Catatonia: Diagnosis, Treatment and Clinical Challenges

Subjects: Neurosciences

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Catatonia is a syndrome that has been associated with several mental illness disorders but that has also presented as a result of other medical conditions. It is defined as a group of symptoms that involve a lack of movement as well as a lack of communication. It can be accompanied by agitation, confusion, and restlessness. Schizophrenia and other psychiatric disorders such as mania and depression are known to be associated with catatonia. The treatment of catatonia often involves the use of benzodiazepines, such as lorazepam, that can be used in combination therapy with antipsychotics. Definitive treatment may be found with electroconvulsive therapy (ECT).

Keywords: schizophrenia ; catatonia ; benzodiazepines ; ECT

1. Catatonia Causes, Presentation, and Pathophysiology

1.1. Types of Catatonia

There are three types of catatonia that clinicians need to be aware of. The first, and most common, is akinetic catatonia. A patient with this type of catatonia will stare and appears to be non-responsive [1]. Response to vocal and noxious stimuli is decreased [2]. These patients are alert and aware of their surroundings. The second type of catatonia is excited catatonia. A patient with this type may move, but their movements seem pointless and impulsive. They can appear agitated, combative, or even delirious [1]. The excess motor activity could cause either harm to the patient themself or harm to others [2]. The last type is malignant catatonia. This type of catatonia is dangerous and is associated with autonomic instability [1]. This can be seen in neuroleptic malignant syndrome and can signal a potential lethal underlying cause of the catatonia. Malignant catatonia can evolve rapidly, within a matter of days [3]. It is because of this rapid evolution that clinicians need to keep this in mind when seeing a person with suspected catatonia and act quickly to treat the underlying cause.

Although not an official subtype of catatonia, periodic catatonia can present as a diagnostic challenge for clinicians and should be discussed. Periodic catatonia is a rare form of catatonia where the symptoms present in phases and can disappear completely in between episodes [4]. The pathophysiology of periodic catatonia is unclear at this time, though it may be related to a dysfunctional GABA signal since acute cases respond well to benzodiazepines [5]. There have been cases reported where treatment with an atypical antipsychotic relieved symptoms [5].

1.2. Causes

It is important to note that catatonia is a constellation of symptoms that are a result of an underlying disorder. Catatonia itself is not a disorder but rather a syndrome. Psychiatric disorders are the first source that comes to mind when thinking about the underlaying causes of catatonia. Patients with bipolar disorder, autism, schizophrenia, major depressive disorder, or mixed psychiatric conditions all have a higher incidence of catatonia than the general population [6]. In fact, roughly 35% of individuals with schizophrenia will show symptoms of catatonia at some point [7]. It is because of this that it is important to keep catatonia in mind in patients with schizophrenia when abnormal movement and communication is present, as this could be a presentation of neuroleptic malignant syndrome, a life-threatening syndrome that can be caused by antipsychotic use. Roughly 20% of patients with catatonia have a medical cause rather than a psychiatric one [8]. Additionally, general medical conditions such as strokes, neoplasms, infections, autoimmune disorders, neurodegenerative diseases, metabolic derangements, and certain drugs have all been associated with catatonia [8]. Infectious and autoimmune etiologies account for roughly 29% of cases associated with general medical causes, and studies have shown that meningitis and encephalitis as well as systemic bacterial, viral, or fungal infections may result in catatonia [9]. Further, autoimmune processes, particularly N-methyl-D-aspartate receptor (NMDAR) encephalitis and systemic lupus erythematous (SLE) also have a strong association with catatonia [9]. In fact, NMDAR encephalitis is

responsible for 72% of all autoimmune cases of catatonia. The percentages presented in this section are meant to highlight that catatonia should be on the clinician's radar whenever the syndrome is even slightly suspected. The exact reason why some medical conditions lead to catatonia is not well understood; however, direct neurotoxic effects, the patient's psychological reaction to the insult, or mediation by acute phase reactants have all been suggested as potential causes [9][10].

1.3. Pathophysiology

The pathophysiology of catatonia is not currently well understood. However, recent studies suggest that three motor pathways within the brain and brainstem are responsible [11][12][13]. The first pathway leads from the primary motor cortex (M1) to the putamen, the internal and external pallidum, the thalamus, and then back to M1. This pathway is responsible for the inhibition and excitation of movements [12][13]. Another circuit runs between the M1, thalamus, cerebellum, and pontine nuclei and is responsible for motor dynamics and timing [11][12][13]. Lastly, the third circuit is composed of the M1, supplementary motor area (SMA), posterior parietal cortex, and medial prefrontal cortex and controls motor organization and speed [11][12][13]. The dysfunction of any of these circuits could lead to catatonic symptoms. Blood flow to the M1 and SMA has been shown to be increased in patients with catatonia compared to those without catatonia, further suggesting the increased neural activity of these circuits, likely resulting in catatonic behavior [14][15][16][17].

