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Jan Bures . Jean Pierre G. Changeux

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The History of Neuroscience in Autobiography

Edward A. Kravitz

William Maxwell (Max) Cowan

James L. McGaugh . Randolph Menzel

Mircea Steriade . Richard F. Thompson

Volume 4

Edited by Larry R. Squire

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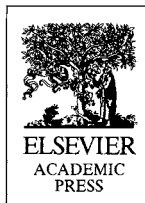
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The History of Neuroscience in Autobiography

VOLUME 4

Edited by Larry R. Squire



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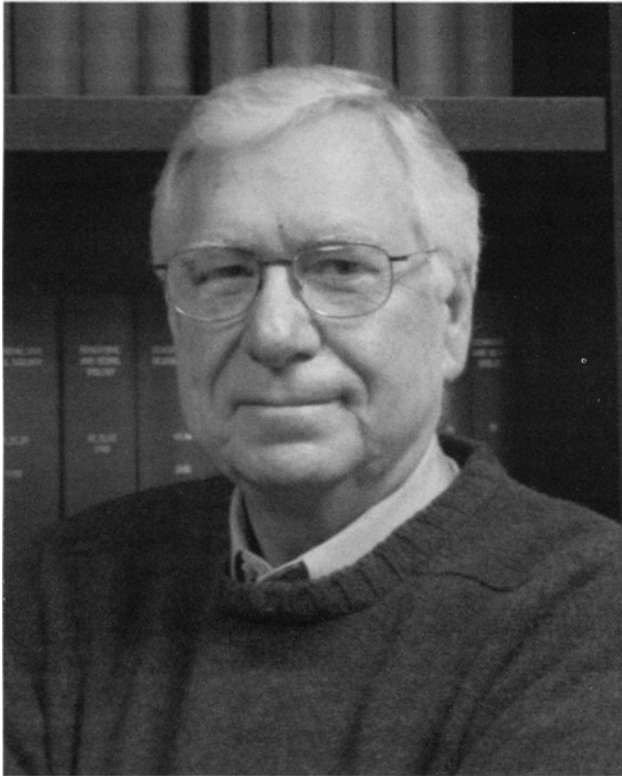
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James E. H. Samp



James L. McGaugh

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Long Beach, California
December 17, 1931

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National Academy of Sciences, USA (1989)
President, American Psychological Society (1989)
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Society of Experimental Psychologists (1991)
American Academy of Arts and Sciences (1992)
UCI Medal, University of California, Irvine (1992)
Foreign Member, Brazilian Academy of Sciences (1994)
John P. McGovern Award, American Association for the
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Mexican Academy of Sciences (2000)
Laurea Honoris Causa, University of L'Aquila, Italy (2001)

James McGaugh pioneered research investigating brain systems mediating the effects of drugs and stress hormones on memory consolidation. He was the first to use posttraining treatments to distinguish between learning and performance effects in studies of drug enhancement of memory. He is also recognized for revealing the role of the amygdala in regulating memory processes in efferent brain regions. He founded the first Department of Neurobiology and Behavior and the first Center for the Neurobiology of Learning and Memory.

James L. McGaugh

I assume that those who discover this chapter, either by chance or on purpose, will, or should, expect to learn about my origins, family background, early experiences, family life, jobs and hobbies, education, friendships, and other kinds of direct or accidental influences that ultimately guided my academic and research career in neuroscience. Much of my story is, of course, based on memory. But, as remembering is a creative act, the story I tell cannot be accurate in all details. Certainly, making retrospective judgments about the causes of critical choices, decisions, and actions that shaped my career is, at best, risky. I will try to tell the truth and most of the truth, but I cannot guarantee that it will be nothing but the truth.

Immigrant Origins

My father, William McGaugh, was a fifth-generation McGaugh in this country. The first William McGaugh, a transplanted Scot from Northern Ireland, arrived in Virginia in the mid-18th century to work on a plantation. We believe that his wife came here as an indentured servant. In 1755 he enlisted in the Virginia Rangers and was then a private in the Revolutionary War. As a veteran, he received a land grant and was one of the first 100 settlers in the area of Nashville, TN. I have wondered about his role in the war as it is well documented that the Scotch-Irish were not fond of their English employers and frequently fought with the British at night and with the Colonists by day. Perhaps it was best that he soon departed for Tennessee. On the move to Tennessee, one of his daughters was killed by Indians near Hickman's Station. My grandfather, Dee Lafayette McGaugh (named after the French General de Lafayette who fought with the Colonies in the Revolutionary War, and the source of my middle name), was a cowboy-rancher-farmer in Texas, Arizona, and California, in that order. When he was young he rode cattle drives on the "Chisholm Trail" several times. I met him a few times when I was young, but did not really know him or know much, if anything, about him at that time. I remember him as a rather distant and forbidding figure. His wife, Nancy Callie Lawrence, was born in Parker County, Texas (a county named after my maternal great-grandfather) in 1873 and died in childbirth when my father was 7 years old.

My mother, Daphne Hermes, was a third-generation immigrant from Germany. Her grandfather, Emil Hermes, emigrated from Prussia to South

Texas in the mid-19th century in order to avoid military conscription. But, perhaps to his surprise, on arrival here he was not able to avoid military service. He fought in the Civil War and is buried in the Civil War Veteran's Cemetery in Austin, TX. There were, of course, many other German emigrants in Texas. At that time, and up to the latter part of the 19th century, German was the most commonly spoken language in the region of San Antonio. My maternal grandfather, James Hermes (source of my first name), was a middle-class, or perhaps upper-middle-class merchant in Beeville, TX. He had a "drayage," or transportation company, that provided taxi and hauling services.

My maternal grandmother was Mattie Parker Hermes. Although the record is unclear, we believe that her family was of English origins. The early to mid-19th century was a very dangerous period in Texas history. In 1836 her 9-year-old second cousin, Cynthia Ann Parker, moved from Illinois to Texas and was abducted by Comanche Indians from a Texas Rangers' settlement now known as Fort Parker. She was raised as a Comanche and eventually married a Comanche chief and had three children. In 1860 Cynthia was discovered and captured by Texas Rangers and was never allowed to return to her Comanche life. She died in captivity in 1870. One of her sons, Chief Quanah Parker, is now one of the most highly recognized of the Indian chiefs of that era. Sadly, he spent most of his life searching for his mother, only to discover her grave. This story is the source of many books and is a well-known part of Texas history. Fort Parker is now a Texas State Park. Yes, the West was wild and my family was part of that wild West history. There is yet more.

My Family

My mother, Daphne Hermes, was born two weeks before the beginning of the 20th century, on the 100th anniversary of the death of George Washington. Her family was sufficiently prosperous to send her to college at what is now Texas Woman's University (TWU) in Denton, TX. I found this to be of special interest only after I learned that at that time only approximately 56,000 women out of a U.S. population of approximately 92 million people attended college. When I was invited to lecture at TWU a number of years ago, they gave me a copy of her college transcript. She should have devoted more study time to her chemistry course. When she was a senior in high school, her father, James Hermes, was murdered. He had received a contract for hauling materials required for the construction of a new post office. The supervisor of the excavation project, R.B. Brown, confronted him at the construction site and shot and killed him. Although his killer was convicted of murder, the conviction was overturned by the U.S. Supreme Court in a decision written by Justice Oliver Wendell Holmes (*Brown v. United States*, May 16, 1921, pp. 501–502). The following was part of the court record: "The

Supreme Court... cannot disregard the considerable body of evidence that the shooting was in self-defense, though there was evidence that the last shot was fired after the deceased was down" (p. 501). It seems that the fact that my grandfather carried a knife made the case for murder less clear-cut—more wild West.

My father was born in Azle, TX, near Ft. Worth. He attended Wesley College for three years, but his studies were interrupted by an "illness." During World War I he was deferred because of his illness and went to Arizona where he worked on the Porter Ranch (the largest in Arizona) where my mother's uncle (twin brother of her mother) was the ranch foreman. There in discussions with her uncle, he learned about my mother and wrote to her when she was a college student. They continued their correspondence after she returned home and got a job as a Spanish teacher in Skidmore, TX. My father then started a bakery (Blue Ribbon Bakery) in Wickenburg, AZ, and then, or soon after, became a Methodist minister. My parents were married in 1920, and for the next 20 years they moved to a series of small towns in Arizona as my father was transferred by the church organization. The hazards in those days included pistols that my father required the churchgoers to deposit at the entrance to the church and occasional bank robberies committed by riders on horseback.

I was born in Long Beach, CA, in 1931, the youngest of four children (two brothers and a sister) at the dawning of the Great Economic Depression. At Long Beach, my father was on a leave of absence from his church position because of yet another illness. The next year our family returned to Arizona, where we lived for several years in Claypool, a small copper mining town in the mountains east of Phoenix. As the mines were closed because of the economic depression, there was no employment. We survived on barter of milk, eggs, and vegetables, as well as a very small salary from the church organization. My first memories are of events that occurred during those years. We then moved to Nogales, AZ, a small town on the border of Mexico. Our home was perhaps a few hundred yards from the border. Reading was highly valued by my family, so we had a home full of books. Also, the city library was directly across the street from our home.

When I was seven years old I became ill with brucellosis (also called "undulant fever" or "Malta fever"), a serious infectious disease that I probably got from drinking unpasteurized milk. As I was confined to a bed and thus unable to go to school (the second grade), my mother became my teacher. It was there that her Prussian heritage emerged. Unceasingly and mercilessly, I was drilled daily on spelling, arithmetic, and reading. Also, as I had nothing else to do, I read whenever I was not being given my lessons. I must have read dozens of books, mainly Western adventure stories. I dreamed of being a cowboy and acquired toy pistols and rifles as birthday and Christmas gifts. I also learned Spanish from our Mexican maid who spoke no English but spent much time with me. In many ways it was a horrible time in my life.

