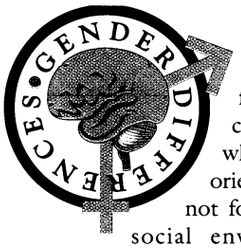
Is Homosexuality Biological?

New work on the hypothalamus suggests the answer may be yes. But that's only part of a broader debate over gender differences and the brain.

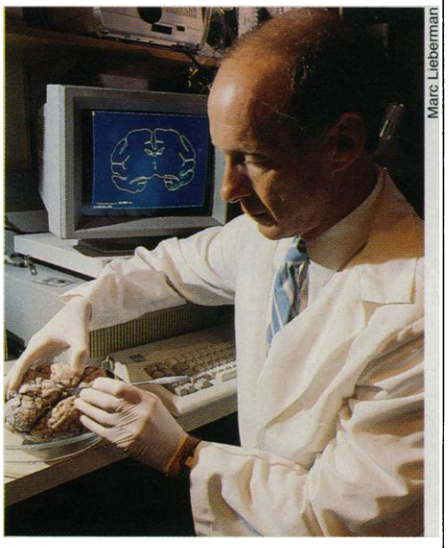


"I'VE ALWAYS KNOWN I'm fundamentally different," is a frequent claim of homosexuals who feel that their sexual orientation is innate and not formed by choice or by social environment. Whether they're right has been the subject of heated debate on many fronts: scientific, social, political—even religious. An article in this week's *Science* (see p. 1034) steps right into the middle of that controversy, presenting new evidence suggesting that homosexuality is at least in part a biological phenomenon.

Simon LeVay, a neuroscientist at the Salk Institute in San Diego, has found that in homosexual men part of the anterior hypothalamus—a brain region that governs sexual behavior—has the anatomical form usually found in women rather than the form typical of heterosexual men. LeVay's is the second report of a difference between the brains of homosexuals and heterosexuals (the first was published last year in *Brain Research**)—though it is the first to find such a difference in the hypothalamus, which is known to be a source of sexual urges. That connection raises the possibility that this difference may not only correlate with homosexuality but also play a role in causing it.

Either interpretation—correlation or cause—suggests that some biological difference is at the root of homosexuality. And that is a potentially explosive notion. Homophobes could exploit the result by pointing to the brain "defect" in homosexuals; they might even envisage screening for homosexuality in utero. Others may interpret the data as evidence that homosexuality is as natural a variation from the average brain as left-handedness. And many gays will see LeVay's finding as welcome confirmation of what they have always believed. "If it's true, the implications are amazing," says Dennis Landis, a neurologist who studies brain structure at Case Western Reserve University. "It would begin to suggest why male homosexuality is present in most human populations, despite cultural constraints. It suggests it's a biological phenomenon."

Indeed, the finding has important implications for science as well as society. Not only does it link sexual orientation to a structure within the brain, it also adds to a small but growing body of observations suggesting that many structural differences in the brain—including those that distinguish typical male and female brains (see p. 957)—may be determined by prenatal hormone levels. Some of those differences may play a role in sexual behavior as well as in cognitive differences between men and women (see p. 959).


Marc Lieberman

Brain man. *Simon LeVay.*

Lest eager believers jump to too many conclusions, LeVay points out that his finding contains no direct evidence that the difference he has observed actually causes homosexuality. He and others in the field acknowledge that the paper needs replication, since such studies are difficult and somewhat subjective. "Simon is very good; he's extremely well-equipped to make those observations," said one neuroscientist who is familiar with LeVay's work. "But we ought to put off big speculation until it is confirmed."

Ironically, given the potential impact of his work, LeVay, whose main research focuses on the visual areas of the brain, says he began this study as a "hobby project." He knew that the research team of Roger Gorski at the University of California, Los Angeles, had examined post-mortem human brains and found two regions, or "nuclei," in the anterior hypothalamus that are more than twice as large in men as they are in women. LeVay extended the study to homosexual men, using brains of men who had died of AIDS. In most of the 19 homosexuals he looked at, he found that one of these nuclei, called INAH-3, was smaller than it is in heterosexual men—in fact it was the same size as it is in women.

