effects of ACTH and MSH on conditioned avoidance behavior. A group of investigators in New Orleans, including Abba Kastin of the Veterans Administration Hospital there, Curt Sandman, who is now at Ohio State University, and Lois Stratten of the University of New Orleans, began their work on MSH with appetitive tasks in order to avoid the extra stress imposed on animals by aversive conditioning. But they have also used avoidance conditioning, and, in recent experiments, the Utrecht group has studied the effects of pituitary peptides on appetitive behavior. In general, the results of the two groups are in agreement for both types of experiment.

Kastin and Sandman, however, think that MSH and ACTH facilitate learning by improving the animal's ability to pay attention to the task rather than by acting on memory processes. They cite the results of task reversal experiments in support of this position. In task reversal experiments the subject (whether animal or human) must learn to make a response to a particular property—a color, for example. Then the experimenter changes the correct answer. The shift may be to a different color (intradimensional shift) or to a new category (extradimensional shift) such as shape. Kastin and his colleagues trained rats to run to a lighted door in one arm of a Y-shaped maze in order to escape an electric shock. Then they made the dark door the escape route from the shock. Rats treated with MSH learned this reversal faster than those receiving the control solution.

According to Kastin, this result is inconsistent with the theory that MSH increases retention of an acquired behavior because, if that were the case, reversal should be slower, not faster, when the animals are given the hormone. But the result supports the hypothesis that MSH improves the rats' ability to pay attention. A highly attentive rat should learn that the lighted door is the correct escape route and also that the degree of brightness is the key characteristic. This should enable it to make the shift to the dark door more readily than an inattentive rat that had not learned what quality to look for.

Although trials to determine the effects of pituitary peptides in humans are not yet very far along, there is evidence that they do affect learning behavior in humans. Lyle Miller of Temple University, working in collaboration with the New Orleans investigators, found that ACTH 4-10 improved the visual memory, as determined by the Benton visual retention test, and decreased the anxiety of volunteers receiving the drug when compared with those injected with a dilute salt solution. In an earlier study, they obtained similar results with MSH. The peptide did not affect the volunteers' verbal retention nor did it have any effect on their retention times.

When the investigators determined the effects of ACTH 4-10 on the electroencephalograms (EEG's) of the subjects, they observed changes indicating that the peptide prolongs the subject's period of mental alertness. When individuals are exposed to a new stimulus of some kind, the alpha patterns of their EEG's, which are generally associated with a relaxed mental state, are normally replaced with a pattern characteristic of the alert state. However, after a time the subject will become accustomed to the stimulus and the alpha pattern will reappear. The alpha patterns of volunteers given ACTH 4-10 returned more slowly than did those of individuals receiving the control solution. The results of reversal experiments with humans were also consistent with the hypothesis that ACTH 4-10 affects attention.

There have been suggestions that these pituitary peptides are involved in the development of tolerance to morphine. Toler-

Observer's Report

Frontiers of Astronomy:

Sir Fred Hoyle celebrated his 60th birthday this year, and a symposium was held to mark the occasion in Venice, 15 to 19 July. Many of Hoyle's colleagues and former students presented current work in some of the fields Hoyle helped to found, including cosmology, the nature of the interstellar medium, and the early history of the solar system. The following is a report from a participant.

There is no longer really anything to be said about the original steady-state picture of the universe, in which matter is continuously created at just the right rate to keep all average properties constant for all time, except that it is a beautiful idea which turned out not to agree with observations. Hoyle has recently suggested an alternative picture, in which our universe changes with time, not because it is expanding, but because the masses of the stable fundamental particles are increasing with time. Our universe is then just one of many patches in a space-time continuum, each with its own properties, which may have started its life with very large place-to-place fluctuations in the density of matter. S. E. Woosley (Caltech) has calculated the nuclear reactions that should occur early in such a universe, and finds that a large fraction of the material in the densest clumps should be converted to elements with atomic numbers near that of iron. Conventional big-bang universes produce only hydrogen and helium early in their history. Besides providing an additional site for the synthesis of heavy elements, this picture has the attractive property that if the center of our sun is made of material processed in this way, the discrepancy between predicted and observed fluxes of solar neutrinos largely goes away. The chief difficulty may well be to avoid having all the iron so produced get trapped in black holes.

In more conventional cosmology, two of the classic tests, which it was once hoped would tell us whether our universe will expand forever or turn around and recontract, now no longer seem able to tell us this. The first of these tests is the relation between the red shift and the apparent brightness of galaxies. Since the apparent brightness of a galaxy decreases with its distance from us, and distant objects are seen as they were in the past, observations of the recession velocity (red shift) versus apparent brightness should tell us whether the expansion of the universe is slowing down enough for it eventually to stop and begin to contract. The number of available red shifts has increased considerably in the past few years (particularly due to the work of Oke and Gunn at Hale Observatories), but the interpretation has become more difficult. In order to determine the distance to a galaxy from its apparent brightness, we need to know how its real brightness changes with time. It was once assumed that such changes were small, but this no longer seems to be the case. On the one hand, B. Tinsley (Yale University) has shown that the general tendency of the aging of the stars in bright, massive galaxies is to make ance is the phenomenon in which an individual becomes less sensitive to a drug and requires progressively higher doses of it to achieve the desired effect. William Krivoy of the Addiction Research Center in Lexington, Kentucky, has shown that ACTH and MSH antagonize the analgesic effects of morphine, and that a vasopressin analog facilitates development of resistance to the drug. Investigators have suggested that development of tolerance to morphine is a form of learning and that it involves protein synthesis. Since the hormones are peptides, if not proteins, and are involved in learning, Krivoy has hypothesized that they may somehow participate in the development of morphine tolerance. However, all of the hormones are known to stimulate adenylate cyclase in certain cells. This enzyme catalyzes the synthesis of adenosine 3′, 5′-monophosphate (cyclic AMP). Morphine inhibits the enzyme in cultured nerve cells (*Science*, 29 August). Consequently, the peptides may antagonize morphine activity by counteracting its effects on adenylate cyclase.

