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Neural mechanisms of individual and sexual recognition in Syrian hamsters (*Mesocricetus auratus*)

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Abstract

Recognizing the individual and sexual identities of conspecifics is critical for adaptive social behavior and, in most mammals this information is communicated primarily by chemosensory cues. Due to its heavy reliance on odor cues, we have used the Syrian hamster as our model species for investigating the neural regulation of social recognition. Using lesion, electrophysiological and immunocytochemical techniques, separate neural pathways underlying recognition of individual odors and guidance of sex-typical responses to opposite-sex odors have been identified in both male and female hamsters. Specifically, we have found that recognition of individual odor identity requires olfactory bulb connections to entorhinal cortex (ENT) rather than other chemoreceptive brain regions. This kind of social memory does not appear to require the hippocampus and may, instead, depend on ENT connections with piriform cortex. In contrast, sexual recognition, through either differential investigation or scent marking toward opposite-sex odors, depends on both olfactory and vomeronasal system input to the corticomedial amygdala. Preference for investigating opposite-sex odors requires primarily olfactory input to the medial amygdala (ME) whereas appropriately targeted scent marking responses require vomeronasal input to ME as well as to other structures. Within the ME, the anterior section (MEa) appears important for evaluating or classifying social odors whereas the posterodorsal region (MEpd) may be more involved in generating approach to social odors. Evidence is presented that analysis of social odors may initially be done in MEa and then communicated to MEpd, perhaps through micro-circuits that separately process male and female odors.

Keywords

Olfaction; Scent marking; Attraction; Odor; Pheromone

Chemical signals are a prominent and often critical means of intra-specific communication for most mammalian species [8]. As in all communicative systems, the extraction of information from within these signals allows animals to adaptively regulate their mating and territorial interactions [10]. The kind of information that scents contain varies across species as do the specific behavioral reactions to them, but it is clear that most well-studied species display the ability to recognize the sexual, kinship and individual identities of conspecifics via odors and modify their behaviors accordingly [8,37,64]. As the social behavior of most mammals, is predicated on recognition and interpretation of odors, a more complete understanding of the biological basis of social behavior requires a thorough understanding of how and where social odors are processed in the nervous system.

To this end, our research program has focused on defining and characterizing the neural circuits underlying individual and sexual odor recognition in our model organism, the Syrian (golden)

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hamster. The hamster is an ideal model species in which to define the neurobiology of social odor recognition as the sociosexual behavior of golden hamsters is mediated almost exclusively by signals processed in the main and/or accessory olfactory system [37]. For example, copulatory behavior and offensive aggression in male hamsters are completely and permanently eliminated by removing the olfactory bulbs [69,71]. This dependence on chemosensory cues has made the study of neural and behavioral regulation of social behavior much more tractable than if these behaviors depended heavily on the integration of several sensory systems. Moreover, the chemosensory systems underlying hamster social behavior are also anatomically simpler and have more direct connections to areas involved in motivational processes than do other sensory systems [12]. These advances in the neurobiology of social behavior have been paralleled by the substantial accumulation of knowledge concerning the production, identity, deposition and behavioral significance of social odors in this species [37,40]. Importantly, hamster social behavior, and especially copulatory behavior, is also tightly regulated by sex-steroid hormones [89,92,98], allowing us to integrate the study of social recognition with neural mechanisms underlying steroid-sensitive changes in social motivation.

1. Chemosensory circuits

Any consideration of the circuitry underlying social recognition must begin with the neural architecture of chemosensory processing. In hamsters and in other macrosmatic species, the basic anatomy of odor-processing circuits is well-defined and is reviewed in detail elsewhere [23,96]. Although other chemosensory systems may, in theory, process social odors [103], the majority of research has implicated the main olfactory system (MOS) and the accessory or vomeronasal system (AOS) in the regulation of social behavior [66]. These two systems appear to process different aspects of the stimulus with the AOS often characterized as detecting non-volatile odor stimuli and the MOS detecting primarily volatile chemicals [25]. Mirroring this possible division of function, these systems are largely separate prior to reaching the amygdala, having both separate sensory neuron populations (main olfactory epithelium (MOE), vomeronasal organ (VNO)) in the nasal cavity and segregated representations in the olfactory bulbs (main olfactory bulbs (MOBs) and accessory olfactory bulbs (AOBs)). For both systems, chemosensory receptor neurons project onto the dendrites of mitral/tufted cells in the olfactory bulbs, although with significant differences in distribution and patterning [25].

From the MOB, these projection neurons course mainly through the lateral olfactory tract (LOT) to the anterior olfactory nucleus or primary olfactory cortex [26], piriform cortex, olfactory tubercle, anterior (ACo) and posterolateral cortical amygdala (PLCo), a small region in the anterior medial amygdala (MEa) and the entorhinal cortex (ENT) [12]. The piriform cortex (PIR), the largest area and the one most extensively innervated by the OB, is heavily interconnected with other olfactory structures and provides the majority of olfactory input to the orbitofrontal cortex (OFC) both directly and indirectly via the mediodorsal thalamus [24]. PIR also has extensive bi-directional connections with ENT, which, in turn, provides the majority of cortical connections with the hippocampus (HIPP) [104].

In contrast, the AOB has a much more restricted projection zone; mitral cells from AOB travel in a segregated bundle adjacent to LOT and synapse onto neurons in the medial (ME) and posteromedial cortical amygdala (PMCo) [25]. These structures, in turn, connect with each other, the bed nucleus of the stria terminalis (BNST) and several basal diencephalic regions including the medial preoptic/anterior hypothalamus (MPOA-AH), ventromedial (VMH) and ventral premammillary (VPM) hypothalamic nuclei [11,50,51].

2. Individual recognition

The ability to recognize individual conspecifics using odors appears across mammalian species [26] and is critical for regulating pair-bonding, maternal behavior, aggression and adaptive copulatory behavior [9,31,49,53,77,79,87]. To recognize and discriminate between individuals on the basis of their odors requires, at minimum, the ability to determine whether a new odor percept matches (familiarity) or does not match (novelty) a previously encountered odor. Consequently, this general ability can be used by hamsters to recognize and discriminate between individual conspecifics across several functional domains and using different techniques. Here we focus on neural mechanisms underlying the habituation/discrimination process as well as learning-related modifications to copulatory behavior (Coolidge effect) in hamsters.

2.1. Habituation/discrimination

Habituation paradigms have been used to investigate the kinds of information available in social odors in several species [26,29,41,42,76,95]. During these tests, decrements in odor investigation are observed following repeated presentation of a particular odor from one individual. On a subsequent test trial, the same type of odor from a novel individual is presented either alone or opposed to the now-familiar odor. Increased or preferred sniffing of the novel odor is taken as a reflection of recognition of the familiar one. Hamsters demonstrate recognition of social odors over delays of several seconds to several weeks using different kinds of conspecific odors [39].

