Modulation by pre-synaptic histamine H_3 receptors of glutamatergic transmission in rat globus pallidus

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The globus pallidus, a neuronal nucleus involved in the control of motor behaviour, expresses high amounts of histamine H_3 receptors (H_3Rs) but very low levels of the corresponding mRNA (1), suggesting a pre-synaptic location for most pallidal H_3Rs. The main synaptic afferents to the globus pallidus are provided by neurones located in the striatum (GABAergic), substantia nigra pars compacta (dopaminergic), subthalamic nucleus and cerebral cortex (glutamategic). In this work we set out to study the effect of the activation of pallidal H_3Rs on depolarisation-evoked neurotransmitter release, neuronal firing rate and turning behaviour. In rat globus pallidus slices perfusion with the selective H_3R agonist immepip had no effect on K^+ (20 mM)-evoked release of either [^{3}H]-dopamine or [^{3}H]-GABA, but reduced [^{3}H]-D-aspartate release (inhibition of 38 ± 4%, n=5, and 63 ± 6%, n=3, at 30 and 100 nM, respectively), an effect blocked by the selective H_3R antagonist A-331440 (10 μM). Intrapallidal injection of immepip (0.1 μl, 10 μM) decreased by 55 ± 9% (n=7) the spontaneous firing rate of pallidal neurones in anaesthetised rats. In free-moving animals local immepip infusion (1 μl, 10 μM) induced ipsilateral turning (42 ± 2 turns/90 min, n=8) following systemic apomorphine (0.5 mg/kg, subcutaneous). Immepip effects on neuronal firing rate and turning behaviour were reduced by the local injection of A-331440 (1 mM, 0.1 or 1 μl respectively). Taken together, our results indicate that pre-synaptic H_3Rs modulate glutamategic transmission in rat globus pallidus and thus participate in the control of movement by basal ganglia. These pieces of information may be relevant for the understanding of the role of histamine and H_3Rs in the control of motor behaviour both in normal and pathophysiological conditions, such as Parkinson's disease in which histamine levels in globus pallidus have been shown to increase (2).

[1]C. Pillot et al., *Neuroscience* 114: 173-193, 2002.
[2]J.O. Rinne et al., *J. Neurochem.* 81: 954-960, 2002.