Gert Holstege, M.D., Ph.D., José Boers, M.A.

The Neuronal Systems of Mating

Introduction

It has been known for a long time that estrogen plays a crucial role in the display of sexual behavior in female mammals. An example is the female hamster, which has an estrous cycle of four days. Of these four days, she is in estrous for only 12-20 hours, i.e. willing to mate with a male hamster (Frank and Fraps, 1945). During this estrous period, the male hamster or even the human experimenter easily triggers the female hamster by moving the fur of the lower back or perineum. During this posture, the female is immobile for several minutes, independent of whether or not a male hamster is in the environment. During that time, she displays lordosis of the back with elevation of the tail (Fig. 1), which enables the male hamster to mount. Possibly, such a remarkable immobility is necessary, because in non-estrous states the female is rather aggressive towards male

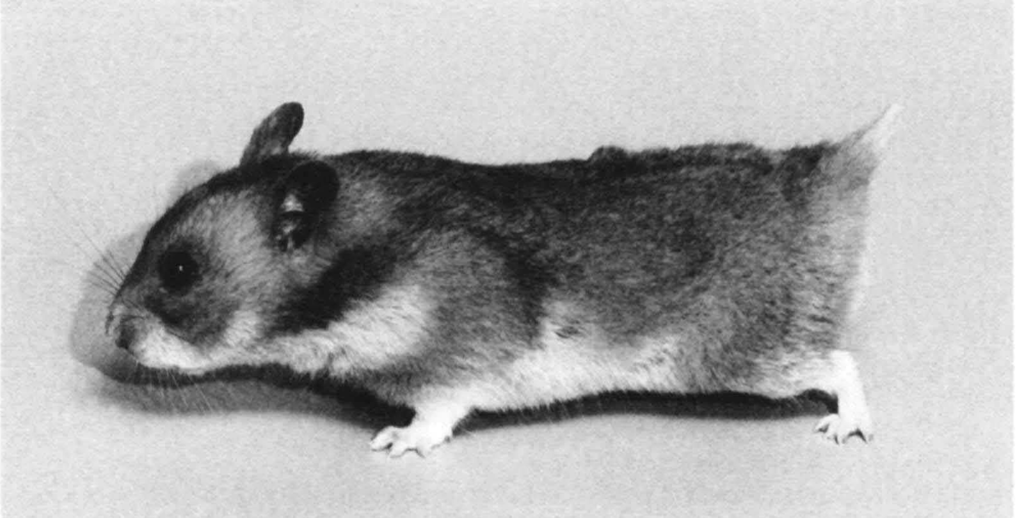

Fig. 1. Female hamster in lordosis posture. Note the erect posture of the tail.

hamsters and only total immobility of the female convinces him that he can mate without being attacked.

Cats have a completely different estrous cycle. Female cats can remain in a state of estrous for more than two weeks, instead of 12-20 hours in the hamster. In cats mating behavior is also more complicated than in the hamster, and consists of lordosis of the back, sideward movement of the tail and treading of the hindlimbs. Similar to the hamster the female cat displays the mating posture after stroking of the lower back or perineum, independent of whether a male cat is present or not. Apparently, in both species there must exists a very strong reflex system that becomes active during estrous but not during non-estrous periods.

Ascending Component of the Reflex System

The stimulus that triggers the estrous female hamster or cat to display the mating posture must originate in the lumbosacral spinal cord, because at that level the afferent fibers from the lower trunk and perineum enter the central nervous system. Ascending pathways from the spinal cord have been extensively described to pass to and terminate in the thalamus (spinothalamic tract), mainly to its ventroposterolateral

