The diagnosis and treatment of catatonia

Authors: Jonathan P Rogers,[A] Michael S Zandi[B] and Anthony S David[C]

ABSTRACT

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

DOI: 10.7861/clinmed.2023-0113

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.[1] 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.[3] At its most severe, malignant catatonia, involving pyrexia and autonomic instability, is associated with a mortality of 10%.[4]

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.[5] 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.[7]

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[8]; thus, clinicians

Authors: [A]Wellcome Trust clinical PhD training fellow, University College London, London, UK, and specialty registrar in general adult and old age psychiatry, South London and Maudsley NHS Foundation Trust, London, UK; [B]consultant neurologist, National Hospital for Neurology and Neurosurgery, London, UK, and honorary associate professor, Queen Square Institute of Neurology, University College London, London, UK; [C]professor of mental health and director, Institute of Mental Health, University College London, London, UK

Box 1. Summary of diagnostic criteria for catatonia in *DSM-5-TR*[2]

Clinical picture dominated by at least three of the following clinical features:

- Stupor (lack of responsiveness to the environment)
- Catalepsy (a posture induced by an external agent is sustained against gravity)
- Waxy flexibility (steady, even resistance to repositioning)
- Mutism (absence of, or dramatic reduction in, speech)
- Negativism (resistance to instructions, which might even entail doing the opposite to them)
- Posturing (spontaneous assumption of postures sustained against gravity)
- Mannerism (caricature of a normal motor act)
- Stereotypy (non-goal-directed movement repeated to abnormal frequency)
- Agitation (which must not be prompted by external stimuli)
- Grimacing
- Echolalia (repetition of another person's speech)
- Echopraxia (mimicry of another person's movements)

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).

Box 2. Examples of important psychiatric and medical conditions that might underlie catatonia

Psychiatric conditions

Depression
Primary psychotic disorders, eg schizophrenia
Mania
Autism spectrum disorder
Postpartum psychosis

Medical conditions

Autoimmune encephalitis (especially NMDA receptor encephalitis)
Systemic lupus erythematosus
Viral or bacterial meningitis/encephalitis
HIV
Thyroid disease
Space-occupying lesion
Traumatic brain injury
Medications/drugs (eg corticosteroids, ketamine)
Medication/drug withdrawal (eg clozapine, benzodiazepines)

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. Treatment of the underlying condition might be psychiatric or medical, such as immunosuppression in NMDAR encephalitis. There is some evidence suggesting that treatment response is better if given sooner. Prevention and management of medical

Table 1. Examples of conditions that can be mistaken for catatonia

Disorder	Similarities to catatonia	Distinguishing features
Stiff person syndrome, progressive encephalomyelitis with rigidity and myoclonus, and related conditions	Anxiety, rigidity, immobility (in severe cases), response to benzodiazepines	Autoantibodies in serum and cerebrospinal fluid to GAD-65, glycine receptors, DPPX and related proteins; enhanced exteroceptive reflexes
Parkinson's disease, progressive supranuclear palsy, multiple system atrophy and other heredodegenerative related disorders (rare)	Hypokinesia, freezing	Insidious onset, tremor, asymmetry, synkinetic rigidity, abnormal dopamine transporter single photon emission computed tomography (DAT-SPECT) scan
Drug-induced dystonia	Similar to catatonic posturing	Absence of stupor; response to anticholinergics
Neuroleptic malignant syndrome	Can be clinically indistinguishable from malignant catatonia	Precipitation by initiation or rapid dose increase of a dopamine D_2 receptor antagonist
Locked-in syndrome	Almost complete absence of movement and speech	Vertical gaze and blinking usually intact; usually abrupt onset
Coma	Unresponsiveness	No resistance to eye opening
Functional neurological disorder	Mutism and paralysis in severe cases	Usually positive signs of functional motor impairments[6]

Box 3. Summary of recommendations for investigations in catatonia

- Consider blood tests, urine drug screen, lumbar puncture, electroencephalography (EEG) and neuroimaging depending on the history and examination
- In a first episode of catatonia or where the underlying diagnosis is unclear, consider computed tomography (CT) or magnetic resonance imaging (MRI) of brain
- In a first episode of catatonia or where the underlying diagnosis is unclear, consider assessing for antibodies to the NMDA receptor and other relevant antibodies in the serum and ideally in cerebrospinal fluid (CSF)
- Where there is a suspicion of or risk factors for seizures (eg prior epilepsy, head injury, central nervous system infection, autoimmune encephalitis, alcohol withdrawal), consider an EEG
- When it is unclear whether catatonia is present, consider a lorazepam challenge

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.

Box 4. Summary of recommendations for using ECT in catatonia

- When ECT is used, use bilateral ECT
- In acute catatonia, when ECT is used, it should be administered at a minimum of two times weekly
- The number of sessions of ECT depends on the treatment response, individualised risks and side effects

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, topiramate 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.

Table 2. Treatment of catatonia in special groups

Clinical scenario	Additional considerations for diagnosis and treatment
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.[5]

References

1 Rogers JP, Pollak TA, Begum N *et al*. Catatonia: Demographic, clinical and laboratory associations. *Psychol Med* 2021, in press (doi:10.1017/S0033291721004402).
2 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-5-TR*. Washington DC: American Psychiatric Association Publishing, 2022.
3 Funayama M, Takata T, Koreki A *et al*. Catatonic stupor in schizophrenic disorders and subsequent medical complications and mortality. *Psychosom Med*. 2018;80:370–6.
4 Mann SC, Caroff SN, Campbell EC. Malignant Catatonia. In: Frucht SJ (ed.). *Movement Disorder Emergencies: Diagnosis and Treatment*. Cham: Springer International Publishing, 2022:115–37.
5 Rogers JP, Oldham MA, Fricchione G *et al*. Evidence-based consensus guidelines for the management of catatonia: Recommendations from the British Association for Psychopharmacology. *J Psychopharmacol* 2023;37:327–69.
6 Stone J. Functional neurological disorders: the neurological assessment as treatment. *Practical Neurol* 2016;16:7–17.
7 Oldham MA. The probability that catatonia in the hospital has a medical cause and the relative proportions of its causes: a systematic review. *Psychosomatics* 2018;59:333–40.
8 Northoff G, Krill W, Wenke J *et al*. Major differences in subjective experience of akinetic states in catatonic and parkinsonian patients. *Cognitive Neuropsychiatry* 1998;3:161–78.
9 Clinebell K, Azzam PN, Gopalan P *et al*. Guidelines for preventing common medical complications of catatonia: case report and literature review. *J Clin Psychiatry* 2014;75:644–51.
10 NICE. *Guidance on the use of electroconvulsive therapy*. London: NICE, 2003.
11 General Medical Council. *Good practice in prescribing and managing medicines and devices*. London: General Medical Council; 2022.

Address for correspondence: Dr Jonathan P Rogers, UCL Division of Psychiatry, 6th Floor, Maple House, 149 Tottenham Court Rd, Bloomsbury, London, W1T 7NF, UK.
Email: jonathan.rogers@ucl.ac.uk
Twitter: @drjprogers; @michael_zandi; @ProfTonyDavid