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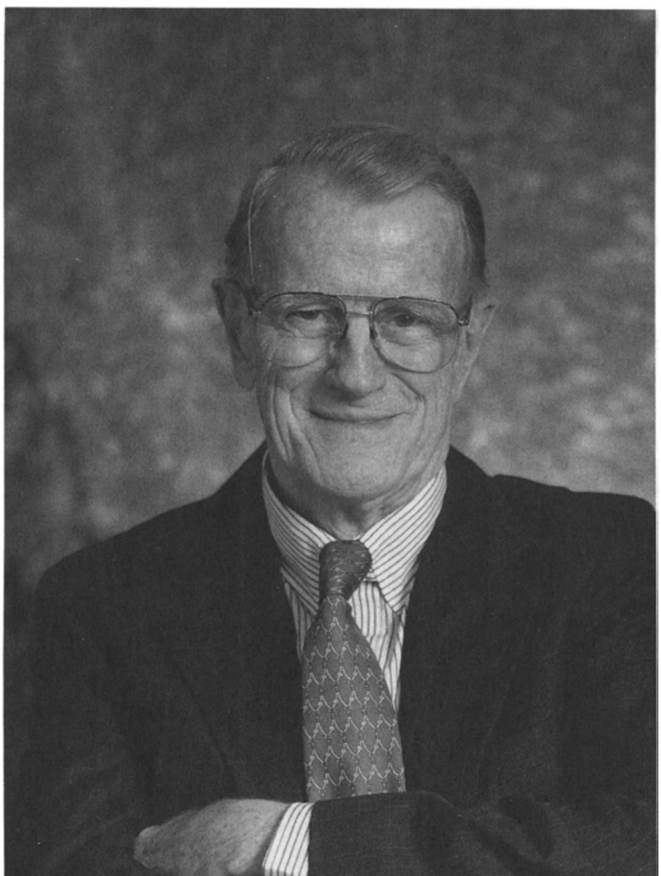

James M. Sprague

BORN:

Kansas City, Missouri
August 31, 1916

EDUCATION:

University of Kansas, A.B., 1938; A.M., 1940 (Zoology)
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APPOINTMENTS:

Johns Hopkins University School of Medicine (1942)
University of Pennsylvania School of Medicine (1950)
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Fellow, John Simon Guggenheim Foundation (1948–1949)
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James Sprague was initially trained in Evolution and Comparative Anatomy, but early on began work on the central nervous system. He carried out fundamental anatomical and physiological research on the spinal motor system, the spinocerebellar tracts, and the zonal organization of the efferent paths of the cerebellum. He performed classical studies that contrasted functions of lemniscal and reticular ascending systems of the brainstem. These studies evolved into research on the mammalian visual system: the cortical and midbrain mechanisms of visual orienting, of form perception and discrimination in the cat, and the interhemispheric transfer of these functions.

James M. Sprague

I was lucky enough to be born into a well-to-do family in Kansas City, Missouri. My mother, Lelia Mather, and my father, James P. Sprague, were both descendants of two of the oldest families in New England that had settled in the Boston area before 1630. This affluence allowed me to have a boyhood experience each summer that was an important determinant for the future. My grandfather Mather, a physician in Kansas City, purchased a cottage on Mackinac Island in 1900. The island lies in the strait connecting Lakes Michigan and Huron, an idyllic spot steeped in the history of the opening of the Northwest by fur traders and Jesuit missionaries. Largely covered by a mixed hardwood-conifer forest, the island is full of birds and small mammals. The handsome fort that dominates the harbor and small village was built in the mid-1700s. Standing in the village of Mackinac is the house in which William Beaumont, an Army physician, in 1822 to 1823 observed the process of digestion through a fistula in one of his patients—a classic study in medicine. Transportation on the island was and still is entirely by foot, horse, or bicycle; no cars are permitted except for emergencies. Because the island was free from hay fever, which plagued my mother throughout her life, we happily traveled to the cottage each summer until I was 12-years-old. The island is small and there is no way to get lost, so I was allowed to roam freely into the forests, to the old fort, along the woodland paths, and the lake—an experience that imprinted a love of nature and a desire to become a naturalist and explorer. My nursemaid, Eliza Nawagezik, was a remarkable woman—an Indian of the Chippewa (Ojibwa) tribe—who lived on Mackinac Island but had graduated from Carlisle College in Pennsylvania.

All of this came to an abrupt end with the collapse of the stock market in 1929 and the advent of the Great Depression. My father, along with many other businessmen, saw his job fall apart; he lost his steel distributorship and much of our livelihood with it, and we could no longer spend summers on this enchanted island.

Nevertheless, my early interest in natural history was sustained by field trips with the Boy Scouts and a friendship I struck up with one of my high school teachers, with whom I tramped the Missouri River bottoms on ornithological trips. This area is one of the major flyways of migrating birds going north in the spring to their nesting areas and south in the fall to Central and South America to spend the winter. The predictable rhythm of the multitude of species moving so faultlessly toward an imprinted destination enhanced my sense of being a part of nature and not some "superior" observer. This cognizance was reinforced during summer months in camps in the Missouri Ozarks and Colorado Rockies. I spent any time free from camp routine seeking the habitats of birds and mammals and immersing myself in nature. It was a stimulating time of life despite family deprivation.

High school, on the other hand, was for the most part mediocre and not stimulating—a pleasant enough experience, in retrospect, due primarily to the positive attitudes of the instructors. Standards were rather lax and instruction was not rigorous. The exception was English literature, a subject in which I received considerable reinforcement from my mother, an inveterate reader. Biology was taught by a kindly lady, but was so routine and uninspired that I almost failed. Even worse was physiology, taught by the football coach!

The big surprise came with ROTC, in which I reluctantly enrolled under parental pressure. ROTC was taught by a regular Army sergeant, a ramrod straight, crew-cut man with unblinking green eyes. Despite his demands for strict discipline and disdain for anything other than clear-cut objectives, I flourished and emerged two years later as second lieutenant with a medal inscribed "Most Military"!

By the time I finished high school in 1932 (with a mediocre scholastic record), the Depression was at its worst point and family finances required "the graduate" to forget the former country club environment of his parents and face the reality of earning a living. Compounding my problems was the separation and divorce of my mother and father. The money put away during former affluent days for my university education was needed to live. Jobs were scarce, but through family connections, I was hired to run an elevator and do various house-cleaning chores in an office building owned by an insurance company. This was indeed an abrupt change in lifestyle, but it proved to be an important learning experience.

I was plunged into a harsh milieu. My fellow workers resented my being given a job that was needed, as one worker said, "about as much as a thrashing machine." I was incredibly naive and took a lot of ribbing, but basically the men were a decent lot and they finally accepted me. In addition to running the elevator and changing light bulbs, I quickly learned how to wash windows and scrub washrooms and as a bonus was tutored in the vocabulary of four-letter words. President Roosevelt had just been elected and among the changes he made was the increase in the minimum wage. Thus, for a 48-hour week I received $62.50 per month, a figure that still sticks in my mind. The chief engineer was worth $100 per month and the building superintendent $150. It was obvious to me that these people had dead-end jobs and little chance for an improved life. I vowed to start working my way out of that depressing situation.