What neural structures are involved in habituation to, and discrimination of individual odors? At the peripheral level, female hamsters discriminate between flank gland or urine odors from different males following removal of their VNO even though overall levels of investigation are reduced [84]. This suggests that discrimination of individual odors by females depends on the integrity of the olfactory, rather than vomeronasal system. However, there appears to be a sex difference in how individual odors are processed by the chemosensory systems [44]. VNO removal in male hamsters impairs discrimination of individual odors but this depends on the type of odor used as well as by testing parameters. In contrast, individual discrimination by females is unimpaired by VNO lesions regardless of odor used or the specifics of behavioral testing.

More centrally, the ability to discriminate individual odors does not appear to require processing by anterior segments of the MOB projection zone (anterior olfactory nucleus, olfactory tubercle, anterior piriform cortex) as transections of LOT caudal to these structures eliminate discrimination without eliminating odor detection in female hamsters [85]. Individual odor discrimination also does not require secondary olfactory connections with OFC as lesions to this and other parts of frontal cortex do not degrade discrimination performance [78]. Similarly, lesions of ME, which receives direct and indirect MOB projections, do not impair individual odor discrimination in female hamsters [83]. By process of elimination, the posterior PIR, cortical amygdala and/or ENT must be the substrates supporting individual recognition. Although the contribution of PIR and cortical amygdala to this process is currently undefined, lesions of ENT in female hamsters do eliminate their ability to discriminate between individual male odors [86]. This effect is not due to disconnection of cortical inputs to HIPP as fornix lesions that disrupt HIPP function neither impair individual odor discrimination in females [86] nor do selective HIPP lesions impair discrimination of female odors by male hamsters [80].

Based on the elimination of individual discrimination by ENT lesions, we predicted that ENT neurons would show cellular correlates of habituation and discrimination of individual odors. Consequently, we recorded from ENT neurons from male hamsters as they investigated volatile

odorants from different female's vaginal secretions [77]. We found that many neurons encode differences between female's odors with many discriminating between odors from different individual females but not between different odor samples from the same female. Other neurons discriminate between odor samples from one female and generalize across collections from other females. This kind of cellular discrimination is observed in altered neural activity during investigation of previously presented odors as well as in response to novel female odors. Consequently, ENT neurons of male hamsters do encode information that is critical for the identification and recognition of individual females by odor cues.

Based both on lesion and physiological data, it appears that MOS input to the ENT, either directly from MOB or from posterior PIR [102] is a critical neural pathway for the ability to discriminate novel from familiar social odors. Interestingly, no neural manipulations alter the ability of hamsters to habituate to repeated presentations of odors, indicating that different neural substrates are responsible for recognition of familiarity and novelty.

2.2. Coolidge effect

Individual discrimination occurs within specific behavioral contexts and so we would expect that manipulations that alter habituation/discrimination performance would also alter individual recognition in more naturalistic contexts. An example of a more naturalistic form of social memory is the bias of male animals to mate preferentially with unfamiliar females, a phenomenon known as the Coolidge effect [14]. Specifically, this phenomenon is one in which males show renewed sexual interest in a novel female following copulation to satiety with another female. This recognition of familiar females requires the males to form memories of past mating partners and compare these memories to current stimuli from a potential mate. In hamsters, this form of recognition depends on the ability to recognize conspecifics using chemosensory cues processed through the MOS, but not AOS [45]. Following evidence that ENT is critical for individual odor discrimination [86], we tested whether olfactory input to ENT is also required for the Coolidge effect in male hamsters [80]. After excitotoxic lesions to ENT or HIPPO, male hamsters were allowed to copulate to satiety with a female conspecific and were then presented with two anesthetized females, the familiar mate and an unfamiliar female that copulated with another male. Males with HIPPO lesions, like sham animals, preferentially investigate the novel female, indicating intact recognition of individual identity. However, ENT-lesioned males spend equal amount of time investigating novel and familiar females indicating failure to behaviorally discriminate between familiar and novel females. Based on similarities in copulatory behavior between groups prior to testing, this deficit is not likely attributable to abnormal encoding of copulatory stimuli.

Precisely how ENT interacts with neural circuits underlying sexual behavior and attraction is not known, but ENT does have reciprocal connections with PMCo [48], a structure that we have shown regulates sexual satiety in male hamsters [62]. It is, therefore, possible that interaction between mnemonic processing within ENT and satiety information from PMCo may be required to suppress copulation with familiar females.

More globally, these results support the idea that both the Coolidge effect and habituation/discrimination task share the same kind of general familiarity/novelty detection process that underlies widely used visual object and odor recognition tasks [6,15,72,79]. For example, lesions that include ENT impair formal tests of recognition memory using non-social odors or objects [68,75] and neurons in this region encode the familiarity and novelty of objects [7]. Indeed, the habituation/discrimination procedure accesses a general olfactory recognition process because hamsters discriminate between individual odors of other species [46] and complex, non-social, odors [59].

3. Sexual odor recognition

Sexual odor recognition in hamsters can be inferred by observation of chemosensory investigation of conspecifics or their odors and also by observing differential scent marking responses toward male and female odors. Not surprisingly, both male and female hamsters spend much more time investigating the anogenital, head and flank areas of opposite-sex individuals as well as isolated odors from these areas [36,54]. In addition, both male and female hamsters show more flank marking toward same-sex odors, supporting the proposed competitive signaling function of this behavior [32,35]. In contrast, female hamsters show considerably more vaginal marking, a proceptive or sexually-solicitation behavior in response to male odors than to female odors [35,82]. We outline what is currently known about the neural regulation of sex odor recognition (in both sexes) via differential flank and vaginal marking as well as by investigatory preferences.

3.1. Flank marking

Both male and female hamsters flank mark by rubbing sebaceous scent glands located on their dorsal flank region onto vertical surfaces [32,35]. Flank marking occurs primarily in response to odors of same-sex conspecifics and after the establishment of dominant-subordinate relationships [32,35]. Based on these characteristics, this behavior likely functions as an advertisement of competitive ability and territorial status in this species [1,33,87].

Flank marking has been extensively studied at the neural level following the discovery that the release of arginine-vasopressin (AVP) within the medial preoptic area-anterior hypothalamus (MPOA-AH) is critical for the behavior [1]. Injections of AVP into the MPOA-AH stimulate high levels of flank marking [18] and both AVP-induced marking and odor-induced marking is blocked by injections of AVP V1a receptor antagonists into the MPOA-AH [2]. These manipulations do alter marking, irrespective of social status, but do not have lasting effects on dominance interactions [19]. This pattern of results suggests that AVP within the MPOA-AH primarily regulates the output of scent marking behavior rather than the evaluation of social signals *per se*.

