

## Spasm: The culprit in heart attacks?

Although a blood clot in a coronary artery hardened with fats has been considered the cause of heart attacks for a quarter-century, the villain may really be something quite different — spasms of coronary arteries. This news, which comes from Italian researchers and is published in the Dec. 7 *NEW ENGLAND JOURNAL OF MEDICINE*, has profound implications for the prevention of heart attacks, the leading cause of death in the industrialized world.

A heart attack, heart scientists generally agree, consists of death of a section of heart muscle due to deprivation of blood coming from coronary arteries. But the cause of this blood deprivation has been tough to pin down because heart attack patients usually seek medical attention only after the fact. Now, Attilio Maseri and his colleagues at the University of Pisa have carefully followed persons at risk of developing heart attacks in the hope of catching heart attacks in the act.

The researchers zeroed in on 76 hospitalized patients suffering from recurrent episodes of angina, which consists of chest pains resulting from the heart being deprived of arterial blood. Angina often, although not always, precedes a heart attack. The patients had their blood dynamics continually monitored, their hearts studied by a technique called thallium myocardial scintigraphy when they weren't experiencing anginal symptoms, and their hearts studied by means of coronary arteriography when they were experiencing anginal symptoms. The investigators found, using these various techniques, that spasms of arteries supplying the heart were the cause of all of the patients' anginal episodes; that the spasms causing angina continued as eight of the patients went on to develop heart attacks; that three of the eight patients developed blood clots only after they experienced spasms and heart attacks; and that these clots formed precisely where arterial spasms had occurred. So coronary arterial spasms, not arterial blood clots, may be the real cause of heart attacks, the researchers conclude.

These findings, Eugene Braunwald of Harvard Medical School writes in an accompanying editorial, have "profound implications" for prevention of heart attacks. When blood clots were considered to be the principal culprit in heart attacks, anticoagulant drugs appeared to be the logical preventive approach. But if coronary arterial spasms are the culprit, then a whole host of new preventive possibilities unfold, notably coronary arterial dilators such as nitroglycerin and aspirin and other drugs that prevent aggregation of platelets in coronary arteries, because it is now known that platelets not only cause

blood clots but also release a chemical capable of constricting blood vessels. What's more, since nerve impulses that constrict blood vessels are transmitted to coronary arteries via alpha-adrenergic nerve receptors on the arteries, drugs that block these receptors may also help in the prevention of coronary arterial spasms.

Braunwald cautions, however, that while the findings of Maseri and co-workers "are impressive and convincing," spasm may only be the culprit in certain heart attack victims — for instance, in those who experience angina before attacks. Also to be clarified is when spasm can occur alone and when it must occur in coronary arteries previously hardened with fats. The data from Maseri and his team suggest that a spasm usually, but not always, takes place in a hardened artery. □

## Pesticides can alter human brain activity

A single exposure to a pesticide can trigger changes in human brain activity — as measured by electroencephalograms (EEG's) — lasting more than one year, according to Frank H. Duffy and James L. Burchfiel of the Harvard Medical School. Duffy said the finding holds serious implications for anyone exposed to organophosphate pesticides. In related tests with monkeys the Harvard pair showed long-term brain changes also occurred after exposure to dieldrin, a chlorinated-hydrocarbon pesticide. Their findings were reported this week at a conference in Washington on pesticides and human health sponsored by the Society for Occupational and Environmental Health.

Duffy, director of experimental neurophysiology at Harvard, said his interest in organo-phosphates developed after learning that civilian army workers complained of behavior problems — which included excessive dreaming, loss of libido, loss of memory, irritability and trouble concentrating — after working near sarin. Pharmacologically, sarin is identical to such commonly used pesticides as malathion and parathion, Duffy says, only many times more potent (so potent, in fact, that the army developed it as a nerve gas for use on humans).

