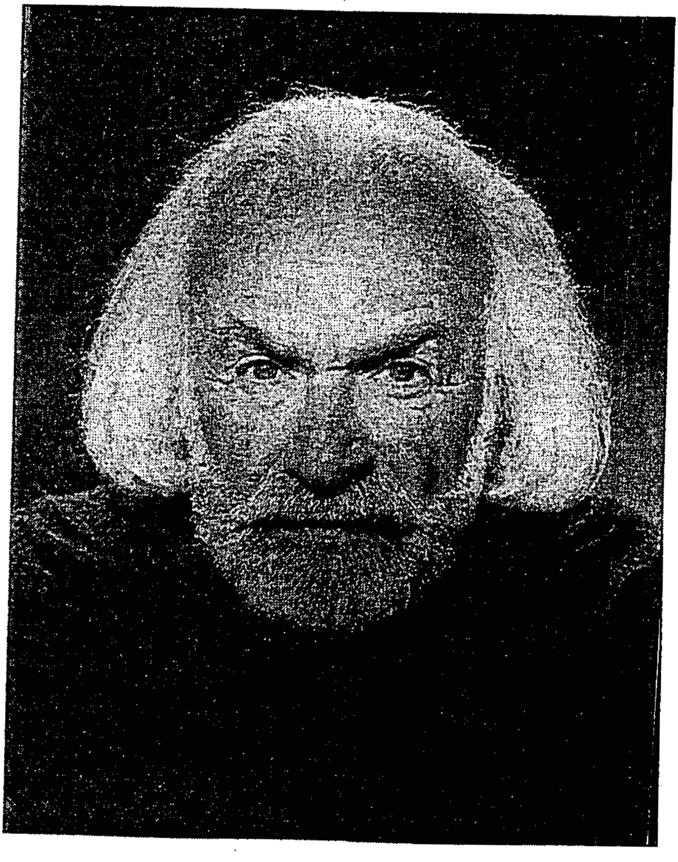
THE HISTORY OF NEUROSCIENCE T-210
IN AUTOBIOGRAPHY
@ 1998

Karl H Pribram



Karl H. Pribram

Born:

Vienna, Austria
February 25, 1919

Education:

University of Chicago, B.S. (1938)
University of Chicago, M.D. (1941)

Appointments:

Yerkes Laboratories of Primate Biology (1946)
Yale University (1948)
Center for Advanced Studies, Stanford University (1958)
Stanford University (1959)
Professor Emeritus, Stanford University (1989)
Distinguished Professor, Radford University (1989)

Honors and Awards (Selected):

NIH Lifetime Research Career Award (1962)
International Neuropsychological Society (President, 1967)
American Psychological Association
Division of Physiological and Comparative Psychology (President, 1967–1968)
Division of Theological and Philosophical Psychology (President, 1979–1980)
Menfred Sakel Award, Society for Biological Psychiatry (197(
Realia Honor, Institute for Advanced Philosophic Research (1986)
Outstanding Contributions Award, American Board of Medical Psychotherapists (1990)
Honorary Ph.D. in Psychology, University of Montreal, Canada (1992)
Neural Network Leadership Award, International Neural Network Society (1994)
Honorary Ph.D. in Neuroscience, University of Bremen, Germany (1996)

Karl Pribram was trained as a neurosurgeon and then devoted his career to elucidating the structure and function of the cerebral cortex, relating human clinical experience to his neurophysiological and neurobehavioral studies on nonhuman primates. He discovered the visual functions of the temporal lobe and the relationship of the anterior frontal cortex to the limbic system. His theoretical writings include the topics of perception, emotion, memory, and planning.

The History of Neuroscience in Autobiography, Volume 2

Karl H. Pribram

Preamble

Summer 1918. The head of the bacterological services of the Austrian Army and a Dutch Red Cross nurse were swimming nude in the Danube somewhere between Vienna and Budapest. Some pigs pulled their clothes from the bushes; retrieval entailed a considerable chase. The child conceived on that occasion was often accused of "pigging out," and his manners were attributed to that chase by the Danube.

February 25, 1919. I was born in Vienna, Austria at 8:00 PM encased in the amniotic sac—taken by my mother to be a most propitious beginning.

Autumn 1923. I set off to a Kinderheim in Gstaadt, Switzerland to protect me and my mother from a stormy relationship.

Summer 1924. Ernest August Pribram, my father, went to America to save me from growing up in a Europe whose future he saw as torn with political turmoil.

Autumn 1926. I joined my mother in Vienna and finished second grade in Catholic school.

Summer 1927. I went to a farm in Geneva, and learned French.

Autumn 1927. I and my mother arrived in the United States and my reunited family settled in Chicago.

The Scientist as a Young Man

It was Labor Day, 1932, when my father put me on a train in Chicago to head for Culver Military Academy near Fort Wayne, Indiana. I had set my sights on going to Culver once I had heard about it from my dentist, a gentle, wonderful man who saved my adolescent cavitous molars which, over the next 70 years, I have had to protect from the more rapacious of the dental profession. Tonsils I still also own, despite the medical fad that no one should reach adulthood with such natural protective devices in place. In each case battles with established practice had to be engaged and each time I won: good training for a career in research.

My attraction to Culver was simple: horses. My father could not afford the additional fees to allow me to become a member of the famed Black Horse Troop which was sent to Washington for each presidential inauguration. But the field artillery was still horse-drawn in that long-ago time when the caissons and French 75's went rolling along.

Before going to Culver, I had a dismal 6-year record in Chicago's public schools, being repeatedly expelled for fighting with bullies who picked on everyone, or from Catholic schools for asking the nuns simple questions such as how God could be both all good and all just. What I saw around me during the depression of the 1930s didn't fit the picture of God that those good women tried to convey. When told to have faith, I lost all faith in what the hooded ladies had to say, and expressed my opinion in no uncertain terms. Over and over. My father had Jesuit friends who tried to reason with me, but as I would not accept their premises, they taught me only that reason can be totally reasonable and that what one needs to ascertain truth or falsity is to search for the premises, the axioms, from which the reasoning takes off.

The public school teachers were being paid with script, so during the last year in elementary school, I took over when teachers were absent—which was often. I figured that each of the students had fathers and that the fathers worked and could tell their children what they did. So, each pupil came to class prepared to tell us about his father's occupation, and what it entailed both intellectually and in practice. We were all fascinated and much preferred our system to the substitute teachers that were foisted upon us. The administration was not altogether pleased.

My father believed that a military environment was just what his son needed. As we said good-bye I hugged him (he didn't like hugging much) and I said that I was proud to be admitted to such an excellent school. My father replied, "Be sure to conduct yourself in such a manner that *Culver will be proud of you* when you leave." Those parting words stayed with me for the rest of my life.

During my senior year science was to be taught for the first time in the history of the Academy, one course in physics and another in chemistry. I immediately registered for both. Although the two courses were not to be taken simultaneously, I pleaded that as a senior, I had been prevented from having an adequate science education. I took the courses and received honors in both, as well as in history and in English literature. Each required a special project that went beyond what had been covered in class. Only one student was to receive honors in a particular subject and each student was eligible to receive honors in only one subject. Fortunately, only the competitive "one subject, one student" part had been made explicit and my projects were completed at graduation when the "one student, only one honor" became elevated to everyone's consciousness, as we would say today. I graduated with all four honors.

The decision as to which university to attend was a difficult one. I had been accepted at Oxford, Harvard, and the University of Chicago, but two related factors favored Chicago: (1) I had decided to study biology and medicine, and my father, an eminent biologist (bacteriologist, pathologist, and immunologist) with whom I hardly ever had interacted, was there; and (2) though a decision for Harvard or Oxford would have carried more prestige, in 1936, Chicago under Maynard Hutchins was more intellectually alive and innovative. So Chicago it was.

My father and I met every Sunday. He portrayed the facts and ideas important to physiology and immunology to me in unforgettable fashion. Just recently I joined in writing two papers that deal with the possibility of superconductivity in dendrite membranes because the formulations are consonant with these early tuitions.

Five years later, in 1941, I received my M.D. According to Hutchins, it was not really considered a doctorate, rather simply a permit to practice a trade. The Chicago colors were withheld from the gowns worn to the graduation ceremonies by the incipient medics.

I had done well at university. I loved my undergraduate courses in history and economics, physics and chemistry, and biological discovery, made straight A's, and took comprehensive exams in stride, often without having attended classes (an O.K. under Hutchins). I took copious notes. The endocrines and the brain were especially intriguing because they served as integrators of the functions of the body. Viewing myself as a potential explorer (I had steeped myself in Amundsen and Admiral Byrd while in my preteens and in Paul DeKruif's *The Microbe Hunters* somewhat later) I saw endocrinology and biochemistry at one extreme—where too much research had already been done to consider them virgin fields—and brain physiology at the other extreme, where too few techniques seemed to be available for fruitful exploration.

All this changed once I engaged the medical clinical curriculum. Seeing patients was wonderfully satisfying from the human and diagnostic standpoint, but the lectures and laboratory sessions were incredibly dull. When I asked questions of "how" or "how come," I was summarily informed that the answer was, "because I say so." I was challenging authority and that was a no-no. Catholic school all over again. This in Hutchins's Chicago? Obviously, Hutchins was correct in his evaluation: medical school was a trade school.

In one class we were to type pneumonias. Thirty-six types were known and during the course of the class, two more were discovered. Sulfanomides had also just been discovered and were on the market. Was it really necessary to learn the typing procedure? The class decided: No. The professor declared: Yes. The class walked out and got away with it. Some of Hutchins's influence permeated even into the depths of the medical establishment. Over the years medical education has, to some extent, remedied this intolerable teaching situation, but one still reads articles by students, interns, and residents who tell a story that is not too different from the one I experienced.

The only way to make the study of medicine outside of the clinic interesting was to attach oneself to one or another of the professors and aid them in their research. One got to know them, the puzzles they were trying to solve, and the broader biological perspective within which medical care operates. I decided to apprentice in the department of physiology. "Ajax" Carlson was its head. He insisted that every student in the department repeat the historically important experiments that led to current views of how the human body functioned. This dictum had an enormous influence on my research career. Over the years, many experiments done in my laboratories were initiated to see for ourselves the details of currently important findings that can only come from first-hand experience in generating data. Thus, when confronted in a discussion of ideas, I would always be able to call up Carlson's other dictum: "Wass iss die effidence?" And, to the extent possible, I would have that evidence first-hand.

I was privy to exploring with my professors the deterioration of the activity of vitamin C in orange juice with storage; the effects in dogs of denervation of the kidneys, and a project I devised and performed myself: How much blood flow does the liver need before deficiencies in function would show up on laboratory tests? I constricted the flow of blood to the liver by placing adjustable clamps on the hepatic artery and the vena cava. The clamps had been devised by Goldblatt to do just this sort of study on the kidneys. Goldblatt found that impairing kidney blood flow produced persistently elevated blood pressure. The liver experiments had no such dramatic effects. Turning the screws on the Goldblatt clamps had no effect whatsoever on the then-available tests of liver function—until the last one-eighth turn of either screw (in the clamp on the vena cava or the one on the hepatic artery). With this last turn, the animal, which had to all intents been perfectly normal for weeks, died. Any small aggregate of surviving liver cells could function in lieu of the entire liver, up to a point.

It was a lesson I remembered when, much later, I learned that memory storage in the brain shows considerable resistance to degradation when large extents of that organ are damaged.

Most exciting of these forays into research, however, was an exposure to the work being done in Ralph Gerard's laboratory. On one occasion, an electrical record from a brain site energized a loudspeaker. Whenever a loud clap was produced near the cat from which the record was being taken, the loudspeaker would give out a distinct sound. A tap to the cat's paw also produced a sharp sound on the loudspeaker. Brain electrical activity reflected the sensory input! A discussion ensued: why couldn't these results be shown outside the laboratory? Electrocardiograms were being made daily, why not electroencephalograms (EEGs)? The answer was that the electrical changes produced by the brain were several magnitudes smaller than those produced by the heart.