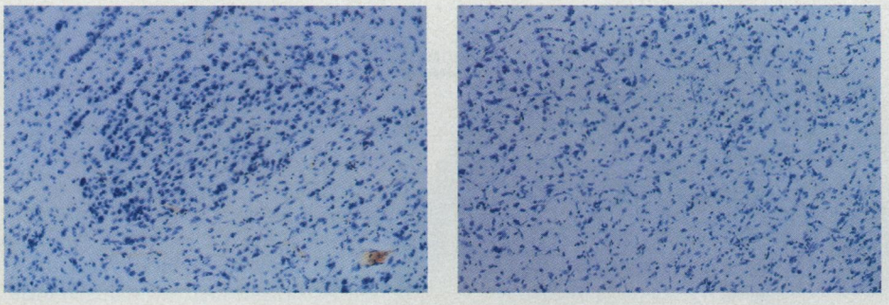
The finding "fits in well with the animal research that shows [hypothalamic differences] that correlate with sexual behavior," says Gloria Hoffman, a neuroendocrine anatomist at the University of Pittsburgh. Indeed, while there is no animal model for studying homosexuality, some researchers have observed that experimental lesions in the anterior hypothalamus of male monkeys reduce behavior such as the mounting of females, while leaving unperturbed other sexual activities such as masturbation—the closest any animal evidence comes to showing a physical effect on sexual orientation.

AIDS provides the first chance to study the brains of homosexual men, LeVay says, since male homosexuality is a risk factor for the disease, and AIDS patients are often categorized by risk group. The brains of lesbians are more difficult to obtain for research, since lesbians are not generally at risk for AIDS, and sexual orientation is rarely recorded in deaths from other causes.

Could the differences LeVay saw be due to AIDS rather than to homosexuality? "AIDS pathologies...could influence the size of the nuclei," says Laura Allen, a postdoc with Gorski at UCLA who studies the INAH nuclei. But she notes that LeVay found that heterosexual men had large INAH-3 nuclei, whether they had died from AIDS or from other causes. That leads Allen to conclude that "LeVay is probably correct," though she reserves final approval until another lab has reproduced the finding.

One reason the work begs for confirmation is that the study of sexual dimorphism in the human brain has had a history of controversy and contradiction. Not only are the structures hard to see clearly in tissue

*D.F. Swaab and M.A. Hofman, "An Enlarged Suprachiasmatic Nucleus in Homosexual Men," *Brain Research* **537**, 141 (1990).



Missing cells. *Oval collection of cells in hypothalamus from heterosexual man* (left) *are absent in homosexual man* (right).

slices, but researchers argue about what is the most reliable measure of size—the volume measurements used by LeVay, or actual cell counts. There is also the nagging possibility that some unknown factors may influence the size of the structures, according to one of the major players in the field, Dick Swaab, a neuroscientist at the Netherlands Institute for Brain Research in Amsterdam.

Despite his words of caution, Swaab says he is glad to hear of LeVay's finding, because it builds on his own group's discovery, reported last year in *Brain Research*, of the first known structural difference between the brains of homosexual and heterosexual men. Swaab's team found that the suprachiasmatic nucleus (SCN), a part of the brain that governs daily rhythms, is twice as large in homosexual men as it is in the typical heterosexual brain.

But the suprachiasmatic nucleus is not known to play a role in sexual behavior, LeVay points out. So while it might be influenced by the same factors that cause homosexuality, it is less likely than the anterior hypothalamus to be part of the cause. Gorski postdoc Allen agrees that the anterior hypothalamus is "exactly where we would expect some nucleus that may control [sexual orientation] to be located."

