British Journal of Psychiatry (1994), **164**, 437–440

Editorial

Homosexual Orientation

The search for a biological basis

JOHN BANCROFT

The origins and determinants of sexual orientation, both heterosexual and homosexual, pose unanswered questions of genuine scientific interest. But the scientific enquiry they have engendered reveals a long history of distortion by moral and political considerations. This is an area, *par excellence*, where scientific objectivity has little chance of survival.

Whether homosexuality has a biological basis or not has been related to whether it is a 'sickness or a sin', and hence whether or not it should be tolerated. Thus, in the 19th century it was attributed first to insanity (e.g. Morrison) and later to a 'congenital anomaly' (e.g. Westphal and Lombroso). In the early 20th century, Hirschfeld put forward the view of a 'hormonal intersex'. Whether homosexual orientation can change, and hence be potentially susceptible to 'treatment', has been similarly compounded; evidence of its mutability has been on the one hand grounds for culpability, placing it back in the 'sin' category, and on the other hand grounds for imposing treatment. According to modern US law, immutability of sexual orientation may need to be proved if the homosexual is to be protected from discrimination (Green, 1988).

Relevant scientific enquiry comes and goes, partly reflecting new technologies and new ways of answering the questions. We are currently in the midst of such a wave, but while the technologies are new, and the explanatory models more sophisticated, the confounding issues of morality and the politics of repression are little changed.

Most research has been guided by two assumptions; firstly, that heterosexuality is the norm and hence requires no scientific explanation; secondly, that homosexuality is a form of 'intersexuality', lying biologically between the 'normal' heterosexual male and the 'normal' heterosexual female, which in its more modern version is seen to reflect a relative failure of sexual differentiation.

We can consider the research evidence under four headings: hormonal mechanisms; brain structure; neuropsychological function; and genetic factors. The first three headings all reflect the 'intersex' assumption; the genetic approach is theoretically more neutral, making no assumptions beyond the idea that genetic factors are in some way involved.

Hormonal mechanisms

The early idea that homosexuals are hormonally different (e.g. in their circulating levels of reproductive hormones) was abandoned some time ago. At least for gay men, the evidence was consistently negative or uninterpretable; the possibility that some lesbian women may be hormonally different remains on the agenda (Meyer-Bahlburg, 1979).

The emphasis switched to the early 'organisational' rather than later 'activational' effects of hormones. This derived not only from the impressive progress in understanding the biology of sexual differentiation, but from an assumption that the rodent provided a model that was relevant to the human. Sexual differentiation of the brain in rodents and other lower mammals is said to result from two effects of androgens during early (foetal or early postnatal) development: 'masculinisation', which is manifested in relatively gender-specific behaviour such as exploration, aggression of certain kinds, and mounting; and 'defeminisation', the absence of lordosis and the essentially female characteristic of the rodent's reproductive cycle, the 'positive feedback' response of the hypothalamus to oestrogen.

The overtly sexual manifestations of this process are clearly unhelpful in studying the human – lordosis has no primate counterpart, and our sexual motor activity cannot be classified in such discrete categories as 'mounting'! Any non-sexual behavioural effects of masculinisation will be hopelessly obscured by the prolonged intervention of psychosocial influences by the time that sexual orientation is apparent. So the researchers were left with the positive feedback response to an oestrogen challenge. Although early studies claimed evidence of 'partial positive feedback' in male homosexuals (Dorner *et al*, 1975; Gladue *et al*, 1984), alternative explanations were obvious (i.e. differences in testicular rather than hypothalamic response; Baum *et al*, 1985). In any case, this approach was doomed when it became clear that in primates, including humans, the positive feedback response is not 'organised' and structurally established in early development, as in rodents, but is a dynamic

consequence of the prevailing hormonal milieu (Gooren, 1986*a*,*b*). Once again, however, we are left with a slightly different picture in the female, where studies of congenital adrenal hyperplasia and exposure to diethylstilboestrol during foetal development have been found to be associated, in some cases, not with homosexual orientation *per se*, but with an increased likelihood of homosexual imagery or interest during adolescence and beyond (Ehrhardt *et al*, 1985; Hines & Collaer, 1993).

Brain structure

The notion of 'intersex' has to some extent retained momentum because of the continuing search for biological gender differences, another highly contentious and politically distorted scientific issue. There are salutary past examples of gender differences in brain structure; when intelligence was thought to be centred in the frontal lobes, men were found to have larger frontal lobes and smaller parietal lobes than women. When the centre of intelligence shifted to the parietal lobes, so the sex difference reversed! Now, the approach is less phrenological and more neuroanatomical, searching for discrete and often tiny structures which are sexually dimorphic.

Recent scientific interest was fuelled by the description of the sexually dimorphic nucleus of the pre-optic area of the rat (SDN-POA), substantially larger in the male than the female (Gorski *et al*, 1980). This has been found in other, but not all, species investigated. Its functional significance remains unclear, although there is certainly no reason to believe that it has anything to do with sexual preferences. A number of other hypothalamic structures have since been shown to be sexually dimorphic, again with no clear functional significance having been identified.

