

Spring 2015

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aging process and preventing disease, just like getting enough exercise, eating well, avoiding too much stress, not smoking, keeping your weight down, and wearing sunscreen,” she says.

To that end, she and her colleagues recently tested the relationship between sleep disturbances and multisystem biological risk in a group of more than 1,000 older adults. Multisystem biological risk is a measure that captures the functioning of multiple physiological regulatory systems—for example, the cardiovascular, immune, glucose metabolic, and sympathetic nervous system. These systems can become poorly regulated with age and use. The study, published in the journal *PLOS ONE*, showed elevated levels of multisystem risk in short sleepers (less than 5 hours of sleep per

night) and long sleepers (more than 8.5 hours) who reported poor sleep quality, compared to their counterparts who got a normal night’s sleep.

“This suggests sleep of short duration, or of long duration with poor sleep quality may accelerate aging across multiple biological systems,” Carroll says.

One way to improve sleep is through cognitive behavioral therapy (CBT), a treatment that helps patients understand the thoughts and feelings that influence their behavior. In a follow-up study published in the journal *Psychoneuroendocrinology*, Carroll and colleagues found that CBT for insomnia lowered multisystem risk among older adults with high multisystem risk at the start of the trial. “This lowering of multisystem risk suggests that the treatment of

sleep disturbances may actually reverse some of the signs of system aging,” she says.

“These initial findings are promising, but do need to be replicated,” Carroll says. “If we continue to see improvements in multisystem risk by treating sleep disturbances, then this would have substantial impact on health. Given the increasing growth of the aging population across the world and in the United States, and the predicted financial cost of chronic disease burden from this aging population, there is a critical need to identify ways to improve the overall healthspan of older adults. We want doctors to consider patient’s sleep problems as part of their routine physical examinations and overall evaluation of lifestyle risk factors. This would improve patient care and also public health.”

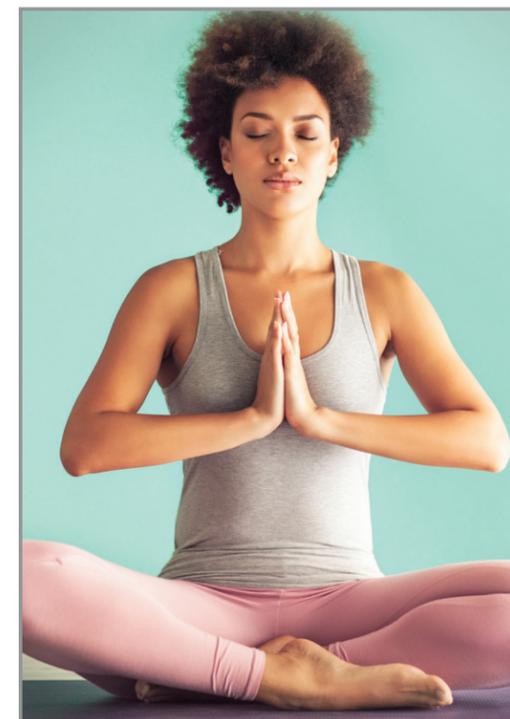


## Enhancing Quality of Life in Breast Cancer Survivors

In Julienne Bower’s lab, a number of research projects are centered on a common goal: improving the quality of life and survival outcomes of breast cancer survivors. Bower, an associate professor of psychology and psychiatry at UCLA and research scientist at the Cousins Center, is trying to understand and reduce the risk factors that contribute to inflammation—from early life stress resulting from adversity during childhood, to the very present stress arising from a cancer diagnosis and treatment. “We know inflammation is associated with fatigue and also predicts poor survival in breast cancer survivors. Inflammation is bad both for your quality of life and potentially breast cancer recurrence,” she says.

