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Y2K MAN AND PHEROMONAL COMMUNICATION

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Among animals chemical sensitivity plays an important role all life long while chemical messengers are involved in many behavioural activities. Pheromones are chemical substances that are released by animals in order to stimulate modifications in the neuroendocrine system of receiving individuals of the same species thus producing a physiological and behavioural response (Karlson and Lüscher,1959).
Pheromones are markers of animal territory and identity and as such are involved in reproductive processes. In mammals they do convey specific information concerning species, gender and physiological phases and identify the animal in order to trigger behavioural and neuroendocrine responses. Such responses do secure hierarchical position in animal groups as well as breeding chances.
Pheromones have influence on male and female sexual behaviour as well as on hormone activity (Marchlewska-Koj 1984). *Females* are able to identify sexually active males by odour. Production of these olfactory stimulants is controlled by gonadal hormones, mainly testosterone. In most species, males can distinguish the scent of females in oestrus or anoestrus phase.. In rodents, rabbits, cow, pigs and a few species of primates, pheromones produced by males can stimulate ovulation and induce oestrus in anoestrus adult females. Moreover a pregnancy lock due to male olfactory signals was observed in mice. That happens only when a recently inseminated female is exposed to a male genetically different from the first partner. Male pheromones stimulate neurohormonal system of female and inhibit secretion of prolactin. The level of progesterone decreases and blastocysts implantation fails. Abortion is followed by oestrus and next copulation can take place. This phenomenon allows females to select “the best” male and prevents inbreeding within a population.
Male mice are not only able to discriminate females in oestrus and anoestrus but also between females genetically different only for one locus. For example, male distinguishes by odour females with different MHC locus and always prefers her to copulate. (Yamazaki et al., 1988). This locus is involved in important immune response including graft rejection, cell-cell interaction and reaction to infection. The ability to discriminate locus helps to generate heterogenic offspring with better immunity.
Generally speaking, any animal is able to use olfaction to discriminate related from unrelated offspring.
In Proscimiae, well known is the ability to recognize subjects of the same species and to mark territory with pheromonal escrets. Many important studies on Primates were conducted by Michael and Keverne (1976, 1980,1983) who demonstrated existence and importance of pheromones even in animals that functionally should be considered “not-microsmatic”.

What about Humans? There are pheromone evidences in humans?
Discussing chemical communication and its role in Social interactions requires checking if the animal under examination is in condition to perceive, identify and work out the incoming chemical signals (like smells or any other perception) and at the same time to generate and transmit the same kind of signals.
In Man, despite the absence of well-differentiated specialized scent glands (except the axillae often characterized as a specialized scent gland) the odour of exocrine substances, enhanced by the enzymatic actions of resident bacteria, and several simple products resulting from bacterial degradation have been proposed as putative semiochemicals (e.g. a series of aliphatic acids of vaginal origin and androstenol-androstenone of mainly axillary origin). The local quality and quantity of exocrine substrates and the composition and density of resident microorganisms and microecological conditions (hair, pH, temperature etc.) generate a highly distinctive scent in different regions of the human body. The conclusion is that *Homo sapiens* is an efficient receiver and sender of chemical signals like all species with an active olfactory communication system (Stoddart,1988).
The secretion of semiochemicals in virtually any part of the body is basically dependent on endocrine activity, which in turn can be strongly affected by psychological-social events-and may be influenced by the environment in which the person live (Shaal et al. 1991). Some of this olfactory signals are perceived consciously and processed through the main olfactory system, some other (pheromones) may be processed unconsciously through the accessory olfactory system.

The main issue now is: *how does Man use pheromonal communication*?
Experiments have shown (Shaal B. 1980) that a mother can identify and discriminate the odour of her new born infant or other child of the same age by smelling an indument worn previously by the child. On the other side infant normally prefers axillary pads from their own mothers over pads from unfamiliar mothers. Therefore body odours can provide important information to identify persons in humans. (Porter et al. 1981, 1983, 1985, Russel et al. 1983). Also adults can recognise gender(73%) and individuality(34%) of non-related children (Ligabue Stricker and Tua, 1993).
But can chemical signals from one human be detected by another without being consciously experienced an odour?
Or might the chemical excrete have an immediate or delayed effects on the neuroendocrinological reproductive systems of other humans?
Tests on adults demonstrated that both males and females are able to identify gender, self odour and partner, simply by smelling T-shirts worn for some hours, without using any deodorants and perfume. Male odour is often described as musky, and female odour as sweet. (Russel, 1976, Hold e Schleidt 1982).
Moreover in women were found compounds similar to "copulin" detected in Primates (Michael et al. 1971, 1974). Copulin is a blend of aliphatic acids (acetic, propionic, butyric,, isovaleric, isocaproic.) usually present in vaginal fluids of healthy women. They are under hormonal control and their fluctuations during the menstrual cycle communicate the ovulatory period (Mc Clintock, 1971). As in Primates,in fact, near the middle of the menstrual cycle their concentration is higher. The use of hormonal contraceptives reduces the production of copulin and its fluctuations.
In Man the " musky " odour " (Kloek 1961), is due to metabolites of androstenone and androstenol, typically pheromonal substances produced by the testes and present with high concentration in urine, saliva and axillary sweat. The effect on social interactions is more constant and stronger than copulin one (Kirk-Smith 1978).. The higher intensity of the male odour compared to female odour is due to greater amounts of skin secretions and concomitantly more odorogenic microflora
As regards perception, women are more able to recognize biological odours than men, especially during ovulatory periods (e.g.. Exaltolide, synthetic lattone of 15-idrossipentadecanoic acid), inducing a correlation between olfactory and reproductive system and the existence, also in mankind, of pheromonal communication. (Le Magnen 1952).

