and the frequency-dependent effect in the paired pulse paradigm can be explained by the highly use-dependent sodium channel blocking activity of AWD 140-190 on neuronal cells (Rostock et al., Soc Neurosci Abstr 1995; 24). The data indicate that AWD 140-190 is a potent anticonvulsant. It is currently undergoing further development.

Seizure Susceptibility in Different Rat Strains Indicated by Cortical Stimulation. R. A. Voskuyl and C. M. van Rijn (Department of Physiology, Leiden, The Netherlands).

The threshold for convulsions can be conveniently determined by stimulation of the cortex with ramp-shaped pulse trains through chronically implanted electrodes. Although the model was developed primarily to study effects of anticonvulsant drugs, the threshold determination can also be used as a general method to assess seizure susceptibility. We studied whether a difference exists in convulsive threshold between epileptic and nonepileptic rat strains. The epileptic strain was the WAG/Rij rat that develops epileptic activity between 3 and 6 months of age. The other strains were the ACI rat and the Wistar rat. A characteristic of the cortical stimulation model is that the threshold initially decreases with repeated testing until a steady-state level is reached after 20-30 sessions. This change is permanent, because it does not regress when stimulation is discontinued for several days to weeks. To compare different rat strains, we determined both the initial threshold and the decrease after 20 test sessions. Rats aged <8 weeks of all strains did not differ with respect to either the initial threshold or the threshold after 20 sessions: average threshold ± SD in session 1 (in µA)—WAG/Rij 641 ± 107 (n = 10), Wistar 604 ± 56 (n = 9), and ACI 628 ± 41 (n = 7); in session 20, WAG/Rij 425 ± 144, Wistar 399 ± 77 and ACI 379 ± 32. In rats aged >7 months, the initial threshold was significantly lower for WAG/Rij rats as compared with young rats. For the ACI rats, a slightly but not significantly lower threshold was observed, that of the Wistar strain was between those of the other two. After 20 sessions, there was no difference either between strains or between age groups. Average threshold in session 1 (in µA)—WAG/Rij 474 ± 29 (n = 10), Wistar 505 ± 32 (n = 10), and ACI 583 ± 63 (n = 8); at session 20, WAG/Rij 404 ± 35, Wistar 370 ± 41, ACI 397 ± 52. The decrease in initial threshold appears to be a marker for the development of absence-like epileptic activity in WAG/Rij rats. In this respect, ACI rats can be considered a clear nonepileptic control. The data also indicate that Wistars may develop an increase in seizure susceptibility with age, although a lesser increase than that in WAG/Rij rats.


Constant 2-h stimulation of the perforant path in rats can lead to extensive damage of the hippocampus similar to that which occurs after status epilepticus (SE). This model may provide a use for halothane under halothane anesthesia (1-2%), 12 adult male Sprague-Dawley rats were implanted with a bipolar steel electrode in the perforant path and a monopolar electrode in the dentate granule cell layer (a subcutaneous silver electrode was used as earth). The positions of the recording and stimulating electrodes were optimized neurophysiologically. With the animals under halothane anesthesia (1-2%), the perforant path was stimulated with 50-µs constant current (3-6 mA) pulses at 20 Hz for 2 h. A similar group of rats that were not stimulated during this period were used as controls. The animals were allowed to recover and were killed 2 weeks later. The brains were perfused and fixed in 4% paraformaldehyde. Neuronal cell counts and morphometry from three serial sections of the hippocampus in control (n = 3) and stimulated animals (n = 3) were compared.

In all rats that underwent stimulation under halothane anesthesia, population spikes were apparent for 5-12 min, but then rapidly disappeared and did not reappear for the remainder of the stimulation period. There was no significant difference in morphology of neuronal cell counts between control and stimulated animals. Halothane thus prevented the continuation of population spikes and the subsequent damage previously reported when this pattern of stimulation was used in freely moving animals and animals under urethane anesthesia.