

Study to Assess Whether Improved Sleep Reduces Depression Risk – *continued from page 2*

significantly linked to sleep difficulties. “If an older adult has a sleep disturbance, they have a four-fold higher risk of having a depression recurrence,” Irwin says—perhaps because sleep problems increase inflammation, which has been linked to mood problems, but also, he adds, because insomnia and other problems can lead to fatigue and the disruption of social relationships, “which can drive depression risk.”

According to Irwin, the results suggest that “treatment of sleep disturbance may prevent depression recurrence, and early identification of those with sleep disturbance and treatment of those sleep problems may prevent depression from developing.”

Irwin and his colleagues are now recruiting elderly (>60 years of age) volunteers with trouble sleeping for a three-year-long study that will assess these hypotheses. In particular, the study will examine whether two behavioral interventions—cognitive behavioral therapy for sleep quality (CBT-SQ) or sleep hygiene education and training (SS)—can improve sleep difficulties and reduce the risk for depression in individuals who are not currently depressed but have a prior history of the mental illness. Because inflammation is linked with depression, the researchers will also monitor changes in a number of cellular and genomic markers of inflammatory processes. “We hope to show that treatment of sleep disturbance can actually prevent depression, which has never been shown before,” Irwin says.

To learn more about the study, call (310) 206-3578.



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T'ai Chi Reduces Inflammation in the Elderly

A recent study by researchers at the UCLA Cousins Center for Psychoneuroimmunology offers new insight into inflammation-reducing benefits of exercise among the elderly.

Eighty-three volunteers, aged 59 to 86 years old, were recruited for the study. Half participated in thrice-weekly 40-minute sessions of T'ai Chi Chih, a Westernized version of the Chinese martial art consisting of a series of 19 movements and one pose. The movements, with names such as “Bird Flaps Its Wings” and “Working the Pulley,” are performed slowly and meditatively, with the goal of balancing what practitioners call “chi”—the essential life energy. The other half of the volunteers took health-related education courses, also for 120 minutes per week.

Over the course of the 16-week study, Michael Irwin, Norman Cousins Chair for Psychoneuroimmunology at the UCLA David Geffen School of Medicine and director of the Cousins Center, and Richard Olmstead, an associate research scientist in the Cousins Center, monitored the blood levels of inflammatory markers including interleukin 6 (IL6), an immune system molecule known to cause inflammation and to promote

cardiovascular disease and some cancers. The subjects were also evaluated for sleep quality, physical activity, and signs of depression.



The researchers found significantly lower levels of IL6 in the T'ai Chi-practicing volunteers, but not in the group of subjects who just took the health education courses; the drop in IL6 in the T'ai Chi group was correlated with a comparable decrease in signs of depression. According to Olmstead, the study—which was published

in the *American Journal of Geriatric Psychiatry*—suggests “it is possible that meditative low-impact exercise may decrease inflammation and risk of inflammatory disorders in older adults. This, in turn, could improve overall health outcomes.”

Does this mean that any form of low-impact exercise would have the same effect in the elderly? So far, Olmstead says, the jury is out (and it remains a completely “open question” whether T'ai Chi Chih would have any benefit in younger people, he adds). Indeed, it is possible that the actual *exercise* aspect of T'ai Chi Chih had no bearing on the results. “There were not any notable changes in overall physical activity in the subjects. The general literature is mixed in terms of whether exercise interventions can reduce IL6. It could be that the meditative aspects of T'ai Chi are indeed an important component,” says Olmstead.

Further studies of IL6 changes after longer periods of meditative exercise compared to non-meditative low-impact exercise, and perhaps examining the effect on common infections such as flu, he says, will help to tease apart exactly what is going on.

Blood Pressure Drugs Have Diverse Effects on Cancer Recurrence

A new analysis by researchers at UCLA's Cousins Center adds to the growing body of evidence showing that lifestyle factors once thought unrelated to cancer may actually exert a powerful influence on the disease. Case in point: drugs for hypertension.

