MYTH OR SCIENCE?
THE POWER OF PHEROMONES

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Critical Appraisal

"Make your crush go crazy over you with only a couple of sprays of this pheromone cologne", "appeal to his desires" or "keep grabbing attention from women" are some of the promises seen in pheromone perfume adverts. An even bigger trust in the power of pheromones is seen at so-called "Pheromone Parties". The participating singles wear the same T-shirt the three nights before, bring it in a zip bag to the party and are given a number [1]. After a night of smelling the numbered t-shirts, matching singles can then decide to meet up. However, will we really meet our significant other through the smell of these specific molecules? And can pheromones really boost our sexual attraction? This article aims to explore the science behind such claims on pheromones in our mating behaviour and choice.

Pheromones (pherein: to transfer, hormon: that which excites) are often associated with sexual attraction and partner choice. However, the scientific origin of pheromones is not that sexy at all. In the 1930s, insect researchers were the first to distinguish chemical signals into endohormones and ectohormones [2]. Endohormones would be what we still call 'hormones' these days, such as the stress hormone cortisol and the sex hormone testosterone. These signalling molecules are secreted into the blood by specific glands [3]. The ectohormones entailed those 'hormones' that were secreted from the body of insects. A wide variety of functions has been ascribed to such ectohormones of insects, including the trailing of routes to their nest and alarming for predators [4, 5]. Only in 1959 were ectohormones renamed to pheromones and associated with sexual attraction by studies focusing on the silk moth [6]. The female silk moth produces Bombykol, a single molecule attracting the attention of every male moth around (Figure 1A) [7]. Darwin had already speculated on such a function of strong-smelling mammals before, stating that "the most odoriferous males are the most successful in winning the females" [8]. Yet, in contrast to the insect pheromones, only a few examples of pheromones have been described in mammals. This can in large part be attributed to the complex social behaviour of mammals, that is heavily intertwined with both context and past experiences [9]. Among the few compounds that have been linked to reproductive behaviour of mammals is androstenone. Male pigs produce and secrete androstenone, which then induces lordosis (mating readiness) in female pigs (Figure 1B) [10]. Androstenone can even be bought commercially by pig farmers to increase reproductive success. The finding of androstenone-like compounds under the armpits of humans led to wild speculations on human pheromones and even a market of pheromone perfumes [11]. But is there really a scientific basis to these perfumes claiming to increase our sexual attraction?

The definition of pheromones

To evaluate the role of pheromones in the mating behaviour and choice of humans, we first have to define what a pheromone is. The original definition of pheromones from 1959 states that pheromones are "substances secreted to the outside by an individual and received by a second individual of the same species, in which they release a specific reaction, for example, a definite behaviour or a developmental process" [6]. This definition was, however, tailored to insect biology, and redefinitions to apply the concept of pheromones to mammals have never reached consensus [12, 13]. Nevertheless, most of the proposed definitions include that pheromones (a) are comprised of one or only a few compounds, (b) are species-specific, (c) have well-defined behavioural or endocrine effects, and (d) are little influenced by learning [12]. Indeed, the androstenone example of pigs concerns only one compound and has a stereotyped response in the female pigs, independent of their past experiences [10]. However, the species-specific criterium would no longer hold if androstenone indeed has similar effects on human females.

The putative human pheromones

The difficulties with the definition of pheromones did not stop the commercialisation of androstenone-like compounds in human products. This commercialisation was further supported by over forty papers that claim physiological and psychological effects of these 'putative pheromones' [14]. On the other hand, a large body of scientific critique has been published as well. Opponents would ask remarkable but critical questions such as "are women attracted to the odours of male pigs?" and "are birth rates higher in countries with pig farms?" [12]. Criticisers point out the use of non-physiological concentrations, small sample sizes, statistical errors, positive publication bias, and experimenter phenomena (where subjects are primed to expect the desired effect) in the forty studies [12, 15]. Moreover, not everybody is able to smell androstenone and related steroids, and the persons who do often find them unpleasant [16]. All in all, the opponents state that these putative pheromones have never been shown to be biologically relevant in humans and, therefore, should not be called pheromones.