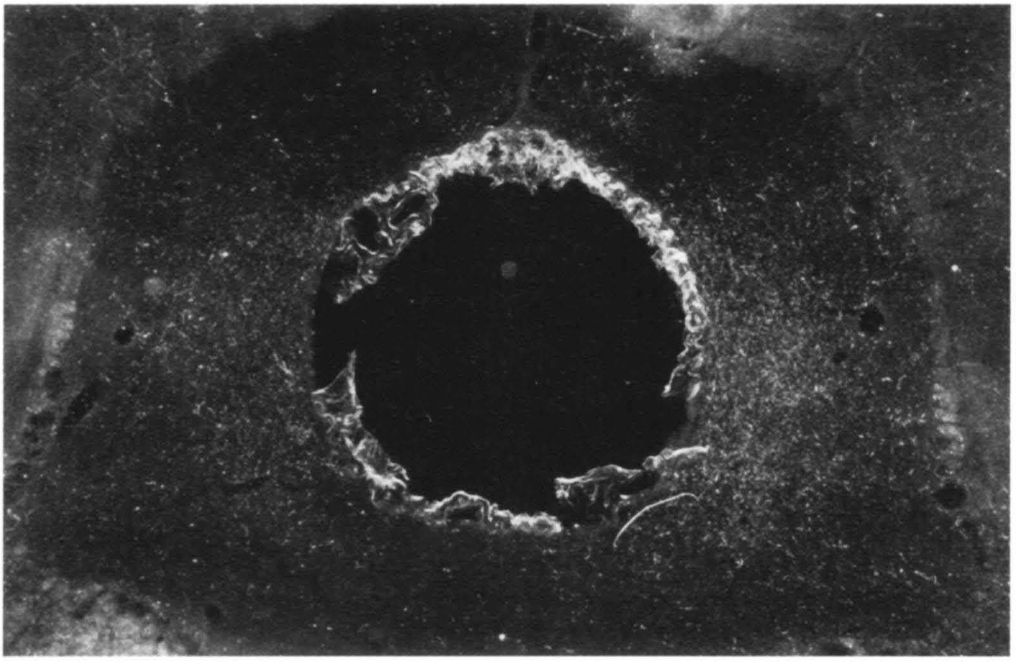

Fig. 2. Termination of ascending labeled fibers in the PAG, after an injection of the tracer WGA-HRP in the sacral spinal cord. Prior to the injection an hemisection was made at L4.

part (VPL) and to certain medial thalamic subnuclei. Recent findings of Mouton et al. (1998) have shown that a much stronger ascending system than the spinothalamic tract terminates in the caudal half of the periaqueductal gray (PAG), which projection is especially strong from the lumbosacral cord (Fig. 2; see also VanderHorst and Holstege, 1996). This termination in the PAG is interesting, because in rats it has been shown that stimulation in this part of the PAG induces the display of the mating posture and lesions in this same area prohibits mating behavior to occur in estrous females (Sakuma and Pfaff, 1979b). It has also been demonstrated that hypothalamic lesions or decerebration rostral to the PAG does not interrupt these mating postures to occur after proper stimulation (Sakuma and Pfaff, 1979a). Apparently, although there is a lot known about the effects of various hypothalamic regions on mating behavior (see Pfaff et al., 1994 for review), the PAG is the crucial structure for triggering it, and it also explains why the PAG receives such a strong projection from the lumbosacral cord.

Descending Component of the Mating Reflex

Since stimulation of the PAG has been shown to elicit the mating posture, it must have access to the motoneurons of the muscles that produce this posture. Although there is a direct PAG projection to the spinal cord, it is unlikely it represents the descending component of the reflex system, because it terminates for the most part in the cervical cord, and mainly on interneurons. Only a few PAG fibers continue into the lumbosacral cord (Mouton and Holstege, 1994).

However, there exists a projection to especially those motoneuronal cell groups that innervate the muscles involved in the display of the mating posture (VanderHorst and Holstege, 1995). This projection does not originate from the PAG, but from neurons in the nucleus retroambiguus (NRA) in the caudal medulla oblongata. However, the NRA, in turn, receives a very strong and distinct projection from the PAG, which suggests the PAG-NRA-lumbosacral motoneuronal projection as being the pathway via which the PAG induces mating behavior. To make this framework even more complicated, the NRA is also involved in the control of abdominal pressure, within the context of expiration (Merrill, 1970), vocalization (Holstege, 1989, Zhang et al., 1994) and vomiting (Miller, 1987). The NRA has distinct projections to all the motoneurons that produce these motor activities, such as projection to the motoneurons of pharynx and larynx intercostal, abdominal, and pelvic floor muscles (Holstege and Kuypers, 1982; Holstege and Tan, 1987; Holstege, 1989; Fig. 3). Thus, the NRA consists of premotor interneurons that have direct access to motoneurons involved in the control of intrathoracic and abdominal pressure as well as of mating posture. Ultrastructural findings (VanderHorst and Holstege, 1997; Boers and Holstege, 1999a) have shown that almost all NRA projections are of an excitatory nature.