That evening, across the table from me sat Frank Offner, a student engineer who became intrigued by the problem when I told him what I had seen. He stated that the current lack of sufficient amplification of the signal with respect to the noise of the system should not be insurmountable. I introduced Offner to Gerard. Frank Offner spent his life making and marketing EEG machines, the hard-copy electroencephalograms we sought that evening at dinner. It was the first time I realized how many contributions to neurobehavioral science could be made in informal settings far removed from the laboratory. There were to be many, many more.

Ralph Gerard was to play a most significant part in my education. Gerard was an incisive thinker and a brilliant teacher. Whenever sloppy reasoning went on in the classroom he propelled a piece of chalk at the perpetrator. On one such occasion, I was the target: my thinking had been teleological, a process forbidden in Gerard's neurophysiology. Many years later, neurophysiologists became aware of the ubiquitous presence of feedback and feedforward processes in the nervous system. I laughed privately at my former master and always cocksure friend. "Ha ha, how wrong you were in your certainty," I exclaimed as I was composing *Languages of the Brain.*

I have spent many hours in the classroom pointing out how our ideas of the functions of the brain have evolved, and that even what I have written and taught has become obsolete. I am not sure that my way of teaching is better than Gerard's. Perhaps uncertainty is too unsettling to a student. Let students be misled and find out for themselves, allowing them to experience the glee of having the "professor" shown to be wrong.

Of course I didn't always wait until later to challenge my professor. On one occasion Gerard was providing the class with the criteria for classifying mammals. Among these was hair. I stroked my long dense locks and asked: "Really, do *all* mammals have hair?" The class roared. Gerard was as bald as Yul Brynner in "The King and I."

For me, the high point of Gerard's classes came at the time of a final exam in an advanced course on neurophysiology. Gerard asked only one question: Discuss the organization of the nervous system. Fortunately for me, John Fulton's classic *Physiology of the Nervous System* had just arrived at the university bookstore the weekend before the exam. In preparation, I had purchased a copy. The book was so fascinating that I could not put it down and spent the entire weekend reading, letting go the rest of my studies and preparation for finals. On Gerard's exam I filled eight blue books, writing as fast as writing could be accomplished. Gerard stated it was the very best he had ever received; how had I achieved such comprehensive knowledge and superb organization? I told Gerard of Fulton's book. Fortunately, Gerard had not as yet seen it; the posing of his exam question was not related to the publication.

The first half of Fulton's *Physiology of the Nervous System* was devoted to sensory receptors, motor units, peripheral nerves, spinal cord, and brain stem. Microanatomy was presented with appropriate pictures. The second half of the book did the same for the brain's cortex and the fiber system coursing to and from it and detailed the discovery of the functions of the occipital (rear) lobes of the brain's hemispheres. In a similar fashion, Fulton reviewed the discovery of the connections of the parietal lobe to somatic sensation and the temporal lobe to hearing. Nothing as yet was known of the functions of the inferior part of this lobe. This was to be my contribution during the first years of work with Fulton.

The most fascinating and important story for me, though I didn't realize it at the time, was composed by the results of damage to the frontal lobes of the brain. Fulton's work had led to the procedure of frontal leukotomy, or lobotomy, as it was commonly known. Severing the fibers connecting the frontal lobes from structures in the brain stem was shown, on occasion, to produce marked changes in personality. What caused these changes was not known. After I had completed my training in neurosurgery (with Paul Bucy, Eric Oddberg, Percival Bailey and Warren McCullock in Chicago, Illinois; Eustace Simmes in Memphis, Tennessee; and Lyerly in Jacksonville, Florida), Fulton asked me to join him in finding out just what they might be. But I am ahead of the story.

Another aspect of neurophysiology that I learned from Gerard and from Fulton's book was that receptor-initiated signals course to the spinal cord via nerves that reach it through a "root" that is separate from the one leaving the cord to reach muscles. Experiments by Charles Bell in England and François Magendie in France had shown that sectioning of the entering root left the animal without sensation while its movements remained intact. The reverse was true of the other, the outgoing root. Until these experiments were completed, no one knew which root provided the input and which the output. The results of the experiment were heralded as a "law" and were the basis for conceiving the basic unit of nervous activity as a reflex arc.

Reflex arcs are segregated in segments which represent the fact that the composition of our bodies is much like that of earthworms. Each segment of the spinal cord is encapsulated by a vertebra. The vertebrae are held together by sheaths which contain disc-shaped cartilaginous cushions. When the sheaths rupture the cartilage oozes out to press on the nerve roots, causing pain. When the compressed nerve roots carry signals from the back of the leg, the patient experiences sciatica. Much of the ordinary practice of neurosurgery is made up of removing such ruptured discs.

Many years later, just before joining Fulton in his laboratory at Yale University in 1948, one of the last major human surgical operations I performed was the removal of such a disc. I had recently read of an innovative technique, by which the operation was done with the patient lying on his side, eliminating pressure on his abdominal blood vessels and thus minimizing bleeding at the operative site. I was able to remove the disc before the operating room nurse had fully completed setting up all the gear we usually needed, and performed the entire procedure in less than 20 minutes. The patient was eating steak a few hours later and had no recurrence of his problem.

However, in all his discussion of reflexes, Fulton did not mention a major component of the output root of the reflex: one-third of the nerves composing this root end in the receptors of muscles. Thus muscle receptor activity is regulated not only by the stretching of the muscle but by signals coming to the receptor from the spinal cord. The spinal cord signals are in turn controlled by signals coming from the brain. Although known to exist previously, the importance of these receptor regulating nerves came into focus in the 1950s through the work of John Eccles and Stephen Kuffler. They investigated the effects of stimulating the nerves going to the receptors after having removed the functions that make muscles contract.

The "law of Bell and Magendie" was, after all, not a law. The reflex arc is not an arc but a mechanism akin to a thermostat that can be set to a particular value which determines the operation (the on's and the off's) of the system. Soon other receptors were found to be regulated in a similar fashion. Years later, Spinelli and I would devote a decade to showing that retinal processes were subject to such central control. In 1960 George Miller, Eugene Galanter, and I wrote a book (*Plans and the Structure of Behavior*) in which we detailed the import of the new neurology and moved psychology from stimulus–response, reflex-arc behaviorism to a cognitive science which paid heed to the brain's control over its own input from the senses.

In 1949 John Fulton presented me with the third edition of his book inscribed, "In warm appreciation. . . ." My main contribution to this edition was to rewrite the chapter on the brain's control over the autonomic nervous system. The autonomic system is called this because it regulates the functions of the viscera which, for the most part, take care of their own process and function automatically without our awareness or conscious intervention. However, I had by then established that the brain's cortex had an input to the hypothalamus of the brainstem which, in Fulton's earlier editions, was called the head ganglion of the autonomic system. Fulton himself had obtained, with Margaret Kennard, results that indicated the possible operation of such cortical control and in fact gave me my appointment at Yale, in part, because of my findings. But I am again getting way ahead of the story as it has unfolded over the years.

Gerard's lectures and laboratory courses with the climactic final exam had me hooked. The brain was to be the continent I was to explore. Many years later, Paul MacLean inscribed a translation (for which he was responsible) of a book written by Ramon y Cajal: "To Karl, Magellan of the Brain." I was delighted with his insight as to my motivation in choosing a research career.

Over these years, Gerard became a close friend, referred to as *Poppa Ralph,* because when my father was killed driving an auto in which my bride and I were passengers, Gerard telegraphed his readiness to fetch us from Montana where the accident had occurred. The Chicago experience was thus a warm and personal one as well as an intellectual feast.

World War II came as expected and the necessities demanded graduation, internship, and residencies. I passed up the opportunity to receive a Ph.D. in physiology although I had passed all the necessary examinations. This was no time to pursue the basic research necessary to finish a thesis. My life as an enthusiastic, unorthodox, and brash young man had to give way to life among medical men, those arch conservatives who threw *Semmelweiss* out of their profession for showing that they were infecting mothers in the hospital during childbirth and put Pasteur temporarily into a jail for administering lockjaw vaccine to a boy who had been bitten by a rabid dog.

What sustained me during those years (1941–1948) of the practice of medicine and surgery were the rewarding experiences with patients which made up the practice and the consuming interest in finding out how the brain works which was fuelled by the signs and symptoms portrayed by these patients. During my externships and internship I was fortunate to have as a colleague, my complement, Joseph Ranzahoff: he abhorred neurology and brain surgery but loved the smelly nether regions of abdominal surgery. Trades of patients were the order of the day: *chaque un a son gout.* Ironically, during his military stint Ranzahoff was assigned to neurosurgery and after the war, he became an eminently successful, though somewhat gruff, practitioner of the art in New York city (see Shainberg, 1979).

In addition to Gerard, the University of Chicago was rich in other neuroscientists. Stephen Polyak was working on the anatomy of the retina and visual system. I was intrigued by the work of Roaf (1927, 1930) on color afterimages and saw in Polyak's detailing of three sorts of retinal bipolar cells a mechanism for analyzing and further separating the Helmholtzian receptor process, accounting for the effects of color afterimages. I wrote up these suggestions with Polyak's help and submitted the result as an unpublished medical student thesis.

Paul Weiss was training Roger Sperry to transplant limbs of *Amblystoma.* I became well acquainted with both of them when Weiss appeared on my medical service during my internship. The friendships lasted a lifetime and centered on the problem of resonance: How could it be that a limb induces in the developing nervous system a code that allows the system to recognize the limb irrespective of its innervation? Sperry's answer to this question invoked specific chemical codes; mine, suggested in *Languages of the Brain,* devolves on the finding by J.Z. Young of the induction of specific nerve fiber size spectra by each muscle. Most likely the specific chemistry induces specific fiber size spectra.

A. Earl Walker became chief of neurological surgery when Paul Bucy left; I learned the details of thalamic anatomy from Walker before joining Bucy. Over the years to come, together with Kao Liang Chow and with the help of Jerzy Rose at Johns Hopkins University, I extended Walker's anatomical research to complete a classification of thalamocortical connectivity. Also during this period, Ward Halstead introduced me to what we now call neuropsychological procedures, which are used to study the effects of brain injury in humans.

But most important to my future were Heinrich Klüver and Paul Bucy, pioneers in investigations of the functions of the temporal lobe of the brain. In 1942, I became Bucy's first resident when he moved to the nearby Chicago Memorial Hospital and wrote up our first 100 brain operations in order to have the residency accredited. Bucy was editing a volume on the precentral motor cortex at the time and I became privy to the controversies and details of explorations of this research, as well as learning the techniques of surgery from a master.

My time with Bucy was exciting and fabulously enriching. Bucy would tell stories as we made rounds. He had started in general practice and had found that his patients were in fact patient and loyal even when he made mistakes or had to bumble through because of his limited experience. What counted, he found, was that he was really trying and that he was totally honest with his patients and their families. On another occasion he recounted that, while in general practice, he had visited a mental hospital only to find that almost all the patients were sedated with bromides. He ordered the patients to be taken off the drug. Within a fortnight more than half of them were well enough to be considered for discharge. (We don't use bromides today, but how will our current drugging practices be evaluated by another generation?)

Most of all, Bucy taught me how to localize brain tumors and, in the course of this, to learn about the localization of brain functions. I read avidly during the few quiet moments while on emergency duty, including the book Bucy had published with Buchanan on intracranial tumors in infancy and childhood, and the section on brain tumors he wrote for Roy Grinker's textbook on neurology. In the section on treatment (p. 621), I saw once again (as I had been taught in obstetrics) the admonition "we must follow the age-old rule of surgery, *primum non nocere*, and curb our enthusiasm to the point where optimum results in length of life, comfort, and happiness are attained."

