

## Human body odour, genetic variability, and sexual orientation: A reply to D. Oliva

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**Bernhard Fink<sup>1</sup> and Nick Neave<sup>2</sup>**

1. Ludwig-Boltzmann-Institute for Urban Ethology, University of Vienna, AUSTRIA.
2. Human Cognitive Neuroscience Unit, Division of Psychology, Northumbria University, Newcastle upon Tyne, UK.

*Correspondence to:* Bernhard Fink

Ludwig-Boltzmann-Institute for Urban Ethology,  
University of Vienna, AUSTRIA. e-mail: bernhard.fink@ieeee.org

*Submitted:* August 13, 2002

*Accepted:* August 13, 2002

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*Neuroendocrinology Letters* 2002; **23**:289–290

pii: NEL230402L02

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*Sir* – In a letter to the Editor, D. Oliva has raised the hypothesis that there might be a guiding thread through pheromone communication from unicellular organisms up to humans, which may serve as an explanation for human homosexual orientation. Although we do not want to reject this hypothesis in its entirety, as links between olfactory signals and human sexual orientation remain poorly understood, the argument seem to be too simplistic in light of evolutionary adaptationism and neurobiological research, and requires further investigation and discussion. Our reply should not be regarded as criticism, but rather to encourage further academic discussion.

Evolutionary theory suggests that humans have evolved adaptive mechanisms to increase genetic variability when searching for a mate. Within the mating game an individual should therefore seek honest signals of genetic quality in a potential partner. This ability is also essential for many other aspects of social behaviour, such as the maintenance of stable social groups, inbreeding avoidance, and the modulation of competitive relationships (see [1]). Several studies have suggested that the polymorphic Major Histocompatibility Complex (MHC) in animals - referred to in humans as the Human Leukocyte Antigen (HLA) - is under natural and sexual selection, and may provide such an honest cue, as its immunological function is the discrimination of self and nonself within the immune system.

In rodents it has been shown that body odour is significantly influenced by the MHC and that it can be discriminated by members of different species [2]. Wedekind *et al.* [3, 4] have shown that the HLA influ-

ences both body odours and body odour preferences in humans, as females rate body odours from males with differing HLA as more pleasant than odours from males with similar HLA's. Further, they report that scorings of pleasantness of body odour were correlated negatively with the degree of MHC similarity. Ober *et al.* [5] found that isolated human populations avoid mating with individuals with same HLA haplotypes than expected by chance. These authors consider this as evidence that the HLA or linked genes influence human mate choice. Consequently, MHC/HLA seems to affect body odour preferences by the degree of similarity or dissimilarity. According to evolutionary theory, the reason for such a conserved mechanism - which is not exclusively human - is the increase of heterozygosity in the progeny.

Of course, it has been proposed that similarities between the regulatory mechanisms governing yeast (*Saccharomyces cerevisiae*) mating-type genes and mammalian MHC genes exist [6] but as D. Oliva states, the fusion of two haploid cells, generating one diploid zygote, creates individuals with different genomic inheritance, and high genetic variability in the population. As for humans, the reason for sexual recombination is the better possibilities of adaptation to the environment. The suggestion of a common pattern in homosexual orientation instead of finding a heterosexual mate through olfactory communication from unicellular organisms up to humans requires further explanations on the possible evolutionary advantages such a mechanism.

From a neurobiological point of view we know that the olfactory systems maintains a significant propor-

tion of the genomes of many higher organisms that is devoted to encoding the proteins of smell [7]. However, the extent to which olfactory signals may contribute to homosexuality remains unknown. Some research has demonstrated that while females demonstrate hypothalamic activation when smelling an androgen-like compound, male hypothalamic activation occurs in the presence of an estrogen-like substance [8]. In other words, it seems that there is a different behavioural response in humans to sex-dissociated olfactory hypothalamic activation. If we theoretically extend this finding, a change in sexual orientation mediated by olfactory signals would mean that the brain of a heterosexual individual is designed in a way that it reacts to olfactory signals of the other sex but the brain of a homosexual individual is activated by same-sex odours. To our knowledge this interesting hypothesis has as yet, received no empirical support.

In humans, hypothalamic nuclei have been shown to have a neuronal density in homosexual men that is approximately half of that seen in heterosexual men [9, 10]. Additionally, homosexual men exhibit a positive Luteinizing Hormone (LH) response to administered oestrogen that is intermediate between women and heterosexual men (see for review [11]), However, Hendricks *et al.* [12] observed no significant differences between heterosexual and homosexual subjects in the likelihood of their exhibiting elevated LH concentrations in response to exogenous estrogens. Elias and Valenta [13] have postulated that anatomic differences in the anterior hypothalamic nuclei that regulate sexual orientation in males may lead to alteration in the gonadotropin releasing hormone (GnRH) pulse/frequency leading to a more female-type pattern of gonadotropin secretion in homosexual males. However, the question remains, what could be the reasons for such a change of density of the hypothalamic nuclei? As a consequence we have to ask when sexual orientation is determined during ontogeny?

There is considerable evidence that sexual orientation is hormonally encoded into the brain in fetal and/or neonatal life influenced levels of testosterone and oestrogen. Robinson and Manning [14] have shown that the ratio of the length of 2nd and 4th digits (2D:4D) is negatively related to prenatal testosterone and positively to oestrogen. They found that 2D:4D was lower in a sample of homosexual men than in sex- and age-matched controls. These data tend to support an association between male homosexuality and high fetal testosterone. Homosexual orientation has also been suggested to be possibly related to hemispheric functional asymmetry [15]. This may fit to the link between lowered 2D:4D in homosexuals and the cerebral lateralization effects caused by prenatal testosterone and estrogens [16, 17].

Taken together, prenatal neuroendocrine events are in all likelihood a factor in the development of human sexual orientation and functional brain asymmetries. However, the precise contribution of biological factors to the development of sexual orientation remains to be elucidated. It is not yet clear if biological factors

directly wire the brain so that this will support a particular sexual orientation but linking yeast and human sexual orientation seems to be at this stage too tentative. Therefore, it seems imperative to consider homosexual orientation not exclusively as biologically dependent, but rather as nature and nurture dependent neuroendocrine alterations of sexual brain organization. Only this may liberate homosexuals from pathological labelling and other forms of discrimination.

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