Response to eperisone in patients of therapy-resistant dissociative convulsions: A report of two cases

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Abstract:
Dissociative convulsions or pseudoseizures are a difficult to treat common psychiatric condition. In a subset of these patients, the chief complaint is clenching of teeth with apparent nonresponsiveness alone. Neither drugs nor psychotherapeutic interventions have been found to be of much help in its management. Report of two such subsets of cases is presented, in which patients with dissociative convulsions showed sudden, dramatic, and sustained good response to the addition of a muscle relaxant eperisone.

Key words:
Dissociative convulsions, dissociative disorder, eperisone

Dissociative disorder is a commonly seen clinical entity in psychiatric practices in developing countries, and dissociative convulsions (pseudoseizures) are its most common presentation. Most often, they respond poorly to the psychotherapeutic, social intervention, and routinely used psychotropics. Management of many such patients is not only challenging but also frustrating. Here, we report cases of two such patients, who had not shown any improvement with earlier mentioned interventions but showed immediate, dramatic, complete, and sustained response to the addition of a muscle relaxant eperisone.

Case Reports

Case 1
A 22-year-old educated, unmarried female presented with the complaint of frequent spells of unresponsiveness for the last 4 years. Her spells were characterized by a variety of symptoms such as teeth clenching, up rolling of eyeballs, tightening of the limbs, and apparent unresponsiveness which would last for several hours. These spells were not preceded by premonitory symptoms such as dizziness, gastric irritation, and déjà vu. There were no tongue bites, urinary or fecal incontinence, or fall injury related to these spells. The patient would gain consciousness immediately without any period of confusion. These spells would occur several times in a day but never while the patient was asleep. Her symptoms differed on different occasions. She was admitted as an inpatient for detailed evaluation. There was no significant past or family history. Physical as well as radiological examinations were unremarkable. Serial mental state examination revealed only anxious affect. Based on the history and examinations, she was diagnosed as a case of dissociative convulsions. Psychological evaluation and intervention were initiated, but the patient did not show satisfactory cooperation in different settings. Anxiolytics and several classes of antidepressants and low-dose antipsychotics were prescribed for adequate duration, but to no avail.

Her symptoms did not seem to respond to any intervention, which made both the attendant and the doctors clueless. To target her possible motor hyperresponsiveness, muscle relaxant eperisone was added presumptively. Eperisone was given orally in the dose of 50 mg twice a day and increased to 150 mg a day in divided doses. Her symptoms disappeared almost completely from the next day. This cannot be explained by any nonspecific “halo effect” of either the drug or the doctor as she was being treated with different drugs earlier too by the same team of doctors. On stopping eperisone, her symptoms recurred, and the symptoms improved on restarting the drug. She has been...
followed up for over a year now and no recurrence or change in symptoms has been observed.

Case 2
The second patient was an 18-year-old girl with 1-year history of similar spells of clenching of teeth with prolonged unresponsiveness as in the earlier case. However, this case had far many spells more than fifty times/day. In addition, she had sadness of mood and decreased interest in activities. No physical abnormality was detected on examination. She was diagnosed as a case of moderate depressive episode with dissociative convulsions. She was started on antidepressant and psychological intervention was also given. Her low mood responded to the treatment, but her dissociative convulsions continued. Going by the positive response in our earlier case, this patient was also given oral eperisone in a similar dose and for a similar duration and her convulsions responded immediately. Frequency of her convulsions decreased from over fifty times/day to <5/day from next day to nil over subsequent period. Her convulsions also recurred after stopping the drug but responded on restarting it. The patient has been maintaining well on follow-up.

Discussion
Both cases provide definite evidence of dramatic and sustained response to addition of muscle relaxant eperisone to the management of therapy-resistant convulsions. It is worthwhile exploring the possible ways in which eperisone might have helped.

Possible mechanisms of action of eperisone as a muscle relaxant include:\[3\]
1. Inhibition of mono- and multi-synaptic reflexes in relation to the inhibitory action on α- and γ-efferent neurons in spinal and supraspinal structures
2. Suppression of frequency of spontaneous afferent discharges of muscle spindle and the dynamic and static responses of spindle to stretch, the latter as a consequence of modifications of descending influences from central structures on the static and dynamic γ-efferent neurons that innervate the muscle spindle
3. Possible calcium antagonistic action
4. Sigma receptor modulation.

