Neuroendocrinology Letters ISSN 0172–780X


INVITED NEL REVIEW

# Human Pheromones: Integrating Neuroendocrinology and Ethology

**James V. Kohl,[1] Michaela Atzmueller,[2] Bernhard Fink[2] & Karl Grammer[2]**

1. JVK Resources, Inc. Las Vegas, Nevada, USA.
2. Ludwig-Boltzmann-Institute for Urban Ethology, University of Vienna, Vienna, Austria.

*Correspondence to:* Bernhard Fink,
Ludwig-Boltzmann-Institute for Urban Ethology,
University of Vienna, Althanstrasse 14, A-1090 Vienna, Austria.
TEL +43 1 4277 54766
FAX +43 1 4277 9547
E-MAIL bernhard.fink@ieee.org

*Submitted:* *August 6, 2001*
*Accepted:* *September10, 2001*

*Key words:* **human ethology; pheromones, odor; olfaction; human sexuality; sexual selection; mate choice**

*Neuroendocrinology Letters 2001; **22**:309–321 pii: NEL220501R01 Copyright © Neuroendocrinology Letters 2001*

**Abstract** The effect of sensory input on hormones is essential to any explanation of mammalian behavior, including aspects of physical attraction. The chemical signals we send have direct and developmental effects on hormone levels in other people. Since we don‘t know either if, or how, visual cues might have direct and developmental effects on hormone levels in other people, the biological basis for the development of visually perceived human physical attraction is currently somewhat questionable. In contrast, the biological basis for the development of physical attraction based on chemical signals is well detailed.

**The human sense of smell**

The importance of the human sense of smell has been largely underestimated. Many people believe that human olfactory acuity and specificity have deteriorated. Other mammals are believed to be macrosmatic (i.e., better smellers) because they have more olfactory receptor cells in their nasal mucosa than humans [1]. For example, dogs have about 230 million olfactory receptor cells, while humans have about 10 million. Accordingly, humans and other primates typically are believed to be microsmatic (i.e., worse smellers) equipped with highly developed powers of vision that supposedly make humans "visual creatures." This concept needs reconsideration since many recent studies have shown that olfaction plays a very important role in human reproductive biology and because human reproductive biology affects human behavior.

The nasal mucosa can functionally be divided into two areas: the respiratory region and the olfactory region, which contains the sensory cells. In the nose, the olfactory region can be found on both sides of the nasal septum in the upper nasal conchae. The ability to discern between many different odors suggests that specific receptors exist in the sensory cells. Excitation of axons from these sensory cells occurs when an odor molecule "docks" with a receptor protein in the membrane of the olfactory ciliae. It is not yet known whether the human ability to distinguish between thousands of different scents is caused by the number of specific receptors or by the simultaneous stimulation of multiple receptors [2, 3]. It is suspected, however, that our superior cognitive power allows us to better use olfactory input when compared with other mammals [4]. The axons of the sensory cells enter the olfactory bulb. Sensory input is then projected via the olfactory tract into the olfactory lobe of the brain. From here, olfactory input is projected via the thalamus to the neocortex and to the limbic system. This pathway allows olfactory stimuli to be consciously detected and interpreted, but also allows olfactory stimuli to directly influence the neuroendocrinology of emotions.

The 'affective primacy hypothesis' [5] asserts that positive and negative affective reactions can be evoked with minimal stimulus input and virtually no cognitive processing. Olfactory signals seem to induce emotional reactions whether or not a chemical stimulus is consciously perceived. We theorize that the importance of human non-verbal signals is based upon information processing, which occurs in the limbic system, and without any cognitive (cortical) assessment. Affect thus does not require conscious interpretation of signal content. Underlying this fact is that affect dominates social interaction and it is the major currency in social interactions [6]. Affective reactions can occur without extensive perceptual and cognitive encoding. They are made with greater confidence than cognitive judgments, and can be made sooner [5, 7]. Olfactory input from the social environment is well adapted to fit such assertions. For example, chemical cues allow humans to select for, and to mate for, traits of reproductive fitness that cannot be assessed simply from visual cues.

The universal nature of emotional expression in different species strongly suggests the shared evolution and the fundamental nature of affect. Affect is clearly primary to language in phylogeny. Affect comes before our evolved language and our present form of thinking. Many studies have shown that the contribution of affect to signal recognition and processing has been underestimated [8, 9, 10]. Despite agreement that the affect-cognition question is important to research in non-verbal behavior, there are still many questions that current data do not answer.

In contrast, the affect of pheromones on our emotions is linked to the effect of pheromones on the hormones of the hypothalamic-pituitary-gonadal axis – an unconscious affect. The ontogenetic link between olfaction and hormones becomes evident in patients suffering from X-linked Kallmann's syndrome. They show underdeveloped gonads, completely lacking secondary sexual characteristics, and both male and female patients are anosmic, which means they are unable to detect odors. This syndrome results from underdevelopment of the olfactory bulb in the embryo. Gonadotropin releasing hormone (GnRH) neurosecretory cells of the hypothalamus originate in the olfactory placode and migrate into the hypothalamus. However, in Kallmann's syndrome this migration does not occurand this is accompanied by underdevelopment of the olfactory bulb and minimal, if any, secretion of hypothalamic GnRH [11]. Preliminary evidence suggests that people with Kallmann's syndrome do not respond to putative human pheromones [12].

Further to our discourse on affect, which includes the effect of human pheromones on hormones like GnRH, and thus on behavior, is the concept that affect is conditioned in the presence of other sensory input. For example, Cooper, Parvopassu, Herbin, and Magnin [13] suggest that mammalian neuroanatomical pathways link vision and olfaction. Social-environmental odor cues, which male rats may learn to visually associate with sexual activity, can be used to condition luteinizing hormone (LH) release [14]. In fact, after minimal conditioning, an arbitrary odor ultimately will elicit a male LH response, even in the absence of odor previously associated with a female. Regardless of whatever non-olfactory sensory input is involved, the functional significance of the conditioned change in LH secretion lies principally in the unequivocal demonstration that olfactory cues

can activate the male pituitary-gonadal axis in a way that mimics, in every respect, the activation achieved by exposure to a female. Short-term exposure of males to females also is linked to increased testosterone (T) in rats, mice, rabbits, bulls, rams, monkeys, and humans [14]. From a neuroendocrine perspective, given the link between LH and T, presumably, the female odor cues that condition LH release, also condition T release, and therefore have the ability to condition human hormone responses to non-olfactory sensory input. This biologically based affective reaction links the social environment to the neuroendocrinology of behavior, and does not require cognition. Based upon a detailed mammalian neuroendocrine model, Kohl [15] proposed that LH is the measurable link between sex and the human sense of smell. Kohl [16] detailed reciprocity in olfactory-genetic-neuronal-hormonal-behavioral relationships that appear to link the nature and nurture of human sexuality. Subsequently, Diamond, Binstock, and Kohl [17] offered a more complete overview of non-gonadal, non-hormonal, influences on sexual differentiation and of the influence of sensory stimuli, especially chemosensory stimuli, on human sexuality. In this regard, the affect of chemosensory stimuli on behavior was integrated with tactile cues. Dellovade et al. [18] suggest that male pheromones and tactile cues lead to the increase they noted in GnRH immunoreactive (GnRN-ir) cell numbers which were correlated with LH modulated estradiol levels and with sexual behavior.

