guideline, published in April 2023. Important investigations may include neuroimaging, electroencephalography and assessment for neuronal autoantibodies in serum and cerebrospinal fluid. First-line treatment comprises benzodiazepines and/or electroconvulsive therapy. The benzodiazepine of choice is lorazepam, which is sometimes used in very high doses. Multidisciplinary working between psychiatrists and physicians is often essential. The main limitation of the guidelines is the low quality of the underlying evidence, comprising mainly small observational studies and case reports or series.

KEYWORDS: catatonia, catatonic schizophrenia, guideline, treatment, benzodiazepine, electroconvulsive therapy, neuroleptic malignant syndrome, encephalitis

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Introduction

Catatonia is a severe neuropsychiatric syndrome involving emotion, speech, movement and complex behaviour. It has an incidence of ∼10 per 100,000 person-years. Although it was considered as a form of schizophrenia for much of the 20th century, the major diagnostic manuals, the International Classification of Diseases (ICD-11) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-5-TR), now recognise catatonia to occur in a wide range of psychiatric, neurological and medical conditions.

Although catatonia is classically conceived as mutism with catalepsy (the phenomenon in which an individual’s limb retains a position against gravity after manipulation by the examiner), the phenotype is broader than this (Box 1). Fear and extreme emotional reactions also commonly feature.

Apart from the severe distress that catatonia often entails, catatonia is an important condition to recognise and manage promptly because it has been associated with a wide range of medical complications, including infection (pneumonia, urinary tract infection and sepsis), venous thromboembolism (deep venous thrombosis and pulmonary embolus), pressure sores, acute kidney injury and cardiac arrhythmia, as well as a substantially increased mortality, even compared with other patients with severe mental illnesses. At its most severe, malignant catatonia, involving pyrexia and autonomic instability, is associated with a mortality of 10%.

Scope and purpose

This concise guidance highlights some of the key recommendations of the Evidence-based consensus guidelines for the management of catatonia: recommendations from the British Association for Psychopharmacology, published in April 2023. In this article, we emphasis points from the guidelines that are of relevance to general physicians.

Differential diagnosis of catatonia

When considering the diagnosis of a patient with possible catatonia, there are two key questions:

> What conditions could account for this patient’s presentation if it is not catatonia? Examples of such disorders and how to distinguish them are provided in Table 1.

> If it is catatonia, what medical or psychiatric disorder might be underlying it? Catatonia occurring de novo, on its own, is rare. The list of disorders associated with catatonia is very long, but some important examples are provided in Box 2. Importantly, underlying medical disorders are at least as common as psychiatric disorders in acute medical and surgical settings.

Work-up

Given that catatonia is associated with intense anxiety, the approach to a patient is crucial. Despite appearances to the contrary, there is evidence that many patients with catatonia are aware of, and recall, their experiences; thus, clinicians...
The diagnosis and treatment of catatonia

In terms of investigations, the approach depends on the clinical situation and the index of suspicion for particular diagnoses (Box 3). Where it is unclear whether a presentation represents catatonia, a lorazepam challenge can be particularly useful. A baseline assessment of catatonic signs is conducted before 1–2 mg of lorazepam is administered. After an interval of 5 min (for intravenous (IV) lorazepam), 15 min (intramuscular; IM) or 30 min (oral), a reduction in catatonic signs of 50% supports a diagnosis of catatonia.

**Treatment considerations**

Treatment should usually be directed at the underlying condition at the same time as giving specific treatments for catatonia. Prevention and management of medical should interact with the person as they would with someone who understands what is happening. History from the patient is often limited; therefore, obtaining a thorough collateral history is essential. As well as ascertaining the course of the current illness, such a collateral should establish the presence of prior psychiatric or neurological disorders, any recent changes in medications and any recreational drug use.

Physical examination should involve attempts to elicit catatonic signs, such as catalepsy, echopraxia and abnormalities of muscle tone. Videos illustrating how to do this are available from https://bfcrs.urmc.edu. Equally important is an examination aimed at establishing volume status, focal neurological signs, evidence of pressure sores and evidence of deep venous thrombosis. Cardiovascular and respiratory examination are important in advance of treatment with high-dose benzodiazepines or electroconvulsive therapy (ECT).

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<th>Disorder</th>
<th>Similarities to catatonia</th>
<th>Distinguishing features</th>
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<td>Stiff person syndrome, progressive encephalomyelitis with rigidity and myoclonus, and related conditions</td>
<td>Anxiety, rigidity, immobility (in severe cases), response to benzodiazepines</td>
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<td>Almost complete absence of movement and speech</td>
<td>Vertical gaze and blinking usually intact; usually abrupt onset</td>
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complications can include thromboprophylaxis, pressure mattresses, intravenous fluids and nasogastric feeding.\(^9\)

The mainstay of specific catatonia management is benzodiazepines and/or ECT. Antipsychotic medications, although possibly helpful in some cases where the underlying diagnosis is schizophrenia, should be used with caution, because catatonia is a strong risk factor for neuroleptic malignant syndrome.\(^3\) If clozapine has recently been discontinued for reasons other than for severe adverse effects, prompt reinstatement should be considered.

