

DO WE HAVE TO TREAT POST-TRAUMATIC SEIZURES FOLLOWING THE FIRST SEIZURE? YES

Alla Guekht

Moscow Research and Clinical Center for Neuropsychiatry, Russian National Research Medical University, Moscow City Hospital № 12, Russia

Traumatic brain injury (TBI) is one of the **major causes of acquired epilepsy**. TBI accounts for approximately 4% of focal epilepsy in the general population (Annegers, 1996).

TBI results in potentially epileptogenic brain damage **through a number of mechanisms**. Among them - cicatrix in the cortex, focal contusions and intracranial hemorrhages, toxic effects of hemoglobin breakdown products, secondary cellular damage through the release of excitatory amino acids, cytokines, bioactive lipids. Epileptogenesis may arise from diffuse injury as a result of selective damage to hippocampus (Willmore, 1990; Coulter et al., 1996; Diaz-Arrastia et al., 2000; 2009; D'Ambrosio, Perucca, 2004; D'Ambrosio et al., 2004).

Post-traumatic seizures (PTS) can occur soon after the injury, presumably as a consequence of the acute pathophysiologic changes secondary to the neurologic insult, or they may first develop months to years (even decades) after the head injury. Accordingly, **early**, or provoked (up to seven days after the injury) or **late**, unprovoked (more than seven days after the injury) PTS are identified. Post-traumatic epilepsy (PTE) is defined as two or more unprovoked seizures after the TBI. The incidence of early seizures ranges from 2.1 to 16.9%, late - from 1.9% to >30% (Frey, 2003)

The risk of developing posttraumatic seizures is substantially determined by the severity of the brain injury; the number of studies identified the following high-risk factors: acute intracranial hematoma, depressed skull fracture, dural penetration, the presence of focal neurological deficits, coma/ prolonged impairment of consciousness.

Risk factors can be identified for the occurrence of both early and late PTSs. The presence of an acute ICH, younger age, and higher injury severity are risk factors for early seizures. The presence of early PTSs, an acute ICH, a brain contusion, age older than 65 years at the time of injury, and higher injury severity increase the risk of late seizures (Annegers et al., 1998; Asikainen et al., 1999; Frey, 2003; Raymond et al., 2010).

PTS are associated with high probability of recurrence. The early PTS predict high (almost 2-fold) increase of incidence of late PTS. Late posttraumatic seizures are correlated with very high rate of recurrence (Englander et al., 2003). In the population-based study, 86 % of patients with one unprovoked post-traumatic seizure experienced a second seizure within 2 years (Haltiner et al., 1997). This confirms that the risk of developing PTE in patients after one unprovoked PTS is extremely high and requires treatment. Seizure frequency in the first year after injury predicted future severity of seizures.

Epilepsy resulting from brain trauma is often difficult to control with medical therapy, and is the cause of epilepsy in approximately 5% of patients referred to specialized epilepsy centers (Semah et al., 1998, De Reuck, 2011).

Also, in **TBI survivors the impact of a seizure disorder extends far beyond the medical intervention and care**. All aspects of the individual's life can be affected, particularly if the seizures are recurrent. Individuals with TBI and PTS, especially late, are exposed to substantial disadvantage regarding ongoing physical, cognitive, psychosocial issues following brain injury and epilepsy.

Treatment strategies should be developed to achieve seizure remission and to ameliorate these ongoing issues.

Taking into consideration:

- ***high incidence and prevalence of seizures and epilepsy after TBI***
- ***multiple mechanisms involved in the epileptogenesis after TBI***
- ***substantial number of identified risk factors of PTS***
- ***very high recurrence rate, especially of late PTS***
- ***difficulties in control of seizures and epilepsy after TBI***
- ***impact of seizures on the QOL***

it is important to initiate long-term AED treatment following the first unprovoked seizure after the TBI.

Regarding the early seizure – the decision should be individual and patient-tailored. In future genetic susceptibility to PTS might be considered. Some ongoing studies suggest genetic susceptibility to seizure disorders after TBI. The role of the APOE genotype in post-traumatic seizure, genetic variability for glutamic acid decarboxylase and adenosine A1 receptor are being investigated (Cavalleri et al., 2007; Wagner et al., 2010; Darrah et al. 2013)

Key references:

- Asikainen I et al., *Epilepsia* 1999 40:584–589.
Annegers JF et al., *N Engl J Med* 1998;338:20-4.
Chang BS, Lowenstein DH. *Neurology*. 2003; 60:10-6.
Coulter DA et al., *Epilepsy Res* 1996 26:81–91.
Darrah SD et al. *Epilepsy Res*. 2013;103(2-3):180-94.
D'Ambrosio R, Perucca E. *Curr Opin Neurol* 200417:731–735.
D'Ambrosio R et al., *Brain* 2004 127:304–314.
De Reuck J. *Clin Neurol Neurosurg*. 2011;113(6):469-71.
Diaz-Arrastia R et al., *Epilepsia*. 2009; 50(suppl 2):14-20.
Diaz-Arrastia R et al., *Arch Neurol* 200 57:1611–1616.
Englander J, et al., *Arch Phys Med Rehabil* 2003;84:365-73.
Jennett B. *Scot Med J* 1973;18:8-13.
Jensen FE. *Epilepsia*. 2009; 50(suppl 2):1-3.
Haltiner AM et al. *Arch Phys Med Rehabil* 1997;78:835-40.
Haltiner AM et al., *J Neurosurg*.1999; 91:588-92.
Hung C. *Chen Curr Treatment Options in Neurology* 2012 14:293–306
Raymont V et al. *Neurology*. 2010;75:224–9.
Wagner AK et al. *Epilepsy Res*. 2010 Aug;90(3):259-72.
Willmore LJ. *Epilepsia* 1990;31:S67–73