
With crystal-blue eyes, wavy hair, and freshly scrubbed faces, the boys look as though they stepped out of a Pottery Barn Kids catalog. They are 7-year-old twins. I'll call them Thomas and Patrick; their parents agreed to let me meet the boys as long as I didn't use their real names.

Spend five seconds with them, and there can be no doubt that they are identical twins - so identical even they can't tell each other apart in photographs. Spend five minutes with them, and their profound differences begin to emerge.

Patrick is social, thoughtful, attentive. He repeatedly addresses me by name. Thomas is physical, spontaneous, a bit distracted. Just minutes after meeting me outside a coffee shop, he punches me in the upper arm, yells, "Gray punch buggy!" and then points to a Volkswagen Beetle cruising past us. It's a hard punch. They horse around like typical brothers, but Patrick's punches are less forceful and his voice is higher. Thomas charges at his brother, arms flexed in front of him like a mini-bodybuilder. The differences are subtle - they're 7-year-old boys, after all - but they are there.

When the twins were 2, Patrick found his mother's shoes. He liked wearing them. Thomas tried on his father's once but didn't see the point.

When they were 3, Thomas blurted out that toy guns were his favorite things. Patrick piped up that his were the Barbie dolls he discovered at day care.

When the twins were 5, Thomas announced he was going to be a monster for Halloween. Patrick said he was going to be a princess. Thomas said he couldn't do that, because other kids would laugh at him. Patrick seemed puzzled. "Then I'll be Batman," he said.

Their mother - intelligent, warm, and open-minded - found herself conflicted. She wanted Patrick - whose playmates have always been girls, never boys - to be himself, but she worried his feminine behavior would expose him to ridicule and pain. She decided to allow him free expression at home while setting some limits in public.

That worked until last year, when a school official called to say Patrick was making his classmates uncomfortable. He kept insisting that he was a girl.

Patrick exhibits behavior called childhood gender nonconformity, or CGN. This doesn't describe a boy who has a doll somewhere in his toy collection or tried on his sister's Snow White outfit once, but rather one who consistently exhibits a host of strongly feminine traits and interests while avoiding boy-typical behavior like rough-and-tumble play. There's been considerable research into this phenomenon, particularly in males, including a study that followed boys from an early age into early adulthood. The data suggest there is a very good chance Patrick will grow up to be homosexual. Not all homosexual men show this extremely feminine behavior as young boys. But the research indicates that, of the boys who do exhibit CGN, about 75 percent of them - perhaps more - turn out to be gay or bisexual.

What makes the case of Patrick and Thomas so fascinating is that it calls into question both of the dominant theories in the long-running debate over what makes people gay: nature or nurture, genes or learned behavior. As identical twins, Patrick and Thomas began as genetic clones. From the moment they came out of their mother's womb, their environment was about as close to identical as possible - being fed,
changed, and plopped into their car seats the same way, having similar relationships with the same nurturing father and mother. Yet before either boy could talk, one showed highly feminine traits while the other appeared to be "all boy," as the moms at the playgrounds say with apologetic shrugs.

"That my sons were different the second they were born, there is no question about it," says the twins' mother.

So what happened between their identical genetic starting point and their births? They spent nine months in utero. In the hunt for what causes people to be gay or straight, that's now the most interesting and potentially enlightening frontier.

**WHAT DOES IT MATTER WHERE HOMOSEXUALITY COMES FROM?** Proving people are born gay would give them wider social acceptance and better protection against discrimination, many gay rights advocates argue. In the last decade, as this "biological" argument has gained momentum, polls find Americans - especially young adults - increasingly tolerant of gays and lesbians. And that's exactly what has groups opposed to homosexuality so concerned. The Family Research Council, a conservative Christian think tank in Washington, D.C., argues in its book *Getting It Straight* that finding people are born gay "would advance the idea that sexual orientation is an innate characteristic, like race; that homosexuals, like African-Americans, should be legally protected against 'discrimination;' and that disapproval of homosexuality should be as socially stigmatized as racism. However, it is not true."

Some advocates of gay marriage argue that proving sexual orientation is inborn would make it easier to frame the debate as simply a matter of civil rights. That could be true, but then again, freedom of religion enjoyed federal protection long before inborn traits like race and sex.

