

Sexual orientation and brain structures: A critical review of recent research

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This paper critically reviews three main studies that have sought to show that there are structural differences between the brains of male heterosexuals and homosexuals. These studies have focused on three regions of the brain, namely, the suprachiasmatic nucleus (SCN), the third interstitial nucleus of the anterior hypothalamus (INAH-3) and the anterior commissure (AC). This paper exposes a number of conceptual and methodological flaws in these studies and concludes by saying that the available evidence does not support the hypothesis that the brains of male homosexuals are structurally different from those of male heterosexuals.

A number of neuroanatomists and endocrinologists have hypothesized that the brains of homosexual and heterosexual men are anatomically different. This hypothesis is based on the idea that because homosexual men like heterosexual women are sexually attracted to men, they must possess a female-like brain. The brain structure hypothesis can also be viewed as a subset of Günter Dörner's prenatal-hormone hypothesis, which states that androgen deficiency during the critical period of fetal development feminizes the male brain, while androgen exposure masculinizes the female brain¹. But the idea that homosexuals are cross-gendered is not entirely new. Karl Ulrichs, the father of the homosexual rights movement, conceived of homosexuals as a distinct class of people in that they possessed the bodies of their biological sex but the minds of the opposite sex². In this paper I will critically examine three studies, which claim to have discovered anatomical differences in three different regions of the brains of homosexual and heterosexual men. These regions are: the third interstitial nucleus of the anterior hypothalamus (INAH-3), the anterior commissure (AC) and the suprachiasmatic nucleus (SCN).

The search for neuroanatomical differences

The existence of structural differences correlated with sexual dimorphism in the human brain has implicitly been presumed since the days of Aristotle. However, the

actual research into these differences can be traced back to the late 1970s, when Roger Gorski and his co-workers discovered a group of cells in the medial preoptic part of the rat's hypothalamus that was 5 to 6 times larger in volume in males than in females³. This sex difference was so clear, it could even be observed without the aid of a microscope. Gorski and his group named this cell group the 'sexually dimorphic nucleus of the preoptic area', or SDN-POA. This region of the hypothalamus has long been associated with general life functions such as eating, sleeping and reproduction. In rats, the SDN becomes sexually dimorphic as a result of perinatal hormone exposure. Investigations have shown that prenatal stress or castration of male rats on the first day of life reduces the volume of this nucleus permanently^{4,5}. Conversely, when newborn female rats are injected with tamoxifen (an anti-estrogen) the volume of their SDN-POA is decreased, suggesting demasculinization⁶. Although the hypothalamus in general is a crucial area for the regulation of sexual drive and behaviour, the exact function of the SDN is not known. However, a study by De Jonge *et al.*⁷ has shown that lesioning the SDN in male rats produces lordosis and affects their libido.

The human analogue of the SDN-POA is thought to be contained in one of the four interstitial nuclei of the anterior hypothalamus or INAH, but precisely which of the four is unclear. One morphometric study of what Swaab and Fliers considered to be the human SDN-POA (formerly known as the intermediate nucleus), revealed that the volume is more than twice in men as it is in women and contains twice as many cells in men⁸. In other words, like the rat SDN-POA, the human SDN-POA was found to be sexually dimorphic. It is important to note that no difference in SDN cell number was observed between homosexual and heterosexual men. This finding has been interpreted as refuting Dörner's hypothesis, which holds that male homosexuals have a female hypothalamus.

Nevertheless, the existence of sexual dimorphism in the SDN-POA is somewhat controversial, as two other groups of researchers have failed to confirm the initial report^{9,10}. Swaab has tried to account for this apparent anomaly by pointing out that the subjects in their own study and that of Allen *et al.* were drawn from two different age groups. He notes that while in Allen's study 70% of the adult subjects came from the age group in which SDN size difference is minimal (50 to 60 years), in their

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own study only 29% of the subjects came from that group¹¹. Unfortunately, this argument cannot be applied to LeVay's study, which also failed to find a sex difference in the volume of this nucleus in spite of the fact that his subjects belonged to the same age group as the subjects in Hofman *et al.*'s study.

