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Sensory innervation of the external and internal genitalia of the female rat

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Using a whole-nerve recording method, the genitalia of the female rat were found to receive afferent innervation as follows. Pelvic nerve: vagina, cervix, and perineal skin; hypogastric nerve: cervix and proximal three fifths of the uterus; pudendal nerve: skin of perineum, inner thigh, and clitoral sheath. It is probable that the pudendal and pelvic nerves are activated during copulation, and that all 3 nerves are activated during parturition.

INTRODUCTION

Genital stimulation mediates a variety of reproductive functions in the female rat. The stimulation may be either internal (e.g. vaginal) or external (e.g. perineal) or both. Under appropriate conditions, these reproductive functions include control of ovulation[5,9,12,19,21,40], pregnancy[44], pseudopregnancy[10,12,23], parturition[34], and analgesia[26] that occurs during pregnancy[16,17]. Certain of these effects are correlated with genital stimulation-induced activation of specific brain regions[4], release of luteinizing hormone-releasing hormone (LH-RH)[45], luteinizing hormone (LH)[36], prolactin[15,42,43,47], oxytocin-like activity[35], progesterone[2] and prostaglandin F[34] (see Komisaruk et al.[28] for review).

The internal genitalia of the rat are innervated primarily by one pair of discrete ganglia supplied by two pairs of discrete nerves, the hypogastric nerves and the pelvic nerves[6]. Peripheral to these ganglia are numerous small bundles which innervate urinary bladder, ureters, urethra, and rectum, of both sexes, as well as the uterus, vagina, and clitoris of the female, and analogous structures of the male[6,13,32,38,39]. The hypogastric nerves (which contain sympathetic efferents) and the pelvic nerves (which contain parasympathetic and sympathetic[20] efferents) terminate peripherally in a pair of ganglia situated on either side of the uterine cervix, referred to as the 'uterine cervical ganglia' or the 'pelvic ganglia'[6].

In the rat, the pelvic nerve responds to mechanical stimulation of the vagina, cervix, and rectum[27]; the type and location of stimuli leading to responding by the hypogastric nerve are unknown. In the cat, the pelvic nerve is relatively unresponsive to electrical stimulation of the vagina[1], and unresponsive to mechanical stimulation of the uterus; the hypogastric nerve responds to mechanical stimulation of the uterus[1,14].

The external genital region of the female rat is innervated by the pudendal nerve which responds to ipsilateral cutaneous stimulation in the area extending laterally along the inner surface of the thigh from the midline between the clitoris and the base of the

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tail[3,27,29]. During copulation, the penis stimulates the sensory field of the pudendal nerve; this stimulation is involved in the elicitation of lordosis, the female's mating stance[3], for lordosis can no longer be elicited by stimulation of the region after its denervation[30].

Copulation and parturition result in differential mechanical stimulation of the external and internal genital structures. In order to have a better understanding of the peripheral neural mediation of neuroendocrine and behavioral responses to stimulation provided by these reproductive events, we surveyed the internal and external genital sensory fields of the hypogastric, pelvic, and pudendal nerves in the rat.

MATERIALS AND METHODS

The majority of the 20 Charles River CD rats used in the present study were either in natural estrus or in the midst of parturition.

Under Chloropent anesthesia (Fort Dodge Labs, Fort Dodge, IA) (0.25 ml/100 g, i.p.), which contains chloral hydrate, magnesium sulfate, and pentobarbital, rats were dissected for nerve recordings. A ventral approach similar to that of Komisaruk et al.[27] was used. For pelvic or pudendal nerve recordings, two 0.006-inch diameter silver hook electrodes were inserted into the nerve under study, 2–5 mm apart, rostromedial to the junction of the internal and common iliac veins, and within 1 cm of the site where the pelvic and pudendal nerves diverge. The fine-diameter hypogastric nerves were generally suspended from the electrodes rather than impaled. The electrodes were placed under the hypogastric nerve at a point between its origin at the inferior mesenteric plexus (associated with the inferior mesenteric artery) and the point where the nerve turns to run caudally with the ureter.

Nerve activity was recorded in a shielded room through a Grass P15 preamplifier and Kopf spike filter and monitored on a Tektronix 564 storage CRO and Grass AM4 audio monitor. The nerve preparation showed little spontaneous spike activity.

Several means of mechanical stimulation were used. Mild compression by small blunt forceps was used on both internal and external structures. The specificity of the stimulation was increased by lightly probing or stretching an area with a small probe while holding the area motionless with forceps. Hollow organs (vagina, uterus, rectum) were stretched with a blunt probe, a hemostat, or a balloon (3 ml Bard–Parker embolectomy catheter) attached to a syringe with which its inflation was controlled. In some cases the ventral surfaces of the vagina and rectum were cut open longitudinally for closer examination of receptive fields, especially those of the cervix. This was made possible by first cutting through the pubic symphysis on the midline.

