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# CHEMOSIGNALS IN OLFACTORY SYSTEM MIGHT ALTER EMOTIONAL STATE: STRATEGY FOR SOCIAL COMMUNICATIONS

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## ABSTRACT

Olfactory system plays a crucial role in social and sexual behavior. Odors as olfactory stimuli can change immediate emotional state and level of arousal in humans. It is demonstrated that brain in the perception, discrimination and recognition of odor memory employs the amygdala and hypothalamus by different sets of cortical areas. Moreover, brain has the potential to instantly recall the emotional valance and personal experiences related to the source of the odor (smell) in human which may affect correct decision making.

Moreover, chemosignals (pheromones) are an important and critical means of communication for most mammalian species. Most mammals respond to chemosignals in many ways, including those surrounding reproduction, parent-offspring interactions and territorial/dominance relationships. They affects the olfactory neurons of the nervous system, then stimulating the central nervous system consequently influencing the hormonal system leading to release of neurotransmitters by indirectly influencing the behavior. In mammalian behavior which affects the living maintenances and quality. This issue has been discussed in religious doctrine in order to protect the nervous system from damage caused by the nuisance odors

**Conclusion**: Therefore chemosignals may play a critical role in sexual selection. Since chemosignals can influence sexual behavior in adulthood their role in social neuroscience is important. Interestingly, this issue is also mentioned in Islamic instructions which may reflect the importance of olfactory system in social interaction.

**Keywords:** Olfaction; Chemosignal; Pheromone; Women; Islam

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## INTRODUCTION

Pheromones or chemosignals are chemical molecules released in humans, insects and animals as a response to the opposite or same sex behavior or hormonal change. The molecules are in body fluids such as urine, sweat, exocrine glands, and genital mucosal secretions [1].

Scientists have identified a connection between pheromones and olfactory system while proving the significance in their emotional and sexual relationships. Human body odor influences sexual attraction hence the choice of sexual partner. Moreover, differences in body odor can be detected on the basis of separating gender and sexual orientation.

Studies have shown women after smelling an androgen-like compound activate the hypothalamus located in the pre-optic and ventro-medial nuclei .In contrast, men activate the hypothalamus in the paraventricular and dorsomedial nuclei when smelling an estrogen-like substance. The activation of the hypothalamic leads to sex differences in human

physiological and behavioral responses [2].

On the other hand, the olfactory system in mammals is considered the main olfactory system (MOS) and an accessory olfactory (vomeronasal) system (AOS) plays a major role in the control of sexual behaviors associated with reproduction [3-5].

Vomeronasal organ is responsible for detecting pheromones [6]. This organ is located above the hard palate on both sides of the nasal septum and is lined with receptor cells with their axons entry to the accessory olfactory bulb sending its inputs to the hypothalamic nuclei [7].

Different responses to sex pheromones result from higher brain function. Main and accessory olfactory bulb enter to various parts of the amygdala an area which can be a convergence point for olfactory and vomeronasal inputs [8]. Vomeronasal organ is very atrophic organ in humans and its role has been moved to the main olfactory system. But this does not mean that it lacks a vital role in the human olfactory system [9].

Research has shown that brain in the perception, discrimination and recognition of odor memory employs the amygdala and thalamus by different sets of cortical areas [10].

Odors as olfactory stimuli can change immediate emotional state and level of arousal in humans [11].Moreover, brain has the potential to instantly recall the emotional valence and personal experiences related to the source of the odor (smell) in human [12].

It has been identified that nasal receptors near the entrance of the nose have the strongest reaction to air containing pheromones, transferring it to stimulate the hypothalamus with a signal of attraction, sexual desire, arousal etc [13].

An interesting point is that men and women are so different in the olfactory cortex, as studies have shown that women have larger orbitofrontal cortex (including spaces smell) than men [14].

An important finding here is that men have greater concentration than females in the entorhinal cortex, a region that it is considered to be primary olfactory cortex receiving direct input from the olfactory bulb [15].