It was also the time I became acquainted with Percival Bailey's treatise on intracranial tumors. After carefully and beautifully reviewing the evidence, he unequivocally states (p. 69): "I merely wanted to impress upon you that in the human brain the parts are not equipotential and that even the defect of intelligence does not, as is sometimes stated (261), depend only upon the quantity of cerebral tissue removed or destroyed." Reference (261) is to Karl Lashley's 1929 monograph *Brain Mechanisms and Intelligence*, which I managed to purchase at a second-hand book store for a dime. Lashley later became a major influence in my life and the tension between his views and those I inherited from Bailey and Bucy formed the thrust of my research career.

Bailey could make his summary statement despite that in the text (p. 67) leading up to it he had to remark that:

> The anatomical correlates of such relatively simple functions as sensation and voluntary motion are somewhat familiar to us. We know also that the central mechanism of the more complicated function of language is usually clustered closely around the left lateral fissure, but when we attempt to discuss a higher mental function such as intelligence, we are greatly hampered by lack of consistent data. Yet certain areas of the brain are known, injury to which is peculiarly liable to disturb intelligence. One of these is the left supramarginal gyrus. Another is the anterior part of the frontal lobe, although in this case the disturbance of character is predominant and I should be less willing to indicate the exact area involved. It is significant that these parts are just the ones in the human brain which are most developed beyond those present in the higher apes.

Later, after I had been given techniques to study such general concepts as intelligence and character by Karl Lashley, I made it my research business to pin down more precisely the localization of the brain/behavior relations entailed. Only much later did I begin to understand what Lashley meant by his dicta regarding equipotentiality and mass action in the storage and retrieval of memories and in the processing of equivalence in perceptions and actions.

In 1943, Bucy was editing a volume on the motor systems of the brain. I was privy to that editing, chapter by chapter, as Bucy explained to me his views and criticisms of what had been submitted. I found out that Wilder Penfield, Warren McCulloch, and Dusser de Barenne all thought of the cerebral motor cortex more as a sensory cortex for movement than as the final common path for all cortical activity, a view that Bucy shared. I learned of how much scholarly activity goes into the writing and editing of such a volume, the great care to provide the best currently available access to knowledge.

My turn to become scholarly came when we admitted a 54-year-old Greek woman who complained of bouts of twitching accompanied by localized sweating over the left side of the face. While in the hospital she actually experienced a grand mal epileptic seizure accompanied by sweating and by flushing. When during surgery we found a small oligodendroglioma in the precentral motor cortex, a tumor which was readily removed with the result of a complete cure for the patient, I suggested that we had come upon a most important finding. Everyone in neurology *knew* that control over the autonomic nervous system was exercised by no higher station than the hypothalamus. Cortical control would mean that the system was not as autonomous, or automatic, as we had been taught to believe. But here was a patient whose cortical tumor had produced epilepsy accompanied by localized sweating and flushing, definitely due to excitation of the autonomic nervous system. I asked Bucy if this observation was worth publishing and he agreed that, indeed, it was. I was eager to get something into print. I was already 24 years old and most of my forebears had published in their early 20's. I was about to become the laggard in the family.

The paper was accepted for publication in the *Archives of Neurology & Psychiatry* (Bucy and Pribram, 1943) and Bucy received a letter from Earl Walker that the Chicago Medical Society wished to have it presented at their next meeting. Bucy showed me the letter and said "you do it." I did. The other speaker that evening was Warren McCulloch, head of the research team at the Neuropsychiatric Institute of the University of Illinois. I did not understand a word of what he was trying to tell us and neither did anyone else. It took me another 40 years of listening to McCulloch (who was at Massachusetts Institute of Technology (MIT) when I was at Yale) and discussion before I was able to grasp the "cybernetic" ideas that were to transform our understanding of the way the nervous system operated. Two decades later, I was offered the headship of the research team at the University of Illinois. It was a most gratifying offer but, by then, I was ensconced in a most productive laboratory at Stanford and could not see myself free to move.

A second research endeavor stemmed from the results of the surgery performed on this interesting woman: I noted that careful removals of cortical tissue that minimally invaded white matter left the patient with no perceptible aftereffects. During the 1950s, when Lawrence Weiskrantz was a graduate student in my laboratory, discussing this insight led to his lifelong pursuit of careful removals of visual cortex and the devising of infinitely sophisticated testing procedures to determine the extent of residual vision; these experiments resulted in his discovery of blind-sight, the ability to perform visual tasks without conscious awareness of the visual stimuli involved.

Within a few months of joining Bucy, I was so completely caught up in neurosurgery (while still attending to all the other services in the small hospital) that I made a decision to pursue the study of the nervous system, as a neurologist, a psychiatrist, or a neurosurgeon. I had never been good with my hands so I asked Bucy to tell me, after some months, whether I could make it as a surgeon. His answer came in typical Bucy fashion. One day he said, "Next month I am going on vacation and turning my practice over to you." I asked if that meant that he wanted me to do the surgery. "Of course," he said. That was all. I had set up a woodworking shop in my home and had practiced using my hands with the aid of machine shop workers who were my neighbors. All my patients and I survived the month. That was it; I became a neurosurgeon. Bucy arranged for me to have a residency with Eric Oldberg at the neighboring St. Luke's hospital if I wanted it. Oldberg was head of the University of Illinois Neuropsychiatric Institute where Percival Bailey, Gerhardt von Bonin, and Warren McCulloch were pursuing their own research. I was to be part of this team.

Thus, after my year with Bucy, I became Oldberg's resident (and also took on the residencies in neurology and psychiatry for extended periods when necessary because of the war) with privileged access to this group. Bailey took on another resident, John Green, and Bailey sat with us over a six-month period detailing the history of his tutelage with Hortega del Rio, whose methods and neuroembryological approach led to Bailey's pioneering work on the classification of brain tumors. Each story was illustrated with microscopic material sectioned from brain tumors which we examined together in great detail.

I occasionally participated in the then-ongoing strychninization experiments of chimpanzee cortex and listened attentively to Bailey, von Bonin, and McCulloch discuss the results. Some years later, at Yale University, I was able to put to good use my surgical skills and the knowledge I had acquired from these discussions to complete the chemical stimulation experiments on cat and monkey by explorations of the medial and basal surfaces of the brain, which had remained inaccessible to the earlier research.

A most exciting part of the research going on at this time was the exploration of the lateral surface of the human brain for suppression of motor activity. Although the results obtained were highly controversial, the process of cortical stimulation in which Bucy also participated, the examination of the patient (sometimes left to me) while this stimulation was in progress, and the discussions which ensued were fascinating. I remember well the occasion during one of these procedures when a telegram arrived from Paul Glees at Oxford University stating that he had just found nerve fibers connecting the precentral cortex to the caudate nucleus, using his newly developed silver staining technique. McCulloch suggested that the term *negative feedback* be applied to explain the suppression of motor activity and that Glees had found the anatomical basis for such feedback. Knowledge of these feedback circuits, in conjunction with those operating on the spinal reflex, were to produce the Test–Operate–Test sequence as a fundamental procedure operating in the formation of Plans in *Plans and the Structure of Behavior* (Miller et al., 1960).

The Universities of Chicago and Illinois were not the only centers for neuroscience research in Chicago at the time. Horace Magoun and Donald Lindsley and their collaborators were beginning their research on the mesencephalic reticular formation at Northwestern University. I was to participate in this work in collaboration with Percival Bailey, having received a fellowship to do so, but Bailey changed his plans and went overseas for a year. The proposed collaboration never took place, but my interest in the project had been piqued so that I kept abreast of developments as they occurred.

Exciting as all of these Chicago experiences were, they did not furnish me with some of the basic tools I needed to accomplish my goals, which were to explore the relationship between brain function and mental processes such as emotion, cognition, and conation (the intention to act). In my search for a hay fever-free location where I might earn my living as a neurosurgeon and at the same time pursue these goals, I heard of the Yerkes Laboratories of Primate Biology near Jacksonville, Florida, where Karl Lashley was director. Fortunately, there was a position open in Jacksonville with J.G. Lyerly. Lyerly, as well as Poppen in Boston, had devised a superior incision for frontal lobotomy which was safer than the classical (lateral) Freeman–Watts procedure and left fewer unwanted side effects. The lateral incision was shown by Fred Mettler and L. P. Rowland to invade Broca's speech area. Although no language disturbances followed the lateral incision, fibers from the medial and orbital cortex were more apt to be saved when Lyerly's superior incision was used. Because of his innovative bent, I felt that Lyerly would be sympathetic to my desire to work at Yerkes. In 1946, I took my Florida State Board examinations and began private practice.

Lyerly agreed to my working two half-days per week, plus any free time, at my research at Yerkes. I called Lashley and he responded favorably, stating that he had been looking for a neurosurgeon to assist him in his primate research. Thus began a collaboration which was to prove most influential in shaping my subsequent research program.

Lashley taught me the techniques of experimental psychology, a field of inquiry which I did not know existed. Paradoxically, although Lashley was almost solipsistic, destructive in his research procedures and interpretations of any finding that would relate brain function to behavior, he provided many of the questions that needed to be answered and that led to the discoveries which make up the substance of my career. Some of the discoveries I made while he was still alive, such as the unique relationship between the frontal cortex and the limbic forebrain, and the sensory specificity of various sectors of the posterior "association" cortex. He ignored or played down these results, as they were contrary to his belief that the mechanisms involved in organizing complex psychological processes were distributed in the brain. But always, his critical wit sharpened my interpretations and provided the basis for further observation and experiment.

The opportunity to work full time in research came in 1948 when I was asked by John Fulton to join him the department of physiology at Yale University. My association with Yale lasted for a decade (1948–1958), during which time I also directed the research laboratories of the Institute of Living, a mental hospital in nearby Hartford, Connecticut. The facilities at

Yale and in Hartford provided ample space for a group of young investigators dedicated to exploring the power of combining the techniques of experimental psychology with those of neurophysiology and experimental neurosurgery. Doctoral students from Yale (Muriel Bagshaw, Martha Helson Wilson), Harvard (Lawrence Weiskrantz), McGill (Mortimer Mishkin), University of California at Berkeley (William Wilson), and Stanford (Jerome Schwartzbaum) formed the nucleus of a most productive team, all of whom received their degrees while working on the program.

During this period I spent one month a year at the Yerkes Laboratory, and Kao Liang Chow, an early student and collaborator, spent a month with me in the north, reestablishing at least in part Yerkes' original vision, a Yale University-related primate research laboratory. This continuing collaboration led to an invitation to succeed Lashley as director of the laboratories, and I filled this post until the president of Yale University sold the laboratories to Emory University in Atlanta in 1956.

Also during this period, I began an intimate association with psychologists at Harvard University. I taught summer school there one year, built operant equipment in the Harvard shops, and learned a great deal from S.S. Stevens, Gary Boring, and Georg von Bekesy. Once a month, Bert Rosner and I drove up to Harvard (and later MIT) to perform experiments with Walter Rosenblith on monkeys in which we evoked electrical potentials in the cortex by auditory stimulation. Somewhat later, these sessions were extended to explore, with Wolfgang Kohler, the evocation of direct current shifts under similar conditions.

My interactions with B.F. Skinner at Harvard were especially memorable and led to a decade of primate operant conditioning experiments, which developed into subsequent research in cognitive neuropsychology. Shortly, I was able to automate and extend the operant equipment to record (including reaction time) the results of individual choices among a dozen possible panel presses. Later, over my three decades at Stanford (1959–1989), these responses were recorded in a large variety of problem-solving situations. The computer-controlled testing apparatus was dubbed Discrimination Apparatus for Discrete Trial Analysis (DADTA).

