



林 桂一郎

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研究論文内容要旨

Mutations in the *SCN1A* gene, which encodes the *a*1 subunit of voltage-gated sodium channels, cause generalized epilepsy with febrile seizures plus (GEFS+) and severe myoclonic epilepsy of infancy (SMEI). N1417H-*Scn1a* mutant rats are considered to be an animal model of human FS+ or GEFS+. To assess the pharmacologic validity of this model, we compared the efficacies of eight different antiepileptic drugs (AEDs) for the treatment of hyperthermia-induced seizures using N1417H-*Scn1a* mutant rats.

The effects of AEDs were evaluated using the hot water model, which is a model of experimental FS. Five-week-old rats were pretreated with each AED and immersed in water at 45°C to induce hyperthermia-induced seizures. The seizure manifestations and video-electroencephalographic recordings were evaluated.

Diazepam and potassium bromide showed potent inhibitory effects against hyperthermiainduced seizures in the *Scn1a* mutant rats, whereas carbamazepine exhibited adverse effects. These responses to hyperthermia-induced seizures were similar to those in patients with GEFS+ and SMEI. N1417H-*Scn1a* mutant rats may, therefore, be useful for testing the efficacy of new AEDs against FS in GEFS+ and SMEI patients.