Meet Me in St. Louis—with Data

St. Louis—*At the annual meeting of the Society for Neuroscience here last week, 12,000 researchers gathered to hear the latest scientific results on subjects as diverse as a new infection pathway for the AIDS virus, a deadly cofactor in cocaine-induced deaths, and an explanation for how female birds recognize the love songs of their mates. These highlights are the first of two reports from the neuroscience meeting; a more comprensive news article will appear in next week's issue of* Science.

Birds Do It

"If music be the food of love, play on. . ." wrote the Bard, but *Homo sapiens* is far from the only species in whose mating behavior songs play a key role.

Male canaries sing an elaborate, species-specific courting song that attracts females for mating. They learn their song by listening to the songs of experienced male singers, and it has been known for some time that a part of the brain called the HVc is needed for this learning.

Females also have the HVc (although it isn't as big as the male version), but it hadn't been known what purpose the brain region served on the distaff side. Researchers speculated that the HVc might be needed for females to recognize and respond to the male courting songs, but there wasn't any hard evidence for that notion until last week, when Eliot Brenowitz of the University of Washington reported studies in which he destroyed part of the HVc in female canaries and found that they lose an essential capacity to discriminate between their and other species' songs.

Brenowitz injected healthy females with hormones to bring them into breeding condition. Then he played them recordings of male canary songs or male sparrow songs. The females responded—exclusively to the canary songs—with a characteristic mating display. Then Brenowitz used electric shock to destroy part of the females' HVc. When he tested them, he said, "They completely changed their behavior. They started responding to sparrow as well as canary song."

The result is "teleologically pleasing," said Mark Breedlove, of the University of California, Berkeley, who studies sexual dimorphism in the brain. Breedlove explained that since males learn their songs by listening, and the stHVc seems to play a role in that recognition, it seems logical that that area of the brain would govern song recognition in females as well.

Brenowitz told *Science* that he had expected to disrupt song recognition, but in the opposite way: he anticipated that the females would not respond to either song, and that he would have to take pains to show that they weren't deaf. But he says the result does make sense if one considers hormonally stimulated females as being primed to respond to song and the HVc as a species-specific filter that allows them to respond only to the right singer.

New HIV Infection Mechanism?

Among many AIDS puzzles, neuroscientists have scratched their heads over one that arises in the brains of AIDS sufferers: call it the case of the missing CD4.

When HIV infects immune system cells such as T cells and macrophages, it binds to a cell-surface receptor known as CD4. But although HIV is known to infect brain tissues (where it is responsible for the dementia seen in many AIDS patients), brain neurons don't have CD4.

Until now, researchers concluded HIV must exert its effects on nerve cells indirectly—perhaps by infecting the brain cells called microglial cells (which do bear CD4 receptors); the glial cells might, in turn, influence neurons. But groups from Columbia University, Bristol-Myers Squibb, and Nova Pharmaceuticals reported here that HIV may enter neurons directly by a mechanism that does not rely on CD4. And if they are correct, neuroscientists will have to revise their picture of HIV infection.

All three groups found that HIV is capable of infecting cell lines derived from neuroblastomas or glioblastomas—tumors stemming from neurons or glial cells. When gp120 (the HIV envelope protein that "docks" on CD4) was added to the soup, the viral binding was interrupted. This implies that the entry mechanism involves a specific receptor on the cells, a receptor that binds to gp120, says Yaffa Mizrachi of the Columbia group. Yet the binding was not blocked by free CD4, suggesting that the cellular receptor is not that molecule.

"It would be nice to do this on primary nerve cells," says Stuart Lipton of Harvard University, noting that immortalized cell lines may differ in some ways from neurons. Nevertheless, Lipton, whose own work suggests that gp120 is toxic to nerve cells, finds the results pleasing. "If neurons don't seem to have CD4, then how do they get injured? It would make sense that there would be a non-CD4 site gp120 might interact with."

Miami Vice Metabolite

Cocaine users know that when they drink alcohol, and then snort coke, they get a higher high than if they had used cocaine alone. Now science has a clue as to why that is—and the implications may be fatal.

Deborah Mash of the University of Miami School of Medicine reported here that in the presence of alcohol, liver enzymes convert cocaine into a potent metabolite called cocaethylene. A decade ago, coca-ethylene was identified in the urine of cocaine and alcohol users, but its functions weren't clear. Mash's group finds that this substance is as potent as cocaine in blocking uptake of the neurotransmitter dopamine at synapses—the activity thought to be responsible for cocaine's pleasurable effects and the reinforcement that makes it habit-forming.

But cocaethylene is 40 times less potent than pure cocaine at blocking the uptake of the transmitter serotonin, something that has been shown to counteract the reinforcing nature of the dopamine blockade. The result, says cocaine researcher Michael Kuhar, is that cocaethylene is a "purer rewarding substance" than cocaine itself.

Working with toxicologist Lee Hearn of the Dade County coroner's office, Mash's team analyzed samples from 124 people who died after using cocaine and alcohol and found cocaethylene in the 60% in whom the blood levels of both cocaine and alcohol were moderate to high at the time of death. They have also found the substance in the blood of 12 of 14 emergency room patients who had recently used both cocaine and alcohol.

Those findings suggest cocaethylene is dangerous stuff. And epidemiological studies show that the cocaine-alcohol combination is 21 times as deadly as cocaine alone for people with underlying coronary artery disease, Mash said. In addition, cocoaethylene is twice as deadly as cocaine when given to mice. But she cautioned that more work is needed before the actual relative risk of cocaine and cocaethylene can be established.

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