MECHANISM OF ACTION OF 8-HYDROXY-2-(DI-N-PROPYLAMINO)TETRALIN (8-OH-DPAT) ON THE EXPULSION PHASE OF EJACULATION IN ANAESTHETISED RATS

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ABSTRACT

INTRODUCTION & OBJECTIVE

Ejaculation consists in two distinct and successive phases i.e. emission and expulsion with the latter caused by rhythmic contractions of pelvic floor striated muscles; the primary role being played by bulbospongiosus muscles (BS) (Gerstenberg et al., 1990).

Neural control of ejaculation likely results from a complex and coordinated interplay between perirenal sensory afferences, spinal nuclei controlling anatomical structures involved in ejaculation, and supraspinal areas modulating the activity of the activity of these spinal nuclei.

It is well established that serotonin (5-HT) plays an inhibitory role on spinal sexual reflexes including ejaculation (Marson & McKenna, 1994). Evidence indicates that 5-HT1A receptors mediate at least partly the central inhibitory effect of 5-HT on ejaculation (Hillgärtner et al., 1998) although their location (pre- or postsynaptic) needs to be clarified.

The goal of the study, using urethro-genital reflex paradigm in anaesthetised rats, is to discriminate between spinal and cerebral site of action for 8-OH-DPAT and to provide further information on its mechanism of action.

METHODS

The urethro-genital reflex paradigm

The urethro-genital reflex (UG reflex) is the ability of a pinch of the glans resulting in the occlusion of the urethra at the urethral meatus combined with distension of the urethra to trigger the rhythmic and synchronized contractions of the BS muscles (expulsion reflex) characteristic of the expulsion phase in urethane-anesthetised rats at the T8 level (McKenna et al., 1991). In these experiments, organized electrical activity within the BS muscles recorded by EMG and corresponding to BS rhythmic contractions occurs during and after urethral occlusion.

A catheter was positioned within the prostatic urethra close to the bladder neck and the prostatic urethra was filled by continuous urethral perfusion, an increase in urethral pressure occurred corresponding to an increase in the volume of delivery of 30 and 90 µg 8-OH-DPAT is decreased for intra-urethral accumulated volume of 40 and 60 µl compared to vehicle.

Surgical preparation

Adult male Wistar rats weighing 200-250 g were anaesthetised with urethane (1.2 g/kg), tracheotomized, and the carotid artery catheterized for blood pressure measurement.

Intracavernous cavernula implantation

A cannula was stereotaxically placed into the cerebral ventricle (coordinates according to Paxinos & Watson rat brain atlas: 0.5 mm anterior to bregma, 1.3 mm lateral to midline, and 4.5 mm below the skull). Cannula was connected to a Hamilton syringe placed in a micropump allowing delivery of microvolume. At the end of the experimental session, methylene blue dye was injected through the cannula, and the brains, removed and grossly dissected, were inspected for the presence of blue dye in the ventricles.

Splanchnization at the T8 level

The T8 spinal cord was exposed through a laminectomy of the T7-T9 vertebra. The dura was incised, xylocaine was dropped over the incision, and a complete transversal section of the underlying T8 spinal cord was performed. The completeness of the section was verified by exposing the transverse surface of the proximal and the distal stumps of the cut spinal cord.

RESULTS

Table 1. Rats exhibiting UG reflex after vehicle or 8-OH-DPAT intrathecal injection.

<table>
<thead>
<tr>
<th>Volume (µl)</th>
<th>Vehicle</th>
<th>8-OH-DPAT 10 µg</th>
<th>8-OH-DPAT 30 µg</th>
<th>8-OH-DPAT 90 µg</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>100</td>
<td>67</td>
<td>60</td>
<td>55</td>
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<tr>
<td>60</td>
<td>100</td>
<td>60</td>
<td>60</td>
<td>50</td>
</tr>
</tbody>
</table>

CONCLUSION

Intrathecal injection of 8-OH-DPAT had a tendency to prevent the occurrence of UG reflex probably acting by post-synaptic 5-HT1A receptors.

Intracavernous injection of 8-OH-DPAT dose-dependently induced BS rhythmic contractions in absence of stimulus. We hypothesised that this supranuclear effect of effect 8-OH-DPAT could be mediated by somatodendritic 5-HT1A autoreceptors.

It is suggested that i.c.v. delivery of 8-OH-DPAT-induced BS contractions can be used as an experimental model mimicking the expulsion phase of ejaculation.