I was alone much of the time, had no playmates, and was constantly confined to my bed. My only contact with the outside world was the view from the front window. My parents placed my bed there so I could at least see something of the outside. My worst memories were those of watching neighbor children play outside in the snow (yes, it snows in southern Arizona). But, it was not a wasted time. It taught me something about personal adversity and challenge. It also prepared me academically for many subsequent years of school. After I was ill for about a year, the world's first miracle drug, a sulfa drug, became available. I was told that I was a subject in an early clinical trial. If that is true, then I certainly was not in the placebo group. My illness vanished, and I returned to school within weeks of receiving the drug. I skipped the second grade and joined the third grade class. Daniel Bovet, a Swiss pharmacologist who was then at the Pasteur Institute, received the Nobel Prize in 1957 for the discovery of sulfa drugs (as well as antihistamines and muscle relaxants). There is more to this story below.

There were also many happy and interesting times in Nogales. Much of our family life centered on church activities. Our summer "vacations" were church camps located at closed and abandoned copper mining company facilities in nearby mountains. In Nogales, our next-door neighbor was the head of the German Consulate. As Nogales was a major commercial inland port of entry, he was responsible for visas and other matters of international German commerce. He and his family organized magnificent fireworks displays on the Fourth of July, and their home was warmly and beautifully decorated at Christmas time. Unfortunately, as we learned only much later, he was also the head of the German spy network for all of Arizona and California during World War II. Our highly respected Japanese dentist was the head of the Japanese spy network for the same area.

In 1940 my father was transferred to Arlington, CA, which is now part of the city of Riverside. It was a major promotion. My oldest brother, Bill (yet another William McGaugh), was in college. My other brother, Dana, was completing high school at the age of 15, having skipped two grades of school because of his extraordinarily precocious intellectual ability. My sister, Daphne, was also an outstanding student. She was the class valedictorian at one of her graduation ceremonies. Thus, my siblings set high (perhaps excessively high) standards for me. But, I was also an excellent student for a number of years, perhaps at least partly because of the "Prussian" education I had received from my mother. School was very easy for me. Later on when I was in high school, I found that it had been much too easy, as I had formed no consistent study habits.

One year after moving to California my father became seriously ill again. This time, he was *very seriously* ill. In the fall of 1941 he committed suicide. The illness that he suffered from on and off for so many years was no doubt bipolar depression, but nothing was known about depression at that

time. His suicide was a catastrophic event for our family. There was huge emotional loss, public (and personal) shame of a suicide of a very prominent member of the community, and an abrupt family financial crisis. Our home and income had always been provided by the church. We were quickly evicted. We had no savings and no source of income. My mother's Texas teaching credentials were not honored in California. I was sent to live on a ranch with relatives until my mother managed to get some temporary financial help and found a house to rent. I then quickly became an entrepreneur. I became a shoeshine boy and sold newspapers on a street corner. The outbreak of World War II (four months after my father's death) was especially good for my business. I received a penny for each paper and sold more than 100 papers when Pearl Harbor was bombed—my first dollar. For me, at the age of 10, war was not Hell. It provided economic salvation.

Within a few months, the nearby countryside foothills were filled with temporary army camps crowded with soldiers confined to tents before they were shipped off to the Pacific war areas. It was a perfect condition for a small-time (and small) war profiteer. I bought needles, thread, matches, candles, candy bars, and other items prized by the soldiers and sold them at a large but acceptable markup. After all, money would be of no use to them where they were headed. More formal and permanent army bases were also established nearby, and my mother was soon able to get a job as a secretary at one close to our home. I also raised and sold rabbits, as meat was rationed during the war. Thus, World War II not only brought an end to the Great Depression, it provided a solution to our family's personal economic crisis. I then got a somewhat more secure job as a newspaper delivery boy and made the daily bicycle trips, a 17-mile route, on dirt roads. It was not much fun during the winter rainy season.

Although my life was difficult during the first several years after my father's death, I think that I learned important lasting lessons. I learned that difficulty does not mean disaster. I also learned that good things did not come my way by chance. My personal initiative was critical. It still is, of course.

Because I was raised in a religious family, I should perhaps mention, at least briefly, the role of religion in my life. I don't recall any deep theological influences. If there were, they were from the Protestant New Testament of the Bible—no hellfire and brimstone. I think I simply learned from my family and my experience in church programs that it is very important to help others, particularly those in need, and to try to make the world a better and more decent place. "*Do unto others as ye would have them do unto you,*" was the minimal condition. The other influences were simply matters of custom. I attended church by requirement when I was young and then by habit, until my agnostic view developed gradually and crystallized in my early years of college. It seemed to me very highly unlikely that an Almighty unwilling or unable to prevent my grandfather's murder and my father's

suicide, not to mention World War II and other catastrophic world events, would or should have any influence on the more minor and routine matters of daily life. Perhaps the tasks of managing the physical universe and guiding evolution preclude any attention to other more minor matters. In any case, I decided that I would look elsewhere for the causes of and solutions to life's challenges and mysteries.

Early Education and Interests

So far, I have not mentioned science, and certainly not neuroscience. No one in my family had any interest in or (as far as I know) knowledge of science. Science was not taught (as I recall) in my primary or middle school. In high school I took the courses in mathematics, chemistry, and physics required for college admission. But, the courses were dull and uninspiring. They were mainly demonstration and drill. There was certainly no spirit of inquiry or wonderment. In school, my main interests were in drama, literature, and music. The teachers who had the greatest influence on me were my drama teacher, Mr. Chester Hess, and my band and orchestra teacher, Mr. Lester Oakes. I was in many school plays (as well as community theatre) and played clarinet and bass clarinet in the school concert band, marching band, and orchestra (that was also the community opera orchestra). In my senior year I was the band commander and Captain of the ROTC band and was a member of the All Southern California Concert Band.

My other major interest was in bicycle and automobile mechanics. Out of financial necessity, I created working bicycles out of broken ones. I made a "motor-bike" when I found a gasoline washing machine engine and attached it to my bike. It was probably the most dangerous 40 mile per hour vehicle in the history of motor-propelled vehicles. When I was in high school my brother Bill was an office manager in a small manufacturing plant and managed to get me an after-school job there. A very kind machinist in the plant loaned me some money to buy a better engine, taught me how to weld, and helped me modify my bicycle so that it looked and drove like a motorcycle. It was modestly less dangerous than the first model. I then found an old rusted car (1929 Nash coupe) that I bought for \$40 and nursed to semi-health. A previous owner had painted "Bonnie Blue Eyes" on the visor above the windshield. Bonnie Blue Eyes was my chariot for several years. Keeping it running in semi-health required that I learn how to repair and replace transmissions and engines and learn about carburetors, generators, etc. In the process I also acquired several other cars that I repaired and sold or pirated for parts. My family was absolutely convinced that I would become an automobile mechanic. I probably thought that as well. Certainly, it never crossed their minds or my mind that I would eventually choose a career in science. There were no signs in my early education, experiences, or interests that pointed in that direction.

College Education

When I was in high school I didn't think much about college. One of the great advantages of living in California was that the highest quality college education was provided free to all qualified resident applicants. The thought of applying to a private college or university never entered my mind. If it had, it certainly would not have remained there for long, as the only money that I had available was what I earned each previous week or month from my part-time jobs. My brother Dana and my sister had both attended the University of California, Berkeley. In 1949 I applied to and was admitted to Berkeley, but decided to go to San Jose State College (now a University) primarily because it had a highly recognized drama department and a good music department. I don't recall it being a difficult decision to make. I guess I simply wanted to continue studying in the areas that interested me most in high school. So, I took a bus to San Jose and enrolled as a drama major and music minor. I found a part-time job loading soft-drink trucks each evening and rented a room. There was, as I noted above, no tuition and there were no fees, so my only expenses were living expenses. Because play auditions, rehearsals, and performances were in the afternoons and evenings, I had to get a different job. So, I worked in a bakery, starting at 3:00 AM daily. I was in plays, played in the concert band, and sang in the chorale. I studied opera and conducting and was elected to the music honor society. My interest in drama, however, waned. The department was production oriented and gave little attention to the literature of drama, which was my major interest. So, I sampled other areas, including cultural anthropology, sociology, and biology. Biology was descriptive, dull, and disappointing. During my sophomore year I discovered psychology, and it seemed like a good fit for my interests. I kept drama, speech, and music as minor areas.

During my first few weeks in San Jose I met a beautiful and charming young woman named Carol Becker at a church youth group. Becky (her nickname) and I dated for several years and were married in 1952. My name changed from "James," the name I had always used, to "Jim," as Becky said I was Jim and who was I to argue with her about a trivial thing such as a name change? I also fell in love with Becky's parents, Ruth and George Becker, two of the kindest, most decent, understanding, and supportive people I have ever known. They were ideal "in-laws" and, eventually, absolutely wonderful grandparents.

Shortly before I started college, a close friend of our family who knew me well warned me that my high school study habits (or lack thereof) would get me flunked out of college in one term. So, with that severe warning, I studied hard and got excellent grades during my first year. In addition to studying, working, and dating, I managed to buy an old abandoned car that needed serious repairs and put it in running order. At the end of the first year, in June, I drove my car down the Pacific Coast Highway on my way

home to Riverside to visit my family. The highway was jammed with a series of military convoys. As I had no radio in the car, it was only later that night that I learned that the Korean War had started. Very soon I was issued a draft card and learned that although I could get a student deferment, the draft boards were drafting students into the army on the basis of their college grades—the poorer the grades, the greater the chance of being drafted. I did not neglect this important bit of information. I decided immediately that I had to receive only “A’s” in my classes from then on. I did, and graduated three years later at the top of my class with highest honors.

