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Roger Sperry
1913–1994

Roger W. Sperry, 1981 Nobel laureate in physiology or medicine and the Institute's Board of Trustees Professor of Psychobiology, Emeritus, died on April 17, 1994, of a heart attack and of complications associated with a neuromuscular degenerative disease from which he had suffered for many years. He was 80.

A native of Hartford, Connecticut, Sperry earned his bachelor's degree in English literature from Oberlin College in 1935, then focused his attention on psychology, earning his master's in that field in 1937, also from Oberlin. For his doctorate, he studied zoology, earning his degree from the University of Chicago in 1941.

Roger Sperry

Sperry's academic career was as diverse as his educational background. After graduating from Chicago, he held fellowships at Harvard from 1941 to 1946, where he worked in the Yerkes Laboratories of Primate Biology, and he performed military service from 1942 to 1945 by taking part in the federal government's Medical Research Project on Nerve Injuries. After the war he taught as an assistant professor in the University of Chicago's department of anatomy until 1952. During 1952 and 1953, he served as associate professor of psychology at the same institution while simultaneously serving as the section chief for neurological diseases and blindness at the National Institutes of Health. In 1954 he became the Hixon Professor of Psychobiology at Caltech, where he remained for the next forty years. He retired from teaching as professor emeritus in 1984.

Among Sperry's many accomplishments is research he carried out in the early 1950s showing the nervous system to be characterized by a very high specificity of neural reconnection—that is, by the ability of neurons, when severed, to regenerate connections to their original targets. This work led in the early 1960s to a new theory explaining how neurons grow, assemble, and organize themselves in the brain by means of amazingly intricate, genetically determined chemical codes.

Sperry is best known for his "left-brain/right-brain" research, work that has had an incalculable impact on fields ranging from neurophysiology to psychology to education. Working in the 1950s and early 1960s with patients who had had their corpus callosum—the bundle of fibers connecting the left and right cerebral hemispheres—surgically cut in an effort to control epileptic seizures, he demonstrated how the two hemispheres function, independently and in concert. The most striking of his discoveries and the one with which his name continues to be most widely associated is the finding that under certain conditions, each hemisphere has the seeming capacity to behave like a separate consciousness, with the left side of the brain generally more specialized for verbal and analytical thinking, and the right side for spatial and visual thought.

In later years, Sperry's own ever-active brain turned increasingly to philosophy, particularly to issues associated with the mind–brain question—that is, the relationship between the observable physiological structure of the brain and the quality of subjective, conscious thought that characterizes the mind. In pondering these questions, Sperry broke with the behaviorist school, which then dominated psychology and the behavioral sciences, and advocated a new approach that placed far greater emphasis on the role of mental states and experiences in influencing the physiological functioning of the brain. He first set out these ideas in 1965 in what the January 1994 issue of *Humankind Advancing*, which was dedicated to Sperry, described as "a remarkable series of philosophical papers"; and he continued to write and publish provocative and influential writings on the nature of consciousness up until the time of his death. It was for this work, more than for his studies of vision, neuronal growth, or split-brain patients, that Sperry wished most to be remembered.

For his work on hemispheric specialization, Sperry was awarded the 1981 Nobel Prize in physiology or medicine, along with David H. Hubel and Torsten N. Wiesel. He also received the National Medal of Science in 1989 from President Bush, the Wolf Prize in Medicine and the Albert Lasker Medical Research Award in 1979, and the California Scientist of the Year Award in 1972, among many other honors.

In addition to his talents as a researcher, Sperry was "the most artistic person I've ever known," said long-time laboratory assistant Lois MacBird in a 1981 interview. "He sculpted phenomenally. The Sperrys' home is filled with his work." Sperry was also an avid paleontologist, with an extensive collection of prehistoric mollusks.

"He was one of the premier experimental neurobiologists of his time," said Norman Davidson, the Norman Chandler Professor of Chemical Biology, Emeritus, and executive officer for biology at Caltech. "Those of us who have known him since those early years will always remember the courage and tenacity with which he continued to carry on his work in later years in spite of a debilitating degenerative disease. It was an inspiration to all who knew him."

The late Caltech professor is survived by his wife of 45 years, Norma Deupree Sperry, of Pasadena; his brother, Russell L. Sperry, of Bend, Oregon; his son, Glenn Tad Sperry, of Philadelphia; his daughter, Janeth Hope Sperry, of Cleveland; and two grandchildren.

The family asks that donations in Sperry's memory be made to the Muscular Dystrophy Association, or to the Children's Lung Fund, Cleveland, Ohio.

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Chicago Tribune

April 23, 1994 Saturday, NORTH SPORTS FINAL EDITION

ROGER SPERRY, 80
STUDIED FUNCTIONS OF HUMAN BRAIN

By Kenan Heise, Tribune Staff Writer.

Roger W. Sperry, 80, a Nobel laureate and professor emeritus of psychobiology at the **California Institute of Technology**, was honored for his research in right-side, left-side brain functions and learning. He was a former professor at the University of Chicago, where he had received his doctorate in zoology.

A resident of Pasadena, Calif., he died Sunday in Huntington Memorial Hospital in Pasadena.

Professor Sperry, a native of Hartford, Conn., received his bachelor's and master's degrees from Oberlin College. He earned his doctorate at the U. of C. in 1941. During World War II, his military duty involved medical research on nerve injuries.

