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Research report

The main and the accessory olfactory systems interact in the control of mate recognition and sexual behavior

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ABSTRACT

In the field of sensory perception, one noticeable fact regarding olfactory perception is the existence of several olfactory subsystems involved in the detection and processing of olfactory information. Indeed, the vomeronasal or accessory olfactory system is usually conceived as being involved in the processing of pheromones as it is closely connected to the hypothalamus, thereby controlling reproductive function. By contrast, the main olfactory system is considered as a general analyzer of volatile chemosignals, used in the context of social communication, for the identification of the status of conspecifics. The respective roles played by the main and the accessory olfactory systems in the control of mate recognition and sexual behavior are at present still controversial. We summarize in this review recent results showing that both the main and accessory olfactory systems are able to process partially overlapping sets of sexual chemosignals and that both systems support complimentary aspects in mate recognition and in the control of sexual behavior.

Among the various communication strategies that have evolved in mammalian species, smell is surely the most widespread and the most conserved [106]. In the field of chemosensory communication, Karlson and Lüscher [43] introduced the concept of "pheromones" as chemosignals that provide information to conspecifics about sex or endocrine status or which stimulate hard-wired species-specific social behaviors. Traditionally, pheromones have been classified as either "releaser pheromones" which trigger an immediate response or as "primer pheromones" inducing long-term changes in behavior or physiology. More recently, a new terminology has been introduced, including "signaler pheromones", which induce behavioral or physiological changes depending on the identity of the individuals emitting or sending the pheromonal signal. However, it is difficult to classify specific pheromonal compounds regarding their neurobiological processing and/or their behavioral action and consequently there has been some controversy about the use and definition of the term "pheromone". For example, a pheromonal compound such as brevicomin can act either as a releaser pheromone, eliciting aggressive responses in conspecific males, or as a primer pheromone, inducing estrus in female mice [81].

Despite these controversies, it is clear that olfactory/pheromonal signals profoundly influence neuroendocrine functioning and regulate a wide variety of social behaviors including sexual interactions, parent–offspring relations and inter-individual aggression. In the field of sexual functioning, olfactory cues and pheromones are probably the most powerful signals mediating the influence of social environment on reproductive function in many species. For example, pheromones have been shown to influence nearly all stages of reproductive life including the modulation of sexual maturation and puberty [110], the suppression of estrous cyclicity [115], the mediation of mate recognition and sexual interactions [3,47], the disruption of pregnancy [13,14,18] or the initiation of maternal behavior at parturition [58,59].

Finally, one noticeable fact in the physiology of olfaction is the existence of at least two distinct but complementary systems for the detection of chemosensory molecules, namely the main and the accessory olfactory systems [12,15,75,102] (see [11] for the newly chemosensory system identified in the Grueneberg ganglion) in most mammalian species. These olfactory systems have evolved so that they differ in their peripheral anatomy, their central projections and also in their function. However, both systems may also function synergistically in sustaining some pheromone-dependent behaviors [7,48,90]. Therefore, a central problem in olfaction is to elucidate the relative roles played by both systems in detecting olfactory information and in regulating chemosensory-dependent behaviors. In this review, we will focus on the relative roles of the

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main versus accessory olfactory systems in the processing of sexual olfactory/pheromonal chemosignals and their involvement in the control of sexual interactions, including mate recognition, as well as how these olfactory systems are regulated by gonadal hormones.

1. Functional organization of both the accessory and main olfactory systems

1.1. The accessory olfactory system

The accessory olfactory system, through its close connections with the reproductive hypothalamus, is usually conceived to be involved in the detection of odors that influence reproductive behaviors and as a consequence triggers neuroendocrine changes leading to puberty acceleration, estrous induction, and pregnancy block, as well as the testosterone increases in males when exposed to urine from estrous females [51,52,91]. The sensory neurons of the accessory olfactory system are found in the vomeronasal organ (VNO), a blind-ended tube located at the basis of the nasal septum which opens via a small duct into the nasal cavity or into the mouth depending on the species. The VNO detects pheromones which gain access to the VNO by a vascular pumping mechanism [78]. Indeed, many mammalian species engage in intense physical investigation of scent sources, thus exposing VNO sensory neurons to chemosignals which are pumped into the lumen of the VNO when the animal is attending to the stimulus [66,76]. Pheromonal ligands then interact with receptors on the membrane of VNO sensory neurons. These vomeronasal receptors have been identified and classified in two distinct families: the vomeronasal type 1 (V1Rs) and type 2 receptors (V2Rs). Both types of receptors share little sequence homology and are thought to have an ancient evolutionary origin [51,52]. In addition, both types of receptors are expressed in different regions of the VNO: V1Rs are expressed in the apical part of the VNO, near the lumen, while V2Rs are expressed in the more basal region [14,38]. This regionalization is conserved at the level of the first olfactory relay, the AOB, where V1Rs neurons send projections exclusively to the rostral part of the AOB while the V2Rs neurons project to the caudal part of the AOB. It has been shown that these subdivisions of the VNO and AOB sustain functional differences as they respond differentially to pheromonal stimuli in mice [16,37]. After the first olfactory relay, mitral cells of the AOB project in turn to the medial nucleus of the amygdala, where information processed in the two parts (rostral vs caudal) of the vomeronasal pathway converge when their projections overlap in this structure [111]. Olfactory information is then dispatched to several hypothalamic and limbic regions involved in the regulation of reproductive behavior such as the bed nucleus of the stria terminalis (BnST), the medial preoptic area (MPOA) and the ventromedial hypothalamus [93] and thus bypass higher cognitive cortical centers.