The role of eperisone can be better understood with a brief overview of muscle spindle physiology.\[4\] Muscle spindle is an encapsulated structure located inside the muscle and is responsible for providing proprioceptive feedback to brain and mediating the reflexes. It is composed of nuclear bag fibers and nuclear chain fibers (intrafusal fibers) which are innervated by I, IIa afferent nerves and the dynamic and static γ-efferent nerves (motor neurons). γ-motor neurons are smaller than α-motor neurons with slow conduction velocity and are responsible for regulating spindle sensitivity. Activation of dynamic γ-motor neurons increases the dynamic sensitivity of Ia nerve endings while activation of static γ-motor neurons increases the tonic activity of Ia, II endings.

When spindle ends are stretched, this is sensed by Ia and II nerves which respond by activation of α-motor neurons and contraction of entire muscle. With γ-motor neuron discharge, ends of fiber contract and this resulting stretch are sensed by afferents which by activating α-motor neuron contract the entire muscle. This γ-efferent discharge is influenced by supraspinal structures.

It is generally acknowledged and accepted that anxiety is the most crucial antecedent to production of convulsive symptoms. In fact the word “conversion” derives its validity from the original concept that it is anxiety that is getting converted into somatic symptom. Neurophysiological studies suggest that anxiety is known to increase γ-efferent discharge so that anxious patients have increased resting muscle tone and increased reflexes. Hence, it appears as if spindle sensitivity is different and variable in anxious patients.

It is a common observation in our clinical setting that in conversive fits, there is a preferential involvement of cranial musculature (teeth clenching due to masseter contraction). It was evaluated whether there exists any significant reason in terms of their structure and function. Indeed several distinct features were found which make them more readily contractile:\[5-7\]
1. They have different isoforms of myosin fibrils
2. Different composition of their motor units
3. Fast contracting fibers being smaller and more readily recruited during muscle contraction
4. Light chains govern the force-velocity kinetics in case of masseter (only muscle known in humans to have such property).

These differences allow for the rapid contraction and relaxation of these muscles and could be the reason for their preferential involvement in some predisposed patients.

Conclusion
These findings pose a question as to whether the clinical and neurophysiological observations can be interrelated. It is possible that evoked anxiety can lead to greater sensitization of muscle spindles of predisposed individuals more specifically in cranial muscles which have inbuilt greater readiness to respond because of their structural differences at the molecular level. This could be the mechanism of production of symptom of “clenching of teeth” which is so commonly seen in a subset of dissociative patients.

In these groups of patients, it is seen that merely prescribing drugs to relieve the anxiety are not sufficient and they need some additional drugs with possibly different target. One such approach could be to target the effector itself, i.e., the muscle. Eperisone and related molecules can be useful in this regard as it decreases the heightened sensitivity of muscles to contract and thereby lead to relaxation.

It was also observed that this approach could at best be an add-on therapy and not monotherapy but any significant relief, of whatsoever quantity, in these therapy-resistant patients is most welcome. The speed and completeness of response of these two patients to this muscle relaxant suggest that these molecules may have a bright future and therefore need to be evaluated more objectively on large samples.
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Conflicts of Interest
There are no conflicts of interest.

References

1. Wig NN, Mangalwedhe K, Bedi H, Murthy RS. A follow up study of hysteria. Indian J Psychiatry 1982;24:120-5.
2. Deka K, Chaudhury PK, Bora K, Kalita P. A study of clinical correlates and socio-demographic profile in conversion disorder. Indian J Psychiatry 2007;49:205-7.
3. Tanaka K, Kaneko T, Yamatsu K. Effects of 4’ethyl-2-methyl-3-piperidinopropiophenone on experimental rigidity and spinal cord activities (author’s transl). Nihon Yakurigaku Zasshi 1981;77:511-20.
4. Barrett KE, Barman SM, Boitano S, Brooks HL. Ganong’s Review of Medical Physiology. 23rd ed. New York: The McGraw-Hill; 2010. p. 130-6.
5. Sciote JJ, Morris TJ. Skeletal muscle function and fibre types: The relationship between occlusal function and the phenotype of jaw-closing muscles in human. J Orthod 2000;27:15-30.
6. Rowlerson AM. Specialization of mammalian jaw muscles: Fibre type compositions and the distribution of muscle spindles. In: Taylor A, editors. Neurophysiology of the Jaws and Teeth. London: Macmillan Press; 1990. p. 1-51.
7. Vignon C, Pellissier JF, Serratrice G. Further histochemical studies on masticatory muscles. J Neurol Sci 1980;45:157-76.