

Making painkillers ... naturally

Three Johns Hopkins University neuroscientists have identified the human enzymes responsible for the manufacture of so-called enkephalins, the brain's own morphine-like hormones. The discovery raises the possibility of a new and more efficient class of psychoactive drugs for appetite control and for the treatment of shock victims.

Psychiatrist and biochemist Solomon H. Snyder, speaking at a recent seminar at the Johns Hopkins Medical Institutions in Baltimore, said that he and Lloyd D. Fricker, a student, have succeeded in isolating "enkephalin convertase," one of the two bodily chemicals necessary for the creation of the body's naturally occurring opiates. In addition, Snyder told *SCIENCE NEWS*, he and another student, Steve Strittmater, have recently identified a second, unnamed enzyme that works in tandem with enkephalin convertase to complete the manufacturing process.

Snyder was a co-discoverer of the enkephalins, neurotransmitters that act in the brain by binding to specific opiate receptors, which Snyder also discovered. Although drugs have been created that block the effects of enkephalins by blocking the receptors, little has been known about the actual formation of these chemical messengers. Enkephalins, which are chains of five amino acids, are trapped in massive "precursor" molecules of 300 to 500 amino acids. In order to become biologically active they must be chemically extracted from the precursor. The recently identified enzymes do the extracting and, according to Snyder, they seem to work exclusively on the enkephalins.

Snyder and his students identified the enzymes by synthesizing a chemical similar enough to the enkephalin precursor to attract and activate specific enzymes, thus mimicking the natural process. They found that two enzymes were required to free the tiny enkephalin molecule—one to sever it on each end from the amino acid chain. The first of these, enkephalin convertase, appears to be specifically designed for this job, Snyder says; the second requires more study.

These findings point to the possibility of a new class of drugs that, by inhibiting the enzymes, could lower the amount of active enkephalins manufactured in the brain. And in fact, Snyder says, Fricker has already found several chemicals that are "very potent and specific" inhibitors of enkephalin convertase. Should these chemicals lead to the development of new drugs, their most obvious applications would be those for which receptor blockers are currently used; naloxone, for example, has been used in animals and humans as an appetite depressant and —

because it raises blood pressure — as a treatment for severe shock.

According to psychiatrist Steven M. Paul of the National Institute of Mental Health, a drug that controls the actual production of a neurotransmitter should be a more efficient and more natural drug than one that blocks transmission. When brain recep-

tors are blocked, he says, they often compensate by becoming supersensitive, and in the case of another neurotransmitter system—the dopamine system—such receptor sensitivity has been implicated in the side-effect called tardive dyskinesia, an involuntary movement disorder.

—*W. Herbert*

Speedier licensing for nuclear power plants

If a nuclear power plant is operating "at an acceptable level of risk," utilities may not be required to make changes to increase the safety of the plant. This recommendation is one of five changes suggested in a Department of Energy task force report on nuclear licensing and regulatory reform. The report, released last week, is a preview of legislation the Reagan administration plans to submit to Congress early next year to help revitalize the nuclear power industry.

The report says that the existing regulatory process "has not produced regulatory stability nor has it kept pace with the evolution of nuclear power as an energy source.... The present process does not offer predictable criteria for siting, designing, constructing and operating nuclear plants, and it does not lead to predictable schedules." The aim is to make it possible to plan and build nuclear plants in six to eight years rather than the 10 to 14 years now required.

The task force proposes:

- The Nuclear Regulatory Commission should provide centralized review and approval of all proposals for changes in nuclear plants to increase safety. Decisions on whether a utility should make alterations in a particular plant would depend on the increase in overall risk from a potential safety concern.
- Hearings that provide for cross-examination of witnesses should be "reserved for genuine contested issues of material fact."
- Instead of the current two-step licensing process, under which a construction permit and an operating license must be obtained separately, utilities would have the option of getting both licenses in one step.
- The NRC could approve sites as suitable for prospective nuclear plants in advance of a utility's desire to apply for permission to construct.
- Utilities could choose to build a plant based on NRC-approved generic designs.

Marcus A. Rowden, former chairman of the Nuclear Regulatory Commission, says he supports the task force recommendations although he doesn't agree with every detail. "It addresses the major points that need treatment through legislation," Rowden says.