The studies of pheromones function revealed that pheromone affects the olfactory neurons of the nervous system then stimulating the central nervous system consequently influencing the hormonal system leading to release of neurotransmitters by indirectly influencing the behavior. It is clear that pheromones may play a critical role in sexual selection [16].

Olfactory signals influence emotional responses even if an olfactory stimulus is not consciously perceived which, due to the fact that olfactory receptors convey projections not only to the neocortex for conscious processing (e.g. the nature of a particular aroma) but also to the limbic system for emotional processing (e.g. memories and experiences associated with a particular smell) [17].

All studies indicate that odours and olfactory system are important for activities which are related to survival of the system and gender generation. Accordingly, may conclude that the olfactory system in both human and mammals highly contributes to the phenomenon called social interaction. Moreover, it was found that Islamic (perhaps other religions) which highlight the importance of controlling odors for both men and women may be highly due to significance of social interaction.

## 1. Olfactory organ

The olfactory system is considered as one of the oldest sensory modalities in the phylogenetic history of mammals. As a chemical sensor, the olfactory system influences social and sexual behavior. The specialized olfactory epithelial cells are classified as the only group of neurons capable of regeneration. Activation occurs when odor molecules come in contact with specialized processes known as the olfactory vesicles [16-17].

In mammals, the primary sensing structure is the olfactory epithelium of the nose that lines the posterior part of the nasal cavity, containing the nasal septum. This olfactory epithelium is made of three cell types: the OSNs, the basal cells and the sustentacular cells.

### 1.2 Types of olfactory system

Most mammalian species, for example monkeys, have a dual olfactory system: the main olfactory system (MOS) and the accessory olfactory (vomeronasal) system (AOS); these systems are interconnected at several levels [5]. The AOS is implicated in the control of sexual [18] and maternal behaviors, [19] and pheromone-mediated phenomena related to reproduction [5,7]. In most mammals, a specialized region of the olfactory system called the vomeronasal organ (VNO), is responsible for pheromone detection. The principal evidence that the VNO plays a role in mammalian pheromone detection comes from lesion studies asserting that removal of the VNO produces reliable impairments in reproductive behaviors [8]. The VNO is located above the hard palate on both sides of the nasal septum, moreover, it is lined with receptor cells whose axons are projected to the accessory olfactory bulb sending its projects to the hypothalamic nuclei [9].

Most mammals have two separated olfactory systems with different functional roles: the main olfactory system for recognizing conventional odorant molecules and the vomeronasal system specifically dedicated to detecting pheromones [20]. In humans, the vomeronasal organ (VNO) was regarded as vestigial, but different researchers presumed its function to have a distinct sensory passage to detect pheromone [20]. The studies have shown that a damaged VNO could affect the patient's social life in terms of selecting mates and relations, in addition, other studies showed that both the main and accessory olfactory systems are able to process partially overlapping sets of sexual chemo-signals complimentarily supporting aspects of controlling sexual behavior [21].

### 1.3 Olfactory tracts

Olfactory tracts consist of olfactory receptor, olfactory bulb, olfactory tract, anterior commissure, olfactory cortex. The primary olfactory cortex is projected to limbic structures, such as the amygdala and the hippocampus, and to the hypothalamus and the ventral striatum, which includes the accumbens nucleus and the olfactory tubercle [22]..

There remain profound statements about structure of the nose and smelling sense of human in debates conducted by Imam Sadiq (as.) with the scientists of the time: "God made the water inside nose cold so that the air we breathe in through the nose can get cold and protect the brain otherwise the brain will be smelted and comes down. There is running humidity in the nose due to which no pain and sickness is found in the brain since the humidity makes it out, if there was no humidity, the brain would get hard and rigid and a place for worms. The nostrils point downward to let brain fluid out and to direct the smells to the olfactory system and also to distinguish good smell from a bad one. If the nostrils were upwardly-located, no fluid would come out and no smell would be sensed [23].

