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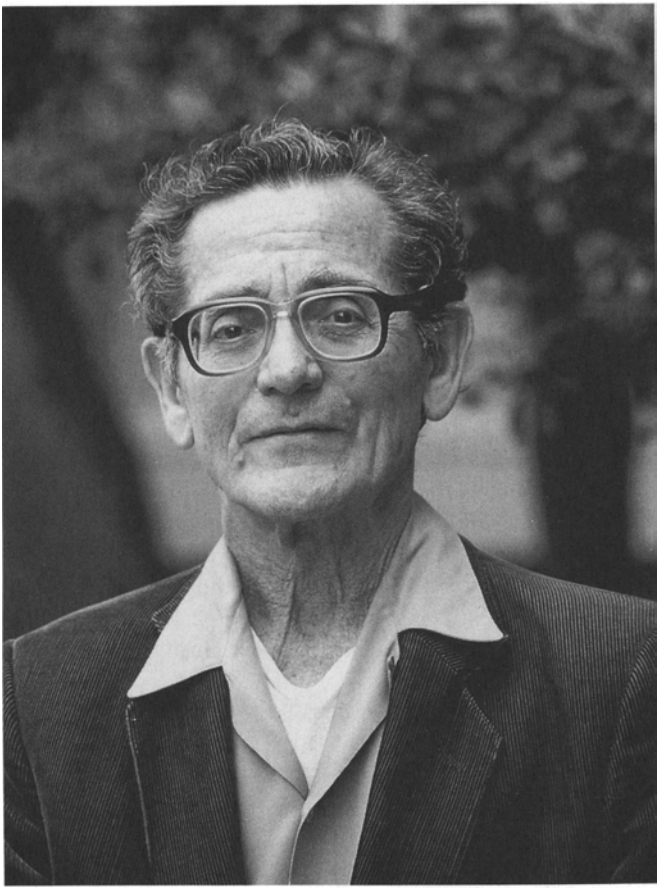

Benjamin Libet

BORN:

Chicago, Illinois
April l2, 1916

EDUCATION:

University of Chicago, B.Sc., 1936
University of Chicago, Ph.D. (Physiology, with Ralph Gerard, 1939)

APPOINTMENTS:

Albany Medical College (1939)
Institute of Pennsylvania Hospital (1940)
University of Pennsylvania School of Medicine (1943)
University of Chicago (1945)
University of California, San Francisco (1949)
Professor of Physiology Emeritus, University of California, San Francisco (1984)

Benjamin Libet was trained in physiology and initially studied cerebral electrical and metabolic activities, and synaptic and nonsynaptic interactions in vertebrates and invertebrates. Later, he carried out a series of novel studies in neurosurgical patients, investigating the physiological bases of conscious sensation, volition, and experience.

Benjamin Libet

How did it all happen—that the first-generation American child of Ukrainian Jewish immigrants, raised during the Great Depression in near poverty in Chicago, developed into a neuroscientist who carried out fundamental experimental research on brain processing in conscious experience (among many other types of research)? Perhaps the adage "only in America" provides the answer, at least for that time period.

My paternal grandfather came to America—Chicago—in 1905 from a town called Brusilov in the Ukraine, not far from Kiev. He came at least in part to avoid being impressed into the czar's army to fight in the Russo-Japanese war of 1905. Grandpa Harry Libitsky was a highly skilled tailor who sewed men's suits entirely by hand. I have sometimes thought that I may have inherited my microsurgical skills from his abilities in needlework.

On his return to the United States after a brief visit to Brusilov in about 1909, my grandfather brought my father, then 13 or 14 years old, back with him. My grandfather left behind his wife and three younger children, with my grandmother expecting another child. World War I intervened before he could arrange for the rest of the family to come to Chicago, and they did not arrive until 1921. My grandmother never forgave him for not getting them out earlier. She suffered greatly during the interval, both from lack of funds and from the terrorizing activities of various gentile gangs, including raids by the cossacks. At one point she came down with an illness that she thought was fatal and fell back on an old superstition that one might mislead and avert the Angel of Death by adopting a different name. She dropped her name of "Bobtsy," vowed to be identified henceforth as "Genia," and would not tolerate my grandfather calling her by her original name later in America.

My father, Morris, had had only the standard Jewish-Hebrew school education back in Brusilov. He wanted to attend a public school after arriving in Chicago, but grandfather Harry would not let him. My father was forced to seek work and become self-sufficient; he became a machine-operating tailor in men's clothing factories. I believe that my father had excellent innate intelligence and that the frustration of being unable to pursue more intellectual activities led to serious personal difficulties for the rest of his life. However, he remained on good terms with my grandfather. Although grandpa Harry was tough about my father's development, he was

a doting gentle grandfather to my siblings and me. In fact, he was an important and early source of familial love for me. "Zaydeh" (the Yiddish term for grandfather) could not understand the importance of my academic work in neurophysiology because I was not becoming a practicing M.D. He was later mollified when he heard that I was *teaching* doctors.

My mother, Anna Charovsky, emmigrated from Kiev in 1913, just one year before the outbreak of World War I in Europe. Had her departure from Kiev been delayed for a year, I, Ben Libet, would not have appeared. Anna's father, Mayer, was a small-time cattle dealer. Her mother, Devorah, died during the birth of Anna's younger sister, Chavah. Anna was unusual among Jewish girls in having attended a state school and the Gymnasium (equivalent to high school and junior college here) and having had some experience as a school teacher before emigrating. Her older brother, Avram, who had himself become an engineer, promoted Anna's academic pursuits. Anna emigrated with a married older sister, Pearl; they all headed for Chicago where another older brother, Louis Charous, had already settled.

Anna and Morris first met in Chicago. They were married in 1915, and somewhat over nine months later I was born, on April 12, 1916. My brother, Meyer, came along a year and a half later, and then my sister Dorothy in July of 1921. At home, my parents spoke Yiddish, and that was my first language until I picked up English playing with other kids in the street. Both my parents soon became proficient in English without studying it formally.

From the start I liked learning at school and found most subjects relatively easy. My mother strongly supported my academic work, perhaps seeing it as an achievement that she (and my father) did not have the opportunity to pursue. Mother seemed to have full confidence that I could and would do well in academic work as well as in most other activities. She was, of course, overly sanguine in that confidence; but I am sure her confidence in me contributed greatly to my ability to face academic and other problems during most of my life. Much later, when J.C. Eccles was awarded the Nobel Prize in 1963, both mother and my sister Dorothy knew I had worked with him in 1956 to 1957. When Dorothy asked mother, "Guess who won the Nobel Prize?" mother promptly answered, "Ben!"

I was also musical and at an early age began singing in a lusty alto voice songs that I heard on records played on our crank-up Victrola phonograph. In 1925 the world-renowned Hebrew-Orthodox cantor, Josef Rosenblatt, was coming to Chicago to sing the High Holy Day services. Mother took me to audition for the a cappella choir that was to accompany Rosenblatt. When the choir director asked me to sing, I boomed out "My Country Tis of Thee" and was promptly taken on. With my $25 earnings mother bought a piano for me. I also earned two $10 tickets (tickets were $10 to $100 each) to the Rosenblatt-conducted services. That enabled my father and grandfather to

attend; both loved to listen to a great cantor even though my father, at least, almost never entered a synagogue otherwise. Every year thereafter until I left Chicago in 1939—except for my fourteenth year with my voice changing to a baritone—I sang in professional choirs in synagogues, earning helpful fees.

I graduated from a public elementary school at age 12 and from the John Marshall High School at 16. In those years the University of Chicago offered scholarships to students who did well in a three-hour competitive examination in one subject of their choice. I took the exam in chemistry (we had an exceptionally good chemistry teacher in high school), and I did well enough to be offered a half-tuition scholarship ($150 in 1932!). My high school provided the other $150 in the form of the "Mary Zimmerman Scholarship" (named for the noble-mannered teacher of Latin, a subject I had studied for four years). Having graduated from high school during the Great Depression, I could not have gone to the University of Chicago without those scholarships. I continued to get scholarships through the undergraduate years and received paid assistantships and a university fellowship as a graduate student (there were no student loans or predoctoral stipends from the government in those times).