In previous studies, Bower reported that Iyengar yoga—a specialized form of yoga that uses restorative poses—relieves cancer-related fatigue in breast cancer survivors. In a follow-up study published in the journal *Psychoneuroendocrinology*, she and her colleagues showed that Iyengar decreases the production of a protein called nuclear factor  $\kappa\beta$  (NF- $\kappa\beta$ ), which induces the production of proinflammatory cytokines—chemicals that signal the brain and trigger “sickness behaviors,” including fatigue. “So at a molecular level,” she says, “yoga was influencing the degree to which these cells are in an inflammatory state and seems to be effective in reducing cancer-related fatigue. If my mother or my friend was going through breast cancer treatment and was experiencing fatigue, I would send her to an Iyengar yoga instructor because I believe that this study demonstrates that this practice is effective.”

Post-treatment fatigue can be a problem for breast cancer survivors of any age, but among young women, depression and stress may be more debilitating. “For them, we want to reduce stress and depression and also we want them to live a long time. So we want an intervention that in addition to improving psychological well being, affects other aspects of quality of life and biological processes,” Bower says.



To that end, she and her lab studied the benefits of mindfulness meditation in younger breast cancer survivors (diagnosed prior to age 50). The practice teaches individuals to pay attention to (but not react to) their moment-by-moment thoughts, emotions, and physiological responses and sensations. As reported in the journal *Cancer*, six weeks of mindfulness sessions led to reductions in

stress and depression—and lower levels of NF- $\kappa\beta$ —in the patients. The benefits were short-lived; three months later, stress and depression were back to their pre-study levels. “But the patients did show some lasting effects, such as positive affect and increased feeling of peace and purpose in life,” says Bower. “I think that is important because it is not all about reducing stress and depression but also about enhancing positive things in life.”

### Sleeping to a Healthier Life?

Aging is the single biggest risk factor for most common chronic diseases, such as cancer and heart disease. While getting older is inevitable, the aging process (and chronic disease development) may be *slowed* through lifestyle changes—including one as seemingly simple as getting a good night’s sleep.

So suspects Cousins Center Adjunct Assistant Professor Judith Carroll, whose research investigates the connections between sleep disturbances, the biological aging process (both at the cellular and systems level), and disease risk. “If we can show that treating sleep problems also improves “healthspan”—a word describing the goal of extending the years of healthy living without chronic disease—then more people might recognize that good sleep is vital to slowing the

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## Insomnia, Inflammation and Older Adults

An estimated 50 percent of people aged 55 and older suffer from some type of sleep problem. These nighttime issues can carry over into the day, causing fatigue, depression, and a diminished quality of life. Equally troubling, sleep disturbances can induce inflammatory responses that may contribute to chronic disease. Although medications can improve sleep, they're usually temporary fixes, and not without risk.

Looking for a better way to help older adults get a good night's sleep, Cousins Center Director Michael Irwin and his colleagues investigated the practice of mindfulness meditation. Mindfulness meditation involves paying attention to—but not reacting to, judging or being distracted by—one's own moment-by-moment thoughts, emotions, and physiological responses and sensations.

As described in a study appearing in the *Journal of the American Medical Association, Internal Medicine*, 49 volunteers aged 55 and older were divided into two groups. One group completed a six-week, two-hour-per-week sleep education and stress reduction program. The second group received instruction in mindfulness meditation. Compared to the first, the second group showed a greater improvement in quality of sleep, similar to the sleep improvements seen with standard behavioral treatment (cognitive behavioral therapy, CBT, which helps patients understand the thoughts and feelings that influence their behavior) or sleeping aids. They also had fewer insomnia symptoms, less fatigue, and less depression.

The *JAMA, Internal Medicine* study didn't track patients to see if mindfulness meditation prevented future sleep problems and also didn't look for any effects relating to inflammation. In a study in the journal *Sleep*, Irwin and colleagues examined these parameters in older insomnia patients receiving sleep education, treated with CBT, or participating in T'ai chi chih—a structured, movement-based meditation previously shown to have positive impacts on sleep quality. CBT led to lasting sleep improvements, and significantly reduced the amount of C-reactive protein, a biological marker of inflammation linked to cardiovascular disease and diabetes risk. T'ai chi chih produced less-robust, and short-term, improvements in insomnia and C-reactive protein levels, “but the benefits didn't last,” Irwin says. Insomnia—and



inflammation—both returned. “People need to practice daily get benefit from T'ai chi,” he says.