Investigators are now trying to identify the neurochemical changes that presumably underlie the effects of the peptides on behavior. De Wied points out that stimulation of adenylate cyclase is one possibility. The known effects of increased cyclic AMP concentrations include changes in membrane permeability, in enzyme activity, and in protein synthesis. Any or all of these could alter neuronal functions and the formation of new connections between neurons.

According to de Wied, ACTH 4-10 does alter protein synthesis. Removal of the pituitary gland decreases the incorporation of the amino acid leucine into protein in the brainstem. The analog of ACTH 4-10 that speeds up extinction of conditioned responses lowers the incorporation even further. But ACTH 4-10 itself restores it to normal. Several investigators have evidence that formation of memory requires protein synthesis. Finally, the idea that the peptide acts through protein synthesis is consistent with the finding that its effects last for several hours even though it is destroyed within minutes.

Studies of the effects of ACTH and MSH on the electrical changes in neurons that occur during transmission of nerve impulses indicate that the hormones increase the excitability of nerve cells. For example, Fleur Strand of New York University showed that ACTH and ACTH 4-10 increase the excitability of peripheral nerve cells and decrease their fatigue during electrical stimulation. And Krivoy, working with Roger Guillemin, who is now at the Salk Institute, showed that MSH increased the excitability of neurons in the spinal cord of cats.

These investigators suggested that MSH, which has no other known function in mammals, might act as a neurohumor (a substance that transmits nerve impulses from one neuron to another). Kastin has shown that the secretion of MSH is controlled very rigorously by means of two hypothalamic factors, one of which inhibits and the other of which stimulates MSH synthesis. Although he admits that the argument is highly teleological, Kastin thinks that such an elaborate mechanism would not have evolved for a material having no function. Transmitting or modulating nerve impulses would, of course, be a very important function.

There have been criticisms of the idea that pituitary hormones affect brain function. One of them centers on the existence of the blood-brain barrier that prevents many substances—especially proteins and peptides—found in the bloodstream from reaching the central nervous system. These hormones, like all others, are secreted into the bloodstream. But vasopressin actually originates in the hypothalamus, and inves-

In Venice

them grow significantly fainter with time, while on the other, J. P. Ostriker and S. D. Tremaine (Princeton) have pointed out that such galaxies will gobble up material from other, nearby galaxies, which will make them grow brighter with time. It does not, at present, seem possible to decide which of the two effects dominates and thus to interpret the red shift–apparent brightness data.

The other classic test is to measure the apparent (angular) diameter of objects whose real size you think you know, as a function of their distance. Because the structure of space-time (within the framework of general relativity) is determined by the amount of matter present, this test should also distinguish an ever-expanding universe from a recontracting one. The optical data on this problem have always been difficult to interpret, but there had been great hopes for using radio sources. R. Ekers and others at the Westerbork Radio Observatory in the Netherlands have recently measured angular diameters of a large number of faint (hence distant) radio sources. Their data, in combination with previous results, say only that the real sizes and brightnesses of radio sources change with time. Since we have no theory of what the changes ought to be, we cannot now do cosmology with angular diameters.

Hoyle was among the first to predict the composition of the dust grains that pervade interstellar space. In the intervening years, his heretical suggestion (graphite) has become part of the conventional wisdom. N. C. Wickramasinghe (Cardiff) has proposed a new heresy, suggesting that polymers of formaldehyde and similar organic molecules may be important components, responsible for the observed ultraviolet absorption features. Even more controversial is the question of what fraction of the interstellar medium's supply of heavy elements is, in fact, locked up in the grains. Analysis of ultraviolet absorption lines in the spectra of distant stars, obtained with the Copernicus satellite, has normally been thought to imply considerable depletion of heavy elements from the gas onto the grains. G. Steigman (Yale University) now points out, however, that most of the absorption probably takes place in ionized regions around the stars themselves, so that the data tell us very little about the heavy element content of the general interstellar gas.

An increasing body of data may require us to rethink our ideas on the history of the solar system during the period when the planets and meteorites condensed and cooled. The traditional view requires a homogeneous gaseous medium to condense quickly and without outside interference. We now know of a variety of place-to-place variations in the ratios of isotope abundances of various elements in meteorites, which require some modification of this picture. D. D. Clayton (Rice University) has suggested that interstellar grains condense in the immediate vicinity of the supernovae where the heavy elements are made and preserve their identity through the condensation process.—VIRGINIA TRIMBLE

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