Preliminary Steps

Despite my optimistic attitude, the situation was not promising—my family's finances were extremely low. One factor in my favor was that I had a general idea of what to do with my life (at least in the immediate future) and that was to become a zoologist. Realization of this aim, however, required much more education. Luckily, Kansas City had a two-year junior college with rather lenient admission requirements, plus a faculty of men and women who were serious and rigorous educators. For the most part they did not hold doctorates and were not qualified for university jobs, but they were excellent teachers and I am forever grateful to them.

Finding the time to go to Kansas City Junior College, however, was the major problem. I started the solution by seeing the building superintendent and explaining my desire. To my great surprise he was quite sympathetic. Apparently, he had always wanted to go to college. He immediately agreed to change my schedule, allowing me to work half-time in the afternoons and evenings. This left the mornings free to go to school, but also reduced my salary to $31.25 per month. The next step was to approach my uncle and aunt (my father was in bankruptcy) for a loan of enough money to make a go of it. My uncle, Harry F. Mather, was a physician and surgeon and was sympathetic to my interests in science, but he had two sons of his own to educate. Nevertheless, a loan was agreed on. So the "end of the beginning" came about and I cannot begin to express the joy I felt to see this small window of opportunity before me.

I entered junior college the fall of my second year after high school with great enthusiasm and found the material fascinating. In the beginning, eagerness exceeded ability. I had not cultivated good study habits in high school, to say the least. Learning to study and to organize material from books was not an easy accomplishment and I struggled, but did it well enough to receive a tuition scholarship for the second year. Life was rigorous and disciplined to an extreme, with me rising at 6 a.m., reaching school at 8 a.m. and going to work at 2 p.m., leaving at 7 p.m. for dinner and study, and going to bed at midnight. I partly compensated for sleep deprivation on the weekends but managed to continue the trips to the rivers and woods around Kansas City, winter and summer.

At that time, a new government office building was being constructed in the center of the city and the *Kansas City Star* announced that fossils were found at the site of excavation. I hurriedly applied to the contractor for permission to go into the pit. Here were piles of gray-black shale, which, when split, revealed a multitude of fossils—pelecypods, brachypods, crinoids, and ferns—and I returned home with backpack bulging. I identified the fossils using library books and placed them lovingly on the shelves of my room along with Indian artifacts, bird nests, animal skulls, and minerals. Only one more trip to the pit was possible before construction continued, after which I grieved that those remnants of long-past lives from ancient seas were lost forever. I would have saved them all!

At junior college, a requirement of the biology course was to make an original effort in the form of a mounted skeleton of animal or bird. Through friends I obtained the carcasses of a fox and a pheasant and mounted them with the help of books. William Hornaday's *Taxidermy* gave instructions how to skin, stuff, and mount the pheasant; the result certainly would not have won any prize, but I was enormously proud of my work and received an "A" from the instructor. I have the fondest memories of that school's rather shabby building and those exacting, but supportive instructors.

At the time of graduation from the two-year college in 1936, good luck struck again in the form of two wealthy and powerful family friends. One, Clifford C. Jones, was the president of a large insurance company in Kansas City. He and his wife each presented me with a check on graduation, not a princely sum, but for a struggling student a significant one. The second piece of luck came from my godfather (Episcopalian, not Mafia!) who was a dermatologist and sportsman and a friend of the then chancellor of the University of Kansas. My godfather (Richard Sutton, M.D.) gave me two important gifts: he obtained a job for me in the Natural History Museum and he paid my out-of-state tuition for the next four years at the University of Kansas until I completed my bachelor's and master's degrees in zoology. So I was on my way to the future that I had dreamed about—developing into a naturalist and explorer.

University Years: Kansas

At the University of Kansas I spent half of each day in class and half at my job, learning about the local fauna in the museum. The curator (Charles D. Bunker) was a man old enough to have seen the piles of skeletons and skulls of the thousands of bison slaughtered on the Kansas and Nebraska plains in the 1870s and 1880s. Another reminder that the Old West was not far behind was located in the museum—the mounted specimen of the horse Comanche, the only survivor of the Battle of the Little Bighorn, when General Custer and his entire command were wiped out by the Sioux and Cheyenne in 1876.

My job at the museum was to care for the large collection of mammal skins and skeletons, and during the summers I went on field trips to different parts of Kansas with an assistant curator (Claude Hibbard) to collect specimens not well represented in the museum's collection. Many of these expeditions were to the fossil beds of western Kansas, a semiarid country of rolling hills and dry washes, of eroded Pliocene and Oligocene rocks loaded with fossils of rodents, carnivores, and small horses. Often these fossils could be picked up after a rain, exposed in the ground of stream beds. More frequently, their recovery required sifting large amounts of sand and earth through a wire mesh to recover the broken remains of a fauna that lived 20 to 40 million years ago. One summer I was the camp cook for four men with voracious appetites, fortunate for me because my experience was limited to preparing food to qualify for a Boy Scout merit badge! By summer's end I could serve up a complete chicken dinner, including biscuits and pie cooked over a two-burner Coleman stove and oven.

My museum job began at $30 per month and topped off at $50 and required laboratory teaching in the comparative anatomy course. The hours were long, the pay low—lunch was frequently a chocolate bar with peanuts and for dinner I ate more chili than in all the rest of my years. In those days my scientific interests were limited to taxonomy, comparative anatomy, evolution, and wildlife distribution and behavior. One of my mentors, Charles Bunker, stimulated the budding careers of many Kansas boys who worked in the museum—Alexander Wetmore, who became director of the Smithsonian Institution; Remington Kellogg, who was curator of mammals and then director of the U.S. Natural History Museum; Raymond Hall, who became curator of mammals at the University of California, Berkeley; Theodore White, who collected fossils for the Museum of Comparative Zoology at Harvard University; and William Burt, who became curator of mammals, and Claude Hibbard, curator of paleontology, both at the University of Michigan. Later, the signatures of these luminaries and many others covered the scapula of a bull bison in Bunker's office. Eventually, I was asked to sign along with these men (and two women) and did so proudly with the knowledge that I was now a qualified naturalist.

The University of Kansas at Lawrence has a beautiful site atop a geological formation called a monadnock, which looks over wooded rolling hills and farm country. The university was dependent on appropriations from a practical-minded state legislature, so surplus funds were hard to come by. Nonetheless, teaching was of a high quality, some of the faculty did research, and the spirit of faculty and students was good. It was an optimistic time for me, and I am indebted to more people than I can acknowledge here for support and encouragement. I found the courses in biology and paleontology fascinating and was attracted especially to Norman Newell, who became professor of paleontology at Columbia University and the American Museum of Natural History. Many years later I met him again at the annual meeting of the National Academy of Sciences, in Washington. Also present on the university faculty at that time was Loren Eiseley, the anthropologist and renowned writer who eventually went to the University of Pennsylvania (Penn), where we made contact again 15 years later.

I was at the University of Kansas for four years, two of which were to accumulate the credits to receive a baccalaureate degree in zoology, and two additional years to qualify for a master's degree, under the supervision of the herpetologist, Edward Taylor. The university required a thesis of original research for a master's and my choice of subject revealed a personal and lifelong characteristic—that is, to work in a field of study off the beaten track. The choice was modest enough in the beginning. The small mammals trapped during the museum's field trips were skinned, treated with alum and arsenic, and stuffed. The carcasses were then placed in separate boxes containing a population of dermestid beetles. These remarkable insects ate the soft parts of the carcasses, leaving complete, articulated skeletons, including the small hyoid bone normally attached to the base of the skull and supporting the base of the tongue and pharynx. The use of that bone was fascinating—for instance, whether the hyoid arch (as it is called) is bony or ligamentous in felines determines whether a specific species can or cannot roar. This hyoid bone had not been described in rodents and appealed to me as a good subject for a master's thesis. The faculty supervisors agreed and I put together a fairly interesting, but limited and not too rigorous, thesis. It was, however, an important step for me to organize my first scientific study, and I laud the wisdom of the university in requiring an experimentally based thesis for a second-level degree. In preparing the thesis I became acquainted with the writings of some of the great European comparative anatomists, chiefly English and German, of the 19th century.