Robert Pollard, a nuclear safety engineer with the Union of Concerned Scientists, argues, "It's the same old thing that's been coming in since 1978. A lot of their

proposals could be accomplished right now under NRC's regulations." He adds, "A lot of these proposals, at least on the surface, are things we recommended in 1978. The difficulty is when you look at the details of how they want to accomplish them."

Rowden says, "The basic underlying concepts have a broad area of acceptance. I'm hopeful that with the appropriate level of political support, we can move this forward during the next Congress and get legislation enacted, and at the same time have the NRC move forward on a parallel path with administrative reforms."

A spokesman for the Atomic Industrial Forum, a group representing nuclear power companies, says, "The industry is mainly interested in the idea of certainty in licensing. Regulatory reform is one of several things that have to happen if there are going to be any more nuclear power plants."

Still to come is the report of an NRC nuclear regulatory reform task force. Rowden expects that the NRC recommendations will roughly parallel those in the DOE task force report.

—*I. Peterson*

Anorexia nervosa: A brain shrinker?

Anorexia nervosa, self-imposed starvation to achieve a sense of thinness, is a widespread problem among young women in Western countries. Now a team of German neuroradiologists and psychiatrists has found that anorexics can experience brain abnormalities coupled with impaired mental performance. However, the abnormalities and impaired performance are largely reversible provided anorexics return to a normal weight. These results were reported last week at the 12th International Symposium on Neuroradiology in Washington, D.C., by the team's chief investigator — Knut Kohlmeyer of the Central Institute of Mental Health in Mannheim, West Germany.

There have been several recent reports in the medical literature of computerized axial tomography (CT) brain scans revealing reversible brain abnormalities in anorexic patients. Scientists have also reported that severe malnutrition can lead to impaired mental performance. But Kohlmeyer and his colleagues appear to be the first to have combined CT brain

scans with mental performance tests to study anorexics.

They performed CT brain scans on 23 teenage anorexics. In 21 they found numerous spaces over the top of the cerebral cortex and a fissure between the two hemispheres of the brain. These are anatomical features not normally present in young people and are the precise features noted by other researchers visualizing anorexics' brains with CT scans. Seven of the 21 patients also showed a slight enlargement of ventricles inside the brain, and two of the 21 with particularly severe anorexia likewise had abnormally wide spaces in the cerebellum of the brain. The two remaining patients out of the 23 showed no brain abnormalities; they were the patients who had suffered anorexia for the shortest time. At the time of the scans, the researchers also gave all 23 patients tests to measure their IQ, concentration, reaction time and perceptual speed. The patients' IQs were comparable to those of the normal healthy population, but their concentration, reaction time and perceptual speed were slightly below those of the normal healthy population.

Eleven of the 23 patients who eventually returned to a normal weight were then given repeat CT brain scans and mental performance tests; the results were compared to the patients' previous ones. There was a significant reduction in the number of cortical and cerebellar spaces and interhemispheric fissures among all the patients. Only one of the 11 had had enlarged ventricles; they were still enlarged. The patients showed no change in IQ, but improvement in concentration, reaction time and perceptual speed.

While anorexia may be caused by psychological problems, the illness itself can lead to mental impairment, and this impairment in turn appears to be due to brain abnormalities. Kolhmeyer and his co-workers conclude. When patients return to a normal weight, though, the brain abnormalities and mental impairment appear to be largely reversible.

Still to be answered is how anorexia triggers the brain abnormalities noted in anorexics. It probably does so by shrinking the brain through nutrition and water loss, contends Arnold E. Andersen, director of the Eating and Weight Disorders Unit at Johns Hopkins University School of Medicine in Baltimore. Daniel Weinberger of the Adult Psychiatry Laboratory in St. Elizabeth's Hospital in Washington agrees: "CT scans are sensitive enough to pick up some variances in fluid status in the brain." However, Kolhmeyer and his co-workers found no indication that their 23 subjects were suffering severe malnutrition or severe water loss during anorexia, as chronically starved persons do. Still, the investigators admit, "it would be valuable to obtain cranial CT findings on chronically starved subjects and to compare them to those of anorexics."