Even so, I had to live at home with my parents throughout my university education, commuting every day for seven years (four for the B.S. plus three for the Ph.D.), mostly by way of the Chicago trolley cars that took an hour each way. I was not alone in that; several other graduates from my high school had a similar history. Some became nationally known professors of chemistry (Irving Klotz, Arthur Jaffey, Theodore Puck), one a zoologist-ecologist and physician (Asher Finkel), and one (my closest friend, Louis Yesnick) a physician-internist. Another (Jacob Mosak) became an eminent economist at the United Nations. My future wife, Fay (Fannie Evans), also commuted from her home to the University of Chicago for three years before our marriage. I wonder whether students today would put up with those kinds of hardships to attend the university, especially at the graduate level.

For some of those years (approximately 1930 to 1936) my whole family (my parents and their three teenage children) lived in one large room directly to the rear of our small candy store. My mother had realized that such a source of income was essential if we were to ride out the Depression without asking for welfare. In the summer of 1932 I worked in delicatessen stores, 12 hours a day, six to seven days a week, for $10 to $12 a week. In 1933, I was lucky to land a job at the Chicago World's Fair at $17 a week. I am not citing all this as a complaint, though I wished it had been easier; I accepted these conditions as a matter of course so I could go to the University of Chicago and work toward my academic goals.

Undergraduate Studies: University of Chicago

My entry into the University of Chicago, at age 16, opened up a whole new vista of intellectual and social experiences. The tone was set at the start

when Robert M. Hutchins, the youthful president of the University of Chicago, greeted the freshman class. He was a tall, handsome, elegant man who talked to us as if we were adults, kidded us with his wry humor, and spoke to us about his "New Plan for the College." In that plan, initiated one or two years earlier, students were given their own responsibility for learning, attendance at classes was not mandatory, all students took four general year-long courses (biological sciences, social sciences, humanities, and physical sciences) in their first two years (plus some electives), and grading in the general courses was based completely on six-hour comprehensive examinations in each course at year's end. These "comp exams" were devised by a professional board of examiners separate from the course instructors; that feature shifted the teaching and learning processes toward longer-range achievements and encouraged questioning and argumentation by students without fear of retribution in the grading.

What an enormous change from high school. The students had initial anxieties about how to cope with such responsibility, but soon relished it. Classroom attendance was close to 100 percent. The university induced its greatest, internationally famous professors to lecture in the general courses; their lectures were so stimulating that we had no thought of skipping them. The University of Chicago had an atmosphere of openness, rationality, and imaginativeness that I have not encountered in other universities. Additional benefits came from associating with other able students.

Although I liked chemistry, I had an affinity for studying living things. In a summer boys' camp, when I was 12 years old, I joined a biology group. In one demonstration the counselor pithed a frog (that is, destroyed its brain) and, after exposing the living viscera, showed us that various organs could still respond and function in the absence of the brain. When he finally excised the heart and it continued to beat in isolation, I was startled and fascinated. Had I just been told that the heart can beat in isolation, or seen it modeled on a computer, I would not have experienced the stimulating impression that the real thing provoked (I also credit a high school biology teacher with further fostering my fascination with the nature of living things).

I first met Ralph Gerard in my freshman general biological science course at the University of Chicago. He was the instructor for the twice-weekly discussion section of about 25 students in the quarter term for physiology. Gerard was an associate professor, 32 years old, and already completely bald. His large, penetrating blue eyes, bald head, and brilliance as a speaker made him a striking figure. Gerard was recognized nationally and internationally for his work on nerve metabolism and for the classical review he had published that year (Gerard, 1932). But he was also interested in educational issues, especially in methods of teaching science. He conducted the section by asking for questions which he then turned back to the students. He treated every student response seriously

and with respect, stimulating some of us to make imaginative inquiries and suggestions. The biological sciences II course in my second year included student lab exercises. Louis Yesnick and I requested that Gerard allow us to repeat von Helmholtz's experiment to measure conduction velocity in the motor nerve of the frog using the sciatic nerve-gastrocnemius preparation. We did the experiment successfully, and I was thrilled to find we could indeed reproduce the values of the elegant experiment Helmholtz had done before the days of amplifiers and oscilloscopes.

Yesnick and I decided to major in physiology for the bachelor's degree. In our senior year we were both assigned to do an undergraduate research project with Professor Arno B. Luckhardt, who told us to test how an increase in intracranial pressure may affect the production of urine. I think that question stemmed from some clinical experiences or reports. Luckhardt was a warm-hearted, gentle man. He had become especially recognized for his discovery of the excellent general anesthetic qualities of ethylene. He reputedly turned down the then immense sum of a million dollars for the patent rights because he wanted the public to benefit from the finding in the most accessible manner. Unfortunately, ethylene was quickly found to be easily ignited and explosive in the operating room.

Graduate Research with Gerard

I had completed the requirements for the B.S. degree in the second of the three quarters in my senior year, and so, deficient in funds, I graduated in March 1936 with an election to Phi Beta Kappa. I applied and was accepted for entry in the fall of 1936 into both the University of Illinois Medical School and the University of Chicago Medical School. I accepted the former because of the much lower costs. But I wavered about entering medical school until the actual day for registration, when I realized more firmly that I wanted to do research in physiology. I found the prospect of the prescribed four years of medical school courses a much less appealing option, and looking beyond that, I did not at the time feel inclined to practice medicine. The long-range prospect of a university research and teaching career seemed more attractive, although much less certain of achievement. On registration day, I also realized that the University of Illinois had my $50 registration deposit, a significant sum in 1936. So I went to cancel my registration by lying shamelessly to the dean that my father was ill and saying truthfully that I would be financially strapped. The dean graciously had my $50 returned and urged me to re-apply the next year if conditions improved.

I was then promptly admitted to the graduate division of the University of Chicago and went to see Gerard about joining his research activities. I admired Gerard and the activities of his research group, and was strongly attracted to neurophysiological issues. Four or five bright graduate stu-

dents were working with Gerard on problems of neural metabolism (Frieda Panimon), sleep (Helen Blake), oxygen and circulatory requirements of brain (Oscar Sugar), and so on. The brilliant biophysicist Franklin (Frank) Offner, had just produced a crystal-type pen-writer for recording changes in bioelectric potentials with frequencies up to about 100 Hz or more. Frank also constructed and maintained the amplifiers for research in the lab, including a "push-pull" amplifier that he invented to provide ungrounded bipolar recording with less external electrical interference. Among those who had already finished and departed from the University of Chicago were Robert Cohen and Mabel Blake-Cohen (electroencephalography, EEG), Herman Serota (local changes in cerebral blood flow with a heated thermocouple), and Wade and Louise Marshall (electrophysiology of the brain). Gerard was in the forefront of studies of the nature of "brain waves," which Hans Berger had recently discovered in humans and reported in 1929. Among those who came to Gerard's lab for experience in that field were Horace Magoun and J.Z. Young.

Young and Gerard had, the year before my arrival, demonstrated that the brain of the frog not only showed spontaneous EEG activities but that it continued to do so after being removed from the frog's skull and being placed in a dish. For my entry into research Gerard suggested that I find out about the nature of the EEG activity in the isolated frog brain. Fundamental arguments were going on about the neuronal basis of the EEG. Gerard left the issue wide open for me to develop leads on my own, and he did not give me any special training in electrophysiological recording methods. Frank Offner helped to introduce me to the equipment in the lab.