Other regions of the brain that have been found to be sexually differentiated include the third and second interstitial nucleus of the anterior hypothalamus, corpus callosum, massa intermedia, amygdala, the bed nucleus of stria terminalis, the anteroventral periventricular nucleus and the anterior commissure. These findings have led some investigators to speculate that the same regions could also vary according to sexual orientation.

The suprachiasmatic nucleus

As already indicated, the brain structure hypothesis predicts that the size and volume of certain nuclei in the brains of homosexual men should differ from that of heterosexual men. The first attempt to test this hypothesis was made by Swaab and Hofman and involved a region of the brain known as the suprachiasmatic nucleus, or SCN in short¹². The SCN acts as the body's internal clock by generating circadian rhythms. It regulates and coordinates the body's daily rhythms such as sleep, temperature and the secretion of hormones.

Swaab and Hofman's study involved 34 postmortem subjects; 18 of whose sexual orientation was not known which served as a reference group, 10 homosexual men who had died of AIDS, 4 heterosexual males who had died of AIDS and 2 heterosexual women who had died of AIDS. The study reported that the SCN of homosexual men was larger in volume and number of neurons than that of heterosexual men. The SCN volume in homosexual men was 1.7 times as large and contained 2.1 times as many cells as the SCN in heterosexual men. Interestingly, the only difference that this study found between heterosexual men and heterosexual women in this area was one of shape. In heterosexual men, this region was shaped like a sphere while in heterosexual women and gay men it was more elongated.

Since the SCN also acts as a biological clock, Swaab and Hofman have hypothesized that sleep patterns of homosexual men should differ from those of heterosexual men. Support for this prediction comes from Hall and Kimura's study, which found that homosexual men had a rise-and-retire pattern that was more like that of heterosexual women than of heterosexual men. On average, homosexual men tended to get up and go to bed earlier than heterosexual men just like heterosexual women¹³. However, it is not clear why the sleeping patterns of homosexual men should resemble those of heterosexual women given that the size of the SCN itself is not sexually dimorphic.

Swaab and Hofman's study can be criticized on both methodological and conceptual grounds. In the first place the researchers relied on hospital records to arrive at the sexual orientation of the experimental subjects. The investigators had no access to the subjects' own assessments of their sexual orientations or to the history of their same-sex or heterosexual contacts. Assessing an individual's sexual orientation is a complicated affair and sexologists have been trained to deal with this. We do not know how the hospital workers assessed the sexual orientation of these subjects when they were alive but it is unlikely that a sexual orientation scale was used. Since most of the experimental subjects had died of AIDS, the hospital records may only have indicated how the patients acquired the virus, e.g. through same-sex contact, heterosexual contact or intravenous drug use. This kind of information can only suggest a behavioural rather than a dispositional account of sexual orientation and is therefore not very helpful. Evidence of sexual relations with members of the same gender is not a suitable criterion for assuming homosexuality since some heterosexuals may engage in homosexual relationship due to situational non-availability of members of the opposite sex, as happens in monasteries, boarding schools and prisons.

Another major difficulty with this study is that although the homosexual and the heterosexual subjects died of opportunistic infections arising from AIDS, they were not matched for clinical diagnosis. In fact, only one set of subjects were diagnosed as suffering from the same type of illness, i.e. cytomegalic infections. The rest were diagnosed as suffering from different combinations of illnesses. This might have contributed to the SCN differences that Swaab *et al.* reported. It is also important to note that, although the SCN is located within the hypothalamus, which is intimately involved in sex hormones and sexual behaviour, the SCN is not known to play any direct role in sexual behaviour. It is therefore difficult to understand its relationship to sexual orientation or to see any significance in Swaab *et al.*'s findings.