Although there exist several brainstem afferent projections to the NRA, (Gerrits and Holstege, 1996), the PAG-NRA-motoneuronal pathway seems to form the motor component of at least vocalization and mating behavior. In respect to the last function,

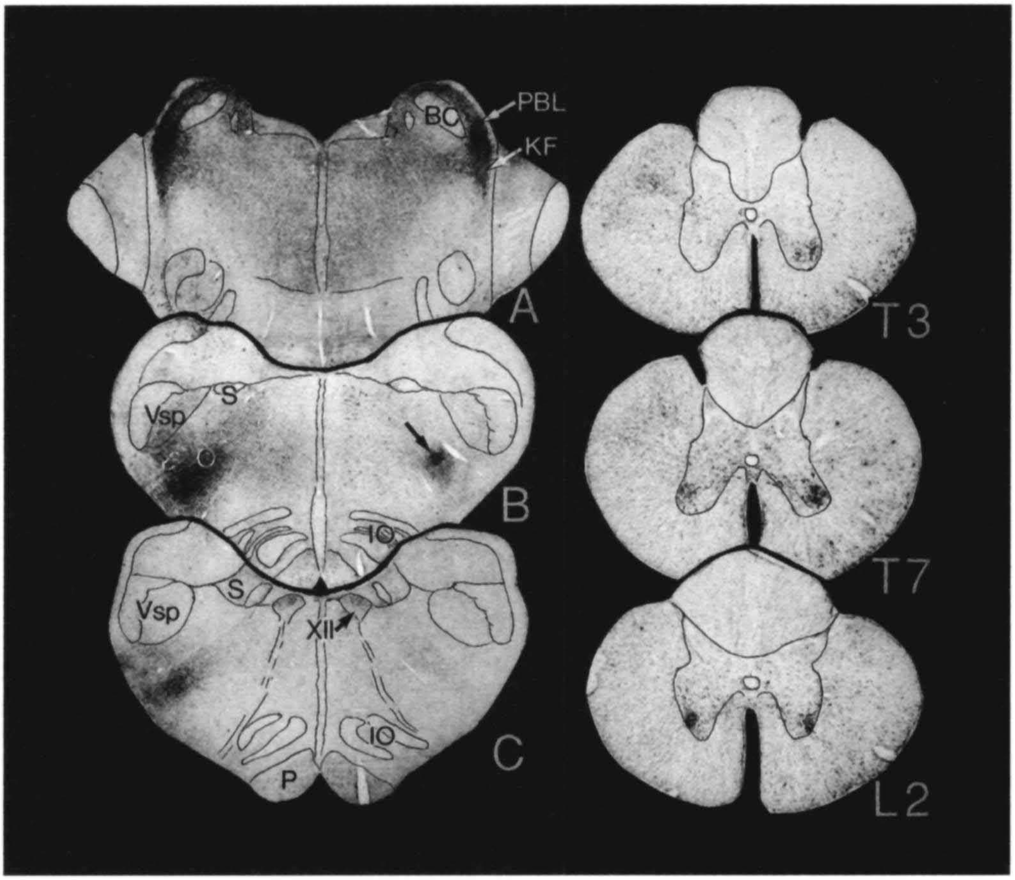

Fig. 3. Reversed darkfield photomicrographs of the caudal brainstem (A-C) and three segments (T3, T7, and L2) of the spinal cord after an injection of tracer in the NRA. Note the strong bilateral projections to the lateral parabrachial nuclei and the nucleus Kölliker-Fuse and the very strong contralateral projection to the dorsal group of the nucleus ambiguus in B (arrow). Note further the bilateral projection to the dorsal part of the hypoglossal nucleus in C and the strong projections to the intercostal (T3) and abdominal (T7 and L2) motoneuronal cell groups in the spinal cord.

according to the concept of VanderHorst and Holstege (1997), there exists a reflex loop in which the ascending loop begins with skin afferents of perineum, vagina, flanks and lower back that enter the lumbosacral cord, where the signal is relayed to the PAG. The PAG, in turn, excites the NRA, which directly activates the mating motoneurons (Fig. 4).