Using monkeys, the researchers showed that those exposed to either a single, large dose of sarin or to a series of low-level doses (so low that any resulting symptoms might have gone unnoticed without scrutiny) brought "significant EEG changes that persisted a year.

Duffy said the "frightening" findings led them to study humans accidentally exposed to sarin from one to three times only; all exposures occurred at least a year earlier. Like the monkeys, the humans showed small but consistent and significant EEG changes — particularly in the

high-frequency beta phases — when compared against a carefully matched unexposed group. So consistent were the changes that a computer could automatically separate the exposed from unexposed with a better than 99 percent accuracy. Without running concurrent behavioral tests (impossible in this study) any correlation between EEG's and the observed emotional symptoms is only circumstantial, Duffy said. On the bright side, Duffy says studies on persons exposed several years ago indicate brain changes may be reversible. □

## Drugs boost brain damper

Librium, valium and the other benzodiazepine drugs are among the most widely prescribed in the world. But the mechanism of their action has not been explained. John G. Tallman of the National Institute of Mental Health told a science writers' seminar last week that recent research at NIMH has clarified one important action of the tranquilizers: They enhance the activity of a naturally occurring brain chemical.

The benzodiazepine drugs help quiet nerve cell firing in the brain by reinforcing the blocking action of the abundant neurotransmitter GABA, the major chemical inhibitor of brain activity. Tallman's colleague Dorothy Gallagher demonstrated that drug effect in one area of the rat brain, and Erminio Costa and co-workers demonstrated it in another area.

Researchers have located the specific receptor proteins that bind benzodiazepine drugs. Those receptors are close to receptors for GABA on the nerve cells. Tallman says the two receptors together mediate flow of chloride ions across the cell membrane, shutting down nerve cell firing. High concentrations of GABA increase binding of the benzodiazepine drugs to their own receptors, indicating further the intimate relationship between the two receptors.

The studies reveal that drugs like librium and valium act by increasing the affinity of GABA receptor protein, rather than by altering the amount of GABA released into a synapse or the number of receptors available. That affinity change has been observed only in the presence of high levels of GABA; thus Gallagher speculates that the drugs may have their most pronounced effects in certain painful (or stressful) behavioral states that seem to increase GABA levels.

The benzodiazepine receptors probably bind naturally occurring brain compounds, as well as prescribed drugs. Frederick K. Goodwin and colleagues, also at NIMH, have isolated brain purines that attach specifically to those receptors. When administered at high concentrations,

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purines have a spectrum of behavioral effects, Goodwin says, including anti-anxiety and anti-convulsant properties similar to the drugs. Goodwin points out that drug companies, independently developing analogs to the anti-anxiety drugs, have synthesized chemicals that resemble purines.

The new understanding of the mechanism of benzodiazepine action should help in the design of better drugs, Tallman says, "and purines may be best." □

## Samuel A. Goudsmit dead at 76

Spin is that mysterious, misnamed, misunderstood property of subatomic particles that dictates so much in their behavior. The amount of it they have determines the statistical laws they obey, and therefore whether they are a secure building block for structures. If electrons did not have spin in the amount they do, there would be no atoms and thus no chemistry, no biology, no geology, no solid state physics.

The spin of electrons was discovered in 1927 by two doctoral students at the University of Utrecht in the Netherlands, Samuel A. Goudsmit and George E. Uhlenbeck. Its discovery was a kind of capstone of early quantum mechanics. It answered the serious outstanding questions about the details observed in the spectra of

atoms. At the time there was great rejoicing.

Many physicists have thought that Goudsmit and Uhlenbeck should have had a Nobel prize for the discovery, and in 50 years the Swedish committee has been repeatedly memorialized to that effect. Now it will never happen. Goudsmit, who had been teaching at the University of Nevada at Reno, died there on December 5. He was 76.

