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Differential involvement of adenosine receptors in rodent models of parkinsonism and essential tremors
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Harmaline is a well-known tremorgenic compound which has been suggested to model essential tremor (ET) in animals. The main cause of harmaline tremor is activation of olivo-cerebellar climbing fibers and excessive glutamate release. Furthermore, mechanisms underlying this behaviour involve GABAergic and glutamatergic connections to the ventral motor thalamic nuclei. Tremulous jaw movements (TJMs), defined as rapid vertical deflections of the lower jaw that are not directed at any particular stimulus, are used as a rodent model of parkinsonian (PD) resting tremor. TJMs can be induced by striatal dopamine depletion (6-OHDA, reserpine) or typical antipsychotics and are dependent upon the striatum.

The aim of our study was to examine the involvement of adenosine receptors in models of ET (harmaline) and PD (TJMs) tremors. We used two highly selective adenosine ligands: (±)-5′-chloro-5′-deoxy-ENBA (A1 agonist) and SCH 58261 (A2A antagonist). For modeling PD tremor acute tetrabenazine (TBZ), a selective and reversible VMAT-2 inhibitor, and subchronic pimozide (PIM), a typical antipsychotic drug were used in rats. The expression of zif-268 mRNA (qRT-PCR) and vGLUT1, vGLUT2, GAD-65 and GAD-67 proteins (western blot) in the striatum, thalamus and cerebellum were determined.

Administration of TBZ (2 mg/kg, i.p.) and PIM (1 mg/kg, i.p.) led to a significant induction of TJMs, caused catalepsy, increased expression of zif-268 mRNA and GAD-67 and vGLUT2 proteins in the striatum. SCH58261 (5 mg/kg, i.p.) reduced TJMs and catalepsy in TBZ-treated rats. Harmaline (15 mg/kg, i.p.) induced generalized tremor, measured in the Force Plate Actimeters. ENBA (0.5, 0.1, 0.05 mg/kg, i.p.) in a dose-dependent manner inhibited harmaline-induced tremor and at the same time lowered locomotor activity. ENBA in the lowest dose (0.01 mg/kg, i.p.) also inhibited rats locomotion but had no effect on tremor. Furthermore, harmaline raised the expression of zif-268 mRNA and GAD-67 protein in the cerebellum, lowered the expression of GAD-65 protein in the thalamus and did not influence vGLUT1 or vGLUT2 proteins in examined structures.

The present results suggest different role of adenosine A1 and A2A receptors in ET vs. PD tremors and involvement of GABA and glutamatergic transmission in both types of tremors.

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