Some critics have also suggested that homosexual behaviour may actually have increased the neuronal number in the SCN of the brains of the homosexual men that Swaab *et al.* studied. This hypothesis is not completely implausible. Laboratory experiments on rats have shown a close correlation between the size of the sexually dimorphic nucleus and the level of sexual activity. Until brain tissue from homosexual men dying of other causes becomes available, this possibility cannot be completely ruled out. Also, at the moment, it is not possible to test whether measuring the SCN in life could allow one to predict future sexual orientation. Another important point to note is that the size of the SCN did not vary with sex. The cell number in the SCN of both heterosexual men and heterosexual women was the same and this contradicts Dörner's hypothesis that homosexuals have an intersexed brain.

The third interstitial nucleus of the anterior hypothalamus

LeVay's research into the brain differences of homosexual and heterosexual men was motivated by the work of Laura Allen, a neuroanatomist in Roger Gorski's laboratory. Allen had identified four small groups of neurons in the anterior portion of the hypothalamus, which she called the interstitial nuclei of the anterior hypothalamus (INAH) 1, 2, 3 and 4 (ref. 14). This study had shown that INAH-3 and INAH-4 were sexually dimorphic in human beings. They were significantly larger in men than in women. LeVay hypothesized that INAH-2 and/or INAH-3 were large in individuals sexually oriented toward women (heterosexual men and homosexual women) and small in individuals sexually oriented toward men (heterosexual women and homosexual men)¹⁵. The study consisted of forty-one cadavers of which nineteen were self-described gay men, all of whom had died of AIDS; sixteen presumed heterosexual men, six of whom had died of AIDS and were intravenous drug users, and six presumed heterosexual women, one of whom had died of AIDS. It is important to note that there was no brain tissue from homosexual women available. LeVay reported that the INAH-3 was half the size in women and homosexual men as it is in heterosexual men. In other words, in addition to finding that INAH-3 was larger in heterosexual males than in heterosexual women, he also found that it was smaller in homosexual men than in heterosexual men. He could not find any differences between the INAH-1 of heterosexual and homosexual men.

Two recent studies have partly corroborated LeVay's findings by showing that INAH-3 occupied a significantly greater volume and contained significantly more neurons in males than in females^{16,17}. However, it is important to note that the size differential was not as large as that reported by LeVay in his 1991 paper. Like LeVay, Byne *et al.* postulate that the sex differences in the human INAH3 may partly depend on sex differences in developmental exposure to gonadal hormones but he also points out that early experience can influence brain structure and that major expansion of the human brain occurs post-natally. In the second study, Byne did not find any difference within INAH-3 based on sexual orientation. However, this nucleus did occupy a smaller volume in homosexual men than in heterosexual men as LeVay had predicted¹⁸.

On the surface, LeVay's findings might appear to offer strong evidence in support of the biological research program. However, closer examination reveals that there are major conceptual and methodological flaws, which weaken the study's conclusions. In the first place, subjects were drawn from a small, highly selected and unrepresentative sample consisting mainly of AIDS patients. A larger sample will be required for a correlation between INAH-3 and sexual orientation to be established.

It is important to note that LeVay did not verify the sexual orientation of his subjects. The heterosexual sub-

jects were assumed heterosexual on the basis of the numerical preponderance of heterosexual men in the general population. Those subjects who did not die of AIDS were assumed (in the absence of evidence to the contrary) to be heterosexual. This, obviously, was a major flaw in scientific method. It is also important to note that LeVay assumed that all the men who died from AIDS but whose sexual orientation was not indicated in the medical records were heterosexual. Again this was a wrong assumption to make given that when this study was carried out, AIDS was confined to homosexual and bisexual men. It is almost certain that some of the men who died from AIDS and whom LeVay classified as heterosexual were in fact homosexual. Furthermore, LeVay failed to take into consideration the complexity of how sexual orientation is variously defined and experienced in the course of an individual's lifetime and across historical periods and cultural contexts. With regard to the brain tissue of the 'homosexual' subjects, he relied on hospital records to determine the subject's sexual orientation. He made no effort to find out how the sexual orientation of these subjects was determined. And since all the brain tissues studied were obtained from cadavers, there was no way that LeVay could have used a sexual orientation scale (such as the well-known seven-point rating scale developed by Kinsey) to determine the range or extent of the experimental subjects' sexual orientation. Furthermore, by adopting a bipolar view of sexual orientation, LeVay eliminated the possibility of a person with a sexuality that is neither heterosexual nor homosexual.

