

NEUROPROTECTION – DO AEDs PROTECT THE BRAIN? (NO)

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For clinical purposes the multifaceted term neuroprotection should be understood as preservation of cerebral functions. Stroke, multiple sclerosis, neurodegenerative diseases and epilepsies could profit from neuroprotection.

Numerous animal experiments with a wide range of substances including AEDs have demonstrated neuroprotective effects (for review see Stepien et al., 2005). Clinical trials with these drugs have been characterized by subsequent failures (Calabresi et al., 2003; Cheng et al., 2004; O'Collins et al., 2006; Willmore, 2005). These disappointing results led to the question, if it is time to definitely abandon neuroprotection from the clinical armamentarium (Sacchetti, 2008).

Since stroke and seizure-induced neuronal injury share some pathophysiological mechanisms, AEDs should play a distinct role as neuroprotective drugs. AEDs are developed to suppress epileptic seizures. AEDs are not successful in preventing the development of epilepsies in people at risk (Temkin, 2001), they are not antiepileptogenic (Schachter, 2002; Walker et al., 2002), and do not cure established epilepsies. They represent a strictly symptomatic treatment of seizures. The proven antiseizure activity per se can act disease modifying. The complex development of temporal lobe epilepsies with initial lesion, quiescent period, second hit, recurrent epileptic seizures and progressive intractability has extensively studied by the group of Pitkänen in animal models of status epilepticus (Pitkänen and Kubova, 2004). Like in stroke experiments positive results could not be translated from bench to bedside.

Where is the evidence that animal research benefits humans? (Pound et al., 2004). Methodological problems in experiments might be responsible for failures (Crossley et al., 2008). However, the question also arises, if we are doing the right thing with clinical trials, especially with timing and dosing.

In summary, with AEDs no neuroprotective abilities besides seizure suppression have reached clinical significance. On the contrary, AEDs can be harmful to the brain, at least for cognitive functions.

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