Harvard

Before completion of my thesis in 1940, I began seriously considering where to apply for training leading to a Ph.D. For a variety of reasons, I had strong interest in three possibilities—the University of Michigan, the University of California, Berkeley, and Harvard, each having an active museum of natural history. A visit was therefore necessary to become a serious candidate for a scholarship, so I once more turned to my godfather for the wherewithal. He again supported my ambition and covered travel expenses; we chose Harvard for the first, and as it turned out, only visit. Lady Luck again played a role as my first appointment was with Professor Alfred S. Romer, the noted vertebrate paleontologist, who taught a major course in comparative anatomy for undergraduates. This course was popular because of Romer's charismatic personality, and it filled a key spot in premedical preparation. I nervously knocked on the front door of the Romer house on Brattle Street, Cambridge. He was confined at home with the flu, but the worst was over and when I arrived he was lying on a chaise lounge covered with a blanket. Soon after I entered the room, however, he got to his feet and greeted me by chanting with full body participation the football cry of the University of Kansas—"Rock-chalk, Jay Hawk, K.U."—beginning slowly and working up in speed and volume to a crescendo. I joined him in this amazing performance and we got along famously. Before the "interview" was over, he offered me a scholarship, assuming that Harvard would admit me as a graduate student, which it did. I was floating on cloud nine when I returned to Lawrence, and reported to my pleased godfather, friends, and mother (who had had a strong preference for Harvard right along).

Naturally, I was high on the manner in which the gates of higher education had opened to allow me to work on a Ph.D. at Harvard. Although I did not realize it, I would be leaving the Midwest for good and making my home on the East Coast in Cambridge, then Baltimore, and finally Philadelphia. While working for the master's degree I had met Isabelle Baird, a young woman who was a graduate student in entomology. We became engaged before I moved to Cambridge and were married a year later in Fort Knox, Kentucky, where her parents lived. She broke off her graduate work at Kansas and went with me back to Harvard for my final year. Soon after my graduation in 1942 we moved to Baltimore where I had an appointment in anatomy at Johns Hopkins Medical School and where our son, Jim, was born. Unfortunately, our marriage was not successful and after several years we separated; she returned to the University of Kansas to finish her doctor's degree and then joined the biology faculty at Mt. Holyoke College, in South Hadley, Massachusetts. Jim was raised in South Hadley, went to Harvard College and the University of Pennsylvania Medical School. He now has a successful practice in pediatric ophthalmology in McLean, Virginia, and lives in Washington, D.C., with his charming wife Elsie (née Youngman) and adopted children, Lena and Julie. He is a fine doctor and a wonderful person and I feel proud to be his father.

When I first went to Harvard I was assigned a small apartment in old Perkins Hall Dormitory, and I shared it with another biology graduate student, Peter Morrison. Peter had a major interest in biochemistry and eventually became director of the Institute of Arctic Biology at the University of Alaska, Fairbanks. In contrast to Perkins, the biological laboratories were in a relatively new building, the entrance of which was framed by two life-sized, bronze figures of the African rhinoceros. I shared a large and beautiful room on the second floor overlooking the rhinos with Dillon Ripley, who later became director of the Smithsonian Institution in Washington, D.C., and George Bartholomew, now professor of biology at the University of California, Los Angeles. They were delightful companions in the stressful pursuit of a Ph.D. degree. This large room, by the way, was the most spacious office, with the best view, that I occupied until I took over the chairman's office at the University of Pennsylvania 27 years later.

I went to Harvard with the full intent of some day becoming a museum curator, specializing in comparative anatomy and life history of mammals. So I attached myself to two people in Harvard's Museum of Comparative Zoology—Alfred Romer, curator of vertebrate paleontology, and Glover Allen, curator of mammals, both men of impressive scholarship. At the end of one of our conversations, Dr. Allen pointed out a large collection of pickled bats from all over the world that had been on the museum shelves for many years and suggested that I dissect these animals for my thesis. Not surprisingly, I chose to study the structure of the hyoid apparatus which, as these were intact specimens and not just skeletons, included the associated pharynx, larynx, and musculature. My area of research opened up in a stimulating way in this environment.

Harvard had a mature attitude toward graduate education, which suited me perfectly. A thesis advisory committee of five faculty members was assembled for each student and because the degree was in biology, the committee was broadly constituted. Mine consisted of Professors Romer, Allen, Hisaw (endocrinologist), Weston (botanist), and Wyman (biochemist and geneticist). No courses were required, although some were recommended to patch up my weaknesses. I was left alone to pursue my education, which hopefully would get me through a comprehensive (and terrifying) oral examination at the end. Once a week the faculty and student body gathered in a common room for tea and a faculty lecture. This "mixer" was a bit stiff, but educational and occasionally inspiring. Attendance was voluntary, hence the more reclusive or belligerent faculty and students were never seen.

I spent a good part of the next two years cheerfully dissecting and describing the hyoid and associated structures of 39 species of 32 genera of bats and writing a monograph on my findings. Of the 17 known families of bats, 13 were available in the Harvard collection. At least one member of one genus of each family was dissected by me and the origin and insertion of 19 muscles were described and figured; in one species the innervation of these muscles was also worked out. In examining my thesis now, I am absolutely amazed at the amount of work accomplished during those two years and by the energy of the young. The thesis was later published in the *American Journal of Anatomy* (1943). So far as I know, few read this work or referred to it subsequently and it is of historical interest only. Nevertheless it gave me much pleasure to complete it and, of course, it directed my reading and deepened my understanding of comparative anatomy and evolution. The only sorrow of those Harvard years was the death of Glover Allen. He was a gentle, shy man of deep erudition and was a model of modesty for his accomplishments and international reputation.

Postbaccalaureate Years: Johns Hopkins

As graduation day approached in the spring of 1942, Romer had lined up an ideal job for me in the Field Museum in Chicago as an assistant curator of mammals. But this was not to be. Ironically, and to my great disappointment, after all the years of study in preparation for just this kind of work, the restrictions imposed by World War II greatly affected museum activity, and the position was not filled. At the same time, the the job market in medical schools was opened up to prepare physicians needed in the Armed Services. I went to see George Wislocki, then professor of anatomy in the Harvard Medical School, and he generously made it possible for a classmate, Marcus Singer, and me to dissect a human cadaver during the summer of 1942 and to learn the rudiments of human anatomy sufficiently, but barely so, to teach first year medical students. With this accomplished, I was offered and accepted a teaching position at Johns Hopkins University Medical School. Romer's advice was to continue my studies until the war was over and then return to my original objectives. But I found myself in a totally new research milieu in which the academic preparation for a career in evolution and comparative anatomy was only of marginal interest.

