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A decrease in the number of SWD was noted after remacemide administration. At the highest dose, SWD were almost completely suppressed and there were no important effects on behavior or on spectral content of the background EEG, suggesting that remacemide has few side effects and might be effective against absence epilepsy. A decrease in the number of SWD was also noted after FPL 12495 gavage, but mean duration was prolonged. Behavioral changes were apparent only after the highest dose, accompanied by changes in spectral content, suggesting that FPL 12495 has other central effects as well. FPL 12495 appeared to be more potent than remacemide in all its effects.

The effects of FPL 12495 are unusual in that no other investigated drug has yet shown a decrease in number together with an increase in mean duration of discharges. FPL 12495 appears to exert a differential action on the two commonly distinguished mechanisms controlling number and duration.


Numerous studies have provided evidence for the involvement of opioids in the mechanisms of various forms of epilepsy. Most have investigated the effects of opioids in the control and genesis of convulsive epilepsy, whereas data on opioids mechanisms with respect to nonconvulsive epilepsy are almost lacking. Therefore, we investigated the role of the opioid subsystems in WAG/Rij rats, a genetic rat model of human absence epilepsy. Six-month-old male WAG/Rij were chronically provided with EEG electrodes and some with cannulas in the lateral ventricle. The baseline EEG was measured, and the drugs or solvent was injected. The EEG was recorded for 1 h, and the number and duration of spike-wave discharges (SWD) was counted.

SWD were facilitated by the non-specific opioid antagonist naloxone (intraperitoneally), suggesting that SWD are tonically inhibited by the endogenous opioid system. Next, specific mu, delta and kappa agonists and antagonists were evaluated. The mu receptor agonist DAMGO increased intracerebroventricularly, i.e.c.v.) markedly the number of SWD, whereas DPDPE, a delta receptor agonist, had no effect. Three kappa agonists (i.e. 5 or subcutaneously) U50488H, U65953, or PD117301 dose-dependently inhibited the number of SWD. These effects could be antagonized by the kappa antagonist Nor-BNI. Nor-BNI itself enhanced the number of SWD, but the mu antagonist naltrindole had no effect.

Endogenous opioids, which act through the kappa receptors, tonically control the initiation of SWD. Kappa agonists, if devoid of psychomimetic effects, might be useful antiepileptic drugs.

Effects of Tiagabine on Spike-Wave Discharges, Behavior, and Spectral Content of the EEG in Rats with Absence Epilepsy. A. M. L. Coenen, E. L. J. M. van Luijtelaar, and E. Blezer (Department of Psychology, University of Nijmegen, Nijmegen, The Netherlands).

The mechanism of action of the new anticonvulsant drug tiagabine (TGB) is reuptake inhibition of GABA. What TGB will do against nonconvulsive epilepsy is unclear. GABA agonists such as muscimol and anticonvulsants such as carbamazepine and phenytoin generally increase the number of spike-wave discharges (SWD). We were interested whether TGB would also facilitate the number of SWD in a genetic rat model for generalized absence epilepsy.

Male WAG/Rij rats with chronically implanted EEG electrodes were given either 0, 1, 3, or 10 mg/kg TGB intraperitoneally. The EEG was recorded for 1 h before and 3 h after drug administration. Behavior was recorded for 30 min postdosing: ambulation, passive behavior, and automatic behavior were scored.

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