**Benzodiazepines**

The response to benzodiazepines in acute catatonia can be dramatic and rapid, sometimes within minutes. Although all benzodiazepines are probably effective, lorazepam has been most studied and, thus, is the preferred option. Routes of administration include oral, sublingual, IM and IV, depending on the clinical setting and availability.

Although many patients with catatonia might respond to doses of lorazepam licensed for other conditions, some require titration over several days to much higher doses. Titration should not be considered complete until catatonia is fully treated, sedation occurs or dose reaches at least 16 mg/day (in divided doses). Benzodiazepines should be gradually titrated down, although occasionally patients require longer-term benzodiazepine treatment.

**Electroconvulsive therapy**

ECT is usually highly effective in catatonia and National Institute for Health and Care Excellence (NICE) also recognises catatonia as an indication.\(^10\) Legal requirements for the administration of ECT depend on different jurisdictions. Box 4 summarises the recommendations for ECT.

**Other treatments**

Numerous other treatments have been suggested for catatonia, mostly based on case reports and case series. The evidence is a little stronger for the NMDAR antagonists amantadine and memantine, which are recommended after benzodiazepines and ECT. After NMDAR antagonists, there is a wide range of options with a low degree of evidence, namely levodopa, a dopamine agonist, carbamazepine, valproate, tiapiramate and a second-generation antipsychotic. However, antipsychotics should be avoided in the absence of a psychotic disorder and, even where a primary psychosis is present, should be used with caution.

**Special groups**

Treatment of catatonia in children and adolescents, older adults, women in the perinatal period, individuals with autism spectrum disorder and certain medical conditions is summarised in Table 2.

**Limitations**

The main limitation of these guidelines is the low quality of the evidence underlying them. Although a few randomised clinical trials have been conducted, they have tended to have been at high risk of bias, poorly reported or poorly applicable to most patients or modern treatments. Therefore, most of the evidence comprises small observational studies, often without a control group, although effects are sometimes dramatic. It should also be noted that most treatments for catatonia are outside the licence of the product; thus, relevant guidance, including providing information to the patient where possible and documenting the need for an unlicensed medication, should be followed.\(^11\)

**Implications for implementation**

Fortunately, benzodiazepines are cheap and widely available. However, access to ECT is patchy, which can delay care. Liaison between local services will be necessary to facilitate this. Multidisciplinary working more generally, particularly between psychiatrists and physicians, is important, because there are few clinicians who have expertise in the entire range of diagnoses detailed in Table 1 and Box 2.

**Conflicts of interest**

JPR, MSZ and ASD were members of the BAP Guideline Development Group. JPR is supported by the Wellcome Trust. MSZ declares honoraria for one lecture each for each of the four mentioned in the last 3 years: Norwegian Neurological Society; Copenhagen Neuropsychological Society, Rigshospitalet; and Cygnet Healthcare. MSZ declares travel and hotel support for a stay in Florence from the European Association of Neurology (EAN) for an EAN meeting on autoimmune encephalitis in April 2022. MSZ represents neurology in the UK for the Association of British Neurologists for matters related to Covid in meetings with NHS England and Royal College of Physicians.
The diagnosis and treatment of catatonia

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Table 2. Treatment of catatonia in special groups

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<th>Clinical scenario</th>
<th>Additional considerations for diagnosis and treatment</th>
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| Children and adolescents           | > Reported in children as young as 5 years  
> As in adults, mainstay of treatment comprises benzodiazepines and/or ECT                                                                                                                  |
| Older adults                       | > Consider catatonia in the differential diagnosis of an apparent rapidly progressing dementia or failure to thrive  
> Medical disorders underlying catatonia more common  
> Benzodiazepines should be used at lower doses                                                                                                                                             |
| Women in the perinatal period      | > Multidisciplinary working between psychiatric and obstetric team is essential  
> Promote contact between mother and baby where appropriate  
> In pregnancy, where catatonia is severe and presents high risks, and treatment for the underlying condition is inadequate, initially consider lorazepam up to 4 mg/day. If ineffective, consider ECT  
> Postpartum women should not breastfeed if lorazepam is used at doses higher than 4 mg/day  
> Women may breastfeed after ECT                                                                                                                                                    |
| Autism spectrum disorder           | > Vigilance is required, because catatonia is particularly common  
> Given the overlap of clinical features between catatonia and autism, diagnosis of catatonia requires a marked change in presentation from baseline  
> In mild cases, first-line treatments are psychological interventions and/or lorazepam  
> In more severe cases, consider benzodiazepines and/or ECT                                                                                                                             |
| Renal impairment                   | > Lorazepam dosing not usually altered, but consider additional monitoring for side effects                                                                                           |
| Hepatic impairment                 | > Lorazepam dosing does not usually need to be altered in mild–moderate hepatic impairment  
> Lorazepam cautioned in severe hepatic impairment                                                                                                                                        |
| Respiratory disease                | > Consider ECT, rather than benzodiazepines, in severe respiratory disease                                                                                                                  |

ECT = electroconvulsive therapy.

Acknowledgements

The contribution of the BAP Catatonia Guideline Development Group is gratefully acknowledged. A complete list of group members can be found in the full published guideline. *

References