At one point in our interaction, Skinner and I came to an impasse over the possible mechanism involved in the chaining of responses. Chaining was disrupted by resections of the far frontal cortex. Skinner suggested that proprioceptive feedback might have been disrupted, but this hypothesis was not supported by my experiments. Furthermore, as I indicated to Skinner, he, as a Ph.D. in biology, could propose such an hypothesis, but I, as a loyal Skinnerian, had to search elsewhere than within the "black box" for an answer to our question. George Miller overheard some of our discussions and pointed out to me that he had available a procedure that made chaining of responses easy: a computer program. Miller explained to me the principles of list programming which he had just learned from Herbert Simon and Alan Newell. The culmination of the collaboration begun by these encounters in the halls of Harvard was *Plans and the Structure of Behavior*, a book influenced also by our interactions with Jerome Bruner, who had organized a conference on thinking at Cambridge University in 1956 to which we had been invited. The book was written in 1958–1959 at the Center for Advanced Studies in the Behavioral Sciences, adjacent to the campus of Stanford University.

Thanks to Jack Hilgard and Robert Sears of the psychology department, and to Tom Gonda (the son of a neurologist who had been a friend of my family in Vienna) in psychiatry, I was given an appointment at Stanford (supported, initially, by a grant from the Markel Foundation for Social Research) in 1959. Soon afterward, in 1962, I received a lifetime research career award from the U.S. National Institutes of Health which, in addition to substantial grants to pursue research interests, sustained me for the next three decades.

At Stanford, another group of doctoral and postdoctoral associates joined these endeavors. (Altogether, some fifty doctoral and fifty postdoctoral fellows were trained in the neuropsychological laboratories at Yale and Stanford under my direction.) At Stanford, Robert Anderson, Muriel Bagshaw, Bruce Bridgeman, James Dewson, Robert Douglas, Daniel Kimball, Abraham Spevack, and Leslie Ungerleider were among those who made major contributions. Nico Spinelli became an integral and almost indispensable collaborator.

When I became emeritus at Stanford at age 70, I was offered the opportunity to continue work at Radford University in Virginia. Radford, sister university to Virginia Tech, built a laboratory for me, and I organized a Center for Brain Research and Informational Sciences (B.R.A.I.N.S.) with the help of Alastair Harris, who chairs the psychology department. The appointment is supported by the eminent scholars fund of the Commonwealth of Virginia and an endowment from the James P. and Anna King Foundation. I developed a close and effective collaboration with Joseph King, who obtained his Ph.D. at neighboring Virginia Tech under the direction of Abe Spevack, who had spent several years with me at Stanford as a postdoctoral fellow.

Research Themes

The results of the research completed over the years at the Yerkes laboratories, at Yale, at Stanford, and currently in Virginia, can be organized according to overlapping themes, each theme representing a problem area and the application of techniques appropriate to that problem area. A description of the themes follows.

Theme I: Establishing a Correlation between Brain Systems and Specific Behavioral Indicators

By the time my research program began, large areas of the primate cortex remained unexplored by experimental investigation. In humans, damage to these areas resulted in agnosia, aphasia, and changes in character, and thus in interpersonal emotional interactions. But it was not known whether these changes in competence and behavior were the result of damage additional to that inflicted on primary sensory-motor systems, or whether the changes could occur without such damage. Furthermore, it was not known whether the changes were specific to one or another location within the silent (known as the "association") cortex.

By using a battery of behavioral tests and resecting large parts of the then-silent cortex of monkeys without invading the primary sensory-motor systems, I found answers to these questions relatively rapidly. A method was devised which used superimpositions of reconstructions of resected cortex. The number of the resections that produced a particular behavioral deficit were summed. The sum of the resections which produced no deficit were also summed and the result was subtracted from the sum of lesions that produced a deficit. This "intercept of sums" technique was the origin of the "double dissociation" technique now used so extensively in clinical neuropsychology and allowed me to make multiple double dissociations among the various deficits produced by the resections and to localize the brain system involved in the behavior represented by each task (reviewed by Pribram, 1975).

The results I obtained at Yale in the early 1950s were unequivocal. One type of deficit was produced when the anterior frontal, the cingulate and hippocampal cortex, and the amygdala and anterior temporal cortex were resected. Another type of deficit followed resections of the posterior cortical convexity and could be further subdivided into sensory-specific components, each of which was related to its own portion of the convexal cortex. In no instance did invasion of the adjacent primary sensory-motor systems produce the deficit or even enhance it. These findings were published in the *Journal of Comparative Neurology* and *Journal of Comparative and Physiological Psychology* in the early 1950s, reviewed in 1954 in *Current Trends in Psychology* (Pribram, 1954), and reprinted in *Behavioral Sciences* (see Pribram, 1969, Vol. I).

Theme II: Determining the Behavioral Categories Denoted by the Indicators

Having identified specific behavioral indicators for the functions of specific areas of the cortex, the next problem was to discover what the indicators meant. Much as a Babinsky sign serves as an indicator of improper functioning of the spinal pyramidal motor system, signs of malfunction of brain cognitive systems were now available to us.

In order to define the meaning of the behavioral indicators we had to explore the effects of each brain resection with a wide range of behavioral tasks related in one way or another to the indicator. Limits were established by showing which tasks could be performed without any deficit. For example, the visual deficit produced by resections of the inferotemporal cortex was observed during discriminations of color, brightness, size, and two- and three-dimensional shapes, but not when the animal was tracking even minute objects. Further, limits to the deficit on the brightness or size discrimination were obtained when the difference between the brightness or size of the cues was either very large or very small. (In the latter case, normal controls had as much difficulty discriminating size or brightness as did the monkeys with brain damage.) I used response operator characteristic curves (ROC) to check whether the deficiency in discrimination was a function of changes in detection threshold or in response bias.

Interpretation was seldom straightforward, despite the wealth of data accumulated. This was in large part due to the lack of agreement about the constructs used in experimental psychology. Just how does one compare the results obtained in a fixed interval operant conditioning study with a result obtained in an ROC decisional experiment? How does one compare either of these with results obtained in a delayed alternation situation tested in a Yerkes box or with the DADTA apparatus? Interpretation had to be made after much cross validation of techniques, often using the same subjects and, of course, comparable resections. Nonetheless, some 80 publications in *Brain, Journal of Neurophysiology, Journal of Comparative Neurology, Journal of Comparative and Physiological Psychology,* and *Neuropsychologia* presented the results of these investigations, each in the technical language appropriate to the behavioral methods used. But in most cases some conceptual leaps were necessary in making the interpretations; these leaps were guided on one hand by findings on human neuropsychological patients and on the other by knowledge obtained about the anatomy and physiology of the neural systems being investigated.

Theme III: Determining the Physiological Processes Mediated by the Systems

Another line of research, which was made possible by the initial findings of Theme I, was an analysis of the anatomy and physiological processes of the neural systems of which the critical cortical areas were a part. Chemical and electrical stimulations in anesthetized or problem-solving monkeys were performed. The effects of such stimulations on electrical recordings of event-related, local field potentials were assessed while monkeys performed in the DADTA. Also, such effects on the microstructure of receptive fields of single units in the visual somatosensory, somatosensory, and motor systems were assayed.

Once again the results of these experiments yielded a good deal of data (some 40 papers), published in the *Journal of Neurophysiology, Brain Research, Experimental Brain Research, Electroencephalography,* and *Clinical Neurophysiology and Experimental Neurology,* which are interesting in their own right. However, as in Theme II, *interpretation* (and in some instances *controversial interpretation*) became necessary. One major controversy centers on whether the sensory specificity of the "association" cortex of the parietal, occipital, and temporal lobes is due to its transcortical input via connections from the related primary sensory cortex, or whether the specificity is to be ascribed to an output which operates downstream on the primary sensory systems. I was able to make massive disconnections, some of which appeared to be complete, between the primary sensory systems and the inferotemporal cortex involved in visual discriminations. None of these disconnections produced lasting deficits in sensory discriminations and this led me to propose the output hypothesis. Controversy hinged on whether the disconnections were in fact total: even a small remnant of connectivity could possibly be sufficient to mediate an input. The facts are reviewed in the paper "The Role of Cortico-cortical Connections" (Pribram, 1986a).

Theme IV: Relevance of the Research Results to Humans

The research program began with the aim to clarify the brain mechanisms involved in cognitive, emotional, and conative (involving the intention to act) processes in humans. The final research phase of the program therefore had to address the relevance of the results of the nonhuman primate research, in which some 1500 monkeys were used, to human neuropsychological findings. Since my early days in the neurosurgical clinic, electrical recordings of event-related scalp potentials, computerized tomography, and nuclear magnetic resonance imaging (MRI) techniques have been developed to aid in the localization of brain pathological conditions. A major task ahead is to compare the results obtained with these techniques with those obtained in monkeys.

Due to the prodigious advances in information processing technology, recordings of the running electrical brain activity show great promise, as well. Differences in patterns can reflect individual differences in character traits and differences in conscious states. To the end of exploiting these possibilities, my laboratory was recently fitted with a 128-electrode recording capability. In addition, my colleagues and I have devised several new methods for quantifying the spatiotemporal dynamics of EEG. Development of these methods was motivated by watching computer-generated animations of EEG voltage recordings. These animations contain a wealth of information about the rapidity (about 100 per second) of change in the patterns of voltages observed across the surface of the scalp. We quantified these spatio-temporal dynamics as scalars, vectors, and cluster analytic plots of EEG activity and have obtained initial findings suggesting that the techniques will prove useful (Pribram et al., 1996).

Theme V: Theoretical Interpretations of the Research Results

The laboratory research has yielded many unexpected results. These results have dramatically changed my views from time to time and posed, as critical to further research, problems which I had thought I could ignore. Much of the theoretical work which has engaged me has stemmed from these surprises.

Discoveries

Karl Popper claims that science is based on conjecture and refutation, and Karl Lashley was always comfortable when he operated in this mode. My own research has proceeded in a more haphazard fashion (see Pribram, 1982). Despite the planning represented by the themes described earlier, my actual research has been a search which stemmed from problems and paradoxes (such as unexpectedly finding relatively direct sensory inputs to the motor cortex) rather than from well-formulated conjectures or hypotheses.

Theses there were, but only rarely did I derive single, testable hypotheses with experiments designed to confirm or disconfirm. Rather, I followed the rule that several more or less clearly defined alternatives presented themselves when the thesis, that is, the reasons for performing the research, became clear. I designed experiments to find out which of the alternatives fit the data I had obtained. Sometimes the data fit none of the alternatives, the thesis itself was found wanting, and new directions had to be taken. Often these new directions stemmed from attempts to systematize the data already obtained and to develop an appropriate frame for sorting and classifying them.

Whatever the merits or deficiencies of this approach, it is shared by many biologists. Claude Bernard, when asked how he proceeded in the laboratory, answered that he simply asked nature some questions. By adopting this perspective, the yield of my research has been substantial and I made many discoveries which might not have been uncovered by a more rigid approach. Some of these discoveries are detailed below.

The Functions of the Frontolimbic Forebrain

The Limbic Forebrain. Early research results led me to redefine the boundaries of the limbic forebrain (also called the olfactory brain) which had hitherto included only the hippocampal and cingulate gyri by establishing the relationship between limbic cortex and visceroautonomic activity (see Pribram & Kruger, 1954).

Based on the earlier work of Warren McCulloch, Percival Bailey, and Gerhardt von Bonin, I established by strychnine neuronography and by electrical stimulation and histological examination, the interrelationship between the amygdaloid complex and the surrounding orbitofrontal, anterior insular, and temporal polar cortex and the direct connections of all of these to the hypothalamus (see Pribram et al., 1950; MacLean and Pribram, 1953; Pribram and MacLean, 1953).

