Vomeronal Mechanisms of Mate Recognition in Mice

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Introduction

The ability of animals to distinguish individual conspecifics influences many aspects of their behaviour, including choice of mate, territorial marking and mother-offspring interactions. In rodents, information about individuality is conveyed by chemical cues in their urine and body secretions. Hence, mice can be trained to discriminate the urine odour of congenic mice that differ only in genes of their major histocompatibility complex (MHC). This ability is likely to be based on MHC-related differences in the profile of urinary volatiles (Singer et al., 1997), which are sensed by the main olfactory system and generate statistically different patterns of activity across large populations of neurons in the main olfactory bulb (Schaefer et al., 2002). In contrast, individual recognition underlying urine countermarking behaviour of male mice depends on the profile of major urinary proteins rather than MHC type (Hurst et al., 2001), suggesting that mice use different chemosignals for signalling individual identity in different behavioural contexts. Furthermore, information about the individual identity of mice can be conveyed by both the main olfactory and vomeronasal systems. Whereas the main olfactory system is adapted to learn and discriminate small differences in the profile of airborne volatiles, the vomeronasal system responds to a more limited range of non-volatile stimuli taken up following direct contact. Moreover, the representation of individual identity in vomeronasal system appears to differ from that in the main olfactory system, as individual neurons in the accessory olfactory bulb (AOB), respond highly selectively to the strain identity of anaesthetized conspecifics (Luo et al., 2003).

Individuality and the pregnancy block effect

Individuality chemosignals sensed by the vomeronasal system are vital for mate recognition in the pregnancy block effect (Lloyd-Thomas and Keverne, 1982). This effect is elicited by exposure of recently mated female mice to male urinary chemosignals from unfamiliar inbred strains, which blocks the implantation of their developing embryos and leads to pregnancy failure. Crucially, female mice learn to recognize the strain identity of urinary chemosignals from the mating male, which subsequently prevents them from blocking her pregnancy. The strain identity of the pregnancy blocking chemosignals is known to be influenced by MHC Class I genotype, as chemosignals from congenic males, which differ from the mating male at only the H2 locus of the MHC, are effective in blocking pregnancy (Yamazaki et al., 1986). However, differences in stimulus access and the low level of sequence homology between main olfactory and vomeronasal receptors (Herrada and Dulac, 1997; Matsumani and Buck, 1997; Ryba and Tirindelli, 1997) suggest that different types of chemosignal may convey MHC-dependent information in the two systems. Indeed, recent evidence suggests that MHC class I peptide ligands form a novel class of chemosignal that convey individuality in the pregnancy block effect (Leinders-Zufall et al., 2004). These nine-amino acid peptides are products of the proteosomal degradation pathway, and are able to convey information about strain identity due to the positions of large hydrophobic side chains of particular amino acids, known as anchor residues, along the peptide chain.

Neural mechanisms of mate recognition

The pregnancy block effect is mediated by a relatively direct neural pathway from the vomeronasal receptors to the hypothalamus, via the accessory olfactory bulb (AOB) and corticomedial amygdala (Li et al., 1989). Activation of this pathway reduces levels of the hormone prolactin, and the consequent removal of luteotrophic support leads to a fall in progesterone and a return to oestrus (Bellringer et al., 1980; Li et al., 1994). But how can synaptic changes in this relatively simple neural system account for its ability to learn about and subsequently recognize the chemosignals of the mating male? A substantial body of evidence has accumulated that suggests that the neural changes underlying this chemosensory learning are localized to the AOB, at the first stage of processing of the vomeronasal information (Kaba and Nakashishi, 1995). The association of elevated noradrenaline levels in the AOB at mating with the activity of those mitral cells that respond specifically to the mating male chemosignals is hypothesized to cause a long-lasting increase in gain of their reciprocal synapses with the inhibitory granule interneurons. This increase in inhibitory control of the mitral cells can account for the mate recognition by selectively disrupting the transmission of the mating male’s chemosignal at the level of the AOB, preventing it from activating the hypothalamic mechanisms that result in pregnancy block (Brennan et al., 1990).

Support for this hypothesis has come from neurochemical investigations using in vivo microdialysis in freely behaving mice (Figure 1). We found significantly higher levels of the inhibitory neurotransmitter GABA in the AOB of mated females, in response to their exposure to male urine.
mate’s pheromones, compared to the response of non-mated females that received the same amount of male exposure. This is consistent with an increase in inhibitory feedback acting on the mating male’s chemosignals. Further support has been provided by recent electrophysiological investigations of the AOB and medial amygdala in freely behaving female mice (unpublished data). Local field potentials (LFPs) recorded from the AOB were found to oscillate across a range of frequencies, with a predominant low frequency oscillation of around 4–8 Hz. Such oscillations of neural activity are a common feature of olfactory systems and result from the synchronous depolarization and hyperpolarization of large neuronal populations. We found that the predominant frequency of LFP oscillation in the AOB increased significantly in the 8–12 Hz theta range in response to exposure to male chemosignals, irrespective of strain identity. However, following mating, the urinary cues from the mating male remained effective in increasing the amplitude of the LFP oscillations, in the 8–12 Hz frequency range, whereas there was no increase in response to urinary cues from an unfamiliar male. Furthermore, the frequency of action potentials recorded from neurons in the medial amygdala was on average twice as great in response to urine from an unfamiliar male compared to urine from the mating male, irrespective of the strains of the males that were used. These differential electrophysiological responses to male chemosignals are consistent with a disruption of the mate’s pregnancy blocking signal at the level of the AOB. Although, the role of oscillating neural activity in conveying vomeronasal information is unclear, the newly discovered individuality chemosignals may provide a useful tool for future investigations into the neural basis for mate recognition in the accessory olfactory system in the block to pregnancy in mice.[4]

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References


