

Why do patients with meningiomas have seizures?

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Abstract

Individuals with brain tumors frequently have seizures, and the seizures can be as difficult to manage as the brain tumor itself. The onset of seizures in someone who has never had a seizure before can be the first sign of a brain tumor. For others, seizures may not begin until after their brain tumor has been removed. Because seizures themselves can be life threatening, it is critical that patients and physicians discuss the causes and treatments of tumor-associated seizures.

This paper explores the current state of research on tumor-associated seizures. Although a great deal of research has been done, our understanding of the mechanisms underlying these types of seizures is incomplete. We *do* know that seizures can accompany other types of injury to the brain as well, such as stroke, trauma, infection, neurodegenerative disease, neurosurgery, and other disorders affecting the brain. It is likely that all of these different disorders set the stage for seizure activity by in some way increasing the excitability of neurons.

Overview of Research on Tumor-Associated Seizures

Tumor-associated seizures can occur with all types of brain tumors, but they are more common with some types of brain tumors than with others¹:

Frequency of seizures in people with specific types of brain tumors

Type of brain tumor	Percent of individuals with this type of brain tumor who have seizures
Ganglioglioma	90%
Low-grade glioma	60-85%
High-grade glioma	54-69%
Glioblastoma	29-49%
Meningioma	29-41%
Metastases to the brain	35%

Some of these types of brain tumors, such as meningiomas, compress adjacent brain tissue but do not invade the normal tissue. Cells of other brain tumors, such as glioblastoma, infiltrate normal brain tissue. Despite differences in behavior, all brain tumors are capable of causing seizures. In order to understand why tumors cause seizures, we must first understand what happens in the brain during a seizure.

Seizure Origin

The brain is comprised of different cell types. The cells in the brain that are responsible for generating and propagating electrical activity are called *neurons*. The connections between neurons are called *synapses*. The term “seizure focus” is often used to refer to a cluster of neurons that show increased electrical activity. The increased electrical activity of the neurons in a seizure focus can be due to a number of factors: altered properties of

¹ Lote K, Stenwig AE, Skullerud K, Hirschberg H: Prevalence and prognostic significance of epilepsy in patients with gliomas. **Eur J Cancer** 34:98-102, 1998. Tandon PN, Mahapatra AK, Khosla A: Epileptic

the neurons, altered synaptic connections between neurons, or altered conditions surrounding the neurons in their extracellular environment. Tumors, blood clots, scar tissue, and brain malformations are all known to alter these factors. The neurons within a seizure focus differ in behavior from most neurons in that they are capable of exhibiting a repetitive and synchronized electrical response known as a *paroxysmal depolarizing shift*. This is a sudden, large change in electrical charge that lasts a fraction of a second. If the abnormal electrical activity remains confined to the seizure focus, a seizure will not occur, but if the abnormal electrical activity spreads beyond the seizure focus, a seizure may occur.

Tumor-associated Seizures

In individuals with brain tumors, where is the seizure focus? It is logical to assume that the seizure focus is in the tumor itself. Since a brain tumor is a collection of abnormal cells, they might be prone to generate abnormal electrical activity. Indeed, tumor cells taken directly from certain types of brain tumors (namely gangliogliomas and dysembryoplastic neuroepithelial tumors) have shown the ability to generate electrical activity.² This has led some researchers to hypothesize that hyperexcitability may be an intrinsic feature of certain types of tumor cells.

There is also evidence, however, that seizures in the setting of a brain tumor may be due to alterations in the brain tissue surrounding the tumor, rather than within the tumor. The fact that seizures commonly persist despite removal of the tumor mass would

seizures in supratentorial gliomas. **Neurol India** 49:55-59, 2001. Beaumont A, Whittle IR: The Pathogenesis of Tumor Associated Epilepsy. **Acta Neurochir** 142:1-15, 2000.

² Blümcke I, Wiestler OD: Gangliogliomas: an intriguing tumor entity associated with focal epilepsies. **Journal of Neuropathology and Experimental Neurology** 61(7):575-84, 2002.

support the idea that the seizure focus lies somewhere outside of the brain tumor, or extends beyond the brain tumor to include surrounding tissue.³ The fact that seizures are common with brain tumors, such as meningiomas, which do not infiltrate surrounding brain tissue, but simply compress or distort surrounding brain tissue, also supports the idea that seizures originate in the tissue surrounding the brain tumor. Indeed, the tissue surrounding a brain tumor has been shown to differ from normal brain tissue with respect to structure and chemical activity.

It is also possible that the seizure focus lies in areas of the brain that are distant from the tumor. These regions have been found to show seizure-like activity, adding more uncertainty to the debate surrounding the origin of tumor-associated seizures.

Conclusion

Because seizures can be one of the main side effects of having a brain tumor, it is crucial that patients understand what a seizure is, what causes it, and what can be done to treat it. There are many types of medications that are highly effective in treating seizures. Many of the newer medications are as effective as the older ones and have fewer side effects. With ongoing research, we are gaining a better understanding of brain tumors and their associated seizures. A better understanding of these disorders will lead us closer to a cure.

³ Elger CE: Epilepsy: disease and model to study human brain function. **Brain Pathol** 12:193-98, 2002. Zentner J, Hufnagel A, Wolf HK, et al: Surgical treatment of neoplasms associated with medically intractable epilepsy. **Neurosurgery** 41:378-86, 1997.