The work of Arthur Ward and Robert Livingston had shown that visceroautonomic responses were obtained from electrical stimulation of the cingulate gyrus and orbitofrontal cortex. With B. R. Kaada and J. A. Epstein (see Kaada et al., 1949) I extended these results to the anterior insula, temporal pole, and amygdala. Initially, this finding was resisted as being due to artifact—a Nobel laureate indicated to John Fulton that he thought our results were due to inadvertent stimulation of the dura—after all, we knew that the hypothalamus was the "head ganglion" of that system. Fulton stuck by me and published our findings. Within 2 years, most of the graduate students in physiology at Yale were doing their theses on limbic-related topics.

Thus, the amygdala and its surrounding cortex were shown to be part of the limbic forebrain, which, as noted above, had previously included only the hippocampal and cingulate systems. Further, an entire extent of mediobasal motor cortex—which included the periamygdaloid cortex, the temporal and the adjacent anterior insular, the orbitofrontal, medial frontal and anterior cingulate cortex—was discovered whose primary function is to regulate visceroautonomic functions (Pribram, 1961).

The Anterior Frontal Cortex and Limbic Forebrain. Next I established the fact that the far frontal cortex is the "association" cortex for the limbic forebrain. This accounted for the psychosurgical effects of frontal lobotomy. Using the delayed response and delayed alternation techniques I extended the work of Carlyle Jacobsen and Henry Nissen, who had shown that resections of far frontal cortex disrupted performance on these tasks. I found that resections of the various structures composing the limbic forebrain (hippocampus, amygdala, cingulate cortex) also disrupted performance of delayed alternation (Pribram et al., 1962). By contrast, resections of the cortex of the posterior cerebral convexity failed to disrupt performance on these tasks; if anything, monkeys with such resections tended to perform better than their unoperated control subjects (Pribram and Miskin, unpublished results).

These findings, and results of anatomical experiments which showed that the organization of the projections from the dorsal thalamus to the anterior frontal, peri-rhinal, and cingulate cortex differed substantially from the organization of the projections to cortex of the posterior cerebral convexity (Pribram, 1958a, b), indicated that the anterior frontal cortex can be considered to be intimately related in both structure and function to the limbic forebrain. This relationship between the anterior frontal cortex and the limbic forebrain was quickly recognized to account for many of the changes in "character" produced by frontal lobotomy in humans.

Neurobehavioral and Psychophysiological Analyses of the Functions of the Frontolimbic Forebrain. In addition to the effects on the performance of delayed alternation, my students and I showed that amygdalectomy affected a set of behaviors I labeled the four F's: *F*ighting, *F*leeing, *F*eeding, and Sex. Aggression—fighting—was assayed in a dominance hierarchy and shown to be dependent on the immediate (48 hour) interaction between the amygdalectomized monkey and his next dominant neighbor (Rosvold et al., 1954). It is as if the familiarization process during which relative dominance becomes established had to be repeated anew with every encounter.

Fleeing was examined in a conditioned avoidance procedure. Not only amygdalectomy but all limbic and anterior frontal resections markedly altered avoidances, although the escape (pain) threshold was unaffected (Bagshaw and Pribram, 1968; Pribram and Weiskrantz, 1957). It is the *memory* of the familiarity with pain, perceived as fear, that is affected, not sensitivity.

A large number of animal experiments were done to measure the effect of food deprivation on the amount eaten, the effect of the amount of food used as reinforcer (size and number of food pellets) in determining the rate of lever pressing, and the amount of food ingested when the animal had unlimited access. Amygdalectomized animals (monkeys, dogs, rats) ate more than their controls but deprivation had very little effect on the amount eaten, nor did changes in the quantity of reinforcer (Schwartzbaum, 1960, 1961). The increase in the amount eaten proved to be the result of eating long after control subjects were satiated (Fuller et al., 1957). Satiation proved to be akin to familiarization in that *memory* of what had just been eaten influenced further eating.

I did not perform any formal experiments on the effects of amygdalectomy on sexual behavior. But informal observation and a careful review and personal observation of the work of the Baltimore, Washington, and UCLA groups led to the conclusion that the degree of familiarization with the situation in which sexual behavior takes place (as well as between the sexual partners) is a potent variable in determining the change in sexual behavior that results from amygdalectomy (Pribram, 1960).

It took a quarter of a century of experimental analysis to reach the conclusion that *familiarization* is the common denominator in disturbances produced by amygdalectomy. Early on, it became apparent to me that the four F's were related to each other in some special way. In lay terms, fight, flight, food, and sex were instincts. But the term instinct had become suspect in experimental psychology because of the lack of an agreed upon definition as demonstrated by Frank Beach's presidential address, titled the

"De-scent of Instinct," presented to Division 3 of the American Psychological Association. Instead, ethologists had substituted "species specific behaviors." But this concept somehow failed to capture the spirit of what is meant by instinct. Human language is species specific and has recently been labeled an instinct, but that label departs considerably from earlier ones.

What makes the four F's so interesting to us—whether they are exhibited by birds, bees, or nonhuman mammals—is not only that we all "do it" but that we all do it in a somewhat similar fashion. Rather than being *species specific,* instincts such as the four F's are *species-shared* behaviors. The question therefore arose, "just what is the property that is disturbed by amygdalectomy and shared by the four F's?" In order to answer this question experimentally, I decided to take a long chance and first ask another: What might it be that is not shared, that is, what are the limits of the impairment produced by amygdalectomy? As almost always, nature answered the question that I posed in a surprising fashion.

I chose to examine monkeys' responses on a set of stimulus equivalence problems in which the monkeys were trained to choose the lighter of two greys and tested on trials in which the absolute values of the greys were changed (Schwartzbaum and Pribram, 1960). Behaviors exhibited in such situations could not be labeled as instinctive, yet equivalences characterize the reinforcing properties of various food and sex objects. In a similar vein, equivalences characterize the deterrent properties of various agonists to be aggressed against or avoided.

Over a decade, with different collaborators [Jerome Schwartzbaum (see Schwartzbaum and Pribram, 1960), Eliot Hearst (see Hearst and Pribram, 1964a, b), Muriel Bagshaw (Bagshaw and Pribram, 1965) and Robert Douglas (Douglas et al., 1969; Douglas and Pribram, 1969; Pribram et al., 1969)], I undertook a series of experiments on amygdalectomized monkeys. The results of these experiments demonstrated first that, indeed, equivalence was disrupted by amygdalectomy, whereas stimulus generalization remained intact (generalization is disrupted by resections of the posterior cortical convexity). Second, disruption of equivalence occurs because amygdalectomized monkeys treat an episode in their experience as novel whereas control monkeys respond to the same experience as familiar.

Equivalence thus depends on treating an episode—a situation—as familiar. The results of the experimental analysis were consonant with observations made in the clinic where patients with epileptogenic lesions of the amygdala experience *déjà vu* and *jamais vue* phenomena. Further analysis of these experimental results indicated that familiarity resides in the context within which the episode is experienced (Pribram, 1991, pp. 217, 233, and Appendix C).

The changes in dominance and in avoidance produced by amygdalectomy can be understood as deficiencies in familiarization: the monkey's position in the dominance hierarchy is no longer familiar after the resection, stimulations of the orbitofrontal cortex and the amygdala. No such disruption was seen after resections or electrical stimulations of parietal cortex (Chin et al., 1976).

I summarized these findings with a proposal that is derived from a distinction made by Henry Head for peripheral nerves: epicritic sensations display local sign (i.e., can be accurately localized in time and space); when local sign is absent, the sensations are described as protopathic (original + pathos). For central processing, the terms *hedonic* or *protocritic* are more appropriate. The proposal states that the frontolimbic forebrain processes the hedonic, protocritic aspects of sensation, whereas the systems of the cortical convexity process the epicritic aspects (Pribram and McGuinness, 1975; Pribram, 1977).

The Functions of the Posterior Cortical Convexity

Sensory Specificity in Cognition and the Posterior Cortical Convexity. In another part of the research program, I was able to show that the cognitive aspects of epicritic processes were dependent on the sensory specificity of restricted regions within the posterior association cortex of the cortical convexity. The cortical terminations of epicritic sensory input were well known when this program of research was initiated. However, at that time it was thought that the expanse of cortex lying between the primary sensory receiving areas served a purely "associative" function. Thus the sensory specificity of agnosias found in human patients was thought to result from lesions of the association cortex which invaded the adjacent primary sensory cortex as well.

The experiments undertaken with Josephine Semmes and Kao Liang Chow, using the multiple dissociation technique, demonstrated that, in the monkey, no such invasion of primary sensory cortex was necessary to produce the sensory deficits. In addition to the cortical systems involved in taste already described, a nonprimary area specific to the tactile sense, another specific to hearing, and a third specific to vision, were identified (Blum et al., 1950).

An extensive series of experiments, which engaged the interest and participation of Mortimer Mishkin, centered on the functions of the inferotemporal cortex, the area shown to be specific to vision (Mishkin and Pribram, 1954; Pribram and Mishkin, 1955; Mishkin, 1954; Mishkin and Hall, 1955). Until this discovery, the temporal lobes were thought to be totally devoted to hearing; visual defects following temporal lobe lesions were thought to be due to involvement of the optic tracts or radiations. It took more than two decades of demonstration and publication before the role of the inferotemporal cortex in vision was accepted as it is now. The results of this series showed that visual sensory functions such as threshold and detection remained essentially intact; resections produced marked deficits whenever selections among visual inputs were demanded.

Electrical recording of local field potentials led to similar conclusions. Recordings made from the primary visual cortex were sensitive to changes in number and kinds of features that characterized the input. Recordings made from the inferotemporal cortex were sensitive to variables that influenced selection or choice, especially when choice had to be made among ones that share features (Rothblatt and Pribram, 1972; Nuwer and Pribram, 1979; Bolster and Pribram, 1993).

Selection was interpreted to be the rudiment of the cognitive process underlying comprehension. [The experimental results that formed the steps leading to this interpretation are detailed in Lecture 7 of *Brain and Perception;* Pribram (1991).] When comprehension is disturbed by a brain lesion in humans, the identification of objects is impaired, which results in an agnosia.

Efferent Control over Sensory Input. One of the main motivations of the research undertaken at Stanford was the overriding need for demonstration of top-down processing in the brain and nervous system. In psychology, computer science, and linguistics, as in cognitive science in general, top-down processing is assumed and essential. In the brain sciences, however, bottom-up processing was (and is) generally acknowledged as sufficient for constructing theories of function. However, Hagbarth and Kerr (1954) had shown efferent control over tactile receptors and efferent control over muscle spindles had also been shown during the 1950s. Thus, in a series of experiments, D. N. Spinelli, J. H. Dewson, and I (Spinelli et al., 1965; Spinelli and Pribram, 1966; Pribram et al., 1966; Spinelli and Pribram, 1967; Reitz and Pribram, 1969; Gerbrandt et al., 1970; Spinelli and Weingarten, 1966; Dewson, 1968) demonstrated a ubiquitous top-down corticofugal control from sensory specific "association" cortex over sensory input, control that extended as far down as the retinal and auditory receptors.

Perceptual Constancy. Experimental evidence was provided to show that, in vision, size constancy is a function of the perisensory system which immediately surrounds the sensory receiving cortex. In an initial experiment, together with Robert Anderson, I showed that object constancy was not related to the functions of the frontolimbic forebrain (Anderson et al., 1976; Pribram et al., 1977). In the complementary study, carried out by Ungerleider and me size constancy was shown to be disrupted by a combined lesion of the pulvinar of the thalamus and the pre- and peristriate cortex (Ungerleider et al., 1977). Following such lesions monkeys responded to the size of the retinal image and did not take distance cues into account.