The various commissures connecting the two sides of the brain have also received considerable attention. The splenium of the corpus callosum has been reported as having a different shape in females, a finding which has not been replicated in a number of studies (see Hines & Collaer (1993) for review). The anterior commissure was found to be larger in women than men in one study (Allen & Gorski, 1992), a finding which awaits replication.

The evidence relating such possibly dimorphic structures to sexual orientation is still very limited and inconsistent (Byne & Parsons, 1993), although it has generated considerable media response. Swaab & Fliers (1985) described a SDN-POA in the human but did not find any relationship with sexual orientation. Others have not found this nucleus to be sexually dimorphic, preferring to call it the first interstitial nucleus of the anterior hypothalamus (INAH1) (Allen *et al*, 1989; LeVay, 1991). Both of these groups found another area, INAH3, to be sexually dimorphic, while LeVay (1991) also found this to be smaller in homosexual than heterosexual men. Swaab & Hofman (1990) found the suprachiasmatic nucleus, which is not regarded as sexually dimorphic, at least in size, to be larger in homosexual men. Allen & Gorski (1992) found the anterior commissure to be smaller in heterosexual men than in women and homosexual men.

The reader is entitled to be sceptical if not confused by these findings. There is either a lack of consistency or of replication. There are methodological problems. Numbers are inevitably small, and in most studies homosexual subjects have died of AIDS; the possibility that such structural changes could be a consequence of disease, such as AIDS, remains. But even if these findings are substantiated, and specific areas of the hypothalamus or elsewhere are found to be linked to sexual orientation, it is difficult to imagine what the nature of such a link would be. It is certainly unlikely that there is any direct relationship between structure of a specific area of the brain and sexual operation *per se*.

Neuropsychological function

One of the more interesting issues in the field of sex differences is the lateralisation of brain function (possibly linked to the commissural structural differences mentioned above). Language lateralisation and hand preference have both been studied, although the relationship between the two is not clear. In general, males show greater language lateralisation and females more consistent right-hand preference (Hines & Collaer, 1983). There is evidence that both female and male homosexuals are more likely to be left handed (McCormick *et al*, 1990). The proposed hormonal mechanism (i.e. increased exposure to androgen during early development) might explain the finding in lesbians; it is difficult to account for this tendency in gay men with a hormonal explanation. Once again, we have a finding which, if substantiated, does not help to explain biological determination of sexual orientation, except perhaps indirectly, either as a marker of other relevant processes, or via the effects of gender-related behaviour on sexual development.

Genetic factors

The possibility of a genetic factor in sexual orientation has been recognised since Kallman (1952) claimed 100% concordance for a sample of homosexuality in

monozygotic (MZ) twins and only 12% concordance in dizygotic (DZ) pairs. Since then numerous examples of discordant MZ pairs have been reported, but there has been a more or less consistent difference in concordance rates across studies, represented by the two most recent, with 52% MZ and 22% DZ concordance in males (Bailey & Pillard, 1991) and 48% MZ and 16% DZ concordance in females (Bailey *et al*, 1993). There is further evidence from family studies, although with male and female lineages probably distinct (Pillard, 1990). Such evidence has remained, while not conclusive, strongly suggestive of a genetic factor.

The most recent evidence has added substantial weight to the genetic case. Hamer *et al* (1993) first carried out a family pedigree study which indicated that the observed increase in homosexual orientation among male relatives involved, apart from brothers, mainly relatives on the mother's side; that is, maternal uncles or sons of maternal aunts. This suggested a sex-linkage and justified a linkage study using DNA markers on the X chromosome. They found a convincing correlation between homosexual orientation and the inheritance of polymorphous markers at the Xq28 subtelomeric region of the long arm of the X chromosome.

This was not, as the media chose to call it, a 'gay gene', but persuasive evidence of a genetic factor or factors, which in this section of the gay community at least, are sex linked. As previously, the genotype remains obscure. It could be of indirect relevance (e.g. relating to some behavioural or gender role 'phenotype' which interacts with other influences on sexual development). It is unlikely to be a gene which determines sexual orientation *per se*. In some respects, this field of enquiry is the most scientifically respectable of those considered – it is free of the dubious assumptions that have been central to the others. But in other respects it is potentially more open to abuse. While it is the hope of these recent researchers that demonstration of a genetic basis to homosexuality will lessen social repression of gay people, the fantasies that surround the remarkable developments in molecular genetics lead some to see scope for 'selecting out' homosexual offspring.

Conclusion

Without questioning the scientific interest of the issues raised, the continuing political need to distinguish between nature and nurture in this respect will serve to obscure the science. 'Sexual orientation' is, in any case, a peculiarly human concept. While homosexual behaviour is commonplace among other species, examples of exclusive homosexual preference are hard to find – except among humans. And even then there have been cultures whose language has no word for it (i.e. it is not an 'emic' concept). Furthermore, if such a characteristic was determined solely by biological factors, it would be inconceivable that no counterpart could be found in other species. And yet there is scant evidence, in other species, of sexual preference which is clearly innate and not the result of learning (Bancroft, 1989). It remains difficult, on scientific grounds, to avoid the conclusion that the uniquely human phenomenon of sexual orientation is a consequence of a multifactorial developmental process in which biological factors play a part, but in which psychosocial factors remain crucially important. If so, the moral and political issues must be resolved on other grounds.