—J.A. Treichel

VA yields control of Agent Orange study

Yielding to congressional pressure, the Veterans Administration has agreed to give up control of an investigation into whether Vietnam veterans were harmed by exposure to the chemical defoliant Agent Orange. "It has become increasingly apparent that a broad consensus has developed supporting the belief that it would be in the best interest of our veterans to have a non-VA scientific body conduct the Agent Orange epidemiology study," VA Administrator Robert P. Nimmo said in an Oct. 14 letter to Health and Human Services Secretary Richard S. Schweiker. "While I remain firm in my belief that the VA has proceeded reasonably," he continued, "I have been persuaded as to the wisdom of the House Veterans Affairs Committee recommendation that the Centers for Disease Control [a division of HHS] conduct the study."

Nimmo's decision to turn the study over to the CDC came shortly after he received a letter signed by more than 100 members of the House of Representatives who requested such a move. Three years ago, Congress ordered the VA to embark on an Agent Orange health-effects study. Veterans exposed to this dioxin-containing

herbicide link it to a variety of health problems, including cancer and birth defects in their offspring. The purpose of the epidemiological study is to determine whether Agent Orange in fact caused such difficulties and whether disability compensation should be paid. When VA officials recently announced that data needed to address these issues probably would not be obtained until 1989 (SN: 9/4/82, p. 149), the agency was accused of deliberately trying to delay the project, and pressure to let CDC officials investigate the veterans' health complaints began to mount. Says HHS official Shirley Barth, "it seems reasonable" to assume that CDC will agree to take over the Agent Orange study. "We've seen this coming," she says. Critics of the Veterans Administration say that such a change of hands ultimately will lead to a speedier resolution of the Agent Orange issues.

Meanwhile, a General Accounting Office report criticizing the VA's handling of the Agent Orange problem is expected to be released this week. The GAO study was undertaken at the request of Sen. John Heinz (R-Pa.) and Rep. Thomas J. Downey (D-N.Y.).

—L. Garmon

EPA restricts use of pesticide toxaphene

The news conference held by the Environmental Protection Agency last week was billed as an opportunity for the agency to announce major restrictions on the use of toxaphene, once the most widely used pesticide spray in the United States. But before EPA Assistant Administrator John A. Todhunter got around to detailing those restrictions, he charged the previous administration with gross inaction in the area of pesticide regulation. After the conference, several members of environmental groups agreed that the event was staged in an attempt to divert attention from the current administration's mishandling of pesticide matters more serious than the toxaphene situation.

Toxaphene, a complex mixture of chlorine-containing compounds, now is used primarily on cotton, soybeans, sorghum, wheat, peanuts and as a spray or dip to fight scabies on beef cattle and sheep. While use of this chemical is confined largely to the South, residues of the pesticide have been detected in fish from the Great Lakes since 1974, suggesting atmospheric transport of a persistent environmental contaminant. In addition, research data indicate that such residues are harmful to fish and other "non-target" species; finally, animal tests suggest that toxaphene could pose a cancer risk to humans.

Because of these risks, EPA last week announced it is banning the widespread spraying of toxaphene on cotton and several other major applications that to-

gether comprise about 95 percent of current toxaphene use. Use of the chemical to dip or spray livestock, to treat pineapple and banana crops in the Virgin Islands and Puerto Rico and to battle "emergency"-size outbreaks of certain pests such as the armyworm, cutworm and grasshopper will continue. The ban on the other toxaphene applications will take effect in about 30 days.

The government first placed the pesticide in a special review category in 1977, as a first step toward restricting its use, Todhunter said at the press conference. "Why the Carter administration failed to resolve the status of toxaphene is not known to us," he said, but "this administration is not indecisive; I don't think we're afraid to face up to and to deal with our environmental problems."

But Ellen Silbergeld of the Environmental Defense Fund says that the most serious pesticide-related environmental problem is not the status of toxaphene, but rather EPA's "systematic abuse" during the Reagan administration of its authority to grant emergency uses of pesticides for situations in which the chemicals are normally outlawed. Silbergeld notes that from July 1, 1978 to July 1, 1979, EPA permitted only 112 such emergency uses of pesticides; from Oct. 1, 1981 to July 31, 1982, 225 emergency uses were granted. Says Silbergeld, "This is the real hot issue in pesticides — just what kind of abuse is going on?"

—L. Garmon