The results of these experiments indicate that at least one form of constancy is dependent on the perisensory visual system. Electrical stimulation of this system produces eye movements. Object constancy is likely, therefore, to depend on eye movements which produce a series of related sensory images. Processing these related images results in constancy. Based on these and other results, a theory of object perception was modelled in terms of symmetry groups (Pribram and Carlton, 1987) and amplified in *Brain and Perception* (Pribram, 1991). I am, at present, extending this model to account for the variety of reference frames, attained by transformations of coordinates, that account for the variety of perspectives with which we encounter our conscious experience.

Reciprocity between the Functions of the Frontolimbic Systems and Those of the Cortical Convexity. Mortimer Mishkin and I (in unpublished studies) demonstrated that reciprocity exists between the functions of the frontolimbic formations and those of the cortex of cortical convexity. Resections of the frontolimbic cortex actually speed the learning of sensory discriminations, while making the learning of delayed alternation well nigh impossible. Resections of the cortex of the posterior convexity actually speed the learning of delayed alternation, making the learning of difficult sensory discriminations well nigh impossible.

This reciprocity was also demonstrated with electrophysiological techniques. Recovery cycles in the visual system were shortened by electrical stimulations of the inferior temporal cortex and the putamen and lengthened by electrical stimulations of the frontolimbic forebrain and the caudate nucleus (Spinelli and Pribram, 1966). The inhibitory surrounds and flanks of receptive fields of neurons in the lateral geniculate nucleus and in the primary visual cortex were made larger by electrical stimulations of the systems of the posterior convexity and made to disappear by stimulations of frontolimibic systems (Spinelli and Pribram, 1967; Lassonde et al., 1981).

Feature Encoding by Neurons in the Visual Cortex. Having utilized plots of receptive fields in the studies on reciprocity, I became interested in classifying the properties of visual receptive fields. Initially with Nico Spinelli and Bruce Bridgeman (Spinelli et al., 1970), and later with M. Ptito and M. Lassonde (Pribram et al., 1981), I attempted to classify "cells" in the visual cortex. This proved to be impossible because each cortical cell responded to several features of the input such as orientation, velocity, and the spatial and temporal frequency of drifted gratings. Furthermore, cells and cell groups displayed different conjunctions of selectivities which included: (1) tuning to auditory frequency, (2) whether a stimulus property had been reinforced, and (3) whether a particular response had been made on a prior occasion. Furthermore, such properties as *simple* and *hypercomplex* could occur in the same recording from single cells. I concluded that cells were not detectors, that their receptive field properties could be specified, but that the cells were multidimensional in their characteristics (see Pribram, 1991, Lectures 1 and 2).

Thus, the pattern generated by an ensemble of neurons is required to encode any specific feature, as indicated also by Vernon Mountcastle's work on the parietal cortex and Georgopoulos' data on the motor cortex. The assumption that single neurons serve as feature detectors or channels therefore, has to be abandoned. Classification of receptive field (network) properties rather than of cells is more appropriate.

When a spike train becomes stationary, without a temporal change in the probability density of the occurrence of spikes, an analysis based on a random walk with drift is potentially relevant. An early study by G. L. Gerstein and Benoit Mandelbrot (1964) indicated that a model based on a random walk with positive drift yields an excellent fit to experimental data of interspike intervals recorded from spontaneous neural activity. There are, therefore, theoretical and experimental reasons to believe that a model based on the first-passage time of a random walk with positive drift realistically describes the process that generates spike-train statistics. We investigated whether, according to the model, different stimulus features would differentially influence the initiation of a spike.

The model implies that one factor is a boundary condition or "barrier height" that reflects the amount of depolarization necessary for the spike to occur; the second is "drift rate" which reflects the rate at which repolarization proceeds. We found that the orientation of a visual stimulus affects the boundary condition; its spatial frequency affects the drift rate (Berger et al., 1990; Berger and Pribram, 1992; reviewed in Berger and Pribram, 1993).

The Functions of the Peri-Rolandic Central Cortex

Gabor Functions in the Somatic-Sensory Cortex. At Radford University, I have available only rats and humans. Surprisingly, we quickly obtained fabulous spike trains from the somatosensory cortex of the rats and immediately set to work to extend findings from visual neurophysiology. Joseph King and I, with two graduate students in engineering, investigated receptive fields in the somatosensory "barrel cortex" of the rat obtained by stimulation of their vibrissae. We rotated grooved cylinders to stimulate the rats' whiskers. The spatial separation between the grooves were different on different cylinders and the cylinders could be rotated at different speeds. Our results were plotted as surface distributions of excitation in dendritic receptive fields and as neuronal population vectors (King et al., 1994; SantaMaria et al., 1995). A computer simulation of our results showed that, according to the principles of signal processing, the somatosensory surface distributions recorded in these circumstances were readily described by Gabor-like functions much as in the visual system, unambiguously indicating that processing can occur in a space time constrained spectral domain.

The Sensory Nature of Motor Control. The finding of a mediobasal motor cortex and the involvement of motor control in the production of object constancy inspired me to look more closely at some aspects of the functions of the classical motor systems.

While at Yale in 1952, quite by accident I discovered direct cutaneous and proprioceptive inputs to the precentral motor cortex. With a postdoctoral student and neurosurgical colleague, Leonard Malis, I had developed and perfected an apparatus to study the brain electrical potentials evoked by sensory stimulation. Together with a graduate student, Lawrence Kruger, Malis placed electrodes on the cortex of a monkey. I had earlier opened the skull to expose the central Rolandic area of the cortex, but had left to test a group of monkeys with the delayed alternation procedure. Returning, I found Malis' oscilloscope displaying crisp, large electrical responses every time the sciatic nerve was stimulated. We were ecstatic. For almost 2 years we had waited for the oscilloscope, a DuMont, the first to be built for use in neurophysiology and designed by Harry Grundfest of Columbia University. Grundfest received the initial production model; we received the second. Finally we were able to do the experiment we had planned.

Our joy was short-lived. I asked where the electrodes had been placed. Malis and Kruger replied in unison, "on the brain, you dummy." I asked, "but where on the brain?" When I looked, the electrode site was squarely in the upper-middle part of the precentral gyrus. "Artifact," I exclaimed.

It took a thesis by Kruger and consultations with Clinton Woolsey and Wade Marshall before we all were convinced that indeed the "motor" cortex received afferents directly from the periphery—not via the cerebellum or the postcentral gyrus. I resected these structures in various experiments without producing any change in the evoked response. Only the incitement of spreading depression diminished the response, attesting to the fact that it was not, after all, artifact (Malis et al., 1963; Kruger, 1956).

With Malis and another postdoctoral student and neurosurgical colleague, Joseph Berman, I explored the effects on behavior of extensive resections of the precentral cortex using latch boxes and cinematographic recordings of the behavior of monkeys in a variety of situations. The results of these investigations showed that all *movements*, defined as sequences of muscle contractions, remained intact. The skill of opening latch boxes was, however, impaired: transition times *between* movements were markedly increased. This increase in transition time was specific to the latch box situation; it was not present in more ordinary circumstances such as climbing the sides of cages, grabbing food, and other movements (Pribram et al., 1955–56).

On the basis of these experiments and the importance of the gamma motor system, I concluded that the precentral cortex exerted its effect by changing the setpoints of the muscle spindles involved. Behavioral *acts* were defined in terms of patterns of these set points which thus resulted from particular consequences of movement. Control over acts had to encode in some way and represent the input resulting from movements rather than control specific muscles or even muscle sequences per se. When this representation was impaired, transition times became prolonged. I was tempted to suggest that the time constant of processing the representation had been extended, a suggestion consonant with a proposal made by Lashley in 1924, who decided that the motor cortex was facilitatory only in its function.

Frequency Encoding of Load in the Motor System. The nature of the encoding process remained opaque to me for almost a decade after completing the initial experiments. Then, a series of events occurred which allowed me to continue the explorations. First, data obtained by Edward Evarts showed that the activity of neurons in the precentral motor cortex was proportional to the load placed on a lever manipulated by a monkey and not the metric extension or contraction of the muscles used in the manipulation. Second, the results obtained in the 1930s by N. Bernstein in the Soviet Union were translated into English. Bernstein had shown that he could predict the course of a more-or-less repetitive series of actions by performing a Fourier analysis of the wave forms produced by spots placed over the joints involved in the action.

These data and analyses fed into the thesis I had by then developed, that certain aspects of cortical function could best be understood by carrying out harmonic analyses. Orthogonal transformations of sensory inputs, such as the Fourier method, were hypothesized to be one "code" used for cortical processing. Together with an engineering student, Amand Sharafat (Pribram et al., 1984), I performed an experiment in which we investigated whether neurons in the cat motor cortex were tuned to certain bandwidths of frequencies of passive movements of their forelimbs. Here, for once, we were testing a specific hypothesis, and the hypothesis was supported by our results. Certain cells in the motor cortex are responsive to the frequency of the movement of a limb. Some of these cells are also selective of phase. The ensemble of cells are therefore performing a spectral analysis of changes produced by the movement. A set of values is computed which, when inversely transformed, represents the load imposed by the situation (the apparatus moving the limb) on the movement. It is this load, not the metric contractions of the muscles nor the sequences involved in movement per se, to which the cells are responding.

Theory

In 1984, on the back page of the front section of the *New York Times,* a full-page advertisement had been placed, ostensibly by *Omni* magazine. In part, the ad read as follows:

> In a recent issue, *Omni* magazine discussed the problems of perception and memory with Dr. Karl Pribram, the Austrian-born neuropsychologist who developed the first holographic model of the brain. According to Pribram, the brain encodes information on a three dimensional energy field that enfolds time and space, yet allows us to recall or reconstruct specific images from the countless millions stored in a space slightly smaller than a melon. The Pribram interview is a rich, provocative example of the journalism that has made *Omni* the world's leading science magazine.

Provocative, it certainly is. I puzzled as to what it might have been that I had said that would make someone—anyone—even the current "media hype"—attribute to me such a view of "the" brain. Ah, yes. The fields are the receptive dendritic fields of neurons recorded as surface distributions of excitation. And true, a three-dimensional orthogonal (spectral) transformation will enfold a four-dimensional space/time image. Storage capacity in the spectral domain is indeed prodigious. This domain is, of course, only one of several "languages of the brain," but on the whole, someone had read me better than I had initially read them.

The *Omni* interview and other similar experiences have made me wonder how it is that my theoretical work has engaged so much popular interest, while discoveries made in the laboratory have often become part of the received wisdom in the neurosciences without acknowledgment even within psychology or neuroscience. The laboratory research has taken up by far the greatest amount of my time and effort, and I therefore welcome this opportunity to show how this research led to theory. For me, theory is data-based and, according to Ajax Carlson's maxim, I have, whenever possible, obtained in my own laboratory at first-hand the data critical to theory.

What led to this notoriety was the publication of *Plans and the Structure of Behavior* in 1960, which had a major impact on moving psychology from a strictly behavioristic stimulus–response or response–reward science to a more cognitive science. In that publication, George Miller, Eugene Galanter, and I called ourselves *subjective behaviorists.* I have already noted how I became involved with Miller after Skinner and I reached an impasse on the problem of the chaining of responses. Clinical considerations, set forth in my contribution to Sigmund Koch's *Psychology as a Science,* were instrumental in taking more seriously the verbal reports of introspection than was the custom in mid-century. Thus came about a major divergence from Skinner, who abhorred the use of subjective terminology because of the difficulty of extracting the exact meaning of a verbal communication. This topic was explored at great length at the Center for Advanced Study in the Behavioral Sciences with Ormond van Quine who was writing *Word and Object* while we were engaged in writing *Plans.*

The thrust of *Plans* was that computer programs can serve as powerful metaphors for understanding cognitive processes and the brain processes involved in them. That thrust has been realized—in the neuroscience community as well as in psychology—in conceptualizations such as "information processing" and "motor programs," which abound.

