Neurotransmitter lateralized in brain

For more than a century, the left and right halves of the human brain have been known to function differently. Only in recent years, however, have the singular abilities of each side come into sharper focus. The left hemisphere is now known to be involved in speech and in logical, analytical thinking. Thr right hemisphere is now known to be concerned with spatial relations and with artistic and holistic thought processes. Indeed, neuroscientists declared at a 1977 symposium that brain asymmetry "impinges upon the entire spectrum of brain behavior research from the synapse to the sentence."

Now, for the first time, a neurotransmitter — a chemical that passes electrical messages between nerves — has been found to have a natural, strongly lateralized distribution in the human brain. Arvin Oke and colleagues at the University of Kansas in Lawrence report in the June 23 SCIENCE that a specific region of the left human brain, but not of the right human brain, is rich in the neurotransmitter norepinephrine, whereas another specific region of the right brain, but not of the left brain, also contains a lot of this neurotransmitter. "Such naturally occurring left-right differences in concentration of a neurotransmitter represent a new aspect of hemispheric specialization," they say. They also believe that these concentration differences might "be correlated in the future with functional and behavioral aspects," for instance, with human speech, or with schizophrenia.

Recently Oke and his colleagues used some relatively new techniques — liquid chromatography combined with electrochemical detection — to map neurotransmitters in various areas of the human brain. In the process of this mapping they noted, to their surprise, that the left and right sides of the brain seemed to differ in their concentrations of these chemicals. So they probed further for evidence of this nature, concentrating on the thalamus. The thalamus is an area of the brain located smack between the left and right brain hemispheres and thus comprising a bit of each. And the neurotransmitter they looked for was norepinephrine.

They found that a particular area of the left brain side of the thalamus — the pulvinar region — is especially rich in norepinephrine, but that the pulvinar region of the right brain side of the thalamus is not. In contrast, the somatosensory input area of the right brain side of the thalamus, but not the somatosensory input area of the left brain side of the thalamus, has a high concentration of norepinephrine. "Thus we believe the results truly represent norepinephrine lateralization in the thalamus," they conclude.

What's more, this appears to be the first time that a natural asymmetry of neurotransmitter in the human brain has been documented. The only other time that lateralized neurotransmitter levels were observed in the human brain was in a patient with Parkinson's disease. The patient had an asymmetry of the neurotransmitter dopamine. This lateralization was probably due to a causal link between dopamine and Parkinson's, however, rather than to any intrinsic chemical laterality, since a dopamine deficiency is known to underlie this disorder.

So why should the left and right sides of the thalamus differ in their norepinephrine distribution? Probably because each side uses the neurotransmitter for its own specific purposes. For instance, surgery of the left pulvinar region of the thalamus, which has much norepinephrine, produces postoperative speech difficulties, but surgery on the right pulvinar region of the thalamus, which has a paucity of norepinephrine, does not. And, as mentioned before, the left hemisphere of the brain is involved in speech. So it's quite possible that norepinephrine helps the left side of the thalamus, and perhaps some other areas of the left hemisphere of the brain as well, to produce human speech. Similarly, because the somatosensory region of the right side of the thalamus has been found to be rich in norepinephrine, and because the right hemisphere of the brain is thought to be involved in schizophrenia, norepinephrine in the right thalamus, and perhaps in other right brain regions as well, may be implicated in this condition. □

R&D: The future looks dim ahead

Optimism was not the tone pervading the colloquium on R&D policy in Washington last week. W. Bowman Cutter, the executive associate director of budget of the Office of Management and Budget, set the tone early when he told the conference, sponsored by the American Association for the Advancement of Science, that federal research money will get tighter, at least for near term, because the economy is in trouble.

The Carter administration will be asking everybody, including the research and development community, to accept a pause, "as yet undefined," in the expected rate of increase in the federal budget in order to make corrections in an economy that seems headed in "some very unfavorable and distasteful directions," Cutter said. "I see the [fiscal year] 1980 budget as the tightest in a decade," he predicted.