And what about the perception related to age? it is possible to demonstrate parallelism between pheromone olfactory sensitivity and hormonal development?.
Olfactory tests on a group of babies by means of pheromone-like substances proved that, at 3 to 6 age, male and female responses to Osmopherine® (female odour like) are mostly identical and described as pleasant (69%) while strong differences were observed using Osmopherone® (male odour like) (Ligabue Stricker and Tua 1993).The interpretation of these results was that both gender recognized in the female synthetic pheromone the maternal odour stimulus, very pregnant and lovely for very young children. Additionally females recognized their own odour. On the contrary male synthetic pheromone is unknown and not yet sexual interesting for young females that described it as unpleasant (69%) but it is recognized like self odour by the young males (62% pleasant response).
Subsequent researches of Franca Ligabue Stricker of the University of Turin (1992,1996) demonstrated that with aging the valuation of pheromone perception varies and evolves accordingly with the physiological stages of life. This study was carried out on 2737 subjects (1394 females; 1343 males aged 6 to 21) by mean of the same "biologically relevant" substances used on babies..
The basic result was that an high percentage (about 60%, 6 years old) of the youngest cases showed *the same responses to the two pheromone-likes* (i.e. both pleasant, unpleasant, neutral or anosmy) with no significant difference between males and females. The percentage of similar responses decrease linearly with age: from 59.6% at 6, to 29.9% at 20. As regards the quality, the equal observed response is mostly "pleasant" in both sex especially until 13 (mean: 63.04% female; 64.23% male) but pleasantness decreases with age, faster in female than in male, and among subjects aged 14-21 we find an average 44.6% of equally pleasant response in male and only 23.1% in female.
Moreover, respecting the not equally perceiving subjects,. in females pleasantness response to female pheromone decreases linearly from 6 (69%) to 13 (12%) according with the increase of positive response to male pheromone (23% at 6, 63% at 13), afterwards it remains unchanged. On the contrary, males, until 13, do not show any significant difference in the perception of the two smells. Some olfactory and behavioural indecision was observed in age 14 to 21 yet.

These results can be explained assuming that the very high olfactory neutrality observed in youngest people coincides with reproductive neutrality and that the sensitivity to biological smells increases with their production and with hormone development which originates them. That's why females were found to distinguish pheromone-active smells earlier than males, as a consequence of getting earlier into puberty..
Since puberty and development of gonadotropins go hand in hand such results show that there is a connection between endocrine and olfactory systems (a relation that is fundamental for pheromone communication in animals).
In order to provide additional evidence to the above conclusion, F.Ligabue Stricker (1996) analysed pheromone perception of 160 subjects with hormonal problems related to reproduction (i.e. impotence, sterility, amenorrhoea etc.) and characterised by abnormal variations in haematic concentrations of gonadotropins and of sexual hormones. The olfactory responses were compared with those of healthy adults.
The results showed that especially males with pathological hormonal levels do show changes in pheromone perception: the positive response to Female odours actually reaches such a minimum value which was never found in healthy people of any age: 6.7%.
But the most interesting result was that differently from healthy control subjects, a very high percentage of persons with hormonal and sexual disorders appears anosmic towards pheromone-like substances.
The above researches confirm the strong interactions between olfactory, endocrine and reproductive systems. This physiological relationship might have been suspected indeed by Pathology where physicians already know the Kallman's syndrome (Kallmann et al. 1944), hypogonadic hypogonadim associated with anosmy due to same gene (Sparkes 1968).
Once the relationship between olfactory and hormonal system is accepted it is easier to understand and recognize social interactive phenomena on reproductive physiology.
Already on 1971 McClintock showed that the menstrual cycles of women who are room-mates or close friends tends to converge over time. It has to exist therefore some factor related to social closeness and interaction that shift the timing of the biological clock in the brain and determine a change in the ovulation and cycling. It seems therefore that the potential for chemical communication involving sexual function has been preserved in human during evolution.
What about partners pheromonal interaction?
Giving to well stabilised pairs synthetic pheromone for four months it was possible to demonstrate that balanced pheromonal overloads don't affect relations between partners, as happens if the chemical compound is given to only one of the partners (Ligabue Stricker 1994). So proving that happy paired couples are also pheromonal balanced.
What about relationship between histocompatibility antigens and pheromone communication ?
The last question is if, also in Man, as found on mice (Beauchamp *et al*., 1985; Lenington, 1994; Potts *et al*, 1991; Yamazaki *et al*, 1981), histocompatibility antigens can act as olfactory markers and help recognising the most suitable partner.
Selecting a companion bearing antigens of different type is likely to lead to an offspring which, being mostly heterozygous, shall show a wider immunitary response thus having a significant advantage in the selection process.
F.Ligabue Stricker and her team demonstrated that even in Man some relation exists between histocompatibility antigens and olfactory perception. In order to evaluate if in our species too there are biological factors which to some extent can influence the choice of the partner, studies were conducted on pairs with proven good fitness. Firstly antigenic difference between single and coupled people was analysed by comparing the frequency of class I HLA antigens found in 1454 coupled persons (727 pairs) against a control population of 133 singles.(Ligabue Stricker *et al.*1995*)*.The analysis showed that, in addition to a different antigenic frequency, singles and paired persons do have a different appreciation of pheromone substances, a difference which is even more evident in pairs whose components have different HLA antigens.
In order to achieve heterozygous offspring, a partner with different HLA antigens has to be selected in Man too, therefore it appears that such choice is likely to be influenced by a pheromone communication system which helps olfactory recognition of genetical identity.

The finding that humans can communicate by pheromones opens many possibilities to future investigation. Human pheromones might be used to interact with interpersonal information or more simply as a natural, alternative to control ovulation timing or as an aid to contraception

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