In a follow-up study in the journal *Biological Psychiatry*, Irwin and colleagues more closely examined the influence of these interventions on biological markers of inflammation, finding that found that CBT reduced signs of systemic inflammation, while T'ai chi produced reductions in *cellular* inflammation. Both treatments reduced the expression of proinflammatory cytokine genes.

“Given the links between insomnia, depression, and inflammatory disease risk,” the authors write, “these findings provide an evidence-based molecular framework to understand how behavioral interventions that target sleep may reduce inflammation and represent a third pillar, along with diet and physical activity, to promote health.”

## Uncovering the Physical Origins of Depression

New research by Cousins Center scientists suggests that some of the same biological processes that underlie certain physical diseases also drive depression. In other words, depression may be much more like a physical disease than previously thought.

In an article in the journal *Psychological Bulletin*, Cousin's Director Michael Irwin and George Slavich, an associate professor of psychiatry and biobehavioral sciences at UCLA and director of Cousins Center's Laboratory for Stress Assessment and Research, reviewed more than 30 years of scientific work on stress, inflammation, and depression. The review revealed that components of the immune system involved in inflammation and at the heart of certain physical diseases also play a role in depression.

Inflammation is typically thought of as the body's primary response to physical injury or infection. However, a growing body of research now shows that psychological stress can trigger inflammation—and that, in turn, can induce profound changes in behavior, including the development of depressive symptoms such as sad mood, difficulty feeling pleasure, fatigue, and social-behavioral withdrawal. The researchers describe the connection using a new integrative, multi-level theory called the Social Signal Transduction Theory of Depression.

Depression, the authors say, is not just a “mental disorder” involving negative thoughts. “We have generally failed to appreciate the full extent to which

depression is also a biological and physical disorder, affecting several parts of the body and potentially leading to other health problems, says Slavich, who notes that the research suggests new opportunities for possibly preventing and treating depression by targeting inflammation.

“We know a lot about the social conditions that precipitate depression and about the cognitive and emotional processes that mediate these effects,” Slavich adds. “With the advent of new techniques, we are now able to go one step deeper and identify the full set of mechanisms that link stress with depression. Inflammation is undoubtedly a key player in this link.”

## RESEARCH BRIEFS

### Stress and pancreatic cancer

Pancreatic cancer is the fourth leading cause of cancer-related death and is notoriously difficult to treat. The pancreas is innervated by fibers of the sympathetic nervous system (SNS)—fibers that are activated during chronic stress, changing cell behavior. Are pancreatic tumors influenced as well by stress? To find out, researchers non-invasively tracked the growth and dissemination of pancreatic cancer in a mouse model that replicates the interaction between pancreatic tumor cells and their microenvironment. When the mice were stressed—by being restrained within a small space—tumor growth increased and tumor cells spread. Drugs that stimulate the SNS by activating so-called  $\beta$ -adrenergic receptors produced the same outcome. But  $\beta$ -blocker drugs reversed the effects. These findings, the authors note, “raise the possibility that chronic stress may contribute to pancreatic tumor recurrence . . . even after resection of the primary tumor,” and suggest that the use of  $\beta$ -blocker drugs “may complement existing chemotherapeutic strategies to slow or prevent pancreatic tumor growth and invasion, and improve survival of patients with pancreatic cancer.” *Brain, Behavior, and Immunity* 31 (August 2014) 40–47.

### Personality and inflammation

Different types of happiness have been found to have varying effects on the human genome. But does personality—our individual collection of psychological attributes—similarly effect gene expression? A recent study examined this question, looking at the relationship between the five major dimensions of personality (neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness) and the genes previously linked to stress, threat, and adverse socioenvironmental conditions. In a sample of 121 healthy individuals, extraversion (characterized by high levels of sociability and appetitive motivation) was found to be associated with increased expression of pro-inflammatory genes while conscientiousness (reflecting planfulness, caution, and harm avoidance) was associated with reduced expression of those genes. “Although the biological mechanisms of these associations remain to be defined in future research,” the authors write, “the present data may shed new light on the long-observed epidemiological associations between personality, physical health, and human longevity.” *Psychoneuroendocrinology* 52 (2015) 72–82.