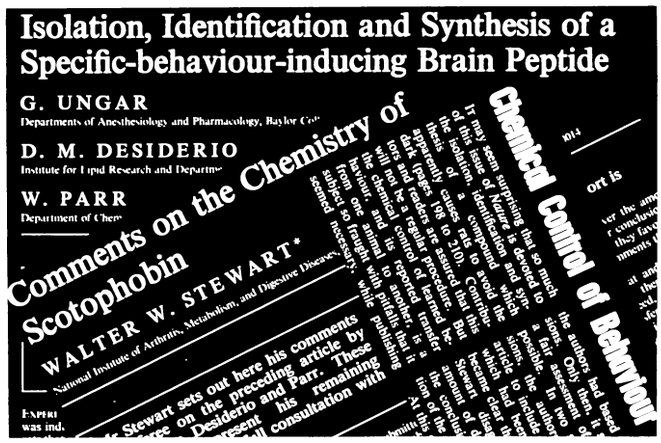
Pro-and-con debate over the chemical transfer of learning

An unusual treatment of a controversial research report casts light on some often-obscured aspects of the scientific process


Isolation, Identification and Synthesis of a Specific-behaviour-inducing Brain Peptide

G. UNGAR

D. M. DESIDERIO

W. PARR

Comments on the Chemistry of Scotophobin

WALTER W. STEWART*

Chemical Control of Behaviour

Four years ago, scientists at the Baylor College of Medicine in Houston reported evidence that avoidance of the dark could be induced in mice treated with extracts of brain taken from rats that were trained to fear the dark. During 1969 and 1970, brain material was collected from more than 4,000 trained rats and the dark-avoidance-inducing substance was isolated. A year-and-a-half ago the Baylor scientists reported identification, sequencing and synthesis of the substance, and dubbed it scotophobin, after the Greek words for "fear of the dark." For all practical purposes this peptide consisting of a chain of 15 amino acids appeared to be the first known mammalian substance involved in the chemical transfer of learned behavior, although some claims for transferring memory from one worm to another by chemical means had been made in the early 1960's (SN: 11/6/71, p. 308).

Word had it that the details of these latest accomplishments, by pharmacologist George Ungar, and by chemists D. M. Desiderio and Wolfgang Parr, would be published in the internationally prestigious scientific journal NATURE. The paper was submitted to the British publication Feb. 8, 1971. Scientists interested in the work waited and wondered. Last week the paper finally appeared.

The time lags between acceptance of a paper and its publication are a continuing source of frustration to scientists. But NATURE, a weekly, prides itself on relatively rapid publication of important papers, and for it, a 17-month delay is extraordinarily long. Even more unusual, the journal published, following the scotophobin paper, a critique that is longer than the paper itself, by the scientist whom NATURE asked to referee the paper before it was published. Referees normally remain anonymous. The critique is followed by the authors' notably brief rebuttal of the critique. In an editorial, the editors of NATURE apologize for devoting so much of the issue to scotophobin but declare, "The chemical control of learned behavior, and its reported transfer from one animal to another, is a subject so fraught with pitfalls that it seemed necessary, while publishing the results of Dr. Ungar and his colleagues, to set out clearly the reservations that many people will doubtless wish to voice among themselves. . . ."

The series of events are worth noting, not only because they concern a controversial scientific subject but also because they cast light on a scientific process the public rarely has the opportunity to witness. Experimental results are not considered valid until they have been scrutinized by a number of scientists and been duplicated in other laboratories. Such scrutiny and attempted duplication are probably as vital as the original results themselves.

The critic of the scotophobin paper is a 27-year-old chemist who, NATURE claims, has no personal interest in the paper beyond the fact he was chosen to referee it. He is Walter W. Stewart of the National Institute of Arthritis, Metabolism and Digestive Diseases in Bethesda, Md. Stewart admits right off he has been intentionally tough. "Fifteen months ago," he writes, "Drs. Ungar, Desiderio and Parr submitted to NATURE a short article which announced a remarkable finding. I was asked to referee the article; in correspondence with the authors it became clear that we disagreed on some basic questions. Because of the great import the authors' work will have if valid and because of the widespread attention this work has already received [by the lay press] it did not seem desirable to delay publication while seeking closer agreement. At the suggestion of the edi-