The quest continues

But if these androstenone-like compounds are not the human pheromones, could there be other human pheromones? The slightly disappointing answer is that we do not know yet; we are not even sure whether human pheromones exist. Nevertheless, many scientists anticipate that there are human pheromones yet to be identified [15]. Like many other mammals, we also undergo changes in smell-producing secretions as we go through puberty that could function in sexual behaviour, and we have a good sense of smell [17]. Our difficulty with abstract thinking about smells seems to be more a cultural than a biological deficiency, related to an underappreciation of smell in the Western world [18]. However, unlike statements of pheromone perfume adverts, we no longer have a functional 'second nose', the vomeronasal organ, that many other animals use to

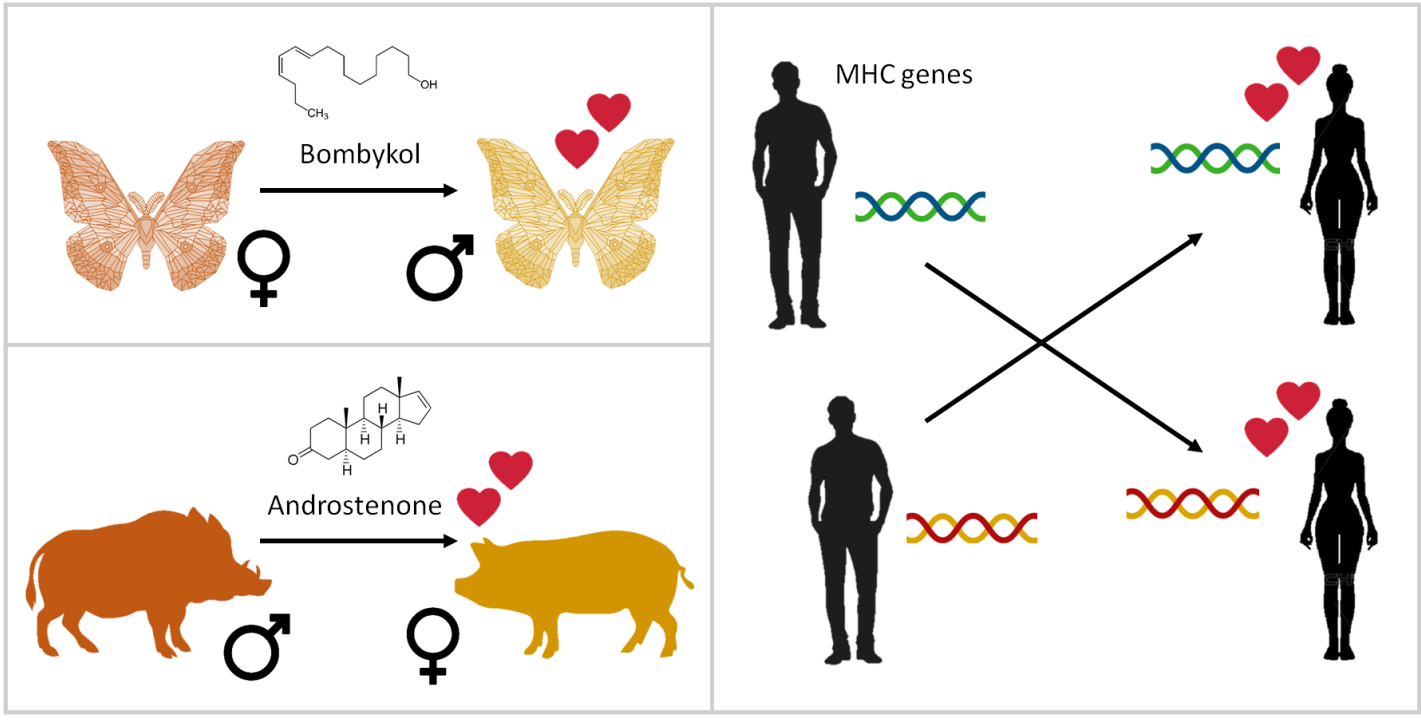

Figure 3: The role of smell in sexual behaviour and mate selection across the animal kingdom
In silk moths, females produce the molecule Bombykol to attract male moths (A). Male pigs produce the molecule androstenone, which induces mating readiness of female pigs (B). Humans may use the sense of smell in a more complicated way as women prefer the smell of men with MHC genes dissimilar to their own (C).

