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Repeated exposure to trimethylolpropane phosphate induces central nervous system sensitization and facilitates electrical kindling.

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Trimethylolpropane phosphate (TMPP), pentylenetetrazol (PTZ) and N-methyl-beta-carboline-3-carboxamide (FG-7142) were evaluated and compared for facilitation of electrical kindling in freely moving rats. Stimulating/recording electrodes were implanted in the left amygdala (LAD), right amygdala (RAD) and left bed nucleus (LBN) of the stria terminalis. TMPP (0.275 mg/kg), PTZ (20 mg/kg), FG-7142 (7.5 mg/kg) or vehicle was administered intraperitoneally (i.p.) to separate groups of rats 3 times/week for 10 weeks. Stimulation of the LAD (0.1 Hz, 0.1-ms duration, 280-1500 microA, 20 pulses) 24 h following the drug administration evoked epileptiform after-discharges (ADs) in the LBN and RAD of 12.5% and 17% of rats after the seventh dose of TMPP and PTZ, respectively, and in 20% of rats from the LBN and RAD after the ninth and nineteenth dose of FG-7142, respectively. The same stimulation also induced myoclonic jerks after nine doses of TMPP or PTZ, or after thirteen doses of FG-7142 in 25%, 30% and 20% of animals tested, respectively. Chemically kindled clonic seizures were observed in 100% of TMPP or FG-7142 and 50% of PTZ treated rats by the thirtieth dosing. Control animals exhibited neither behavioral nor electrographic seizures to vehicle injection or to the LAD stimulation. Kindling stimulation applied to the LAD (60 Hz, 2-s train duration, 20-1500 microA, 0.1-ms pulse duration) 4 weeks following the completion of drug treatments evoked epileptic after-discharges from the LAD, LBN and RAD in all treated groups, with generally decreased threshold and latency to onset of after-discharges, compared to vehicle controls. The present study suggests that repeated exposure of rats to sub-convulsive doses of TMPP, PTZ and FG-7142 induces long-term central nervous system sensitization that may be related to both chemical kindling and the facilitation of electrical kindling.

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