ABSTRACT # 520

MECHANISM OF ACTION OF p-CHLOROAMPHETAMINE (PCA)-INDUCED EJACULATION IN ANAESTHETISED RATS

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ABSTRACT

Introduction and Objective: PCA is an amphetamine derivative that induces ejaculation in conscious and anaesthetised rats. Serotonin (5-HT) and norepinephrine (NE) are suggested to play respectively primary and secondary roles in mediating PCA effects likely occurring at the spinal and peripheral levels. The aim of the present study is to investigate the mechanism of action of PCA by carrying out, in anaesthetised rats, differential selective lesions at distinct levels of the peripheral autonomic pathways involved in the command of the various physiological events leading to ejaculation i.e. the emission and the expulsion of sperm.

Methods: Under urethane anaesthesia, a catheter was inserted into the seminal vesicle (SV) and recording electrodes were placed into the bulbospongiosus muscles (BS) to monitor SV pressure and BS electro-myogram (EMG) respectively. Acute bilateral transection of hypogastric (HNx), pelvic (PNx) and dorsal penile nerves (DPNx) as well as the paravertebral sympathetic chain (PSCx) were performed in different groups of Wistar adult rats. SV pressure and BS EMG were recorded before and over 30 min following PCA intraperitoneal injection (5 mg/kg) in the different experimental conditions and compared to control conditions.

Results: After PCA i.p. delivery, 4 out of 6 rats in intact and DNPx groups, 3 out of 6 rats in PSCx group, 2 out of 6 in HNx group and none of the 6 rats in PNx group ejaculated. Increase in SV pressure and contractions of BS were not systematically accompanied with expulsion of a seminal plug. In comparison with intact rats, PCA-induced increase in SV pressure was significantly reduced in PNx rats and almost abolished in HNx and PSCx rats, while DNPx did not affect the contractile response of VS to PCA. PCA-induced BS contractions were not impaired by any nerve section and was even enhanced in HNx compared to PNx rats. Time synchronisation between increase in SV pressure and BS contractions was not impaired by any nerve section.

Conclusions: It appears that both sympathetic (HN, LSC) and para-sympathetic (PN) innervations participate to the contraction of SV and that decrease in SV activity is responsible for a decrease in the occurrence of ejaculation. The autonomic innervation to the urogenital tract seems not to be involved in the occurrence of BS contractions that are crucial for the expulsion of sperm.

INTRODUCTION & OBJECTIVE

- p-chloroamphetamine (PCA) is an amphetamine derivative that liberates catecholamines and serotonin within the CNS and noradrenaline at the periphery.
- PCA induces ejaculation in both conscious (Humphries et al., 1980; Rènyi, 1985) and anaesthetised rats by acting at spinal and/or peripheral levels (Yonezawa et al., 2000).
- The goal of the study is to investigate the mechanism of action of PCA by carrying out, in anaesthetised rats, differential selective lesions at distinct levels of the peripheral autonomic pathways involved in the command of the various physiological events leading to ejaculation.

MATERIAL & METHODS

Surgical preparation

Adult male Wistar rats weighing 200-300 g were anaesthetised with isoflurane (1.5-2%), tracheotomized, and the carotid artery catheterized for blood pressure measurement.

Seminal vesicle pressure (SVP) was measured with a catheter, filled with mineral oil, inserted in the seminal vesicle through the apex.

A pair of stainless steel electrodes were placed within the bulbospongiosus muscles (BS) for recording BS electrical activity (BS EMG). Electrical signal from BS was amplified (gain, 10000; Low pass, 10 KHz; High pass, 10 Hz) before being digitised.

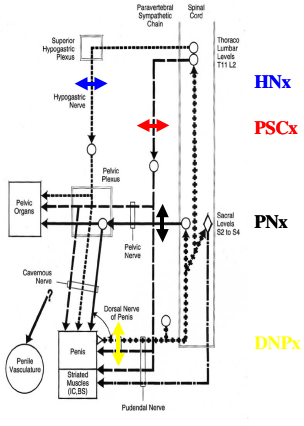
Bilateral nerve transections

Pelvic nerves (PN) were freed from surrounding connective tissue on the lateral aspect of the prostate and sectioned 5 mm posterior to the major pelvic ganglion.

