Neuro-endocrinology

11 BRIEFINGS

PHEROMONES AND REPRODUCTION

SUMMARY

The information humans receive from their nose is rarely of vital significance and although perfumers and masters of wine have developed a large vocabulary of descriptors, most of us categorise odours into pleasant or unpleasant. Not surprisingly therefore, most of our olfactory receptor genes are non-functional pseudogenes. Rodents, on the other hand, not only have a vast repertoire of olfactory genes (1000-1500) but also possess two additional sets of receptors in the vomeronasal organ that is specialised for pheromone reception.

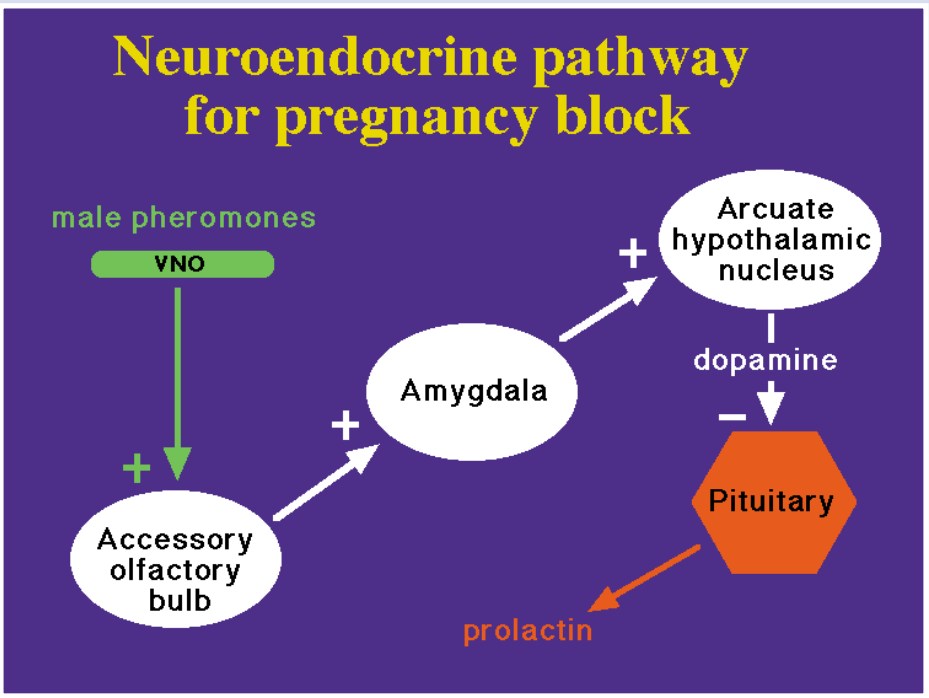
Using the pathway shown, male pheromones induce dopamine release into the pituitary portal blood vessels. Dopamine acts on the pituitary to inhibit prolactin release and luteotrophic support of the ovary is lost. Progesterone levels then decrease, permitting oestrogen levels to rise, thereby promoting the oestrus condition.

Strange males

The reproductive biology of rodents is strongly influenced by chemical cues, both in the context of behaviour (signalling pheromones) and reproductive endocrinology (primer pheromones). An important effect of primer pheromones, observed in the female, is the control of oestrus. This occurs in a number of species by invoking the onset of puberty and the onset of oestrus after a period without ovarian cycles.

A special case of oestrus control which occurs in the mouse and a few other rodent species, is the olfactory block to pregnancy. This was first described by Hilda Bruce in 1959 who found that newly mated female mice returned to oestrus if they were exposed to strange males within 72h of the initial mating. The fact that pregnancy block cannot occur after implantation of the embryo suggests that the effect of male primer pheromones is on the pre-implantation hormonal status.

In both the block to pregnancy and the induction of oestrus, the primary endocrine change is a fall in serum prolactin. Evidence that prolactin is the hormone mainly responsible for pregnancy block comes from experiments which show that restricted exposure of female mice to primer pheromones coincident with prolactin surges, following mating, blocks pregnancy.



Neuro-endocrinology Briefing 11: Pheromones and Reproduction

Where do pheromones act?

In parallel to the common neuroendocrine mechanisms for oestrous induction, all of the pheromone effects involve the vomeronasal organ (VNO), an accessory structure in the nose. Damage of the vomeronasal organ or to its neural processing centre, the accessory olfactory bulb (AOB), prevents female odours from inducing anoestrus and male odours from inducing oestrus, accelerating puberty onset, and blocking pregnancy. These pheromones are non-volatile peptides, hence females must make contact with male urine to stimulate the sensory receptors in the VNO. Pheromone information received in the AOB is relayed to a group of nerve cells in the arcuate nucleus of the hypothalamus, at the base of the brain, which secrete dopamine; a powerful regulator of the production of prolactin from the pituitary gland.

Why not all?

The pheromonal mechanism for inducing pregnancy block has much in common with pheromonal mechanisms for promoting early puberty and inducing oestrus in grouped females. Since these occur in response to urinary pheromones from any male the question arises as to why pregnancy block only occurs with strange male pheromones. Mechanisms appear to exist which bring about recognition of the pheromonal signal from the familiar male and several features which characterise the neural basis of this olfactory recognition memory have now been elucidated.

It is known that memory formation occurs in a critical period after mating; that it is a function of the vomeronasal accessory system and is dependant on neural pathways to the AOB which produce the neurotransmitter, nor-adrenaline. A series of studies has shown that the relatively primitive structure of the AOB has the capacity for synaptic changes of importance for the recognition memory and subsequent 'gating' of pheromones from the male that mates.

"memory formation occurs in a critical period after mating"

Human pheromones?

Evolutionary enlargement of the brain's neocortex has enabled the rapid processing of information from a number of sensory channels simultaneously and human behaviour does not come under the obligatory regulation of any one of our senses. It would therefore seem implausible that humans might experience significant behavioural or endocrine regulation by pheromones. Nevertheless there have been claims for human pheromones based on a tendency for females to synchronise their cycles and for a functional human VNO.

There is strong anatomical evidence for a foetal human VNO but the recent molecular genetic studies suggest that human olfactory sensibilities are in decline (72% of human olfactory receptor genes investigated in a recent study were shown to be pseudogenes, and only pseudogenes have so far been identified for the human VNO receptors). Anatomical studies lend support to this viewpoint. A study of 564 adults has located the vomeronasal vestibule bilaterally in only 8% of subjects, while it was unilateral in 22% and absent in 70%. Biopsy and autopsy investigations have failed to identify nerve cells in the adult human VNO using a variety of neural and olfactory markers. This finding is supported by the absence of an AOB in humans, apes and Old World primates. The overwhelming evidence would therefore not give support to a human VNO that is functional in any meaningful way.

Nevertheless, the main olfactory system in humans could have taken over the functions of the VNO in responding to odour cues of behavioural significance. There is a strong olfactory input to prefrontal cortex and, in some aspects of human decision-making, this area of the brain is guided by emotional signals. We tend to identify these decisions as 'gut feelings', but perhaps this feeling in our guts is really secondary to the sensation from our noses.

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