Epilepsy Etiology

There is evidence suggesting that alterations in astrocyte chloride homeostasis may contribute to the development and maintenance of epileptic activity. The excitatory and inhibitory neurotransmission in the brain involve the release of neurotransmitters such as glutamate (excitatory) and GABA (gamma-aminobutyric acid, inhibitory). Changes in the concentration of chloride ions can affect the efficacy of GABAergic neurotransmission, as the direction and strength of the GABAergic response depend on the intracellular chloride concentration.

In some cases of epilepsy, it has been observed that the expression or function of the NKCC1 cotransporter in astrocytes and neurons may be altered. The NKCC1 cotransporter is responsible for importing chloride ions into cells, and increased activity of NKCC1 can result in elevated intracellular chloride levels. This, in turn, can lead to a shift in the GABAergic response from inhibitory to excitatory, a phenomenon known as “GABAergic depolarization.”

GABAergic depolarization can contribute to hyperexcitability in the brain, potentially facilitating the generation and propagation of epileptic seizures. Astrocytes may modulate the expression and function of NKCC1, influencing chloride homeostasis and, consequently, the balance between excitatory and inhibitory neurotransmission [1)]

see Epileptogenesis.

symptomatic (AKA “secondary”): seizures of known etiology (e.g. stroke, tumor…)

a) temporal lobe epilepsy:

●mesial temporal sclerosis

2. idiopathic (AKA “primary”): no underlying cause. Includes:

a) juvenile myoclonic epilepsy

3. cryptogenic: seizures presumed to be symptomatic but with unknown etiology

a) West syndrome (infantile spasms, Blitz-Nick-Salaam Krämpfe)

b) Lennox-Gastaut syndrome

4. special syndromes: situation-related seizures

a) Febrile seizures

b) seizures occurring only with acute metabolic or toxic events: e.g. alcohol

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Benzodiazepines increases the activity of seizure foci which may be used for mapping foci during seizure surgery but may also induce seizures

Craniotomy

Tumor-related

Seizures may be manifestation of intracranial tumor (IT) and demand thorough neurological evaluation. Tumor histology does not seem to affect seizure predisposition. Most seizures associated with IT occur in fifth and sixth decades of life and affect frontal lobe most often [2].

Thery are a common symptom in patients with Low-grade glioma (LGG), negatively influencing quality of life, if uncontrolled.

Seizures are the most frequent and often the only manifestation in patients with brain tumors of glial origin, and medical treatment appears to be less effective for seizure control because of incomplete understanding of underlying pathophysiological mechanisms. Particularly, patients with slow-growing low-grade tumors (low-grade gliomas (LGGs) and glioneuronal tumors) in cortical areas of the temporal lobe are more frequently associated with seizures than high-grade tumors [3] [4] [5].

Clinically, tumor-related seizures manifest as simple or complex partial seizures with or without secondary generalization and, in more than 50% of cases, are pharmacoresistant. When uncontrolled, tumor-related epilepsy affects patients' quality of life, causes cognitive deterioration, and may result in significant morbidity [6] [7].

Seizures during status epilepticus (SE) cause neuronal death and induce cyclooxygenase-2 (COX-2).

Traumatic brain injury (TBI)

see Posttraumatic seizures.

Seizures may cause diagnostic confusion and be a source of metabolic stress after Pediatric traumatic brain injury. The incidence of electroencephalography (EEG)-confirmed seizures and of subclinical seizures in the pediatric population with TBI is not well known.

Seizure after aneurysmal subarachnoid hemorrhage

see Seizure after aneurysmal subarachnoid hemorrhage.

see Epilepsy in cerebral arteriovenous malformation.

see Epilepsy in Sturge-Weber syndrome.

Fibromuscular dysplasia

Neurocysticercosis

1)
Untiet V, Nedergaard M, Verkhratsky A. Astrocyte chloride, excitatory-inhibitory balance and epilepsy. Neural Regen Res. 2024 Sep 1;19(9):1887. doi: 10.4103/1673-5374.390981. Epub 2023 Dec 15. PMID: 38227511.
2)
Mezue WC, Ndubuisi CA, Chikani MC, Onyia E, Iroegbu L, Ohaegbulam SC. Epilepsy in primary

intracranial tumors in a neurosurgical hospital in Enugu, South-East Nigeria. Niger J Clin Pract. 2015 Sep-Oct;18(5):681-6. doi: 10.4103/1119-3077.158980. PubMed PMID: 26096250.
3)
van Breemen MS, Wilms EB, Vecht CJ. Epilepsy in patients with brain tumours: epidemiology, mechanisms, and management. Lancet Neurol. 2007;6:421–430. doi: 10.1016/S1474-4422(07)70103-5.
4)
Chang EF, Potts MB, Keles GE, Lamborn KR, Chang SM, Barbaro NM, et al. Seizure characteristics and control following resection in 332 patients with low-grade gliomas. J Neurosurg. 2008;108:227–235. doi: 10.3171/JNS/2008/108/2/0227.
5)
Lee JW, Wen PY, Hurwitz S, Black P, Kesari S, Drappatz J, et al. Morphological characteristics of brain tumors causing seizures. Arch Neurol. 2010;67:336–342.
6)
Klein M, Engelberts NH, van der Ploeg HM, et al. Epilepsy in low-grade gliomas: the impact on cognitive function and quality of life. Ann Neurol. 2003;54:514–520.
7)
Taphoorn MJ, Klein M. Cognitive deficits in adult patients with brain tumours. Lancet Neurol. 2004;3:159–168.