In the hamster a similar but much less complicated PAG-NRA-motoneuronal pathway exists, which reflects the simplicity of the mating behavior in the hamster compared to the cat.

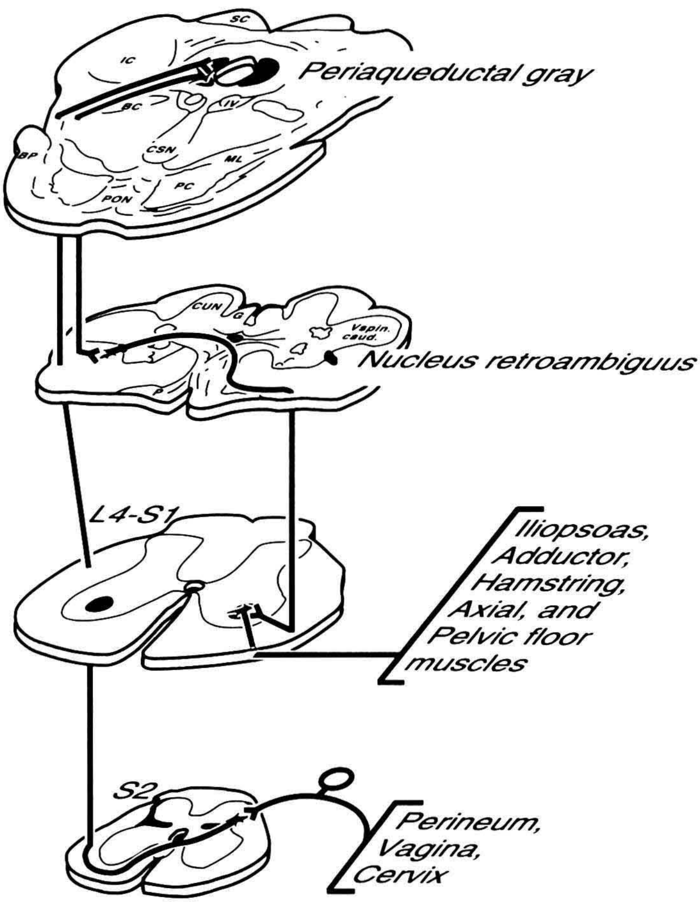

Fig. 4. Schematic representation of the reflex loop for eliciting the mating posture in the female cat.

Effects of Estrogen

In hamster and cat, for mating to occur, the females have to be in estrous. It also takes place in artificial estrous, i.e. in ovariectomized female cats, when given subcutaneous injections of estradiol. Apparently, estrogen is able to 'change' the function of the reflex of mating behavior, because an identical stimulus (stroking the flanks, perineum, vagina, and lower back) never produces this effect in cats with low estrogen levels. The question is how and where estrogen influences this reflex arc.

Whether there is any influence of estrogen on the ascending loop is not known, but in the cat VanderHorst and Holstege (1997) have found great differences in the strength of the descending loop. These differences appear to be located at the