Pairing of a neutral odor with access to a receptive female rat was shown to result in an ejaculatory preference for a female with that odor [19]. Plaud and Martini [20] recently found that the sexual arousal of human males could be classically conditioned. This was confirmed by Lalumiere & Quinsey [21] who showed that sexual interest in human males might result from Pavlovian conditioning. It seems likely that odor-induced, GnRH-directed conditioning of human LH release may be used to evoke functional changes in the mammalian neuroendocrine pathways that mediate the release of T and E, with or without visual awareness of any associated stimuli. Given mammalian models, olfactory conditioning of a GnRH-directed neuroendocrine response may lead to a change in the sex steroid hormones T and E, which would be a change that also is manifest in behavior. This neuroendocrine link between social environmental sensory (i.e., olfactory) input and the neuroendocrinology of reproduction appears to preclude any involvement of cognition. Thus, the affect-cognition question is sublimated by the effect of pheromones on the neuroendocrine system, and presumably on behavior. For example, though neuroendocrine effects were not measured, Jacob, Kinnunen, Metz, Cooper, and McClintock [22] showed through brain imaging that androstadienone has distributed effects on cortical processes and brain metabolism even when it is not detected consciously. Accordingly, this human "chemosignal" modulates psychological state without being consciously discernible as an odor (see also [23]).

## The vomeronasal organ

The vomeronasal organ (VNO), also termed Jacobson's organ, is a special part of the olfactory system(s) and can be found in most tetrapods at least in the embryonic stages. In most mammals, it is located above the hard palate on both sides of the nasal septum and consists of a pair of blind-ended tubes that open into the nasal cavity. In some mammals, it is connected to the oral cavity by the nasopalatine duct. Receptor cells in the epithelium of the mammalian VNO are not equipped with cilia [24, 25, 26] and their axons extend to an "accessory" olfactory bulb, that projects directly into the limbic system, bypassing the thalamus, and thus cortical integration. Simply put, the VNO is representative of an accessory olfactory system [27] that directly translates olfactory cues into neuroendocrine responses. In the past, the VNO was believed to exist only in lower mammals, and only at embryonic stages in primates. However, recent data have shown that the VNO also exists in adult humans [28]. Monti-Bloch and Grosser [29] found the adult human VNO responds to picogram amounts of human skin pheromones with depolarization. These findings suggest, that the human VNO may function as a pheromone detector as it does in other mammals. However, so far there is no evidence that the human VNO is connected to a functional accessory olfactory system. This lack of evidence, in the past, has caused considerable scientific debate about whether or not there is such a thing as a human pheromone.

## Pheromones

The term "pheromone" comes from the ancient Greek words "pherein": to carry, and "hormon": to excite. Karlson and Luscher [30] introduced this term in 1959. Pheromones are referred to as ecto-hormones: chemical messengers that are transported outside the body that have the potential to evoke certain responses, such as physiological (e.g., hormonal) or behavioral changes in a conspecific. Thus, pheromones play an important role in inter-individual communication, and are known to do so in species from single-celled yeasts to primates, despite different manifestations of what might be considered "behavior".

Pheromones can be divided into at least two classes, according to the physiological effects they cause in the recipient: "signal" and "primer" pher-

omones [31]. Signal pheromones cause short-term changes, such as the release of neurotransmitters that can directly modify the recipient's behavior. For example, Moss and Dudley [32] suggest that a fraction of the GnRH molecule functions directly as a neurotransmitter in rats to elicit a behavioral effect (i.e., lordosis). This behavioral effect is characteristic of a "signal" pheromone, which activates a response.

Primer pheromones evoke long lasting changes in the body by influencing the hypothalamic-pituitary-gonadal axis, which allows both for organizational and activational effects of primer pheromones. Primer pheromones are believed to exert their affect by altering the hypothalamic secretion of GnRH. Hypothalamic GnRH triggers the secretion of gonadotrophic hormones from the pituitary. The gonadotropins follicle stimulating hormone (FSH), and LH affect gonadal hormone secretion. In females, FSH stimulates follicle maturation in the ovaries and the secretion of estrogens; LH stimulates the ovarian theca cells to produce androgens, which diffuse to the granulosa cells of the ovarian follicle, where they are converted to estrogens, and LH also stimulates the growth of the corpus luteum and secretion of progesterone. In males, FSH stimulates spermatogenesis and probably affects T production and secretion by acting indirectly on an as-yet-unidentified Sertoli cell protein [33]. In males, the LH/FSH ratio controls T production by Leydig cells in the testes. Sex steroid hormones like T and E alter neurotransmission by influencing synaptogenesis, synaptolysis, and apoptosis during development.

GnRH pulsatility is unequivocally required for LH release (see [34]), and GnRH pulsatility is directly associated with changes in LH and in FSH pulsatility that are manifest in LH/FSH ratios, which modulate steroidogenesis. Thus, LH and the LH/FSH ratio are human measures of GnRH pulsatility and so are T and E levels, though these measures are less direct. The effect of primer pheromones on GnRH allows pheromones to influence LH/FSH ratios and the production of T and E, or simply put, primer pheromones influence the entire hypothalamic-pituitary-gonadal axis, which influences behavior by altering neuroanatomy and thus neurotransmission.

The odors produced by humans are a function of the location on the body where the odor is being produced. The amount of available oxygen as well as water and skin gland secretions determine the type and number of cutaneous flora, which are present on different body areas. Moist areas of the body, such as the mouth, axillae, genital region, and feet, support greater varieties and numbers of bacteria because they are occluded, or are moist because of their function (e.g., mouth, vaginal barrel). The type and density of cutaneous microorganisms on different areas of the body interacting with skin and other glandular secretions give rise to a variety of odors from various body sites.

### Human body odor

In humans, pheromone production is primarily linked to the apocrine glands of the skin, but also is linked to other glandular secretions and to skin flora present in moist areas of the body, like the axillae, mouth, feet, and genitals. For example, concentrations of $C_2$-$C_5$ aliphatic acids that are secreted from the vaginal barrel, and that have been referred to as "copulins," vary with menstrual cycle phase. The odor of the copulins and its behavioral effects also appear to vary with the menstrual cycle. Thus, copulins are also referred to as pheromones [35, 36].

In sufficient quantity, pheromones are consciously detected as natural human body odor. Apocrine glands are found in areas that include the genital area, around the navel, on the chest, breasts, and areola, and are concentrated in the axillae. Like ecrine (watery sweat) glands and sebaceous (sebum-secreting) glands, apocrine glands are associated with hairs. The high concentration of apocrine glands found in the armpits led to the term: "axillary organ", which is considered an independent "organ" of human odor production. Apocrine glands have a tubular, coiled structure and are about 2 mm in diameter [37]. Human apocrine glands develop in the embryo, but become functional only with the onset of puberty [38]. This link between apocrine gland function and puberty reflects that function is closely linked to levels of sex steroid hormones that increase with the onset of adrenarche and puberty. Freshly produced apocrine secretion has no odor [39], and is transformed into odorous products by microorganisms (see [40] for review).

For reasons that remain unclear, humans produce a relatively high amount of odor production, when compared to other primates. The odors of the skin, the saliva, urine and, genital secretions, contribute to the amount and hedonic quality that is characteristic of natural human body odor. In this regard, we note that any odor, even the scent of rose, becomes aversive when it is produced in suprathreshold quantities. Thus, though pheromonal communication typically occurs without consciousness, pheromones, when produced in high concentration, may still have both conscious and aversive effects on others.