I was unable to get the isolated frog brain to show any activity in almost daily trials for about four weeks. Then suddenly the brain exhibited a beautifully regular six-per-second rhythm at and near the olfactory bulbs. I later decided that the earlier attempts had failed because of the way the decapitation scissors were angled. The blades had to be positioned at a sharply oblique or flat angle, so as to be almost horizontal to (in the same plane as) the antero-posterior axis. Apparently with angles more perpendicular to this axis the intracranial space experienced some crushing during the quick cut. The brain did not "like" being squeezed or pulled, and precautions also had to be observed when pulling off the top of the cranium and transferring the brain to the dish of Ringers solution.

Use of the isolated frog brain allowed the possibility of modifying the extracellular environment by simply changing substances or adding them to the bath fluids. Electrophysiological studies, including intracellular ones, are also easier to do when the brain is not *in situ*. These possibilities were achieved later for mammalian brain by the use of thin slices, presumably done first by Henry McIlwain. But the isolated frog brain, in contrast to slices, provides intact neural circuitry and exhibits fine EEG rhythms. I have wondered why this frog brain preparation has not come

into more general use. I myself became extremely allergic to frog's blood during my three years working with it; I would get almost intolerable bronchial asthma after each study period with the frog. The asthma prevented me from continuing to study the isolated frog brain.

Gerard and I found that various changes in ionic composition of the bath could convert the almost sinusoidal six-per-second rhythm to a variety of different frequencies and wave configurations (Libet and Gerard, 1939). That finding lent strong support to the view that the normal EEG represented potentials with a similar frequency and wave shape in the individual neurons, with a large number of these "beating" in relative synchrony. This view is still current, based on further evidence with intracellular recordings. The alternative view, held at that time by Herbert Gasser and others, regarded the relatively long-duration EEG waves (the roughly 100 msec waves in the Berger rhythm of human brain) as each reflecting a proper composite of short-lasting "spikes" (with about 1 msec durations) or possibly of their after-potentials, as seen for nerve impulses. Our finding in the frog brain made it almost impossible to imagine how that alternative view could account for the radical changes that we could produce in the recorded EEG. Additionally, we found that even a tiny bit cut from the olfactory bulb could still exhibit a regular rhythm; that finding argued against the requirement of elaborate networks for the EEG.

Because the results were so interesting, Gerard asked me to give a paper at the April 1938 meeting of the American Physiological Society, in Baltimore, Maryland. At that time the neurophysiology presentations were few enough to require only a single session for each time slot. And so this 22-year-old beginner presented the paper in a room full of luminaries such as Herbert Gasser, George Bishop, Lorente de Nó, Francis Schmitt, and Hallowell Davis. My talk was received well. In another session I heard the young Alan Hodgkin, from England, present one of his first landmark findings—he proved that conduction of the action potential involved passive electrotonic spread from the active site.

I should also tell a story about the trip to Baltimore. Gerard decided to drive his car from Chicago, taking me along with Helen Blake. On the way we stopped in Cincinnati to visit an experimental psychiatrist, a Dr. Tietz as I recall. Gerard had induced Dr. Tietz to try administering methylene blue to patients with catatonic schizophrenia, on the basis (I suppose) that this hydrogen acceptor molecule would facilitate oxidative brain metabolism (a hot topic at the time). Dr. Tietz brought in a catatonic woman who displayed the usual nonresponsiveness to questions. Dr. Tietz then gave the patient an intravenous injection of 50 ml of a methylene blue solution. The patient turned the sickly color of green cheese, and I almost fainted with nausea. However, the patient became remarkably responsive and rational for about 30 minutes. But she reverted to the catatonic state as the color wore off. That striking effect should merit a follow-up study.

Gerard had the idea that the presumed synchronization of the electrical waves in a large number of neurons was achieved by intercellular currents, initially started by some "pacemaker" cells. A high concentration of nicotine altered the EEG wave shape but did not stop the rhythm. As that procedure should block all cholinergic synapses, we thought the result supported the intercellular field idea. Of course, we now know that cerebral synapses are not simply cholinergic or even all nicotinic when they are cholinergic. I think it would still be of considerable interest to test the synchrony mechanism by at least blocking all nerve conduction, which could be done by applying both tetrodotoxin (TTX) and a calcium-channel blocker (to stop both the Na^+-type and Ca^{++}-type nerve impulses), agents not available at that time.

Gerard and I produced another startling finding that supported the transmission of neural actions via intercellular field currents. At the end of an experiment that left the brain still showing activity, I added caffeine to the bath, because that substance was known to affect brain function. The caffeine converted the normal EEG waves to very large seizure-type waves that appeared in intermittent bursts; this finding clearly presented a model for an epileptic condition. I also established that these "caffeine waves" first appeared at the anterior pole of a cerebral hemisphere and traveled to the posterior end at the rather slow speed of about 5 cm per second.

In a discussion with Gerard, we considered the possibility that transmission of the caffeine wave was mediated by the large intercellular currents that were reflected in the surface-recorded potential changes. To test this hypothesis we hit on the bold idea of seeing whether the caffeine waves would be transmitted across a complete transection of the brain. I transected the brain completely at a level about halfway between the anterior and posterior cerebral poles and allowed the cut halves to come back in closely normal apposition (Gerard and Libet, 1940; Libet and Gerard, 1941). We were astonished to find that a distinct fraction of the traveling caffeine wave appeared in the cerebral portion posterior to the transection.

Twenty-five years later (in 1964) I was in Paris at a dinner party given by Alfred Fessard and Denise Albe-Fessard for my wife Fay and me and the Marshalls (Wade and Louise). Wade told me that he, like some others, had not believed my report of caffeine-wave transmission across a cut. Wade liked to repeat experiments by others when he had serious doubts about them; he did that for the "suppressor strip" proposal by McCulloch and Dusser de Barenne and showed that their findings were almost certainly due to artificially induced "spreading depression" (SD) rather than to an inhibitory motor cortex mechanism. Wade told me he had repeated my caffeine-wave experiment and obtained a similar result. I told him he should have published that confirmation; had he found an opposite result, he would no doubt have published it! I suggest that the caffeine-wave

transmission experiment merits attention and perhaps a reinvestigation with modern technical capabilities.

The final product of those wonderfully productive three years of graduate work with Gerard was the discovery and analysis of slow, so-called "steady potentials" (SPs) in the frog brain (Libet and Gerard, 1941). Bipolar recording of the pia-ventricular potentials (with one electrode inserted into the cerebral ventricle so as to lie directly below another electrode on the pial surface) indicated that the recorded SP might reflect a resting steady potential gradient along the long axis of neurons in the pallium. Shifts in that SP could be made by applying currents from an external source; shifts in a given direction produced changes in the magnitude and even the polarity of endogenous EEG components, seen especially well with the caffeine waves. Subsequently, others (e.g., James O'Leary and Sidney Goldring) carried out investigations of SPs in the mammalian brain.

When my first publication with Gerard was to appear in 1938, I had to decide whether to keep my family name of Libitsky. Both Gerard and our department chairman, the great Anton J. Carlson, told me that, with few job opportunities in 1939, the Libitsky name might turn off prospective employers in an era of fairly common anti-Jewish bias, even in universities. Additionally, I felt inclined to adopt a more Americanized name; I felt that the Ukrainian source of the "sky" ending did not deserve any loyalty in view of the history of anti-Semitism and pogroms there. I think I also desired to adopt a symbolic indicator of my forging a career outside the confines of the conditions from which I had come. That wish definitely did not include an intention to disavow any of my family or my Jewish background, to which I have remained proudly committed. Instead of just dropping the "sky," I also changed the second "i" to an "e," winding up with Libet. I liked that partly because it sounded more French, like Gerard's name. That got me into embarrassing moments later when my French colleagues assumed I was indeed French—my ability to speak French was almost zero. My brother Meyer also adopted the name Libet, although a number of cousins on my father's side changed their names to Libit. At times I have regretted changing my name, but mostly I have been satisfied with the decision.

