

ARE CURRENT ANIMAL MODELS FOR SEIZURE AND EPILEPTIC DISORDERS USEFUL FOR DISCOVER NOVEL ANTIEPILEPTIC DRUGS?

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Several animal models are available for the study of epilepsy and these models have a proven history in advancing our understanding of basic mechanisms underlying epileptogenesis and have been instrumental in the screening of novel antiepileptic drugs. *In vivo* animal models have been categorized into models of seizures and those of epilepsy. Since human epilepsy is defined by the appearance of multiple spontaneous recurrent seizures, induction of acute seizure activity alone without chronic epileptiform behaviour is considered a model for seizures and not epilepsy (1). For example, adult rodents will have a severe, generalized seizure in response to a single exposure to the potent neurotoxin flurothyl, but will not develop spontaneous seizures; in comparison, a convulsant dose of kainic acid (KA) causes dramatic, permanent brain damage and subsequent spontaneous seizures (2,3).

Genetic models in rats and mice have been valuable in understanding basic mechanisms of partial or generalized seizure-related phenomena and are standard techniques for evaluating new therapeutics. I shall try to address the criteria that should be met in a valid animal model and to provide an overview of current animal models that are relevant to human conditions. In fact, the validity of animal models has been challenged for several reasons. First, many of the models draw mechanistic conclusions about epilepsy based on studies performed in a normal and not an epileptic brain. Second, behavioural manifestations associated with each model can differ and look nothing like a human's behavior. In addition, models not specific for any one human condition but rather exhibiting partial or generalized seizures are discussed. Perhaps future animal models in epilepsy research will be designed that can alert the investigator of an oncoming spontaneous seizure. Experiments designed to address these issues may be practical for developing novel therapeutic strategies for better controlling seizures in patients with epilepsy.

1) Engel J. (1992) *Epilepsy Res Suppl* 8: 9–20.

2) Mody I, Schwartzkroin PA. (1997) In: Engel J, Pedley TA, editors. *Epilepsy: a comprehensive textbook*. Philadelphia: Lippincott–Raven, 397–404.

3) Avanzini G, Moshe SL, Schwartzkroin PA, Engel J. (1997) In: Engel J, Pedley TA, editors. *Epilepsy: a comprehensive textbook*. Philadelphia: Lippincott–Raven, 427–42.