Reduced GABA activity, specifically GABA-A receptor activity, in the right lateral orbitofrontal and right posterior parietal cortex is thought to be another driver of the dysfunction seen in catatonia syndrome [18]. This dysfunction could explain the motor and affective symptoms seen in catatonia. This would explain why patients with catatonia respond well to and why benzodiazepines remain the mainstay of treatment for catatonia. This class of drugs stimulates GABA-A binding and relieves the symptoms of catatonia, presumably by lowering the increased neural activity in the circuits described above. Dysfunctional connections between the orbitofrontal cortex and the medial prefrontal cortices can be partially reversed by the administration of benzodiazepines, and imaging shows reduced GABA-A receptor density in cortical areas such as the left sensorimotor cortex [19][20]. Therefore, dysfunctional GABA-A signaling also seems to contribute to catatonia.

2. Catatonia Current Treatment

The early initiation of treatment in patients presenting with catatonia can reduce the risk of complications. When patients develop catatonia, their risk of developing deep venous thrombosis and pulmonary embolism increases substantially and occurs frequently [21]. This is due to the patient's immobility. Other complications include malnutrition, infection, and muscle contractures, as the patient's mobility is decreased, and they may refuse oral intake [22][23][24]. Despite the development of possible complications, most patients experience a resolution of symptoms with proper management [25].

The first-line treatment for catatonia is generally benzodiazepines, unless malignant catatonia is present. Benzodiazepines work on the GABA-A receptors and help to relieve the GABA dysfunction seen in some patients presenting with catatonia syndrome. Various benzodiazepines have been studied, and while lorazepam is typically used, others can also be considered, especially when additional symptoms or disorders are present. Caution must be used in patients exhibiting delirium, as their presentation can worsen; such patients may require lower doses for treatment [26]. When catatonia is suspected, a lorazepam challenge can be performed. This is done by giving a dose of lorazepam, either through IM or IV, and watching for a response. A response indicates the need for high suspicion of catatonia. In the case of substance-induced catatonia, a combination of lorazepam and diazepam has been shown to be an effective treatment plan, with the resolution of symptoms occurring within a day [27].

Electroconvulsive therapy (ECT) has been used to treat various mental disorders for many years and is an established treatment modality that has been proven to be highly effective for several conditions. Treatment involves brief electrical brain stimulations under anesthesia. ECT is a first-line treatment in neuroleptic malignant syndrome, malignant catatonia, and delirious catatonia. ECT is thought to work by increasing cerebral blood flow to the orbitofrontal and parietal cortices, which increases GABA activity and GABA receptor expression [28]. It can also be a definitive treatment when treatment with benzodiazepines has failed. The response rate of catatonia symptoms when ECT is used is around 80–100% [29] It can take several ECT treatments to achieve the desired results [30]. It can take at least six sessions for symptom relief to be seen [28]. The number of total ECT sessions needed cannot be predicted. The termination of ECT can be considered when a full clinical response is achieved or when there is further clinical improvement after two consecutive sessions [29].

Predictors of a favorable response to ECT are noted to be young age, the presence of autonomic dysregulation at baseline, daily ECT during the first week of treatment, longer duration of motor and EEG seizure activity at the final ECT sessions, and less morbidity in the year after ECT [29]. Contraindications to ECT include myocardial infarction within 3

months, elevated intracranial pressure, pheochromocytoma, cerebral tumors, and cerebral aneurysms [31]. Associated side effects may include impaired new learning, anterograde and retrograde amnesia, and autobiographical memory; these side effects usually resolve within weeks to months, but it may take up to 6 months for cognitive function to return to baseline [32][33][34]. A previous history of cognitive impairment places patients at higher risk of developing side effects [32]. If patients experience recurrent episodes, ECT may be continued for maintenance treatment [35].

3. Clinical Challenges

While ECT has been proven to produce a positive response in patients with catatonia, there are challenging aspects aside from the possible side effects resulting from this treatment modality. One such difficulty is obtaining consent from the patient. Patients in a catatonic state may be unable to provide full consent or refuse such treatment. In the USA, the guardian in these cases may make medical decisions; however, ECT treatment is typically not included, and a petition must be obtained [36]. A catatonic patient's autonomy sets ethical challenges, as they are unable to fully comprehend the details of ECT treatment [36][37]. This same challenge presents in adolescent patients; however, healthcare professionals must consider the risks versus the benefits [37]. ECT has been found to be safe and effective in the pediatric population and is available as a form of treatment for them.

Other challenging aspects of catatonia involve its various forms of presentation, one of them being periodic catatonia. Periodic catatonia is a subtype of catatonia in which patients regularly experience multiple episodes. Although rare, it is a difficult subtype to diagnose and treat, as it may disappear before it can be treated [4]. Tang et al. describe a case of a 73-year-old woman with episodes of appearing ill for 45 years, which was initially thought to be a non-specific psychosis. She was initially placed on antipsychotics but was noted to have a good response to benzodiazepines. It was later discovered that her symptoms and presentation were consistent with periodic catatonia, and she was treated with multiple sessions of ECT. Her catatonia remained in remission for one year [38]. In patients presenting with multiple episodes of psychosis with symptoms meeting the criteria for catatonia, periodic catatonia should be considered in the differential diagnosis. Treating patients with antipsychotics in such cases may exacerbate catatonia and may induce neuroleptic malignant syndrome or malignant catatonia [39][40]. When neuroleptic malignant syndrome or malignant catatonia occurs, benzodiazepines have been proven to be an effective form of treatment for both conditions [40].

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