But what factors might influence the development of this part of the brain? A possible answer comes from studies in rats, which also have a sexually dimorphic area in their anterior hypothalamus, larger in males than in females, that governs sexual behavior. In rats, the development of the area is dependent on testosterone levels before and immediately after birth. Male rat pups that are castrated at birth, reducing their testosterone levels, have a smaller sexually dimorphic nucleus than normal males, and when they grow up they show less male-type sexual behavior, such as mounting. Testosterone injections enlarge the nucleus in female pups. The resulting adults show more "male" sexual behavior.

Extending that kind of data to humans involves a huge step, but that's just the step some researchers are trying to take. Sandra J. Witelson and her colleagues at McMaster University have found lesbians to be twice as likely as heterosexual women to show left-hand preference on a variety of tasks; gay men also show such a tendency. Since studies of people with abnormal sex-hormone levels suggest that handedness is a brain feature that can be influenced by sex hormones during brain development, Witelson says her team's results suggest there "might be atypical brain organization" in homosexuals, also caused by atypical sex-hormone levels.

In a paper in the current issue of *Psychoneuroendocrinology* (v.16, p.131), Witelson proposes that the brain is a mosaic of areas that may respond to sex hormones at various times during early development. Typical female or male hormone levels would produce a typical female or male brain, she says. But unusual levels of sex hormones at any given time may switch the development of susceptible brain areas. "This could cause different areas in the same brain to undergo different sexual differentiation," says Witelson. Depending on levels and timing, sex-hormones could influence handedness, sexual orientation, or other characteristics.

Witelson emphasizes that her model is speculative, based on a rather eclectic assortment of data. But that model—and LeVay's finding—raises questions that offer a program for future research. Does INAH-3 have sex-hormone receptors, for example, indicating that it could be influenced by those hormones? And when during brain development does the difference between the sexes emerge?

No matter how such questions are answered, it may be difficult ever to establish that INAH-3 or any other brain structure actually causes homosexuality, or to rule out the possibility that childhood or adolescent experience may have altered the size of INAH-3 in homosexuals. But Witelson, for one, is not discouraged. "The important [point] is that several independent studies have shown that various brain structures are different between people of different sexual orientation," she says. And Swaab agrees with Witelson that this is what one would expect. The difference between homosexuals and heterosexuals, he quips, "should be in the brain, not in the heart."

■ MARCIA BARINAGA

The Brain as "Sexual Organ"

When Oxford University anatomists Geoffrey Raisman and Pauline Field set out to study the differences between the brains of male and female rats in the late 1960s, most researchers were skeptical. The prevailing view was that male and female brains were alike. "People just didn't believe these significant structural differences existed," recalls Rockefeller University neuroscientist Bruce McEwen, who studies sex differences in rodent brains. But the pair forged ahead and, 20 years ago this month, published a study in *Science* that was the first to show conclusively a structural difference in the brains of male and female mammals: Male rats have fewer synapses connecting two parts of the hypothalamus than females do. McEwen says it's only since Raisman's and Field's study, which he calls "monumental," that researchers "have felt there could be structural sex differences in the brain."

Raisman and Field were quickly joined in these studies by an entire new generation of researchers who entered the field just in time to make use of high-tech tools that could show them the brain in minute detail. Electron microscopes gave a view of differences in autopsied brain structures the size of the period at the end of this sentence. Noninvasive imaging techniques, such as magnetic resonance imaging (MRI), helped show the interior of living heads for the first time. At the same time, rodent studies reached a new level of sophistication, allowing researchers to trace the way sex hormones work.

As a result of data gathered with these new tools during the 1970s and 1980s there is now a solid body of data indicating sex differences in the brains of almost every mammalian family examined so far: rodents, birds, monkeys, and—most recently and most intriguingly—human beings. "I see more and more studies involving different species and different parts of the brain," says McEwen. "Without question, these differences do exist, because they have been documented at