

The unique nature of seizures in autoimmune encephalitis



What are seizures?

Seizures can be scary events both for people who suffer from them and for their loved ones. Symptoms of a seizure typically include muscle spasms; loss of consciousness; sudden, rapid eye movements; or sudden mood changes; among other symptoms, and these can last from seconds to minutes¹. These are the most severe seizures, but mild seizures, with more moderate physical and behavioral symptoms — such as stiffness of the muscles, feelings of déjà vu, anxiety, temporary confusion, or nausea — can also happen and may negatively affect health. During seizures, the body parallels what is happening in the brain: uncontrolled movements of the body can result from uncontrolled bursts of electrical activity in the brain.

Seizures are a response to hyperexcitability, meaning increased activity, of neurons in the brain, and hypersynchrony, meaning more neurons fire at the same time than normal. Seizures are very different across and within conditions. They can be generalized, affecting the entire brain from the beginning of the seizure, or focal, affecting one specific area although it may later spread. Frequent, unprovoked seizures called recurrent seizures may indicate that the person has a condition called epilepsy. Epilepsy is a chronic neurological disorder in which seizures can cause periods of unusual behavior, sensations, and negative effects on cognition such as a loss of awareness. However, because abnormal electrical activity can happen in response to other alterations in the brain such as brain injury

Written by: Claudia Lopez Lloreda, [PennNeuroKnow](#)



ALLIES IN AUTOIMMUNE ENCEPHALITIS
AND NEUROSCIENCE EDUCATION

and in response to medications, seizures can also be seen in other conditions.

One of these conditions is autoimmune encephalitis (AE). In AE, the body attacks the brain by creating antibodies against important neuronal proteins. Because these proteins help neurons communicate, the antibodies alter neuronal activity. Altering neuronal activation can lead to the changes that are seen in seizures (hyperexcitability and hypersynchrony). In fact, research shows that seizures in some patients can be a common symptom during the acute phase (early on in disease) of AE². It is believed that antibodies against the neuronal proteins contribute directly to the disease processes and the development of seizures. It's also possible that the process of neuroinflammation associated with AE, which increases the amount of toxic inflammatory molecules in the brain, can also contribute to the development of seizures². Even once the inflammation has been resolved, the brain can still be predisposed to seizures or developing epilepsy, especially if the inflammation resulted in neuronal death³. However, whether epilepsy, a chronic disease, is developed in response to AE is not entirely clear. Some studies suggest that the risk of developing chronic epilepsy is low, from 10-15%⁴.

In different types of AE, seizures appear differently. Apart from the well-known tonic-clonic seizures (associated with jerking muscle movements), seizures in AE can also show up as faciobrachial dystonic seizures. These are characterized by abrupt involuntary movements, typically on one half of the face and arm of the same side. The frequency, response to therapies, and symptoms of the seizures themselves can all vary. However, the AE that most frequently manifest with seizures and chronic epilepsy are those mediated by antibodies against the LGI1, GABA_BR, and GABA_AR; all important proteins involved in neuronal communication⁵.

Are seizures associated with AE treated the same way as in epilepsy?

Antiepileptic drugs are the standard of care for people with epilepsy. Since seizures are a result of uncontrolled electrical activity and an imbalance of excitation and inhibition in the brain, antiepileptic drugs work by trying to restore that balance. For example, the drug clonazepam prevents seizures by increasing the effectiveness of a molecule in the brain called GABA, which helps the brain dampen the uncontrolled brain activity.

Now, although the normal path for people with epilepsy is treatment with antiepileptic drugs, it may not be particularly effective for people with seizures associated with AE. A study looking at a population of AE patients found that resolution of seizures happened even after discontinued antiepileptic drugs therapy⁶. In these young patients with AE who experienced unprovoked seizures at the onset of the disease there was a remission rate of 94%, meaning they stopped suffering from seizures, after they stopped taking antiepileptic drugs. Rather, immunotherapy seemed to be the important factor in controlling seizures. The researchers suggested that "long-term use of antiepileptic drugs appears not to be necessary to control seizures in AE"⁶.