The study evaluated data from 1779 women in the Life After Cancer Epidemiology (LACE) Study who had been diagnosed with and treated for early-stage breast cancer. Twenty-three percent of the women had been given a beta blocker, an angiotensin-converting enzyme (ACE) inhibitor, or both types of drugs, for the treatment of high blood pressure—with surprisingly different outcomes.

The use of beta blockers, the research revealed, was associated with a lower risk of cancer recurrence and mortality. In contrast, patients who took ACE inhibitors showed more than 50 percent higher levels of cancer recurrence. That two drug classes used to treat high blood pressure had such disparate effects suggests that the results were not actually related to blood pressure, says UCLA's Steven Cole, a professor of medicine in the division of hematology-oncology and a research scientist in the Cousins Center, and a co-author of the study. Instead, the effects are

probably related to the specific biological systems affected by each type of drug. For example, beta blockers appear to block the ability of tumor cells to recruit the macrophages that aid their spread and to prevent the formation of new tumor-nourishing blood vessels. ACE inhibitors, however, do not appear to block either of those processes.

The study findings, the researchers say, are "provocative," and raise awareness about the possible benefits of beta blockers in reducing recurrence risk—as well as concerns about the potential risk of ACE inhibitors when used by cancer patients. "We don't yet know why ACE inhibitors might be detrimental," says Cole, "but it's probably related the specific biology by which ACE inhibitors affect angiotensin," a hormone that causes blood vessels to constrict, "although we don't understand how that interacts with cancer," he says.

The take-home message of the study, Cole says, is that "drugs that are prescribed for one disease have the potential to influence other diseases, especially cancer." The result, he adds, "is not surprising if you think about the body as one integrated organism, and cancer as a whole-body, integrated system disease. When one part of the body starts to behave badly, drugs that target another part might be helpful."

Study to Assess Whether Improved Sleep Reduces Depression Risk



In addition to being considered a routine part of normal aging, sleep problems like insomnia are a common symptom of depression—which, in the elderly, can raise both disease and mortality risks. But could the link between the mood disorder and sleep disturbance be more causal, with impaired sleep actually leading to depression?

This question was addressed in a 2008 study of community-dwelling elderly individuals conducted by Cousins Center Post-Doctoral Fellow Jin Cho and colleagues. As reported in the study, which was published in the *American Journal of Psychiatry*, a prior history of depression increased the chance that depressive symptoms would eventually return. More significantly, the recurrence of depression was

