This is your brain on meth: 3-D Images Illustrate Drug Devastation

The first high-resolution MRI study of methamphetamine addicts vividly reveals what UCLA scientists call “a forest fire of damage” to the brain’s reward, emotion and memory systems. The *Journal of Neuroscience* published the findings on June 30, 2004.

“We expected some brain abnormalities but not so much damage,” says Dr. Paul Thompson, associate professor of neurology. “We saw about 10 times the cell loss caused by normal aging in a healthy brain.”

Dr. Edythe London, a professor at the UCLA Neuropsychiatric Institute, imaged the brains of 22 people who had abused methamphetamine for 10 years and then imaged the brains of 21 age-matched controls. Both groups also performed a series of memory tests.

The drug abusers performed significantly worse on the memory tests than healthy people their age. In addition, the addicts showed an 11 percent tissue deficit in the limbic region, the brain’s reward and emotion center, and an 8 percent deficit in the hippocampus, the brain’s memory center. The tissue shortfall directly correlated with the level of memory impairment.

“The addicts’ brain tissue loss resembled that of Alzheimer’s disease,” says Thompson. “Memory, emotion and reward areas were affected the most, while other parts of the brain remained intact.”

White matter, the bulky nerve fibers that connect different regions, was severely inflamed, making the addicts’ brains a whopping 10 percent larger than normal.

“We think this inflammation results from repeated drug abuse,” says Thompson. “The brain inflames when its glial cells multiply in response to injury.”
UCLA Study Calls for Earlier Treatment of Fungal Infections in Critically Ill Newborns

A UCLA study demonstrates that early treatment can mean the difference between life and death for high-risk babies born with fungal infections.

Presented May 1, 2004, at the Pediatric Academic Society’s annual meeting, the findings show that the infant’s likelihood of death rose with each day physicians delayed antifungal therapy after the newborn’s first positive culture.

“Because fungal infections are considered ‘slow-moving,’ the standard protocol has been to wait for laboratory results before starting treatment,” explains Dr. Heather Cahan, neonatology fellow at Mattel Children’s Hospital at UCLA. “We wanted to investigate how long physicians are waiting to start treatment and if this adversely affects the baby’s outcome.”

The UCLA team examined the histories of 68 patients with 77 episodes of invasive fungal infections at a neonatal intensive care unit from 1998 to 2002. Thirty-four percent of the newborns died.

After lab results confirmed a positive culture, physicians waited an average of 10 days before starting antifungal treatment. The infant’s risk of death rose 11 percent with each day of delayed therapy.

“We found that treatment delay was the most important factor in newborns’ mortality rate from fungal infections,” Cahan says. “We recommend that neonatologists start antifungal treatment within 48 hours of drawing cultures in high-risk infants.”

New Therapy Fights Resistance to Leukemia Pill, Targets Mutations That Cause Relapse

UCLA’s Jonsson Cancer Center scientists discovered that an experimental therapy improves survival in an animal model for drug-resistant chronic myeloid leukemia (CML). With early human studies already underway at UCLA, the findings were published July 16, 2004, in Science.

Gleevec targets a cancer-causing gene linked to CML, which strikes more than 70,000 adults worldwide each year. Some 20 percent of patients develop secondary genetic mutations that prevent Gleevec from binding to the gene and cause the leukemia to recur.

Developed by Bristol-Myers Squibb, the new compound, BMS-354825, is also administered in a pill form. It targets and binds to 14 of the 15 secondary mutations in the CML gene.

“In the future, we may combine therapies to override the resistance mechanisms that allow cancer to evade individual therapies,” says Dr. Neil Shah, assistant professor of hematology/oncology. “We may treat cancer like HIV, with a cocktail of drugs.”

Future studies may eventually pair Gleevec with the new drug, if it proves to be safe and effective in human clinical trials.
Obesity Disrupts Appetite Hormone, May Sabotage Body’s Cues for Hunger, Fullness

UCLA scientists have discovered that lean people experience a huge nighttime surge of ghrelin that obese people do not. Ghrelin, the hormone that stimulates hunger, helps the body control its weight as part of a complex system that regulates food intake and energy output.

Published June 28, 2004, in the Proceedings of the National Academy of Sciences, the UCLA research suggests that obesity suppresses the ghrelin spike.