One of the strong points then in basic sciences at Hopkins was the study of the central nervous system in my home department of anatomy, in the physiology department, and in the Carnegie Institution of Washington's department of embryology, located in the Medical Center. Making contact with these departments and reading the publications of their faculty opened a new world to me, both conceptually and in the possibility of doing experimental research. I was caught up in the fascination of the structure and function of the brain and, after several false starts, I picked up an interesting problem with considerable help from discussions with William Straus, comparative anatomist and physical anthropologist in the anatomy department.

Interestingly, the experimental problem grew out of embryology and comparative anatomy, of which I had some knowledge, and it had to do with the derivation of spinal musculature from embryonic myotomes or lateral plate and their respective innervations from dorsal and ventral rami of the ventral roots of the spinal nerves. The problem was to localize the position in the spinal gray matter of the motor neurons innervating myotonic or lateral plate muscles that had very different functions. Localization was achieved by severing dorsal or ventral rami respectively and waiting for retrograde chromatolysis to occur to identify the cell bodies of which the axons had been cut. In an unforeseen coincidence, I was not given rats, as might be expected for a beginner, but instead the study was done using rhesus monkeys, which were part of Marion Hines' research in the department. My modest beginning of a career in neuroscience was helped in great measure by the supportive environment in which I worked, specifically by discussions with Bill Straus and Marion Hines in anatomy; Louis Flexner in the Carnegie Institution; Vernon Mountcastle, Jerzy Rose, and Reginald Bromiley in physiology; and by the critical reading of my manuscript by Clinton Woolsey.

Two men came into my life in important ways during this early period of my development—Donald Barron, professor of physiology at Yale, and Horace Magoun, professor of anatomy at Northwestern. Both contacts were serendipitous. Louis Flexner was my contact with Barron whom he knew from their days of working with Joseph Barcroft in Cambridge, England, and Flexner knew of Barron's interest in the development of the brain in sheep. Barron was a wonderful person with whom I had marvelously exciting and formative discussions about science, and he loaned me a series of silver stained slides of the sheep spinal cord at various ages, fetal and newborn, which showed the differentiation of the dorsal and ventral primary rami. These I studied and later published on.

My relationship with Magoun began at a meeting when I delivered a paper, after which I sought him out for discussion about the possibility of spending a semester in his laboratory. After he returned to Chicago, he sent me a letter in which he agreed to my visit and provided financial support. In Chicago with Magoun, Donald Lindsley, and Leon Schreiner, I learned some neurophysiology and electroencephalography in a study of reticulospinal control of stretch reflexes. Tid Magoun was a brilliant investigator of mercurial temperament. He made great demands on his collaborators, but was a decent and generous man. At the time of my visit he was in full stride on a series of remarkable discoveries on the function of the brainstem reticular formation. When I went to Northwestern in the spring of 1948, I had already received a Guggenheim Fellowship and had made arrangements to spend a year in England. Otherwise I would have spent the following year with Magoun, who was joined by Giuseppe Moruzzi from Italy. Because of the timing I missed being a partner in the wonderful discoveries they made on the role of reticular formation in the control of arousal and wakefulness.

Soon after Moruzzi returned to Italy to accept the chair of physiology in Pisa, Magoun moved to the University of California, Los Angeles. With a series of colleagues he went on to work out the details of neural circuitry in midbrain, thalamus, and cortex by which the brain controlled waking, alerting, and attention. That research galvanized an entire area of research worldwide, including anatomy, physiology, and experimental psychology, and made him an international leader in neuroscience. The conceptual advances of Magoun's research during the years 1948 to 1960 were such that he was a strong contender for the Nobel Prize and, in my opinion, should have received it.

Oxford and Cambridge

In the early summer of 1948, I boarded the *Mauretania* for Southampton and a wonderful year divided between Professor (later Sir Wilfrid) LeGros Clark in Oxford and Dr. Bryan Matthews in Cambridge. Both were distinguished investigators. Clark was professor of anatomy, widely known for his research on the connections of the mammalian visual system, and as a physical anthropologist. It was he, with his colleague Jeffrey Winer, who proved several years later that the Piltdown man was a fraud. Bryan Matthews had done brilliant work as a young man, growing up in the remarkable department of physiology at Cambridge, and he published what became a classical paper on a new neural mechanism—the gamma motoneuron and its influence on stretch reflexes. The onset of World War II had interrupted his developing career, but his services during the war earned him a knighthood. Later he succeeded Lord Adrian as professor of physiology in Cambridge. Matthews owned a 60-foot boat which he sailed to the Mediterranean each summer. I once crewed for him across the English Channel, up the river Scheld to Antwerp, and then via canals to Brussels where we attended an international physiology meeting. I came to know both LeGros Clark and Bryan Matthews as friends and we kept in touch until they died.

In Oxford I learned the silver technique developed by Paul Glees for staining degenerating axoplasm and through the use of it I worked out connections of the hippocampus in the rabbit with a colleague in the department, Margaret Meyer. The technique was a marked advance over the classical Marchi method for tracing pathways in the central nervous system. The classical method traced the degenerating axons only so far as they were myelinated, whereas the silver method impregnated the axon sheath itself and revealed the terminal arborization to the synapse.

While in Cambridge I lived in the house of a retired professor of German literature and his wife, whose dining room provided lively discussions of every sort. From there it was a short walk through a meadow, with cows and a millpond, to reach the physiology laboratories on Downing Street. The scientific environment was unique to me. The investigators were expected to do everything for themselves and few general facilities were available. I was joined in Matthews' lab by Michael Fuortes from Torino, Italy, and each of us was given a set of directions on how to build an electronic amplifier from components that Matthews provided. I remember that Fuortes' amplifier was more handsome than mine and when Matthews came around to take a look at it, I was discouraged and defensively stated that I had produced a pile of junk. He checked it out and said, "Yes, but a pile of junk that works." Mike Fuortes later came to the United States, eventually moving to the National Institutes of Health (NIH) where he did outstanding research on the retina.

In any case, I scraped together enough electronic equipment to begin some recording experiments on the spinal cord of cats, but I ran up against a serious obstacle I had not foreseen. Matthews' laboratory was heated totally by one electric glowing wire burner, which was insufficient to maintain the warmth of the investigator, much less that of an anesthetized animal in the months of January to March. I was intrigued to learn how Professor Adrian had solved this problem in his studies of the cortex. I asked his secretary for an appointment and one morning, some days later, he met me in his laboratory to show me his screened, recording cage that was encased in folds and twists of metal pipe through which he ran hot water from the sink to warm his preparation by radiation. This solution was beyond my reach as a young visitor in a famous laboratory, so I delayed the experiments until spring furnished the necessary warmth. Meanwhile, I read voraciously in the physiology library, attended lectures on Roman history as well as science, talked with many people, went frequently to Kings College Chapel for Evensong, and enjoyed fully exploring the myriad facets of Cambridge, both the university and the adjoining countryside. I learned there, without a doubt, that the opportunities afforded by sabbaticals should not be limited to working day and night in a laboratory.

One day Professor Adrian stopped by Matthews' laboratory to chat and told me he had just returned from a visit to Sir Charles Sherrington, who was confined to a nursing home in the seaside town of Eastbourne. Sir Charles had been a scientific hero of mine since I read *The Integrative Action of the Nervous System,* and I asked if it would be possible to visit him. Adrian told me Sir Charles would enjoy visitors and kindly made the arrangements for me. Sir Charles was then over 90 and frail, but he asked what I was doing in research and we talked for several hours about various subjects, including Santiago Ramón y Cajal's visit to Oxford many years before. Cajal had been invited to give some lectures in Oxford and stayed in Sherrington's house. Cajal asked for a key to his bedroom and requested Mrs. Sherrington not to have the room cleaned or the bed made, and further asked that no one enter the room. This behavior was mystifying and never explained. Before leaving Eastbourne, Sir Charles gave me a signed copy of his book, *Goethe on Nature and on Science*, published and partly rewritten that year, 1949, in honor of the bicentenary of Goethe's birth.