The main and accessory olfactory bulbs are commonly projected to different parts of the amygdala which could be a convergence point for olfactory and vomeronasal input [24]. Therefore, the studies have shown that odor perception and recognition memory is mediated by different sets of brain structures, i.e.odor perception involves not only the amygdala-piriform and orbitofrontal cortices but also the medial thalamus, and insular and cingulate cortices [25].

### 1.4. Olfactory tracts and central pathway

Generally, it is considered to be three pathways of transmission for olfactory system: 1-The very old olfactory system: this tract starts olfactory tract to medial olfactory area then is transferred to hypothalamus and limbic system. This system is related to licking lips, salivation and other basic operations as well as reflexes and unconscious actions. This system is found in primate animals. 2- The less old olfactory system: this system starts olfactory tract to central olfactory area then is transferred to perpyriform, pyriform and center pyriformthence, to amygdale, limbic system and hippocampus. This Part is related to desire and aversion to food. 3- The newer pathway: this pathway is found in human and animals with strong smell sense. This tract is transferred to thalamus thence to orbitofrontal. It is related to conscious centers of olfactory and accurate detection of odor [26]

## 2. Pheromone and olfactory system

The phrase ''pheromone'' stems from the Greek words Pheran – to transfer – and Horman – to excite [27]. These chemical molecules are released by humans, insects, and animals to trigger a response to or to elicit specific behavioral expressions or hormonal changes from the opposite sex, the same sex or both sexes of the same species. These signaling molecules contain in such body fluids as urine, sweat, specialized exocrine glands, and genital mucous secretions [1]. These chemical molecules are broadly divided into two classes: (1) releaser pheromones that produce short-term behavioral changes in addition to acting as attractants or repellents; and (2) primer pheromones that produce long-lasting changes in behavior or development by activating the hypothalamic–pituitary–adrenal axis [28]. On the other hand, pheromones are divided into aggregation pheromones, alarm pheromones, epideictic pheromones, territorial pheromones, trail pheromones, information pheromones and sex pheromones [29,5, 30]. In humans, the main odor-producing organ is the skin via its apocrine sebaceous glands developed during puberty and associated with sweat glands and tufts of hairs [31]. Four specific functions of pheromones have been identified: opposite-sex attractants, same-sex repellents, mother–infant bonding attractants and menstrual cycle modulators [32].

The apocrine axillary glands, regarded as pheromone-producing scent glands, do not begin functioning until puberty when sex hormones have an impact on their activity. In this Regard, studies have shown a possible link between steroid hormone action and induction of pheromone production by investigating the localization of androgen receptor and estrogen receptors (α and β) in these glands ,[33] moreover, other studies have shown the synchronization of the menstrual cycles among women based on unconscious odor cues in an experiment where a group of women were exposed to a scent of perspiration from armpits of other women. Then, this caused their menstrual cycles to speed up or slow down depending on the time when the sweat was collected; before, during, or after ovulation [34].

Other studies reported that the age of Menarche (the first menstruation for girls) had a direct correlation with the time young girls spend with boys, due to their exposure to odors of the opposite sex [35]. Furthermore, studies showed that smelling androstadienone of male sweat maintains higher levels of cortisol in females and therefore influencing the endocrine balance of the opposite sex [36]. Different opinions suppose that human body odor may contribute to selection of partners or may influence sexual preference. Other studies showed that women smelling an androgen like compound activate the hypothalamus, in the pre-optic and ventro-medial nuclei but men activate the hypothalamus in the paraventricular and dorsomedial nuclei when smelling an estrogen-like substance. Thus, this sex difference of hypothalamic activation suggests a potential physiological substrate for a sex-differentiated behavioural response in humans [3]. Additionally, pheromones are a mediator for proper psychosexual behavior. In this context, studies have shown that the psychosocial environment may influence the fertility of females by altering urinary pheromone activity in the male [37]. Also, other studies showed that exposure to the endogenous steroid androstadienone have the ability to modulate women's mood to make them feel more focused [38].