What then are the neural systems that mediate perception and evaluation of social stimuli required for regulating flank marking? The evidence from both male and female hamsters suggests that odor-elicited flank marking requires input from both the main olfactory and vomeronasal systems. Peripheral lesions of the MOS, via intra-nasal zinc sulfate infusion, reduces flank marking in male and female hamsters when investigating areas containing both male and female odors [38,43]. Although VNO removal does not reduce flank marking in this context, removing the VNO in females eliminates the high rate of marking to female odors when tested separately; the modest response to male odors remains unaffected [84]. This suggests that maintaining flank marking requires MOS input, but also that the AOS transmits information about same-sex odors to neural structures that generate flank marking. Indeed, combined damage to both systems, by removing MOB/AOB [47] or LOT transection [57, 85], eliminates flank marking completely.

Since flank marking is regulated by MOS processing, we might expect that areas posterior to LOT cuts (such as posterior PIR, ME and ENT) would be important for flank marking. In fact, flank marking is critically dependent on chemosensory input to ME as large lesions to this area virtually eliminate flank marking behavior in females [83]. Similarly, smaller lesions of anterior (MEa) or posterodorsal (MEpd) medial amygdala also disrupt male hamster's flank marking responses toward male odors (unpublished observations). As MEa and MEpd have substantial input to MPOA-AH and other hypothalamic areas that are known to be responsible for the control flank marking [1], it is likely that odor modulation of flank marking is mediated by ME efferents to these diencephalic targets. Other targets of chemosensory input appear to

have either unclear or lesser involvement in flank marking. For example, severing PIR connections to OFC does not alter flank marking behavior [78]. High levels of flank marking toward same-sex odors by females are impaired after ENT lesions, but not by subcortical disconnection of HIP [86]. However, these ENT lesions also damaged PMCo and so we cannot separate the role of MOB input to ENT from that of AOB input to PMCo in the regulation of flank marking.

3.2. Vaginal marking

Vaginal marking is a female proceptive behavior that serves to synchronize reproduction in hamsters by advertising impending receptivity and by guiding males to the female's burrow [30]. As such, this behavior is greatly increased by specific male odors, peaks on the day before estrus, and deposits a secretion that both attracts and sexual excites male hamsters that investigate them [34-36,81,82]. Vaginal marking itself consists of at least two basic behavioral components. The first is the observable stereotyped lowering and dragging of the anogenital region on the substrate [4]. The motoric mechanisms of this behavior are unknown but do not require peripheral sensory feedback as it survives anesthesia of the perineum (unpublished observations). The second component of vaginal marking is the actual extrusion of vaginal secretion, presumably by vaginal smooth muscle contraction, from storage pockets just within the vaginal opening during the anogenital drag. This behavioral component also does not require sensory feedback as perineal anesthesia does not reduce the number of observable marks on the substrate (unpublished observations). In order to trace the motor control of the vaginal smooth muscle, we injected a retrograde, trans-synaptic tracer (pseudorabies virus) into the vaginal wall and observed labeling of the ventrolateral medulla, periaqueductal grey, MPOA-AH and VMH as well as the MEpd and BNST [4]. Several of these regions have been implicated in the sensory and/or hormonal control of vaginal marking (see below).

Although the motor control of vaginal marking remains relatively obscure, the neural circuitry underlying its chemosensory and hormonal regulation has been better characterized. As the behavior is regulated by odors it is not surprising that vaginal marking in response to male odors is greatly reduced by OB removal [47]. More selective damage to MOS, via peripheral ZnSO₄ lesions, produces decrements in vaginal marking but less than those following OB removal [38]. Although overall levels of vaginal marking to an arena containing male and female odor is not impaired after VNO removal [38], destroying the VNO eliminates differential marking to male odors [84]. That is, following VNO removal, levels of vaginal marking are similar between male and female odor conditions. Similar effects are found after LOT cuts but, surprisingly, drastic reductions in overall vaginal marking levels are not observed [85]. This may indicate involvement of more medially projecting OB fibers, perhaps to structures like the olfactory tubercle.

More centrally, MOS structures such as OFC or ENT are not critical for preferential vaginal marking toward male odors as removal of these structures do not impair vaginal marking [78,86]. In contrast, vaginal marking is reduced by large ME lesions. Interestingly, animals with these lesions still vaginal mark more toward male odors than to female odors [83]. A similar effect was observed after unintentional damage to the ventrolateral septum following lesions of the fimbria/fornix [78,86]. Consequently, AOS and MOS input to ME might regulate overall levels of vaginal marking but not the bias in marking toward male odors, perhaps through connections with the septum. Other connections such as AOB inputs to BNST or PMCo may regulate differential vaginal marking toward male odors.

As ME has substantial input to MPOA-AH and other hypothalamic areas that, through steroid implant studies, are known to mediate hormonal control of vaginal marking [58,100], it is likely that odor modulation of scent marking is mediated by ME efferents to these areas. The cell groups critical for marking within these target areas are unknown, but release of the

neuropeptide oxytocin (OT) within MPOA-AH may regulate marking in response to odors. Specifically, injections of OT receptor antagonists within MPOA-AH of proestrus females block increased vaginal marking to male odors without changing marking responses to clean bedding or female odors [63]. We are currently determining if these results are due to changes in odor processing as well as attempting to define which MPOA-AH cells contain OT-receptors.

3.3. Investigatory preference

Sexual recognition, as indexed by differential investigation of opposite-sex odors in a Y-maze or similar testing environment is, unsurprisingly, dependent on OB processing in both male and female hamsters. Removing OB or cutting the majority of its efferent connections eliminates preferences for investigating opposite-sex odors and conspecifics as well as abolishing other social behaviors [13,70].

3.3.1. Peripheral lesions—Which system, MOS or AOS, is critical for attraction to, and preference for opposite-sex odors in hamsters? In males, removing the VNO or cutting the vomeronasal nerves (VN) does not reliably impair anogenital investigation (AGI) or attraction to vaginal secretions. For example, although VN cuts reduce investigation of anesthetized males scented with vaginal secretion [90], VNO removal does not effect AGI toward anesthetized female hamsters [74] or reduce investigation of vaginal secretion [99] nor do VN cuts influence the preference for investigating conspecific females or their vaginal secretions [70]. It does appear, however, that the chemoinvestigatory behavior of sexually inexperienced males is more vulnerable to AOS damage than if the animals had copulated prior to surgery [65]. Reducing MOS function, via nasal ZnSO₄ irrigation, decreases investigation of isolated vaginal secretion [90] but may or may not reduce AGI of anesthetized female surrogates [74, 90]. In female hamsters, removing the VNO has no effect on their preferential investigation of male volatile odorants compared to those from another female, but did reduce overall investigation of male odor when direct contact was allowed [84]. It appears that for both sexes, preferential attraction toward opposite-sex odors at a distance is mediated by the MOS but that the AOS may play a role in chemoinvestigation when direct contact with odorants occurs.

3.3.2. Central lesions—LOT transections at the level of anterior PIR in both male and female hamsters eliminate preference for opposite-sex odors and greatly reduce interest in them without eliminating odor detection [57,85]. This demonstrates that the AON and anterior PIR are not critical for attraction to, or preference for, social odors. Of course, this deficit is likely not specific to social odors as LOT cuts may impair discrimination of other, non-social odors [97]. These results do, however, indicate that chemosensory structures caudal to LOT cuts, such as posterior PIR, ME, cortical amygdala nuclei and/or ENT, are critical for hamster sex odor preferences.