One can certainly question the social policy underlying the decision to have college grades influence eligibility for the draft. But, it is not clear to me what policy is best for selecting 18-year-old boys and girls/men and women to fight in our wars. The Korean War is often referred to as “the forgotten war.” For those who have seen either the movie or television episodes of “MASH,” it would be easy to get the impression that the Korean War might have been some fun mixed in with some occasional battle casualties. At least 52,000 U.S. soldiers were killed in that war and thousands more were seriously wounded. For many of us of military age at that time, the case for U.S. involvement in the Korean War was considerably less convincing than was the case for our prior involvement in World War II. I was certainly not alone in wishing to avoid being sent to Korea as a ground soldier. But the fact that I was not drafted into the military made the issue moot.

When I changed my major from drama, I quit my early morning job in the bakery and then had a series of unpleasant part-time afternoon jobs. I eventually got a job on a chicken ranch just outside of town and worked there for a year. I ate a lot of chicken and eggs that year. I also got a job as a church choir director to provide some additional, much-needed income. Becky’s dad did commercial grain harvesting each summer, and for two summers I worked for him. On some days I worked on the self-propelled harvester, sewing the sacks after each was filled with freshly harvested grain, and on other days I drove a truck alongside the harvester, making every effort to make sure that the grain spewed into the back of the truck and not on to the ground. Eventually, I was able to get a full-time job as a psychiatric technician at Palo Alto Veteran’s Hospital. These were the final years *before* the introduction of the first antipsychotic drugs (reserpine and thiorazine). So, I interacted with very ill, unmedicated mental patients on a daily basis. Rather, it was on a nightly basis, as I worked the graveyard shift from midnight to 8:00 AM. There were also many prefrontal lobotomy patients there, as the popularizer of prefrontal lobotomies, Walter Jackson Freeman, was still performing those highly questionable operations there at that hospital.

Some years later I was able to draw on my experiences at that hospital in my classroom teaching. That experience also helped forge my scientific interest in the biological bases of behavior. It seemed very clear to me that those patients had serious brain problems that could not be cured by the “talk”

therapies popular at that time. It was also clear that prefrontal lobotomies provided no cure. The psychiatric technician position was a perfect job for me because it fit well with my psychology major and allowed me at least 6 hr each night for studying. I don't recall clearly how I managed to find time to attend classes, sleep sometime during the day, and hold evening choir practices, but I also don't recall it being a critical or difficult problem. Besides, there was the omnipresent Draft Board to think of.

When I discovered psychology it was, for me, much like the change from black and white to Technicolor in the film "The Wizard of Oz"—a world of wonderment. It was in psychology classes that I first learned about the excitement and challenge of science and found my academic home. In classes on experimental psychology, I learned about developing hypotheses and selecting appropriate methods of inquiry. I learned that hypotheses, however clever and integrative, must, ultimately, be potentially falsifiable. A course in philosophy helped. The required two years of statistics significantly aided that understanding. I learned about the fundamental difference between correlation and causation. Also, I learned a lot of what was known about brain and behavior in courses in physiological psychology, as well as required courses in anatomy and physiology. Robert S. Woodworth's *Experimental Psychology* (1938) and Ernest Gardner's *Fundamentals of Neurology* (1948) became my "bibles." Although Woodworth's book was published in 1938, it was only 12 years old when I first got a copy, and four of those years were the years of World War II when the most prominent and productive experimental psychologists worked exclusively on studies related to the war effort. Thus, it was still the most up-to-date and comprehensive summary of research in experimental psychology.

As I also served (for very modest pay) as a teaching assistant in several courses, including Experimental Psychology and Statistics, I had to know the content of those classes well in order to prepare and grade examinations. Edward Minium was my most demanding and inspiring teacher. Edward Chace Tolman was his Ph.D. thesis advisor when Minium was a graduate student at UC Berkeley. Recently, Minium endowed a lectureship at Berkeley in honor of another one of his professors, Ed Ghiselli. I was honored to be invited to give the inaugural Ghiselli lecture and was further honored to have my undergraduate teacher, Edward Minium, who had long been retired, attend my lecture.

Joseph Cooper was another very influential teacher. His course in "Theories of Learning" firmly established my interest in this area. I also took courses in theories of personality and theories of abnormal psychology. In all of these courses, the various views were presented as equally valid alternatives. That bothered me. As the various theories were at odds with each other on many issues, why weren't the issues resolved? In the area of learning theory, certainly Thorndike, Guthrie, Tolman, and Hilgard had very different views about the causes and nature of learning. Which ones

were the correct ones? Better still, which *one* was the correct *one*? I wanted to know that. The textbooks all adopted ecumenical positions, leaving the impressions that the different views were equally valid. In the area of personality and abnormal psychology, I readily dismissed the then enormously popular Freudian theory simply because there was no experimental evidence to support it. The beauty of Freud's ideas, I decided, was also their fatal flaw: no matter the finding, there was always an alternative explanation within the theory. I did not, and do not, share the commonly held belief that Freud's ideas were among the most important scientific ideas of the 20th century. In fact, as I indicated, I don't think they should even be regarded as scientific ideas. They may have been good ideas for bad novels, but they were bad ideas for good science.

At the end of my third year at San Jose it was clear that I would plan to go to graduate school and aim for an academic career in experimental psychology. I wanted to help discover answers to important and as yet unanswered questions concerning the nature and bases of behavior. I did not think at that time that there might also be many important, but not yet asked, questions. Stanford University is about 20 miles from San Jose and Berkeley is about 45 miles. In the fall of 1952 I applied to both of their graduate programs in psychology and was admitted to both. I chose Berkeley because I was offered a teaching assistantship there. Also, I think my prior admission as an undergraduate as well as the fact that my brother and sister had attended Berkeley probably influenced my decision. I knew that both departments had very distinguished faculty, but did not know enough to make a judgment about which department would be best for my background and interests. Whatever the reasons for my choice, I chose well.

In the spring of 1953, just before I was to graduate, I learned that my student deferment from the military draft ended with my graduation. There was to be no extension of my deferment to allow continued study in graduate school. I also learned that I could join the Air Force as an officer (for an additional year's commitment) as an alternative. So, I enlisted in the Air Force. I had my physical examination at a local Air Force base and prepared to become a second lieutenant in the Air Force that summer. Events in late spring and summer altered those plans. On July 27, 1953, a cease-fire agreement was signed in Korea and the Korean War ended. I received a letter from the Air Force telling me that my enlistment was terminated without any military benefits. I was, of course, very happy with the alternative benefits of going to graduate school.

Graduate Studies at the University of California, Berkeley

Becky and I moved to Berkeley in the fall of 1953. She got a position at the Radiation Laboratory (now the Lawrence Laboratory), located in the

hills above the campus, and I started graduate studies and began to serve as a teaching assistant. The graduate program consisted of a "proseminar," a first-year seminar that seemed to be designed only to eliminate weak graduate students; "Prelims," a two-day set of comprehensive exams on *all* areas of psychology given in the second or third year; submission of a Ph.D. thesis; and a final oral exam. The program was very clearly designed, either by plan or by accident, for the highly self-motivated student. When I arrived there many of the graduate students were World War II veterans who enjoyed graduate student life and were in no hurry to complete their degrees. The average number of years for completing a Ph.D. at that time was about eight or nine years. I immediately decided that I was on a four-year program.

My first teaching assistant assignments were to work with David Krech and Edward Tolman. Krech, who later became one of my most supportive graduate advisors and had a very significant influence on my career, was, on my arrival at Berkeley, a crusty, intimidating grouch. So, I initially avoided him whenever possible. So did most of the other graduate students. When I approached Tolman for the first time, he invited me to go off campus for a cup of coffee to get acquainted. As he was without doubt one of the most important and influential psychologists of that era, I was enormously honored just to meet him.

Tolman had just returned to Berkeley after four years of exile at the University of Chicago and Harvard. On June 14, 1949, the Regents of the University of California mandated that all faculty were to sign a loyalty oath. Tolman refused to sign, became a leader of the University of California faculty non-signers, and was fired. He also encouraged younger faculty to sign and keep their jobs. He was able to return to Berkeley in 1953 after the special loyalty oath was declared unconstitutional. Tolman and all of the University of California faculty members who had refused to sign the Regents' loyalty oath were reinstated with full back pay.

On the first day of the undergraduate class he was teaching, and for which I was his teaching assistant, Tolman asked me to walk to class with him and said that he had a special favor to ask of me. It was a great moment in my personal history. The great Tolman himself asked me for a favor! He then handed me his pack of cigarettes and asked me to take them and sit in the back of the class, as he was trying to quit smoking. He said that at some time during the class he would probably walk up the aisle to me and ask me to give him a cigarette. My assignment was to tell him, "No." We played out that ritual during each class, and, of course, each time he asked I meekly handed him his cigarette.