Postdoctoral Activities, 1939–1945

I achieved my Ph.D. from the University of Chicago in June 1939, and Fay and I were married on July 1. We had met in 1936 and "gone steady" for three years. When I received the Ph.D. hood at the convocation in Rockefeller Chapel, President Robert M. Hutchins (who was over six feet tall) seemed to be a bit surprised to see this five-foot-eight-inch, slightly built youngster of 23 (who looked like he was not yet 20). There had been, of course, other young Ph.D. recipients; in fact, Ralph Gerard got his Ph.D. at 21, also from the University of Chicago, and served as a professor in a Midwest college the following year.

I was fortunate in that period of job scarcity to have been offered an instructorship in physiology at the Albany Medical College in Albany, New York, at a salary of $1,800 a year. After spending the summer of 1939 continuing the study of slow potentials in Gerard's lab (he had dug up a private donation of $100 to help support me for that time), Fay and I headed for Albany by bus in September. The chairman of the department in Albany was Harold Himwich, whose interests centered on brain metabolism and its functional implications in normal brain and in human psychiatry.

I carried out one or two worthwhile experiments on the cat brain. In one of these, together with Joseph Fazekas and Himwich, I studied the sensitivities of brain electrical activities to a sudden and complete stoppage of cerebral blood flow. We showed that an auditory-evoked potential—recorded simply with an electrode on the exposed surface of the auditory cortex—in response to a simple clap of hands, could continue to be elicited for up to 50 seconds, long after the resting EEG was gone (Libet et al., 1941). The response consisted of the "primary" initial EP (cortical evoked potential); the later EP components (which we did not understand well at the time) had been largely eliminated by the general anesthetic. The relative persistence of the primary EP could have interesting relevance to reports of near-death experiences by patients who survive a period of cardiac arrest. While in Albany, I also lectured extensively to the medical class, in which a fair number of the students were my age or older.

In April 1940, my wife and I took the train, coach seats, from New York City to New Orleans for the American Physiological Society meeting. In the same coach were Birdsey Renshaw and Donald Barron, who were engrossed in discussions of the latest spinal cord physiology during the two-day trip. My talk at the meeting dealt with work done in Chicago on SPs and on the transmission of the caffeine waves across a transection. *The New York Times* gave feature treatment to my report, with the headline "Brain Lightning."

Back in Albany, I found Himwich a well-intentioned and likable person. However, the style of his research and the expectations he had for me did not appeal to me. On Gerard's recommendation, I was taken on by K.A.C. (Allen) Elliott in June 1940. Elliott's lab was in the Institute of the Pennsylvania Hospital for Nervous and Mental Disorders in Philadelphia. The scientific experience with Elliott was very valuable, even though my long-range research interest did not lie in his neurochemistry field. Elliott's desk was in the large lab room itself, so he was always accessible and was involved with each day's experimental runs. I learned much about rigorous controls and quantitative results, as well as some neurochemistry.

Elliott and I measured O_2 uptake with Barcroft manometers and matched that with biochemical analyses (done mostly by Dwight B. McNair Scott). We established some fundamental points about carbohydrate metabolism of brain tissue: (1) We found that homogenized suspensions of rat

brain had an O_2 uptake similar to that of brain slices for the initial few hours at 37°C. When we used homogenized preparations, the biochemical measurements were easier to quantify (Elliott and Libet, 1942). (2) We found that homogenizing the brain in hypotonic solutions (NaCl omitted from the Kreb-Ringers solution) resulted in a severe loss in O_2 uptake, even when we measured the latter with normal Ringers restored. That result indicated that some cellular structures were necessary for normal O_2 metabolism and were disrupted by the hypotonic treatment. Had we then pursued the question of which cell structures were affected by the hypotonic treatment, we might have discovered the crucial role of mitochondria some years before Lehninger did. Ah, well, that is another example of a missed discovery. (3) We found that O_2 uptake of isotonic homogenates was almost completely accounted for by the amount of glucose metabolized, including some of the increases in lactate and pyruvate (Elliott et al., 1942). (4) When we omitted glucose from the medium, we found that O_2 uptake was reduced to about 60 percent of that with glucose. Most of that O_2 uptake was due to combustion of noncarbohydrate material. Such "internal combustion" of cell constituents does not occur when glucose is available. The possibility that nonglucose combustion might affect neuron structure was of considerable interest to the psychiatrist who was using insulin-hypoglycemic shock treatment for schizophrenia at that time. The discovery could also be relevant to electroconvulsive shock therapy and to epileptic seizures. It seems likely that neuronal energy metabolism rises to such high levels during cerebral seizures that the glucose available from the circulating blood is temporarily insufficient to sustain these levels, and that neurons resort to some noncarbohydrate energy sources during such functional hypoglycemic periods.

Elliott and I (1944) also made an interesting discovery that ferrous compounds, together with ascorbic acid, could considerably enhance O_2 uptake by brain tissue, probably with phospholipid as substrate. We then partially isolated an iron protein from liver, one that could replace inorganic iron, and named it "ferrin" (Libet and Elliott, 1944). Ferrin was different from iron-carrier ferritin. We did not pursue ferrin further, but it would seem to merit more interest.

World War II Activities

On December 7, 1941, we heard the announcement of the Japanese attack on Pearl Harbor on the radio in our small apartment in Philadelphia. And our first child, Julian, was born January 31, 1942. The engagement of the United States in World War II led to speeded-up medical school curricula and to war-related research. The department of physiology at the University of Pennsylvania, chaired by H.C. Bazett, took me on as an instructor in 1943. That terminated my three-year stint with Elliott, with

his acquiescence. Elliott later moved to McGill University in Montréal as chairman of biochemistry and as neurochemist in the Montréal Neurological Institute, with Wilder Penfield, Herbert Jasper, and others. At the University of Pennsylvania I lectured to the medical students on endocrinology and gastrointestinal physiology. Grayson McCouch was the resident neurophysiologist, and I had a solid background in endocrinology from my studies at the University of Chicago. Merkel Jacobs, the distinguished general physiologist at the University of Pennsylvania, attended all the medical lectures and told me he liked the style and content of my lectures. One of the students in those classes, Robert Fishman, identified himself to me many years later after he took up the chair of neurology at the University of California, San Francisco (UCSF).

For research I joined Bazett in his studies of body temperature and principles of clothing insulation as related to military requirements. We also assembled a small portable O_2 cylinder fitted to a face mask with an intervening demand-only valve for the O_2. The device was to give aviators who might be shot down over the North Sea a few minutes of breathing during which to escape from the airplane underwater (this development was before scuba gear). The Canadian Air Force asked us to demonstrate the mask in Toronto. I walked about in a pool of deep water with this device (and without my glasses, so I could barely see where I was going). Bill Gibson, then a Canadian Air Force officer, told me he has a film of that demonstration.

In August 1944, I had a stressful time when my father suffered a skull fracture in an accident and died after a week in a coma. He was 48 years old and had been in good health. Shortly thereafter the Personal Equipment Lab at the Army-Air Forces Wright Field near Dayton, Ohio, needed a physiologist, and Bazett suggested me for the job. My family and I moved into a pre-fab housing structure in "Harshman Homes," situated just outside the western edge of Wright Field. The B-17 "Flying Fortresses" flew in over our heads for their landing, rattling the house and our teeth. The walls between us and our neighbors in the duplex allowed us to hear much of their talking, and vice versa. The house was heated with a little coal-burning stove. In all this, our second child, Moreen, was born on November 7, 1944. We did not complain much; we were making our contribution to a war effort we were keenly in favor of.