Another time during that sabbatical I visited Charles Darwin's house at Down, where he wrote *The Origin of Species,* among other books. The house was charming, overseen by the gentle presence of Sir Arthur Keith, the anthropologist who lived there. Sir Arthur invited me to lunch, after which he took an hour's postprandial nap and left me to ruminate in Darwin's study, which remained just as the great man had left it. I should not leave a description of England without comment on the wonderful friendliness and hospitality found everywhere in that beautiful country.

Hopkins—My Last Year

The return to Baltimore was a cultural wrench, made particularly difficult by the animosity of the newly appointed chair of the department of anatomy. His animosity was not reserved for me, but was carried through to all members of the department. He succeeded in driving out a distinguished faculty, including two members of the National Academy of Sciences.

During 1949 to 1950, my last year at Hopkins, I tried to continue using the Glees silver method for tracing degenerating nerve fibers but without success; the technique that worked well using Oxford tap water refused to cooperate with Baltimore city water! While in England, I had read a paper by Cooper and Sherrington that described large, multipolar neurons in the ventral horn of the spinal cord, which were not motoneurons; they proposed these cells as the origin of the ventral spinocerebellar tract. I began to study this system after making lesions in the ventrolateral funiculus of the thoracic cord, using chromatolysis of the Cooper-Sherrington cells below the lesion and Marchi degeneration of the ascending tract that terminated chiefly in the bulbar reticular formation, as well as the cerebellum. At the same time I sought job opportunities elsewhere, surreptitiously I might add, because had he known, my chair would have tried to run me down in any way possible! An attractive job in anatomy at the University of Pennsylvania was offered by William Windle and eagerly accepted. I moved to Philadelphia in the fall of 1950 and have remained there happily up to the present.

University of Pennsylvania

I went to Penn with reasonable experience in teaching gross and microscopic anatomy and neuroanatomy, but with only a modest research achievement. I had gone to Hopkins immediately after graduate school, with no postdoctoral experience. During my first three years in Baltimore (1942–1945) I taught medical students in the mornings and worked in the National Research Council in Washington, D.C. in the afternoons. Both Army and Navy had deferred me from active service because of minor physical deficiencies and, to make some contribution to the war other than training medical students for the Armed Services, I joined the "Army of the Potomac" working in the National Research Council. At that time I was chagrined not to be in the South Pacific, but in retrospect I was lucky. After the war was over, there remained the rather considerable problem of reorienting my research efforts away from comparative anatomy to the developing area of neuroscience. Eight years after obtaining my Ph.D., my modest bibliography listed five papers in comparative anatomy, five in neuroanatomy, and one in neurophysiology.

I found two colleagues at Penn working on the anatomy and physiology of the spinal cord—William Chambers and John Liu—and with them pursued the study of the spinocerebellar tracts in the cat and monkey. This work led naturally to investigation of the structure and function of the cerebellum, and Bill Chambers and I collaborated on the problem intensely for the next five years. With him, I discovered the value and pleasure of a long-term collaboration with a gifted colleague and friend. By that time in the early 1950s, Walle Nauta had introduced the first of a series of superior silver techniques for staining degenerating axons, and Bill and I applied these to trace, in greater detail than had been possible in previous studies, the efferent projections from cerebellar cortex to the three deep paired nuclei, and from these nuclei to the brainstem and thalamus.

These anatomical studies in the cat expanded those done earlier in Norway by Jan Jansen and Alf Brodal using the Marchi method; this study had shown that the cerebellar outflow was organized into three zones. The medial cortical or vermal zone projected to the medial fastigial nuclei, the lateral cortex projected to the dentate nuclei, and the intermediate or paravernal cortex projected to the interpositus nuclei. Our research demonstrated that each fastigial nucleus projected bilaterally to the medullary and midbrain reticular formation and vestibular nuclei and to the thalamus, including ventral and ventrolateral nuclei. Each interpositus and dentate nucleus projected contralaterally and heavily to the red nucleus of the midbrain and to the ventral and ventrolateral nuclei of the thalamus. These anatomical studies were done with Donald Thomas and Donald Cohen, first-year medical students.

Bill Chambers and I were interested in working out the functions of these three systems, and we approached this problem by making specific lesions in cortical or nuclear zones and following the animals' deficits. In addition, we stimulated these zones electrically in intact and lesioned cats and after decerebration. The results indicated that vermal cortex and fastigial nuclei are involved in the control of gross postural tone, equilibrium, and locomotion of the entire body. The intermediate zone is involved only with skilled movements and tone of the ipsilateral limbs. The lateral zone (hemispheric cortex and dentate nuclei) is involved with spatially organized and skilled movements of ipsilateral limbs, but without regulation of posture and tone. All parts of the cerebellum exert influence via the thalamus on the motor cortex of the cerebrum. The functions of these zones were summarized by Sprague and Chambers in detail in 1959 after unilateral and bilateral lesions; deficits and recovery after cerebellectomy were studied by us over long periods of time.

Closely allied to the cerebellar research was our follow-up of the lesion studies of Magoun, Lindsley, and Moruzzi done at Northwestern; their important results had been obtained for the most part in acute animals or chronic animals of rather short-term survival. A significant conclusion of their work had sharply separated the function of the neural paths that ascended in the reticular core of the brainstem from those more peripheral sensory paths. They concluded that the latter, termed lemniscal systems, provided specific topographically organized sensory information to the forebrain; the reticular or extralemniscal path controlled wakefulness and sleep, arousal, alertness, and attention and many visceral functions.

We devised a battery of tests that were applied to cats for several months preoperatively and for long periods, up to two and a half years, after midbrain lesions. These lesions interrupted either the reticular core or the sensory systems that at the midbrain level included somatosensory, acoustic, and part of the visual sensory paths. Analysis of data obtained in this longitudinal study used electroencephalographic (EEG) recording and neurological and behavioral examinations; psychophysical and psychological testing; and, finally, anatomical evaluation of the lesions. Our results revealed a widespread spectrum of deficits in attentive, adaptive, and affective behavior after lesions that interrupted ascending sensory paths to the midbrain and forebrain as well as descending pathways from the cortex to the midbrain. The reticular lesions were followed by variable periods of somnolence with deficits in arousal, hypokinesis, catatonia, and spasticity; animals with such reticular lesions often showed considerable recovery with good attention to and localization of visual, acoustic, tactile, and nociceptive stimuli and full, often exaggerated, affective responses. This work provided a richer and more meaningful picture of the contribution of the sensory and reticular systems to the behavioral repertory of the animal than had previous studies using animals of short-term survival. The work was the result of collaboration over several years with Bill Chambers, Eliot Stellar, and John Liu and postdoctoral fellows Tom Meikle, Mel Levitt, and Ken Robson, who all contributed much to the rather arduous, but rewarding study (Sprague et al., 1961, 1963).