However, it has also become clear that brain processes are considerably different, even in the fundamentals of their operation, from current serial processing computers. Brain processing proceeds, to a large extent, in parallel, and addressing occurs by content rather than by location. Our mails are representative of location-addressable systems. Content-addressable systems are akin to those in which a broadcast is receivable by a properly tuned instrument, irrespective of location within the broadcast range.

These differences were highlighted in *Languages of the Brain* (Pribram, 1971), published a decade after *Plans. Languages* continued to explore the power of hierarchically arranged information processing mechanisms but added the mechanisms of image processing which, although they had been integral to the conceptions proposed in *Plans,* were not explored because no appropriate metaphor was available at that time. Such a metaphor became available in the early 1960s in the form of optical holograms. Image processing depends on parallel processing and thus is better fitted to some aspects of brain anatomy and function than is serial programming.

One of the consequences of considering parallel as well as serial processing was the introduction of a model for feedforward operations. In *Plans,* we had made much of hierarchically organized feedback loops. As Roger Brown pointed out in his review of our volume, this left the mental apparatus almost as much at the mercy of input as did the earlier stimulus–response psychologies. In *Languages,* this deficiency was remedied by showing that coactivation of two or more feedback loops by a parallel input would produce the kind of feedforward organization basic to voluntary control. This proposal was in consonance with similar suggestions put forward by Herman von Helmholtz, Ross Ashby, Roger Sperry, and Hans-Lukas Teuber, but was more specific in its design features than were the other suggestions.

Of the many languages described in *Languages of the Brain,* the language of the hologram has engendered the greatest lay interest and professional controversy. This controversy has resulted because the optical hologram displays vividly the operations of image processing. Image processing relies on orthogonal transformations such as the Fourier which, because of their linearity, are readily invertible. This means that image and transform are reciprocals, that is, duals of one another, and that transformation in either direction is readily achieved.

The transform domain has properties which make it ideal for storage and for computation. Gigabytes of retrievable information can be encoded in a cubic centimeter of holographic memory. IBM uses such storage devices in the barcode machines that identify grocery store items. Correlations are computed by simply convolving (multiplying) one input with the next. The ease with which such correlations can be computed in this fashion accounts for the value of the fast Fourier transform (FFT) in statistics.

There are other properties of the transform domain which are not so obviously useful but which have had a tremendous theoretical impact. Information becomes distributed in the transform domain so that essentially equivalent images can be reconstructed from any portion of the stored representation. Computer simulations of such parallel distributed processes (PDP) have become commonplace. Such simulations can "learn language" by going through stages similar to those developed during language learning in human infants. The relations between such simulations and neurophysiological and neuropsychological data are reviewed in my book *Brain and Perception: Holonomy and Structure in Figural Processing* (Pribram, 1991).

Holography was a mathematical invention designed by Dennis Gabor to enhance the resolution of electron microscopy. Optical realizations of the mathematics came more than a decade later. It is important to emphasize that other realizations of the mathematics such as those made by computer (as in the IBM example above) are also holographic. Certain aspects of brain function realize Gabor's mathematics, to that extent they too can be thought of as holographic.

During the 1970s considerable evidence accumulated that one of the properties of receptive fields of cells in the primary visual cortex can be expressed in terms of Gabor elementary functions. In a 1946 paper, before his invention of holography, Gabor became interested in determining the maximum compression of a telephone message which could be transmitted across the Atlantic cable that would still leave that message comprehensible. To accomplish this, he developed a phase space for psychophysics which had as its coordinates not only space and time but the spectral properties of the process (later to be embodied in holography). Because he used Hilbert's mathematics as had Heisenberg in developing the formulation of quantum physics, Gabor recognized the elementary functions populating the phase space as *quanta of information. Brain and Perception* further develops the implications for brain function of Gabor's quanta of information, and their relation to Shannon's measure on the amount of information, to PDP theory, and to the data obtained in my investigations.

Recently, together with Mari Jibu and Kunio Yasue (who collaborated on the mathematical appendices to *Brain and Perception*), I provided some speculations indicating how, at the synaptodendritic level, quantum mechanical processes can operate. Something like superconductivity can occur by virtue of boson condensation over short ranges when the water molecules adjacent to the internal and external hydrophilic layers of the dendritic membrane become aligned by the passive conduction of postsynaptic excitatory and inhibitory potential changes initiated at synapses (Jibu et al., 1996).

The characteristics of the spectral and phase space domains are very different from the familiar space–time dimensions which characterize the image domain. Consider, for example, the dimensions of a spectral representation of an electroencephalographic record: its dimensions are frequency and power. Time is not represented as such; it has become enfolded into the representation of frequency.

I have put together a narrative that describes the importance of these theoretical and laboratory results to understanding the brain/mind relation. The story runs as follows: Take computer programming as a metaphor. At some point in programming, there is a direct correspondence between the programming language and the operations of the hardware being addressed. In ordinary sequential processing configurations, machine language embodies this correspondence. Higher-order languages encode the information necessary to make the hardware run. When the word processing program allows this essay to be written in English, there is no longer any similarity between the user's language and the binary (on/off) procedures of the computer hardware. This, therefore, expresses a dualism between mental language and material hardware operations.

Transposed from metaphor to the actual mind–brain connection, the language describing the operations of the neural wetware, the connection web, made up of dendrites and synapses and the electrochemical operations occurring therein seem far removed from the language used by behavioral scientists to describe psychological processes. But the distance which separates these languages is no greater than that which distinguishes word processing from machine language.

However, the mind–brain connection is different from that which characterizes the program–computer relationship. The mind–brain connection is composed of intimate, reciprocal, self-organizing procedures at every level of neural organization. High-level psychological processes such as those involved in cognition are therefore the result of cascades of biological bootstrapping operations.

If we take seriously the possibility that at the level of the connection web something is occurring which is akin to a computer being programmed in machine language, the Gabor, or some similar function, fulfills the requirements. This function was devised not only to operate on the material level of the Atlantic cable but also to determine comprehensible telephone communication, the aim of which is mutual minding.

Therefore, at the level of processing in the connection web, a formal correspondence (such as the correspondence between machine language based on a binary code and the operations of computer hardware based on on/off switches) is an accurate and productive philosophical approach that describes this process. Correspondence occurs as a result of algebraic rather than geometric homomorphisms. But the actual procedures are instantiations not only as programming and natural languages but in a variety of media. In music, these instantiations may be a performance, a compact disc, a cassette tape or a radio or television broadcast. The procedures involved thus bind together the various scales of operation by way of reciprocal processes that lead to self-organizing embodiments. At the same time, their mathematical structure defines the process and thus avoids the pitfalls of a promissory materialism and those of an evanescent unspecifiable mentalistic process.

A convenient label for this resolution of the mind–brain issue is *isonomy.* Isonomy is defined as obeying a set of laws that are related to one another by a change in coordinates. Isonomy, by taking into account levels of instantiation, encompasses epistemological dualisms and pluralisms and avoids the category error of an ontological identity position.

There is thus good evidence that a class of orders lies behind the classical level of organization we ordinarily perceive and which can be described in Euclidean and Newtonian terms and mapped in Cartesian space–time coordinates (see also C.J.S. Clarke, 1995). This other class of orders constitutes distributed organizations described as potential because of their impalpability until radical changes in appearance are realized in the transformational process. When a potential is realized, information (the form within) becomes unfolded into its ordinary space–time appearance; in the other direction, the transformation enfolds and distributes the information, as this is done by the holographic process. Because work is involved in transforming, descriptions in terms of energy are suitable, and as the form of information is what is transformed, descriptions in terms of entropy (and negentropy) are also suitable. Thus, on the one hand, there are enfolded potential orders; on the other, there are unfolded orders manifested in space–time.

Dualism of mental versus material holds only for the ordinary manifest world of appearances—the world described in Euclidean geometry and Newtonian mechanics. I gave an explanation of dualism (Pribram, 1965) in terms of procedural difference in approaching the hierarchy of sciences that can be discerned in this world of appearances. This explanation was developed into a constructional realism. But it was also stated that certain questions raised by a more classical dualistic and identity position were left unanswered.

Two issues can be discerned: (1) What is it that remains identifiable across algebraic transformations? (2) Is the correspondence between machine language (program or musical notation) and the machine or instrument's operation an identity or a duality? I believe the answer to both questions hinges on whether one concentrates on the order (form, organization) or the embodiments (the media) in which these orders become instantiated (Pribram, 1986b).

Instantiations depend on transformations among orders. What remains invariant across all instantiations is in-formation, a form within. The measure of information (in terms of negentropy, the amount of organization of energy) in Gabor's terms applies both to the organization of the material wetware of the brain and cable hardware in telecommunication, and to the organization of the mindful communication itself. Thus the *in-formation* is neutral to the material/mental dichotomy. Surprisingly, according to this analysis, it is a Platonism that motivates the information revolution (e.g., "information processing" approaches in cognitive and neurosciences) and distinguishes it from the materialism of the industrial revolution. Further, according to my perspective, as in-formation is neither material nor mental, a scientific pragmatism akin to that practiced by Pythagoreans, will displace mentalism and dualism as well as materialism as the central philosophical concern (Pribram, 1997).

Thus, by temperament, I need to be grounded in the nitty gritty of experimental and observational results as much as I am moved by the beauty of theoretical formulations expressed mathematically. Therefore, in my opinion, in the 21st century the tension between idealism and realism which characterized the dialogue between Plato and Aristotle and which has been elaborated by Bertrand Russell, will replace that between mentalism and materialism, a new tension that, at its most productive, will lead to new directions in experimentation, observation, and mathematical theory construction in the spirit of a Pythagorean pragmaticism: that is, a tension between an appearance and the potential process that generates it.

These considerations suggest that these new directions in experimentation will change the venue of science. Currently our emphasis is on what Aristotle called efficient causes, the "this causes that." According to the proposals presented in this essay, 21st century science will supplement searches guided by efficient causation with research guided by Aristotle's final causes. Searches guided by formal and final causation ask how things and events are put together to be what they are and what they tend to become. This type of research, which is by no means new (especially in thermodynamics and psychophysics), emphasizes transfer functions, transformations that occur as we search for ways to understand relations among patterns at different scales of observation.

Pythagoras examined by experiment and mathematical (thoughtful) description orders at all scales of observations available to him. These scales ranged from universal (spiritual) to those composing musical tones produced by vibrating material objects. There is every evidence, from what has occurred in the second half of the 20th century, that in the coming millennium, a similar range of experience will be the grist of our explorations. At the very center of such endeavors is humankind's understanding of its relation to the universe—and at the center of this understanding lies the relation between the orders invented or discovered by the operations of that three-pound universe, the brain, and those orders in which it is embedded.

As of now, these are speculative but historically well-grounded proposals that are set forth to provoke 21st century dialogue, research, and theorizing. For my part, in order to give body to the speculations, I need to continue to incorporate current research findings with the earlier ones obtained by me and my students into a systematic theoretical framework sensitive to the ever-changing landscape of data. In order to do this properly, I must, as heretofore, heed Ajax Carlson's two dicta: (1) Wass iss die effidence? (2) Try to access that evidence first hand. This should keep the explorer in me occupied for a good long while.

Selected Bibliography

Anderson RM, Hunt SC, Vander Stoep A, Pribram KH. Object permanency and delayed response as spatial context in monkeys with frontal lesions. *Neuropsychologia* 1976;14:481–490.

Bagshaw MH, Benzies S. Multiple measures of the orienting reaction and their dissociation after amygdalectomy in monkeys. *Exp Neurol* 1968;2:175–187.

Bagshaw MH, Coppock HW. Galvanic skin response conditioning deficit in amygdalectomized monkeys. *Exp Neurol* 1968;20:188–196.