For much of the 20th century, the dominant thinking connected homosexuality to upbringing. Freud, for instance, speculated that overprotective mothers and distant fathers helped make boys gay. It took the American Psychiatric Association until 1973 to remove "homosexuality" from its manual of mental disorders.

Then, in 1991, a neuroscientist in San Diego named Simon LeVay told the world he had found a key difference between the brains of homosexual and heterosexual men he studied. LeVay showed that a tiny clump of neurons of the anterior hypothalamus - which is believed to control sexual behavior - was, on average, more than twice the size in heterosexual men as in homosexual men. LeVay's findings did not speak directly to the nature-vs.-nurture debate - the clumps could, theoretically, have changed size because of homosexual behavior. But that seemed unlikely, and the study ended up jump-starting the effort to prove a biological basis for homosexuality.

Later that same year, Boston University psychiatrist Richard Pillard and Northwestern University psychologist J. Michael Bailey announced the results of their study of male twins. They found that, in identical twins, if one twin was gay, the other had about a 50 percent chance of also being gay. For fraternal twins, the rate was about 20 percent. Because identical twins share their entire genetic makeup while fraternal twins share about half, genes were believed to explain the difference. Most reputable studies find the rate of homosexuality in the general population to be 2 to 4 percent, rather than the popular "1 in 10" estimate.

In 1993 came the biggest news: Dean Hamer's discovery of the "gay gene." In fact, Hamer, a Harvard-trained researcher at the National Cancer Institute, hadn't quite put it that boldly or imprecisely. He found that gay brothers shared a specific region of the X chromosome, called Xq28, at a higher rate than gay men
shared with their straight brothers. Hamer and others suggested this finding would eventually transform our understanding of sexual orientation.

That hasn't happened yet. But the clear focus of sexual-orientation research has shifted to biological causes, and there hasn't been much science produced to support the old theories tying homosexuality to upbringing. Freud may have been seeing the effect rather than the cause, since a father faced with a very feminine son might well become more distant or hostile, leading the boy's mother to become more protective. In recent years, researchers who suspect that homosexuality is inborn - whether because of genetics or events happening in the womb - have looked everywhere for clues: Prenatal hormones. Birth order. Finger length. Fingerprints. Stress. Sweat. Eye blinks. Spatial relations. Hearing. Handedness. Even "gay" sheep.

LeVay, who is gay, says that when he published his study 14 years ago, some gays and lesbians criticized him for doing research that might lead to homosexuality once again being lumped in with diseases and disorders. "If anything, the reverse has happened," says LeVay, who is now 61 and no longer active in the lab. He says the hunt for a biological basis for homosexuality, which involves many researchers who are themselves gay or lesbian, "has contributed to the status of gay people in society."

These studies have been small and underfunded, and the results have often been modest. Still, because there's been so much of this disparate research, "all sort of pointing in the same direction, makes it pretty clear there are biological processes significantly influencing sexual orientation," says LeVay. "But it's also kind of frustrating that it's still a bunch of hints, that nothing is really as crystal clear as you would like."

Just in the last few months, though, the hints have grown stronger.

In May, Swedish researchers reported finding important differences in how the brains of straight men and gay men responded to two compounds suspected of being pheromones - those scent-related chemicals that are key to sexual arousal in animals. The first compound came from women's urine, the second from male sweat. Brain scans showed that when straight men smelled the female urine compound, their hypothalamus lit up. That didn't happen with gay men. Instead, their hypothalamus lit up when they smelled the male-sweat compound, which was the same way straight women had responded. This research once again connecting the hypothalamus to sexual orientation comes on the heels of work with sheep. About 8 percent of domestic rams are exclusively interested in sex with other rams. Researchers found that a clump of neurons similar to the one LeVay identified in human brains was also smaller in gay rams than straight ones. (Again, it's conceivable that these differences could be showing effect rather than cause.)

In June, scientists in Vienna announced that they had isolated a master genetic switch for sexual orientation in the fruit fly. Once they flicked the switch, the genetically altered female flies rebuffed overtures from males and instead attempted to mate with other females, adopting the elaborate courting dance and mating songs that males use.