I was in a clothing section of the survival-and-rescue operations as a "materials engineer." We helped design and test clothing for fliers in the Air Force—antigravity suits for fighter pilots and waterproof coveralls for use by fliers who might fall into the icy waters of the North Sea. Among other things, our civilian head of the section (a fine person, Richard Goldthwait) assigned me to deal with the "General Gerow boot." Although the problem of trench foot, or immersion foot, was not prevalent in the Air Force, an Air Force general named Gerow devised a boot that he thought would solve the problem (we felt his motivation may have been to show that the Air Force

could solve an Army problem and thus to help the push for the Air Force to become a separate military branch). To start that study, I demanded to see what the Navy was doing about immersion foot. A combat-experienced major and a lieutenant were assigned to fly me to Washington, D.C. to visit the Naval Medical Research Institute. I had never flown before, and I requested a parachute for the trip in the two-engine military plane. When we landed in Washington it was too late in the evening for business. My pilots, both from the same town in Georgia, decided to fly home for an overnight visit and invited me along. Because they did not have authorization for this, the major flew the plane close to the ground most of the way to Georgia to avoid detection, freezing me with anxiety. He landed the plane at night on a simple concrete strip near his home town in Georgia; the strip was illuminated by the headlights from his relatives' cars!

We returned to Washington the next day and at the Naval Medical Research Institute I found that the Navy had solved the problem of immersion foot. Damage from immersing feet in cold water was due primarily to heat loss and the resulting poor circulation. The Navy came up with closed cell-sponge rubber, a material now used by divers in their wet suits, and had devised a boot insert of rubber that retains its insulating quality even when wet. General Gerow mistakenly thought that immersion/trench foot was simply due to long exposure of feet to the water in wet socks. His boot had a rubber tube going down to the foot; the upper end of the tube was attached to a rubber bulb which the wearer could pump by hand to force air down around the foot. Because I could not lightly dismiss a general's product I set up a test of the Gerow boot, the Navy boot, and another ordinary hip-length rubber boot offered by one of the military officers in the lab. A group of about five soldiers had thermocouples affixed to their feet and, wearing the boots in question, were asked by their sergeant to slog into the cold muddy banks of the nearby river. After some extensive time with cold mud in their boots, I measured their foot temperatures with a portable potentiometer. The non-Navy boots, including Gerow's, failed badly. When I left Wright Field in September 1945 I was given an "Award of Merit."

University of Chicago and the Woods Hole Marine Biological Laboratory, 1945–1949

I returned to the University of Chicago in September 1945, again on Gerard's recommendation. As an instructor in biological science, I taught in the general course that I myself had taken as a freshman in 1932. I enjoyed that teaching experience much more than my other teaching in professional schools. The students were generally bright and eager to learn the subject for its own interest and relevance to human life rather than in the mode of what-do-I-have-to-know-for-clinical-practice often encountered in professional students. The topics covered all of biology, from botany through psychology, and so I learned much myself.

In research I was involved in the studies of functional neurochemistry carried out by some of the graduate students (including Lou Boyarsky and later, Sidney Ochs). But I also got back to the issue of SPs in the brain. Looking about for some cerebral process likely to exhibit distinct slow potentials, I hit on looking at the spreading depression (SD) that had been described by Aristides Leão (1947).

Amplifiers with sufficiently long time constants were not available to me. I simply set up a sufficiently sensitive galvanometer in a Wheatstone bridge circuit, recorded the deflections beamed to a large semicircular scale, and plotted the SP changes on ordinary graph paper. Julius Kahn, then a graduate student in neuropharmacology, worked with me. We indeed found a large SP shift when SD, initiated by a brief but strong stimulus to a spot on the rabbit's cerebral cortex, progressed through the area on which sat our Ag-AgCl recording electrodes.

Hiss Ferreira (from Brazil) was then at the University of Chicago for some research experience with K.S. Cole. When I described these results to Ferreira, he said he thought his compatriot Leão was working along the same line. On writing to Leão, then in Robert Morison's lab at Harvard, I found that Leão had carried out the same experiments a few months before I did, and was about to send off a paper for publication. He graciously acknowledged our activity in a postscript of that paper (Leão, 1951). Somehow, I was demoralized by being "scooped" on this story, and I felt any paper by me would be passé. And so I did not write up those results until some 15 years later (Libet and Gerard, 1962).

Gerard brought Stephen Kuffler to the University of Chicago on a research fellowship in 1947. Steve picked up on the small motor nerve system that Lars Leksell had described for mammalian muscle spindles, and proceeded to analyze the actions in frog muscles.

Also, in that period of 1945 to 1948 in Gerard's group, Gilbert Ling developed the technique of making the glass microelectrode for intracellular studies. Judith Graham Pool had begun this use of a glass microelectrode earlier, when Gerard had her develop such an electrode to deliver acetylcholine (ACh) intracellularly; that research served as a test in his debate with David Nachmansohn about the role of ACh in conduction of the impulse. Gilbert was able to reduce the electrode tip to a 0.5 μm level by a suitably quick pull of the molten glass capillary tube. That smaller size tip gave recordings of consistently high membrane potentials in frog muscle (Ling and Gerard, 1949), and it opened the way for the breakthrough research by way of intracellular recordings in the nervous system. Among the visitors who came to see Ling's technique was Alan Hodgkin in, I believe, late 1947. Hodgkin then designed the cathode-follower pre-amp, which permitted recordings of rapid changes in membrane potential (like action potentials), with these electrodes, rather than being suitable only for resting membrane potentials.

In the summers of 1947 and 1948, I had a marvelous experience at the Marine Biological Laboratory (MBL) in Woods Hole, Massachusetts, made possible by fellowships from the Lalor Foundation. Going to the MBL had the dual benefit of allowing me to pursue an interesting problem with the squid's giant axon and of getting my family out of the Chicago summer into the refreshing coastal, academic, and social environment at Woods Hole. An additional achievement was my role in introducing Stephen Kuffler to Woods Hole. When I wrote to him back in Chicago about the great qualities of the MBL/Woods Hole environment, Kuffler promptly came there with his family. He quickly became a permanent summertime leader at MBL.

I had for some time thought that the increase in membrane conductance during a nerve impulse might be due to conformational changes in molecules related to the actomyosin system in muscle. As a partial test of the hypothesis, one should expect that ATPase, closely associated with muscle actomyosin, would also be associated with the axon membrane. To test that hypothesis, I homogenized the axoplasm and the cleaned sheath of the giant axons of the squid separately and tested each for ATPase activity. I indeed found a substantial ATPase activity that was about 100 times as concentrated in the sheath as compared with the axoplasm; ATPase in sheath was even greater than in muscle. In my second summer (1948) at Woods Hole, I tried to pin down the localization of the enzyme within the sheath. I found that muscle-free connective tissue, like that making up most of the sheath, had ATPase activity about one-third that of the axon sheath. That finding indicated that the axolemma itself would have ATPase activity many times greater than that of the whole axon sheath. One reason for describing those results here is that I never wrote a full paper on them; at that time I was in the midst of moving to California (in September 1948) and also having to deal with new jobs in 1948 and again in 1949. Actually, these results were fully summarized in two abstracts (Libet, 1948a and b). Skou noticed these and credited that work for the first cytochemical localization of membrane ATPase when he later reviewed the evidence relating enzymatic ATPase activity to the Na-K pump (the enzymatic mediation of Na-K transport was not known in 1948) (Skou, 1965).

There is an interesting footnote to the ATPase story: I presented my findings at the summer's-end conference at the MBL in 1947. I added that ATPase was not more concentrated in optic ganglion than in axon sheath, unlike cholinesterase, and that this finding supported a role for ATPase in nerve conduction rather than in synaptic transmission. David Nachmansohn thought this threatened his view that ACh and cholinesterase somehow mediated the nerve impulse. He gave a vigorous defense of his view, suggesting that the lack of a higher ATPase concentration in the ganglion argued against my proposal, as there were likely more small-axon membrane lengths in ganglion than in the giant axon,

per unit weight. With a calm style that surprised myself, I pointed out (1) that my values were for axon sheath, a small fraction of the whole axon, not for the tissue in bulk; and (2) that I could turn his own argument around and suggest that his much higher cholinesterase findings for the ganglion could more readily fit with a role in synaptic transmission than in nerve conduction, as there were no synapses in the nerve. That generated a laugh from the audience. K.S. (Casey) Cole later complimented me for picking up the other end of a double-ended argument; and old Otto Loewi told me in his charming way that he did not follow the discussion too well but that he thought I had the better of it. On the other hand, George Wald later berated me for attacking such an important scientist; Wald surprised me, as he generally gave the impression of being a liberal and on the side of truth, not of authority. In any case, Nachmansohn himself did not harbor any antagonism, and we became good friends.