RESULTS

Only the hypogastric nerve responded to mechanical stimulation of the uterus. Only the pelvic nerve responded to mechanical stimulation of the vagina (the most sensitive portion thereof being the rostrolateral wall). Distention of the uterus by internal probes or balloons elicited only weak responses, whereas compression of the outside of the uterus, either in non-pregnant rats or around the fetuses of pregnant rats, elicited relatively strong responses. There were topographical differences in uterine sen-

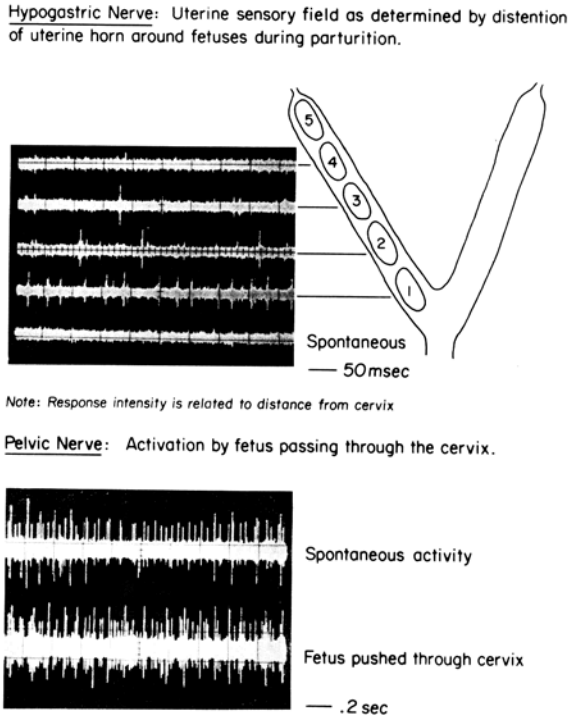

Fig. 1. a: recordings from hypogastric nerve during gentle stretching of the uterine wall around fetuses, showing a greater response to stretching of the cervical end than the ovarian end. b: pushing a fetus through the cervix increases activity recorded from the pelvic nerve.

sitivity, with stimulation of the cervical end eliciting the strongest responses and stimulation of about the last 40% of the tubal end eliciting no responses (see Fig. 1a).

This suggests that the tubal end of the uterus may receive sensory innervation from another nerve, perhaps the ovarian nerves, or the nerve of the ovarian ligament identified by Lawrence and Burden[33].

In order to examine the innervation of the uterine cervix it was necessary to use a preparation with a distended, accessible cervix. Therefore we recorded from nerves of rats immediately after they had delivered 3 or 4 pups.

Mild stimulation of the tissues within the cervical canal and the papillae that normally cover it on the vaginal surface seldom elicited any response in the pelvic or hypogastric nerves, as long as care was taken not to disturb adjacent tissues. However, when the stimulation was increased to stretch deeper tissue as well, both the pelvic and hypogastric nerves responded strongly. When fetuses were manually pushed through the cervix (in 6 rats) we observed clear activation of the pelvic nerve (Fig. 1b) and strong contractions of the female's abdominal muscles which closely resemble the abdominal contractions observed in rats after artificial or copulatory vaginal stimulation[37] and which may be involved in delivery.

The pelvic nerve responded to stimulation of the bladder and somewhat less strongly to distention or