Tolman was an interesting (to me), but rather unsystematic lecturer. But his research and writings influenced me enormously. In his book *Purposive Behavior in Animals and Men* (Tolman, 1932) and in many theoretical and experimental papers, he made what seemed (and still seem) to me to

be three fundamental observations. First, behavior consists of acts and sequences of acts, not *merely* muscle movements and glandular secretions. Second, learning consists of acquiring cognitive information about “what-leads-to what,” enabling us to adapt to changes in experiences. Responses are “docile,” that is, changeable according to the specific circumstances. Third, although rewards (reinforcements) influence what we do and thus, indirectly, what information we acquire, rewards are not essential for learning. These observations were supported by evidence from a variety of original and clever studies of “latent learning” (learning by experiences without explicit rewards) and “place vs. response.” Underlying all of these conclusions was his fundamental distinction between learning and performance. Tolman was the first to emphasize that learning is not directly observed, but is *inferred* from performance. As a great many factors can influence performance, the difficult but necessary task is that of determining the contribution of learning to the changes observed in performance. Tolman’s observations and inferences profoundly influenced my thinking at the time and have explicitly and consistently guided my own research and my interpretations of research findings. Despite his confrontation with the Regents of the University of California, he received an honorary degree from Berkeley in 1959, a few months before his death. Three years later the psychology building was named “Tolman Hall” in his honor.

Although all of Tolman’s findings and interpretations were readily available from his writings as well as from many textbooks, my understanding of it was increased by participating, each term, in Tolman’s “Animal Seminar.” This was a weekly evening seminar attended by many faculty, including David Krech, Mark Rosenzweig, Al (Donald) Riley, and Leo Postman, as well as visiting faculty, including, in different years, Jeff Bitterman, Harry Harlow, Wolfgang Köhler, and Donald Hebb. A few students (usually three or four) also attended. It was a heady experience listening to the intense, heated, and complex discussions of the latest theoretical and experimental controversies. For me it was, during the first few months, like being transported to a foreign country without knowledge of the language. But, I gradually learned the language and eventually came to regard participation in this seminar as one of the most important opportunities of my graduate experience. The graduate students at Berkeley at that time included, among others, John Garcia, Robert Bolles, and Lewis Petrinovich. It was an outstanding group of bright, original, and industrious graduate students who subsequently made very significant contributions to our understanding of the nature and bases of behavior. As they were slightly older (and very much wiser) graduate students, I turned to them for advice, support, and, as I discuss below, research collaboration.

For the graduate students, one of the most important events of each year was the big party at which we presented a musical comedy. Petrinovich and I wrote, produced, directed, acted, and sang in those ribald reviews. All

graduate students attended and many performed. Although most of faculty usually attended, many of them thought that our musical sketches poking fun at the faculty and the graduate program (and, sometimes, the graduate students) were in bad taste. We thought that the faculty were sometimes too "thin-skinned." On reflection, I think we were both correct.

In my second year at Berkeley, Krech and Rosenzweig, together with Edward Bennett, a young biochemist working in Melvin Calvin's laboratory, initiated a "Brain Chemistry and Behavior" research project. The research focused on the role of acetylcholine in behavior using acetylcholinesterase as the index of cholinergic activity. I was fortunate to be asked to work on the project and eventually to investigate, as part of my Ph.D. thesis, the relationship between acetylcholinesterase activity and maze learning in rats. I did the biochemical assays (using a newly invented and only marginally cooperative automatic pH recorder) in Bennett's facilities in Calvin's laboratory and participated in Calvin's weekly lab seminar. I was also fortunate to get a very well-paying research assistantship. As the work of Calvin's lab focused on photosynthesis, I understood only my own presentations in that seminar. A few years later Calvin received the Nobel Prize for his work on photosynthesis.

Although my graduate work was very exciting and satisfying, another much more important and exciting event occurred in my second year at Berkeley. Our son, Douglas, was born.

Krech, Rosenzweig, and Bennett also held a weekly seminar on brain chemistry and behavior. As a project for the seminar, my graduate student colleague Lew Petrinovich and I decided to do a comprehensive review of all published studies of drug effects on learning. It was difficult detective work because there was, of course, no Internet, no PubMed or any other bibliographic aid, and no copying machines. We found a total of approximately 100 references, including many reporting the effects of vitamins. After presenting our findings at the seminar, we continued to revise and update our review and finally published it a decade later when we decided, quite arbitrarily, that it either was or it soon would be impossible to summarize the findings in this very rapidly growing research area in a single review paper (McGaugh and Petrinovich, 1965).

In searching through old journals, we discovered a paper by Karl Lashley (1917) reporting that strychnine administered to rats before daily training trials improved rats' maze learning. This was of particular interest because it was the only report of drug enhancement of learning. Additionally, we found some evidence suggesting that strychnine inhibited acetylcholinesterase activity. So, we decided to replicate Lashley's study. We built the maze, acquired rats from the vivarium, and conducted the study. We were delighted to find that we replicated Lashley's results. Harry Harlow, the Editor of the *Journal of Comparative and Physiological Psychology*, was not delighted. He rejected the paper in a multipaged letter that included, among other things,

the advice that publication of these findings might adversely affect our research careers. But, the main reason given for the rejection was that he did not believe the findings. As Harlow put it, "The results of your paper upset a fundamental pharmacological assumption that no drug improves behavior." We eventually published the paper in a different journal (McGaugh and Petrinovich, 1959).

Our paper was rejected for the wrong reason. In it we suggested that strychnine "... *facilitates learning by increasing the efficiency of transmission in the central nervous system*" (p. 102). But, our findings, as well as those of Lashley, only indicated that maze *performance* was improved. And, as Tolman taught us, learning is not observed, but is inferred from performance. As strychnine might influence rats' maze performance by affecting processes other than those underlying learning, our interpretation of the findings was, at best, only speculation. I decided to pursue this problem further as part of my Ph.D. thesis research. More specifically, I decided to tackle the learning-performance problem. The major clues came from an experiment by Carl Duncan and a book by Donald Hebb, both published in 1949. Duncan (1949) reported that electroconvulsive shock administered to rats after training produces retrograde amnesia. These findings supported Müller and Pilzecker's "Perseveration-Consolidation Hypothesis" proposed a half-century earlier (1900), which was largely ignored. In his now well-known book, *The Organization of Behavior*, Hebb (1949) proposed that reverberatory neural activity initiated by training was essential for establishing synaptic connections underlying learning. These findings and theoretical speculation suggested, to me, the possibility that a drug might facilitate learning by acting on posttraining neural activity initiated by training. Thus, I reasoned, it should be possible to enhance learning with a drug administered *after* training, during the postlearning period of memory consolidation. This procedure, if effective, would solve the learning-performance problem, as the "enhancing" drug would not be in the animals either during the training or the subsequent testing for memory of the training. I decided to test this hypothesis.

With enormous excitement (and an equal amount of anxiety), I told Krech of my reasoning and my plans to study the effect of posttraining drug injections. He responded with less enthusiasm than Harlow had expressed for our rejected strychnine paper. Fortunately, Krech soon went off to Norway for a sabbatical leave and my other research advisor, Rosenzweig, was more enthusiastic. So, as soon as I could get some rats, I repeated the previous experiments investigating the effects of strychnine on maze learning, but gave the strychnine (or saline) injections *after* each daily training trial. The drugs were coded so that I did not know which animals received the drug and which received saline injections. When I broke the code after the experiment was completed, I was astounded, delighted, and extremely elated to find that the post-trial strychnine injections enhanced the rats' maze learning. It was

clearly one of the most euphoric moments in my entire scientific career. The drug-effect learning-performance problem appeared to be solved.

San Jose State College Reprise

It was at about this time that my self-imposed, four-year Ph.D. plan required urgent action. I informed my advisors that I would be completing my thesis at the end of the year and would like to have a university position. In those days, all faculty recruiting was in solid secrecy. Jobs at the best universities were not advertised. Thus, I was simply informed that I would receive offers of assistant professor positions from Cornell University and Ohio State University. I received the offers: \$5000 salary plus \$500 moving expenses. There were no invitations for interviews or visits. Although those were excellent universities with outstanding departments of psychology, they were in the wrong part of the country. My roots, as well as Becky's, were firmly in the West. As I was not offered any positions in the West, I contacted faculty friends at San Jose State and asked if there might be a position for me there. There was. So, Becky, Douglas, and I moved to the San Jose area in 1957, and I was appointed to my first faculty position; Assistant Professor of Psychology at a higher salary (\$5700) than that offered by the other universities. There was, however, one small immediate problem. Completion of my thesis research was delayed because of a problem in the rat colony at Berkeley. As all of the rats in my experiments were bred in that colony, I had to wait several months in order to have the rats needed to complete my thesis research. I completed the research during the summer after moving to San Jose, wrote the thesis during that year, and handed in the thesis in June 1958, one day after the deadline for receiving my Ph.D. that year.

San Jose State College emphasized teaching, almost exclusively. Research was optional, but not encouraged or supported. I was assigned to teach introductory psychology, social psychology, and a graduate course in perception. I was never given a chance to teach courses in learning or physiological psychology. To compensate for this restraint, I developed an undergraduate honors seminar and started an undergraduate research opportunity program that has continued for over four decades. The teaching "load" was four courses per term. After several years I was able to get the honors seminar included as one of the four courses. The main consequence of the seminar was that I was able to find the very best students and invite them to help me in my research program.