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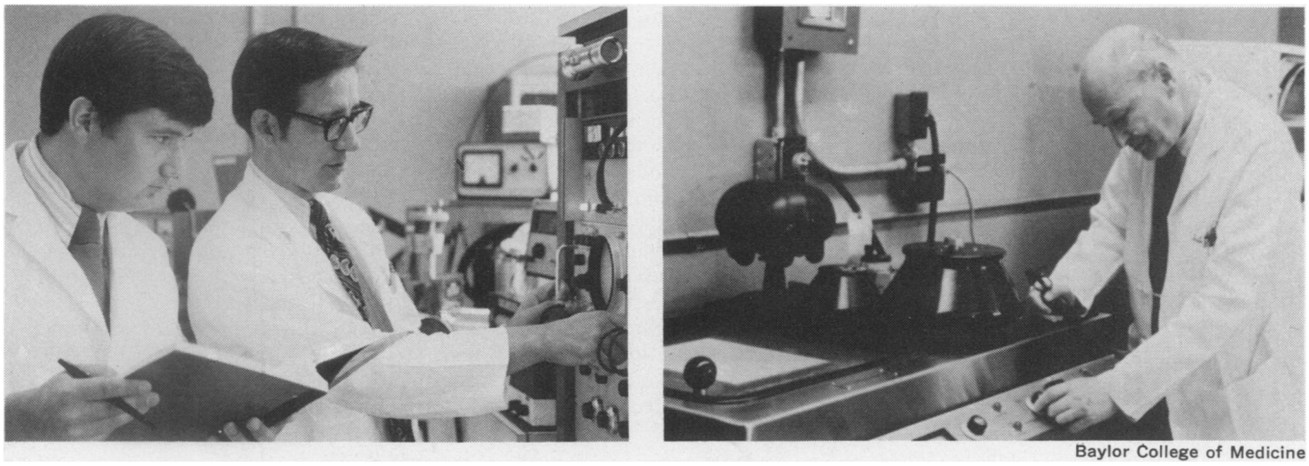

Baylor College of Medicine

Peer criticism spurs Parr, Desiderio and Ungar to defend the authenticity of their memory molecule.

S. 32: Civilianizing Federal science

Next week, the Senate is expected to vote on one of the most far-reaching science policy bills to come before it in a long time. The National Science Policy and Priorities Act (S. 32), introduced by Sen. Edward Kennedy (D-Mass.), would greatly expand the role of the National Science Foundation and change the orientation of Government-funded research from defense to civilian needs.

As it now stands, the bill is a revised and enlarged version of one Kennedy introduced two years ago. Since then, it has picked up 33 co-sponsors and has been unanimously approved by the Committee on Labor and Public Welfare. The bill has fared somewhat less well in the House, where a companion to Kennedy's original bill has been moldering for more than a year. Rep. John Davis (D-Ga.) introduced a bill identical to S. 32 late in June, which has been referred to Davis' Subcommittee on Science, Research and Development.

S. 32 begins with two radical propositions: that Federal investment in science and technology should increase at a rate equal to, or greater than, the gross national product, and that Federal spending for civilian research should equal or exceed spending on defense-related research. Over the past eight years, spending on science in proportion to GNP has decreased, and the Department of Defense traditionally gets the lion's share of Federal science funding.

S. 32 would authorize NSF to designate problems in areas such as health care, poverty, public safety, pollution, unemployment, housing, education, transportation, nutrition, communications and energy resources that should receive priority. Over the next three years, NSF would receive a total of $1.8 billion to conduct or contract for research aimed at solving designated problems. The bulk of this money would go to a new agency to be established within NSF, the Civil Science Systems Administration. CSSA would receive $1.2 billion for research, design, testing, evaluation and demonstration of systems to solve national problems. Kennedy describes CSSA as a NASA-type agency that would become the focus for science in the Seventies "in much the same way as the space program did in the Sixties."

Another major provision of the bill is for "technical manpower transition." The vagaries of Federal science funding, notably reductions in expenditures on the space program, have thrown thousands of scientists and engineers out of work. In many cases, their specialized training is inapplicable to other fields. Some $560 million would be provided over the next three years to assist in transition of manpower from research programs that have been terminated or cut back to civilian-oriented R&D. Specific programs would include: grants to state and local government agencies to enable them to hire unemployed or underemployed scientists, engineers and technicians; establishment of "community conversion corporations" which would conduct or contract for R&D focused on the problems of a particular community and would give preference in hiring to unemployed scientists and technicians; grants to nonprofit organizations and private firms to enable them to hire scientists, engineers and technicians for work on civilian projects while receiving on-the-job training; fellowships to enable unemployed scientists, engineers and technicians to acquire new skills, and establishment of placement programs. Kennedy predicts that S. 32 would directly provide jobs for 40,000 scientists and engineers.

