Craving fat? Blame it on a brain protein

If your favorite foods include items such as potato chips, fried chicken, and ice cream – and if you find it nearly impossible to "eat just one"—the problem may literally be in your head, new research suggests.

A team of neuroscientists led by Sarah F. Leibowitz at Rockefeller University in New York City has uncovered evidence in rats that a brain protein called galanin dictates the craving for fatty foods. Moreover, the group has found that a drug that blocks galanin's activity can reduce an animal's appetite for fat.

Leibowitz described these results last week at the Society for Neuroscience's annual meeting in Anaheim, Calif. She and her colleagues studied the brains of rats that had been allowed over a three-week period to eat as much as they wanted of three specially prepared foods: milk protein, a high-carbohydrate mixture of sugar and cornstarch, and lard.

Leibowitz's team found that rats with high natural concentrations of galanin in a brain region called the hypothalamus ate more lard each day and gained more weight over the study period than did rats with low galanin concentrations – despite the fact that both groups consumed roughly the same amount of protein and carbohydrate each day. In addition, the researchers observed, the rats with high galanin levels almost always began their meals by lapping up lard, indicating that they might be trying to satisfy a craving.

In a second study reported at the conference, Leibowitz' group ruled out the possibility that the extra galanin might have arisen elsewhere in the rats' bodies and then traveled to their brains. The researchers discovered high concentrations of galanin messenger RNA (mRNA) – the chemical intermediary through which the galanin gene directs the production of galanin – in brain cells taken from overweight rats with a strong predilection for fat. They also found that these rats had reduced concentrations of insulin in the blood, indicating that galanin serves as a biochemical link between obesity and diabetes.

"Animals with high galanin levels have high fat intake," summarizes Leibowitz, "and these animals also have lower levels of insulin." However, she adds, her team has not yet determined how galanin and insulin interact.

"The data are quite interesting," comments Michael Schwartz of the Veterans Administration Medical Center in Seattle. But he cautions that Leibowitz's group needs to study rats fed only fat to make certain that the elevated galanin they observed is not simply the result of a high-fat diet. Until then, he contends, the researchers "don't know whether the galanin is causing the increased fat intake or if the increased fat intake is causing the increased galanin."

Leibowitz counters that earlier experiments by her group and others have shown that rats receiving galanin injections in a specific region of their hypothalamus eat much more fat than do control rats given galanin injections elsewhere in their brains. Moreover, she says, the galanin injections make the fat-gobbling rats sluggish, reducing their metabolism and leading to weight gain.

Leibowitz and her colleagues have recently found that an experimental drug called M40 can slash a rat's fat craving by blocking the activity of galanin in its hypothalamus. In the November/December BRAIN RESEARCH, she and Rockefeller colleague Taewan Kim report that rats given extra galanin to boost their fat intake resume eating normal amounts of fat following injections of M40.

Several drug companies are now developing compounds similar to M40. Leibowitz says she and her co-workers hope to begin clinical trials of M40 "within the next couple of years" among patients with eating disorders. She adds that the drug might also benefit diabetics who have difficulty controlling their weight. *– C. Ezzell*

Hypertension battle plan

Despite several decades of progress in reducing the prevalence of high blood pressure, federal health officials believe more can be done to combat this disease. Last week, the National Heart, Lung, and Blood Institute (NHLBI) unveiled a new program aimed at preventing hypertension.

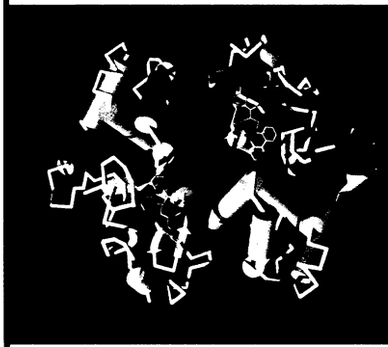
Americans can reduce their risk of developing hypertension with life-style changes, including cutting back on salt consumption, says Paul K. Whelton, chairman of an NHLBI committee that produced a report outlining the prevention strategy. Noting the relationship between salt intake and blood pressure, his group advises people to ingest no more than 6 grams (approximately 3 teaspoons) of salt per day. In addition, it urges Americans to increase their physical activity, reduce alcohol consumption, and shed excess weight.

The prevention message is especially important for people at high risk of hypertension, such as African Americans and those with a family history of the disease, the committee noted. It urges special efforts to reach people whose blood pressure is slightly elevated but still within the normal range.

Scientists now believe that vascular complications of hypertension can begin well before people develop overt high blood pressure. The committee urged life-style changes for people with "high normal" blood pressure, which is defined as systolic pressures between 130 and 139 millimeters of mercury (mm/Hg) and diastolic pressures between 85 and 89 mm/Hg. Men with pressures that fall into this category have twice the risk of dying from cardiovascular disease.

Life-style changes are also important for people with established hypertension, defined as systolic pressures of at least 140 mm/Hg and diastolic pressures of 90 mm/Hg or more. If that strategy fails to bring pressures down, however, NHLBI reemphasizes lowering blood pressure with drug therapy. □

Anticancer enzyme imaged



Center for Advanced Research in Biotechnology

A computer image reveals that this liver enzyme's 434 amino acids arrange in twin sections. Weak interactions help hold the two sections together. In each section, the amino-acid chain spirals (blue barrels) and zigzags (yellow stripes), forming two docking sites: one for a detoxifying molecule called glutathione (pink) and one for a toxin (not shown). A side chain (red) of one amino acid, tyrosine, chemically alters the glutathione in such a way that the sulfur in the glutathione reacts and links with the toxin to disarm it, says biochemist Richard N. Armstrong of the University of Maryland in College Park.

Each of the dozen or so glutathione S-transferases, as these enzymes are called, has evolved a slightly different amino acid sequence at its toxin docking site, which alters the site's shape slightly, says Armstrong. Thus, the enzymes provide protection against a wide variety of cancer-causing substances that enter the body.

Armstrong worked with researchers at the Center for Advanced Research in Biotechnology in Rockville, Md., to obtain the first three-dimensional picture of this type of enzyme. They describe the X-ray diffraction studies, computer analysis, and the resulting high-resolution structure of the enzyme in the Oct. 27 BIOCHEMISTRY. □