More importantly, some of the individuals that LeVay identified as homosexual had an INAH-3 that was larger than the average size of the INAH-3 of the heterosexuals and some of the heterosexuals had an INAH-3 that was smaller than that of the homosexual men. In other words, the differences were statistical rather than absolute. What this in essence means is that although the two groups considered as groups showed some clear differences, one could not tell an individual's sexual orientation by simply looking at his hypothalamus. In other words, if all that we know about LeVay's subjects is INAH-3 size, we cannot predict whether they are heterosexual or homosexual. LeVay also does not give a satisfactory explanation of why the only bisexual subject in the study had an INAH-3 that was the same size as the heterosexual subjects.

It is also noteworthy that all the tissue processing as well as anatomical measurements and statistical tests in this study were carried out by one investigator. A double blind approach would have been more appropriate since it is methodologically superior. This, as Byne says, is the standard practice even in animal work¹⁹. Moreover, the INAH-3 is quite small and it is questionable whether it can be accurately measured considering that it is made up of the same type of cells as the surrounding tissue. Indeed, scientists disagree on the question of whether this

nucleus should be measured by its volume or by the number of neurons. Swaab, as quoted in Marshall, argues that the results of LeVay's study could have been stronger had he counted the number of cells within INAH-3 instead of just measuring the volume²⁰. This, he says, would have gone a long way in ruling out errors that may have been caused by swelling and shrinkage.

A more profound objection to the findings of LeVay's study is that all homosexual subjects had died from complications arising from AIDS, but most of the control group of heterosexual men had died of other causes. People with AIDS are known to suffer from testicular dysfunction and this may directly affect their brains²¹. A related point is that some of the drugs used to treat opportunistic infections associated with AIDS may have lowered the level of testosterone in the bloodstream of the study subjects and this could have had an effect on the size of the INAH-3 (ref. 22). What this means is that the differences in the size of INAH3 that LeVay observed may actually have been caused by endocrine imbalances associated with AIDS. Research by Deborah Commins and her co-workers has shown that the size of the SDN-POA of Mongolian gerbils, which is thought to be analogous to INAH-3 in humans, varies with the level of the circulating testosterone²³. It is also noteworthy that when this study was carried out, those who contracted AIDS through homosexual intercourse tended to receive better medical care than those who contracted the disease in other ways such as intravenous drug use. What this in essence means is that the homosexual patients may have lived longer than non-homosexual patients. This may have affected the hypothalamic structures differentially.

LeVay has countered some of these objections by pointing out that: (i) The INAH-3 size difference was apparent even when comparing homosexual men with heterosexual AIDS patients; (ii) the volumes of the other nuclei (INAH-1, 2 and 4) were not affected by AIDS and (iii) there was no correlation between the volume of INAH-3 and the length of survival from the time when the subjects were diagnosed with AIDS. (If AIDS had an effect on this nucleus, those who had suffered from the disease longest should have had a smaller INAH3 than those who did not.) These may appear to be strong arguments in defence of the study. However, taking into account that the number of heterosexuals who died of AIDS was very small, it is still possible that the observed differences in the size of INAH-3 resulted from complications associated with AIDS. Furthermore, LeVay's findings are partly contradicted by William Byne's study, which found that AIDS significantly influenced the volume of INAH-1 in both heterosexual men and women (the nucleus was 8% larger in heterosexual men and women with AIDS relative to individuals who did not have AIDS)²⁴. Interestingly, the other three INAH were not influenced by the HIV status of the study subjects, which makes LeVay's findings difficult to interpret.