He taught after the war, first as an assistant professor and then an associate professor at the U. of C. He then was section chief for neurological diseases and blindness at the National Institute of Health and was a professor at **Cal Tech** from 1954 to 1984.

Through study of animals and human patients who had had the connections between the right and left sides of their brains severed, he demonstrated the functions of the two hemispheres of the brain. His research and observations helped establish concepts now regularly taught in the areas of art, education and philosophy.

Other work he did explained how neurons use chemical codes to grow, assemble and organize themselves following hereditary patterns.

Professor Sperry shared the 1981 Nobel Prize in physiology or medicine with David Hubel and Torsten Wiesel. He also received the National Medal of Science, the Wolf Prize in Medicine and the Albert Lasker Medical Research Award.

Survivors include his wife, Norma; a son, Glenn; a daughter, Janeth; a brother; and two grandchildren.

Services are pending.

GRAPHIC: PHOTO; PHOTO: Roger W. Sperry in 1979.

Pasadena Star-News

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Brain research pioneer Sperry dead at 80

Nobel winner taught at Caltech

By Roberto Ceniceros
STAFF WRITER

PASADENA — Retired Caltech professor Roger Wolcott Sperry, a 1981 Nobel Prize winner for discoveries showing that the two hemispheres of the brain function independently, has died of a heart attack.

Sperry, a Pasadena resident, was 80 when he died Sunday at Huntington Memorial Hospital in Pasadena. Memorial services were pending.

Sperry's work ethic drove him to research and write until his hospitalization April 11, friends and relatives said yesterday. For the last 25 years, he suffered from a degenerative nerve disease.

"He was so single-minded that if he was working, that was all he thought about," said his assistant, Mary Jeffries. "I would say, 'See you tomorrow,' and he would very meticulously put his middle finger over his index finger. I guess he was saying, 'With any luck.' "

Sperry won the Nobel Prize in medicine-physiology for his pioneering research involving "split-brain" patients whose left and right brain hemispheres were surgically cut. He showed how the two brain hemispheres function independently and together.

His discovery revolutionized the way doctors, psychologists and scientists understood the brain. Before Sperry's work, the right hemisphere had been considered nearly useless.

Sperry's results substantiated that analytic process and higher verbal skills tend to be located in the left hemisphere, while the right side is more holistic and copes better with spatial relationships.

Sperry also received the National Medal of Science in 1989 from then-President George Bush.

In the 1940s, Sperry researched the functions of brain cells and vision. In the 1960s he introduced groundwork for a theory explaining how neurons grow, assemble and organize themselves in the brain by means of chemical codes controlled by heredity.

Before his death, Sperry had been studying the role of consciousness and its importance in preserving values, said Norma Deupree Sperry, his wife of 45 years.

He was concerned about the earth's condition and population growth. His wife said he believed people should set values that preserve the quality of life.

Sperry continued working at Caltech as a professor emeritus of psychobiology after his official retirement in 1984.

About six months ago, he began using a walker. Jeffries said Sperry held a pencil with great difficulty but pressed on with his work.

The illness forced Sperry to give up the Baja California fishing vacations that he had purchased a camper to enjoy. He was in Baja when the 1981 Nobel Prize was

awarded and learned about it over the radio.

"From the time we got the camper, in about 1973, we were down there several times a year until two years ago," Norma Deupree Sperry said. "We were unable to go after that. It was too difficult for him to get around."

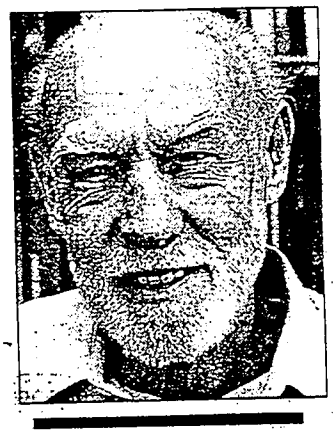
Sperry's list of accomplishments extended beyond science.

Friends knew him for his square dancing, sculpture and fossil collection.

His wife said he once held the Connecticut state high-school record in the javelin throw. He was captain of the basketball team during his days at Oberlin College in Ohio.

He earned his doctorate degree in zoology in 1941 from the University of Chicago.

In addition to his widow, Sperry is survived by his son, Glenn Tad Sperry of Philadelphia; daughter, Janeth Hope Sperry of Cleveland; brother, Russell L. Sperry, of Bend, Ore.; and two grandchildren.



ROGER W. SPERRY

- **Birthplace:** Hartford, Conn., Aug. 20, 1913
- **Education:** Bachelor's degree in English literature, Oberlin College, 1935; master's degree in psychology, Oberlin College, 1937; doctorate in zoology, University of Chicago, 1941
- **Major awards:** Nobel Prize in medicine-physiology, 1981; National Medal of Science, 1989; Wolf Prize in Medicine, Albert Lasker Medical Research Award, both in 1979; California Scientist of the Year Award, 1972
- **Occupation:** Among other positions, joined Caltech in 1954 as Hixon Professor of Psychobiology. Retired in 1984
- **Family:** Married Norma Deupree on Dec. 28, 1949; brother Russell Sperry of Bend, Ore.; son Glenn Tad Sperry of Philadelphia; daughter Janeth Hope Sperry of Cleveland; two grandchildren

Roger W. Sperry (1913–1994)

Colwyn Trevarthen
Dept of Psychology, The University of Edinburgh, Edinburgh, UK.