At San Jose, I first built a laboratory in the garage at our new home and then moved it to a storeroom where the department kept its office supplies. That caused many well-justified complaints, as that room was not air conditioned, had no windows, and was across the hallway from departmental and faculty offices. After a lot of searching, I found two large abandoned basement rooms in the oldest building on the campus (San Jose State was

established in 1857) and turned them into a laboratory. I moved several mazes from Berkeley and made many more. As a graduate student I had acquired a lot of carpentry experience by making mazes and other equipment. We made animal cages out of wire and used aluminum baking pans for the cage bottoms. All of these activities were fun, rather than work, because I enjoyed building the laboratory equipment. I obtained unused rats from Berkeley and talked my department into buying food for the rats. I then started a very active research program investigating further the effects of posttraining drug injections on memory for different kinds of training. A first study found that, like strychnine, the GABAergic antagonist picrotoxin enhanced memory consolidation (Breen and McGaugh, 1961). We also found that posttraining injections of a strychnine-like compound obtained from a lab in Italy enhanced "latent learning" (Westbrook and McGaugh, 1964). Rats given posttraining injections after each non-rewarded trial made fewer errors than saline controls when a reward was subsequently introduced. This finding remains as the strongest evidence that a drug can enhance learning without directly affecting performance. So, these findings confirmed and extended my initial report that posttraining drug injections can enhance memory and strengthened the conclusion that the effects were due to facilitation of memory consolidation. But, the evidence for memory consolidation based on ECS came under attack from several sources. One suggestion (Coons and Miller, 1960) was that the treatment was simply a punishment. A simple experiment using what we now call "inhibitory avoidance" in our lab challenged that interpretation (Madsen and McGaugh, 1961). Animals given foot-shock punishment on stepping from a platform to the floor of a cage showed good retention of the shock the next day by remaining on the platform. Rats given the foot shock followed by an ECS treatment readily stepped off of the platform on the subsequent test trial. Clearly, the ECS treatment did not provide additional punishment. Because of the initial rejection of the first strychnine paper, I prepared manuscripts based on all of these findings, but did not immediately submit them for publication. I'll return to that issue below.

The research environment at San Jose State (or lack thereof) was abysmal. As the course in social psychology remained my primary teaching responsibility, I accepted an invitation to co-author a textbook in social psychology with my former undergraduate teacher, Joseph Cooper. However, my main interactions were with Karl Pribram and Tony Deutsch at Stanford. Both were very interested in my research findings and very supportive of my research program. We had a great many meetings and discussions. I owe a great deal to them for keeping my morale up under my less than optimal conditions. During those years I kept an active research program and received an NIMH research grant, the first research grant ever awarded to anyone at San Jose State College. Because of this achievement I was interviewed on the local television station—my first television appearance. The

total amount (direct costs) for three years was \$29,500 and included funds for a summer salary. The other very good news for Becky and me was the birth of our daughter, Janice, in 1959.

At the beginning of my fourth year at San Jose, Krech and others at Berkeley nominated me for a National Academy of Sciences-National Research Council (NAS-NRC) Senior Postdoctoral Fellowship. I was very excited to learn this. I decided that if I received the fellowship I would ask Daniel Bovet if I could work with him in the Istituto Superiore di Sanità in Rome, Italy. Krech had told Bovet of my work and he had sent me the strychnine-like drug that we used for our latent learning experiment. Bovet had developed a research program investigating the effects, on learning and memory, of drugs newly synthesized at the Istituto. As I noted above, Bovet received a Nobel Prize in 1957 for his prior work at the Pasteur Institute where he pioneered the discovery of many important drugs, including the miracle sulfa drug that cured my brucellosis when I was a child.

I was invited to be interviewed for the fellowship, but was dismayed to learn that Harry Harlow was to interview me. I had hoped that one of the other members of the committee, Karl Pribram or Frank Beach, would do the interview. When I met with Harlow I took along several of my unsubmitted manuscripts. Although he was tough and grumpy, he liked my recent findings, the interview went well, and Harlow recommended me for the NAS-NRC fellowship, which I was granted. He also accepted the papers for publication in the *Journal of Comparative and Physiological Psychology*. Also, 20 years later, Harlow and I co-authored a textbook in psychology (with Richard Thompson; Harlow, McGaugh, and Thompson, 1971). As soon as I learned that I had received the fellowship, I wrote to Bovet to ask if I might come there for postdoctoral study. His response appeared to be written in French, but, although I could read some French (I had had to pass French and German language exams as part of the requirement for my Ph.D.), I couldn't understand whether he had said "yes" or "no" to my request. So, I took a chance and wrote to him to thank him for inviting me to come to his Institute for postdoctoral study. Later, when I was working with him, I found out that he routinely and liberally mixed French with Italian in both his speaking and writing. I noticed that no one ever brought that to his attention.

Rome, Italy

In September 1961, Becky, Doug, Jan, and I took a plane from San Francisco to New York, where I was a speaker in a symposium on memory. While we were there, Becky and I spent most of our time deciding whether I should return to San Jose after the year in Italy or accept one of three offers I had recently received from other institutions (two universities and a research institute). Just before we left New York, I sent a telegram to Robert Leeper and Fred Attneave at the University of Oregon, accepting their offer of a

position there in the Department of Psychology. We then boarded the new ship, the *Leonardo da Vinci* (sister ship of the “unsinkable” *Andrea Doria* that sunk near the island of Nantucket in 1956) for an 11-day cabin class trip to Genoa. We picked up a new Volkswagon bug and drove south to Rome. All of these experiences were highly novel and very exciting for a family from the far West.

My postdoctoral fellowship provided my university salary, all family travel expenses, private school tuition for Doug, and travel expenses for me to visit European research laboratories. It did not pay for our family dog’s flight to Rome. We had left our dog, Cisco, with friends, but as they informed us that he was despondent and had stopped eating we decided to send for him. In addition to his airfare, we had to pay for his breakfast in London on the way to Rome. At the institute in Rome, Bovet very graciously provided me with a laboratory, a large corner office, and a technician. As I knew no Italian, except for some Italian arias that I learned in college and two or three phrases that I memorized from listening to language records, I had to learn some Italian quickly. That effort was greatly aided by the technician who did not understand or speak any English. Bovet very warmly welcomed me to his laboratory and arranged for us to meet frequently. He was very interested in my use of posttraining drug injections for studying memory enhancement so that procedure was added to their experimental program. I collaborated with Enzo Longo in studies of the effects of drugs on behavior and EEG activity in rabbits, and I had many discussions about drug influences on avoidance conditioning with Giorgio Bignami, whose laboratory was next to mine. I also attended Bovet’s weekly seminar, listened in my slowly improving Italian, but spoke mostly in English. The fact that all of the scientists in the laboratory spoke English certainly did not aid my efforts to learn Italian. During the year I took trips to visit the laboratories of Holgar Hyden in Sweden, Larry Weiskrantz in Cambridge, and Aubrey Manning in Edinburgh. At Rome, I also met many well-known scientists who came to visit with Bovet. I met Lucio Bini who, in 1938 with Ugo Cerletti, was the first to administer electroconvulsive shock to a human subject (Cerletti and Bini, 1938). I regret that I did not take advantage of that opportunity to discuss that historic event with him. I also enjoyed many discussions with Bovet’s wife, Filomina Bovet-Nitti. She was the daughter of the last premier of Italy before Mussolini.

It was also a year of adventure for our family. We learned a lot about Rome and traveled extensively in Italy, as well as Switzerland and France, on holidays. We, including Cisco, climbed to the top of Mt. Vesuvius, looked down at the crater, and found it to look rather disappointingly benign. We took a spring vacation on the island of Ischia. We visited the newly excavated city of Ercolano (Herculaneum) that was buried by the same eruption of Vesuvius that buried Pompei in AD 79. We all learned to love the food, and Becky and I also learned to love the wine and espresso. We still do.

During that year we established lasting friendships with Italian colleagues and subsequently visited with them both in Italy and in the United States. I also established continuing research collaborations. My visibility there resulted in my subsequently being invited to speak at many international scientific meetings. Thus, the year with Bovet had an enormous influence on my academic research career. In the summer of 1962 we drove to Calais, crossed the English channel, visited London, and then boarded the *Staatendam* for the ocean voyage back to New York. We drove across the country in our VW bug to San Jose before moving to Eugene, OR, in September 1962. Shortly after our arrival, a huge storm hit Eugene and the "Pioneer Grove" of trees on the campus was destroyed. The Cuban missile crisis occurred the following month. It was clearly a month to remember.

The University of Oregon

My new position as Associate Professor of Psychology at Oregon offered everything that I had hoped for. I was given a recently constructed laboratory and was asked to teach graduate and undergraduate courses and seminars in learning and physiological psychology. The teaching responsibilities were very modest compared to my experiences at San Jose. I attracted excellent graduate students into my laboratory. I also had some very bright and industrious undergraduate students, including Bill Greenough and Ron Racine. I received new NIMH research grants and started new studies of drug effects on memory consolidation. My faculty colleagues were highly interesting, collegial, and supportive. Fred Attneave had a Dixieland band that needed a clarinet player so I was asked to join the group. We played badly, but frequently, at many departmental occasions.

In 1963, Karl Pribram invited me to participate in a conference on "The Anatomy of Memory" held in September at Princeton. The meeting was organized by Pribram and co-organized by Frank Fremont-Smith of the New York Academy of Sciences. The speakers at the conference included, among others, Sir John Eccles, Larry Kruger, Holgar Hyden, Albert Uttley, Heinz Von Foerster, and me. Other participants at that conference included Jan Bures, Robert Hinde, E. Roy John, Seymour (Gig) Levine, James McConnell, Neal Miller, David Rioch, Eugene Roberts, Roger Sperry, Hans-Lukas Teuber, and Larry Weiskrantz. It was my first presentation at a conference devoted solely to brain, learning, and memory. It was a heady experience for me to discuss my research with such an august group of distinguished scientists. Pribram included me as part of the core group that subsequently participated in meetings in Princeton each year for the next several years. At those meetings I had the opportunity to meet with most of the world's major researchers in brain and memory. This was another important way in which Karl Pribram greatly influenced my research career. The proceedings

of the conferences were edited by Dan Kimble, my colleague at Oregon who had studied with Pribram as a postdoctoral fellow.