detect pheromones [19-21]. This vomeronasal organ is actually found within the nose and consists of sensory neurons that detect liquid organic compounds. However, in humans, this organ is believed to be vestigial, like our tailbone, and non-functional. If we would be able to (unconsciously) smell pheromones, we would have to detect them with our main olfactory system. Nevertheless, based on such reports in rabbits and sheep, we can conclude that, biologically speaking, there is no reason to think that humans do not use pheromone or pheromone-like molecules as social information [15]. However, the identification of human pheromones has proven to be a challenge, since up to this date, not one compound has been isolated that meets all the criteria of the pheromone definition. The difficulties in finding human pheromones lay in this strict definition of pheromones, the required study designs that are hard to translate from animal to human research, and the possibility that we may have lost our responses to pheromones [12, 15]. It is almost impossible to perform an adequately controlled trial, as human judgements of smell heavily depend on context and years of learning [9]. The continued quest for pheromones may, therefore, require adaptation of the pheromone concept to also address the individual differences in body odour production and perception.

Smelling T-shirts

Even though no human pheromones have been identified yet, we have a strong belief in the power of smell. Then where does this strong belief come from? Apart from pheromones, all kinds of non-pheromone smells affect our physiology and mood. Famous examples include the odours of rose oil to lower blood pressure, and lemon oil to enhance positive mood [22, 23]. Also, our own body odours can in fact influence others [24]. What we smell like is mainly determined by our diet, age, gender, and genetic make-up [9]. In addition, how we perceive the smell of others seems to vary between individuals [9]. A famous example of non-pheromone individual odours brings us to the 'sweaty T-shirt' experiments from 1995 [25]. Men were asked to sleep in the same T-shirt for two nights in a row and not to use odour-producing products. Women were asked to rate the scent of these T-shirts for pleasantness. Remarkably enough, women preferred the T-shirts of men that had variations in the *major histocompatibility complex* (MHC) genes different from their own (Figure 1C). These MHC genes, in humans also known as *human leukocyte antigen* genes, are important in the presentation of antigens to immune cells, and thereby play an essential role in the defence against pathogens [26]. The small but specific variations in these MHC genes determine which antigens will be presented, and thereby which pathogens can be attacked. The large individual differences in MHC variants can trouble organ transplantation with transplantation rejections, but also ensure a wide recognition of pathogens on a population level. On an individual level, MHC-dependent mate selection would allow women to choose an immunological complementary partner, such that their children would have a larger MHC diversity to recognise more pathogens. This would mean that humans use smell to select mates with favourable genes!

An immunological complementary mate

To better grasp this MHC-dependent odour selection, it is important to gain insight into the underlying biological basis. It seems that indeed, humans produce MHC-dependent odours [27, 28]. Although it remains unclear how exactly MHC molecules lead to specific odour profiles, trained rats can discriminate between the urine of people with different MHC genes [29]. Moreover, humans also show MHC-dependent odour perception [30]. Even the preferences in choosing our own perfumes seem to correlate with our MHC genotype, leading to speculations that perfume use has evolved as a means to advertise our own MHC type for potential mates [31]. Yet, the 'sweaty T-shirt' experiment from 1995 has been repeated over and over with only variable success [32]. Proponents of the theory state that the importance of MHC-dependent mate selection differs between study populations. Under certain contexts and in different geographic regions, MHC dissimilarity preferences may be stronger [27]. Opponents state that MHC-dependent mate selection

may have existed, as it is scientifically widely sustained in for example mice and rats, but that it is greatly overruled by cultural and social factors.

Conclusion

All in all, it seems that the term pheromone is confusing and often misused and that not one human pheromone has been conclusively identified yet [15]. But poor scientific validity of the pheromone perfumes does not mean that smell is not important in mating. Smells are actually very important in recognition and bonding, and possibly even in the finding of an immunologically complementary partner [32]. However, these smells are our individual smells and are not perceived the same by every person of the human species, and should therefore not be confused with or misnamed as pheromone molecules [15]. While the scientific quest for human pheromones continues, it would not harm you to take a good sniff of your potential future mates. In the end, a "Complementary Immune Gene Party" may not sound as sexy as a "Pheromone Party", but it might be a nice party after all.

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