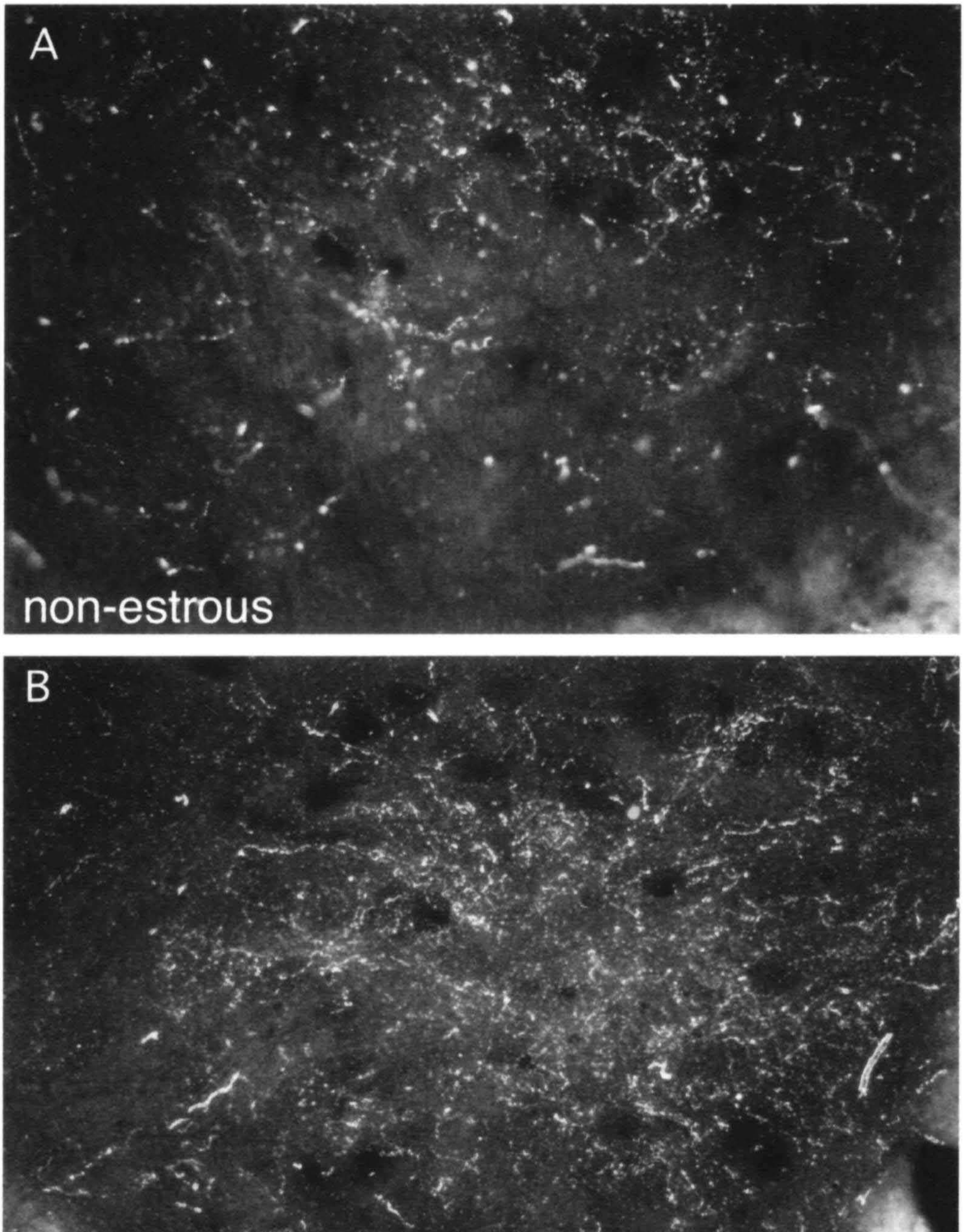

Fig. 5. Darkfield-polarized light photomicrographs of labeled NRA fibers in the motoneuronal cell group of the semimembranosus in non-estrous (5A) and estrous case (5B). Note the large difference in density of NRA fibers.

termination site of the NRA fibers on the motoneurons of the muscles producing the mating posture (Fig. 5). Light- and electronmicroscopical studies have revealed that the number of NRA terminals is almost nine times as numerous in estrous than in non-estrous cats. This enormous difference is caused by a process of growth, because at the ultrastructural level many growth cones were found in the terminals of the NRA fibers, because the growth cones contained the tracer that was injected in the NRA (Fig. 6). Growth cones were never found in non-estrous female cats. Cats take four days to get into estrous, i.e. the growth process takes four days to change the strength of the NRA-motoneuronal pathway so that it 'overrides' most other motor programs. In the hamster the complete estrous cycle takes only four days, and the estrous part of it only 10-20 hours. Such a short duration makes it impossible to develop growth cones in the NRA terminals, which indicate that another mechanism activates the descending system activating the mating posture. Perhaps the crucial difference between hamster and cat appeared to be the presence or absence of estrogen receptors in the nuclei of the cells in the reflex arc. In both species some of the PAG-NRA projecting cells were found to contain estrogen-alpha-receptors (Boers et al., 1999b;