Family life was wonderful in Eugene. Becky and I found a wooded lot with a panoramic view of the city and built our dream home. We were there to stay, we thought. But our time in Eugene, though sweet, was short. Late in the fall term of my second year at Eugene, Krech told me that he had nominated me for a position at the yet-to-be established University of California, Irvine (UCI) located near Newport Beach in Southern California. I thought little about that until I received a telephone call from Edward Steinhaus, Dean of the School of Biological Sciences at UCI asking me to come to UCI for an interview. Steinhaus and Ralph Gerard (one of the subsequent founders of the Society for Neuroscience six years later, in 1970) met the helicopter that took me to Newport Beach from Los Angeles for the interview. As the UCI campus was in its very early stages of construction, we met in temporary metal buildings located about a mile from what was to become the campus. Almost four decades later, these temporary buildings are, of course, still in use. In the discussions with Steinhaus I learned that a Department of Psychobiology was to be one of four departments in the School of Biological Sciences and that I was being considered as a candidate for the founding chair of that department. I was the final potential candidate interviewed for the position. Although I did not like the thought of leaving a very good and highly supportive department at Oregon, the possibility of building an entire department devoted to brain and behavior, the first of its kind in the world, was simply too attractive and exciting to ignore. So, on the flight back to Eugene I decided that if the position were offered to me, I would accept, pending Becky's approval. She approved. The next day I received a call from Steinhaus offering me the position and I accepted it. So, with much sadness, but little regret, Becky, Doug, Janice, Cisco, and I moved to Newport Beach in June 1964. We couldn't move to Irvine as the city of Irvine was not established until 1971.

Department of Psychobiology at the University of California, Irvine

The move to UCI was complicated by a commitment I had made to teach in a Summer Institute on Behavioral Genetics run by Gerald McClearn at UC Berkeley. So, Becky and I settled our family in a new home and I commuted to Berkeley each week. Participating in that Institute gave me a chance to learn about the behavior of different strains of mice, and I subsequently introduced genetic strains of mice into my own research program. At Berkeley, I also met Fred Elmadjian who was responsible for interdisciplinary training programs in brain and behavior at NIMH. As I discuss briefly below, meeting Elmadjian had significant consequences for the development of our new Department of Psychobiology at UCI.

Two important events occurred in the spring before the move to UCI. First, I met, interviewed, and recruited Norm Weinberger to the yet-to-be-established Department of Psychobiology. He joined me in January 1965 as a founding faculty member of UCI. Second, Steinhaus called me to tell me that the Dean of the School of Social Sciences at UCI had the opportunity to recruit several very well-known psychologists, including Kenneth Spence, Gardner Lindzey, and Leon Festinger to UCI, but that they would come only if Psychobiology were integrated within a Department of Psychology in the School of Social Sciences. I was asked to meet with Lindzey at Stanford and then send a report to Steinhaus. Steinhaus then informed the Chancellor of UCI, Daniel G. Aldrich Jr., that if the Department of Psychobiology did not remain in the School of Biological Sciences he would resign from UCI and return to his position at UC Berkeley where he had not yet sold his home. As Steinhaus was very clearly a very distinguished “dean of deans” (the following year he was elected to the National Academy of Sciences), it was an easy decision for the Chancellor. Psychobiology remained as a Department in the School of Biological Sciences. I was very happy to learn of that critical decision as I had already resigned from my position at Oregon, sold our home, and bought a new home in Newport Beach. I didn’t have Steinhaus’ options.

For the third position allocated to our Department (the minimum required for department status), we recruited Richard Whalen from UCLA. My graduate student at Oregon, Marvin Luttges, joined me at UCI and became the very *first* UCI student. As there was, as yet, no admissions office at UCI, he was registered as a UCLA student during his first year at UCI. We quickly attracted many other outstanding graduate students, including Phil Landfield, Steve Zornetzer, Len Kitzes, Ossie Steward, and Rick Robertson, among others. For our first few years at UCI the number of applicants for our graduate program exceeded the total number of applicants for all other graduate programs at UCI. In the next several years, we recruited Marcel Verzeano from UCLA, Richard Thompson from Oregon, and Carl Cotman from Indiana. Those were exciting, roller-coaster-like days. We had launched the first Department of Brain and Behavior and had done so with great success in recruiting faculty and students and in developing our research programs. Steinhaus had told me on my arrival at UCI that I had three years to convince him that the Department was viable. He was convinced. So was Fred Elmadjian at NIMH. We received the only NIMH brain and behavior interdisciplinary training grant awarded to a graduate program located *within* a single department.

Three years later Steinhaus asked me to serve as acting dean of the school so that he could take a sabbatical leave. I agreed to do that and he subsequently resigned because of illness. I was named dean of the school and served for two more years until I was able to recruit Howard Schneiderman, a developmental biologist from Case Western University, and convince him

to replace me as dean. I returned to the department and once again served as chair. I was beginning to become one of the more experienced administrators at this very young campus. In 1974 Chancellor Aldrich asked me to become the Academic Vice Chancellor. After first declining, I agreed and served in that position and, subsequently, as Executive Vice Chancellor (the position of provost at most universities) until the fall of 1982. I then founded, with Norm Weinberger and several other faculty, the Center for the Neurobiology of Learning and Memory (CNLM) and have continued to serve as Director for over two decades. I also served one more term as department chair. In these several roles I have had extensive opportunity to influence the development of UCI. However interesting they were, however, those various administrative responsibilities certainly did not aid my research career. It is now obvious to me that the administrative and academic aspects of my career probably occurred in the wrong order. Usually one assumes administrative responsibilities later in one's career, *after* firmly establishing an academic career. Perhaps someone should have informed me about that.

Consolidating Consolidation

When I arrived at UCI, I quickly set up a laboratory in a building adjacent to the one in which I had been interviewed and, with the help of graduate students and postdocs, continued to investigate drug effects on memory consolidation. Science is a skeptical enterprise. New findings and new ideas are generally not warmly welcomed. Harlow was not the only one to be skeptical about my findings suggesting that posttraining injections of stimulant drugs can enhance memory consolidation. As the consolidation hypothesis had been largely ignored for half a century before Duncan's (1949) findings of ECS-induced retrograde amnesia, it was not a popular idea. Also, as I indicated above, alternative interpretations of Duncan's findings were offered. Although Petrinovich and I countered the criticisms and alternative hypotheses of post training treatment effects in review commentaries, it was clear that what was required was more and stronger experimental evidence. So, the aim of my initial research program at UCI was to obtain that evidence. We conducted an extensive series of experiments examining the effects of posttraining injections of many CNS stimulants. We examined such effects in many kinds of training tasks, including appetitive as well as aversively motivated training tasks. The findings provided strong and consistent evidence that stimulant drugs administered after training can enhance memory for different kinds of information. In all experiments the effects were dose dependent and time dependent. Drug injections administered several hours after training were ineffective. Thus, the findings provided strong support for the hypothesis that the drugs improved retention by enhancing memory consolidation (McGaugh and Herz, 1972). Although those findings seemed to me to provide the needed evidence, my effort to counter the skepticism

required booster shots a couple of decades later (McGaugh, 1989). My laboratory also initiated a series of studies investigating the retrograde amnesia induced by ECS in order to confirm that the impaired performance was due to disruption of memory consolidation. We also investigated the neural bases of ECS-induced retrograde amnesia.

As our evidence began to accumulate, Neal Miller, who was on the editorial board of *Science*, (and whom I had met at Pribram's 1963 conference in Princeton), invited me to write a review for *Science*. My paper, "Time-Dependent Processes in Memory Storage" (McGaugh, 1966), summarized our basic findings of drug and ECS effects on memory consolidation. Publication of that paper probably gained more recognition for my findings from studies of treatments influencing memory consolidation than any other paper I have published. It is still cited frequently, but, it is probably read *infrequently*. The following year, Bovet invited me to participate in and serve as co-organizer of an international conference sponsored by the Accademia Nazionale Dei Lincei and held in Sardinia and Rome (Bovet, Bovet-Nitti, and Oliverio, 1968). The other participants included E.A. Asratyan (a student of Pavlov), Harry Harlow, Mark Rosenzweig, Alberto Oliverio, and Jean Piaget. On a historical note, Piaget held the professorship previously held by Bovet's father, Pierre Bovet. In my presentation at that conference I suggested that the experimental findings supporting either a single-trace (e.g., Müller and Pilzecker, 1900) or dual-trace (e.g., Hebb, 1949) hypothesis of memory consolidation were equally compatible with the possibility that an experience initiates several independent memory traces that have different durations (McGaugh, 1968). I suggested that experiences may initiate short-term, intermediate-term, and long-term memory traces that are not sequentially linked. I did not pursue this idea because I couldn't think of any way or ways to test it. Recent findings from the laboratories of Tom Carew and Ivan Izquierdo have now provided critical evidence. In *Aplysia*, short-term synaptic facilitation and long-term facilitation are not sequentially linked (Emptage and Carew, 1993). In rats, drugs infused into the hippocampus or entorhinal cortex posttraining can block short-term memory without blocking long-term memory (Izquierdo et al., 1998; Barros et al., 2002).

The most important event at that time, however, had nothing to do with science. Our third child, Linda, was born in 1967 in Newport Beach.