Some critics have gone on to postulate that the length of the time between death and autopsy may have affected the hypothalamic structures that LeVay studied. It is also important to note that LeVay based his study on the assumption that the human INAH-3 was essentially the same as the SDN-POA in rats yet, as mentioned previously, the SDN-POA does not play a critical role in male-typical behaviour in rats although it is located in area that is associated with sexual behaviour. It is not clear whether it is INAH-3 or INAH-2 that actually corresponds to the SDN-POA of the rat²⁵.

On a more theoretical level, one could argue that even if LeVay was able to establish a correlation between homosexuality and INAH-3, he did not establish a causal connection. It remains to be proven that the enlarged INAH-3 was the cause rather than the result of altered sexual orientation. Indeed, we do not have any proof that the size of INAH-3 has any causal effect on sexual orientation, heterosexual or homosexual. LeVay himself has admitted that the results of the study do not allow one to decide whether the size of the INAH-3 in an individual is the consequence or the cause of that individual's sexual orientation. It is possible that the enlarged INAH-3 that LeVay observed in the brains of homosexual men was in fact the result rather than the cause of homosexual behaviour. As Harrison *et al.* explain, 'the promiscuous behaviour and associated lifestyle likely to have been common among the homosexual men who die of AIDS may have caused the shrinkage of the INAH-3 (ref 26). This possibility cannot be completely ruled out. Brain's neural networks are known to reconfigure themselves in response to certain experiences. For example, research has shown that when blind people learn Braille, the area of the brain that controls their reading finger becomes more active and enlarged²⁷. As another example, Eleanor Maguire and her co-workers at the University College London have shown that the hippocampus (a region of the brain involved in navigation and memory) of licensed London taxi drivers is larger compared with that of other people²⁸. The effect of behaviour on selected brain cells has also been demonstrated in studies of cichlid fish²⁹. Research has shown that specific cells in the preoptic area of the brains of a male cichlid become enlarged when it acquires territory after dominating others. However, these particular neurons shrink in size when the same male loses its territorial status. Thus it is possible that differences in brain structure between homosexuals and heterosexuals that LeVay observed were caused by the frequency of sexual activity. Indeed, a number of studies have shown that homosexual men are sexually more active than heterosexual men^{30,31}.

The anterior commissure

Shortly after the publication of LeVay's INAH-3 findings, Allen and Gorski reported another difference between the

brains of homosexual and heterosexual men in another part of the brain known as the anterior commissure (AC)³². The anterior commissure is one of the two clusters of nerve fibers that connect the two hemispheres of the brain. It has been found to vary according to sex. The other commissure is known as the corpus callosum. The exact function of the AC is not known but it is unlikely to be directly involved in sexual behaviour.

An earlier study by Allen *et al.* had shown that the anterior commissure is sexually dimorphic³³. This nucleus was found to be 12% or 1.17 mm larger in females than in males. The results of this study led Allen and co-workers to hypothesize that the AC is also dimorphic according to sexual orientation. When Allen and Gorski compared the size of the structure in homosexual and heterosexual men, they found that it was larger in the homosexual men than in heterosexual men. The size of AC of the homosexual men was found to be 18% larger than in heterosexual men and 34% larger than in heterosexual women. This study supported the hypothesis that factors operating during the critical period of an individual's development 'differentiate sexually dimorphic structures and functions in a global fashion'³⁴. As LeVay has noted, this study seems to strengthen his earlier finding that the brains of homosexual and heterosexual men are indeed different³⁵.

This study suffers from many of the problems affecting LeVay's study. In the first place, the researchers relied on autopsied brains, many of them from men who had died after a long period of being infected with AIDS. It is noteworthy that 24 out of the 30 homosexual subjects had AIDS while only 6 of the 30 heterosexuals died of AIDS. Although deliberate effort was made to exclude the brains of all persons who showed any evidence of pathology affecting the brain tissue, critics have pointed out that AIDS could cause subtle brain pathologies that might not be easily detected³⁶. Moreover, as with LeVay's study, Allen did not obtain adequate information on the sexual background of his subjects and relied on medical records to determine the sexual orientation of the subjects. We do not know how the health workers who were attending to these subjects as patients arrived at the conclusion that they were homosexual. Was it because they contracted AIDS through homosexual contact? How were they rated on the Kinsey sexual orientation scale? It was not possible to verify the sexual orientation of these subjects since they were all dead. It is also noteworthy that the 'heterosexuals' were classified as heterosexual if the hospital records did not indicate otherwise. Again, as with LeVay's study, given that homosexuality is a stigmatized trait, it is likely that some of the patients who were classified as heterosexual were in fact homosexual. Anticipating this criticism, Allen asserts that erroneous classification is likely to have decreased the chances of observing significant differences rather than resulting in apparent non-existent differences. However, one could