And now, a large-scale, five-year genetic study of gay brothers is underway in North America. The study received $2.5 million from the National Institutes of Health, which is unusual. Government funders tend to steer clear of sexual orientation research, aware that even small grants are apt to be met with outrage from conservative congressmen looking to make the most of their C-Span face time. Relying on a robust sample of 1,000 gay-brother pairs and the latest advancements in genetic screening, this study promises to bring some clarity to the murky area of what role genes may play in homosexuality.

This accumulating biological evidence, combined with the prospect of more on the horizon, is having an
effect. Last month, the Rev. Rob Schenck, a prominent Washington, D.C., evangelical leader, told a large gathering of young evangelicals that he believes homosexuality is not a choice but rather a predisposition, something "deeply rooted" in people. Schenck told me that his conversion came about after he'd spoken extensively with genetic researchers and psychologists. He argues that evangelicals should continue to oppose homosexual behavior, but that "many evangelicals are living in a sort of state of denial about the advance of this conversation." His message: "If it's inevitable that this scientific evidence is coming, we have to be prepared with a loving response. If we don't have one, we won't have any credibility."

AS THE 21-YEAR-OLD COLLEGE JUNIOR IN A HOSPITAL JOHNNY slides into the MRI, she is handed controls with buttons for "strongly like" and "strongly dislike." Hundreds of pornographic images - in male-male and female-female pairings - flash before her eyes. Eroticism eventually gives way to monotony, and it's hard to avoid looking for details to distinguish one image from the rest of the panting pack. So it goes from "Look at the size of those breasts!" to "That can't be comfortable, given the length of her fingernails!" to "Why is that guy wearing nothing but work boots on the beach?"

Regardless of which buttons the student presses, the MRI scans show her arousal level to each image, at its starting point in the brain.

Researchers at Northwestern University, outside Chicago, are doing this work as a follow-up to their studies of arousal using genital measurement tools. They found that while straight men were aroused by film clips of two women having sex, and gay men were aroused by clips of two men having sex, most of the men who identified themselves as bisexual showed gay arousal patterns. More surprising was just how different the story with women turned out to be. Most women, whether they identified as straight, lesbian, or bisexual, were significantly aroused by straight, gay, and lesbian sex. "I'm not suggesting that most women are bisexual," says Michael Bailey, the psychology professor whose lab conducted the studies. "I'm suggesting that whatever a woman's sexual arousal pattern is, it has little to do with her sexual orientation." That's fundamentally different from men. "In men, arousal is orientation. It's as simple as that. That's how gay men learn they are gay."

These studies mark a return to basics for the 47-year-old Bailey. He says researchers need a far deeper understanding of what sexual orientation is before they can determine where it comes from.

Female sexual orientation is particularly foggy, he says, because there's been so little research done. As for male sexual orientation, he argues that there's now enough evidence to suggest it is "entirely in-born," though not nearly enough to establish how that happens.

Bailey's 1991 twin study is still cited by other researchers as one of the pillars in the genetic argument for homosexuality. But his follow-up study using a comprehensive registry of twins in Australia found a much lower rate of similarity in sexual orientation between identical twins, about 20 percent, down from 50 percent. Bailey still believes that genes make important contributions to sexual orientation. But, he says, "that's not where I'd bet the real breakthroughs will come."

His hunch is that further study of childhood gender nonconformity will pay big. Because it's unclear what percentage of homosexuals and lesbians showed CGN as children, Bailey and his colleagues are now running a study that uses adult participants' home movies from childhood to look for signs of gender-bending behavior.

Cornell psychologist Daryl Bem has proposed an intriguing theory for how CGN might lead to homosexuality. According to this pathway, which he calls "the exotic becomes erotic," children are born
with traits for temperament, such as aggression and activity level, that predispose them to male-typical or female-typical activities. They seek out playmates with the same interests. So a boy whose traits lead him to hopscotch and away from rough play will feel different from, and ostracized by, other boys. This leads to physiological arousal of fear and anger in their presence, arousal that eventually is transformed from exotic to erotic.

Critics of homosexuality have used Bem's theory, which stresses environment over biology, to argue that sexual orientation is not inborn and not fixed. But Bem says this pathway is triggered by biological traits, and he doesn't really see how the outcome of homosexuality can be changed.