Bagshaw MH, Kimble KP, Pribram KH. The GSR of monkeys during orienting and habituation after ablation of the amygdala, hippocampus and inferotemporal cortex. *Neuropsychologia* 1965;11:111–119.

Bagshaw MH, Pribram KH. Cortical organization in gustation (*Macaca mulatta*). *J Neurophysiol* 1953;16:399–508.

Bagshaw MH, Pribram KH. Effect of amygdalectomy on transfer of training in monkeys. *J Comp Physiol Psychol* 1965;59:118–121.

Bagshaw MH, Pribram JD. Effect of amygdalectomy in stimulus threshold of the monkey. *Exp Neurol* 1968;20:197–202.

Bailey P. *Intracranial Tumors.* Springfield, IL: Charles C. Thomas, 1993.

Bailey P, Buchanan DN, Bucy PC. *Intracranial tumors of infancy and childhood.* Chicago: University of Chicago Press, 1939.

Berger DH, Pribram KH. The relationship between the Gabor elementary function and a stochastic model of the inter-spike interval distribution in the responses of visual cortex neurons. *Biol Cybernet* 1992;67:191–194.

Berger D, Pribram KH. From stochastic resonance to Gabor functions. In: Pribram K, ed. *Rethinking neural networks: Quantum fields and biological data.* 1993; 47–66.

Berger D, Pribram KH, Wild H, Bridges C. An analysis of neural spike-train distributions: Determinantes of the response of visual cortex neurons to changes in orientation and spatial frequency. *Exp Brain Res* 1990;80(1):129–134.

Blum JS, Chow KL, Pribram KH. A behavioral analysis of the organization of the parieto-temporo-preoccipital cortex. *J Comp Neurol* 1950;93:53–100.

Bolster B, Pribram KH. Cortical involvement in visual scan in the monkey. *Perception psychophysics,* 1993;53(5):505–518.

Lashley KS. *Brain mechanisms and intelligence.* Chicago: University of Chicago Press, 1929.
Lassonde M, Ptito M, Pribram KH. Intracerebral influences on the microstructure of receptive fields of cat visual cortex. *Exp Brain Res* 1981;43:131–144.
MacLean PD, Pribram KH. Neuronographic analysis of medial and basal cerebral cortex. I. Cat. *J Neurophysiol* 1953;16:312–323.
Malis LI, Pribram KH, Kruger L. Action potential in "motor" cortex evoked by peripheral nerve stimulation. *J Neurophysiol* 1953;16:161–167.
Miller GA, Galanter E, Pribram KH. *Plans and the structure of behavior.* New York: Henry Holt, 1960. [Also in Japanese, German, Spanish, Italian, and Russian]
Mishkin M. Visual discrimination performance following partial ablations of the temporal lobe: II. Ventral surface vs. hippocampus. *J Comp Physiol Psychol* 1954;47:187–193.
Mishkin M, Hall M. Discrimination along a size continuum following ablation of the inferior temporal convexity in monkeys. *J Comp Physiol Psychol* 1955;48: 97–101.
Mishkin M, Pribram KH. Visual discrimination performance following partial ablations of the temporal lobe. I. Ventral vs. lateral. *J Comp Physiol Psychol* 1954; 47:14–20.
Nuwer M, Pribram KH. Role of the inferotemporal cortex in visual selective attention. *Electroenceph Clin Neurophysiol* 1979;46:389–400.
Pribram KH. Toward a science of neuropsychology (method and data). In: Patton, RA, ed. *Current trends in psychology and the behavioral sciences.* Pittsburgh: University of Pittsburgh Press, 1954a;115–142.
Pribram KH. Concerning three rhinencephalic systems. *Electroenceph Clin Neurophysiol* 1954b;6:708–709.
Pribram KH. Neocortical function in behavior. In: Harlow HF, Woolsey CN, eds. *Biological and biochemical bases of behavior.* Madison: University of Wisconsin Press, 1958a:151–172.
Pribram KH. Comparative neurology and the evolution of behavior. In: Roe A, Simpson GG, eds. *Behavior and evolution.* New Haven, CN: Yale University Press, 1958b:140–164.
Pribram KH. A review of theory in physiological psychology. *Annu Rev Psychol* 1960; 11:1–40.
Pribram KH. Limbic System. In: Sheer DE, ed. *Electrical stimulation of the brain.* Austin: University of Texas Press, 1961:311–320.
Pribram KH. Proposal for a structural pragmatism: Some neuropsychological considerations of problems in philosophy. In: Wolman B, Nagle E, eds. *Scientific psychology: Principles and approaches.* New York: Basic Books, 1965:426–459.
Pribram KH, ed. *Brain and behavior,* Volumes I–IV. London: Penguin, 1969.
Pribram KH. *Languages of the brain: Experimental paradoxes and principles in neuropsychology.* Englewood Cliffs, NJ: Prentice-Hall, 1971; Monterey, CA. Brooks/Cole, 1977; New York: Brandon House, 1982. [Translations in Russian, Japanese, Italian, and Spanish].

Pribram KH. Psychosurgery. In: Bradley PB, ed. *Methods in brain research.* New York: Wiley, 1975:531–544.

Pribram KH. Peptides and protocritic processes. In: Miller LH, Sandman CL, Kastin AJ, eds. *Neuropeptide influences on the brain and behavior.* New York: Raven, 1977:213–232.

Pribram KH. Scientist vs. philosopher on the mind/brain issue and induction. In: Levinson P, ed. *In pursuit of truth.* Atlantic Highlands, NJ: Humanities Press, 1982:193–200.

Pribram KH. The role of cortico-cortical connections. In: Lepore F, Ptito M, Jasper H, eds. *Two hemispheres–one brain; functions of the corpus callosum.* New York: Liss, 1986a.

Pribram KH. The cognitive revolution and mind/brain issues. *Am Psychol* 1986b; 41(5):507–520.

Pribram KH. *Brain and perception: Holonomy and structure in figural processing.* Hillsdale, NJ: Erlbaum, 1991.

Pribram KH. What is mind that the brain may order it? In: Mandrekar V, Masani PR, eds. *Proceedings of symposia in applied mathematics,* Vol. 2: *Proceedings of the Norbert Wiener Centenary Congress, 1994.* Providence, RI: American Mathematical Society, 1997:301–329.

Pribram KH, Bagshaw M. Further analysis of the temporal lobe syndrome utilizing front-temporal ablations. *J Comp Neurol* 1953;99:347–375.

Pribram KH, Blehert SR, Spinelli DN. Effects on visual discrimination of cross-hatching and undercutting the inferotemporal cortex of monkeys. *J Comp Physiol Psychol* 1966;62:358–364.

Pribram KH, Carlton EH. Holonomic brain theory in imaging and object perception. *Acta Psychol* 1987;63:175–210.

Pribram KH, Douglas R, Pribram BJ. The nature of non-limbic learning. *J Comp Physiol Psychol* 1969;69:765–772.

Pribram KH, King JS, Pierce TW, Warren A. Some methods for dynamic analysis of the scalp recorded EEG. *Brain Topography* 1996;8(4):367–377.

Pribram KH, Kruger L. Function of the "olfactory" brain. *Ann NY Acad Sci* 1954;54: 109–138.

Pribram KH, Kruger L, Robinson F, Berman AJ. The effects of precentral lesions on the behavior of monkeys. *Yale J Biol Med* 1955–56;28:428–443.

Pribram KH, Lassonde M, Ptito M. Classification of receptive field properties in cat visual cortex. *Exp Brain Res* 1981;43:119–130.

Pribram KH, Lennox MA, Dunsmore RH. Some connections of the orbito-fronto-temporal limbic and hippocampal areas of *Macaca mulatta. J Neurophysiol* 1950;13:127–135.

Pribram KH, MacLean PD. Neuronographic analysis of medial and basal cerebral cortex. II. Monkey. *J Neurophysiol* 1953;16:324–340.

Pribram KH, McGuinness D. Arousal, activation, and effort in the control of attention. *Psychol Rev* 1975;82:116–149.

Pribram KH, Mishkin M. Simultaneous and successive visual discrimination by monkeys with inferotemporal lesions. *J Comp Physiol Psychol* 1955;48: 198–202.

Pribram KH, Plotkin HC, Anderson RM, Leong D. Information sources in the delayed alternation task for normal and "frontal" monkeys. *Neuropsychologia* 1977;15:329–340.

Pribram KH, Reitz S, McNeil M, Spevack AA. The effect of amygdalectomy on orienting and classical conditioning. *Pavlovian J Biol Sci* 1979;14:203–217.

Pribram KH, Sharafat A, Beekman GJ. Frequency encoding in motor systems. In: Whiting HTA, ed. *Human motor actions: Bernstein reassessed.* Amsterdam: North-Holland, 1984:121–156.

Pribram KH, Wilson WA, Conners J. The effects of lesions of the medial forebrain on alternation behavior of rhesus monkeys. *Exp Neurol* 1962;6:36–47.

Pribram KH, Weiskrantz L. A comparison of the effects of medial and lateral cerebral resections on conditioned avoidance behavior in monkeys. *J Comp Physiol Psychol* 1957;50:74–80.

Reitz SL, Pribram KH. Some subcortical connections of the inferotemporal gyrus of monkey. *Exp Neurol* 1969;25:632–645.

Roaf HE. *Q J Exp Physiol* 1927;16:379.

Roaf HE. *Proc R Soc B* 1930;106:276.

Rosvold HE, Mirsky AJ, Pribram KH. Influence on amygdalectomy on social behavior in monkeys. *J Comp Physiol Psychol* 1954;47:173–178.

Rothblat L, Pribram KH. Selective attention: Input filter or response selection? *Brain Res* 1972;39:427–436.

SantaMaria M, King JS, Pribram KH, Xie M, Zheng B, Doherty D. Responses of Somatosensory Cortical Neurons to Spatial Frequency and Orientation: A Progress Report. In: King JS, Pribram KH, eds. *Scale in conscious experience: Is the brain too important to be left to specialists to study.* Hillsdale, NJ: Lawrence Erlbaum, 1995:155–168.

Schwartzbaum JS. Changes in reinforcing properties of stimuli following ablation of the amygdaloid complex in monkeys. *J Comp Physiol Psychol* 1960;53: 388–395.

Schwartzbaum JS. Some characteristics of "amygdaloid hyper-phagia" in monkeys. *Am J Psychol* 1961;74:252–259.

Schwartzbaum JS, Pribram KH. The effects of amygdalectomy in monkeys on transposition along a brightness continuum. *J Comp Physiol Psychol* 1960;53: 396–399.

Shainberg, Lawrence. *Brain surgeon: An intimate view of his world.* New York: Lippincott, 1979.

Spinelli DN, Pribram KH. Changes in visual recovery functions produced by temporal lobe stimulations in monkeys. *Electroenceph Clin Neurophysiol* 1966;20: 44–49.

Spinelli DN, Pribram KH. Changes in visual recovery functions and unit activity produced by frontal and temporal cortex stimulation. *Electroenceph Clin Neurophysiol* 1967;22:143–149.

Spinelli DN, Pribram KH, Bridgeman B. Visual receptive field organization of single units in the visual cortex of monkey. *Int J Neurosci* 1970;1:67–74.

Spinelli DN, Pribram KH, Weingarten M. Centrifugal optic nerve response evoked by auditory and somatic stimulation. *Exp Neurol* 1965;12:303–319.

Spinelli DN, Weingarten M. Afferent and efferent activity in single units of the cat's optic nerve. *Exp Neurol* 1966;15:347–362.

Ungerleider L, Ganz L, Pribram KH. Size constancy in Rheusus monkeys: Effects of pulvinar, prestriate, and inferotemporal lesions. *Exp Brain Res* 1977;27:251–269.