“We expected to find a different ghrelin pattern in obese people, but the big shock was that it happened at night,” says Dr. Julio Licinio, professor of psychiatry and a senior researcher at the UCLA Neuropsychiatric Institute.

“You’d expect the blood levels of the heavier men to contain more hunger hormone, not less. Something must be overriding obese persons’ ghrelin,” he says.

Cells in the stomach secrete ghrelin into the blood, where it rises and falls in predictable daily patterns, spiking before meals when you are hungry and dropping after you eat.

Licinio’s colleagues monitored ghrelin patterns in five lean men and five obese men every seven minutes for 24 hours. The team collected more than 200 blood samples per subject.

The scientists discovered a giant burst of ghrelin in the lean men’s blood between midnight and 6 a.m. that surpassed pre-mealtime peaks of the hormone. Yet ghrelin levels remained flat in the obese men.

“The most powerful ghrelin surge was missing in the obese men, suggesting that their regulatory system has gone awry or is no longer able to listen to its own cues,” Licinio says.

The team’s findings may point to new targets for treating obesity, says Licinio.

“It’s possible that obese people have developed biological mechanisms that make them resistant to their own hormones,” he says. “We must try to solve this mystery and explore new drugs to make them more sensitive to their bodies’ internal cues.”
Lung Inflammation Linked to Heart Disease, UCLA/Penn Research Discovers

Researchers from UCLA and the University of Pennsylvania found that patients with an inflammatory lung disease called pulmonary fibrosis are four times more likely to develop heart disease related to coronary artery disease.

Published March 8, 2004, in the *Archives of Internal Medicine*, the findings observed that both diseases cause inflammation that can lead to tissue scarring and eventual blockage of coronary arteries.

“We were very surprised to see the large number of pulmonary fibrosis patients who also developed advanced coronary artery disease,” says Dr. David Zisman, director of the Interstitial Lung Disease Program and assistant professor of pulmonary and critical care medicine.

The researchers reviewed the coronary angiograms of 630 patients evaluated for lung transplants at the University of Pennsylvania. They discovered that pulmonary fibrosis put patients at twice the risk for coronary artery disease and at four times the risk for more extensive heart disease.

“Our next step will be to examine the inflammation mechanisms that underlie development of these two diseases,” says Dr. Robert Strieter, vice chair of medicine and division chief of pulmonary and critical care medicine.

**RISK FACTORS:** A lung-tissue sample shows the inflammation and scarring caused by pulmonary fibrosis. New findings suggest a common mechanism may lead to heart disease.

African Americans and Asian Americans Less Likely to Seek a Medical Specialist

A UCLA study discovered that African American and Asian American patients are less likely than Caucasians to prefer a medical specialist for initial care. Published May 1, 2004, in the *American Journal of Medicine*, the findings suggest a possible explanation for racial differences in health care.

“Researchers have struggled to understand why African Americans and other minorities receive worse health care and have poorer health status,” says Dr. Mitchell Wong, assistant professor of medicine. “Obvious reasons, such as income and health insurance, only partly explain these disparities.”

Wong’s team randomly selected 646 patients from three academic-based internal medicine outpatient practices in Los Angeles and New York City. Of those, 48 percent were Caucasian, 29 percent African American, 9 percent Latino and 9 percent Asian American.

Researchers asked patients their preference for seeing a specialist for the health problem that brought them to their physician’s office, as well as for three hypothetical scenarios: two weeks of new chest pain, two months of knee pain and a four-week rash.

Patients who were older, possessed Medicaid insurance or had more confidence in their primary-care physician’s ability to diagnose or treat their illnesses were also less likely to prefer a specialist for their initial care. In contrast, patients who knew which tests or treatments they needed or had been to a specialist in the past year were more likely to seek a specialist.

After adjusting for these variables, researchers found that African Americans and Asian Americans still were less likely than Caucasians to prefer initial treatment from a specialist.

Wong suggests that unexamined factors, such as negative attitudes or less understanding about specialists, may illuminate the racial disparities.

“Seeing a specialist is often the first step toward obtaining advanced therapies,” says Wong. “So our findings may explain why African Americans are less likely to receive certain treatments, such as cardiac bypass surgery or chemotherapy.”