Roger Wolcott Sperry, born in Hartford, Connecticut on 20 August 1913, died 17 April 1994 in Pasadena. He was Emeritus Professor of Psychobiology at the California Institute of Technology (Caltech), where he had been Hixon Professor from 1954 to 1984. Sperry received the 1981 Nobel Prize for Physiology and Medicine for research on the functions of the cerebral hemispheres, sharing the honour with Torsten Wiesel and David Hubel, whose research on visual mechanisms was inspired by Sperry's early studies of visual embryology and the functional anatomy of visual cortex.

Sperry devoted his scientific life to exploration of the innate powers of the mind, and he became the leading nativist and most articulate mentalist in behavioural and brain science. He believed totally in the scientific method but fearlessly extended his experimental understanding of the neural machinery of intentions and awareness into a philosophical theory of values and a scientific ethic [Sperry, 1952, 1983, 1988 (Details of references are given in Box 1)]. He pioneered research into experimental embryology of brain circuits[1], perception and learning in the mammalian cerebral cortex, and specializations of consciousness in the human cerebral hemispheres. He was first recognized as an extremely skilled and imaginative researcher in the early 1940s when he published the findings of his PhD thesis with the eminent neuro-embryologist Paul A. Weiss at the University of Chicago[2]. Analysis of the disordered movement patterns following surgical transposition of the insertions of extensor and flexor muscles or exchange of motor nerves showed that the rat's motor system was 'hard-wired' and resistant to re-education. Experiments on the effects of surgical rearrangements of peripheral nerves continued from 1941 to 1946 with Karl Lashley at Harvard and at the Yerkes Laboratories of Primate Biology in Orange Park, Florida (Sperry, 1945). Sperry confirmed experiments by Leon Stone and Robert Matthey showing that a newt's eye dissected from the head, and replaced so that the optic nerve could regrow, would establish normal vision. He added the important experiment of a rearrangement of the eye in the body, changing the relation of the retinal array with respect to the motor system. When the eye was rotated 180° before regeneration of the optic nerve, the recovered vision was also rotated. The animal never regained the ability to move in the correct direction to seize food. This showed that the nerves were guided to re-establish the same retina–brain connections as before the operation, and, moreover, it ruled out learning as the mechanism for recovery of function (Sperry, 1963).

At Yerkes, experiments on the effects of rearranging motor nerves were extended to monkeys, which also failed to recode the aberrant neuromuscular connections; but, unlike rats, they quickly learned to suppress maladaptive movements and to substitute effective acts performed by intact parts of the motor apparatus. Evarts[1] explains the significance of this work on animals of differing evolutionary grade for the development of Sperry's ideas of the role of the cerebral neocortex in voluntary motor co-ordination, perceptual control of movement and consciousness (Sperry, 1952). The work led Sperry, in 1945, to advise neurosurgeons that the human brain could not readily adapt to rearrangements of peripheral motor nerves. From 1942 to 1945, Sperry performed military service on the Medical Research Project on Nerve Injuries.

Returning to Chicago in 1946 as Assistant Professor of Anatomy, Sperry continued nerve-growth experiments on other sensory and motor systems and began work with small tropical fish at the Lerner Marine Laboratory at Bimini, British West Indies, showing that nerves from eye to brain and from brain to fin muscles obeyed the law of innate specification of regenerated connections[1]. In these studies he was assisted by Norma Deupree, who became his wife in 1949. In 1950 he reported that fish and amphibians with surgically inverted vision consistently displayed compulsive circling whenever they moved. Sperry showed that the midbrain was the site of a predictive adjustment of vision inside the brain, triggered by the motor impulse, and anticipating the sensory displacement caused by movement. Instead of stabilizing the perceived world, the input from the inversed eye had the reverse effect, generating an illusory drift of surroundings in the same direction as the movement[3]. Sperry postulated a 'corollary discharge from efference' or 'central kinetic factor' that explained perception of self-movement and constancy of perceived surroundings during movement (Sperry, 1950). The same perceptual-constancy mechanism was discovered simultaneously by Erik von Holst and Horst Mittelstaedt, and named by

Box 1. Key publications of R. W. Sperry

The problem of central nervous reorganization after nerve regeneration and muscle transposition. (1945) *Quart. Rev. Biol.* 20, 311–369
Neural basis of the spontaneous optokinetic response produced by visual inversion. (1950) *J. Comp. Physiol. Psychol.* 43, 482–489
Neurology and the mind–brain problem. (1952) *Am. Sci.* 40, 291–312
Chemoaffinity in the orderly growth of nerve fiber patterns and connections. (1963) *Proc. Natl Acad. Sci. USA* 50, 703–710
Split-brain approach to learning problems. (1967) in G. C. Quarton, T. Melnechuk and F. O. Schmitt (eds), *The Neurosciences: A Study Program*, pp. 714–722, Rockefeller University Press
Some effects of disconnecting the cerebral hemispheres (Nobel Lecture). (1982) *Science* 217, 1223–1226
Science and Moral Priority (1993), Columbia University Press
Psychology's mentalist paradigm and the religion/science tension. (1988) *Am. Psychol.* 43, 607–613
The impact and promise of the cognitive revolution. (1993) *Am. Psychol.* 48, 878–885

them 'the reafference principle' using an 'efference-copy' signal.