also argue that the significant size differences that were observed in spite of the misclassification may actually be an indication that even within each group the variation in the size of the AC was very big. What this would imply is that differences in the size of the AC might not be very helpful in distinguishing homosexuals from heterosexuals.

A related point is that male and female subjects were classified as heterosexual when the medical records did not indicate homosexual orientation. It is not clear whether those subjects that Allen *et al.* classified as heterosexual (at least the ones who died of AIDS) were ever asked to state their sexual orientation. If this was done, why was the sexual orientation not stated in the medical records?

As already pointed out, there is no proof as yet that the anterior commissure is directly involved in regulating sexual behaviour. The only possible connection comes from the observation that homosexual men are much more likely to be stutterers, left-handed and dyslexic than heterosexual men and these conditions are related to the two brain hemispheres that are joined by the AC³⁷⁻³⁹. However, this possible connection is yet to be fully explored.

It is also important to note that there was considerable overlap between the AC sizes of the two groups. The sizes of the AC in 27 of the 30 homosexual men in the study were within the range of sizes found among the 30 heterosexual men in the control group. This made it difficult to determine whether a given brain specimen was from a homosexual or heterosexual male individual. Again, as with LeVay's study, the homosexual men in this particular study may have had a smaller anterior commissure as a result of years of action peculiar to a homosexual lifestyle, rather than the structure of the AC causing them to be homosexual. Another possibility is that there is no causal connection between sexual orientation and the size of the AC, but both co-vary under the influence of some third, unknown variable. Allen's hypothesis has been contradicted by two separate studies, the first by Demeter *et al.*⁴⁰ who found the AC to be larger in males than in females and a more recent one by Lasco *et al.*⁴¹ who failed to detect any variation in the size of the AC with either sex or sexual orientation. Studies in rats have also produced discrepant results regarding possible sexual dimorphism of the AC^{42,43}. The contradictory nature of these findings does not allow us to conclude that the size of the anterior commissure can be used to distinguish male homosexuals from heterosexuals.

Summary and conclusion

We have seen that although an array of evidence has been adduced in support of the brain structure hypothesis, this

evidence is riddled with inconsistencies and the studies designed to test this hypothesis suffer from methodological weaknesses that prevent us from concluding that sexual orientation is determined by the brain. Furthermore few of these studies have been successfully replicated. The results of these studies are also open to different interpretations. However, even if these studies are successfully replicated, it will not justify drawing extravagant conclusions. As already argued, establishing a distinction in the brain structures of homosexuals and heterosexuals is not the same as establishing a cause. The direction of causation may be difficult to establish because behaviour both affects and is affected by brain structure and function. In any case, our current understanding of the brain is inadequate to explain how such quantitative differences could account for such a complex phenomenon as homosexuality. Besides, there need not be a causal connection between sexual orientation and the brain structures in question. The two may be caused by a third variable such as a developmental event during gestation or early life. It is also important to note that the brain structure hypothesis is based on the questionable presumption that homosexual men more resemble females than males, and that therefore one should expect to find a female brain in a male homosexual. This supposition, as a review of human sexual history reveals, is culture bound and inadequate. In some societies, those with predominantly same-sex desires were considered the 'most manly of men and womanly of women'¹⁹. Among the Sambia of the highlands of Guinea and the ancient Greeks, for example, homosexual relations between men was regarded as perfectly compatible with masculinity.

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