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Further evidence for the involvement of 5-HT_{2C} receptors in the pentylenetetrazole model of epilepsy

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To clarify the role of 5-HT_{2C} receptors in the generation of epilepsy this study investigated the effects of the 5-HT_{2C} receptor-preferring agonist 1-(m-chlorophenyl)-piperazine (mCPP) and the subtype-selective 5-HT_{2C} receptor antagonist SB 242084 in pentylenetetrazole (PTZ)-evoked seizures in mice. All drugs were given subcutaneously (s.c.) 60 minutes before PTZ injection (100 mg/kg s.c.). The seizure patterns were recorded during a 60 min period following the injection of PTZ. The following parameters were evaluated: survival rate, duration of survival, seizure latency, seizure level (from 0 to 4) and seizure duration. The activity score for each mouse was defined as the seizure duration time-weighted average of the seizure levels. The significance of the survival rate was assessed by the Chi-square test, for the other parameters we applied one-way ANOVA. mCPP (1, 5 and 25 mg/kg s.c.) significantly increased the rate and the duration of survival and changed the pattern of seizure levels. These effects followed a bell-shaped dose-response curve and were completely abolished by 5 mg/kg of SB 242084, although the antagonist alone did not modify the seizure parameters. These results indicate that the anticonvulsant effects of mCPP might be mediated by activation of 5-HT_{2C} receptors. However, the lack of the effect of the selective antagonist SB 242084 (1, 2.5 and 5 mg/kg s.c.) on the seizure parameters suggests that the function of this 5-HT receptor subtype depends on the level of 5-HT tone.