My allergic asthma was becoming intolerable in the Chicago winters, and so I reluctantly left the University of Chicago and Gerard's lab in the fall of 1948. I accepted my only offer from California, to be director of research in the Kabat-Kaiser Institute for Neuromuscular Rehabilitation in Vallejo. (I almost wound up in marine biology when the institute in Coral Gables, Florida expressed an interest in me. However, the institute backed off after receiving my application form, in which I gave my religion as one of Jewish descent. In retrospect, I have silently thanked the institute, as I would never have gotten into the research on brain and conscious experience had I gone to Coral Gables instead of San Francisco.) Herman Kabat was applying an interesting reflexology approach to enhancing motor behavior in patients with multiple sclerosis, etc. However, I felt the program in Vallejo did not meet my goals in science. And so I was happy and fortunate to be taken on as an assistant professor to fill a teaching opening at UCSF, starting in July 1949.

The stress of looking for a position in California more suitable than the one in Vallejo and then moving to San Francisco enhanced a chronic duodenal ulcer. On the day in September 1949 that I had taken my wife to the University of California Hospital to deliver our third child, Ralph, my ulcer eroded into a small artery and I almost bled to death. I was rescued by the skillful surgery of a young but up-and-coming surgeon, Orville Grimes, with the aid of 14 pints of blood. Fortunately, AIDS had not yet arrived.

Early Years in San Francisco, 1949–1956

At UCSF, I taught the full course in human physiology single-handedly to the classes in dentistry, pharmacy, and dental hygiene. The medical class was still receiving the first two preclinical years of study on the U.C. Berkeley campus, and so I gave lectures in neurophysiology to them in Berkeley, especially after the retirement of the chairman, J.M.D. Olmsted, in 1952. Olmsted was succeeded by Leslie L. Bennett, a kindly and schol-

arly endocrinologist. The University of California, Berkeley faculty invited the school of medicine to move completely from San Francisco; that was something I and others were in favor of. But it was rumored that it was the powerful clinical faculty in San Francisco that prevailed on the University of California regents to move the basic medical science departments from Berkeley to San Francisco (some of the surgeons and cardiologists were the personal doctors for some of the University of California regents and for high state officials). Vigorous new building then took over on the UCSF campus. The medical school departments in Berkeley moved to San Francisco in 1958 to 1959.

In San Francisco I had joined the "Biomechanics Laboratory" on my arrival in July 1949. This group was engaged in a massive team effort to measure the mechanics, muscle physiology, and energy demands in human locomotion in normal and amputee subjects. The effort was led by Verne Inman, a professor of orthopedic surgery, and Howard Eberhart, a professor of engineering at the University of California, Berkeley, and it produced some extraordinary quantitative reports. I teamed up with Bertram Feinstein, then a neurologist, to study the human electromyogram in the context of the group's interest. In that work we established a role for tendon organ inhibition in strong muscle actions (Libet et al., 1959). That study involved locally anesthetizing the entire tendon of the anterior tibial muscle. I realized that we might improve the spread of the injected procaine, as well as eliminate the painful sting produced by the acid in the procaine-HCl, by bringing the pH up to about 7.4 before the injections. We did this by mixing in an appropriate amount of sterilized $NaHCO_3$, which also converted most of the procaine into the more tissue-diffusible un-ionized free alkaloid. That procedure indeed produced the desired effects; I do not know why it has not been adopted widely to eliminate the painful sting from injections of cocaine derivatives in their acid forms.

With Henry J. Ralston II (father of Henry [Pete] Ralston III, chair of our anatomy department since the 1980s) we also studied the effect of stretch on frog muscle. After getting some coaching on the recording of end-plate-potentials (EPP) from Steve Kuffler at Woods Hole in 1951, I showed that modest stretch of the rectus muscle produced a substantial increase in EPP amplitude (Libet and Wright, 1952). Kuffler picked up on that finding, and later an elaborate analysis of that effect was carried out in his lab. In 1952 I was promoted to associate professor with tenure.

In 1950 to 1951, faculty members were required to sign a "loyalty oath." This was promulgated by the Truman administration during the prevailing McCarthyite atmosphere of a witch hunt for alleged "reds" in government. The oath included items like "I have not belonged to any organization listed as subversive by the Attorney General." I would have been happy to give a simple denial of being a Communist, but the requested statement was a serious affront to freedom of assembly and expression. As a young assistant pro-

fessor I could not afford to face possible dismissal, so I signed the oath "under protest," and accompanied it by a letter that expressed my feelings. At the time I periodically gave a brief series of lectures for residents at the Letterman Army Hospital in the Presidio of San Francisco. I refused to sign the loyalty oath connected to that small job. That refusal prompted a visit by two officers from Army Intelligence. After some tricky questioning they went away apparently satisfied about my political status; even so, I was not again asked to give lectures at Letterman.

Research on Synaptic and Postsynaptic Responses

In 1954 or 1955, John Eccles stopped in San Francisco on his way back to Australia from a conference in the United States. When I expressed an interest in getting back into research on the CNS, Eccles invited me to come to his lab in Canberra. In 1956, I obtained a fellowship grant from the Commonwealth Fund and took off for a sabbatical year with my whole family (four children then, with Gayla having arrived in 1952). On the trip to Canberra, we had a few hours' stopover in Sydney and were roaming about in a small park. A tall stranger approached us to ask if we were the Libets! This turned out to be Anders Lundberg, whose wife Ingeline correctly guessed our American identity from the children's clothing and behavior. In Canberra, the Lundbergs occupied a house adjacent to ours, and we became good friends. The friendship was later cemented when we visited them in Göteborg, Sweden. I have spent some wonderful times with Anders at his country place in Flaton, an island in the archipelago west of Göteborg.

Eccles' department was in the forefront of research on synaptic mechanisms and spinal cord functions, and it was an exciting and informative experience for me. Being exposed to the newer ideas and techniques there helped to reset my research outlook and provided a crucial turning point for my future work. Among the stimulating people there were David Curtis (just getting his Ph.D.), William Liley, Anders Lundberg, Ricardo Miledi, Kris Krnjevic, and of course Rose Eccles and Jack Coombs (who had produced our electronic gear) and Jerry Winsbury (the mechanical engineer who designed and constructed our special research hardware and vertical microelectrode puller). Eccles had about five fully equipped lab rooms, each with a shielded recording room, all served by a capable and congenial "diener" (laboratory assistant), Arthur Chapman.

I had begun to acquire the habit of morning and afternoon tea back in Philadelphia with Elliott, and that became a fixed pattern with me in Canberra. My family and I also had to learn how to make an adequate fire in the large fireplace of the pleasant house assigned to us, and to tuck hot-water bags into our beds on cold nights.

Eccles suggested that Bob Young and I work with him on a problem to test for "plasticity" of function in the CNS (Bob was then a graduate stu-

dent from Harvard and is presently professor of neurology at the University of California, Irvine). Working directly with the master was just what I wanted. The experiment involved cutting some lumbar ventral roots to see whether the resulting chromatolysis of motoneurons would produce a reconfiguration of their synaptic inputs. On the day of experiment, Eccles himself isolated and set up most of the muscle nerves related to the affected spinal segments. By the time Bob and I exposed the spinal cord with all the proper fixations and set the cat in the recording room, the testing did not begin until after dinner. I recall the thrill when we first achieved a solid intracellular penetration of a motoneuron and saw as well as heard the large antidromic action potential with its "overshoot" of the resting potential. We worked well into the night, until 2 or 3 a.m. Eccles did this with unflagging energy and enthusiasm, while I sagged. It was then that I decided to orient my future research so as not to require that kind of effort.