In spite of its impressive Senate support, parts of S. 32 are opposed by the Administration and by NSF itself. The Administration's opposition is mostly on grounds that the bill would involve NSF in activities traditionally belonging to the mission agencies. Former NSF head William D. McElroy questioned the need for CSSA, noting that the RANN (Research Applied to National Needs) program already carries out many of the proposed activities. At a deeper level, NSF officials seem concerned about the implied change in NSF orientation, from its traditional role as supporter of basic research to an emphasis on applied research.

tor of NATURE therefore, and with the cooperation of Drs. Ungar, Desiderio and Parr, I present here those of my reservations that remain unresolved."

The most impressive feature of the Baylor group's article, in Stewart's view, is the similar biological effects natural and synthetic scotophobin produced in untrained mice. Yet these comparable effects, he challenges, do not prove that natural scotophobin contains memory in the first place. Can the results with the natural and synthetic scotophobins be reproduced? Some researchers claim that they can, Stewart concedes; yet their effects, he notes, were small compared with those observed by the Baylor researchers.

It is not clear, Stewart continues, how the authors determined the peak of biological activity in the isolated brain material. The first set of experiments, he says, gives essentially no information about purity. "Quantitative analysis [of the second set] indicates that the isolated material was impure."

Stewart scores the authors for making errors in amino acid analysis, carrying out ambiguous chemical degradation experiments and for refusing to publish mass spectrometry data that does not reinforce their interpretations. He applied the authors' interpretation methods to a chemical unrelated to scotophobin "to illustrate the point that if one departs from sound practice in interpreting a mass spectrum, it is possible to prove virtually anything."

Stewart notes that the amino acid composition of the active material the authors report is somewhat different from what they have reported before. On the whole, he concludes, "the weaknesses in those parts of the article that deal with the isolated material are so grave . . . that the authors' conclusions are more likely false than true."

In their rebuttal, Ungar, Desiderio and Parr reply tartly, "It would be impossible, within the limits of five days and 1,500 words granted us to answer in detail the criticisms for which Mr. Stewart was given over a year and apparently unlimited space. We hope, however, to produce enough arguments to reverse his evaluation that 'our conclusions are more likely false than true.' "

The authors note that while Stewart refers to six successful replications of their experiments, he questions the validity of some of them. On the other hand, they argue, he takes at face value the three unsuccessful experiments, as if their negativity made them immune to criticism. He also asks for control experiments, all of which, they counter, have been done and published.

"We are ready to plead guilty to omission of some details in the description of our isolation procedures," they admit, "partly because of what we believed to be space limitations, partly because they were published elsewhere or were not considered critical." They say they fail to understand why Stewart does not understand how they determined the peak of biological activity in the isolated brain material. They are particularly disdainful of Stewart's skepticism about the purity of their final product. "Even by the most generous estimate," they assert, "the impurities cannot represent more than a few percent."

Their mass spectrometric data, they say, are closely linked with chemical

data they had obtained previously. As for Stewart's application of their mass spectrometry methods on a pseudoscotophobin, they declare "it is a good example of what happens when mass spectra are interpreted out of the context of known chemical data. . . ."

In a telephone interview from Spokane, Wash., Ungar told SCIENCE NEWS, "I really don't know" what prompted Stewart to be so harsh in his criticism, nor why NATURE decided to print such a lengthy critique. "We probably made a mistake," Ungar admits, "in agreeing to these publishing conditions. On the other hand we will be coming out soon with new results that will change the whole situation."

Stewart told SCIENCE NEWS this week that he has not seen the new results, "but they could completely change my mind. I have a lot of admiration for anybody like Dr. Ungar, who has the courage to work on a tough, unfashionable topic. The main reason I wrote my article was in hopes that it would make people take his work more seriously, particularly since many people are skeptical of it and do not think it could be true. I would hope they would sit down and do experimental tests to test it out that way."