All these data indicate that the olfactory system activation which arises from the odors in the environment is functioning in a concert manner for establishing better relationships between the species of the same kind.

## 3. The chemosensory function of the Amygdala and chemical signal

### 3.1 The chemosensory function of the amygdala

In the middle of $20^{th}$ century, Herrick and Johnston indicated that the amygdaloid formation of different vertebrata species was related to the olfactory system such information was approved in mammals in the 1960s [39].

The amygdala receives direct chemosensory (olfactory and vomeronasal) inputs from the main and accessory olfactory bulbs. A great deal of projections from main and accessory olfactory bulbs to amygdala proposed to the chemosensory inputs to amygdala perform a key role in survival and reproduction [40].

Lanuza and etalproposed a relation between the chemosensory role of the amygdala and its key component in the network mediating emotional responses [41].

However, there is an important chemosensory input to amygdala; its role in chemosensory processing is disregarded in contrast to the fact that there has been some mediation on emotion learning associated with fear.

The behavioral study in rodents suggest that the chemosensory amygdala interfere in procedure of olfactory and/or vomeronasal stimuli. Therefore, amygdala is taken into account as a structural and functional unit. The vomeronasal system is specializing in detecting pheromones [42].

Chemosensory amygdala is divided to olfactory amygdala, vomeronasal amygdala and mixed chemosensory amygdala that receive projections from main olfactory bulb (MOB) to olfactory amygdala and accessory olfactory bulb (AOB) to vomeronasal amygdala [43]. Also, the received convergent inputs from both bulbs enter mixed chemosensory amygdala (MXCA).A number of reports demonstrate that the AHA (amygdalo-hippocampal area) is related to the vomeronasal amygdala (it receives indirect inputs from AOB) [43].

It is revealed that posterolateral cortical nucleus of the amygdala (PLCO) is targeted by inputs from MOB. PLCO projects to the central extended amygdala and also gives rise to important projections to the hippocampal formation. Hence, the PLCO apparently plays an important role in the processing of olfactory stimuli and in the generation of olfactory memories and in the formation of odor fear conditioning which is the result of important projections to the hippocampal formations due to PLCOs connections to the ventral striatum [44].

It is suggested that PLCO may be involved in processing the rewarding properties of odor with chemical signals or sexual pheromones. APir is part of the olfactory cortex and receives important thalamic afferents from gustatory and also APir connected to the CA1 layer of the hippocampus [44].

This convergence of gustatory and olfactory stimuli makes APir mediate emotional responses to feeding or specific food items. Posterior medial cortical nucleus of the amygdala (PMCO) could be considered as the primary vomeronasal cortex. PMCO modulate the pheromone signal processing through a glutamatergic projection to the granular layer of AOB [45].

The amygdala exists in the innate response to sexual vomeronasal-mediated pheromones as well as in the learning process leading to a conditioned response to male-derived odorants [41].

Therefore, the chemosensory amygdala seems to be involved in processing sexual chemosignals that induce unconditioned emotional responses, as well as in relaying this chemical information to the basolateral amygdala for emotional learning. Consequently, there is actually no clear-cut separation between the chemosensory and the emotional divisions of the amygdala.

Moreover, sexual pheromones are apparently not the only chemical signals inducing emotional responses discriminated by the vomeronasal organ and processed in the amygdala [46].

The adaptive value of conditioning which occur in the amygdala, in which vomeronasal stimuli act as unconditioned emotional triggers allowing the emotional attachment of other chemical and non-chemical stimuli, explains the great success of the amygdala as neural system for survival and reproduction. The chemosensory function of the amygdala cannot be separated from its role as part of the emotional brain [41].