At Chicago, Sperry experimented with cats to test theories of Wolfgang Kohler and Lashley that form recognition is mediated by electrical or magnetic 'field' effects in grey matter, or interference patterns generated by waves of activity in random cortical fibre feltworks. With Nancy Miner and Ronald Myers he then tested the visual discrimination to the limit, and found that the animals' acuity and form recognition were not affected. They concluded that perception depends on information passing vertically into and out of the cortex by axons looping below the grey matter. The behavioural-test apparatus later served to study learning in cats and monkeys with split-brains. The theories that Sperry discredited with these experiments resemble current ideas of emergent integrations in dynamic neural assemblies, which also take insufficient account of motivation (Sperry, 1952).

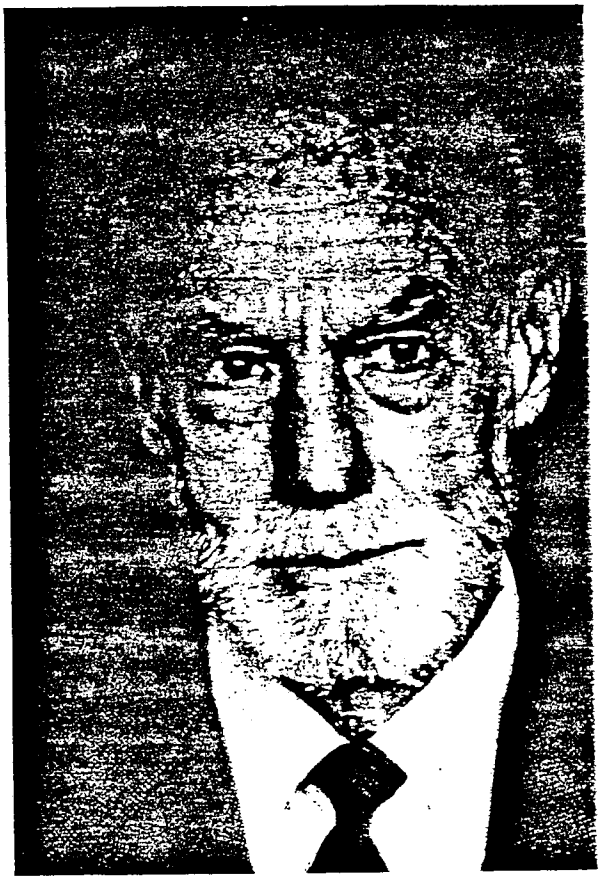
At Lashley's laboratory, Sperry shared discussions of the functions of the corpus callosum, the functions of which were a mystery. Ronald Myers undertook PhD research with Sperry on this problem. He sectioned the optic chiasma and corpus callosum of cats, and then proceeded to show that visual learning was divided in two by the surgery, and that the corpus callosum could transfer perceptual learning from one hemisphere to the other. Thus, what Sperry later called the 'split-brain' was created (Sperry, 1967).

In 1952, Sperry was appointed Section Chief at the National Institute for Neurological Diseases and Blindness. Then, in 1954, he accepted the Hixon Chair at Caltech. In the Biology division, Sperry's laboratory became a centre for new research on nerve regeneration in amphibia and fish, adding evidence for nerve guidance by 'intricate chemical codes under genetic control' (Sperry, 1963)[4]. Sperry suggested that learning would prove to be by modification, of the same process that creates adaptive nerve circuits in the embryo. In 1955, he published a prophetic paper on the nature of the conditioned response, emphasizing the role of transitory facilitatory motor sets and 'perceptual expectancy'.

At Caltech, Myers and a growing group of Sperry's post-graduate students and visiting scientists developed the split-brain experiments with cats, and extended these experiments to monkeys, enabling a classical series of studies of the mechanisms of eye–hand co-ordination (Sperry, 1967). The division of visual learning was confirmed and extended to touch, and the role in visual awareness of the intention to respond with one or other hand was explored. The monkey experiments confirmed that commissurotomy had truly divided consciousness in two. Then, in 1960, Joseph Bogen, a Los Angeles neurosurgeon, proposed that the split-brain experiments justified a re-examination of commissurotomy as a treatment for epilepsy. Split-brain monkeys retained intelligence and co-ordination, and it was thought that disconnection of the cerebral cortices might reduce seizures, and prevent their propagation.

In 1962, a paratrooper with progressively worsening seizures was operated on by Bogen and Philip Vogel. Psychological tests performed by Michael Gazzaniga, under the direction of Sperry and Bogen, determined the effects of commissurotomy on perception, speech and motor control. The startling findings of divided awareness and the lateralization of the capacity of speech to the left hemisphere, revealed by commissurotomy, in Bogen's patient were then published. Sperry's laboratory became the source of a stream of pathfinding papers on the functional differences in the two separated hemispheres of a small group of patients who had accepted the operation, and benefited by reduction of epilepsy. The hitherto little-known functions of the so-called 'minor' hemisphere were fully explored and demonstrated to be far more elaborate than had been believed. The now accepted view of the human brain as comprising laterally specialized and complementary realms of consciousness and cognition is summarized in Sperry's Nobel Address published in 1982.