The effects of lesions to posterior PIR have not been reported, but its connections with OFC may mediate opposite-sex attraction in male, but not female, hamsters [78,94]. Although this suggests a sex difference in neural control of odor preference, the behavioral tests used in these two studies are sufficiently different to warrant more detailed investigation before a definitive conclusion can be reached. Indeed, using the immediate-early gene Fos as a marker for neuronal activation, no sex differences or increases above baseline were detected in response to vaginal secretion in MOS structures [17,20] of hamsters.

The role of ENT in preference seems to be limited to learned discriminations between individuals (see above) as damage to ENT does not alter a female's preference for male odors [86]. Damage to a nearby structure, the PMCo, also has no effect on social odor attraction and

preference in male hamsters, even though it alters patterns of chemoinvestigation of females as well as sexual satiety in these animals [62].

3.3.3. Medial amygdala—The one brain region that has shown to be critical for preference and attraction to opposite-sex odors is the extended ME, including the ME proper and posterior BNST. Large lesions of the ME eliminate differential investigation of opposite-sex odors by female [83] and male hamsters [55]. Similarly, damage to the posterior BNST reduces investigation of female odors by male hamsters [91] and eliminates preference for female odors over male odors [5].

The ME is a heterogeneous structure characterized by both heavy chemosensory input and substantial steroid hormone sensitivity. Detailed connectional analysis of the ME has revealed that the region that receives the majority of chemosensory information is separate from the area that contains the greatest concentration of steroid receptors [73,111]. This division between steroid-sensitive and chemosensory sub-regions of the ME is maintained within the BNST and basal diencephalic structures to which it is connected. Specifically, the ME can be divided into the chemoreceptive zone which includes the anterior medial amygdala (MEa) and the hormone-sensitive posterodorsal medial amygdala (MEpd). Likewise, the BNST can be divided into a chemosensory region, the posterior intermediate BNST (BNSTpi) and the hormonal region, the posteromedial BNST (BNSTpm). Similar distinctions exist in the VMH, VPM and MPOA-AH. Nevertheless, within each anatomical element (ME, BNST, diencephalic areas), the steroid-sensitive and chemosensory sub-regions are interconnected with one another [11,22]. This provides a locus whereby steroid hormones and chemosensory systems could interact. For example, neurons in the MEa are bilaterally connected mostly to the BNSTpi and the MEpd neurons are bilaterally connected mostly with the BNSTpm. Interactions between these hormonal and chemosensory regions are likely mediated by direct, bilateral connections between the MEa and the MEpd and between the BNSTpi and the BNSTpm. This distinction between hormonal and chemosensory aspects of the ME and the BNST is not absolute, as the MEa does contain sex-steroid receptors [106,110] and the MEpd does receive main olfactory input from the ACo and other areas as well as limited direct and indirect (via PMCo) AOB input [50,51].

We know that the ME is critical for sexual odor preference but what role do these different sub-regions serve in sexual attraction and preference? Earlier evidence suggested that the effects of hormones on investigation of social odors are mediated by the MEpd and regions connected with it. For example, testosterone or estradiol implants into the MEpd or the BNST, but not the MEa, of male hamsters alleviate deficits in copulatory behavior and anogenital investigation induced by gonadectomy [105,109]. Moreover, using unilateral placements of testosterone in the MEpd or the BNST ipsi-lateral to an ablated olfactory bulb of castrated hamsters, Wood and co-workers demonstrated that hormonal and chemosensory signals interact at the level of the MEpd and the BNST in the regulation of male copulatory behavior and chemoinvestigation [107,108].

More recently, we have shown functional differences between the MEa and the MEpd control of social odor investigation. Selective lesions of either the MEa or the MEpd in male hamsters eliminates preference, as tested in a Y-maze, for volatile female odors compared to male odors [59]. However, the deficits are qualitatively different: the MEa lesions cause a dramatic increase in investigation of both male and female odors while MEpd damage reduces investigation of female odors. This pattern is maintained in attraction tests where the choice was between a male or female odor and a clean bedding odor. That is, MEa-lesioned males show greatly increased investigation of female odors compared to shams and also an attraction to male odors not normally seen in male hamsters. In contrast, males with MEpd lesions show no attraction to either female or male odors. These deficits are not due to an inability to

discriminate between odors as both groups of lesioned males distinguish between male and female odors and also between two biologically neutral odors in habituation-discrimination tasks. Moreover, the heightened investigation seen in MEa-lesioned animals is specific to social odors as their overall level of investigation of neutral odors is similar to shams. This pattern of results suggests that the MEpd regulates motivation to approach a sexual stimulus, possibly via a hormone-sensitive mechanism, whereas the MEa provides an evaluative mechanism that directs this motivation toward an appropriate goal.

Support for the idea that MEa-mediated evaluation precedes and informs MEpd processing comes from the observation that lesions of MeA reduce c-fos expression in MEpd and other areas (BNST, MPOA-AH, PMCo) in response to male or female social odors [60]. Importantly, comparable MEpd lesions do not reduce social odor-induced c-fos expression in MEa or connected structures. While suggestive, there are numerous examples in which c-fos expression does not faithfully represent neural activity [28] and so finding reduced levels of c-fos expression does not mean that neurons in that particular area are not active and processing information [52,88]. Conversely, neurons in limbic areas often show behaviorally specific inhibitory responses or temporal changes to stimuli that cannot be detected by c-fos expression [93].

Consequently, to delineate the information carried by MEa and MEpd neurons, we recorded simultaneously from multiple single MEa and MEpd neurons in male hamsters as they investigated male, female or neutral odors [56]. Approximately half of neurons recorded in MEa ($n = 78$) and MEpd ($n = 82$) change their firing rates to odors. A quarter of neurons alter their activity specifically to male or female odor with only a very small number (<5%) responding preferentially to neutral odors (artificial strawberry or chocolate). Importantly, virtually no neurons have dual representation of social odors; they either respond to male or to female odor, but not to both. This suggests that the discrimination of male and female odors involves separate micro-circuits rather than by a population of neurons responding at differing rates to both male and female odors. We also observed substantial correlated firing between MEa and MEpd neurons during investigation of social odors. Further analysis of this functional connectivity will allow us to determine the flow of information within this circuit and where chemosensory and hormonal inputs converge.

Based on this data, our working hypothesis is that MOS and AOS information important for sexual recognition converges primarily in the MEa and it is there that male and female odors are differentiated. This sexual identity information is then likely sent to the MEpd (as well as other regions) which, in turn, provides hormonally mediated, motivational drive back to the MEa as well as other areas. Unfortunately, the flow of information is very poorly defined at present and requires additional electro-physiological and disconnection experiments to disentangle these interactions. Nevertheless, at minimum, processing by the MEa and the MEpd interacts with that in the BNST and hypothalamic structures, such as the VMH and MPOA-AH [21,111] to generate appropriate investigation of social odors.

