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responses triggered in response to injury or infection by bacteria, viruses, and other pathogens—can signal the brain to alter neural sensitivity to the social environment, leading to increases in sensitivity to social threat and social connection. Meanwhile, experiences that threaten social connection, such as rejection and isolation, can activate systems that increase the activity of these cytokines.

Why? It may be an artifact of our ancient history. "Essentially, in our evolutionary past, being socially disconnected or isolated put us at a greater risk of attack from predators or hostile conspecifics—which meant a greater risk of infection," Eisenberger says. "Over our evolutionary history, our immune system may have evolved to 'listen in' to these cues of social disconnection/isolation and prepare our body for the greater risk associated with these states by increasing inflammatory activity."

As one example, Eisenberger and colleagues recently showed that people who are highly sensitive to social disconnection exhibit greater inflammatory responsiveness to endotoxin—a portion of the cell wall of *Escherichia coli* bacteria that is used to experimentally induce inflammation in humans. The work, reported in a 2015 paper in the journal *Psychoneuroendocrinology,* suggests that these individuals may be "primed to exhibit heightened inflammatory responses to immunological insults, which may eventually lead to chronic inflammatory-related illnesses," Eisenberger says.

Ultimately, she says, viewing sickness as a social phenomenon, in addition to a physical phenomenon, may help us to better understand emerging relationships between inflammation and mental health problems like depression.

"Indeed," she adds, "we are finding that the immune system can profoundly influence our sensitivity to the social world. Findings such as these may help us to better understand how heightened immune system activity can lead to mental health problems characterized by feelings of social disconnection, such as depression."

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Helpfulness May Make Us Healthier

In a 2013 study, Cousins Center researcher Steve Cole, Professor of Medicine and Psychiatry & Biobehavioral Sciences in the UCLA School of Medicine and UCLA Semel Institute for Neuroscience and Human Behavior, found that the two types of happiness—eudaimonic well-being (working toward a higher life purpose beyond simple self-gratification) and hedonic well-being (from experiencing, acquiring, or consuming nice things)—manifest as different patterns of gene expression in the cells of the immune system.

Cole and colleagues recently followed-up these findings "to replicate the initial result and hone in more closely on the psychological 'active ingredient' for the positive molecular correlates of eudiamonia," Cole says. In the 2015 follow-up, one study group involved adults recruited in North Carolina, and a second group was recruited from the Vancouver, British Columbia, metropolitan area.

The new research, published in the journal *PLoS One,* found the same sorts of favorable molecular correlates of eudaimonia as in the first study. "The results of this study suggested that the favorable genomic correlates of eudaimonic well-being are most tightly associated with the social components of eudaimonic well-being, rather than their more internal psychological components," Cole says. Based on that observation, studies are currently underway to see if specific interventions targeting pro-social behavior might have favorable effects on gene expression. "Analyses have just begun, but the initial results are promising," he says.

In related work published in the *Proceedings of the National Academy of Sciences,* a team led by Cousins Center researcher Andrew J. Fuligni, Professor of Psychiatry and Biobehavioral Sciences at the Semel Institute for Neuroscience and Human Behavior, and Adriana Galván, the Wendell Jeffrey and Bernice Wenzel Term Chair in Behavioral Neuroscience, followed 47 adolescents aged 15 to 17 years old for one year to see whether neural sensitivity to eudaimonic and hedonic rewards—as determined by brain scans—could differentially predict changes in depressive symptoms.

The researchers specifically looked at a brain region called the ventral striatum, which is known to be involved in motivational learning and reward-related experiences. "It also is particularly sensitive during the adolescent years due to pubertal changes and continuing brain development in other regions and networks," Fuligni says.

The study—first-authored by Eva Telzer, a former student of Fuligni's and Galvan's, now at University of North Carolina, Chapel Hill—showed that activation of this brain region during eudaimonic decisions

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predicted longitudinal declines in depressive symptoms, whereas its activation in hedonic decisions was related to longitudinal *increases* in depressive symptoms.

"Although the reward-related neural networks of the adolescent brain have typically been blamed as the culprit of problem behavior, our results suggest that they are also sensitive to more prosocial, developmentally-positive behaviors," says Fuligni. "The findings tell us that individuals who have greater neural activation in reward-related neural regions while helping the family show better psychological health over time. "It is a neural marker of individual differences."

"One important area of future work is integrating these two existing lines of research so we can understand better how the brain basis of eudaimonic well-being may influence the peripheral nervous system and hormonal systems to ultimately alter gene expression dynamics in circulating immune cells," Cole says. "That kind of work can provide neural and genomic biomarkers that might help us rapidly test and optimize new strategies for promoting eudaimonic well-being and its favorable health correlates."

Cousins Researcher Studies How Sleep May Influence How Fast We Age

Aging is the single biggest risk factor for most common chronic diseases, including cancer, diabetes, dementia, and heart disease. Cousins Center researcher Jude Carroll, Assistant Professor, UCLA Semel Institute for Neuroscience and Human Behavior is trying to identify the biological mechanisms through which both behavioral and psychosocial factors influence our vulnerability to age-related disease and accelerated aging—and how changes in our behavior could possibly offset those effects.