### Human pheromones

By definition a human pheromone elicits changes in the physiology and/or behavior of a conspecific. Stern and McClintock [41] showed that the phero-

mones of women regulate ovulation in other women, presumably by affecting levels of LH and FSH. Berliner, Monti-Bloch, Jennings-White and Diaz-Sanchez [42] suggest that a progesteronic pheromone alters LH pulsatility in men. These studies show that human pheromones, or that a putative human pheromone, elicit change in hormones. Similarly, Juette [43] showed that an aqueous mixture of five ovulatory fatty acids evoked increased saliva T levels in men, and produced better judgments of female photos and of female voices than in controls. Thus, both physiology (i.e., T levels) and behavior (i.e., judgment) were affected. The putative human pheromone androstadione also has been shown to elicit physiological (i.e., hormonal) and behavioral (i.e., mood) changes [44, 23]. Shinohara, Morofushi, Funabashi, and Kimura [45] showed that axillary pheromones from women either in the follicular or in the ovulatory phase of the menstrual cycle differentially modulate pulsatile LH pulse frequency in other women, a hormonal effect. Preti, Wysocki, Barnhart, Sonheimer and Leyden [46] recently showed that male axillary extracts effect LH and mood in female recipients, and suggested that the LH response may be used to determine precisely what compound is involved in this pheromonal effect, which is a typical mammalian female response to pheromones from a male conspecific [14]. Minimally, human pheromones appear to alter both physiology and behavior in other humans.

It is still unknown how many different pheromones are produced in human axillae, but some of them have been investigated in recent years. Most studies focused on the 16-androstenes, metabolites of the characteristically male sexual hormones, the androgens, which are secreted by the apocrine glands. Dorfman [47] assumes that the 16-androstenes develop with the metabolism of testosterone. Two of these androstenes, the alcohol 5-androst-16en-3ol (androstenol) and the ketone 5α-androst-16en-3-one (androstenone) have odorous characteristics that bear a similarity to the smell of male axillae. Androstenol has a musk-like scent, while androstenone smells urinous. It is important to note that the odors arise only via the activity of microorganisms [48]. Among these microorganisms are the aerobic bacteria Corynebacterium ssp., which transform the odorless precursors androstadienol and androstadienone, into the odorous 5α-androstenone [49]. If the axillae are treated with antibacterial detergents, the production of androstenone decreases significantly [50].

Male axillary sweat contains approximately five times more androstenone than female sweat [51]. This sex difference can be explained by sexually dimorphic levels of blood androgens, and by sex differences in the colonization of microorganisms. For example, Jackman and Noble [52] investigated the axillary bacteria of 163 male and 122 female subjects and were able to show that in most men the axillae were dominated by the bacteria Corynebacteria ssp., whereas in women they found the bacteria Micrococcaceae. Other putative human pheromones, whether secreted primarily in the axillae, or in other areas, can be expected to be identified upon the examination of sexually dimorphic adrenal hormone metabolites, and with the identification of other sexually dimorphic microorganism colonization.

## Do pheromones influence human behavior?

Pheromones seem to play an important role in mammalian social and sexual behavior. This suggests that the investigation of pheromone effects in humans is warranted. An early study showed that skin conduction in subjects exposed to androstenone was 1.5 times higher than in the control group [53]. These findings provided clues to the potential physiological effects of the 16-androstenes. In a study by Cowley and Brooksbank [54] 38 men and 38 women wore a necklace with a pendant containing androstenol during sleep. The next morning, the number of social interactions of the subjects was assessed and it showed that women wearing the necklace had had significantly more and more intensive contact with men than subjects in the control group. It was presumed that human pheromones had the potential to facilitate inter-sex communication.

Another research team investigated the influence of odorous substances on photo assessment [55]. Two hundred men and women were told to rate a photo of a male person and to rate their own mood under the influence of androstenone. Men rated the person in the photo as "passive" and women reported their own mood to be less "sexy". In a follow-up study men under the influence of androstenone rated photos of males positively, if they liked the scent of androstenone [56]. In a similar study, male and female subjects rated photos of people, animals, and buildings under the influence of androstenol [57]. Subjects wearing masks impregnated with androstenol rated the photos of women as more attractive, more sexy, and friendlier, and rated the photos of men warmer and friendlier than subjects in the control groups.

The influence of human pheromones on social behavior may pale by comparison to the influence that pheromones may have on human reproduction. Olfactory cues are essential in animal, especially mammalian, sexual behavior. In humans these olfactory cues are difficult to isolate and related discussions have lead to controversy. Nonetheless, humans are capable of discriminating between males and females by olfac-

tory cues alone [58]. The afore-mentioned sex differences in the composition of human axillary secretions may be the basis for such discrimination. Pheromones also influence the human menstrual cycle. McClintock [59] found that female college students, who spent significant amounts of time together showed synchrony of their menstrual cycle, and attributed this synchrony to odors (pheromones). A few years later this finding was bolstered by another study [60]. Sweat samples of 5 women with regular 29-days-cycles were taken daily. These donor samples were applied to the upper lips of the female test subjects 3 times a week for 4 months. By the end of the test period, test subjects menstruated significantly more often at the same time as the donors than subjects in the control group. It became clearer that menstrual synchrony, which also is indicative of ovulatory synchrony, is controlled by pheromones. In a parallel study, the influence of male odors on the menstrual cycle was tested [61]. Odor samples of male axillary secretions were again applied to the upper lips of female test subjects. Those who were not sexually active had irregular menstrual cycles at the beginning of the experiment. After 4 months the mean cycle length was 29.5±3 days length in a majority of the test subjects. This strongly suggested that male pheromones have a regulatory effect on the menstrual cycle.

Many authors have speculated that both androstenone and androstenol are male pheromones, raising the questions of whether and how females perceive them. Filsinger, Braun and Monte [62] showed that the application of androstenone to females led to negative descriptions of males whereas the application of androstenol led to a description of males as being sexually attractive. It has been shown repeatedly that females either find the odor of androstenol to be attractive, or that the perception of this odor results in heightened female sexual arousal [63]. These results indicate that androstenol can induce positive, while androstenone induces negative emotions towards males, and suggest that androstenol may be a male pheromone that enhances attractiveness.

Maiworm [64] found that females perceive males positively under exposure to androstenol and negatively under exposure to androstenone. The finding that females are emotionally more affected by androstenone and androstenol than by control substances like rose water, led to the hypothesis that both androstenone and androstenol might be male pheromones. The role of androstenol in any hypothetical signaling system is clear, since it seems to promote female sexual attraction towards males. However, problems arise in attempts to determine the function of androstenone, which induces negative female emotions towards males. Besides, androstenone is the more prominent odor. Thus, the odor of androstenone will prevail, whereas the fresh sweat odor of androstenol disappears quickly. The fact that the production of attractiveness-enhancing androstenol inevitably produces the repellent androstenone makes it difficult to propose a definite advantage for the sender of such chemical signals compared to a non-sender. Arguably, a pheromone function of both substances is unlikely. If a male repels females with androstenone, this would contradict hypotheses, which assert male promiscuity on an evolutionary basis [65]. A less odorous male could out reproduce a more odorous male, simply because he could approach more females in less time and with less energy. This only holds if the costs of the more odorous androstenone production are greater than the benefits reached through producing the more sexually attractive androstenol. As androstenol oxidizes to androstenone the initial attractive signal becomes repellent. Because this effect takes place within 20 minutes [66], a less odorous male would be better off, since the repellent smell of androstenone is the long-term prevailing signal. If androstenone is a signal for females, then what advantages do more odorous males have?

The situation is further complicated by the fact that olfactory acuity and specificity is modulated by the menstrual cycle [67]. Both acuity and sensitivity to putative human male pheromones appears to peak at ovulation. Schneider [68] proposed that females have a higher olfactory acuity at ovulation and Doty, Snyder, Huggins and Lowry [69] showed a direct correlation between estrogen levels, LH levels, and heightened olfactory sensitivity. These changes in olfaction during the menstrual cycle extend well to the odor of androstenol, and in general to the more "musky" odors typical of males. Benton [70] showed that the application of androstenol to the upper lip of females made them rate their mood at the time of ovulation as more submissive. In contrast, Filsinger and Monte [71] found no clear link between sexual history and the perception of androstenone. However, the absence of a correlate might well be explained by research design that did not discriminate between females who take hormonal contraceptives and those who do not, since the estrogen component of contraceptive hormones can be expected to influence olfactory ability. Quite notable, however, is that nearly all studies have found that androstenone is rated negatively independent of the female cycle.