Dorsal nerves of the penis (DNP) were freed as proximally as possible at the base of the penis and sectioned.

Hypogastric nerves (HN) were freed and sectioned 3 mm proximal to the major pelvic ganglion.

Both trunks of the lumbar paravertebral sympathetic chain were removed at the L4-L5 spinal level together with the inferior mesenteric ganglion.



RESULTS

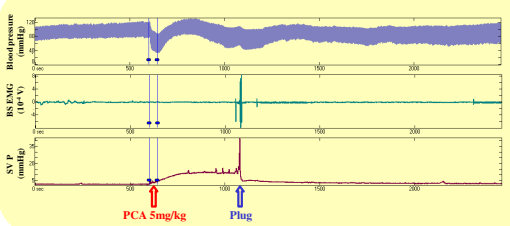


Figure 1: Typical recording obtained after i.p. injection of PCA.
Blood pressure, BS EMG, and intra-seminal vesicle pressure (SVP) were monitored before and after i.p. delivery of PCA (5mg/kg) in intact anaesthetised rats. Note the slow increase in SVP immediately after PCA delivery and the peak of SVP accompanied by BS burst of contractions occurring contemporaneously with ejaculation (plug).

Lesion	Proportion of ejaculating rats	Mean number of ejaculation
None	4/6	1.4 ± 0.4
Pelvic nerves	0/6	0 *
Dorsal nerves of the penis	6/6	1.3 ± 0.2
Hypogastric nerves	2/6	0.3 ± 0.2 *
Sympathetic chain	3/6	1.2 ± 0.6

Table 1: Proportion of ejaculating rats and mean number of ejaculation after PCA i.p. delivery (5mg/kg).
Ejaculation was abolished in rats with pelvic nerves sectioned. The lesion of hypogastric nerves consistently decreased the mean number of ejaculation while other lesions had no effect. Statistics: ANOVA + Bonferroni's post-hoc test; *P<0.05.

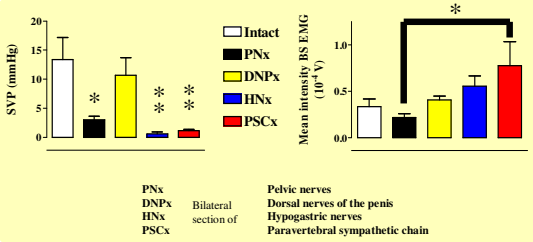


Figure 2: Effect of nerves section on SVP and BS activity measured after PCA i.p. delivery (5mg/kg).
Amplitude of SVP peaks was lower in rats with PN, HN or PSC sectioned compared to intact animals. Mean intensity of BS contractions was decreased in PN sectioned rats compared to PSC sectioned animals. Statistics: ANOVA + Bonferroni's post-hoc test; *P<0.05, **P<0.01.

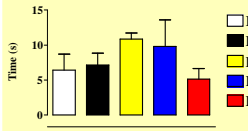


Figure 3: Effect of nerves section on synchronisation between SV and BS contractions.
Temporal synchronisation between SV and BS contractions induced by PCA i.p. delivery (5mg/kg) remained unchanged whatever the nerves sectioned.

CONCLUSION

- Pelvic nerves, which drive parasympathetic tone to SV, play an important role in PCA-induced SV contraction. In addition, they are mandatory for the occurrence of PCA-induced ejaculation.
- Hypogastric nerves and paravertebral sympathetic chain, which drive sympathetic tone to SV, are crucial in PCA-induced SV contraction. However, the occurrence of PCA-induced ejaculation appears unchanged after section of paravertebral sympathetic chain.
- It is suggested that PCA-induced ejaculation can occur when seminal vesicle contraction is impaired. This may be explained by more intense BS contraction.

References

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- Rènyi L. (1985) Ejaculation induced by p-chloroamphetamine in the rat. Neuropharmacol. 24: 697-704.
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