

## EFFECTS OF ADENOSINE RECEPTOR AGONISTS AND ANTAGONISTS ADMINISTRATION ON SPIKE-WAVE DISCHARGE IN A GENETIC MODEL OF GENERALIZED ABSENCE EPILEPSY

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Adenosine exerts inhibitory effects in convulsant epilepsies, mainly by inhibitory A<sub>1</sub> receptors, whereas the pharmacological blockade or genetic inactivation of the facilitatory A<sub>2A</sub> subtypes seems to attenuate convulsions<sup>1</sup>. However, the effects of A<sub>1</sub> and A<sub>2A</sub> receptor activation were not yet evaluated in a particular type of epilepsy such as absence seizures, characterised by an abrupt and brief impairment of consciousness (absence) associated with electroencephalographic sign, that is, characteristic paroxysmal electrical activity consisting of generalized 3–4 Hz spike-wave discharges (SWDs) ‘‘invading the whole brain’’. Thus, we wanted to test whether the focal bilateral microinjection of A<sub>1</sub> and A<sub>2A</sub> selective adenosine receptor agonists and antagonists into brain areas involved in absence seizure triggering and maintenance affected the number and/or duration of SWDs in WAG/Rij rat, a genetic animal model of absence epilepsy. These brain areas corresponded to the thalamic nuclei (nucleus reticularis thalami, NRT; ventroposterolateral, VPL; ventroposteromedial, VPM) and the peri-oral region of the somatosensory cortex (S1po). Animals were equipped with fronto-parietal cortical electrodes for EEGraphic recordings and two additional guide cannulae for bilateral focal microinjection (0.5 µl/site)<sup>2</sup>. We evaluated the effects of drugs selectively active on A<sub>1</sub> (agonist= CCPA; antagonist= DPCPX) and A<sub>2A</sub> receptors (agonists= CGS21680 and 2HE-NECA; antagonist= SCH58261). Independently of the site of administration, CCPA dose-dependently reduced the number of SWDs, while affected their duration differently, CCPA increased and decreased SWD duration when microinjected in VPM and VPL, respectively, while duration was not significantly modified in the other areas examined. The A<sub>2A</sub> agonists had no effects in the VPL, reduced the number and increased SWD duration in the VPM and S1po, while, in the NRT, they increased SWD number without affecting the duration. The A<sub>1</sub> antagonist dose-dependently reduced the SWD number in all the examined areas, without affecting the duration, except in NRT, where the duration was significantly increased. Similarly, the A<sub>2A</sub> antagonist significantly reduced SWD number in all injected areas, modifying their duration only in NRT (increase) and VPL (reduction). In conclusion, these results are mostly in agreement with a few previous findings indicating either a protective activity by non selective adenosine receptor blockade with theophylline<sup>3</sup> or a pro-convulsive adenosine<sup>4</sup> effect in the same animal model of absence epilepsy. Further studies need to better evaluate whether, in this kind of epilepsy, is prevailing the pro-convulsant A<sub>1</sub>-mediated effect, probably related to an increased inhibitory function in the brain, which plays a significant role in the absence seizure pathogenesis, or the pro-convulsant activity of the excitatory A<sub>2A</sub> receptors.

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