Markley Roberts, an economist for the AFL-CIO labor union, questioned whether the administration's planned budget restraint was consistent with the kinds of healthy, full-employment economic growth that provide incentives and resources to support research and development. Cutter countered, saying, "We're not moving toward a restrained budget for the hell of it. We're doing it because ... productivity seems to have fallen off on a cyclical basis in the last year or so, inflation is up much above our guesses, and we are now in the fortieth month of a recovery with a deficit somewhere in excess of $50 billion." He warned that if federal budget planners don't tighten their purse strings voluntarily, other agencies with clear power in this area, such as the Federal Reserve Board, will step in and take over with a much heavier hand and use "much more blunt instruments than we have. We see the choice we're making as being far and away the best among the real possibilities."

New York University President John C. Sawhill challenged that analysis, saying that the federal budget deficit was "somewhat counterbalanced" by the size of the states' budget surpluses together with the federal trade deficit. "If you look at the total impact of these three on the economy, the federal deficit really is not having that large an inflationary impact," he said.

Sawhill went on to say that "one of the ways you improve productivity, at least in the longer range, to bring inflation under control, is by maintaining increasing investment in research and development."

The AAAS meeting, the third in an annual series, was devoted to examining the relationship between innovation, the economy and investments in research and development. One of the few points on which all discussants agreed was that economic and regulatory uncertainties were discouraging private industry from investing in basic research or any long-term research ventures. At the same time, the government has been questioning its role in funding technological development (as opposed to basic research), particularly, Cutter pointed out, because the government hasn't the acumen industry has for analyzing the market potential of a development product.

Basic research, three-quarters of which is carried out by universities, may also be in trouble. Although the administration in its 1979 budget proposal called for a five percent growth in the proportion of money devoted to basic research, at least in the academic sector, this increase "will easily be absorbed in the acquisition of up-to-date equipment alone, leaving little or nothing for an increase in the man-hours devoted to basic research or for assuring that younger scientists receive a share of the funds," Sawhill said. Universities have been operating for several years on a "very stringent budget" and must now upgrade their laboratory equipment if they are to accomplish research that will keep the United States competitive in the world market, he said.

Together, these factors were seen as weakening the U.S. world technological superiority. According to Arthur Bueche,

vice president for research and development at the General Electric Co., "We are losing position to major foreign competitors in terms of R&D as a percent of GNP [gross national product]." What's more, he said, "Figures don't tell the entire story, because half of the U.S. federal R&D funds are for defense. In Japan and West Germany, by contrast, R&D budgets for defense are minimal; virtually all of their R&D funds are aimed at economic development."

He said that Japan, with less than half the population of the United States, is estimated to have as many engineers and scientists working in that type of activity as we do. "And while our effort appears not to have grown between 1970 and 1976, Japan's effort increased 50 percent" — from around 160,000 people in 1970 to about 240,000 in 1976.

Research and development is linked with increasing employment and productivity, several speakers explained. Bueche cited a recent study by Data Resources, Inc., showing that during the past 10 years U.S. high-technology companies increased employment nine times faster than low-technology companies, "and these same high-technology companies increased overall productivity by about four percent per year, or twice the national rate of two percent."

But high technology is dependent on innovation, Bueche said, and there are signs that the rate of innovation may be slowing in the United States. "Our performance in patented inventions is perhaps one of the best single measures of what's happening in terms of R&D output," he said. "The number of patents granted U.S. residents declined 21 percent between 1971 and 1976," he said, "while patents to foreign residents grew by 16 percent to total 37 percent of all U.S. patents granted in 1976."

The Commerce Department will be conducting at least two studies on the R&D problem within the next year. The first, scheduled at the behest of the President, will examine factors that affect and may have discouraged industry investment in research. The second will look for ways in which the government might influence the rate and direction of industrial innovation. □

Viruses prepare to plug into chromosome

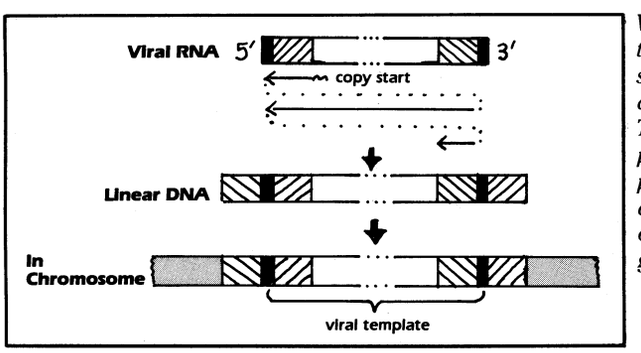
Recent focus on genes that hop in and out of chromosomes has stolen some of the spotlight from the previously recognized genetic transients. Yet there is continuing progress on understanding the mechanics of viruses, which can drop their essential genetic baggage into cellular chromosomes and have it maintained and reproduced there briefly or for millions of years.

