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Publication

Efficacy of anticonvulsant substances in the 6Hz seizure test: Comparison of two rodent species

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Abstract

Usually performed in the mouse, the 6Hz seizure test is used for screening potential new anticonvulsant substances against complex partial seizures. Nevertheless, advanced models of temporal lobe epilepsy (TLE) are more often performed in rats, so that possible species-related differences may complicate the development of anticonvulsant substances. The aim of the present study was to evaluate the feasibility of adapting the 6Hz test in the rat. We first compared the effects of increasing current intensities for inducing seizures in the mouse and in the rat. This step was followed by the evaluation of the activity of anticonvulsant substances. Animals received an electrical stimulation with a constant current via corneal electrodes. The seizure was characterized by the presence of forelimb clonus immediately after stimulation. Spontaneous locomotion was evaluated following the 6Hz test. In the rat, the forelimb seizure score was intensity-dependently increased and seizures were observed in all animals tested at 44mA. In the mouse, the seizures were of lower magnitude and they were not observed in all mice stimulated at 44mA. In both species, levetiracetam (LEV) clearly decreased the forelimb seizure score over the dose-range 100-300mg/kg without affecting locomotion. Valproate (VPA) displayed anticonvulsant activity at 200mg/kg and fully protected both species at 300mg/kg, a dose producing sedative effects in the mouse. Phenytoin (PHT) showed slight to moderate anticonvulsant activity at 100mg/kg in the mouse and at 60 and 100mg/kg in the rat without modifying locomotor activity. Lamotrigine (LTG) partially antagonized forelimb seizure at 60mg/kg in the mouse and at 30-60mg/kg in the rat, but it induced clear motor impairments at high dose in both species. Our data suggest that in the 6Hz test, the magnitude and the nature of seizures differed between the mouse and the rat for a given current intensity. Nevertheless, the pharmacological profile of anticonvulsant substances was similar in both species for the 4 substances tested. Dose-dependent efficacy of LEV and VPA was observed and LTG and PHT also showed anticonvulsant activity, even though the magnitude of the effects remained moderate for these two last substances. The 6Hz test in the rat therefore appears as a useful model which may be performed prior to follow-up models of partial seizures performed in the same species.