Sperry considered the role of consciousness in daily experience and education in his writings on the mental life of commissurotomy patients. In line with comments he made as early as the 1950s, he



concluded that consciousness and its communication should be viewed as a causal and explanatory principle, not a metaphysical epiphenomenon. In 1965, Sperry published the first of a series of philosophical papers. Under the title *Mind, Brain and Humanist Values*, he proposed a new mentalistic monist theory of mind that broke with behaviourist traditions in giving subjective experience a prime controlling role in brain function and behaviour (Sperry, 1983, 1988). Sperry portrays consciousness as a special example of a general principle, 'macrodeterminism', in which the higher, more evolved forces throughout nature exert control over their lower components. Conversely, the highest of human motives are constrained by inherent cerebral design. Sperry's renunciation of the traditional science-values dichotomy stimulated some hostile criticism initially, but, after the mid-1970s, gained wide acceptance in what is now seen as a new era in value philosophy. Sperry had always advocated objective scientific enquiry as the brain's most reliable basis for arriving at belief, and now argued that the same applies to value judgements, which he held

were the true causes of human action and in need of scientific examination and methodical improvement if humanity was to avoid ecological, economic and social catastrophies, the signs of which have become increasingly apparent to all thoughtful and well-informed persons in recent decades. He sought both a new ethics for science, and a new scientific examination of the source of ethics in the workings of consciousness (Sperry, 1993). Sperry's efforts to explain the emergence of dynamic order and purpose in the psychological field and of motives in consciousness lead to the question: how do human populations guide their increasingly powerful dominion over one another and over every other element of natural order on earth? Writing on this global problem actively occupied him at the time of his death.

Roger Sperry received many high honours in addition to the Nobel Prize, including The Albert Lasker Basic Medical Research Award (1979) and The National Medal of Science (1989). He was also elected to many national societies including the National Academy of Sciences of the United States of America, and Foreign Membership of the Royal Society of the United Kingdom. Later, a progressive neuromotor impairment from primary lateral sclerosis forced him to forego participation in ceremonies.

Sperry was a taciturn, socially reticent person with a rich and creative private life. Something of a maverick, he shunned formalities and preferred to vacation in remote, wild places. With the company and help of his wife Norma and children Tad and Jan, he discovered giant fossil dinosaur bones and record-breaking ammonites in the deserts and canyons of the southwestern states of the USA, and caught big fish off the shores of Baja California. When the announcement of his Nobel Prize came, he and Norma were camping alone on a beach in Baja with their dog Chadwick, stranded by a hurricane and out of touch with Caltech for days. Sperry was an industrious artist and scientific illustrator, filling his home with sculptures and ceramics, including busts of his family, and life drawings.

His students remember him as an inspiring teacher and perceptive critic with a precise, ironic sense of humour tempered by gentle kindness[5].

Selected references

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2 Hamburger, V. (1979) *Neurosci. Newsletter* 10, 5–6
3 Evarts, E. V. (1990) in *Brain Circuits and Functions of the Mind* (Trevarthen, C., ed.), pp. xiii–xxvi, Cambridge University Press
4 Levi-Montalcini, R. (1990) in *Brain Circuits and Functions of the Mind* (Trevarthen, C., ed.), pp. 3–18, Cambridge University Press
5 Trevarthen, C., ed. (1990) in *Brain Circuits and Functions of the Mind*, pp. xxvii–xxxvii, Cambridge University Press

perspectives on disease

Synuclein proteins and Alzheimer's disease

Anthony J. Brookes and David St Clair

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In Alzheimer's disease, synuclein/NAC (non-amyloid β component of Alzheimer's disease amyloid) proteins are found in presynaptic cholinergic nerve terminals that degenerate early in Alzheimer's disease, and they are also found closely linked to β-amyloid fibrils in senile plaques. Synuclein/NAC proteins provide a potential molecular link between the degeneration of cholinergic nerve terminals, and the formation of plaques, and might have a primary role in their development.

Our understanding of the molecular aetiology of Alzheimer's disease (AD) is currently incomplete. Evidence suggests that both genetic and environmental factors can contribute to the development of this disorder[1]. With respect to the genetic basis of AD, significant recent advances include:

(1) the demonstration that the gene for the amyloid precursor protein (APP – the precursor of β amyloid, the primary component of the amyloid 'plaques' deposited in AD brains) can be the site of causative mutation, albeit in a minority of cases[2];

(2) the determination that a gene of major influence for familial AD (FAD) lies on chromosome 14 (Ref. 3);

(3) the discovery that possessing the ε4 isoform of apolipoprotein E predisposes at least to the late onset form of AD (Ref. 4).

Although important, these are probably only the first of many components that will need to be defined in order to understand the molecular pathology of AD. Therefore, the cloning of a cDNA for an unrecognized component of AD amyloid deposits was noted with great interest[5]. This cDNA was given the name NAC; its precursor was called NACP. Immunochemical analyses of AD brains, with antibodies raised against two separate fragments of NAC peptide, showed staining of amyloid on diffuse, primitive and mature plaques, as well as on cerebral blood vessels. Electron microscopy reveals localization of NAC peptide on amyloid fibrils specifically. In this respect, NAC peptide differs from most other components of plaques where co-association with amyloid is demonstrable using light microscopy only; this suggests that NAC peptide and amyloid are especially tightly linked. By searching the database with the gene for NACP, we observed a highly significant match to rat 'synuclein' sequences[6]. When the 423-nucleotide coding domain of the human NACP gene was aligned with rat synuclein, the overall identity was 90% with 32 of the 42 differences being in third codon positions. The proteins translated from these sequences were 95% identical, indicating that these are equivalent genes within different species. By mapping the gene for synuclein/NAC to chromosome 4 using monochromosome hybrids, it has been shown that this gene is not the FAD-predisposing locus on chromosome 14 (A.J.B. and D.StC., unpublished obser-