4. Conclusions and future directions

Several conclusions are warranted by the existing data and lead naturally to several future directions. First, it is clear that the neural mechanisms controlling recognition of individual and sexual identity via odor cues are different and require processing by different anatomical structures. Individual odor recognition, or at least the aspects dependent on novelty detection, depends on the integrity of direct and/or indirect olfactory projections to the ENT. Although the extensive connections between the ENT and the HIPPO are not critical to this process, we do not know what other structures are involved. However, based on the neural architecture of PIR and on recent advances in understanding this structure's role in odor memory [3,24,27,

101], it is likely that ENT instantiates social odor memory through its extensive connections with PIR.

Second, even a seemingly unitary phenomenon like “sexual recognition” is not unitary in its underlying neural structure. For example, high levels of flank marking by females toward same-sex odors are attenuated by VNO removal, but female investigatory preference for male odors survives this manipulation [84]. Moreover, large ME lesions in females eliminate attraction to male odors, but these females still vaginal mark (albeit at a reduced rate) more to male odors than to female odors [83]. So, while sexual recognition via investigatory behavior clearly requires olfactory input to ME, vaginal marking to male odors is mediated by OB projections to both ME and to PMCo. Perhaps this reflects a general feature of sexual recognition where information is distributed early in sensory processing to parallel and separate effector circuits.

Third, sex differences in odor preferences are apparent behaviorally but little is currently known about the neurobiology underlying these differences. Not surprisingly, several brain regions are critical for sexual and individual recognition in both male and female hamsters (e.g. ENT, ME). However, unlike male hamsters [89,92], females do not require high levels of circulating sex steroids to show an investigatory preference for opposite-sex odors. That is, females show preference for male odors across all days of the estrous cycle and even following ovariectomy [16]. As such, the neural mechanisms regulating chemoinvestigatory preference in females may be under less hormonal control than those of male hamsters.

Lastly, the ability of hamsters to recognize familiar individuals highlights the role that experience plays in the lives of these animals. However, comparatively little attention has been paid to how hamsters develop preferences or responses to social odors. To address this issue we tested whether female hamsters require exposure to male odors during development in order for them to preferentially investigate, and vaginal mark toward, male odors [61]. Surprisingly, even after removing male siblings from the litter at 3–5 days of age, adult females still prefer male odors over female odors. However, growing up in an all-female litter prevents differential vaginal marking toward volatile male odors. This effect is not observed if females are allowed to contact male or female bedding during testing. The pattern of results suggests that, like chemoinvestigation in female mice [67], high rates of vaginal marking to volatile male odors are conditioned through previous association with non-volatile components of these odors. It also suggests that sexual attraction to odors requires either perinatal/intra-uterine experience with male odors or that it is largely experience-independent.

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Abbreviations

ACo, anterior cortical amygdala
 AGI, ano-genital investigation
 AOB, accessory olfactory bulb
 AOS, accessory olfactory system
 AVP, arginine vasopressin
 BNST, bed nucleus of the stria terminalis
 BNSTpi, posterior intermediate bed nucleus of the stria terminalis
 BNSTpm, posterior medial bed nucleus of the stria terminalis
 ENT, entorhinal cortex
 HIPPO, hippocampus
 ME, medial amygdala

MEa, anterior medial amygdala
 MEpd, posterodorsal medial amygdala
 MOB, main olfactory bulb
 MOE, main olfactory epithelium
 MOS, main olfactory system
 MPOA-AH, medial preoptic area-anterior hypothalamus
 LOT, lateral olfactory tract
 OB, olfactory bulb
 OFC, orbitofrontal cortex
 OT, oxytocin
 PIR, piriform cortex
 PLCo, posterolateral cortical amygdala
 PMCo, posteromedial cortical amygdala
 ST, stria terminalis
 VMH, ventromedial hypothalamus
 VN, vomeronasal nerve
 VNO, vomeronasal organ
 VPM, ventral premammillary hypothalamus
 ZnSO₄, zinc sulfate

References

1. Albers, HE.; Huhman, KL.; Meisel, RL. Hormonal basis of social conflict and communication. In: Pfaff, DW.; Arnold, A.; Etgen, A.; Fahrbach, S.; Rubin, R., editors. *Hormones, brain and behavior*. Vol. 1. Academic Press; New York: 2002. p. 393-433.
2. Albers HE, Pollock J, Simmons WH, Ferris CF. A V1-like receptor mediates vasopressin-induced flank marking behavior in hamster hypothalamus. *J Neurosci* 1986;6:2085–9. [PubMed: 3016215]
3. Barkai E, Saar D. Cellular correlates of olfactory learning in the rat piriform cortex. *Rev Neurosci* 2001;12:111–20. [PubMed: 11392453]
4. Been, L.; Petrulis, A. The neurobiology of sexual solicitation: vaginal marking in female Syrian hamsters (*Mesocricetus auratus*). In: Hurst, J.; Beynon, R.J.; Roberts, S.C.; Wyatt, T., editors. *Chemical signals in vertebrates XI*. Springer; New York: 2007. p. 231-9.
5. Been L, Petrulis A. The role of the posterior bed nucleus of the stria terminalis on sexual odor preference in male Syrian hamsters. *Society for Behavioral Neuroendocrinology XI*. 2008
6. Brown MW, Aggleton JP. Recognition memory: what are the roles of the perirhinal cortex and hippocampus? *Nat Rev Neurosci* 2001;2:51–61. [PubMed: 11253359]
7. Brown MW, Bashir ZI. Evidence concerning how neurons of the perirhinal cortex may effect familiarity discrimination. *Philos Trans R Soc Lond B Biol Sci* 2002;357:1083–95. [PubMed: 12217176]
8. Brown, R.E.; Macdonald, D.W., editors. *Social odors in mammals*. Vol. 1–2. Clarendon Press; Oxford: 1985.
9. Carr WJ, Hirsch JT, Balazs JM. Responses of male rats to odors from familiar vs novel females. *Behav Neural Biol* 1980;29:331–7. [PubMed: 7417195]
10. Colgan, P.W. *Comparative social recognition*. Wiley & Sons; New York: 1983.
11. Coolen LM, Wood RI. Bidirectional connections of the medial amygdaloid nucleus in the Syrian hamster brain: simultaneous anterograde and retrograde tract tracing. *J Comp Neurol* 1998;399:189–209. [PubMed: 9721903]
12. Davis BJ, Macrides F, Youngs WM, Schneider SP, Rosene DL. Efferents and centrifugal afferents of the main and accessory olfactory bulbs in the hamster. *Brain Res Bull* 1978;3:59–72. [PubMed: 75756]
13. Devor M. Components of mating dissociated by lateral olfactory tract transection in male hamsters. *Brain Res* 1973;64:437–41. [PubMed: 4781352]
14. Dewsbury DA. Effects of novelty on copulatory behavior: the Coolidge effect and related phenomenon. *Psychol Bull* 1981;89:464–82.