References

ALLEN, L. S., HINES, M., SHRYNE, J. E., *et al* (1989) Two sexually dimorphic cell groups in the human brain. *Journal of Neuroscience*, **9**, 497–506.

—— & GORSKI, R. A. (1992) Sexual orientation and the size of the anterior commissure in the human brain. *Proceedings of the National Academy of Sciences, USA*, **891**, 7199–7202.

BAILEY, J. M. & PILLARD, R. C. (1991) A genetic study of male sexual orientation. *Archives of General Psychiatry*, **48**, 1089–1096.

——, ——, NEALE, M. C., *et al* (1993) Heritable factors influence sexual orientation in women. *Archives of General Psychiatry*, **50**, 217–223.

BANCROFT, J. (1989) *Human Sexuality and its Problems* (2nd edn). Edinburgh: Churchill Livingstone.

BAUM, M. J., CAROLL, R. S., ERSKINE, M. S., *et al* (1985) Neuroendocrine response to estrogen and sexual orientation. *Science*, **230**, 960–961.

BYNE, W. & PARSONS, B. (1993) Human sexual orientation. The biologic theories reappraised. *Archives of General Psychiatry*, **50**, 228–239.

DÖRNER, G., ROHDE, W., STAHL, F., *et al* (1975) A neuroendocrine predisposition for homosexuality in men. *Archives of Sexual Behavior*, **4**, 1–8.

EHRHARDT, A. A., MEYER-BAHLBURG, H. F. L., ROSEN, R. L., *et al* (1985) Sexual orientation after prenatal exposure to exogenous estrogen. *Archives of Sexual Behavior*, **14**, 57–77.

GLADUE, B. A., GREEN, R. & HELLMAN, R. E. (1984) Neuroendocrine response to estrogen and sexual orientation. *Science*, **225**, 1496–1499.

GOOREN, L. (1986*a*) The neuroendocrine response of luteinising hormone to estrogen administration in heterosexual, homosexual and transexual subjects. *Journal of Clinical Endocrinology and Metabolism*, **61**, 1158–1164.

—— (1986*b*) The neuroendocrine response of luteinising hormone to estrogen administration in humans is not sex specific but dependent on the hormonal environment. *Journal of Clinical Endocrinology and Metabolism*, **63**, 589–593.

GORSKI, R. A., HARLAN, R. E., JACOBSON, C. D., *et al* (1980) Evidence for the existence of a sexually dimorphic nucleus in the pre-optic area of the rat. *Journal of Comparative Neurology*, **193**, 529–539.

GREEN, R. G. (1988) The immutability of (homo)sexual orientation: behavioral science implications for a constitutional (legal) analysis. *Journal of Psychiatry and Law*, Winter, 537–575.

HAMER, D. H., HU, S., MAGNUSON, V. L., *et al* (1993) A linkage between DNA markers on the X chromosome and male sexual orientation. *Science*, **261**, 321–327.

HINES, M. & COLLAER, M. L. (1993) Gonadal hormones and sexual differentiation in human behavior: new developments from research on endocrine syndromes and studies of brain structure. *Annual Review of Sex Research*, **4**, 1–48.

KALLMAN, F. J. (1952) Comparative twin study of the genetic aspects of male homosexuality. *Journal of Nervous and Mental Disease*, **115**, 288–298.

LEVAY, S. (1991) A difference in hypothalamic structure between heterosexual and homosexual men. *Science*, **253**, 1034–1037.

MCCORMICK, C. M., WITELSON, S. F. & KINGSTONE, E. (1990) Left-handedness in homosexual men and women: neuroendocrine implications. *Psychoneuroendocrinology*, **15**, 69–76.

MEYER-BAHLBURG, H. F. L. (1979) Sex hormones and female homosexuality: a critical examination. *Archives of Sexual Behavior*, **8**, 101–119.

PILLARD, R. C. (1990) The Kinsey scale: is it familial? In *Heterosexuality/Homosexuality: Concept of Sexual Orientation* (eds D. P. McWhirter, S. A. Sanders & J. M. Reinisch), pp. 88–100. New York: Oxford University Press.

SWAAB, D. F. & FLIERS, E. (1985) A sexually dimorphic nucleus in the human brain. *Science*, **228**, 1112–1115.

—— & HOFMAN, M. A. (1990) An enlarged suprachiasmatic nucleus in homosexual men. *Brain Research*, **537**, 141–148.

John Bancroft, *MRC Reproductive Biology Unit, Behaviour Research Group, The Kennedy Tower, Royal Edinburgh Hospital, Morningside Park, Edinburgh EH10 5HF*

(*Received September 1993, accepted September 1993*)