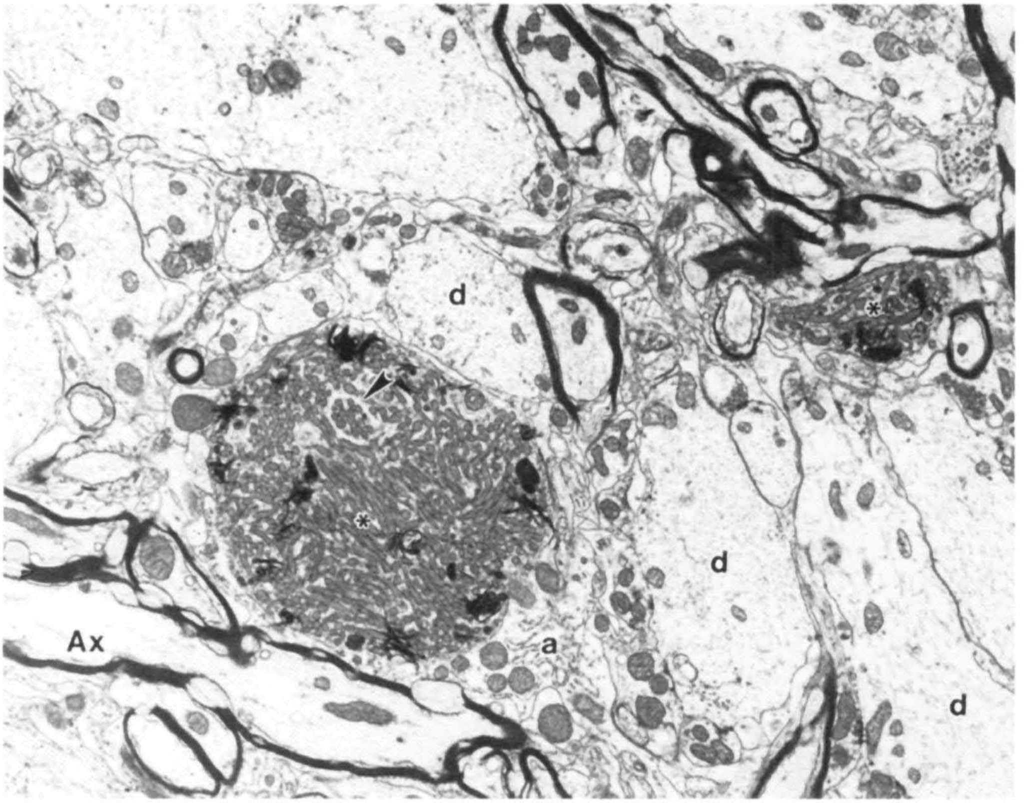

Fig. 6 Electronmicrograph representing labeled growth cones (asterisks) in the semimembranosus motoneuronal cell group. a = astrocyte; Ax = axon; d = dendrite; arrowhead = small groups of mitochondria sequestered within agranular membrane.

VanderHorst et al., 1998). In the NRA the situation is different. In the cat almost none of the NRA cells contain estrogen receptors (VanderHorst et al., 2000), but in the hamster about 80% (Boers and Holstege, 1998). In summary, in cat but not in hamster high estrogen levels induce outgrowth of NRA terminals on lumbosacral motoneurons. In the hamster, estrogen elevates the level of functioning of the NRA cell bodies projecting to the lumbosacral cord. Accordingly, in both species during estrous the same excitatory effect of the PAG on the NRA neurons will result in a much stronger excitatory stimulus on the lumbosacral motoneurons than in non-estrous animals. In the hamster the estrogen receptors are activated, in the cat the number of terminals has increased nine times (Fig. 7). When the trigger is given (palpation of the flanks etc.), the signal is relayed to the PAG from where it is relayed via the spinal cord to the NRA, which, in contrast to the situation in non-estrous hamsters in turn strongly excites the mating muscle motoneurons, resulting in the mating posture.