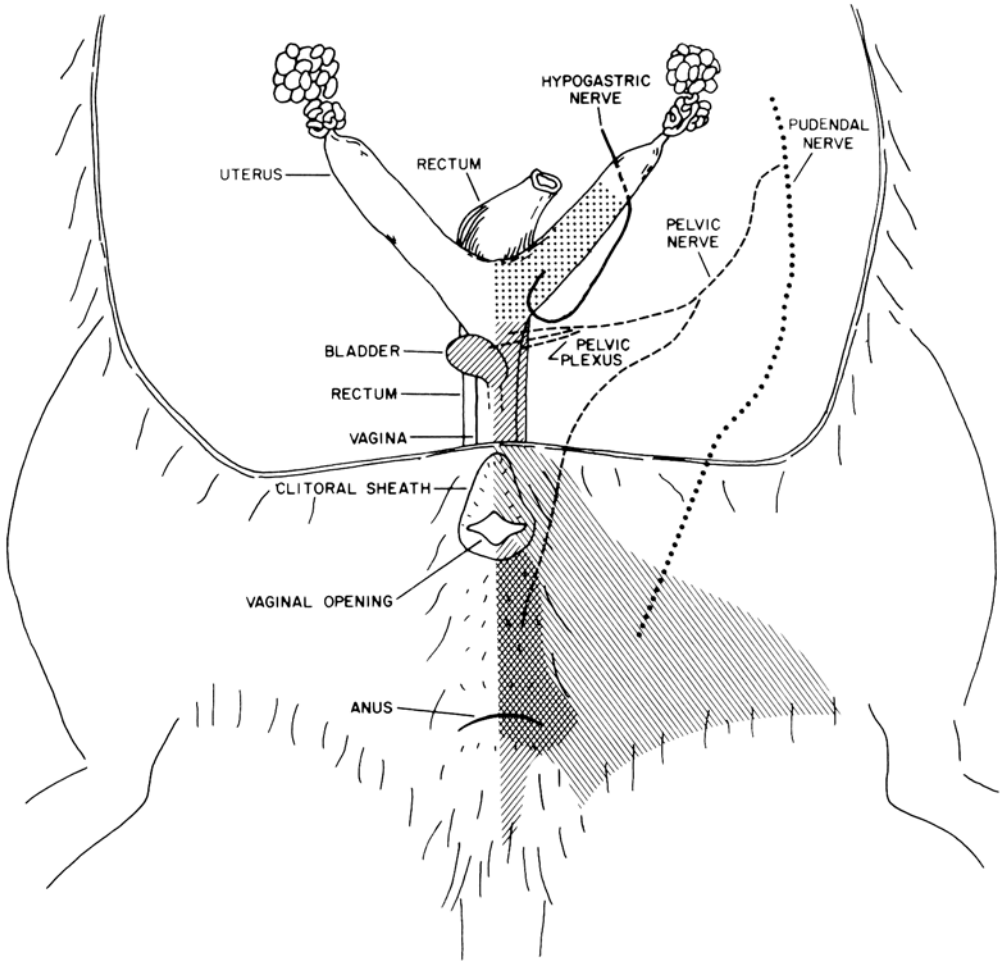

Fig. 2. Schematic representation of sensory fields of pelvic, pudendal, and hypogastric nerves. Nerves are shown displaced laterally for clarity.

compression of the inner surface of the rectum. The hypogastric nerve did not respond clearly to rectal stimulation.

The receptive field of the pudendal nerve appeared much as in previous reports[3,27]. The pudendal nerve did not respond to any internal stimulation. It also did not respond when the clitoris was stimulated by probing through the urethral opening, despite anatomical evidence that the clitoris is innervated by the pudendal nerve[39]. However, the pudendal nerve did respond strongly to brushing of the clitoral sheath.

The pelvic nerve was observed in all subjects to have an external genital sensory field. The external field of the pelvic nerve was observed to overlap the field of the pudendal nerve partially and to include some areas that the pudendal nerve does not innervate (Fig. 2). Dissection of the pelvic nerve peripheral to the recording site revealed that it has two principal branches, one that travels medially toward the pelvic plexus, and another that turns caudally and sends branches into muscle and, apparently, terminates in perineal skin.

When any of these nerve types were cut proximal to the recording site, we observed no change in sensory field size, indicating that afferent rather than efferent activity had been recorded.

DISCUSSION

The afferent and efferent fibers of the hypogastric and pelvic nerves innervate different portions of the pelvic viscera. Whereas both hypogastric sympathetic fibers and pelvic parasympathetic fibers are distributed over all the internal genitalia[11], the sensory fields of the hypogastric and pelvic nerves do not overlap. The present hypogastric nerve recordings are consistent with recordings from the cat that show the hypogastric nerve to be sensitive to uterine stimulation[1,14]. However, we found regional variations in uterine sensitivity, particularly a large region at the tubal end that did not appear to receive hypogastric innervation. Our recordings from the pelvic nerve are consistent with those previously reported in the rat[27] but not in the cat[1], in that we found clear and consistent sensitivity to vaginal stimulation. In addition, we observed particularly marked sensitivity at the cervical end of the vagina. The newly observed external cutaneous sensory field of the pelvic nerve partially overlaps that of the pudendal nerve.

Both the internal and external pelvic nerve sensory fields may play a role in mating. The internal field is apparently responsible for the lordosis response to experimental vaginal stimulation, since lordosis to this stimulus is no longer seen after pelvic neurectomy[10]. The external field includes areas that are struck by the penis prior to intromission[3], and are probably involved in triggering lordosis or enabling the female to position her vagina in the area of the male's thrusts[3,30]. Vaginal stimulation strongly facilitates, but is not essential for, mating responses[7,24].

It is interesting that both the hypogastric and pelvic nerves respond strongly to stretching of the cervix as must occur during labor. Whereas the human analog of the hypogastric nerve (afferents that enter the spinal cord between T_{10} and L_1, inclusive) mediates the pain of labor[8], stimulation of the pelvic nerve by vaginal probing, in rats, produces analgesia. Analgesia was inferred in rats from the vaginocervical stimulation-induced suppression of flexion responses to noxious stimuli[25], inhibition of thalamic neuronal responses to noxious but not innocuous stimuli[26], and operant responding for vaginal stimulation during skin shock[41]. Further evidence that vaginal stimulation produces analgesia is based on verbal report by women, that vaginal self-stimulation differentially elevates pain thresholds but not tactile thresholds[46]. Activation of both nerves during labor could be related to the elevated pain thresholds of rats during late pregnancy[16,17]. Furthermore, activation of these nerves by fetal growth and activity at the end of parturition may be involved in triggering immediate and appropriate maternal behavior at delivery[18,22,31].

Based on the present findings, it is probable that mechanical stimulation provided by copulatory thrusting by the male with or without intromission would activate the pudendal and pelvic nerves, but not the hypogastric nerve. By contrast, during parturition, the hypogastric and pelvic, but not pudendal nerves would be stimulated by the fetuses as they pass down the birth canal, and the pudendal nerve would be activated as they emerge.

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