At the recent Cold Spring Harbor Symposium on DNA: Replication and Recombination, researchers described analyses of an intriguing set of viruses. The RNA tumor viruses, which produce animal cancers, use RNA instead of DNA to encode their genetic information. They are often called "retroviruses" because they reverse a step in one central dogma of biology: DNA makes RNA makes protein. Viral RNA, once in a cell, must create double-stranded DNA molecules. Then the viral genes can slip into an animal chromosome.

The DNA copy deposited in the cell's chromosome must contain all the information of the virus. Yet copying the RNA requires priming. An RNA molecule (transfer RNA) from the cell's cytoplasm binds to about 16 nucleotides of the viral RNA and the DNA copy grows at the end of that chain. The transfer RNA is later clipped off. Therefore, if DNA were simply produced from one end to the other of the linear viral RNA template, the stretch bound to the primer would be lost.

The virus's way out of the dilemma involves at least one jump of the replicating enzyme from one end of the RNA molecule to the other. Results from the laboratories of Harold E. Varmus at the University of California in San Francisco, David Baltimore at the Massachusetts Institute of Technology and John Taylor of the Institute for Cancer Research in Philadelphia indicate that the replicating machinery actually makes that jump twice.

Synthesis of DNA from the viral RNA template begins near one end (called the 5′ end) of the RNA molecule. Test-tube experiments with isolated components show distances of 100 to 150 nucleotides, depending on the virus, from that start to the end of the molecule, reports William A. Haseltine of Harvard Medical School. In the June 1 NATURE Haseltine and Dennis G. Kleid of Stanford Research Institute propose that retro-viruses of various animals can be classified on the basis of the length of that initial copy, running from the primer to the 5′ end.



Viral RNA *serves as a template for the* DNA *that slips viral genes into an animal cell chromosome. Tricky maneuvering produces a* DNA *segment padded at each end with an extra copy of the opposite end of the viral genetic message.*

Varmus and colleagues have looked at DNA copies of viral RNA made in infected animal cells. The linear DNA molecule has the same sequence at both ends and is longer than the RNA molecule. The repeated stretch includes one copy of the sequences at each end of the RNA molecules. Haseltine proposes that the DNA forms from the start on the RNA to the 5′ end and then that DNA reanneals with the short repeat at the RNA 3′ end and continues copying. Near the 5′ end, it again jumps, either to an RNA or DNA template, in order to finish.

In his test-tube experiments with disrupted viruses, Baltimore and co-workers find mouse leukemia virus gives two major DNA products. The longer product seems to include the repeated sequences, as if the copying apparatus successfully made the second jump.

In the nuclei of cells, linear DNA is converted into circles. Varmus finds two major circles, one equal in length to the linear DNA molecules and with two copies of the end region side-by-side, and the other circle missing one copy of the repeated regions (300 base pairs in avian sarcoma virus and 1,200 base pairs in mouse mammary tumor virus.)

The researchers are not yet certain which form of the DNA joins the cell's chromosome. But the inserted DNA contains the repeated end regions. Unlike SV40, a DNA-containing animal tumor virus, the RNA tumor viruses always connect to a host chromosome at the same viral site. Thus the central stretch that will be the template for new viral RNA is bordered by virus-specified segments, the repeats of the viral RNA ends. Taylor and Varmus propose that the extra segments may be important in controlling viral genes.

Although there is no direct evidence that the viral stretches of DNA hop around in chromosomes, Varmus suggests that the genetic inserts by RNA tumor viruses do resemble the movable genetic elements, transposons (SN: 6/17/78, p. 390). The viral genes in the chromosome, like the genes of a transposon, are flanked by a natural repeat. Varmus and Robert A. Weinberg of the Massachusetts Institute of Technology showed that the viral genes can insert into cellular chromosomes in many sites, although researchers do not know yet whether the genes prefer specific regions. The investigators now plan to determine exact sequences of the repeated end regions for comparison with the insertion sequences that flank transposon genes. □