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

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ABSTRACT # 518
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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 perineal sensory afferences, spinal nuclei controlling anatomical structures involved in ejaculation, and supraspinal areas modulating the activity of the spinal site of action.

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

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

METHODS

The urethral-genital reflex paradigm

The urethral-genital reflex (UG) 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-anesthetized spinalized rats at the T8 level (McKenna et al., 1991). In these experiments, organized electrical activity within the BS muscles recorded by BS EMG and corresponding to BS rhythmic contractions occurs during and/or after urethral occlusion.

A catheter was positioned within the prostatic urethra close to the bladder neck and the prostatic urethra was filled by urethral content. The glans pinching was released when a predefined volume (20, 40, or 60 µl) has been intraurethrally infused independently of the occurrence of the rhythmic BS contractions. Electrical activity of BS muscles was recorded by placing two thin bared silver electrodes into the muscles. Electrical signal from the BS muscles was amplified (gain, 10000; amplification bandwidth, 10 Hz-1KHz).

Intrathecal catheter insertion

The rat’s head was placed in a stereotaxic frame, and was rotated nose downwards. The atlanto-occipital membrane was opened and the catheter (PE10), cut to the required length so that its distal opening reached L4-L5 spinal segment, was carefully advanced in the caudal direction. The exact location of the caudal tip of the catheter was visually checked at the end of each experiment.

Intracerebroventricular cannula 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 laterad to midline, and 4.5 mm below the skull). Cannula was connected to a Hamilton syringe placed in a microapparatus 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.

Splanization at the T8 level

The T8 spinal cord was exposed through a luminoectomy of the T7-T9 vertebrae. The dura was incised, subarachnoid space was opened, 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 stump of the cut cord.

CONCLUSION

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

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

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

References


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

<table>
<thead>
<tr>
<th>UG reflex</th>
<th>Vehicle (n=7 rats)</th>
<th>8-OH-DPAT (n=5 rats)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 µg</td>
<td>43%</td>
<td>0%</td>
</tr>
<tr>
<td>30 µg</td>
<td>50%</td>
<td>40%</td>
</tr>
<tr>
<td>60 µg</td>
<td>40%</td>
<td>0%</td>
</tr>
</tbody>
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Figure 1. Typical recording obtained after L.L. injection of 8-OH-DPAT.

Blood pressure, BS EMG, and urethral pressure were monitored before and after LL injection of 30 µg 8-OH-DPAT in T8 spinalized rats. Pinches (vertical double bars) were applied at 5 min intervals. Occurrence of UG reflex is indicated by ●.