

Humans

How older siblings may shape sexual orientation via mother's immune system

It has long been observed that men with older brothers are more likely to be gay, but an association has also been found with older sisters. This sheds further light on how a mother's immune system may be involved in shaping sexual orientation

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▲ Birth order of a fetus may influence sexual orientation in later life

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For decades, researchers have known that the more older brothers a man has, the [greater his likelihood of being gay](#). More recently, this has also been [linked to having older sisters](#). Now, a modelling study suggests that the latter link could be explained by older sisters being a proxy for their mother previously having multiple pregnancies, some of which may have involved miscarried male embryos. The scientists have stressed, however, that this is just an idea and further research is needed.

Carrying boys during pregnancy is thought to cause an immune response towards specific male proteins involved in fetal [brain](#) development, which becomes stronger with successive male pregnancies. If the resulting antibodies enter the brain of a male fetus, they could influence his sexual orientation later on. But that doesn't explain the link to older sisters.

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One proposed explanation is that older sisters provide clues about a mother's reproductive history. The idea goes that the more children a woman has, the more times she has been pregnant, some of which could have ended in miscarriages, including extremely early ones. If male embryos were miscarried, they may have sensitised her immune system against those male proteins. "It's nothing more than a possibility right now," says [Michel Raymond](#) at the University of Montpellier in France.

To explore this, Raymond and his colleagues built a model to uncover whether miscarriages could generate an older-sister effect for male sexual orientation. For simplicity, it assumed that all women have the same probability of miscarriage for each [pregnancy](#), says Raymond. In reality, miscarriage risk probably varies among women, even when accounting for age, which should be investigated in further research, he says.

The researchers compared the model's predictions with data from eight populations. This suggested that each additional older brother is associated with about a 30 per cent increase in the odds of a man being gay, while each additional older sister is linked to about a 20 per cent increase. The team calculated that between 37 and 58 per cent of fertilised eggs would need to be miscarried to fully explain the older sister association. Information about whether the participating mothers included non-binary people and trans men wasn't routinely collected across the eight population datasets.

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About [10 to 20 per cent of known pregnancies end in miscarriage](#) in the US, but Raymond says, “there’s huge variation, depending on what you consider a miscarriage”, with some occurring [before a pregnancy is known about](#).

This study doesn’t definitely show that miscarriages explain the older-sister effect, says Raymond. “It shows that miscarriage is potentially an important phenomenon to take into account,” he says. “However, it is also possible that the maternal immune hypothesis is not correct, and at this stage, it is not possible to decide.”

[Ray Blanchard](#) at the University of Toronto in Canada, who has also proposed that older sisters could act as a proxy for miscarried male pregnancies, says the study adds weight to his idea. “It could have come up with results saying that my hypothesis was basically very unlikely, but it came up with results indicating that, while my hypothesis may not 100 per cent account for the effect of older sisters, we’re within the realm of what is possible.”

It is also unclear how far a pregnancy may need to progress to trigger the proposed maternal immune response.

[A 2017 study](#) found that mothers of gay sons with older brothers had higher levels of antibodies against a Y-chromosome-linked protein involved in brain development called NLGN4Y, compared with mothers of heterosexual sons. [Elena Jazin](#) at Uppsala University in Sweden has documented the expression of NLGN4Y in [8 to 11-week-old human embryos](#), and says its expression probably begins even earlier.





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A study of more than 10 million siblings suggests that firstborns are more likely to be autistic and have allergies, while conditions like migraine and shingles tend to affect their younger sibling

[Jan Kabátek](#) at the University of Melbourne in Australia previously found that [birth order may influence the odds of same-sex unions](#). This included linking older siblings to a greater likelihood of a woman entering a same-sex union, which can't readily be explained by a maternal immune response to male-specific proteins. This response could be to proteins that aren't sex specific, says Kabátek.

Sexual orientation probably can't be explained through one mechanism. [Genetic factors](#) are thought to play a role, with identical twins being more likely to share a sexual orientation than fraternal ones. [Prenatal hormone exposure has also long been investigated](#) as an influence.

"I believe, as do probably most researchers in this area, that there are likely a few different biological causes of homosexuality," says Blanchard. "Therefore, evidence in favor of genetic causes, or [hormone-related] causes, neither supports nor undermines evidence for immunological causes."

Reference:

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