I found interesting the elegant physiological research on the spinal cord by David Lloyd and John Eccles, who differed in whether "direct" reciprocal inhibition by dorsal root 1a fibers on motoneurons was mono- or disynaptic. If the 1a inhibition was monosynaptic, then the axon terminals of the same cell that mediated both excitation and inhibition would be producing different transmitters at different terminals. This would be an important exception to the generally held "law" that a single neuron secreted a single transmitter. The pattern of degeneration in the spinal gray matter after section of dorsal spinal roots appeared to offer an anatomical solution to this controversy. I was invited by Dr. Lloyd to carry out some of these experiments in his laboratory at the Rockefeller Institute for Medical Research in New York City in the fall of 1955 during my sabbatical leave from the University of Pennsylvania. The second and third sacral segments of the cat spinal cord provided the necessary anatomical structure because these dorsal root fibers not only terminated ipsilaterally but also contralaterally. Ipsilaterally, degenerating fibers were found on cell bodies and dendrites of motoneurons controlling movements of the tail, but the contralateral fibers ended on dendrites only, suggesting that the reciprocal inhibition exerted contralaterally might be mediated monosynaptically by these axodendritic synapses (Sprague, 1958).

This hypothesis was put to the test by Karl Frank and myself (1959) using intracellular recordings. We found a difference in latency of 0.3 to

0.7 msec between ipsilateral excitatory postsynaptic potentials (EPSPs) and contralateral inhibitory postsynaptic potentials (IPSPs) in the same motoneuron. Because no adequate explanation could be found to account for this extra latency on the basis of monosynaptic connections, the presence of an interneuron in the direct inhibitory pathway was a definite possibility, confirming Eccles, Fatt, and Landgren (1956). A detailed study with Hongchien Ha of the terminal fields of dorsal root fibers in the cat spinal cord and of the dendritic organization of the motor nuclei was presented at a symposium held in Amsterdam and published in *Progress in Brain Research* in 1964. With this paper my active involvement with the spinal cord was over.

I must break at this point with a most important personal happening that began with the entrance of Dolores Joseph into my life. She had come to Penn from New York University to enter the graduate group in physiology, which required many of its students to take the introductory course in the nervous system. She was in my laboratory section, and after the course ended we became better acquainted as she visited my research lab to see animal experiments at first hand. One thing led to another. I found her marvelous company, and we were married in November of 1959 and recently celebrated our 37th wedding anniversary. She did not complete her Ph.D. but left the university and entered art school at the Philadelphia Museum of Art. She became an excellent graphic artist and her etchings and silk screens became well known in the Philadelphia art community.

To pick up the thread of the discussion of research, I noticed in analyzing the extralemniscal lesions in the midbrain, that there was always a wedge-shaped extension of the lesions below the superior colliculus into the lateral edge of the periaqueductal gray matter. This extension interrupted several afferent pathways into the deep layers of the colliculus and many efferent pathways from these same laminae, with cell loss in the middle and deep layers. Thus it was likely that the unexpected visual deficits found after lesions that severed the ascending lemniscal paths from spinal cord and brainstem might be due to involvement of the superior colliculi.

With Thomas Meikle, a postdoctoral fellow in my laboratory, I began a study of this fascinating and complex structure, the superior colliculi, in 1961, which would stimulate my interests up to the present, 35 years later. The results of our first step in this investigation (published in abstract form in 1962) were from unilateral ablation of the colliculus, which did not extend directly into the tegmental area destroyed by the lemniscal lesions as mentioned above. We found two major behavioral deficits—complete neglect of visual stimuli in the contralateral hemifield, and a motor asymmetry consisting of ipsilesional forced circling, with compulsive responses to ipsilateral stimuli. Both sensory and motor deficits lessened within a few weeks after collicular ablation, but persisted permanently in the form of contralateral extinction to bilateral stimulation and of heightened ipsilateral responses.

This research on the neurological effects of unilateral and bilateral aspiration of the colliculi in the cat was published in full in 1965 with Meikle. The work postulated a new concept that visual attention was a tectal function in addition to the classically accepted control of head and eyes in orienting responses. I later related this attentional dysfunction of the colliculus to deficits in discrimination tasks after cortical lesions.

From 1962 on, my research was involved with the central visual system—anatomy, physiology, and discriminative behavior. Ophthalmologist Alan Laties and I restudied the projection of the retina onto the visual centers in the brain of the cat, using the Nauta silver technique after small retinal lesions made either by photocoagulator or laser. This approach made possible a lesion of a limited number of ganglion cells in an area of retina and the subsequent degeneration of their axons to midbrain and thalamus provided a detailed picture of the organization of this part of the central visual system not previously available. Our study coincided with a widespread, surging interest among neuroscientists in the organization of the visual system. In carrying out this particular study we were indebted to ongoing work of Peter Bishop, Jonathan Stone, and William Hayhow in Australia; and of Torsten Wiesel and David Hubel at Harvard.

Meikle and I wrote a review on the anatomical organization of the visual pathways in the cat as it was understood in 1964. Our research on visually guided behavior after collicular lesions, which resulted in profound sensory and emotional neglect and inattention, led to the question of to what extent these deficits were related to or dependent on the visual cortex. At that time, only visual areas 17, 18, and 19 had been defined, and lesions of these cortices indeed resulted in contralateral neglect which, however, showed considerable recovery. If this cortical lesion was followed by collicular lesion on the same side of the brain, the recovery following the former was abolished and the resulting loss of orienting was permanent.

So clearly, we discovered, there is marked interaction between cortical and midbrain levels in visual orienting. Only when the cortical lesions were much larger and included all of what is now recognized as visual sensory and association cortex, could the deficit be termed hemianopia with total and enduring loss of orienting. However, an astonishing recovery of orienting followed subsequent ablation of the colliculus on the opposite side of the brain (Sprague, 1966). This dramatic result, later called the Sprague effect, forced a new concept of brain function: the paired orienting centers in the superior colliculi have a reciprocal inhibitory mechanism that suppresses activity in one colliculus when the other is directing orienting responses toward contralateral space. This inhibitory mechanism is unbalanced by the effects of the cortical lesion so that the colliculus ipsilateral to the lesion receives a chronic influx of inhibition, resulting in lack of orienting contralaterally and the presence of visual neglect of contralateral space. This idea was supported by cutting the collicular commissure, which also restored orienting. These experiments were exciting for me because in them I had discovered a previously unknown neural mechanism that controlled visuomotor orienting and orienting of attention through interaction between cortex and midbrain. Discovery of a new system is a rare occurrence and formed a peak in my career.

Later experiments with Steve Wallace and Alan Rosenquist (1989, 1990) made a major advance in explaining this phenomenon by showing that the "cross-tectal" inhibition originated in the substantia nigra, and was mediated by the nigrotectal tract, the axons of which passed in the tectal commissure. In other words, it was not a tecto-tectal system as I originally thought. Important in our decision to initiate research on the substantia nigra was the elegant physiological exploration of that structure by Hikosaka and Robert Wurtz (1983) in the macaque and the anatomical studies of nigrotectal pathways in several species, especially the seminal work of Ann Graybiel (1978) in the cat. Linking the Sprague effect with the substantia nigra brought it into a larger neural mechanism controlling visual orienting that was being worked out in several laboratories in the hamster, rat, cat, and macaque.

The mechanism appears to work as follows. Visual input from the retina reaches extrastriate cortex, which projects to the striatum and there activates a striatonigral path (using glutamate), which terminates in the substantia nigra, pars reticulata. This system (using GABA) exerts a controlling influence on nigral neurons which project to the superior colliculus by way of a nigrotectal tract. The nigrotectal path is a tonically active GABAergic tract that suppresses firing of the orienting neurons in the colliculus; these nigral neurons are phasically inhibited by GABAergic activity in the striatonigral path, thus releasing the colliculus to trigger contralateral orienting responses.

