immune response that has run its course, because the effects of IL-1 and -6 on the brain include triggering the HPA by stimulating CRF production, which creates an immune-suppressing feedback.

That damping down can have a downside, though, possibly leading to decreased ability to fight infections. At Ohio State University, Janice Kiecolt-Glaser and Ronald Glaser found that in stressed medical students, overactive HPA responses decreased the effectiveness of the hepatitis-B vaccination. Then working with immunologist John Sheridan, also from Ohio State, they found that the flu vaccine was less likely to work in people caring for spouses with Alzheimer's disease—a task known to cause a lot of stress—than in people of similar age and background not in those caretaker roles.

Yet, the immune-suppressing feedback can be helpful, says NICHD's Chrousos, as it may explain the lessened rheumatoid arthritis symptoms during pregnancy. His group found that during the last trimester, the fetus produces CRF that gets into the mother's circulation and tends to make the HPA axis overly active. In addition, the estrogen increase during pregnancy may stimulate cortisol secretion. Test tube studies suggest that corticosteroid concentrations similar to those in late pregnancy suppress the cell-mediated branch of the immune system, which causes the symptoms of rheumatoid arthritis.

Conversely, there is mounting evidence that a depressed HPA axis, resulting in too little corticosteroid, can lead to a hyperactive immune system and increased risk of developing autoimmune diseases. NIMH's Sternberg and her colleagues found the first evidence for such a connection 8 years ago in studies of two strains of rats that differ in their inflammatory responses and their susceptibility to many experimentally induced autoimmune diseases. They found that Lewis rats, the sensitive strain, release much less CRF and less corticosteroid in response to stress or exposure to antigens than do the resistant Fischer rats.

Such a correlation does not necessarily prove a connection, but at the meeting, Sternberg and Barbara Misiewicz of NIMH reported that transplanting cells from the hypothalamus of embryonic Fischer rats into adult Lewis rat brains makes the recipients as unlikely to develop autoimmune disease as are the Fischer rat donors. By producing more CRF than the Lewis rat's own brain does, the transplanted tissue may prompt more vigorous HPA responses and tame the animals' hyperactive immune system.


GAYKEMA, GOEHLER, WATKINS, AND MAIER

Close ties. Immune cells (red) stimulate the vagus nerve (seen in cross section, in green) via paraganglia cells (green and yellow).

A depressed HPA axis may contribute to an overly sensitive immune system in people, too. "The evidence is mounting that these principles apply not only in chickens, not only in rats, but also in humans," Sternberg emphasizes. For example, at the University of Trier, Germany, psychologist Angelika Buske-Kirschbaum has found that children known to suffer from atopic dermatitis—allergies that result in itchy skin and rashes—or from asthma have a blunted HPA response. When asked to tell a story or do mental math, these children show less increase in the glucocorticoid concentrations in their saliva than do their healthy peers. "They showed this very dramatic difference in the salivary cortisol response," says Sternberg. The researchers propose that the children's lower HPA function may make them susceptible to allergies in the same way it makes Lewis rats prone to autoimmune disease.

These kinds of studies, suggesting intimate links between the endocrine and immune systems and mental states, are inspiring new studies that aim to draw even tighter connections. NIMH's Gold, for example, hopes to learn how the neuroendocrine patterns of depression affect the immune system. In one form of the disease, the HPA axis is underactive, suggesting that those with this condition "may be immunologically disinhibited," he says, while in another other form, corticosteroid levels are unusually high. Ultimately, he hopes that studies of these interconnections will "provide us targets for drug treatments," Gold says, not only for depression but also for the physical symptoms associated with this condition. At the same time, his group hopes to learn whether inflammation or disease can cause depression to flare.

That holistic approach is what neuroendocrine immunology is all about, its pioneers argue. "This is the coming together of these fragmented sciences," says neuroscientist Bruce McEwen of Rockefeller University in New York City. "We're putting the body back together again."

–Elizabeth Pennisi

ATOMIC PHYSICS

Atoms Take a Turn for the Better

Every time a 747 jetliner maneuvers, patterns of light and shadow in a device called an interferometer measure the change in angle. Now, photons have a rival for sensing small rotations: interfering atoms. In the 3 February issue of *Physical Review Letters*, Massachusetts Institute of Technology (MIT) physicists describe how they used an atom interferometer, which takes advantage of the wavelike nature of matter described by quantum mechanics, to measure rotations as subtle as a quarter of a degree per hour. The paper marks a first step toward practical applications for atom interferometers, which physicists first developed in 1991.

The sensitivity of the MIT instrument is "on par with the interferometer in a 747," says Edward Smith, a member of the team that built it. And it may be just the beginning for this atom-based instrument. Because atoms have wavelengths many orders of magnitude shorter than light, he adds, "in the end, atom interferometers will be 10,000 times better than the very best commercial optical interferometers ... and probably less costly."

Like a beam of light, a beam of atoms can be split with a fine grating, sent down separate paths, and brought together again. Because of atoms' wavelike nature, the converging beams produce an interference pattern of "bright" and "dark" spots, which indicates the relative arrival times of the crests and troughs in the two beams. Anything that affects the path lengths should shift the interference pattern—and because atom wavelengths are so short, atom interferometers promise unparalleled sensitivity.

Measuring rotations was a tempting application. Interferometers can sense rotations because any twisting of the interferometer shortens one beam's path and lengthens the other, so when the waves reach the end of the device, they are no longer in phase. The phase difference—manifested in the interference pattern—shows how much the interferometer has twisted.

To realize this scheme with atoms, the MIT physicists needed exquisite vibration control and larger, finely etched gratings to control the atoms. The technology was ready a year ago, and it has now yielded a device that rivals commercial optical interferometers.

Mark Kasevich, a physicist at Stanford University, already has something even better in the works, he says: an atom interferometer that will be two orders of magnitude more sensitive than the best commercial devices. "There's a number of groups quietly trying to improve [atom interferometers]," says Steven Chu, also at Stanford. "It's getting exciting."

–Charles Seife

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