15. Eichenbaum H, Otto T, Cohen NJ. Two functional components of the hippocampal memory system. *Behav Brain Sci* 1994;17:449–518.
16. Eidson LN, Maras PM, Epperson E, Petrulis A. Female hamster preference for odors is not regulated by circulating gonadal hormones. *Physiol Behav* 2007;91:134–41. [PubMed: 17374544]
17. Fernandez-Fewell GD, Meredith M. C-fos expression in vomeronasal pathways of mated or pheromone-stimulated male golden hamsters: contributions from vomeronasal sensory input and expression related to mating performance. *J Neurosci* 1994;14:3643–54. [PubMed: 8207479]
18. Ferris CF, Albers HE, Wesolowski SM, Goldman BD, Luman SE. Vasopressin injected into the hypothalamus triggers a stereotypic behavior in golden hamsters. *Science* 1984;224:521–3. [PubMed: 6538700]
19. Ferris CF, Meenan DM, Axelson JF, Albers HE. A vasopressin antagonist can reverse dominant/subordinate behavior in hamsters. *Physiol Behav* 1986;38:135–8. [PubMed: 3786493]
20. Fiber JM, Swann JM. Testosterone differentially influences sex-specific pheromone-stimulated Fos expression in limbic regions of Syrian hamsters. *Horm Behav* 1996;30:455–73. [PubMed: 9047271]
21. Floody OR. Time course of VMN lesion effects on lordosis and proceptive behavior in female hamsters. *Horm Behav* 2002;41:366–76. [PubMed: 12018932]
22. Gomez DM, Newman SW. Differential projections of the anterior and posterior regions of the medial amygdaloid nucleus in the syrian hamster. *J Comp Neurol* 1992;317:195–218. [PubMed: 1573064]
23. Haberly LB. Neuronal circuitry in olfactory cortex: anatomy and functional implications. *Chem Senses* 1985;10:219–38.
24. Haberly LB. Parallel-distributed processing in olfactory cortex: new insights from morphological and physiological analysis of neuronal circuitry. *Chem Senses* 2001;26:551–76. [PubMed: 11418502]
25. Halpern M, Martinez-Marcos A. Structure and function of the vomeronasal system: an update. *Prog Neurobiol* 2003;70:245–318. [PubMed: 12951145]
26. Halpin ZT. Individual odors among mammals: origins and functions. *Adv Study Behav* 1986;16:39–70.
27. Hasselmo ME, McClelland JL. Neural models of memory. *Curr Opin Neurobiol* 1999;9:184–8. [PubMed: 10322183]
28. Herdegen T, Leah JD. Inducible and constitutive transcription factors in the mammalian nervous system: control of gene expression by Jun, Fos and Krox, and CREB/ATF proteins. *Brain Res Brain Res Rev* 1998;28:370–490. [PubMed: 9858769]
29. Heth G, Todrank J, Johnston RE. Similarity in the qualities of individual odors among kin and species in Turkish (*Mesocricetus brandti*) and golden (*Mesocricetus auratus*) hamsters. *J Comp Psychol* 1999;113:321–6. [PubMed: 10497798]
30. Huck UW, Lisk RD, Gore AC. Scent marking and mate choice in the golden hamster. *Physiol Behav* 1985;35:389–93. [PubMed: 4070412]
31. Insel TR, Young LJ. The neurobiology of attachment. *Nat Rev Neurosci* 2001;2:129–36. [PubMed: 11252992]
32. Johnston RE. Scent marking by male golden hamsters (*Mesocricetus auratus*). I. Effects of odors and social encounters. *Z Tierpsychol* 1975;37:75–98. [PubMed: 1172341]
33. Johnston RE. Scent marking by male Golden Hamsters (*Mesocricetus auratus*). III. Behavior in a seminatural environment. *Z Tierpsychol* 1975;37:213–21. [PubMed: 1170699]
34. Johnston RE. Sexual excitation function of hamster vaginal secretion. *Anim Learn Behav* 1975;3:161–6.
35. Johnston RE. The causation of two scent-marking behaviour patterns in female hamsters (*Mesocricetus auratus*). *Anim Behav* 1977;25:317–27. [PubMed: 560812]
36. Johnston RE. Olfactory preferences, scent marking, and “proceptivity” in female hamsters. *Horm Behav* 1979;13:21–39. [PubMed: 521019]
37. Johnston, RE. Chemical communication in golden hamsters: from behavior to molecules and neural mechanisms. In: Dewsbury, DA., editor. *Contemporary issues in comparative psychology*. Sinauer; Sunderland, MA: 1990. p. 381–412.
38. Johnston RE. Vomeronasal and/or olfactory mediation of ultrasonic calling and scent marking by female golden hamsters. *Physiol Behav* 1992;51:437–48. [PubMed: 1523219]