OBITUARY

VII-7

Roger W. Sperry (1913–1994)

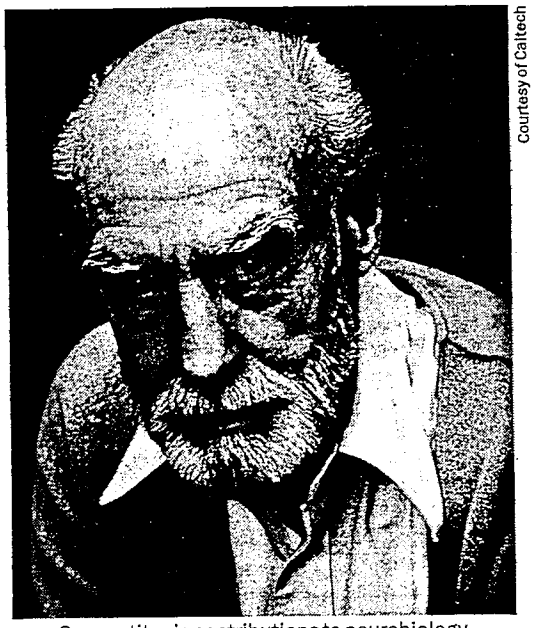
ROGER Sperry, co-winner of the 1981 Nobel Prize in Physiology or Medicine with Torsten Wiesel and myself, died on 17 April in Pasadena, California, of a heart attack. For many years he had suffered from a neuromuscular degenerative disease, but until recently had continued to be active in thinking and writing about the brain, consciousness and the mind. His contributions to neurobiology were titanic.

I first came across Sperry in the fall of 1953, when I heard him speak at an international physiological congress in Montreal. I had just begun my training in clinical neurology, and had not yet done any research. Sperry's talk came as a revelation.

It is hard today to recapture our state of knowledge of the nervous system in the early 1950s, a time when it was widely thought that the wiring of the brain came about largely through experience. In his talk, Sperry described the simple experiment of surgically interchanging the tendinous insertions of flexor and extensor muscles, or the nerves that supplied them, in a limb of a rat, to see whether the nervous system would relearn to use the muscles properly. The relearning never took place. Even the circuits responsible for spinal reflexes such as limb withdrawal in response to a painful stimulus to the foot remained quite unchanged.

A similar simplicity and lucidity characterized all of Sperry's work on neural development during that era. One of his best known developmental studies established that in a fish the fibres of a severed optic nerve grew back precisely to their former targets in the brain, even if at the time of severing the nerve the eye was rotated 180° in its socket. Here no adaptive relearning or rewiring of the circuits responsible for normal visual behaviour seemed to occur, so that the fish continued to snap downwards at bait placed above it. Such experiments suggested that when individual nerve fibres in a growing nerve trunk find their proper targets they do so by specific chemical cues that somehow recognize complementary cues in the targets. These ideas have still not been proven directly, but they have had a profound influence on the entire experimental field of neurodevelopment, today one of the most active branches of neurobiology.

In the 1950s the nervous system, and in particular the cerebral cortex, was supposed by some (who were taken seriously) to function not by nerve conduction and synapses but by a poorly spelled out process of electrical fields or waves in a volume conductor. Two experiments cleanly disposed of these ideas. In one, Sperry inserted into the cortex many tantalum plates or metal wires, which should have profoundly disturbed or short-circuited any such currents. In the second, he diced up the cortex with radially arranged pieces of insulating mica. In neither experiment was cortical function seriously disturbed. This was before Vernon Mountcastle's discovery of cortical columns, but Sperry did know of the predominance of radial cortical connections from the work of Santiago Ramón y Cajal and Lorente de Nó, and realized that the inserts should leave these connections relatively intact.



Courtesy of Caltech

Sperry: titanic contributions to neurobiology.

My next encounter with Roger Sperry was again indirect; in 1955 I found myself in the army and posted to Walter Reed Army Institute of Research, sharing a suite of laboratory cubicles with Ronald Myers, who had just got his PhD under Sperry at the University of Chicago. Myers's thesis topic involved behavioural studies of deficits resulting from severing the corpus callosum in cats. Up to that time, no one had any idea of the function of this huge bundle of nerve fibres, which connects the two hemispheres; together, Myers and Sperry showed that it had a very specific function in vision, and this was the beginning of the split-brain studies.

In the 1960s, Sperry, along with Joseph Bogen, Michael Gazzaniga and others, extended this line of research to humans. The work appeared first in two beautiful papers in *Brain*, in 1965 and 1967. Almost overnight a wealth of facts and concepts became available. The left hemisphere was known to be largely responsible for speech, but the new observations showed that the right hemisphere has language capabilities too, comprehending much of what it hears. It could even be shown that certain specific functions are better done by the right hemisphere than the left; for example the left hand (hence the right hemisphere) could carry out some visuospatial tasks far better than the right. In one marvellous passage we find a description of the right hand coming across and messing up what until then had been a successful three-dimensional drawing of a cube by the left hand. In these papers we learned that one person could have, literally at one and the same time, two consciousnesses.