We found no evidence of alterations in the input-motoneuron pattern, but we hit on a different important discovery (Eccles et al., 1958). The strange form of the motoneuron action potentials led us to postulate that these had a *dendritic firing* origin in these chromatolyzed neurons. Eccles designed experimental tests that confirmed that hypothesis. We had thus demonstrated for the first time that CNS neurons could fire dendritic action potentials. The design of our tests was subsequently employed by others, e.g., in the Kandel, Spencer, and Brinley work (1961) on dendritic spikes in the brain.

My subsequent work in Canberra on synaptic responses in sympathetic ganglia was conditioned by my coming down with infectious hepatitis A in January 1957. The disease apparently resulted from my eating the delicious whipped cream scones served by Mrs. Rene Eccles on Sunday afternoon gatherings at the Eccles' home. She obtained the cream without pasteurization from a neighbor who, it turned out, was himself down with hepatitis at the time. The others were given gamma globulin injections, and no one else got the disease.

During my month of recovery at home I read Rose Eccles' Ph.D. thesis with leisurely thoroughness. I became excited by the possibility that the slow ganglionic potentials she had recorded at the surface of the rabbit superior cervical ganglion (SCG) might represent genuine postsynaptic responses with extraordinary durations in seconds. My early experience with slow potentials in the brain (when I was with Gerard in Chicago) had sensitized me to look for slow synaptic responses that might provide the neural basis for SPs in brain. An earlier report by Laporte and Lorente de Nó (1950) had indicated the likelihood of a slow inhibitory postsynaptic potential (IPSP) in turtle ganglia and was also a stimulating factor.

When I returned to work, I explained to John Eccles what I had in mind and, with his approval, I induced Rose Eccles to introduce me to her meth-

ods for studying the rabbit SCG. Her methods involved making surface recordings, with one Ag-AgCl electrode on the ganglion and a second electrode on the crushed end of the internal carotid branch of the postganglionic nerve, with stimulating electrodes on the preganglionic nerve. Most studies were carried out on the excised preparation, cleaned and mounted in a neatly designed chamber that permitted dipping the preparation into the oxygenated bath medium when it was not up in the air for recording. Rose had reported (Eccles, 1952) that the curarized ganglion exhibited a depressed initial N wave (the well-known excitatory postsynaptic potential [EPSP]), so that it did not fire an action potential; this was followed by a P wave (surface positive, duration about 0.5–1 second) and an LN wave (late-negative, lasting some seconds). Repetition of preganglionic volleys rapidly built up the P and LN waves but not N.

We first applied botulinum toxin to test whether preganglionic release of ACh was necessary for producing the slow P and LN waves. The toxin slowly abolished all of the ganglionic responses. This result indicated that P and LN (as well as N) were dependent on a release of ACh. Because P and LN potentials were not abolished even by strong cholinergic-nicotinic blockers (like curare) that wiped out the N wave, I decided to test a muscarinic blocker like atropine. The "doctrine" at that time was that the sympathetic ganglion response was a purely nicotinic one, as in striate muscle. We were delighted to find that a weak concentration of atropine could wipe out the P and LN components while leaving the N wave alone. That result indicated that the slow P and LN components were also postsynaptic responses mediated, at some step, by ACh acting on muscarinic receptors.

Those findings set me off on a series of studies that dominated my laboratory experimentation for about 25 years. My other line of research, on the cerebral basis for conscious experience, began about that same time and has continued even after my retirement in 1984. I would like to organize most of the remaining history around each of these research programs separately.

I shall digress briefly to note my small role in the founding of the Society for Neuroscience. Gerard invited me to join an initiating committee for the Society that met during the meetings of the International Physiology Congress in 1968 in Washington, D.C. I was appointed a coordinator for the northern California region. Actually, I had, in the early 1950s, started and conducted a monthly discussion group for neuroscientists in the San Francisco Bay area that became known as BANG (Bay Area Neuro-Group). BANG went on fruitfully until the mid-1960s. It was a kind of forerunner of a chapter of the Society for Neuroscience.

I would also note my shock and depression after my mother's death in 1967. While on corticosteroid treatment for a nasty skin disease, pemphigus, she developed an uncontrollable infection. I did not learn how serious this was until it was too late for me to come from San Francisco to Chicago to spend some time with her in her last days. She deserved a better fate.

Slow Synaptic Actions

I concluded the series of experiments begun with Rose Eccles after returning to San Francisco. I first had to set up my own lab (patterned after those in Canberra) in the newly constructed building into which the department of physiology moved from Berkeley in 1958. In the first paper (R.M. Eccles and Libet, 1961), I proposed a diagram for the intraganglionic pathways in which, on the basis of our evidence, the existence of a functional interneuron was postulated to mediate the P wave (presumed to be an IPSP). Monoaminergic small intensely fluorescent (SIF) cells had just recently been described histologically (see Eränkö and Eränkö, 1971). I proposed that the SIF cell received preganglionic ACh input that excited the cell by a muscarinic action, and that it then delivered a catecholamine that elicited a hyperpolarizing response of the ganglion cell. (In a quantitative study of changes in monoamine fluorescence of the SIF cells, done with Christer Owman in Lund, Sweden, we showed that depletion and restoration of DA content in the SIF cells were causally related to the loss and restoration of slow IPSP (sIPSP) responses, respectively (Libet and Owman, 1974).) That proposal elicited considerable interest and pro and con arguments (see Libet, 1992). The electron microscopists soon demonstrated preganglionic endings on SIF cells (Elfvin, 1963; Williams, 1967) as well as some close synaptic-like contacts by SIF cells with ganglion cells. I went on to show that the P and LN waves should be regarded as slow IPSPs and slow EPSPs, respectively (Libet, 1964); and that the synaptic latencies for these responses were also extraordinarily long (about 10 and 300 msec, respectively) (Libet, 1967).

Those long durations and long latencies indicated one was dealing with novel kinds of PSPs, strikingly different from the well-established fast PSPs, whether the latter were in autonomic ganglia, skeletal neuromuscular junctions, or in the CNS. When I began to report these findings and views in the early 1960s, I met with disbelief from some neuroscientists. Admittedly, the experiments employed surface field recordings. But the arrangement of neurons with their axons bundled into the extended postganglionic nerve made the interpretations convincing; there was perhaps the unlikely possibility that some specially arranged glial cells could be responsible for the slow potentials. However, with intracellular recordings, we laid these doubts to rest.

With the first of a series of capable Japanese visitors (Shiko Chichibu, later professor in Kinki University in Osaka; and Tsuneo Tosaka, professor at Tokyo Medical College), we made the initial intracellular studies on frog ganglia. Tosaka reported these findings at the International Physiological Congress in 1965. I presented them at the FASEB meetings in the United States (Libet, 1966). Nishi and Koketsu (1968) then quickly entered the field with their talents for microelectrode studies and pro-

duced a full paper in 1968 that confirmed our reports while adding further findings. In my usual style of being slow to write up full papers, we got ours out just in time to appear in the same issue of the *Journal of Neurophysiology* (Libet et al., 1968; Tosaka et al., 1968).

In a return visit by Tosaka in 1968, we managed to make intracellular studies on the mammalian (rabbit) SCG (Libet and Tosaka, 1969). Good intracellular penetrations of neurons in mammalian ganglia are difficult to make. These ganglia are full of elastic connective tissues and behave like sponge rubber balls. Attempts to soften the ganglia with elastase and collagenase result in a loss of synaptic responses; presumably the synaptic contacts are loosened away from the ganglion cells.

The intracellular studies conclusively established the neuronal, postsynaptic nature of these slow responses. The studies also proved that more than one type of receptor was present on the same ganglion cell. Both the nicotinic and muscarinic receptors for ACh were present, as well as one for catecholamines. That finding was a relatively novel proposition. Of course, various slow PSPs have since become widely recognized and studied in many different types of neurons.