These mixed findings do not rule out the possibility that the female hormonal status may directly influence the perception of androstenone and androstenol. Maiworm [64] found that at different periods in the menstrual cycle androstenone and androstenol had different effects. Contrary to expectations, these substances showed no effect during the middle period

of the menstrual cycle, in which ovulation is possible. Rather, effects are greatest during the first period of the menstrual cycle. At the same time, both pleasant and less pleasant effects may be observed in the final period of the cycle.

Overall, results suggest the existence of two different olfactory signals: androstenol, which induces female attraction to males, and androstenone, which induces negative emotions in females. The functional assessment of such a positive-negative mood-inducing signal requires consideration of a set of evolutionary hypotheses.

### Pheromones and the battle of the sexes

Parental investment theory [65] predicts that females who look for long-term relationships should seek out and choose males who are ready to invest resources in their offspring. This minimizes female investment, but maximizes overall investment through added male assistance. In contrast, males are expected either to attempt copulation frequently with as many fertile females as possible, or to develop a pair bond. This helps to ensure that either a large number of offspring survive without significant paternal investment, or that paternal investment occurs primarily when another male does not father offspring.

According to this theory, it is adaptive for females and males to develop and use cognition in mate selection, which takes into account biological constraints. Thus, mate selection is a task of information processing, and evolution would favor individuals who were able to quickly and reliably process information that allowed them to make appropriate mating decisions. Adaptive cognition could be expected to lead to optimal decision-making under a wide spectrum of socioeconomic constraints. The existence of ubiquitarian sex specific differences in mate selection criteria [72] attests that male and female cognition is adapted to the biological constraints of mate selection. For example, neither males nor females consciously perceive human ovulation. Since ovulation is associated with a number of overt physiological and behavioral changes, it is surprising that it is not consciously detected. However, olfactory perception is one "unconscious" mechanism that is associated both with the physiological and behavioral changes of the menstrual cycle. Alexander and Noonan [73] and also Symons [74] have argued that concealed ovulation evolved because females need to trick males into forming a bond. Males who were not aware of optimal (i.e., ovulatory) female fertility would remain bonded to ensure impregnation and paternity. A female who provided cues to ovulation might risk losing paternal investment, due to paternal uncertainty and limited temporal reproductive interaction. This hypothesis implicates male fear of cuckoldry as an evolutionary pressure [65]. One evolutionary outcome would be that the female's ability to secure paternal care is affected by mechanisms that increase temporal aspects of the pair bond and enhance male confidence of paternity. Concealed ovulation is a mechanism that fits this hypothesis.

In contrast, Benshoff and Thornhill [75] as well as Symons [74] have proposed an alternative evolutionary scenario where concealed ovulation evolved to increase the chances of successful cuckoldry by females so they "can escape the negative consequences of being pawns in marriage games" [76]. Once monogamy is established, a female's best strategy would be to copulate outside the pair bond because she could then obtain superior genes with a certain expectation of paternal investment, and the increased survival of genetically superior offspring. These two hypotheses imply different impacts of heritable traits. If genes, which induce paternal care, were relevant for offspring success, a male paternity-securing function for concealed ovulation would be possible. If there were other traits not related to paternal care but relevant to offspring survival, then concealed ovulation would allow females to exploit occasional opportunities to mate outside the pair bond [77]. In both cases, overt cues of ovulation may be selected against because it would hinder the female's mating strategies [73, 78].

The second hypothesis has received considerable support from Bellis and Baker [79]. They conducted a study of 2708 females and found those 13.8% of 145 "unprotected" extra-pair copulations (EPC) occurred during the ovulatory phase of the menstrual cycle and were preceded in most cases by intra-pair copulations (IPC). EPCs were rarely followed by IPCs. According to his study EPCs, and thus, female infidelity peak at ovulation. The authors conclude that these results hint at female-induced sperm competition, which would be expected by the second hypothesis of the evolutionary function of concealed ovulation discussed above. It is still unclear what proximate mechanism or mechanisms cue female EPC at ovulation. The possibility has been raised [80] that conditioning might facilitate response to sexual stimulation should it first be encountered during the follicular phase. In this regard, pheromonal stimuli from a male, first encountered during ovulatory sexual intercourse, might help to neuroendocrinologically condition a female's sexual response. Similarly, pheromonal stimuli from a female, first encountered during ovulatory sexual intercourse, might help to neuroendocrinologically condition a male's sexual response, and help to ensure properly timed reproductive sexual behavior [81]. In any case, the assumption that concealed ovulation serves to deceive males

is common to all these theories. Supposedly, females deceive males about the fertile phase of the menstrual cycle to help ensure male parental investment, which yields an optimal number of offspring. Additionally, concealed ovulation helps females to monopolize reproduction, and – as a consequence - forces males to develop reproductive strategies for gaining access to ovulating females.

It is reasonable to expect male counter strategies would develop against deceptive attempts by females to conceal ovulation. Grammer [82] described a possible male counter strategy: the evolution of the androstenone-androstenol signaling system. In a study, 290 female subjects rated the odor of androstenone. A change in assessment throughout the menstrual cycle was found: ovulatory women found the scent of androstenone, the most dominant odor of the male armpit, to be more pleasant than on the other days of the menstrual cycle. These results suggest that there is a change in the emotional evaluation of males triggered by the reaction to androstenone. The findings support previous results by Maiworm [64], which were of borderline significance. Male body odor is usually perceived as unattractive and unpleasant by females but this evaluation changes when conception is most likely, and androstenone, minimally, becomes less aversive. This finding is underlined by the fact that anosmia to androstenone also varies with cycle. With optimal likelihood of conception, we find fewer anosmic females [82].

It seems possible that changes in the ability to perceive musky male odors during the menstrual cycle could also be a female strategy, although more data need to be gathered to support this hypothesis. However, the change in female attitude towards male body odor can be expected to impact mate selection and perhaps self-initiated copulations by females. With regard to the androstenol-androstenone signaling system, the situation for androstenol seems clear – it makes males more attractive to females. But females are less likely to act on this olfactory-based attraction unless fitter males produce more androstenol.

The situation is more complicated because producing androstenol inevitably produces androstenone. The androstenone production has a disadvantage because of its unpleasantness. Attractiveness-enhancing androstenol immediately oxidizes to androstenone, which repels females. A non-producing male could do quite well in a population of producers, because females would not be repelled by his body odor. Thus the attractiveness-enhancing component of the smell does not seem to be the main, or at least only, function of the signaling system. Regarding androstenone, the fact that ovulatory females assess its odor as more pleasant could be advantageous for males, as odorous males would be more successful when approaching ovulating females, rather than non-ovulating females. This suggests that males use a kind of passive "ovulation-radar" for the detection of concealed ovulation. The concept of ovulation radar fits our hypotheses about affective reactions. For example, a pheromone from the male elicits change in the hormonal milieu of the female. However, the female is not aware of this change, even though the hormonal change affects her behavior. Similarly, pheromones from the female elicit changes in the hormonal milieu of the male that affect his behavior by chemically signaling him that the female is ovulating. Females faced with an evolved male strategy to detect concealed ovulation would be likely to develop a counter strategy. One possible strategy could be to manipulate male cognition and thus adaptive male information processing in mate selection. Other mammalian males, including non-human primates (especially rhesus monkeys) perceive both estrogen-related reproductive fitness and ovulation through olfaction. Although normally motivated to copulate, when sexually inexperienced rhesus males were made anosmic, they showed no further sexual motivation, despite a powerful visual cue: the female's swelling [83]. Furthermore, rhesus males show no interest in ovariectomized rhesus females, presumably because ovariectomized rhesus females lose the odor characteristic of higher estrogen levels at ovulation. Rhesus males regain interest in copulation when the vaginal secretions from intact (e.g., estrogenized) females are applied to ovariectomized females. Studies on menstrual cycle fluctuations in the fatty-acid composition of women's vaginal fluids indicated that a similar type of estrogen-based chemical signaling system might also exist in humans [84, 85, 86, 87]. For example, human vaginal secretions have a composition that is similar to the vaginal secretions of female rhesus monkeys. The application to ovariectomized female rhesus monkeys, either of human, or rhesus vaginal secretions, induced similar activation of rhesus male sexual interest [88].