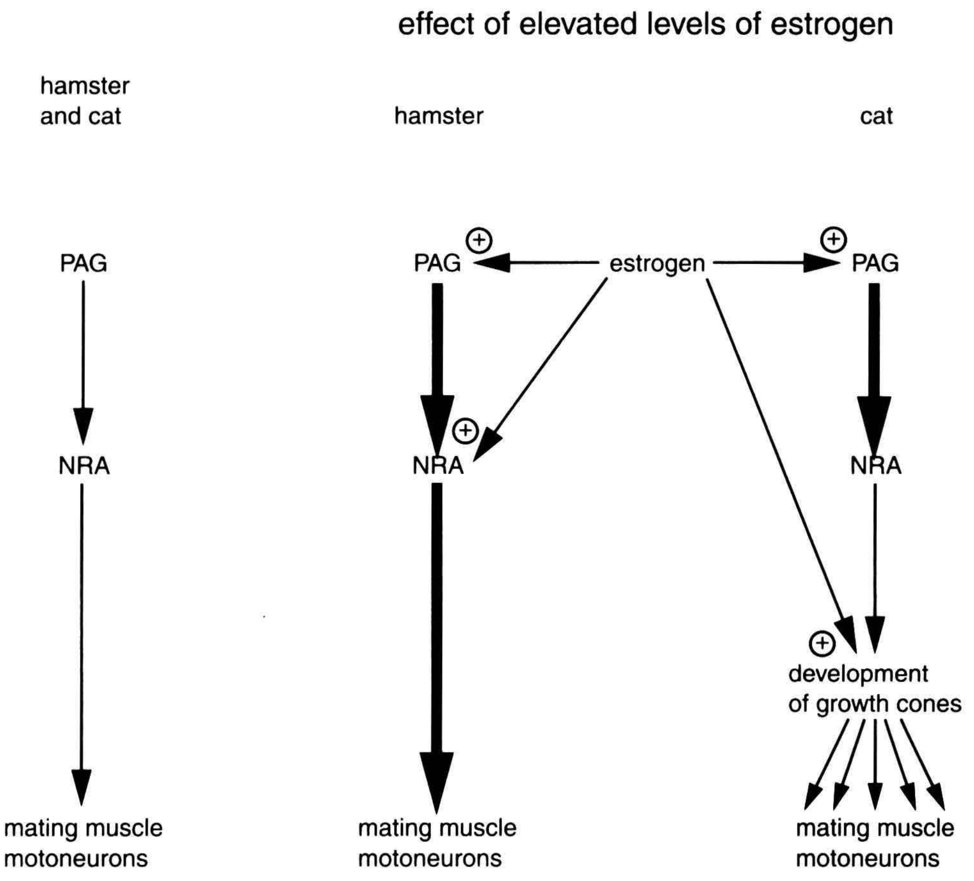

Fig. 7. Schematic representation of the site of action of estrogen in hamster and cat.