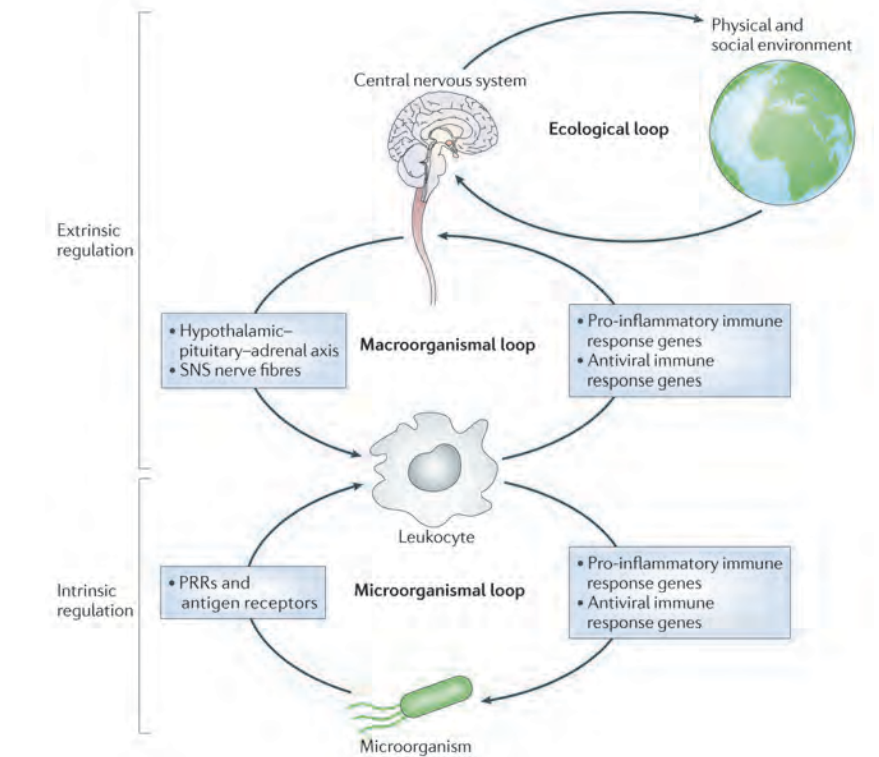
Continued on page 4

Cousins Researchers Explore Neural and Immune System Feedback Loop

The innate immune system represents the body's first line of defense against assaults by foreign invaders and its initial response to cellular injury and death. There's more, however, to this already complex system. Recent work by researchers at the Cousins Center for Psychoneuroimmunology and at other centers suggests that, in addition to being triggered by the activation of specific immune-related genes, our immune system is mediated by signals from the nervous and endocrine systems. The resulting immune responses then signal back to the brain, via chemical messengers, to modulate the central nervous system (CNS) and endocrine activity—producing a feedback loop known as the neuro-immune circuit that, ultimately, can have profound effects on behavior.

In a recent editorial in the journal *Nature Reviews Immunology*, Cousins researchers Michael R. Irwin and Steven Cole discuss this surprising circuit, which, they write, "links physiological, social, and environmental conditions, as perceived by the CNS, with transcriptional 'decision-making'" in white blood cells and "coordinates immune responses with other physiological processes—such as fight-or-flight stress responses—to maximize the overall fitness of the organism within complex environments that bear multiple threats." Understanding the circuit and developing ways to exploit its function, Irwin and Cole argue, could lead to new therapeutic approaches for controlling inflammatory diseases and psychiatric conditions like depression, insomnia, and the sometimes-debilitating fatigue suffered by cancer survivors.

Among the key players in this circuit are proinflammatory cytokines, such as interleukin 6 (IL6) and tumor necrosis factor (TNF), chemicals that are marshaled into action after infection or injury and coordinate the body's responses. Proinflammatory cytokines also activate a suite of symptoms called "sickness behaviors" that include fatigue, reduced appetite, and irregular sleep. These behaviors, Irwin and Cole write, "function together with lymphocyte activation dynamics to limit the



spread of infectious disease both within and between individuals." (In other words, by feeling sick, we may be helping others from getting sick.)

But sickness behaviors aren't always beneficial. The effects, the duo note, "are highly reminiscent of some common adverse behavioural syndromes with poorly understood etiology, suggesting that dysregulated activation of cytokine-mediated sickness behaviours might underlie some cases of medically unexplained fatigue, sleep impairment or major depressive disorder." If that is indeed the case, therapies that block the action of proinflammatory cytokines may help alleviate depressive symptoms, improve sleep disorders, and reduce fatigue.

Just as these cytokines seem to influence behavior, so too, Irwin and Cole note, can behavioral interventions affect the action of these chemicals—via the same feedback loop. Indeed, randomized controlled trials have detected reductions in proinflammatory cytokines

following a variety of behavioral interventions, including cognitive behavioral therapy, aerobic exercise, meditation, and Tai Chi.

"As the relationship between environmental conditions and infectious disease has changed over the past century," the researchers write, "the historically beneficial crosstalk between the CNS and the immune system has become misaligned with our current ecology. Now, this crosstalk may allow abstract non-physical threats to induce inflammation-related cardiovascular, neurodegenerative and neoplastic diseases, while undermining our innate antiviral defences. Nevertheless," they conclude, "it may still be possible to harness reciprocal neural-immune regulation through pharmacological or behavioural interventions to redirect the basic transcriptional stance of the innate immune system and more effectively accommodate the health ecology that we now inhabit."