Many of these ideas became distorted when they percolated down to the public, and one could easily get the impression that the right hemisphere was 'for' emotions and art, and that the left was 'for' reasoning and other dry intellectual pursuits. The original papers in *Brain* are the best antidote to such simplifications. They are highly readable and well within the grasp of a high-school student.

In later life, Sperry became increasingly interested in theories of mind and consciousness, concentrating on the relationship between mind and consciousness and ethical values. Many of his fellow neurobiologists could not easily follow his arguments, which seemed to come closer to philosophy than to neurology. But one could sympathize with his contention that brain mechanisms would never be understood solely on a basis of the chemistry and biophysics of single nerve cells. The revolution in these areas in the past generation has made it abundantly clear that without such a basis brain mechanisms are totally out of reach. Sperry's point was that more than chemistry and biophysics is required. It is like the relationship between chemistry of bricks and mortar, and the finished cathedral.

Our week together in Stockholm, in December 1981, with Torsten Wiesel, was marvellous fun. Our family and his were next-door neighbours at the Grand Hotel. In one lovely incident, just before the first banquet, a knock came at our door. It was Roger Sperry's son, holding an untied white bow tie in his hand. "Does anyone have any idea what to do with this?", he asked. I, of course, had no idea, because I have too little sense of style to use anything but the already-tied kind. But our youngest son, who plays the trumpet, had had to wear formal attire so often at concerts that he had become an expert in the difficult procedure. So Paul went next door and tied all the Sperry family's bow ties.

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NEUROSCIENZE

Addio a Sperry, esploratore dei due cervelli

Scoperse la specializzazione degli emisferi cerebrali ed ebbe il Nobel

POCHI giorni fa è scomparso Roger Wolcott Sperry, professore emerito di psicobiologia al California Institute of Technology di Pasadena, una delle figure più significative fra gli studiosi del sistema nervoso di tutti i tempi. Nato a Hartford nel Connecticut nel 1913, aveva ricevuto il Premio Nobel nel 1981 per i suoi fondamentali studi sulla specializzazione funzionale degli emisferi del cervello umano.

Sperry ha fornito un contributo decisivo al cambiamento delle concezioni sull'asimmetria funzionale degli emisferi cerebrali. Fin dalle scoperte anatomo-cliniche di Dax, Broca e Wernicke nel secolo scorso, queste concezioni erano improntate alla dottrina della dominanza assoluta dell'emisfero sinistro, riconosciuto come il substrato fondamentale delle funzioni cerebrali per il linguaggio e per i processi cognitivi. Le ricerche di Sperry hanno invece dimostrato che entrambi gli emisferi cerebrali partecipano all'attività mentale, pur con specializzazioni funzionali diverse e complementari. Anche l'emisfero destro possiede un'ampia gamma di capacità cognitive che pur non esprimendosi attraverso il linguaggio sottendono tuttavia forme elaborate di ideazione e di ragionamento, qualitativamente diverse, ma non inferiori a quelle dell'emisfero sinistro.

Gli esperimenti che hanno portato a queste nuove concezioni sono stati eseguiti su pazienti con cervello «diviso», cioè con sezione del corpo calloso formato da fibre che collegano i due emisferi cerebrali. Precedenti esperimenti su gatti e scimmie avevano provato che il corpo calloso è necessario per trasferire a ciascun emisfero informazioni di senso inviate selettivamente all'altro emisfero, permettendo così l'unificazione cognitiva dei due emisferi. Con tecniche analoghe a quelle applicate sugli animali, egli dimostrò che nei pazienti con cervello diviso le informazioni sensoriali limitate ad un solo emisfero davano origine ad esperienze coscienti inaccessibili all'altro emisfero, tanto da suggerire l'esistenza di due menti separate sotto la stessa volta cranica.

A Sperry va anche riconosciuto il merito di aver rivelato nei suoi studi giovanili, degni anch'essi del Nobel, alcuni principi fondamentali che regolano lo sviluppo del sistema nervoso. Le complesse connessioni selettive fra le miriadi di neuroni del cervello adulto si organizzano già prima della nascita sulla base di complessi codici chimici sotto il controllo di istruzioni genetiche. Su questo primo livello di organizzazione l'ambiente esercita poi le sue importanti azioni di raffinamento e di mantenimento dell'organizzazione cerebrale. In accordo con le idee di Sperry, David Hubel e Tornsten Wiesel, con lui vincitori del premio Nobel, hanno dimostrato che l'organizzazione della parte visiva del cervello è almeno in parte predisposta alle funzioni della vista già durante la vita intrauterina, quando nessun segnale luminoso raggiunge gli occhi.

La grandezza di Roger Sperry non si limita alle sue fondamentali scoperte scientifiche. Già dagli Anni 60 era divenuto famoso come neurofilosofo per aver sostenuto un'ipotesi di monismo emergentista che aveva perfezionato successivamente fino alla sua scomparsa. Si tratta di «una nuova forma di monismo in cui le entità mentali hanno un ruolo *emergente* e *causale*, in cui non è data esperienza cosciente al di fuori del cervello, né vi è posto per un'entità disincarnata, la si voglia chiamare coscienza, mente o spirito».