Goudsmit was born in The Hague into a family of business people. He once confounded a sociologist, who was interviewing physicists to prove the proposition that pure scientists came from families of intellectuals, by saying: "My father was the manager of a toilet seat factory. My mother had a millinery business." And then, when the audience had tumbled to what he had said about his father: "Don't laugh. Toilet seats were a good business—at least until the bottom dropped out." It was always dangerous to hand Goudsmit a straight line, but, if you didn't, he would hand himself one of his own.

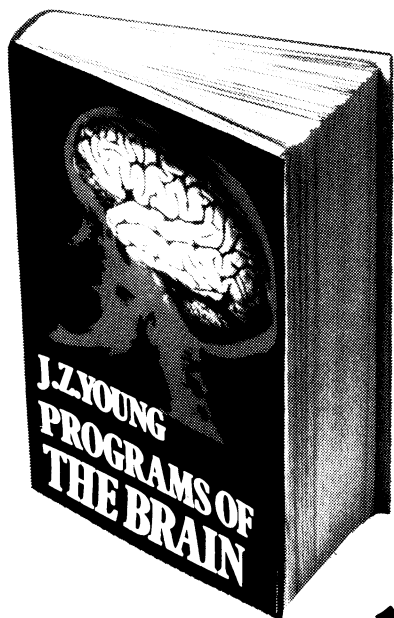
Against the family's advice he went to Utrecht to study under Paul Ehrenfest, one of the greatest of Dutch physicists. When his doctorate came, in spite of his already existing world fame among physicists, the best job offer in the Netherlands was secondary teaching in a provincial town. Then the University of Michigan offered him and Uhlenbeck faculty positions, which they both accepted. Of his move to the United States Goudsmit later made a

revealing remark. In response to a question about an American physicist who had moved to the Netherlands at the same time: "It was an exchange reaction. He became a Hollander, and I became an American."

During the Second World War Goudsmit was a member of Project Alsos, a group of American scientists who monitored German research on nuclear weapons. In the course of that work, Goudsmit was with some of the first Allied troops into Holland and discovered that his parents had been murdered in the Nazi massacre of the Dutch Jews.

After the war he became chairman of the physics department at Brookhaven National Laboratory. He served concurrently as editor of *THE PHYSICAL REVIEW*, *PHYSICAL REVIEW LETTERS* and finally managing editor of all the publications of the American Physical Society. Here he promulgated Goudsmit's Law, the physical equivalent of Ingelfinger's Rule in medicine. Goudsmit's Law says that newspapers and magazines shall not mention a physics result until it has been published in *PHYSICAL REVIEW LETTERS* first. Many science reporters must have gained an appreciation of his forthright and somewhat acerbic personality by arguing with him over that. After he "retired" from Brookhaven, he went to the University of Nevada.

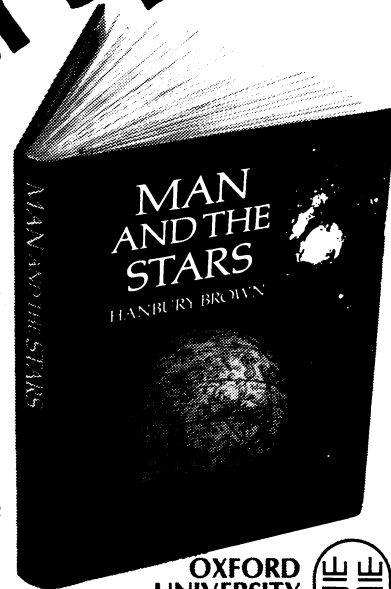
It would be nice to be able to say that he departed this world with an appropriate one-liner, but the fact is he was found dead of a heart attack in his car. □



Based on recent findings of neurosurgeons, clinicians and psychologists as well as the author's own experiments and observations, this path-breaking study shows how we think and why we behave as we do. Written for both the scientist and general reader, it covers basic human capacities (speaking, learning, loving, hating, dreaming) as well as the philosophical problems of creating, knowing, and believing. Illus. \$14.95.

# Inner space, outer space.

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