"While there is a lot of amazing research looking to identify pharmacological ways to intervene in the aging process," Carroll says, "my work specifically asks whether behavioral factors, like sleep disturbances, might impact the biological aging process, and if so, whether we might be able to intervene at the behavioral level to improve sleep and also influence the aging process—ultimately altering disease risk."

Carroll's first exposure to these biobehavioral processes came when she was an undergrad. "I was in a course learning how emotions affected the health of people living with HIV. Amazed by the ability of the mind to influence the body, I was eager to understand how this worked." She changed her major to psychology and enrolled in courses on the biology and psychology of aging, neuroscience, and human physiology.

Judith Carroll

Carroll's first research study was a deeply personal one, inspired by her grandfather's experience with bereavement after the death of her grandmother. "He said that it seemed to him that some people did a lot better than others in coping with the loss of a spouse and it seemed to impact their health," she recalls. "This project, which became my master's thesis, focused on how older adults coped with a loss of a spouse, and whether this process of bereavement contributed to health vulnerability." The work stimulated her interest in pursuing more in-depth research on processes contributing to health vulnerability, especially in later life. "If emotional adversities contributed to worse health, what were the physiological pathways through which this occurred?"

Around the same time, other investigators were narrowing in on possible pathways. One study suggested that psychological stress might impact biological systems through accelerating biological aging. In this study, the marker of aging was the shortening of telomeres—repetitive stretches of DNA that cap the ends of chromosomes. "This was the first study that used telomere length as a marker of biological aging and linked it to psychological experiences, and it offered researchers a way to track rates of aging prior to disease onset," Carroll says.

Now at the Cousins Center, Carroll's Aging Biology and Behavior laboratory is measuring various biological indicators of the aging

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process, including telomere length and telomerase activity. Her "overarching theory" is that *sleep*—or the lack thereof—contributes to increased disease risk by accelerating the aging process, which occurs within cells and within regulatory systems of the body, such as the cardiovascular system. In one study, published in the journal *Sleep,* Carroll's lab showed that insomnia is associated with shortened telomeres in immune cells, an effect that was most pronounced with increasing chronological age. In a second study recently released online in the journal *Biological Psychiatry,* Carroll found that in a sample of over 2,000 postmenopausal women, those who had insomnia symptoms appeared biologically older according to a new measure of biological aging called the epigenetic clock.

In another recent paper published in the journal *Brain, Behavior, and Immunity,* Carroll and colleagues describe how one night of partial sleep deprivation—with participants sleeping only from 3 am to 7 am—activated genes suggestive of an increase in DNA damage that can lead to cellular senescence. Senescent cells, when they accumulate in large numbers within the body, have been shown to be the source of toxic secretory elements that trigger inflammation, tissue aging, and cancer; removing senescent cells, meanwhile, can delay many aspects of aging. In the study, sleep deprivation also increased expression of genes related to these toxic secretory elements that trigger inflammation, "indicating that sleep loss promotes biological aging processes," she says.

The studies indicate that "chronic sleep problems might be detrimental to rates of aging, but also points to the possibility that effective treatments to improve sleep may be particularly protective and slow down rates of aging. This is precisely what we plan to look at in future research in my lab," Carroll says.

These data are important, Carroll says, because they support the hypothesis that inadequate sleep causes changes within our cells that age. "These findings link sleep to the biological processes intrinsic to aging. Those who have healthy sleep may be slowing down this aging process while those with chronic sleep difficulties may be accelerating it. Our next set of research studies is focused on treating the sleep problems as a way to slow aging, or possibly even reverse it."

Among the take home messages from Carroll's work and other research on sleep and health: sleep is crucial to maintaining overall health and preventing disease—and just as important as diet and exercise for maintaining a healthy lifestyle.

Uncovering the Links Between Inflammation and Social Behavior

Inflammation is usually thought of as a response by the body to injury or infection, but increasing evidence suggests that psychological stress can also trigger inflammation—and that inflammation, in turn, can lead to profound changes in behavior, including the development of depressive symptoms such as difficulty feeling pleasure, sad mood, and social withdrawal.

Through her research, Cousins Center researcher Naomi Eisenberger, Associate Professor, UCLA Department of Psychology, is hoping to understand the biological underpinnings of this profound connection between our physical and emotional well-being and our social relationships.

In particular, Eisenberger and her colleagues have been expanding on earlier work showing that inflammation can lead to depression, by further exploring how inflammation might alter certain types of social experiences that might make depression more likely. Indeed, she says, "very little research has examined how inflammation alters our perception of the social world. Given that humans are highly social beings, it is important to understand how being in an inflamed or 'sick' state—a very vulnerable situation—might change an individual's sensitivity to their social world, so they can navigate this situation."

In a series of recent studies, Eisenberger and her colleagues showed, among other findings, that inflammation seems to increase threat-related neural activity in individuals in response to negative social experiences such as rejection and negative social feedback as well as reward-related neural activity when individuals see members of their social support system. "We think that each of these changes—that is, being more sensitive to negative social cues in order to avoid social threat and being more sensitive to positive social cues in order to approach close others who might be able to provide help and support—might be adaptive during times of sickness," she says.

These changes, Eisenberger and her colleagues say, occur through interconnected pathways that link the immune system and brain. For instance, the presence of proinflammatory cytokines—chemical messengers produced by the immune system that serve to increase inflammatory

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