The controversy over the chemical transfer of learned behavior is far from over. In fact it is probably just beginning. Some peptide hormones from the pituitary gland of rat brains, as well as scotophobin, now appear to be involved in chemical transfer of memory (SN: 5/20/72, p. 334). Yet as the controversy in the July 28 NATURE illustrates, dialectics are probably as crucial to science as empirical experiments. Laboratory results distilled by peer scrutiny are what make science run. □

A 2,100-year-old Chinese noblewoman

Through a diplomatically negotiated breach in the Great Wall of China the Western world is gradually forming a more complete picture of the traditionally inscrutable Orient. The most recent piece in the puzzle came last week in the form of an archaeological find. Hsinhua, the official mainland China news and photo agency, reported that a 2,100-year-old tomb had been unearthed near the city of Changsha in southern China.

The discovery of the tomb is important, but even more significant is the extraordinary state of preservation in which it was found. The tomb contains what is believed to be the wife of a local feudal lord of the Han Dynasty (202 B.C.-220 A.D.). The woman, about 50 years old, was partially soaked in a preservative, wrapped in 20 silk garments and placed in the

Wide World Photos

innermost of six protective coffins—one inside the other. This, in turn, was covered by five tons of charcoal and sealed with a four-foot layer of clay.

These precautions protected the contents of the tomb from the decaying effects of the air and preserved the corpse in a clearly distinguishable state. The well preserved corpse, however, is not the most important part of the find. Buried with the woman were hundreds of artifacts that will be useful in recreating the life style of the Chinese nobles of the Han Dynasty.

In addition to the woman's well preserved silk garments the tomb contained a painting on silk depicting the life and legends of the period and 126 wooden figurines clothed in the style of the period. Various foods were also found in the tomb.

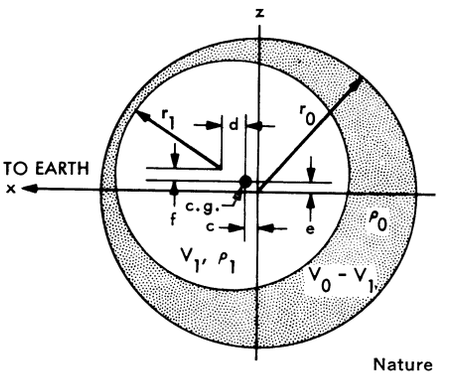
In 1937 the Chino-Japanese war put an end to much Chinese archaeology and since then China has kept many of her secrets to herself. This particular find, however, may be getting prominent play not only because of its historical and archaeological importance but because of its propaganda potential. Changsha is the capital of Chairman Mao Tse-tung's native province. The Han Dynasty was an important period in Chinese history when tyrannical rulers unified the country geographically, politically and philosophically. Describing the find, the Chinese Communist party newspaper Jenmin Jih Pao said, "These are the most important and extremely rare relics recently found. They are of great value to studying the history, culture, handicrafts, agriculture, medicine and preservatives of the age. . . . The great creations by the laboring people are now returning to their hands." □

The beauty of an offset lunar core

Laser-altimeter and gravity data from Apollo 15 and 16 orbital instruments revealed that the far side of the moon is on the average two to four kilometers higher than the mean radius and that the near side is two kilometers lower than the mean radius. Scientists interpret this to mean that the crust on the far side is thicker than on the near side. If there is a core under the crust, it would be closer to the near-side surface. Then as the thinner near-side crust is bombarded by meteorites, these impacts are more likely to weaken the crust, tapping lava beneath and causing upwelling to the surface (SN: 9/18/71, p. 194). This in turn could explain why there are more maria—low areas filled with lava—on the near side. The mascons can be explained this way too; but, says Farouk El-Baz of Bell Laboratories, extra mass such as a near-surface mantle is also needed.

Additional analysis of gravity data has also shown that the moon's center of mass is not at the geographical center of the moon. Instead, it is displaced from the center in a direction 37 degrees east of the direction of the earth (SN: 1/29/72, p. 73).

Now, Gary Ransford and William Sjogren of the Jet Propulsion Laboratory report in the Aug. 4 NATURE that a lunar model having an asymmetric core would explain the offset center of gravity as well as the maria, mascons and the moment of inertia. In their model the distance from the geographical center of the moon to the center of the core is 446 kilometers. This distance is much greater than had been expected. If the density differential between the core and the crust is 0.4



Nature

Proposed geometry of an offset core.

grams per cubic centimeter, the diameter of this core would be 700 kilometers. The crust would be 572 kilometers thick on the near side, and 1,504 kilometers thick on the far side. The model requires a molten moon at one time and that it have been in earth-synchronous orbit as the crust solidified. □