Other studies support the idea that immunotherapy is more effective in attacking seizures in AE. One study looked at three different types of autoimmune encephalitis (anti-LGI1, anti-NMDAR, and anti-GABA_BR) and their response to immunotherapy and antiepileptic drugs⁷. They found that seizure freedom was achieved faster and more frequently after the use of immunotherapy than after the use of antiepileptic drugs. However, there may be a specific window in which immunotherapy is effective at controlling seizures.

Importantly, the researchers do mention that differences in seizures characteristics and therefore response to treatment may be due to the specific type of encephalitis. For example, patients with anti-GABA_BR encephalitis had an increased risk of developing seizures, meaning that the development of seizures may depend on the type of encephalitis⁷.

Written by: Claudia Lopez Lloreda, [PennNeuroKnow](#)

What do these findings mean for people with AE?

These differences in treatment response between AE and epilepsy point to an important trait that needs to be considered: the cause of seizures. In AE, antibodies generated against important neuronal proteins make the brain go awry. Therefore, one of the most effective ways to treat seizures may be attacking the root of the problem with immunotherapy. However, due to the variable nature of AE and the seizures associated with the condition, proper treatment with immunotherapy and/or antiepileptic medication will change from patient to patient.

What to do if someone is having a seizure?

During the most severe seizures, the person may not be able to control their body movements. For this reason, you may help them clear the area around them to prevent possible injury. If possible, place them on their side and provide cushioning for their head. There are additional indications suggested by the Center for Disease Control (become familiar with these [here](#)).

References

1. Epilepsy. (2019, August 10). Retrieved March 6, 2020, from <https://www.mayoclinic.org/diseases-conditions/epilepsy/symptoms-causes/syc-20350093>
2. Rana, A., & Musto, A. E. (2018). The role of inflammation in the development of epilepsy. *Journal of Neuroinflammation*, *15*(1). doi: 10.1186/s12974-018-1192-7
3. Vezzani, A., Fujinami, R. S., White, H. S., Preux, P.-M., Blümcke, I., Sander, J. W., & Löscher, W. (2015). Infections, inflammation and epilepsy. *Acta Neuropathologica*, *131*(2), 211–234. doi: 10.1007/s00401-015-1481-5
4. Steriade, C., Moosa, A. N., Hantus, S., Prayson, R. A., Alexopoulos, A., & Rae-Grant, A. (2018). Electroclinical features of seizures associated with autoimmune encephalitis. *Seizure*, *60*, 198–204. doi: 10.1016/j.seizure.2018.06.021
5. Spatola, M., & Dalmau, J. (2017). Seizures and risk of epilepsy in autoimmune and other inflammatory encephalitis. *Current Opinion in Neurology*, *30*(3), 345–353. doi: 10.1097/wco.0000000000000449
6. Huang, Q., Ma, M., Wei, X., Liao, Y., Qi, H., Wu, Y., & Wu, Y. (2019). Characteristics of Seizure and Antiepileptic Drug Utilization in Outpatients with Autoimmune Encephalitis. *Frontiers in Neurology*, *9*. doi: 10.3389/fneur.2018.01136
7. Bruijn, M. A. D., Sonderen, A. V., Coevorden-Hameete, M. H. V., Bastiaansen, A. E., Schreurs, M. W., Rouhl, R. P., ... Titulaer, M. J. (2019). Evaluation of seizure treatment in anti-LGI1, anti-NMDAR, and anti-GABABR encephalitis. *Neurology*, *92*(19). doi: 10.1212/wnl.00000000000007475

Cover Image from Pixabay: <https://pixabay.com/illustrations/epilepsy-seizure-stroke-headache-623346/>

Written by: Claudia Lopez Lloreda, [PennNeuroKnow](#)

