

## Roger W. Sperry (1913–1994)

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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<sup>1</sup>, 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<sup>2</sup>. 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<sup>1</sup> 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<sup>1</sup>. 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<sup>3</sup>. 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).

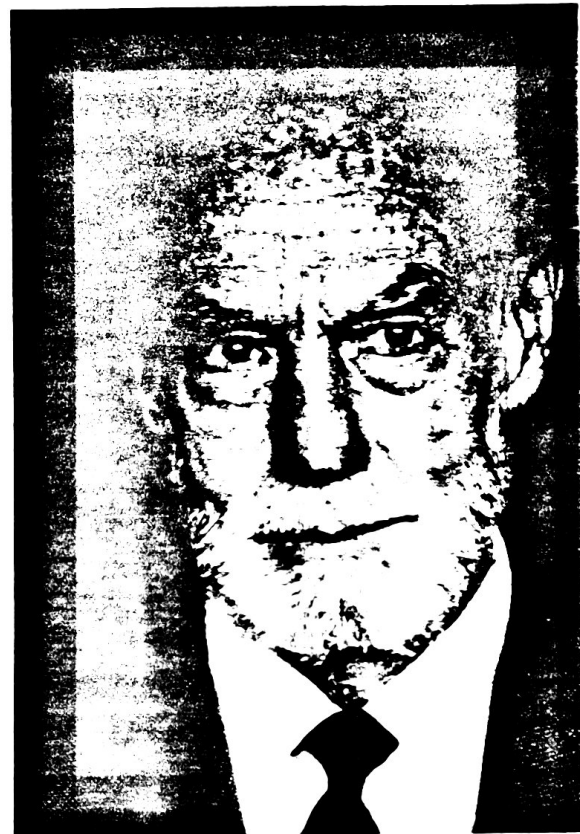
At Lashley's laboratory, Sperry shared discussions of the functions of the corpus callosum, the functions of which were a mystery. Ronald Myers undertook PhD research with Sperry on this problem. He sectioned the optic chiasma and corpus callosum of cats, and then proceeded to show that visual learning 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)<sup>4</sup>. 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 catastrophes, 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<sup>5</sup>.

#### Selected references

- 1 Hunt, R. K. and Cowan, W. M. (1990) in *Brain Circuits and Functions of the Mind* (Trevarthen, C., ed.), pp. 19–74, Cambridge University Press
- 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

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*In Alzheimer's disease, synuclein/NAC (non-amyloid  $\beta$  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  $\beta$ -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<sup>1</sup>. 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  $\beta$  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<sup>2</sup>;

(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  $\epsilon 4$  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<sup>5</sup>. 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<sup>6</sup>. 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-