39. Johnston RE. Memory for individual scent in hamsters (*Mesocricetus auratus*) as assessed by habituation methods. *J Comp Psychol* 1993;107:201–7. [PubMed: 8370274]
40. Johnston RE. Pheromones, the vomeronasal system, and communication. From hormonal responses to individual recognition. *Ann N Y Acad Sci* 1998;855:333–48. [PubMed: 9929626]
41. Johnston RE, Chiang G, Tung C. The information in scent over-marks of golden hamsters. *Anim Behav* 1994;48:323–30.
42. Johnston RE, Derzie A, Chiang G, Jernigan P, Lee H-C. Individual scent signatures in golden hamsters: evidence for specialization of function. *Anim Behav* 1993;45:1061–70.
43. Johnston RE, Mueller UG. Olfactory but not vomeronasal mediation of scent marking by male golden hamsters. *Physiol Behav* 1990;48:701–6. [PubMed: 2082370]
44. Johnston RE, Peng M. The vomeronasal organ is involved in discrimination of individual odors by males but not by females in golden hamsters. *Physiol Behav* 2000;70:537–49. [PubMed: 11111009]
45. Johnston RE, Rasmussen K. Individual recognition of female hamsters by males: role of chemical cues and of the olfactory and vomeronasal systems. *Physiol Behav* 1984;33:95–104. [PubMed: 6505058]
46. Johnston RE, Robinson TA. Cross-species discrimination of individual odors by hamsters (Muridae: *Mesocricetus auratus*, *Phodopus campbelli*). *Ethology* 1993;94:317–25.
47. Kairys DJ, Magalhaes H, Floody OR. Olfactory bulbectomy depresses ultrasound production and scent marking by female hamsters. *Physiol Behav* 1980;25:143–6. [PubMed: 7413811]
48. Kemppainen S, Jolkkonen E, Pitkanen A. Projections from the posterior cortical nucleus of the amygdala to the hippocampal formation and parahippocampal region in rat. *Hippocampus* 2002;12:735–55. [PubMed: 12542226]
49. Kendrick KM, DaCosta APC, Broad KD, Ohkura S, Guevara R, Levy F, et al. Neural control of maternal behaviour and olfactory recognition of offspring. *Brain Res Bull* 1997;44:383–95. [PubMed: 9370203]
50. Kevetter GA, Winans SS. Connections of the corticomedial amygdala in the golden hamster. I. Efferents of the “vomeronasal amygdala”. *J Comp Neurol* 1981;197:81–98. [PubMed: 6164702]
51. Kevetter GA, Winans SS. Connections of the corticomedial amygdala in the golden hamster. II. Efferents of the “olfactory amygdala”. *J Comp Neurol* 1981;197:99–111. [PubMed: 6164703]
52. Kovacs KJ. c-Fos as a transcription factor: a stressful (re)view from a functional map. *Neurochem Int* 1998;33:287–97. [PubMed: 9840219]
53. Lai W-S, Johnston RE. Individual recognition after fighting by golden hamsters: a new method. *Physiol Behav* 2002;76:225–39. [PubMed: 12044595]
54. Landauer MR, Banks EM, Carter CS. Sexual and olfactory preferences of naive and experienced male hamsters. *Anim Behav* 1978;26:611–21.
55. Lehman MN, Winans SS, Powers JB. Medial nucleus of the amygdala mediates chemosensory control of male hamster sexual behavior. *Science* 1980;210:557–60. [PubMed: 7423209]
56. Lewis CM, Petrulis A. Neural encoding of social and non-social odors in the medial amygdala of male Syrian hamsters. *Society for Behavioral Neuroendocrinology XI*. 2008
57. Macrides F, Firl AC Jr, Schneider SP, Bartke A, Stein DG. Effects of one-stage or serial transections of the lateral olfactory tracts on behavior and plasma testosterone levels in male hamsters. *Brain Res* 1976;109:97–109. [PubMed: 1276912]
58. Malsbury CW, Kow L-M, Pfaff DW. Effects of medial hypothalamic lesions on the lordosis responses and other behaviors in female golden hamsters. *Physiol Behav* 1977;19:223–37. [PubMed: 607234]
59. Maras PM, Petrulis A. Chemosensory and steroid-responsive regions of the medial amygdala regulate distinct aspects of opposite-sex odor preference in male Syrian hamsters. *Eur J Neurosci* 2006;24:3541–52. [PubMed: 17229102]
60. Maras PM, Petrulis A. Functional interactions between sub-regions of the medial amygdala during the processing of sexual odors in male Syrian hamsters. *Society for Behavioral Neuroendocrinology XI*. 2008
61. Maras PM, Petrulis A. Olfactory experience and the development of odor preference and vaginal marking in female Syrian hamsters. *Physiol Behav* 2008;94:545–51. [PubMed: 18485425]

62. Maras PM, Petrulis A. The posteromedial cortical amygdala regulates copulatory behavior, but not sexual odor preference, in the male Syrian hamster (*Mesocricetus auratus*). *Neuroscience* 2008;156:425–35. [PubMed: 18762231]
63. Martinez L, Petrulis A, Albers HE. Oxytocin in the medial preoptic area/anterior hypothalamus regulates vaginal marking in female Syrian hamsters. *Society for Behavioral Neuroendocrinology* XI. 2008
64. Mateo JM, Johnston RE. Kin recognition and the 'armpit effect': evidence of self-referent phenotype matching. *Proc R Soc Lond Ser B-Biol Sci* 2000;267:695–700.
65. Meredith M. Vomeronasal organ removal before sexual experience impairs male hamster mating behavior. *Physiol Behav* 1986;36:737–43. [PubMed: 3714848]
66. Meredith M. Sensory processing in the main and accessory olfactory systems: comparisons and contrasts. *J Steroid Biochem Mol Biol* 1991;39:601–14. [PubMed: 1892791]
67. Moncho-Bogani J, Lanuza E, Hernandez A, Novejarque A, Martinez-Garcia F. Attractive properties of sexual pheromones in mice: innate or learned? *Physiol Behav* 2002;77:167–76. [PubMed: 12213516]
68. Mumby DG. Perspectives on object-recognition memory following hippocampal damage: lessons from studies in rats. *Behav Brain Res* 2001;127:159–81. [PubMed: 11718890]
69. Murphy MR. Olfactory stimulation and olfactory bulb removal: effects on territorial aggression in male syrian golden hamsters. *Brain Res* 1976;113:95–110. [PubMed: 986227]
70. Murphy MR. Sexual preferences of male hamsters: importance of preweaning and adult experience, vaginal secretion, and olfactory or vomeronasal sensation. *Behav Neural Biol* 1980;30:323–40. [PubMed: 7193452]
71. Murphy MR, Schneider GE. Olfactory bulb removal eliminates mating behavior in the male golden hamster. *Science* 1970;167:302–4. [PubMed: 5409714]
72. Murray EA, Richmond BJ. Role of perirhinal cortex in object perception, memory, and associations. *Curr Opin Neurobiol* 2001;11:188–93. [PubMed: 11301238]
73. Newman, SW. Pheromonal signals access the medial extended amygdala: one node in a proposed social behavior network. In: Pfaff, DW.; Arnold, A.; Etgen, A.; Fahrbach, S.; Rubin, R., editors. *Hormones, brain and behavior*. Vol. 1. Academic Press; New York: 2002. p. 17-32.
74. O'Connell RJ, Meredith M. Effects of volatile and nonvolatile chemical signals on male sex behaviors mediated by the main and accessory olfactory systems. *Behav Neurosci* 1984;98:1083–93. [PubMed: 6508913]
75. Otto T, Eichenbaum H. Complementary roles of the orbital prefrontal cortex and the perirhinal-entorhinal cortices in an odor-guided delayed-nonmatching-to-sample task. *Behav Neurosci* 1992;106:762–75. [PubMed: 1445656]
76. Penn D, Potts WK. Untrained mice discriminate MHC-determined odors. *Physiol Behav* 1998;64:235–43. [PubMed: 9748088]
77. Petrulis A, Alvarez P, Eichenbaum H. Neural correlates of social odor recognition and the representation of individual distinctive social odors within entorhinal cortex and ventral subiculum. *Neuroscience* 2005;130:259–74. [PubMed: 15561442]
78. Petrulis A, DeSouza I, Schiller M, Johnston RE. Role of frontal cortex in social odor discrimination and scent-marking in female golden hamsters (*Mesocricetus auratus*). *Behav Neurosci* 1998;112:199–212. [PubMed: 9517828]
79. Petrulis, A.; Eichenbaum, H. Olfactory memory. In: Doty, RL., editor. *Handbook of Olfaction and Gustation*. Marcel Dekker; New York: 2003. p. 409-38.
80. Petrulis A, Eichenbaum H. The perirhinal–entorhinal cortex, but not the hippocampus, is critical for expression of individual recognition in the context of the Coolidge effect. *Neuroscience* 2003;122:599–607. [PubMed: 14622903]
81. Petrulis A, Johnston RE. A reevaluation of dimethyl disulfide as a sex attractant in golden hamsters. *Physiol Behav* 1995;57:779–84. [PubMed: 7777617]
82. Petrulis A, Johnston RE. Causes of scent marking in female golden hamsters (*Mesocricetus auratus*): specific signals or classes of information? *J Comp Psychol* 1997;111:25–36. [PubMed: 9090136]