The behaviorally active fraction of the rhesus vaginal secretions - referred to as "copulins" - consists of volatile, short-chained fatty acids [89]. These same substances (i.e., the short-chained fatty acids: acetic-, propanoic-, butanoic, methylpropanoic-, methylbutanoic-, methylpentanoic acid) occur in human vaginal secretions, albeit in slightly different amounts [85]. In addition, the composition of these copulins varies during the menstrual cycle. Preti and Huggins [86] confirmed this observation. Cowley, Johnson, and Brooksbank [90] found that rhesus vaginal secretions change peoples' assessment of other people, and that the application of copulins tends to yield a more positive impression of females. Doty, Ford, and Preti [91] used a questionnaire to evaluate the intensity

and pleasantness of different vaginal fluids from a complete menstrual cycle. They found that odor at ovulation was both the most intense odor, and the least unpleasant odor.

Juette [43] synthesized female vaginal secretions ("copulins") and tested for their ability to act as chemical signals for males. Menstrual, ovulatory and pre-menstrual fatty acid compositions of copulins and an odorless water control were presented to 60 non-smoking male subjects for 25 minutes in a double-blind experiment. To control for changes in sex hormones that were induced by copulins, saliva-samples were taken before and after presentation. While inhaling, either a composition of copulins or a control, males rated pictures of females for attractiveness. Ovulatory fatty acid compositions stimulated male androgen secretion and changed the discriminatory cognitive capacities of males with regard to female attractiveness. Males became less discriminating. Therefore the copulins may act as putative human pheromones and provide beautifully balanced "strategic weapons" in the "battle of the sexes" and the "war of signals" resulting from sex differences in parental investment theory.

However, it is not necessary to view these "battles" or "wars" only from the perspective of parental investment theory. Mammalian pheromones ensure properly timed reproductive sexual behavior in many species. It should surprise no one that pheromones would be involved in properly timed human reproductive sexual behavior. If one examines what is known about the interaction between pheromones and our neuroendocrine system, there is support for the extension of mammalian olfactory communication to human behavior. First and foremost is the effect of mammalian pheromones on conspecifics of the opposite sex: the LH increase and reported ovulatory increase in male T, for example. Persky, Lief, O'Brien, Straus, and Miller [92] commented on the observed ovulatory increase in T levels of human males, and suggested that, somehow, the female was signaling the male that she had ovulated, and that he responded, like a male rhesus monkey with an increase in T. Morris, Udry, Khan-Dawood, & Dawood [93] replicated this work and described their findings as an unobserved event that causes increased intercourse. Though neither of these studies specifically mentioned human pheromones, affective reactions were present both in the male and in the female, and pheromones are the most likely cause of the affective reactions. For example, the increased T in the male can readily be linked to increased intercourse, whether or not the increased T was an observable event. Finally, Singh & Bronstad [81] showed that human males find the natural body odor of ovulatory females to be most pleasant, when compared to the natural body odor during other phases of the menstrual cycle. The male's hedonic rating of pleasant ovulatory odor; the increased T, and the increased intercourse, collectively offer significant support for the concept that chemical communication is more important to properly timed reproductive sexual behavior than is visual or other sensory input. If, for example, male canines were able to tell us that they preferred the scent of estrus odor, and estrus odor increased male T, we would readily explain the affective reaction of the "bitch in heat" which correlates with increased copulation.

Because sexual activity is not limited to the ovulatory phase of the menstrual cycle, human sexual behavior is considered to be more complex than that of other mammals who depend upon properly timed reproductive sexual behavior for species survival. There are other cues, besides chemical cues, that are involved. However, it is remarkable that many people consider visual cues to be more important than olfactory cues, when consideration is given for the mammalian mechanisms that ensure properly timed human reproductive sexual behavior.

### Pheromones as honest signals in mate selection

It is presumable that human scent, apart from the above-mentioned functions, could - like other cues in mate selection - also signal aspects of reproductive fitness. Several studies have found that bodily and facial symmetry play a role in attraction and thus in choice criteria for human mating. Symmetry is believed to signal developmental stability, which refers to an individual's ability to cope with genetic and environmental perturbations during early development. Recent research has focused on the significance of developmental stability as mate choice-criterion. Sex steroid hormone dependent human body odor could transmit information about an individual's developmental stability as an additional, redundant olfactory signal. Since olfactory and visual cues have different physiological roots, the signaling errors are likely to be uncorrelated. Thus, taking the information of both signals into account reduces the error and allows much more reliable mate choice decisions (see [94] for details).

Rikowski and Grammer [95] compared ratings of body odor, attractiveness, and measurements of facial and bodily asymmetry of 16 male and 19 female subjects. Subjects wore a T-shirt for three consecutive nights under controlled conditions. One group of opposite-sex raters then judged the odor of the T-shirts, and another group evaluated portraits of the subjects for attractiveness. Additionally, bodily and facial symmetry of the odor-donors were measured. Facial attractiveness and sexiness of body odor

showed a significant positive correlation for female subjects. In men, the situation was different. Positive associations between body odor and attractiveness and negative associations between odor and bodily asymmetry could only be found if female odor raters were in the most fertile phase (i.e., ovulatory phase) of their menstrual cycle. Thus, simply put, ovulatory women preferred the scent of symmetry.

This effect, replicated by Gangestad & Thornhill [96], could be explained by the above-mentioned female preference of androstenone around ovulation. Metabolic pathways suggest a link between α-androstenes and testosterone [97]. It is presumed that only individuals with high immunocompetence can afford the immune-suppressing effect of a high testosterone level [98]. Immunocompetence appears to correlate with high developmental stability [99]. Thus, human pheromones could indeed be regarded as honest signals for human mate choice based on the testosterone-immunocompentence-developmental stability link to pheromone production.

In humans, female olfactory preferences also seem to induce disassortative mating for components of the major histocompatibility complex (MHC) as is observed in other mammals [100]. In other words, olfactory cues may be able to reflect parts of an individual's genome, and body odor seems to influence female mate choice in order to find a partner who possesses fitting MHC-dependent immune system components. Simply put, ovulatory women seem to prefer the scent of genetic diversity. Indeed, both women who are not taking oral contraceptives, and men rate similar genetically determined odors as less attractive than dissimilar genetically determined odors. Thus, not only are men and women able to distinguish among genetically distinct, self versus non-self odors, they prefer the scent of non-self (i.e., genetic diversity) [101]. Men and women with shared markers of genetic diversity also select perfumes that may amplify body odor that is linked to their genetic diversity [102].