Modulation of Memory Consolidation

Most of the research in my laboratory was focused on the effects of various stimulant drugs on memory consolidation. But, the original purpose of the research was to use drugs as tools to investigate the neural processes underlying memory formation. Unfortunately, the actions of most of the drugs that we used were poorly understood. At the time that we first studied the effects

of picrotoxin, for example, it was not known that this drug acts by blocking GABA receptors. Amphetamine was one of the drugs that we (and others) found to enhance memory consolidation. As amphetamine was known to act via catecholamines, I decided to focus the subsequent experiments on the involvement of catecholamines, especially norepinephrine (NE), in memory consolidation. I also decided to use one-trial inhibitory avoidance training tasks for these experiments as we had used them productively for studies of ECS effects on memory. We adopted (and adapted) these tasks from ones originally developed by Murray Jarvik. Interestingly, Jarvik had adapted them from training procedures originally developed by Bradford Hudson in Tolman's laboratory. Using these procedures and this strategy we found that posttraining intracerebral ventricular (icv) injections of NE or dopamine enhanced memory. Norepinephrine injected icv posttraining also blocked the memory-impairing effects of a dopamine beta hydroxylase inhibitor that blocked the synthesis of NE. Thus, as Seymour Kety had suggested (1972), NE seemed to be involved in some way or ways in memory consolidation.

We also continued our studies of the effects of posttrial electrical stimulation of the brain on memory consolidation. The most commonly accepted hypothesis concerning the basis of the effects was that the stimulation created an "electrical storm" that disorganized brain activity as reflected in brain seizures. When Paul Gold came to my lab as a postdoc in the early 1970s, he continued studies of ECS that he had initiated during his graduate studies at the University of North Carolina and found that the effect of the electrical stimulation on memory varied with the locus of stimulation of the cortex, suggesting that brain seizures play no critical role in inducing amnesia. The additional finding that subseizure electrical stimulation of the amygdala administered after training induced retrograde amnesia confirmed Goddard's original report (Goddard, 1964) that amygdala stimulation induces retrograde amnesia and added the critical evidence that the induction of brain seizures played no role.

Two findings of these studies, the effects of NE and the effects of amygdala stimulation, set the stage for much of the subsequent research in my laboratory. Although these two lines of research were initiated as independent projects, as I discuss below, they converged and led to the development of an integrated hypothesis of the role of NE within the amygdala in memory consolidation. But I first need to discuss additional findings that led to that development.

It seemed very clear from all of our findings, as well as those from other laboratories, that memory consolidation can be enhanced as well as impaired by treatments administered shortly after training. In discussing these many findings, and focusing on the evidence of memory enhancement, Gold and I wondered what adaptive purpose would be served by enabling post-learning enhancement. An obvious (to us) possibility was that some endogenous process activated by learning might serve to select important

information for memory. Further, as the importance of an experience is known only at the time of the experience, the endogenous process must, we thought, act after the experience during the early posttraining period when memory consolidation is initiated. Thus, some endogenous process or processes, such as our experimental treatments, may modulate memory consolidation to provide selective storage of important experiences (Gold and McGaugh, 1975). One possibility was that epinephrine released by the foot-shock training experience may play a role in modulating memory consolidation. Gold and Rod van Buskirk, a graduate student in my laboratory, investigated this possibility and found strongly confirming evidence. Epinephrine injected after inhibitory avoidance training produced dose- and time-dependent enhancement of memory (Gold and van Buskirk, 1975). Subsequently, and very importantly, Gold and van Buskirk also found evidence suggesting that epinephrine induces the release of forebrain NE (Gold and van Buskirk, 1978). Many subsequent studies provided extensive evidence that epinephrine and NE play a role in modulating memory consolidation (McGaugh, 1983).

Epinephrine, Norepinephrine, and the Role of the Amygdala in Modulating Memory Consolidation

In a chapter discussing "The Fixation of Experience," Ralph Gerard (1961) discussed my early findings, as reported to him by David Krech.

Strychnine, according to an informal communication from Dr. Krech, shortens the fixation time. . . . The above facts fit well into a theory of continued activity in the nervous system. . . in the course of which a dynamic memory is fixed as a structural one. . . . Any change that would enhance the extent or intensity of reverberation should hasten the fixation process. . . . A fall in the threshold of cortical neurons, or an increase in impulse bombardment, should hasten fixation. Since epinephrine lowers thresholds, and is released in vivid emotional experiences, such an intense adventure should be highly memorable.

In that same paper Gerard also suggested that activation of "... the amygdala. . . could easily modify the ease and completeness of experience fixation *even if the nuclei were not themselves the loci of engrams* (italics mine)." Although I knew Gerard and interacted with him considerably here at UCI, he did not refer me to this chapter or discuss its implications with me. I discovered it only a couple of years ago. Had I discovered it in 1961, or even a decade later, it might have accelerated my research program. I cite Gerard's comments only as significant and prescient, but neglected suggestions.

The problem with epinephrine as a modulator of memory process in the brain is that it passes the blood-brain barrier either poorly or not at all. But, we knew from Gold and van Buskirk's work that it influenced the release of brain NE. We also knew from our concurrent studies that electrical stimulation of the amygdala could enhance, as well as impair, memory consolidation. Thus, we began to think of the amygdala and NE release in the amygdala as possibly playing roles in epinephrine influences on memory. Findings reported by Michela Gallagher and Bruce Kapp and their colleagues (Gallagher et al., 1977, 1981) greatly influenced our thinking about this possibility. They reported that posttraining infusions of the β -adrenoceptor antagonist propranolol impaired inhibitory avoidance retention and that concurrent infusions of NE blocked the impairment. A series of experiments conducted by two graduate students in my laboratory, Keng-Chen Liang and Cate Bennett, provided critical evidence linking epinephrine effects with amygdala activation. Posttraining electrical stimulation of the amygdala, which produced amnesia in controls, *enhanced* memory in adrenal demedullated animals (i.e., animals unable to secrete epinephrine). But, importantly, the amygdala stimulation produced amnesia in demedullated rats that were given epinephrine before the stimulation. The additional finding that propranolol infused into the amygdala blocked the memory-enhancing effects of posttrial injections of epinephrine provided compelling evidence that epinephrine affects memory consolidation by influencing activation of adrenoceptors in the amygdala. Evidence that NE infused into the amygdala posttraining enhances memory consolidation provided additional essential support for this hypothesis (Liang, Juler, and McGaugh, 1986). This set of findings suggested an integrating hypothesis concerning the central role of the amygdala in regulating the consolidation of memory for emotionally arousing experiences that has guided most of the subsequent research in my laboratory.

Integrating Neuromodulatory Influences on Memory Consolidation

Our findings, as summarized above, indicated that epinephrine released from the adrenal medulla influences memory by altering the release of NE in the amygdala. The findings of Cedric Williams and Rob Jensen indicate that the effect is mediated by activation of the ascending vagal projections to the nucleus of the solitary tract (NTS) that, in turn, sends noradrenergic projections to the amygdala (Jensen, 2001; Williams and Clayton, 2001). Some of the critical experiments were conducted when Williams was a postdoc in my lab, but the studies were initiated previously when Williams was a graduate student in Jensen's lab. However, as Jensen was a postdoc in my lab in an earlier decade, I suppose I could at least claim to have had some indirect influence on their studies of the involvement of the NTS.

Many drugs that influence memory consolidation readily enter the brain and, thus, don't need to use the vagal-NTS connection. But do any of the drugs also influence memory by altering NE functioning in the amygdala? That question motivated the next series of studies in my laboratory. To address this question we returned to two classes of drugs that we had studied extensively in our previous research: drugs that affect GABA receptors such as picrotoxin, a GABA receptor antagonist and one of the first drugs that I had studied several decades earlier, and drugs that affect opiate receptors such as naxolone, an opiate receptor antagonist. The findings of a series of experiments were unambiguous. Propranolol and other adrenoceptor antagonists infused into the amygdala blocked the memory-enhancing effects of GABA and opiate receptor antagonists administered either peripherally or directly into the amygdala posttraining. Two postdocs in my lab, Ines Introini-Collison and Jorge Brioni, both from Argentina, were responsible for conducting most of those experiments. In another, more recent series of experiments in my laboratory using *in vivo* microdialysis and HPLC, we found that naxolone and picrotoxin increase NE release in the amygdala. We also found that inhibitory avoidance training induces NE release in the amygdala, and the magnitude of the increase correlates very highly with subsequent retention performance.

Our evidence very strongly suggests that the interaction of neuromodulatory influences of drugs and hormones affecting memory consolidation is integrated via common actions on NE functioning within the amygdala. In an extensive series of studies conducted by Benno Roozendaal, a research colleague in my lab, we found that the adrenal stress hormone corticosterone (in the rat), like the adrenal stress hormone epinephrine, modulates memory consolidation via influences on noradrenergic receptors within the amygdala (Roozendaal, 2000). Other findings indicated that muscarinic cholinergic influences on memory consolidation also involve the amygdala, but may act "downstream" from the noradrenergic effects. Finally, but importantly, experiments using selective lesions of amygdala nuclei and selective drug infusions into specific amygdala nuclei determined that the basolateral nucleus (BLA) is the critical region of the amygdala mediating the modulatory influences on memory consolidation (McGaugh, 2002; McGaugh and Roozendaal, 2002).

Amygdala Interactions with Other Brain Systems in Consolidating Memories

The studies summarized briefly above provided no compelling clues to the locus of the neural changes underlying memory consolidation. It is theoretically possible, of course, that the amygdala might be a locus of the changes or part of a circuit involving other brain regions as well. These possibilities are strongly advocated by other laboratories studying the role of the amygdala

in learning and memory (LeDoux, 2000; Davis, 2000). Although these possibilities cannot be excluded, our evidence provides no support for them. Or, at least, our evidence indicates that an intact amygdala is not *critical* for learning and retaining information. Complete lesions of the amygdala or complete lesions of the BLA do not prevent the learning of the many kinds of tasks we have used in our experiments (e.g., Cahill, Vazdarjanova, and Setlow, 2000; Lehmann, Treit, and Parent, 2000). Such lesions do, however, prevent the memory-modulatory influences of the drugs and hormones that we have investigated.