### 3.2 Chemical Signal

Chemical signals or chemosignals often called “pheromones” are an important and often critical means of communication for most mammalian species. Most mammals respond to chemosignals in many ways, including those surrounding reproduction, parent–offspring interactions and territorial/dominance relationships [47]. The basic anatomy and physiology of chemosignal-processing circuits consists primarily of the main olfactory system (MOS) and the accessory olfactory system (AOS) [48]. These two systems are largely separate and respond to different types of chemosignals: primarily volatile chemicals for the MOS and primarily non-volatiles molecules for the AOS.

### 3.3 Chemosignals and females’ behavior

The studies have shown that the presence of male chemosignals prior to reproductive maturity accelerates the onset of puberty (first day of estrus) in juvenile female house mice and other species such as [49] meadow voles, Siberian hamsters, prairie voles, pine voles [50].

The presence of chemosignals from adult males can also promote ovulation in an ovulatory group-housed mice [51] or rats through increases in LH and decreases in prolactin (PRL) secretion [52]. This pro-ovulatory “male effect” of chemosignals also occurs in different induced-ovulatory species such as prairie voles and gray short-tailed opossum as well as in anestrous domestic sheep and goats [53]. There has been observed a modest advancement of LH surges in women when experiencing prolonged exposure to male axillary scent [54].

Several reports suggest that mammals show chemosignal- induced synchronization of their ovulatory cycles. The studies presented evidence showing that cohabitating female humans synchronize their menstrual cycles over time and postulating that this was mediated by chemosignals [34].

The beginning of puberty can be delayed by several days in single-sex, group-housed female mice and pine voles [55] exposed to urine from group-housed females. With puberty-acceleration, this delay of sexual maturation is the same as that produced by group-housing itself indicating that social odors are the critical social factor retarding puberty in mice.

Lately, inseminated female mice exposed to novel males have shown a high rate of pregnancy failure and early resumption of estrous cycles, but not if the male is the one that mated with the female [56]. This selective pregnancy block is mediated by chemosensory cues as urine from novel males only can disrupt pregnancy [57].

In contrast with the literature concerning chemosignal effects on female reproductive physiology, there is substantially less information about similar effects in males [58]. The studies suggest that development and function of male reproductive physiology are also sensitive to chemosignal exposure. For instance, the development of puberty in male mice is delayed by exposure to male urine, grouped-female urine, and a puberty-delay chemosignal derived from urine of grouped females [59]. However, non-grouped females do not advance puberty in male mice.

Chemosignals can change male gonadal physiology in adulthood. For example, male mice show increased sperm density when housed with female bedding suggesting that exposure to female chemosignals increases spermatogenesis [59].

The studies have shown that Post-pubertal male mice, Syrian hamsters [60], Siberian hamsters, rats, common marmosets and macaques [61] release LH within 15–30 min, followed by a dramatic peak in circulating androgens, in response to conspecific female odors. A like effect occurs in humans: exposure to chemosignals from peri-ovulatory women modestly reduces a decrease in testosterone in male humans normally observed during laboratory testing [62].

Chemosignals are able to affect animals and human behavior. The studies have shown that Post-pubertal female Syrian hamsters, rats and other species are preferentially attracted to the chemosignals of reproductive male conspecifics, independent of sexual experience [63]. In addition, in humans, women are reported to be able to discriminate sex specific body odors [64] but this effect may be due to known intensity differences between male and female odors. For instance, strong body odors from women are labeled as “male” and both sexes rated male odors as less pleasant and more intense than female odors [65]. Nonetheless, several studies have suggested that androgens (androstenol, androstenone, androstadienone: ANDs) act as putative human male “pheromones” in that they may increase ratings of attractiveness of people's photographs, prevent a decrease in positive mood in laboratory settings for both men and women and influence measures of physiological arousal in women [66].The studies reported that the lack of a sex difference in behavioral response to ANDs [67], difficulties in replicating effects in more naturalistic settings [68], the highly variable concentrations of ANDs on the human body [69]as well as the fact that a significant number of people are selectively anosmic to these odors [70] militates against assigning ANDs as a unique status as sex-attractant chemosignals. Indeed, human mood, cognition and physiology can be modified by non-social odors [71]