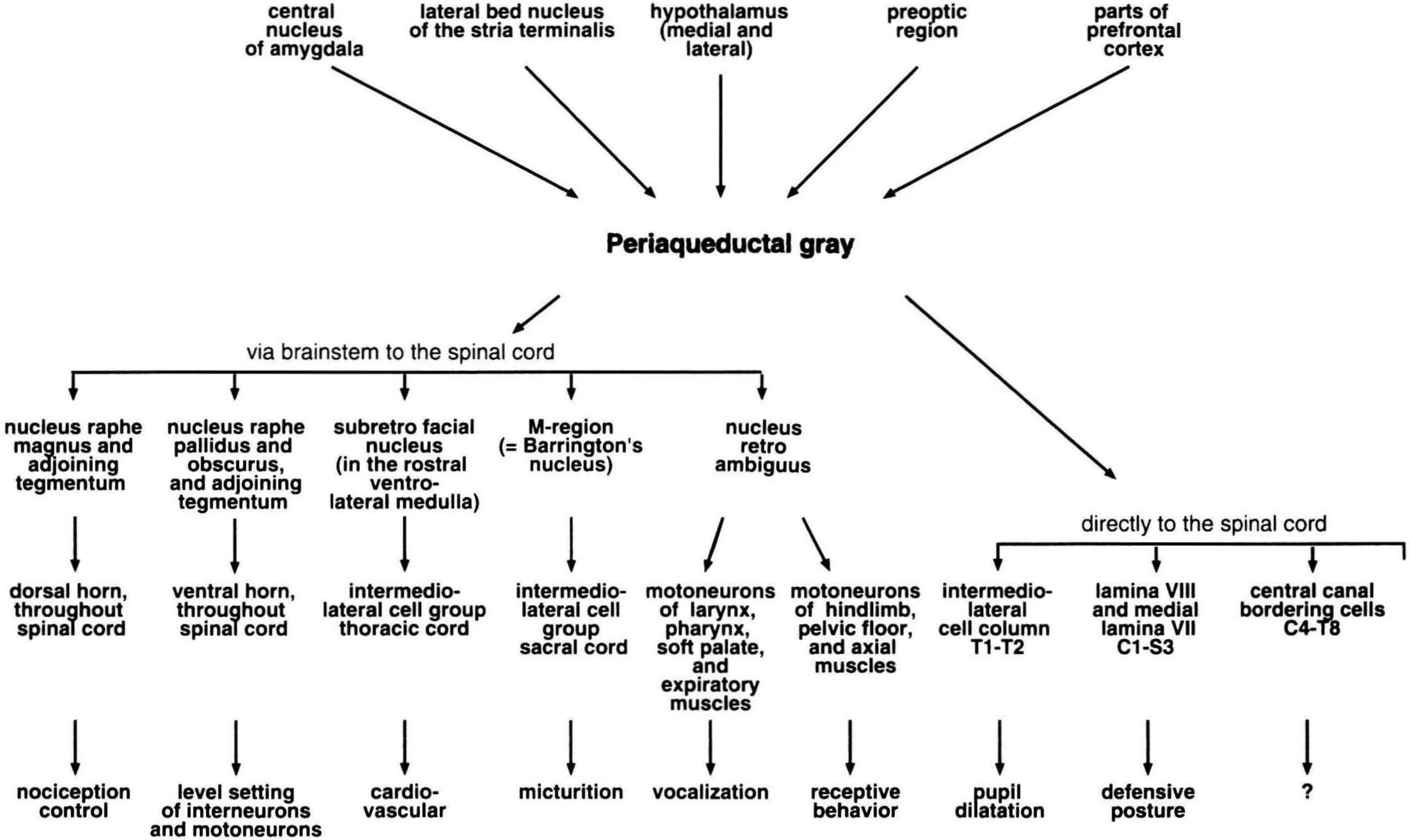

Fig. 8. Schematic overview of the efferent pathways of the PAG to more rostrally located structures and to more caudally located structures in the brainstem and spinal cord. The function in which each of the descending projections might be involved are also indicated.

Most recently, VanderHorst et al. (1999a) have shown that a similar PAG-NRA-motoneuronal system exists in the monkey as in the cat, i.e. no estrogen receptors in the NRA, and, albeit to a somewhat lesser extent, traces of growth cones at the end of the NRA fibers among motoneurons (VanderHorst et al., 1999b).

Epilogue

A concept is presented in which mating behavior in hamster and cat is based on a reflex arc, starting from the skin of lower back, flanks, and perineum, via the lumbosacral cord to the PAG. The descending loop is the PAG-NRA-motoneuronal pathway. Estrogen influences this reflex arc at the level of the PAG (hamster and cat), NRA cells (hamster) or NRA terminals (cat). The PAG plays a crucial role in this reflex arc, because it not only receives many afferents from the lumbosacral cord, but also many fibers from the hypothalamus and many other limbic system regions. Moreover, it projects to various other relay systems in the caudal brainstem (Fig. 8) which allows the PAG to control basic survival behavior of the individual and of the species. For example, the PAG, in case the survival of the individual is threatened, elicits basic survival behavior as aggression or submission, but inhibits sexual behavior.

A similar procedure occurs in humans in whom survival of the individual is first, survival of the species is second. In concentration camps in the Second World War, survival of the individual was crucial, but sex was of negligible importance.

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Department of Anatomy and Embryology, University of Groningen, A. Deusinglaan 1, 9700 AD Groningen, The Netherlands. E-Mail: g.holstege@med.rug.nl