GUANOSINE MAY INCREASE ABSENCE EPILEPTIC ACTIVITY IN WISTAR ALBINO GLAXO RIJSWIJK RATS

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One-third of epileptic patients are drug refractory due to the limited efficacy of antiepileptic therapy. Thus, there is an immense need to find more effective, but safe and well-tolerated antiepileptic drugs. A great deal of results suggests that not only adenosine (Ado) but also non-adenosine nucleosides such as guanosine (Guo) are endogenous antiepileptogenic modulators. To investigate the involvement of the adenosinergic system in Guo-evoked changes in absence epileptic activity, we used a non-selective Ado receptor antagonist theophylline (intraperitoneally, i.p.; 5 mg/kg) in combination with both i.p. 50 mg/kg and 100 mg/kg Guo in Wistar Albino Glaxo Rijswijk (WAG/Rij) rats. We also applied i.p. a selective A_{2A} Ado receptor antagonist SCH 58261 (7-(2-phenylethyl)-5-amino-2-(2-furyl)-pyrazolo-[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine) (1 mg/kg) and a cyclooxygenase (COX) 1 and 2 inhibitor indomethacin (10 mg/kg) in combination with i.p. 100 mg/kg Guo to decide whether Ado/A_{2A}R/COX/PGE2 system has a role in the Guo-evoked modulation of absence epileptic activity. We strengthened our previous result that lower dose of Guo (i.p. 50 mg/kg) decreased the SWD number, whereas higher dose of Guo (i.p. 100 mg/kg) was found to enhance the number of SWDs in WAG/Rij rats. Combined i.p. injection of theophylline or SCH 58261 or indomethacin with 100 mg/kg Guo decreased the SWD number compared to i.p. 100 mg/kg Guo alone. The results suggest that i.p. 100 mg/kg Guo can increase SWD number by means of the adenosinergic system in WAG/Rij rats, which system may have a role in neuroinflammation- and age-evoked increase in SWD number. Consequently, we argue against the previously suggested usability of Guo as an effective drug for the treatment of absence epilepsy.