

Researching how stress among sexual minorities affects health on genetic level

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Credit: University of California, San Francisco

Stress is a natural part of life; everyone experiences it to some degree. But a growing body of research suggests that chronic stress can have a negative effect on health, ranging from relatively mild complaints like sleeplessness to more serious problems like heart disease. Researcher Annesa Flentje, assistant professor in the Department of Community Health Systems at UC San Francisco School of Nursing, is looking at ways stress among sexual minorities – those whose sexual orientation, identity or practices differ from the majority – can affect physical and

mental health, starting at the genetic level, with a particular focus of late on the effect of stress on human immunodeficiency virus (HIV)-positive men.

The Sexual Minority Stress Model

Flentje, a clinical psychologist who received a PhD degree from the University of Montana and completed her postdoctoral studies at UCSF, has long been interested in [health disparities](#) among sexual and gender minorities. Her recent work is based on the sexual minority stress model, which theorizes that [sexual minorities](#) experience [chronic stress](#) due to unique factors such as discrimination, expectation of discrimination, concealment of sexual identity, and internalization of sexual stigma.

"I got interested in the idea that there's an explanation for health disparities, like substance use, which occurs at higher rates among sexual minorities," says Flentje. "It isn't that these individuals are inherently more flawed, but external stressors account for an additional burden of stress on that community, which increases things like substance use for coping."

Current literature suggests that minorities, including sexual minorities, are also at higher risk for some physiological disorders, including some cancers and cardiovascular disease. This led Flentje to consider how all these disparities might be related to stress. She began looking at inflammation – one of the body's responses to stress – as a potential culprit, and thinking about what happens on a molecular level in response to experiences like discrimination and internalized stigma.

Internalized Stress: A Pathway to Genetic Change?

Research has already shown that [different stressors can change how](#)

[genes are expressed](#), Flentje says, but she hypothesizes that one reason for those changes is the internalization of stress. "One plausible pathway is that if these negative experiences aren't cognitively challenged, they may be processed in other ways. In essence, they may infiltrate our bodies," she says.

The hypothesis is bolstered by what we know about how stress can affect the neuroendocrine system, Flentje notes. A complex set of interactions between the hypothalamic, pituitary and adrenal glands, known as the HPA axis, regulates the body's reaction to stress, which can involve a wide variety of physiological systems. For example, [stress has been found to affect immune function in both positive and negative ways](#), but the mechanisms by which this happens remain unclear.

"That's one of the reasons I wanted to look at the level of the gene," Flentje says. "If you look at all the different biological systems, there are multiple things going on, but ultimately I think there's an upstream system that activates all these other paths."

Can an Intervention Change Gene Expression?

Flentje is examining the ways stress affects gene expression from several angles. In a study of HIV-positive men who have sex with men and use stimulants, she's trying to see if there are differences in gene expression based on specific stress-related experiences such as discrimination and living in a state of ongoing hypervigilance in expectation of discrimination.

She is also recruiting HIV-positive, stimulant-using men for a randomized controlled trial of a nine-session cognitive-behavioral intervention developed to reduce the impact of minority stress on individuals. Flentje wants to see if there are changes in the men's gene expression related to inflammatory processes before and after

completing the intervention series.

"As a clinical psychologist, I'm inclined to want to find ways to help people cope with stressors," Flentje says of the trial. The intervention, used in a successful pilot study, is based on stress and coping theory, which advances the idea that we can make choices about how we interact with our environment, including stressors.

Flentje will introduce subjects to the sexual minority stress model, and to summaries of research that shows how stress can affect health. The purpose is to reframe subjects' thinking about coping mechanisms, like alcohol or methamphetamine use, that happen at higher rates in the LGBT community than in the general population.

The goal is not to tell people how to behave in response to stress, says Flentje, but to make them more conscious of the choices they make in their environments, and to give them additional skills and choices for coping with stressors.

There are practical as well as humanitarian benefits to this approach. Flentje hopes it will help shed light on the direct physiological effects of stress itself and on the indirect effects of "downstream" [stress](#) reactions – in this case, substance use. "There hasn't been a lot of work on how substance use changes gene expression. One potential pathway is that these stressors increase substance use, and that the substance use itself could have an impact on [gene expression](#)," she says.

The study, which is funded by the National Institute on Drug Abuse, an arm of the National Institutes of Health, looks at HIV-positive men specifically because [the effects of prolonged inflammation can be especially pronounced and damaging in this population](#). This means the effects of inflammation may be easier to observe, and the potential benefit of the intervention may be greater for these patients. Flentje is

also seeking funding to extend the trial to other groups.

In the end, Flentje's work is about improving the health of the community by reducing stigma and increasing understanding. She says, "We want to tell people, 'This isn't in your head, and it's not your fault.'"

Provided by University of California, San Francisco

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