About this time (1965) I asked for a sabbatical leave of absence from the university and spent most of 1966 in the Institute of Physiology in Pisa, Italy. The director, Giuseppe Moruzzi, had worked with Magoun at Northwestern in 1949 to 1950. The sabbatical was a marvelous choice for both my wife and me; she continued her art work making etchings and wood blocks of the beautiful parks, old buildings, and countryside of Tuscany. I was given a small office on the top floor of the institute, overlooking a garden of cypresses bounded by the medieval city wall, miles beyond which rose the peaks of the Appenines. I found stimulating and productive collaboration with three younger members of the institute.

Giovanni Berlucchi and I began training cats in a series of visual discriminations—brightness and shapes—to learn to what extent they depended on processing in the superior colliculi and in different visual cortical areas (Sprague et al., 1970; Berlucchi et al., 1972). Animals with optic chiasm and various commissures split mid-sagitally were used to isolate the input from each eye to the corresponding side of the brain. Lesions were then placed on one side of the brain in the colliculus and/or cortex. Training was carried out monocularly and performance could be compared using the eye on the lesion side of the brain with that obtained using the eye on the unoperated side; thus both experiment and control are contained within each animal. Marked deficits in learning form discriminations follow unilateral lesions in the superior colliculus and pretectum, compared to the unoperated side. When the discrimination tests were trained preoperatively, no loss in retention after collicular lesions was found. Additional removal of cortical area 17 did not worsen the deficit. The shape discriminations were degraded by the collicular lesions, probably because of the consequent defects in visuomotor orienting and in shifts of visual attention.

Other experiments while in Italy, with Lorenzo Marchiafava and Giacomo Rizzolatti, were among the first to record single unit activity in the superior colliculus of mammals. This study was unique in using alert, unanesthetized cats rendered pain-free by mid-pontine section. All three of these men became close friends and I continued research collaboration with Berlucchi for many years thereafter. We returned to Pisa numerous times—indeed those visits to that beautiful country were among the highlights of both my personal and my scientific life.

Development of the Department of Anatomy

Shortly after returning from Italy in 1966 I was nominated to fill the chair of anatomy at the University of Pennsylvania, which had been vacated by the retirement of Louis Flexner. Up to that point I had avoided major administrative positions, but this was a department that Louis had built to preeminence and one that had supported and nurtured me in more ways than I can mention. I had also played a significant role in 1953 to 1954 in organizing an Institute of Neurological Sciences (INS) that provided the nucleus for the development of a large and productive neuroscience community at Penn. The concept and initiation of INS was the brainchild of Louis Flexner and coincided with the great upsurge of interest in the nervous system in this country and abroad. The influence of the institute brought many distinguished faculty to Penn and regularly attracted some of the brightest graduate students and postdoctoral fellows.

I became director of the institute in 1973 and served in that capacity until 1980. Throughout the directorships of Flexner, Eliot Stellar, and myself (1953–1980) INS was a loosely organized institute supported by NIH, Ford, and Grant Foundations and the University of Pennsylvania. The institute's academic focus was to foster multidisciplinary research and training, university-wide. The institute maintained skilled personnel in the machine, electronic, art, and photography shops that members of INS used for themselves and for their graduate students and postdoctoral fellows. When I was succeeded as director by Robert Barchi, the neuroscience community in this country had grown in size and influence to such an extent that it was time to restructure the institute with allocation of space and a Ph.D. graduate program with a separate budget. A large grant from David Mahoney established a named chair for the director and support of the programs. INS thus became known as the Mahoney Institute of Neurological Sciences. These timely changes were soon followed by the establishment of a department of neuroscience in the school of medicine, with Bob Barchi as chair.

All these factors led me to accept the chair for a term of nine years, from 1967 to 1976. At that time, research in the department of anatomy had three major areas—cell and tissue differentiation, neurochemistry and ultrastructure, and neuroscience. My colleague Bill Chambers and I organized an introduction to the nervous system course, an interdisciplinary neuroscience course which was a meld of anatomy and physiology and was pitched at a level to educate graduate students and fellows in the institute and first-year medical students. The position of the course in the medical curriculum was such that it was followed by neuropathology and clinical neurology, a sequence that directed many students toward a future in neurology.

One of the necessary but onerous responsibilities of the chair was to obtain funds from the university and various foundations for improvements in the department. Anatomy was housed in a wing of the medical school, which had lain untouched since 1926 to 1928 when the wing was built. Fundraising was certainly not a joy; nevertheless we were successful in obtaining the appropriate money and the physical facilities of the department and its appearance were considerably improved. On the other side of the coin of being chairman, however, was the pleasant and stimulating experience of appointing new young faculty to replace those who were retiring. This turnover provided me the chance to create a small group in the department working on the visual system—Paul Liebman, Peter Sterling, Alan Rosenquist, and Larry Palmer. The group acted as a focus with others in psychology and ophthalmology to obtained funds from the National Eye Institute (of NIH) to form a Vision Center to facilitate faculty research and obtain a training grant to attract and support graduate students. These efforts continue to the present day and are part of the research and educational program of INS.

The demands of the department and the institute, as well as a full teaching load, cut deeply into the time I could devote to research, despite allocating at least two hours every afternoon to go to the laboratory and participate directly in the occupation that had attracted me to academic life in the first place. Nevertheless, after six years of administrative responsibilities I began to wonder whether my capacity to "think" creatively about research was still intact, and I asked for a sabbatical away from Penn to find out. My close friend and colleague, Bill Chambers, agreed to look after the shop while I was away, so I applied for and received a Josiah Macy Foundation Faculty Award to help fund a leave of absence in Pisa in 1974 to 1975. Giovanni Berlucchi had maintained close contact with me since my sabbatical of 1966, and I was received again with warm hospitality from him and Giuseppe Moruzzi.

As before, the experience in Italy was both restorative and productive. Robert Doty's work in 1971 had shown clearly that cats had impressive visual abilities, including pattern discrimination, after removal of area 17. Berlucchi and I pursued this seminal finding, beginning in 1971 and 1972. We expanded Doty's finding by making our lesion include not only striate cortex (area 17), but also adjacent area 18; these two primary areas have many similarities in their parallel thalamic connections and in the responses of their constituent neurons. Our approach was to train cats in a number of discriminations—luminance (light-dark), patterns (gratings), and forms—preoperatively and again after lesions that removed areas 17 and 18. These animals retained criterion performance immediately, with perfect retention, which indicated that these suprathreshold discriminations do not require preoperative processing in 17–18. In contrast, after cortical lesions that left 17–18 intact, cats showed deficits in the pattern and form tasks, which required retraining to reach criterion. These results dealt a serious blow to the concept of serial cortical processing in pattern and form perception beginning with striate cortex (Berlucchi et al., 1981).

At least two major questions arise from these findings: what pathways are used to reach other cortical areas in the absence of areas 17 and 18, and what functions do depend on 17 and 18? The first question can be answered by the anatomy of the cat's visual system reviewed by Rosenquist (1985). In contrast to the monkey, the lateral geniculate in cats projects not only to areas 17 and 18 but also to many parts of the extrastriate cortex, which also receive projections from the superior colliculus and pulvinar (the second visual system). Thus, several parallel paths exist between the thalamus and the visual cortices in the cat. It would appear that the suprathreshold or multicued stimuli can be perceived and discriminated by extrastriate cortex without using the geniculocortical path to areas 17 and 18.