Bailey says whether or not Bem's theory holds up, the environment most worth focusing on is the one a child experiences when he's in his mother's womb.

LET'S GET BACK TO THOMAS AND PATRICK. BECAUSE IT'S UNCLEAR why twin brothers with identical genetic starting points and similar post-birth environments would take such divergent paths, it's helpful to return to the beginning.

Males and females have a fundamental genetic difference - females have two X chromosomes, and males have an X and a Y. Still, right after conception, it's hard to tell male and female zygotes apart, except for that tucked-away chromosomal difference. Normally, the changes take shape at a key point of fetal development, when the male brain is masculinized by sex hormones. The female brain is the default. The brain will stay on the female path as long as it is protected from exposure to hormones. The hormonal theory of homosexuality holds that, just as exposure to circulating sex hormones determines whether a fetus will be male or female, such exposure must also influence sexual orientation.

The cases of children born with disorders of "sexual differentiation" offer insight. William Reiner, a psychiatrist and urologist with the University of Oklahoma, has evaluated more than a hundred of these cases. For decades, the standard medical response to boys born with severely inadequate penises (or none at all) was to castrate the boy and have his parents raise him as a girl. But Reiner has found that nurture - even when it involves surgery soon after birth - cannot trump nature. Of the boys with inadequate penises who were raised as girls, he says, "I haven't found one who is sexually attracted to males." The majority of them have transitioned back to being males and report being attracted to females.

During fetal development, sexual identity is set before the sexual organs are formed, Reiner says. Perhaps it's the same for sexual orientation. In his research, of all the babies with X and Y chromosomes who were raised as girls, the only ones he has found who report having female identities and being attracted to males are those who did not have "receptors" to let the male sex hormones do their masculinizing in the womb.

What does this all mean? "Exposure to male hormones in utero dramatically raises the chances of being sexually attracted to females," Reiner says. "We can infer that the absence of male hormone exposure may have something to do with attraction to males."

Michael Bailey says Reiner's findings represent a major breakthrough, showing that "whatever causes sexual orientation is strongly influenced by prenatal biology." Bailey and Reiner say the answer is probably not as simple as just exposure to sex hormones. After all, the exposure levels in some of the people Reiner studies are abnormal enough to produce huge differences in sexual organs. Yet, sexual organs in straight and gay people are, on average, the same. More likely, hormones are interacting with other factors.

Canadian researchers have consistently documented a "big-brother effect," finding that the chances of a
boy being gay increase with each additional older brother he has. (Birth order does not appear to play a role with lesbians.) So, a male with three older brothers is three times more likely to be gay than one with no older brothers, though there's still a better than 90 percent chance he will be straight. They argue that this results from a complex interaction involving hormones, antigens, and the mother's immune system.

By now, there is substantial evidence showing correlation - though not causation - between sexual orientation and traits that are set when a baby is in the womb. Take finger length. In general, men have shorter index fingers in relation to their ring fingers; in women, the lengths are generally about the same. Researchers have found that lesbians generally have ratios closer to males. Other studies have shown masculinized results for lesbians in inner-ear functions and eye-blink reactions to sudden loud noises, and feminized patterns for gay men on certain cognitive tasks like spatial perception and remembering the placement of objects.

New York University researcher Lynn S. Hall, who has studied traits determined in the womb, speculates that Patrick was somehow prenatally stressed, probably during the first trimester, when the brain is really developing, particularly the structures like the hypothalamus that influence sexual behavior. This stress might have been based on his position in the womb or the blood flow to him or any of a number of other factors not in his mother's control. Yet more evidence that identical twins have womb experiences far from identical can be found in their often differing birth weights. Patrick was born a pound lighter than Thomas.

Taken together, the research suggests that early on in the womb, as the fetus's brain develops in either the male or female direction, something fundamental to sexual orientation is happening. Nobody's sure what's causing it. But here's where genes may be involved, perhaps by regulating hormone exposure or by dictating the size of that key clump of neurons in the hypothalamus. Before researchers can sort that out, they'll need to return to the question of whether, in fact, there is a "gay gene."