### 3.4 Chemosignals and males’ behavior

The studies have shown that adult males of numerous mammalian species approach female scent and engage in prolonged investigation of these odors as part of their precopulatory behavior [72,73], moreover, males use the arrangement, spatial patterning and freshness of female scent marks to guide their search toward nearby mating partners [74] and toward areas associated with female odors [75].The studies reported in male humans showed a very modest ability to discriminate chemosignals from ovulatory and non-ovulatory women but did not judge these odors as either attractive or unattractive [76]. Moreover, human males appear to have a modest reduction in self-reports of sexual arousal, testosterone levels and brain responses to visual erotica when exposed to odors from human female tears [77] indicating a possible role for chemosignals in human sexual responding. Other studies have shown that Exposure to EST (estratetraenol) decreased positive mood in men as well as increasing their sympathetic tone but neither of these effects have been replicated [78]. EST has also been reported to increase activity in the hypothalamus of men, but no women, using PET scans [79], and no sex difference in hypothalamic response was found using fMRI with physiological concentrations of EST [47].

## 4. Olfactory management for social communications

As mentioned earlier, pheromones and chemosignals which play significant role in the process of reproduction such as making mate appealing, increasing libido and boosting sex drive have particular performance of their own the negative effects of which should be prevented by regulating relationships and social relations and also avoiding inappropriate relationships between men and women.

Therefore, Islam has prohibited all women and men from establishing a physical and emotional provoking connection. Any relationship outside regulation between men and women will lead to emergence of negative effects of chemosignals interference in their body and spirit, social promiscuity and if continuously done, it can result in such adverse effects as disrupting the process of puberty and menstruation, change of temperament, sexual desire disorder, and damaging brain function and memory.

In this regard, it is important to manage these interactions to avoid any irregularity in the society which can help reduce function of other parts of the brain.

It is interesting to note that religious teachings especially those presented in Islam offer some instructions which help us better manage our social relations [78,79]; methods and instructions which provide tools for better management of social relations regarding olfactory system.

### 4.1 Prohibition to incite sexual excitement with perfume in Islam

It is clear that olfactory system activity can activate different parts of the brain including amygdala and hippocampus [80,81]. Due to frequent communication of the system with the above parts, an olfactory stimulus like nice fragrance can arouse parts of amygdala (medial) associated with olfactory and sexual system and through activation of this pathway strong emotional responses are resulted.

This activation can induce both emotional and non-emotional memory which can be used for further decision making in the society i.e. Irregularity in the relationships [82-84]. Wearing perfume is not forbidden to any group or gender in Islam. There is no problem in using nice fragrance for women according to Islam teaching. It must be mentioned that in Islamic teaching. the right of men to enjoy their wife`s perfume is strongly emphasized. The sentence that: "Of major rights of men is that his wife should use the best perfume" [85], and this saying that: "No one got fragrant unless he got wiser" [86] are among the most famous narrations in Islamic literature.

However, Islam considers some limitations and regulations for wearing perfume in the society to avoid sexual arousal.

Islam intends to prevent the spread of any factor stimulating sexual emotion in the society by issuing these commands. These sentences and other orders that focus on the odor and perfume and their role in relationship between the individuals can be considered as the platform for construction and/or management of social interaction in human society (for review see [87-92].

## 5. Conclusion

Olfactory system has an amazingly complicated structure among the most important of them one can refer to its influence on emotions and the role it plays in sexual desires and social relationships. Olfactory system activity can affect the behavior of the mammalian as well as humans upon which they regulate the relationships with other individuals in their societies and/or other societies (species), on the other hand.

Chemosignals can affect different parts of the brain (e.g. the amygdala and hippocampus) through olfactory receptor stimulation (and olfactory system activity as a result), on the other. This activity can produce long term memories which help the individual make appropriate decision to regulate his/her relationship in the society.

Interestingly, some instructions can be found in religious teachings, especially those of Islam, which help the individuals manage their social relationships in this regard.

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