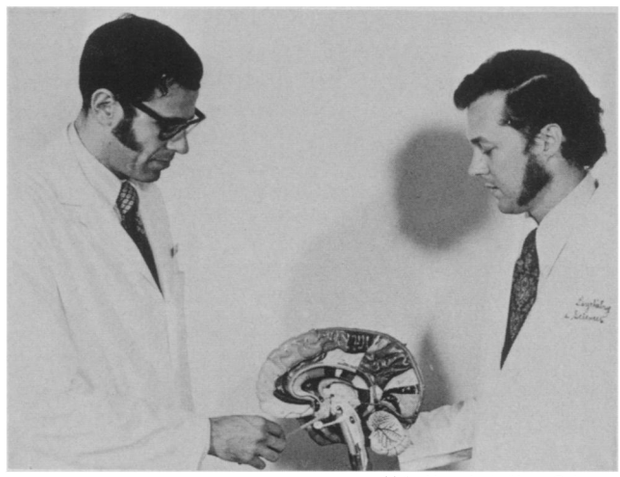
Turning off depression

The brain hormone TRH shows clinical promise for early treatment of depressed patients



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Kastin and Ehrensing mark site of the hypothalamus.

by Joan Arehart-Treichel

Depression is nothing new. Some of the great men of history, such as Abraham Lincoln and Winston Churchill, were susceptible to it. Yet there is little doubt that feelings of loss, loneliness, fatigue, lethargy and acute mental anguish are particularly hallmarks of modern society. Psychiatrists noted that the incidences and types of depression soared in the 1960's. Today 8 million Americans annually are depressed enough to seek the help of a physician. Some 250,000 of them suffer depression so severe, often suicidal, that they must be hospitalized. And in this sophisticated medical age, treatment for depression is strikingly inadequate.

Most antidepressant drugs must be taken two or three weeks before a patient starts to obtain psychological relief. Most have serious side effects. Since electric shock usually brings quicker relief, psychiatrists often prefer to use it instead of drugs. However the patient who submits to shock stands to be stigmatized by society. Witness the recent Sen. Thomas Eagleton (D–Mo.) affair (SN: 8/5/72, p. 85).

In recent months, two independent groups of investigators have rallied clinical evidence that they may indeed have found a superior treatment for depression. It is thyrotropin-releasing hormone (TRH), a small peptide hormone put out by the hypothalamic region of the brain. TRH's usual endocrine activity is to stimulate the tiny pituitary gland in the brain to produce thyroid-stimulating hormone (TSH), which in turn prompts the thyroid gland to produce thyroid hormone. By alleviating depression, TRH joins several other brain hormones as mounting support that they can alter not just straight endocrine functions of the body, but behavior as well (SN: 1/9/72, p. 78; 5/20/72, p. 334). This also appears to be the first time that a brain hormone has been used to treat depression, although several target hormones in the body, such as thyroid hormones and estrogens, have been used, with variable success, for this purpose.

Arthur Prange and Ian Wilson of the University of North Carolina Medical School and of the North Carolina Department of Mental Health at the Dorothea Dix Hospital in Raleigh conducted a double-blind crossover study of 10 depressed patients. Five of the patients received one injection of TRH the first week, then a placebo the following week. The other five patients received a placebo the first week and an injection of TRH the following week. The psychiatrists found that most of the patients responded extremely well to the TRH injection, but only a little to the placebo. This, and related clinical evaluation, led them to conclude that depression is related to some kind of hypothalamic dysfunction.

They reported their work for the first time at the International Congress of Neuropsychopharmacology, held in Copenhagen in August, and again in October at a meeting of the Psychiatric Research Society in Washington. A report also appears in the Oct. 27 SCIENCE.

The other group includes endocrinologist Abba Kastin of Tulane University and the Veterans Administration Hospital in New Orleans, psychiatrist Rudolph Ehrensing of Louisiana State University, Don Schalch of the University of Rochester School of Medicine and Michael Anderson of Abbott Laboratories in Chicago. They have been working on TRH from several points of view for several years now. Although their approach has been entirely different from that of Prange and Wilson, they too have come up with evidence that TRH can relieve depression in patients. As they report in the Oct. 7 LANCET, they studied five depressed patients as part of a double-blind crossover study. All patients received TRH for three days and showed some improvement.

During a control period in which the same patients received a placebo, none of them showed improvement. This evidence, bolstered by other clinical measurements, led the investigators to conclude that depression must be linked with some sort of TRH abnormality.

In interviews, Prange, Kastin and Ehrensing stressed that their studies are preliminary and that much more work must be done to confirm the value of TRH in treating depressed patients. Nonetheless, they admit that they are hopeful. "A single dose of TRH," Prange observes, "might get people out of depression quickly, and then they might be sustained by standard treatment." TRH has been synthesized, so Kastin says there should be no problem in getting enough of it for widespread clinical treatment.

David Elkind of the University of Rochester's Department of Psychiatry and Psychology, an authority on depression, says, "If we could get a substance that would work more quickly and without side effects, it would be a blessing." He cautions, though, that "there is no panacea as far as depression is concerned," and that drug therapy for depression often has to be bolstered by psychotherapy.

Even if TRH does not pave the way toward better treatment of depression, Prange stresses, it should help delineate the physiological and biochemical bases of depression. The biochemistry of depression is not now well understood. But few scientists would quibble that most mental disorders occur via nerve chemical pathways in the brain. Some are even convinced that a depletion of some of these chemicals, such as norepinephrine, causes depression, and that antidepressant drugs alleviate depression by making more norepinephrine available to nerve cells. Since TRH is known to potentiate the effects of the nerve chemical L-dopa, a precursor of norepinephrine, this action might indeed explain how TRH can relieve depression. □