THE CROWD ON BOSTON COMMON IS THICK ON THIS SCORCHER of a Saturday afternoon in June, as the throngs make their way around the 35th annual Boston Pride festival, past booths peddling everything from "Gayopoly" board games to *Braveheart*ian garments called Utilikilts. Sitting quietly in his booth is Alan Sanders, a soft-spoken 41-year-old with a sandy beard and thinning hair. He's placed a mound of rainbow-colored Starbursts on the table in front of him and hung a banner that reads: "WANTED: Gay Men with Gay Brothers for Molecular Genetic Study of Sexual Orientation."

Sanders is a psychiatrist with the Evanston Northwestern Healthcare Research Institute who is leading the NIH-funded search for the genetic basis of male homosexuality ([www.gaybros.com](http://www.gaybros.com)). He is spending the summer crisscrossing the country, going to gay pride festivals, hoping to recruit 1,000 pairs of gay brothers to participate. (His wife, who just delivered their third son, wasn't crazy about the timing.) When people in Boston ask him how much genes may contribute to homosexuality, he says the best estimate is about 40 percent.

Homosexuality runs in families - studies show that 8 to 12 percent of brothers of gay men are also gay, compared with the 2 to 4 percent of the general population.

Sanders spends much of the afternoon handing out Starbursts to people who clearly don't qualify for a gay brothers study - preteen girls, adult lesbians wearing T-shirts that read "I Like Girls Who Like Girls," and elderly women in straw hats who speak only Chinese. But many of the gay men who stop by are interested in more than free candy. Among the people signing up is James Daly, a 31-year-old from Salem. "I think it's important for the public - especially the religious right - to know it's not a choice for some people," Daly says. "I feel I was born this way."
(In fairness, there aren't many leaders of groups representing social and religious conservatives who still argue that homosexual orientation - as opposed to behavior - is a matter of choice. Even as he insists that no one is born gay, Peter Sprigg, the point person on homosexuality for the Family Research Council, says, "I don't think that people choose their sexual attraction.")

In the decade since Dean Hamer made headlines, the gay gene theory has taken some hits. A Canadian team was unable to replicate his findings. Earlier this year, a team from Hamer's own lab reported only mixed results after having done the first scan of the entire human genome in the search for genes influencing sexual orientation.

But all of the gene studies so far have been based on small samples and lacked the funding to do things right. Sanders's study should be big enough to provide some real answers on linkage as well as shed light on gender nonconformity and the big-brother effect.

There is, however, a towering question that Sanders's study will probably not be able to answer. That has to do with evolution. If a prime motivation of all species is to pass genes on to future generations, and gay men are estimated to produce 80 percent fewer offspring than straight men, why would a gay gene not have been wiped out by the forces of natural selection? This evolutionary disadvantage is what led former Amherst College biologist Paul Ewald to argue that homosexuality might be caused by a virus - a pathogen most likely working in utero. That argument caused a stir when he and a colleague proposed it six years ago, but with no research done to test it, it remains just another theory. Other scientists have offered fascinating but unpersuasive explanations, most of them focusing on some kind of compensatory benefit, in the same way that the gene responsible for sickle cell anemia also protects against malaria. A study last year by researchers in Italy showed that female relatives of gay men tended to be more fertile, though, as critics point out, not nearly fertile enough to make up for the gay man's lack of offspring.

But there will be plenty of time for sorting out the evolutionary paradox once - and if - researchers are able to identify actual genes involved in sexual orientation. Getting to that point will likely require integrating multiple lines of promising research. That is exactly what's happening in Eric Vilain's lab at the University of California, Los Angeles. Vilain, an associate professor of human genetics, and his colleague, Sven Bocklandt, are using gay sheep, transgenic mice, identical twin humans, and novel approaches to human genetics to try to unlock the mystery of sexual orientation.

Instead of looking for a gay gene, they stress that they are looking for several genes that cause either attraction to men or attraction to women. Those same genes would work one way in heterosexual women and another way in homosexual men. The UCLA lab is examining how these genes might be turned "up" or "down." It's not a question of what genes you have, but rather which ones you use, says Bocklandt. "I have the genes in my body to make a vagina and carry a baby, but I don't use them, because I am a man." In studying the genes of gay sheep, for example, he's found some that are turned "way up" compared with the straight rams.