Howard Hughes, then a postdoctoral fellow, and I investigated the cortical mechanisms for global and local analysis of visual space (1986). We used as stimuli orderly arrays of identical elements (dots) whose pattern could be perceived and discriminated only through grouping of the units by spatial proximity (i.e., global structure). This function using basic pattern-recognizing components of the visual system was not affected by removal of areas 17–18. Similar results were obtained when small line-segments were used; deficits occurred only when high resolution was required (acuity).

The answer to the second question has been partly revealed in a collaborative study with Mark Berkley (department of psychology, Florida State University) in which cats were trained in a totally different way in threshold discriminations of elementary visual stimuli using only single cues—grating acuity, contrast sensitivity, vernier alignment, or line orientation. The thresholds of all of these difficult tasks were elevated after 17–18 lesions, the vernier test was the most severely affected; grating acuity was elevated only 25 to 30 percent. Multicued form discriminations similar to those described above were either normal or somewhat slowed postoperatively (Berkley and Sprague, 1979). Much of my subsequent research done in collaboration with Mark, including detailed studies of the effects of striate or extrastriate lesions on thresholds of contrast sensitivity and vernier alignment in the cat, has remained unpublished because of his untimely death in 1995 from pancreatic cancer.

Berlucchi and I also studied the role of different cortical areas in the interhemispheric transfer of form discriminations in the cat (Berlucchi et al., 1979). These experiments required splitting the optic chiasm to limit the direct input from each eye to the homolateral brain hemisphere, followed by unilateral lesions in either the commissural parts of areas 17, 18, and 19, or the adjacent suprasylvian cortex (areas 7, 21a, part of 19). Transfer of the form discriminations from the intact to the lesioned hemisphere was blocked by the second lesion, but was present after the first lesion. Thus, we found that this important function of interhemisphere communication in the brain was mediated by extrastriate cortex and did not depend on processing in areas 17 and 18.

I designed a study that used the findings of this research and those of the Sprague effect described earlier. Again, the cats had optic chiasm split and a unilateral lesion placed in the suprasylvian cortex. The animals were taught gratings and form discriminations using the eye connected to the intact hemisphere; transfer of the form to the lesioned hemisphere was lacking (confirming Berlucchi et al., 1979), but transfer of the gratings was excellent. Stimuli with global repetitive features (gratings) apparently can be discriminated using preattentive vision, but stimuli with local features (forms) that require serial exploration using focal vision and attention were not transferred. The next step was section of the tectal commissure and training in new gratings and forms. This commissurotomy, which restored orienting in the Sprague effect, also restored transfer of form discrimination. I hypothesized that the perceptual deficit on the lesioned side of the brain was due to poor spatial attention, and its restoration after midbrain lesion was due to improved function of those collicular cells that mediate orienting of attention (Sprague, 1991).

These interesting results provided evidence of an additional role of the midbrain in a function (form discrimination) that is widely considered wholly cortical, and as such sheds light on the neural mechanisms underlying visual perception. I repeated the experiment with the second lesion in the substantia nigra, pars reticulata (rather than the tectal commissure) that had restored orienting (Wallace et al., 1990), and obtained the same restoration of transfer of form discrimination. My application in 1992 to NIH for a research grant to follow up these findings was not, however, funded—my first failure since 1951. This was a blow because I felt these were original and significant findings, and despite the generosity of my colleague Alan Rosenquist in the use of his facilities, I was no longer able to do experimental research at the University of Pennsylvania after age 76.

Research in Belgium

I frequently attended the annual meeting of the Association for Research in Vision and Ophthalmology (ARVO), in Sarasota, Florida, and on several occasions my son Jim, a pediatric ophthalmologist, and I attended together. It was there that I met and began collaborating with Mark Berkley in 1972 and it was with Jim and Mark that I celebrated my election to the National Academy of Sciences in 1983. I also met Guy Orban at the ARVO meeting in 1983. Guy had organized a laboratory of neurophysiology and behavior at the University of Leuven, Belgium, and with his colleague Erik Vandenbussche was training cats in visual discrimination tasks using the testing methods devised by Berkley at Florida State.

The Belgian laboratory seemed to me the ideal place to study visual behavior in a way I had long dreamed of using anatomy, physiology, and carefully controlled paradigms of discrimination. From 1984 to 1995, Guy, Erik, Peter DeWeerd, Balázs Gulyás, Steven Raiguel, and I pursued an active collaboration that took me to Leuven once or twice a year. The overall plan was a psychophysical study—to train cats to discriminate single-oriented lines or bars, a simple stimulus considered a basic element, or primitive, of visual perception, upon which the brain composed more complex forms. Once stable thresholds were obtained, using parameters of length, width, and contrast comprising optimal visibility, lesions were made in specific cortical areas. These areas in the cat had been clearly defined by histological structure and connectivity, and by single neuron responses. We showed that the perception and discrimination of this visual primitive was processed primarily in visual cortex 17 and 18, that threshold was not determined by those neurons most tightly tuned for orientation, and that the task was achieved by population processing, spread across two cortical areas. Both areas were necessary. When lesions removed 17 and spared 18, or removed 18 sparing 17, no deficit in threshold discrimination occurred unless contrast was greatly reduced or bar length and width were diminished.

The next tasks used the same primitive element (oriented bars) but were more complex, consisting of illusory bar contours and textures composed of line segments. In contrast to the results obtained using single bars, both of these discriminations required processing in two cortical areas: 17–18, in which primary filtering took place, and extrastriate cortex, in which an additional step of the discrimination occurred. These findings require a modification of the widely accepted hypothesis that texture segregation is solely a function of early vision, that is, primary visual areas. It is important to point out that these results were derived from deficits in discriminative behavior performed by the animals and were not extrapolated from single-unit activity recorded in the cortical areas.

On all of those visits to Belgium I was housed in a beautiful facility (Begijnhof) owned by the University of Leuven. The renovated hospice had until recently been occupied by the Beguines, a semireligious order of women. Living in that remnant of old Flanders, in addition to the friendship and warm hospitality of my colleagues, made that final scientific collaboration not only productive but a distinct pleasure.

Winding down an active life of research is not an easy adaptation to make, but one that must be faced by every investigator. Certainly, I have had an exciting and rewarding life of discovery, and as a professor I had the unique privilege of controlling the use of much of my time for scholarship and teaching. Over a span of 50 years many wonderful colleagues and stimulating students added to the richness of my life. A large number of others—postdoctoral fellows, technicians, and secretarial staff—contributed in numerous ways to create a harmonious research environment in the department over the years. Few of them have been specifically mentioned here because a proper account of what they did and what they are doing now would not be possible in the space allowed. Some mention is essential, however, of colleagues other than those mentioned in the text, with whom I collaborated from Penn (Alan Epstein, Adrian Morrison, Larry Palmer, Murray Sherman, Howard Hughes, Louis Flexner, Alan Church), from Japan (Kahee Niimi, Takeshi Kaneseki, Syosuke Kawamura), from England (Ray Lund), from Italy (Mirko Carreras, Franco Lepore, Antonella Antonini), from France (J. Flandrin, J. Courjon), and from Duke University (Irving Diamond).

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