Johnston, Hagel, Franklin, Fink and Grammer [103] propose that male facial attractiveness is mediated by hormones, and generally support a hormonal theory of facial attractiveness dependent on the interaction between visually displayed hormone markers and the hormonal state of the viewer. There is no biological pathway that directly links visual input either to neuroendocrine function, or to the hormonal state of the viewer, and male and female visual systems are not sexually dimorphic. Accordingly, the means and biological mechanisms by which sexually dimorphic, hormone-dependent facial features become attractive have yet to be detailed. However, the olfactory pathways link the hormonal state of the "viewer" to chemical signals of reproductive fitness that correlate well with the degree of hormone-dependent, sexually dimorphic facial features. For example, higher T levels correlate with the visual appeal of a "stronger" jaw. The interaction of these visually displayed hormone markers of reproductive fitness and the effects of the hormones on pheromone production and distribution suggest that the effects of pheromones on reproductive neuroendocrine function might provide a critical, well-detailed, mammalian link between hormone-mediated facial signals and what we consciously perceive as facial attraction.

We would be remiss if we failed to address yet another aspect of what is most commonly believed to be visually perceived physical attraction: the waist-to-hip ratio (WHR) Sex steroid hormones control regional fat distribution [104], which interacts with reproductive control mechanisms. For example, fat tissue converts androgens to estrogens [105]. Circulating E levels appear to lower WHR, while circulating T levels appear to increase WHR, which is believed to signal reproductive fitness in women, and perhaps in men [106]. In addition, high levels of LH and FSH as well as estradiol levels are linked to lower WHR and to the earlier pubertal endocrine activity of females. However, the conscious or unconscious mechanisms linked to the perception of WHR and its link to physical attractiveness, have not been detailed. Presumably, these mechanisms exist cross-culturally, but they have defied explanation. The conditioning of visually perceived physically attractive WHR by association with steroid hormone-dependent chemical cues (e.g., human pheromones) seems to be a very likely explanation for the increased desirability of men and women whose weight and height are proportionate.

Each example above, of symmetry, genetic diversity, hormone-mediated facial attraction, and of WHR, has some as yet undetermined link to what we visually and consciously perceive to be attractive. The simplistic statement, we think about what we see and decide whether or not it is attractive, summarizes these examples. In contrast, other mammals don't think but somehow manage both to decide and to choose for genetic and hormonal traits of reproductive fitness.

In other mammals, links among olfactory acuity and specificity, genetically determined odors, and hormones and odor production provide clear examples of affective primacy, like the chemical cues that affect GnRH-directed hormone responses in limbic structures. This impact of these chemical cues on hormones allows for rapid responses, and accurate choices that do not require cognition. For example, unconscious odor cues link genetic diversity and all aspects of hormone-mediated mate choice. Affective primacy is best explained by mammalian, including human, olfactory acuity and specificity. The explanatory power of visual input pales by comparison.

## Conclusion

We have addressed several aspects of what is consciously perceived to be visual attraction both from an ethological and neuroendocrinological approach. In other mammals, the olfactory link among hormones, pheromones, and a conspecific's hormones and behavior would readily establish that visually perceived facial attractiveness, bodily symmetry, attractive WHRs, and genetically determined HLA attractiveness, are due to the neuroendocrinological conditioning of visual responsivity to olfactory stimuli. Yet, we have merely scratched the surface with regard to the pheromonal basis of human mate choice. As we can "see", the model of humans being primarily visual creatures may require some reconsideration. Human life and interactions are influenced by pheromones whether or not affect or effect are part of our consciousness. The affective hormonal reactions caused by olfaction and pheromones dominate social interaction, and these affective reactions may be the primary influence on social interactions.

Human pheromones have more potential than any other social environmental sensory stimuli to influence physiology and, therefore, behavior. Predictably, we will soon address other aspects of human attraction, and social confounds such as the paraphillias – and even sexual orientation in future discourse. Finally, we might even address the obvious question of how our everyday social lives and future human reproductive success will be affected by the modern striving for cleanliness and the reduction of natural body odor.

REFERENCES


1 Schaal B, Porter RH. "Microsmatic humans" revisited: The generation and perception of chemical signals. In: Slater P, editors. Advances in the Study of Behavior. New York: Academic Press; 1991. p. 135-199.
2 Burchell B. Turning on and turning off the sense of smell. Nature 1991; **350**:16–17.
3 Freedman DH. In the realm of the chemical. Discover 1993; **14**:69–76.
4 Dobb E. The scents around us. Sciences, November-December, 1989; 46-53.
5 Zajonc RB. Feeling and Thinking: Preferences need no inferences. Am Psychol 1980; **35**:151–75.
6 Ekman P, Friesen W. The repertoire of non-verbal behavior: Categories, origins, usage, and coding. Semiotica 1969; **1**, 49–98.
7 Zajonc RB. On the primacy of affect. Am Psychol 1984; **2**:117–23.
8 Niedenthal PM, Kitayama S. (editors) The Heart's Eye: Emotional Influences in Perception and Attention. New York: Academic Press; 1994.
9 Murphy ST, Zajonc RB. Affect, cognition, and awareness: affective priming with optimal and suboptimal stimulus exposures. J Pers Soc Psychol. 1993; **64**:723–39.
10 Seamon JG, McKenna PA, Binder N. The mere exposure effect is differentially sensitive to different judgment tasks. Conscious Cogn. 1998; **7**:85–102.
11 Schwanzel-Fukuda M, Blick D, Pfaff DW. Luteinizing hormone-releasing hormone (LHRH)-expressing cells do not migrate normally in an inherited hypogonadal (Kallmann) syndrome. Mol Brain Res 1989; **6**, 311–26.
12 Monti-Bloch L & Jennings-White C. personal communication: Kohl.
13 Cooper HM, Parvopassu F, Herbin M, Magnin M. Neuroanatomical pathways linking vision and olfaction in mammals. Psychoneuroendocrinology 1994; **19**:623–39.
14 Graham JM, Desjardins C. Classical conditioning: Induction of luteinizing hormone and testosterone secretion in anticipation of sexual activity. Science 1980; **210**:1039–41.
15 Kohl JV. Luteinizing hormone: The link between sex and the sense of smell? Paper presented at the Annual Meeting of the Society for the Scientific Study of Sex; 1992.
16 Kohl JV. Human pheromones: linking the nature and the nurture of human sexuality through reciprocity in olfactory-genetic-neuronal-hormonal-behavioral relationships. Poster presented at the International Behavioral Development Symposium: Biological Basis of Sexual Orientation and Sex-Typical Behavior; 1995.
17 Diamond M, Binstock T, & Kohl JV. From fertilization to adult sexual behavior. Hormones and Behavior 1996; **30**:333-53.
18 Dellovade TL, Hunter E, and Rissman, EF. Interactions with males promote rapid changes in gonadotropin-releasing hormone immunoreactive cells. Neuroendocrinology 1995; **62**(4), 385–95.
19 Kippin TE, Talianakis S, Schattmann L, Bartholomew S, Pfaus JG. Olfactory conditioning of sexual behavior in the male rat (Rattus norvegicus). J Comp Psychol 1998; **112**, 389–99.
20 Plaud JJ, Martini JR. The respondent conditioning of male sexual arousal. Behav Modific 1999; **2**:254–68.
21 Lalumiere ML, Quinsey VL. Pavlovian conditioning of sexual interests in human males. Arch Sex Behav 1998; **27**:241–52.
22 Jacob S, Kinnunen LH, Metz J, Cooper M, McClintock MK. Sustained human chemosignal unconsciously alters brain function. Neuroreport 2001; **239**:1-4.
23 Jacob S, McClintock MK. Psychological state and mood effects of steroidal chemosignals in women and men. Horm Behav 2000; **37**:57-78.
24 Vacarezza OL, Sepich LN, Tramezzani JH. The vomeronasal organ of the rat. J Anat 1981; **132**:167-85.
25 Morrison EE, Constanzo RM. Morphology of the human olfactory epithelium. J Comp Neurol 1990; **297**:1-13.
26 Moran DT, Jafek BW, Rowley III JC. Ultrastructure of the human olfactory mucosa. In: Laing DG, Doty RL, Breipohl W, editors. The Human Sense of Smell. Berlin: Springer –Verlag 1992. p 3-28.
27 Stoddart DM. The scented ape: the biology and culture of human odor. Cambridge University Press; 1990.
28 Moran DT, Jafek BW, Rowley III JC. The vomeronasal (Jacobson's) organ in man: Ultrastructure and frequency of occurrence. J Steroid Biochem Mol Biol 1991; **39**:522-45.
29 Monti-Bloch L, Grosser BI. Effect of putative pheromones on the electrical activity of the human vomeronasal organ and olfactory epithelium. J Steroid Biochem Mol Biol 1991; **39**:573-82.
30 Karlson P, Luscher M. Pheromones: a new term for a class of biologically active substances. Nature 1959; **183**:55-6.
31 Kohl JV, Francoeur RT. The Scent of Eros: Mysteries of Odor in Human Sexuality. New York. Continuum; 1995. p. 41.
32 Moss RL, Dudley CA. Differential effects of an luteinizing-hormone-releasing hormone (LHRH) antagonist analogue on lordosis behavior induced by LHRH and the LHRH fragment Ac-LHRH5-10. Neuroendocrinology 1990; **52**:138–42.
33 Levalle O, Zylbersztein C, Aszpis S, Aquilano D, Terradas C, Colombani M, Aranda C, Scaglia H. Recombinant human follicle-stimulating hormone administration increases testosterone production in men, possibly by a Sertoli cell-secreted nonsteroid factor. J Clin Endocrinol Metab 1998; **83**:3973–6.
34 Hoffman GE, Lee WS, Attardi B, Yann V, Fitzsimmons M. Luteinizing hormone-releasing hormone neurons express c-fos antigen after steroid activation. Endocrinology 1990; **126**:1736–41.

