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Somatostatin Receptors in the Ventral Pallidum Modulate Rat Locomotor Activity

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S u m m a r y. The aim of the present study was to examine the effect of somatostatin and selective ligands on locomotor activity, after infusion in the ventral pallidum of the rat.

INTRODUCTION

The neuropeptide somatostatin is found in medium sized aspiny neurons in nuclei of the basal ganglia, such as the striatum and the nucleus accumbens, where it is implicated in dopamine-mediated behaviors. Somatostatin mediates its actions by activating six somatostatin receptor subtypes, namely sst_1, sst_{2A}, sst_{2B}, sst_3-sst_5. Somatostatin receptors (sst_1 and sst_2) have been localized in areas implicated in motor control such as the nucleus accumbens (NAc), the globus pallidus (GP), and the ventral pallidum (VP) (1), yet their role in locomotor activity has not been established.

METHODS

Male Sprague-Dawley rats weighing 300-350g were used for all experiments. Animals were housed one per cage before and after the surgery, in a room maintained at 22 ^{0}C with an alternating 12h light/dark cycle. Food and water was provide ad libitum. Each rat was anaesthetized [ketamine HCl (100 μg/kg), xylazine (10 μg/kg)] and secured in the stereotaxic frame. Guide cannulae made from 24 gauge stainless steel tube were positioned bilaterally towards the ventral pallidum [AP-0.8, ML ±2.2, VD-7.9] according to Paxinos and Watson (2). A six days post-operative interval was allowed. A cannula for injecting drug solutions into the brain through the guides was made with a 30 gauge needle connected by polyethylene tube (PE 10) to a 1 μl Hamilton syringe. The injection sites were reached by the cannula tip extending beyond the implanted guides by 0.5 mm. Somatostatin (60, 120, 240 ng/0.5μl/side), CH275 (sst_1 analog;120, 240, 480 ng/0.5μl/side), MK678 (sst_2 analog;120, 240, 480 ng/0.5μl/side), and L-809,087(sst_4 agonist, 240ng/0.5μl/side) were delivered bilaterally via the 30 gauge needle. Sterile normal saline (0.5 μl/ side) was injected into control animals. Spontaneous motor activity was measured using a rectangular activity cage (56x56x30cm), provided with horizontal/vertical infra-red sensors. Each rat was adapted to the room for 60min, and then in the activity cage for 30 min (habituation). The animal was then removed, microinjected bilaterally with somatostatin ligands or saline and returned to the activity cage for 60 min.

RESULTS

Somatostatin infusion in the ventral pallidum attenuated the locomotor activity of the rat in a concentration dependent manner. This effect was mimicked by both sst_1 and sst_2 selective ligands. The sst_1 agonist CH275 decreased locomotor activity at concentrations of 240 and 480 ng/0.5ul/side. This decrease was reversed by the selective sst_1 antagonist SRA-880, while the antagonist alone had no effect. The sst_2 agonist MK678 also decreased locomotor activity in a concentration dependent manner. This effect was reversed by the selective sst_2 antagonist CYN-154806. The selective sst_4 agonist L-809,087 had no effect on locomotor activity.

CONCLUSIONS

The present data complement the immunohistochemistry findings supporting the presence of sst_1 and sst_2 in the ventral pallidum.Somatostatin via the activation of sst_1 and sst_2receptors regulates the physiology of the ventral pallidum and reduces locomotor activity. The mechanism of somatostatin's actions may involve the decrease of somatostatin either in the nucleus accumbens via the GABAergic projection from the VP to the NAc [3] or the inhibition of the VTA dopaminergic neurons again via a GABAergic projection from the VP to the VTA, and subsequent activation of GABA-B receptors [4,5]. This hypothesis is presently under investigation in our laboratory.

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