1.2. The main olfactory system

The vomeronasal system has traditionally been the main focus for pheromonal research, while the main olfactory system has been considered as a general analyzer that detects and differentiates among complex chemosignals that are present in the physical and social environment of individuals [31]. However, some mammalian pheromones have long been known to be detected by the main olfactory system (MOS; [12]. In the MOS, chemosignals are detected by olfactory sensory neurons located in the main olfactory epithelium (MOE). These sensory neurons represent the start point of the central treatment of olfactory information as they project their axons through the cribiform plate to converge at the first relay of the central olfactory system in the brain: the glomeruli of the main olfactory bulb (MOB) [19]. It should be noticed that individual sensory neurons in the MOE project a single axon to a single glomerulus in the MOB, therefore, the glomerular layer of the MOB forms a map of olfactory axons terminals [19,120]. These projections of the MOE sensory neurons are precisely organized so that MOE sensory neurons expressing a given odorant receptor send their axons to a few converging glomeruli with a fixed topographical localization. The mitral and tufted cells abutting these MOB glomeruli then transmit olfactory signals to various forebrain and cortical targets including the piriform cortex, the entorhinal cortex or the anteriorcortical nucleus of the amygdala [93].

1.3. Convergence between main and accessory olfactory pathways

While main and accessory olfactory systems exhibit segregated pathways at the level of the first olfactory relays, the two systems converge downstream at several levels, including the cortical-medial amygdala [33,53,54,75,77,93,107]. Indeed, electrical stimulations of both the MOB and vomeronasal organ induce electrophysiological activation of this structure [61,77]. More interestingly, single neurons have been shown to respond to these stimulations, suggesting that both systems can interact in the processing of olfactory/pheromonal signals at the single cell level in the amygdala and interact downstream towards the BnST or MPOA which are of great importance in the regulation of sexual behavior. In addition, it has been recently suggested that the AOB receives backward connections from several forebrain sites including the bed nucleus of the accessory olfactory tract, the rostral portion of the medial amygdala (MeA), and the posteromedial cortical nucleus of the amygdala (PMCo). When exposed to male urinary volatiles, these connections show specific activation, suggesting that main olfactory–MeA–AOB signaling may motivate approach behavior to opposite-sex pheromonal signals that ensure successful reproduction [71].

Another site of cellular convergence of both olfactory systems appears to be the gonadotropin-releasing hormone (GnRH) neurons. Indeed, it is widely accepted that the effects of pheromones on neuroendocrine status are mediated by GnRH neurons which are found scattered in the anterior hypothalamus [77,80,113,114]. Several sets of experiments have repeatedly demonstrated that the vomeronasal system sends projections to the GnRH neurons, and that pheromonal signals processed through the vomeronasal system can activate these neurons [80,113,114]. However, while recent experiments confirmed that GnRH neurons receive signals from subsets of neurons located in the vomeronasal system, they also, and more surprisingly, demonstrated that GnRH neurons receive connections from the main olfactory system [10,119] suggesting that GnRH neurons can receive information about odorants processed by both olfactory systems. Interestingly, GnRH neurons have bidirectional contacts with both main and accessory olfactory systems-relay areas, implying that they can also modulate the processing and transmission in both olfactory systems. Finally, GnRH neurons contact brain areas associated with sexual behavior whose connections exhibit sexual dimorphism. All these results suggest that both olfactory systems converge on and can impact GnRH neurons and in turn influence sexual behavior [10,119].

2. Functional roles of both the main and the accessory olfactory systems in pheromonal processing

The vomeronasal system is known to be involved in several pheromone-induced physiological responses in mice, including puberty acceleration, estrus induction, and pregnancy block—confirming the traditional view of the vomeronasal pathway. In the case of pregnancy block (Bruce effect) the pregnancy of recently mated females is disrupted if these females are exposed to the urine of an unfamiliar male [12,15,18]. This effect is based