Per citare un suo esempio: la geometria di una ruota *emerge* da una particolare disposizione delle molecole che compongono la ruota stessa, ma a sua volta condiziona la traiettoria che le molecole percorrono durante il movimento della ruota: «Rispetto agli eventi interni alla ruota, le molecole sono guidate dalle consuete leggi fisico-chimiche. Rispetto al resto del mondo, il comportamento delle molecole è dettato, per lo più, dalle macroproprietà della ruota presa nel suo insieme». Già nel 1965 egli scriveva: «La potenza causale di un'idea o di un ideale diventa non meno causale di quella di una molecola, di una cellula o di un impulso nervoso... L'errore ormai secolare del materialismo scientifico consiste precisamente nell'avere ignorato questa seconda forma di causazione».

Il paradigma «macromentale» di Sperry sostiene dunque che tutte le differenti e ricche qualità dell'esperienza e tutte le forze vitali e mentali dell'individuo e della società, legate a multiformi interessi, propositi ed impegni personali e collettivi, devono acquistare agli occhi della scienza una dignità ontologica ed un potere causale paragonabili a quelli degli atomi e delle particelle subatomiche e delle loro interazioni. Se accettiamo questa impostazione, il mondo in cui viviamo e il nostro stesso essere ci appariranno governati non solo «dal basso», cioè dalle leggi della fisica e della chimica, ma anche governabili, e in modo assai più influente e denso di significati trascendenti, «dall'alto», cioè dalla forza dei valori umani.

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A REMEMBRANCE OF ROGER W. SPERRY

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In the era of modern science, it is seldom that anyone ventures far from their field of expertise, and nearly unheard of for someone to make major contributions in such diverse disciplines as psychology and developmental biology. **Roger Sperry**, who passed away in April of this year, was one of these rare individuals. Sperry received a Nobel prize in 1981 for his "split brain" studies on cortical hemispheric specialization, but there were many who felt he also deserved one for his earlier work on the formation of nerve connections.

The 60's and 70's were a transition time in which both areas were being actively pursued in his laboratory at Caltech and, for those of us in the lab, it was a remarkable experience in scientific cultural diversity. In the "human wing," split brain patients were being tested with everything from exotic image stabilization devices to tinker toys. The rest of the lab contained a veritable zoo. There was a colony of monkeys and cats, mostly with split brains, being tested with elaborate electromechanical devices. There was a room full of newly-hatched chicks pecking bad-tasting beads to study memory formation; and various frogs and fish were having nerves cut to study selective nerve growth using electrophysiological and neuroanatomical methods.

Sperry was happy to let us work on whatever we wanted as long as we could convince him that we were asking an important question. Although he was happy to give general advice about what to do, it was largely up to us to figure out how to do the experiments, and we did so with a great deal of independence. Writing up the experiments, however, was a different reality. Sperry, who majored in English literature as an undergraduate, was an excellent writer and expected every paper that came from his lab to be well written, down to the choice of the best synonym for every word. For those of us who were less gifted writers, this was a traumatic ordeal of endless revisions which could easily last a year or more. The papers and our writing skills, but not our egos, were the better for it. Generously, Sperry did not put his name on most of our papers.

Sperry's contribution to developmental neurobiology was fundamental, but to really appreciate this one has to go back to the late 1930's and early 1940's when he did his work. At that time, it was generally believed that individual nerve fibers were essentially identical in the way they responded to their local environment during axonal growth. Tissue culture studies seemed to show that axons were guided solely by mechanical structures, and a number of *in vivo* studies had purportedly shown that fibers would form connections with whatever targets they were made to encounter. Astoundingly, these misconnected fibers even appeared to support normal function. The conclusion was that nerve fibers were intrinsically identical and that neuronal function depended on learning, not on specific neuronal connections.

Sperry tested this then current wisdom by rotating the eye of a frog by 180 degrees and then cutting and scrambling the optic nerve. When the nerve grew back, he tested the frog's vision by presenting it with a fly on the end of a wire. When the fly was in front of the frog, the frog turned 180 degrees, and when the fly was behind it, the frog snapped as if the fly were in front. The frog saw a visual world upside down, never learning to see correctly. It would have starved if left on its own. From this simple experiment, Sperry concluded that optic fibers from different parts of the retina must

have grown to specific locations in the brain and therefore fibers must possess chemical identities that allow them to differentially respond to different chemospecific cues in the brain. The experiment also showed that specific connections, not just learning, were fundamental for neuronal function.

As a young assistant professor when this pioneering work was done, Sperry showed remarkable courage, considering that his thesis advisor and colleague at the University of Chicago, Paul Weiss, was the major proponent of mechanical guidance. Perhaps too much courage, because in spite of having published a number of papers extending and confirming his early findings in several different systems, he was denied tenure. (Chicago later gave him an honorary degree.) At Caltech, Sperry continued this work, culminating in the early 60's with direct anatomical evidence for the directed growth of optic fibers and the elaboration of his chemoaffinity hypothesis.

Today, the idea that growing axons differentially respond to chemical cues in their environment to form specific connections during development and that specific connections are actually important for neuronal function is hardly controversial. It is a fact of life for developmental neurobiologists. Many examples of selective growth have been reported in diverse systems from mammalian cortex to *Drosophila* nervous system, and a few guidance molecules have now been identified. It is good to remember that there was a time that we did not know about chemospecificity and that it was Roger Sperry who told us about it.

Note: Ron Meyer was one of Roger Sperry's last graduate students

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