35 Michael RP, Bonsall RW, and Kutner M. Volatile fatty acids, "Copulins", in human vaginal secretions. Psychoneuroendocrinol 1975; **1**:153–162.
36 Michael RP, Bonsall RW, and Warner P. Human vaginal secretions: Volatile fatty acid content. Science 1974, **186**:1217–1219.
37 Craigmyle, MBL. The Apocrine Gland and the Breast. Chichester: Wiley; 1984.
38 Cohn BA. In search of human skin pheromones. Arch. Dermatol 1994; **130**:1048–1051.
39 Shehadeh N, Kligman AM. The effect of topical antibacterial agents on the bacterial flora of the axilla. J Invest Dermatol 1963; **40**:61–71.
40 Zeng X-N, Leyden JJ, Brand JG, Spielman AI, McGinley K, and Preti G. An investigation of human apocrine gland secretion for axillary odor precursors. J Chem Ecol 1992, **18**:1039–1055.
41 Stern K, McClintock MK. Regulation of ovulation by human pheromones. Nature 1998; **392**:177–9.
42 Berliner DL, Monti-Bloch L, Jennings-White, C, Diaz-Sanchez V. Functionality of the human vomeronasal organ (VNO): Evidence for steroid receptors. J Steroid Biochem Mol Biol 1996; **58**:259–65.
43 Juette A. Weibliche Pheromone – Wirkung und Rolle von synthetischen "Kopulinen" bei der versteckten Ovulation des Menschen. Diplomarbeit an der Universität Wien; 1995.
44 Grosser BI, Monti-Bloch L, Jennings-White C, Berliner DL. Behavioral and electrophysiological effects of androstadienone, a human pheromone. Psychoneuroendocrinology 2000; **25**:289–99.
45 Shinohara K, Morofushi M, Funabashi T, Kimura, F. Axillary pheromones modulate pulsatile LH secretion in humans. Neuroreport 2001;**12**:893–895.
46 Preti G, Wysocki CJ, Barnhart K, Sonheimer SJ, Leyden JJ. Male axillary extracts effect lutenizing hormone (LH) pulsing in female recipients. Poster presentation at the 23rd Association for Chemoreception Sciences Annual Meeting; 2001.
47 Dorfman RI. A system for evaluating the functional status of the adrenal cortex. Metabolism 1961; **10**:902–916.
48 Gower DB, Nixon A, Jackman PJH, Mallet AI. Transformation of steroids by axillary coryneform bacteria. Int J Cosm Sci 1986; **8**:149–58.
49 Gower DB, Holland KT, Mallet AI, Rennie PJ, Watkins WJ. Comparison of 16-Androstene Steroid Concentrations in Sterile Apocrine Sweat and Axillary Secretions: Interconversions of 16-Androstenes by the Axillary Microflora-a Mechanism for Axillary Odor Production in Man? J Steroid Biochem Mol Biol 1994; **48**:409–18.
50 Bird S, Gower DB. Axillary androstenone, cholesterol and squalene in men: preliminary evidence for androstenone being a product of bacterial action. J Steroid Biochem Mol Biol 1982; **17**:517–22.
51 Gower DB, Bird S, Sharma P, House FR. Axillary androstenone in men and women: relationships with olfactory acuity to odorous 16-androstenes. Experientia 1985; **41**:1134–6.
52 Jackman PJH, Noble WC. Normal axillary skin microflora in various populations. Clin Exp Dermatol 1983; **8**:259–68.
53 Van Toller C, Kirk-Smith M, Wood N, Lombard J, Dodd GH. Skin conductance and subjective assessment associated with the odor of androstenone. Biol Psychol 1983; **16**:85–107.
54 Cowley JJ, Brooksbank BWL. Human exposure to putative pheromones and changes in aspects of social behavior. J Steroid Biochem Mol Biol 1991; **39**:647–59.
55 Filsinger EE, Braun JJ, Monte WC, Linder DE. Human (Homo sapiens) responses to the pig (Sus scrofa) sex pheromone 5 alpha-androst-16-en-3-one. J Comp Psychol 1984; **98**:219–22.
56 Filsinger EE, Braun JJ, Monte WC. Sex differences in response to the odor of alpha androstenone. Percept Mot Skills 1990; **70**:216–8.
57 Kirk-Smith M, Booth DA, Carroll D, Davies P. Human social attitudes affected by androstenol. Res Comm Psychol Psychiat Behav 1978; **3**:379–84.
58 Hold B, Schleidt M. The importance of human odor in non-verbal communication. Z Tierpsychol 1977; **43**:225.
59 McClintock MK. Menstrual Synchrony and Suppression. Nature 1971; **229**:244–5.
60 Preti G, Cutler WB, Krieger A, Huggins GR, Garcia CR, Lawley RJ. Human Axillary Secretions Influence Women's Menstrual Cycle: The Role of Donor Extract From Women. Horm Behav 1986; **20**: 463–73.
61 Cutler WB, Preti G, Krieger A, Huggins GR, Garcia CR, Lawley RJ. Human Axillary Secretions Influence Women's Menstrual Cycle: The Role of Donor Extract From Men. Horm Behav 1986; **20**:474–82.
62 Filsinger EE, Braun JJ, Monte WC. An examination of the effects of putative pheromones on human judgments. Ethol Sociobiol 1985; **6**:227–36.
63 McCollough PA, Owen JW, Pollak EI. Does Androstenol affect emotion? Ethol Sociobiol 1981; **2**:85–8.
64 Maiworm RE. Influence of androstenone, androstenol, menstrual cycle, and oral contraceptives on the attractivity ratings of female probands. Paper presented at the Ninth Congress of ECRO; 1990.
65 Trivers RL. Parental investment and sexual selection. In: Campbell B, editors. Sexual selection and the descent of man 1871–1971. Chicago: Aldine; 1972. p. 136–136.
66 Labows JN, Preti G, Hoelzle E, Leyden E, Kligman A. Steroid analysis of human apocrine secretion. Steroids 1979; **34**:249–58.
67 Doty RL. Reproductive endocrine influences upon human nasal chemoreception: a review. In: Doty L R, editor. Mammalian olfaction, reproductive processes and behavior. New York: Academic Press 1976.
68 Schneider RA. The sense of smell and human sexuality. Med Asp Hum Sex 1971; **5**, 157–68.
69 Doty RL, Snyder PJ, Huggins GR, Lowry LD. Endocrine, cardiovascular, and psychological correlates of olfactory sensitivity changes during the human menstrual cycle. J Comp Physiol Psychol 1981; **95**:45–60.
70 Benton D. The influence of androstenol-a putative human pheromone – on mood throughout the menstrual cycle. Biol Psychol 1982; **15**:249–56.
71 Filsinger EE, Monte WC. Sex history, menstrual cycle, and psychophysical ratings of alpha androstenone, a possible human sex pheromone. J Sex Res 1986; **22**:243–48.
72 Buss DM. Sex differences in human mate preferences – Evolutionary hypothesis tested in 37 cultures. Behav Brain Sci 1989; **12**:1–49.
73 Alexander RD, Noonan KM. Concealment of ovulation, parental care, and human social evolution. In: Chagnon NA, Irons WG, editors. Evolutionary biology and human social behavior. Scituate: North Duxbury Press; 1979. p.436–36.
74 Symons D. The evolution of human sexuality. Oxford: Oxford University Press; 1979.
75 Benshoof L, Thornhill R. The evolution of monogamy and concealed ovulation in humans. J Soc Biol Struc 1979; **2**:95–106.
76 Gray JP, Wolfe LD. Human female sexual cycles and the concealment of ovulation problem. J Soc Biol Struc 1983; **6**:345–52.
77 Strassman B. Sexual selection, paternal care, and concealed ovulation in humans. Ethol Sociobiol 1981; **2**:31–40.
78 Daniels D. The evolution of concealed ovulation and self-deception. Ethol Sociobiol 1983; **4**; 96–87.
79 Bellis MA, Baker RR. Do females promote sperm-competition? Data for humans. Anim Behav 1991; **40**:997–9.
80 Slob AK, Bax CM, Hop WCJ, Rowland DL, Van der Werfften, Bosch JJ. Sexual arousability and the menstrual cycle. Psychoneuroendocrinology 1996; **21**:545–558.
81 Singh D, Bronstad PM. Female body odour is a potential cue to ovulation. Proc R Soc Lond B Biol Sci 2001; **268**:797–801.
82 Grammer K. 5 alpha-androst-16-en-3-one: A Male Pheromone? A Brief Report. Ethol Sociobiol 1993; **14**:201–8.
83 Michael RP, Keverne EB. Pheromones in the communication of sexual status in primates. Nature 1968; **218**:746–9.
84 Michael RP, Bonsall RW, Warner P. Human vaginal secretions: Volatile fatty acid content. Science 1974; **186**:1217–9.
85 Michael RP, Bonsall RW, Kutner M. Volatile fatty acids, "copulins", in human vaginal secretions. Psychoneuroendocrinology 1975;