The lab is also testing an intriguing theory involving imprinted genes. Normally, we have two copies of every gene, one from each parent, and both copies work. They're identical, so it doesn't matter which copy comes from which parent. But with imprinted genes, that does matter. Although both copies are physically there, one copy - either from the mom or the dad - is blocked from working. Think of an airplane with an engine on each wing, except one of the engines is shut down. A recent Duke University study suggests humans have hundreds of imprinted genes, including one on the X chromosome that previous research has tied to sexual orientation.
With imprinted genes, there is no backup engine. So if there's something atypical in the copy from mom, the copy from dad cannot be turned on. The UCLA lab is now collecting DNA from identical twins in which one twin is straight and the other is gay. Because the twins begin as genetic clones, if a gene is imprinted in one twin, it will be in the other twin as well. Normally, as the fetuses are developing, each time a cell divides, the DNA separates and makes a copy of itself, replicating all kinds of genetic information. It's a complicated but incredibly accurate process. But the coding to keep the backup engine shut down on an imprinted gene is less accurate.

So how might imprinted genes help explain why one identical twin would be straight and the other gay? Say there's an imprinted gene for attraction to females, and there's something atypical in the copy the twin brothers get from mom. As all that replicating is going on, the imprinting (to keep the copy from dad shut down) proceeds as expected in one twin, and he ends up gay. But somehow with his brother, the coding for the imprinting is lost, and rather than remain shut down, the fuel flows to fire up the backup engine from dad. And that twin turns out to be straight.

IN THE COURSE OF REPORTING THIS STORY, I EXPERIENCED A good deal of whiplash. Just when I would become swayed by the evidence supporting one discreet theory, I would stumble onto new evidence casting some doubt on it. Ultimately, I accepted this as unavoidable terrain in the hunt for the basis of sexual orientation. This is, after all, a research field built on underfunded, idiosyncratic studies that are met with full-barreled responses from opposing and well-funded advocacy groups determined to make the results from the lab hew to the scripts they've honed for the talk-show circuit.

You can't really blame the advocacy groups. The stakes are high. In the end, homosexuality remains such a divisive issue that only thoroughly tested research will get society to accept what science has to say about its origin. Critics of funding for sexual orientation research say that it isn't curing cancer, and they're right. But we devote a lot more dollars to studying other issues that aren't curing cancer and have less resonance in society.

Still, no matter how imperfect these studies are, when you put them all together and examine them closely, the message is clear: While post-birth development may well play a supporting role, the roots of homosexuality, at least in men, appear to be in place by the time a child is born. After spending years sifting through all the available data, British researchers Glenn Wilson and Qazi Rahman come to an even bolder conclusion in their forthcoming book *Born Gay: The Psychobiology of Sex Orientation*, in which they write: "Sexual orientation is something we are born with and not 'acquired' from our social environment."

Meanwhile, the mother of twins Patrick and Thomas has done her own sifting and come to her own conclusions. She says her son's feminine behavior suggests he will grow up to be gay, and she has no problem with that. She just worries about what happens to him between now and then.

After that fateful call from Patrick's school, she says, "I knew I had to talk to my son, and I had no clue what to say." Ultimately, she told him that although he could play however he wanted at home, he couldn't tell his classmates he was a girl, because they'd think he was lying. And she told him that some older boys might be mean to him and even hit him if he continued to claim he was a girl.

Then she asked him, "Do you think that you can convince yourself that you are a boy?"

"Yes, Mom," he said. "It's going to be like when I was trying to learn to read, and then one day I opened the book and I could read."
His mother's heart sank. She could tell that he wanted more than anything to please her. "Basically, he was saying there must be a miracle - that one day I wake up and I'm a boy. That's the only way he could imagine it could happen."

In the year since that conversation, Patrick's behavior has become somewhat less feminine. His mother hopes it's just because his interests are evolving and not because he's suppressing them.

"I can now imagine him being completely straight, which I couldn't a year ago," she says. "I can imagine him being gay, which seems to be statistically most likely."

She says she's fine with either outcome, just as long as he's happy and free from harm. She takes heart in how much more accepting today's society is. "By the time my boys are 20, the world will have changed even more."

By then, there might even be enough consensus for researchers to forget about finger lengths and fruit flies and gay sheep, and move on to a new mystery.

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