So, where does the amygdala act to influence memory consolidation? As the amygdala is richly interconnected with many brain regions (Young, 1993), it no doubt influences memory processing in many brain regions. When they were postdocs in my lab, Mark Packard (who did his graduate work with Norm White) and Larry Cahill found that the answer to that question depends on the training task used or, more specifically, the kind of information learned. Posttraining drug (amphetamine) infusions administered into the amygdala enhance spatial learning in a water maze, a task known to involve the hippocampus, as well as visually cued learning in a water maze, a task known to involve the caudate nucleus (Packard, Cahill, and McGaugh, 1994). In an extensive series of experiments, we subsequently found that lesions of the BLA or infusions of β -adrenoceptor antagonists selectively into the BLA block the memory-enhancing effects of hormones and drugs infused into the hippocampus or entorhinal cortex after inhibitory avoidance training. Conversely, lesions of the basal forebrain that provides cholinergic innervation of the cortex block the memory-enhancing effects of NE infused into the BLA posttraining (McGaugh, 2002).

Findings from Larry Cahill's studies of memory in human subjects, while he was in my laboratory, provide strong evidence implicating the amygdala in the consolidation of emotionally significant memory. Amygdala activity assessed by PET scanning during subjects' encoding of emotionally arousing material correlated very highly with memory of the material tested several weeks later (Cahill et al., 1996). This finding has been replicated and extended in other laboratories in studies using different emotional material and brain imaging techniques (Canli et al., 2000; Hamann et al., 1999). As these studies examined explicit or declarative memory, which is known to involve the hippocampus, these findings fit well with the findings of our studies with rats discussed above in suggesting that amygdala interactions with other brain regions are critical for its memory-modulating influences (McGaugh, Cahill, and Roozendaal, 1996). Cahill's finding that adrenergic activation is critical for the effects of emotional arousal on memory in human subjects (Cahill et al., 1994) also fits well with the extensive evidence from our experiments with rats.

Perhaps the best overall conclusion offered by our findings is that Gerard was correct. Epinephrine does have effects on memory like those of

strychnine, and the amygdala does appear to “. . . modify the ease and completeness of experience fixation,” even if it may not be the locus of engrams. But, it took my laboratory almost half a century to obtain the confirming evidence. But, of course, our findings are considerably more complex (McGaugh, 2000, 2002). Beyond that, our findings constitute only the very beginning of the next phases of research. We need to understand the specific actions of the amygdala that influence memory consolidation elsewhere in the brain and the changes at those sites that enable memory. My view is that most memories are not based on simple circuits. It seems much more likely to me that memories are enabled by the actions of highly complex, widely distributed circuitry capable of complex computations required for integrating representations of past experiences as they are activated by our ongoing experiences. How neuromodulatory systems and the amygdala act to regulate the formation of such circuitry remains to be investigated and understood. I presume that my present and former graduate students and postdoctoral researchers, or perhaps their students or the students of their students, will eventually find the answers to these questions.

Other Significant Influences

As I discussed above, scientific conferences, particularly small conferences, have very significantly influenced my research career. About the time that I began the series of experiments investigating epinephrine and amygdala influences on memory consolidation, Aryeh Routtenberg, Ray Kesner, Larry Squire, and I thought it would be useful to establish a small (i.e., fewer than 100 participants) annual meeting to enable us to meet and discuss our findings concerning these and other topics in the neurobiology of learning and memory in an informal setting. So, we organized the Winter Conference on the Neurobiology of Learning and Memory and held the first meeting in January 1976. The sessions at this annual conference held in Park City, UT, enabled me, as well as graduate students and postdocs in my laboratory, to present the findings from my laboratory and discuss them with other investigators, including Ray Kesner, Paul Gold, Michela Gallagher, Bruce Kapp, and Norm White, among others, who were investigating the effects of drugs and electrical stimulation of the amygdala on memory consolidation. Our discussions at this conference very significantly influenced all of our research programs. Of course, the program also included discussions of many other problems and issues in the neurobiology of learning and memory—a different set each year. Most neuroscientists studying learning and memory have attended at least several of the conferences. We celebrated the 25th anniversary of the founding of the conference at our meeting in January 2001.

I also participated in many conferences in Mexico, Argentina, and Brazil. These interactions created collaborations and lasting friendships with

many colleagues, including Ivan Izquierdo, Rene Drucker-Colin, Federico Bermudez-Rattoni, and Roberto Prado Alcalá, each of whom have spent many months working on collaborative research in my laboratory. Many of my postdocs received their graduate training in the laboratories of these colleagues. During the “Cold War” days I also participated in a series of conferences organized by Hans Matthies in Magdeburg, East Germany. At those meetings, those of us from the West (including Steven Rose, Aryeh Routtenberg, Paul Gold, Bela Bohus, and Ivan Izquierdo, among others) were able to learn about neuroscience research on memory being conducted in Eastern European countries. There I had many discussions with Jan Bures, one of the pioneers in memory consolidation research, and later, after the Berlin Wall came down, invited him to come to UCI as a visiting Professor.

In 1982 our Center for the Neurobiology of Learning and Memory (CNLM) at UCI organized the first of a series of conferences on brain and memory, each attracting several hundred speakers and participants from the international community of neuroscientists. These conferences, held every two to four years, provided additional important opportunities for interactions with researchers investigating brain processes mediating memory and have served as “family reunions” for graduate students and postdocs who have worked in my laboratory. We held our seventh conference in 2001. The informal interchanges at these many conferences significantly shaped my thinking and my research. A few years ago I was extremely honored when Paul Gold and Bill Greenough organized a conference in my honor and subsequently edited a Festschrift based on the papers presented by my friends and former students (Gold and Greenough, 2001). Discussions of memory and many other matters at these many meetings created many new ideas and good memories, renewed old friendships, and established new lasting friendships.

I also made many friends and learned a great deal when I served on training grant and research grant review committees (then called “study sections”) at the NIMH and, later, as a member of the NIMH National Advisory Council. I also played an active role in the founding of the American Psychological Society and served a two-year term as the first elected President of that Society. My role as founding Editor of the journal *Neurobiology of Learning and Memory* also provided many opportunities for interactions with international colleagues. But, the role of editor is not always a happy one, for authors of submitted papers are not always pleased with editorial actions. The general rule appears to be that if a paper is accepted it is because the authors are creative and if a paper is rejected it is because the editor is mentally deficient. Nonetheless, I managed to enjoy the role of journal editor *most of the time* during the several decades that I served in that role.

The CNLM has given me the opportunity to work closely, for many years, with colleagues, students, and visiting researchers who share a common interest in understanding the neural bases of memory. Over the years we

have managed to raise funds from generous donors to enable the construction of beautiful and wonderfully functional research, office, and conference facilities. The CNLM has also adopted outreach to the public as part of its mission. We have organized the “Distinguished Lecture Series on Brain, Learning and Memory,” a very well-attended public lecture series, each year for the past decade. This lecture series, as well as tours of the CNLM laboratories offered to school children, allow us to share with the public the excitement and importance of research investigating brain and memory.

Retrospection

Memories are good things to have, generally. As my research quest has emphasized, it is good that we have brains that sort out our experiences so that the most important ones are saved. Memories of significant experiences help us prepare for future experiences. But they also make us who we are. I have tried to use the memories I have preserved to summarize some of the major influences in my life and, in particular, the critical influences that aided my academic research career. I have had a very rewarding career in the Department of Neurobiology and Behavior (originally, as discussed above, called Psychobiology) and the Center for the Neurobiology of Learning and Memory at UCI. I was extremely honored to have my Department establish the McGaugh Award for Excellence in Research (awarded each year to a graduate student) and to have the School of Biological Sciences at UCI name a biology building McGaugh Hall.

My efforts over the half-century since I entered graduate school have been aided by inspiring and supportive mentors, superb graduate students and postdoctoral researchers, visiting researchers from other institutions, and creative and collegial colleagues. Norm Weinberger and I have been close colleagues for almost four decades. I have also been very fortunate to have the assistance of outstanding administrative staff. Nancy Collett has been an exceptionally supportive assistant for over a quarter of a century. Lynn Brown has been a highly creative and effective Assistant Director of the CNLM since its founding. Their superb and sustained assistance and guidance enabled me to focus my efforts on research and teaching.

But, much is missing in my report. It does not even begin to capture the uncountable subtle influences of many teachers, students, staff assistants, colleagues, and friends—including those unrelated to my academic life. Nor does this report say much about my life apart from the university. When I am not thinking and writing on the research topics discussed above, I enjoy my hobbies of making toys and furniture in my woodshop and playing clarinet and alto sax in jazz groups. Dave Schetter, a good friend and great jazz sax musician at UCI, is responsible for seeing that I get ready for wedding receptions (including Jan’s, Linda’s and Doug’s), dinner dances, and other “gigs” with the *Butler Street Blues Band*. Science and jazz get mixed when I play

with the *Synaptic Plasticity Band* whose members include my good friends, for many decades, Aryeh Routtenberg, Len Jarrard, and Mike Gabriel.

I enjoy skiing on fresh powder on sunny days, hikes in the mountains near our family cabin at Big Bear Lake, and walks in the nature preserve at the bay near our Newport Beach home. Family barbecues with swimming during the summer months provide special pleasures. Becky and I recently celebrated our 50th wedding anniversary. Doug, Jan, and Linda and their spouses helped with the celebration, as did our grandchildren, Billy, Scotty, Kaitlin, Kirby, Addie, Tristan, and Phoebe. My family has been superbly and consistently supportive of my academic career and highly proficient in providing experiences that make good and lasting memories—the kinds that are clearly worth preserving.

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