**1**:153–63.
86 Preti G, Huggins GR. Cyclical changes in volatile acidic metabolites of human vaginal secretions and their relation to ovulation. J Chem Ecol 1975; **1**(3):361–76.
87 Waltman R, Tricom V, Wilson GE Jr., Lewin AH, Goldberg NL., Chang MMY. Volatile fatty acids in vaginal secretions: human pheromones? Lancet 1973; **2**:496.
88 Michael RP. Determinants of primate reproductive behavior. Acta endocrinol (Suppl) 1972; **166**:322–61.
89 Curtis RF, Ballantine JA, Keverne EB, Bonsall RW, Michael RP. Identification of primate sexual pheromones and the properties of synthetic attractants. Nature 1971; **232**:396–98.
90 Cowley JJ, Johnson AL, Brooksbank, BWL. The effect of two odorous compounds on performance in an assessment-of-people test. Psychoneuroendocrinology 1977; **2**:159–172.
91 Doty R L, Ford M, Preti G. Changes in the intensity and pleasentness of human vaginal odors during the menstrual cycle. Science 1975; **190**:1316–18.
92 Persky H, Lief HI, O'Brien CP, Straus D, & Miller W (1977) Reproductive hormone levels and sexual behavior of young couples during the menstrual cycle. In: Genne R, & Wheeler CC, editors. Progress in Sexology: Selected Papers from the Proceedings of the 1976 International Congress of Sexology. New York: Plenum Press. p. 293–310.
93 Morris NM, Udry JR, Khan-Dawood F, Dawood MY. Marital sex frequency and midcycle female testosterone. Archives of Sexual Behavior 1987 **16**:27–37.
94 Grammer K, Fink B, Juette A, Ronzal G, & Thornhill R. Female faces and bodies: n-dimensional feature space and attractiveness. In: G. Rhodes & L. Zebrowitz (editors). Advances in Visual Cognition. Volume I: Facial Attractiveness. Westport: Ablex Publishing; 2001.
95 Rikowski A, Grammer K. Human body odour, symmetry and attractiveness. Proc R Soc Lond B Biol Sci. 1999; **266**:869–74.
96 Gangestad SW, Thornhill R. Menstrual cycle variation in women's preferences for the scent of symmetrical men. Proc R Soc Lond B Biol Sci 1998; **22**:927–33.
97 Gower DB, Ruparelia BA. Olfaction in humans with special reference to odors 16-androstenes: their occurrence, perception and possible social, and sexual impact. J Endocrinol 1993; **137**:167–187.
98 Folstad I, Karter AJ. Parasites, bright males, and the immunocompetence handicap. Am Nat 1992; **139**:603–22.
99 Grammer K, Thornhill R. Human (Homo sapiens) facial attractiveness and sexual selection: the role of symmetry and averageness. J Comp Psychol 1994; **108**:233–42.
100 Wedekind C, Seebeck T, Bettens F, Paepke AJ. MHC-dependent mate preferences in humans. Proc R Soc Lond B 1995; **260**:245–9.
101 Wedekind C, Furi S. Body odor preferences in men and women: do they aim for specific MHC combinations or simply heterozygosity? Proc R Soc Lond B Biol Sci 1997; **264**:1471–9.
102 Milinski M, Wedekind C. Evidence for MHC-correlated perfume preferences in humans Behavioral Ecology 2001; **12**:140–149.
103 Johnston VS, Hagel R, Franklin M, Fink B, Grammer K. Male facial attractiveness: Evidence for hormone mediated adaptive design. Evol Hum Behav 2001; **32**:251–67.
104 Bjorntorp P. Hormonal control of regional fat distribution. Human Reproduction Suppl 1997; **1**:21–25.
105 Newmark SR, Rossini, AA, Naftolin, FI, Todd R. Gonadotropin profiles in fed and fasted obese women. American Journal of Obstetrics and Gynecology 1979; **133**:75–80.
106 Singh D. Adaptive significance of female physical attractiveness: role of waist-to-hip ratio. Journal of Personality and Social Psychology 1993; **65**:293–307.