83. Petrulis A, Johnston RE. Lesions centered on the medial amygdala impair scent-marking and sex-odor recognition but spare discrimination of individual odors in female golden hamsters. *Behav Neurosci* 1999;113:345–57. [PubMed: 10357459]
84. Petrulis A, Peng M, Johnston RE. Effects of vomeronasal organ removal on individual odor discrimination, sex-odor preference, and scent marking by female hamsters. *Physiol Behav* 1999;66:73–83. [PubMed: 10222476]
85. Petrulis, A.; Peng, M.; Johnston, RE. Lateral olfactory tract transections impair discrimination of individual odors, sex-odor preferences, and scent marking by female hamsters (*Mesocricetus auratus*). In: Johnston, RE.; Muller-Schwarze, D.; Sorensen, P., editors. *Advances in chemical communication in vertebrates*. Plenum Press; New York: 1999. p. 549-62.
86. Petrulis A, Peng M, Johnston RE. The role of the hippocampal system in social odor discrimination and scent-marking in female golden hamsters (*Mesocricetus auratus*). *Behav Neurosci* 2000;114:184–95. [PubMed: 10718273]
87. Petrulis A, Weidner M, Johnston RE. Recognition of competitors by male golden hamsters. *Physiol Behav* 2004;81:629–38. [PubMed: 15178156]
88. Pfau JG, Heeb MM. Implications of immediate-early gene induction in the brain following sexual stimulation of female and male rodents. *Horm Behav* 1999;35:224–40. [PubMed: 10373335]
89. Powers JB, Bergondy ML. Androgenic regulation of chemoinvestigatory behaviors in male and female hamsters. *Horm Behav* 1983;17:28–44. [PubMed: 6862391]
90. Powers JB, Fields RB, Winans SS. Olfactory and vomeronasal system participation in male hamsters' attraction to female vaginal secretions. *Physiol Behav* 1979;22:77–84. [PubMed: 451041]
91. Powers JB, Newman SW, Bergondy ML. MPOA and BNST lesions in male Syrian hamsters: differential effects on copulatory and chemoinvestigatory behaviors. *Behav Brain Res* 1987;23:181–95. [PubMed: 3555537]
92. Powers JP, Bergondy ML, Matochik JA. Male hamster sociosexual behaviors: effects of testosterone and its metabolites. *Physiol Behav* 1985;35:607–16. [PubMed: 4070435]
93. Rose JD. Changes in limbic neuronal function during hormonal induction of lordosis in behaving hamsters. *Physiol Behav* 1992;51:1135–45. [PubMed: 1641414]
94. Sapolsky RM, Eichenbaum H. Thalamocortical mechanisms in odor-guided behavior. II. Effects of lesions of the mediodorsal thalamic nucleus and frontal cortex on odor preferences and sexual behavior in the hamster. *Brain Behav Evol* 1980;17:276–90. [PubMed: 7397487]
95. Schellinck HM, Rooney E, Brown RE. Odors of individuality of germfree mice are not discriminated by rats in a habituation-dishabituation procedure. *Physiol Behav* 1995;57:1005–8. [PubMed: 7610125]
96. Shipley MT, Ennis M. Functional organization of olfactory system. *J Neurobiol* 1996;30:123–76. [PubMed: 8727988]
97. Slotnick BM, Schoonover FW. Olfactory pathways and the sense of smell. *Neurosci Biobehav Rev* 1992;16:453–72. [PubMed: 1480342]
98. Steel E. Testosterone-dependent non-copulatory behaviour in male hamsters (*Mesocricetus auratus*). *Physiol Behav* 1983;31:453–9. [PubMed: 6657766]
99. Steel E, Keverne EB. Effect of female odour on male hamsters mediated by the vomeronasal organ. *Physiol Behav* 1985;35:195–200. [PubMed: 4070382]
100. Takahashi LK, Lisk RD. Estrogen action in the anterior and ventromedial hypothalamus and modulation of heterosexual behavior in female golden hamsters. *Physiol Behav* 1985;34:233–9. [PubMed: 4001186]
101. Wilson DA, Stevenson RJ. The fundamental role of memory in olfactory perception. *Trends Neurosci* 2003;26:243–7. [PubMed: 12744840]
102. Wilson DA, Stevenson RJ. Olfactory perceptual learning: the critical role of memory in odor discrimination. *Neurosci Biobehav Rev* 2003;27:307–28. [PubMed: 12946684]
103. Wirsig-Wiechmann CR, Wiechmann AF, Eisthen HL. What defines the nervus terminalis? Neurochemical, developmental, and anatomical criteria. *Prog Brain Res* 2002;141:45–58. [PubMed: 12508560]
104. Witter MP. Organization of the entorhinal-hippocampal system: a review of current anatomical data. *Hippocampus* 1993;3:33–44. [PubMed: 8287110]

105. Wood RI. Estradiol, but not dihydrotestosterone, in the medial amygdala facilitates male hamster sex behavior. *Physiol Behav* 1996;59:833–41. [PubMed: 8778874]
106. Wood RI, Brabec RK, Swann JM, Newman SW. Androgen and estrogen concentrating neurons in chemosensory pathways of the male Syrian hamster brain. *Brain Res* 1992;596:89–98. [PubMed: 1468005]
107. Wood RI, Coolen LM. Integration of chemosensory and hormonal cues is essential for sexual behaviour in the male Syrian hamster: role of the medial amygdaloid nucleus. *Neuroscience* 1997;78:1027–35. [PubMed: 9174071]
108. Wood RI, Newman SW. Integration of chemosensory and hormonal cues is essential for mating in the male syrian hamster. *J Neurosci* 1995;15:7261–9. [PubMed: 7472480]
109. Wood RI, Newman SW. The medial amygdaloid nucleus and medial preoptic area mediate steroidal control of sexual behavior in the male syrian hamster. *Horm Behav* 1995;29:338–53. [PubMed: 7490009]
110. Wood RI, Newman SW. Androgen receptor immunoreactivity in the male and female Syrian hamster brain. *J Neurobiol* 1999;39:359–70. [PubMed: 10363909]
111. Wood, RI.; Swann, JM. Neuronal integration of chemosensory and hormonal signals in the control of male sexual behavior. In: Wallen, K.; Schneider, JE., editors. *Reproduction in context: social and environmental influences on reproduction*. MIT Press; Cambridge, MA: 2000. p. 423-44.