An even slower EPSP ("LLN," or late-late negative) was discovered in the frog ganglion by Nishi and Koketsu (1968). This PSP had a duration of up to 30 *minutes*, after a brief repetitive preganglionic input. This late-slow EPSP was not mediated cholinergically or adrenergically. Jan et al., 1979 later showed that the transmitter was the polypeptide known as LH-RH (the releasing hormone for the luteinizing hormone in the pituitary gland)! Lily and Y.N. Jan (1982) went on to show that LH-RH was released only by preganglionic C fibers. But the LLN response was also elicited in the B neurons that received no innervation by C fibers at all. This finding provided a proven example of a synaptic transmitter diffusing for at least some micrometers to elicit a response. We had earlier proposed such "loose" synapses for the slow EPSP.

Some years later we demonstrated a similar late-slow EPSP in the rabbit SCG in the presence of complete cholinergic and adrenergic blockade (Ashe and Libet, 1981a). This response also lasted about 30 minutes after a brief repetitive train of preganglionic volleys, even when these were at low frequencies of three per second. This late-slow PSP in rabbit SCG had a synaptic delay of about one *second* and an amplitude greater than that of a maximal fast EPSP.

Electrogenic Mechanisms

With my third Japanese collaborator, Haruo Kobayashi in 1966 to 1968, we found that the slow EPSP was produced with *no increase* in membrane conductance (Kobayashi and Libet, 1968). That was probably the first example of a chemically transmitted PSP that was not generated by the well-known increases in ionic conductance. In frog ganglia the slow EPSP was actually

related to a *decrease* in membrane conductance. We dismissed the possibility that this finding represented a decrease in K^+ conductance because the slow EPSP did not show a reversal of polarity at E_{K^+} (about –80 to –90 mV in those cells). However, these peculiar characteristics led Brown and Adams (1980) to discover a new K^+ conductance; the ionic channels for this K^+ conductance were open only in the depolarized range of membrane potentials below –60 mV, and these channels opened or closed slowly, with time constants in seconds. These K^+ channels, when open, could be closed by a muscarinic ACh action which thereby results in a slow depolarization; they were thus named the "M" channels. This M-channel mechanism appears to account fully for the slow EPSP in frog ganglia; it is in accord with our finding that this PSP was absent in cells with normal resting potentials of –70 mV (Libet et al., 1968; Kobayashi and Libet, 1968; Tosaka et al., 1983). That was not the case for the mammalian ganglia, which exhibit a large slow EPSP in normal cells at –70 mV. The slow EPSP in rabbit SCG is therefore not equivalent to that in frog ganglia; indeed it was an early example of a "metabotropic" synaptic action; its generation appears largely to be mediated intracellularly via cyclic GMP, produced by the muscarinic activation of guanyl-cyclase (Libet et al., 1975; Hashiguchi et al., 1978, 1982).

Long-Term-Enhancement (LTE) of Slow PSPs

When Tosaka and I were experimenting with the possible role of dopamine (DA) as the transmitter for the sIPSP (in 1969 to 1970) we serendipitously made an extraordinary discovery (Libet and Tosaka, 1970). Temporary exposure of the rabbit SCG to DA was followed by a prolonged enhancement of the slow depolarizing response to a muscarinic action (by ACh, or by methacholine, etc.). This LTE persisted for at least as long as the ganglion remained in functional condition (three to four hours in the chamber). Amines other than DA did not produce LTE. Later, Ashe and I showed a similar effect of DA on the slow IPSP and slow EPSP, but not on the nicotinic fast EPSP (Ashe and Libet, 1981b).

Finally, Sumiko Mochida and I demonstrated that such an LTE could be obtained simply with a brief train of preganglionic volleys, even at relatively low frequencies of repetition (Mochida and Libet, 1985; Libet and Mochida, 1988). That finding was in accord with our earlier demonstration that intraganglionic DA in the SIF cells could be released by preganglionic stimulation. Also, the LTE could be blocked by D_1, but not by D_2 antagonists; and the application of cyclic AMP, whether extra- or intracellularly, could substitute for DA to give LTE (Libet et al., 1975; Kobayashi et al., 1978; Libet, 1979). The latter results indicated that DA acted by stimulating adenyl-cyclase (a property already established by others) and that the resulting increase in cyclic AMP mediated the long-lasting increase in the effectiveness of the muscarinic receptor for the slow EPSP (and for the sIPSP, whether on SIF cell or ganglion cell).

Our reports of LTE, starting with Libet and Tosaka (1970) provided, perhaps, the first example of the modulation of a postsynaptic response to one synaptic transmitter (ACh, acting muscarinically) by another transmitter, DA. After a seminar I gave in Stockholm in 1971, Ragnar Granit commented that it was the first time he had heard of an example of a "synaptic amplifier." The modulating action is not only specific for DA but is produced by DA (or cyclic AMP) without any change in membrane potential or conductance (Kobayashi et al., 1978).

LTE modulation by DA was discovered some eight years before long-term potentiation (LTP) (Bliss, 1978). There are similarities but also important differences between the two. Both last many hours after a brief, repetitive input; they are sensitive to reduction in extracellular Ca^{++} and to the specific inhibitor of Ca-calmodulin, calmidazolium; the inhibitor of protein synthesis anisomycin has no effect on the first several hours of LTE and LTP. They are different as follows: (1) in the specific postsynaptic response that is enhanced; (2) in the frequency of the effective neural inputs (3 to 10 per second for LTE, usually a high frequency for LTP); (3) in the requirement of a second transmitter, DA, for LTE, rather than a large depolarization of whatever origin for LTP; and (4) in that LTE does not require a conjunction or near-synchrony between DA input and the ACh response that is subsequently enhanced, whereas LTP does require such a conjunction between a depolarizing input and a weaker synaptic (glutaminergic) input. The last difference makes LTP a better model for mediating classical learning. But LTE could provide a basis for enduring changes in synaptic reactivity that may underlie the shifts in vigilance and mood thought to be controlled, in part, by DA systems (see Libet, 1986, 1988).

Another remarkable feature of LTE deserves attention: Cyclic GMP, the putative intracellular mediator of the slow EPSP, was found to disrupt or block the production of LTE but only if applied within the first 5 to 10 minutes after the exposure to DA; it had no effect on the test-expressions of LTE once that has been produced (Libet et al., 1975). That temporal discrimination in the effectiveness of cyclic GMP distinguishes between the processes that produce or consolidate an enduring plastic change and those involved in expressing the change.

I would suggest that the LTE phenomenon deserves more attention, for it may have a potentially important role in brain functions.

Brain Processes in Conscious Experience

The question of how the brain produces conscious experience had been lurking in my mind since my time as a graduate student. I am sure that question has been and is on the minds of many neuroscientists, but excruciatingly little direct experimental research has appeared. Neurosurgeons like Harvey Cushing, Otto Foerster, and especially Wilder Penfield, have produced valuable studies mapping the conscious responses that could be

elicited by electrical stimulation of the cerebral cortex, but they did not go into the physiological questions of the neural dynamics—of *how* rather than *where* neuronal activities specifically resulted in conscious experience, an awareness of something.

My entry into this field was made possible by my good fortune in having the neurosurgeon Bertram Feinstein as a colleague and friend. Feinstein was one of the relatively small group of neurosurgeons who had an interest in using the opportunities (set up by therapeutic procedures) to study experimental questions of both fundamental and clinical importance. He had the additional, uniquely humble quality of allowing someone more expert in a given research matter to take the leadership in the design and conduct of an experiment. When Bert invited me to study some important physiological questions that would benefit from access to intracranial electrodes, I jumped at the chance of studying conscious experience in awake human subjects. Feinstein's new operating room (at the Mt. Zion Hospital in San Francisco) was designed to foster electrophysiological studies and was completed in 1958 to 1959. I was also fortunate in the composition of the research team (including W. Watson Alberts and E.W. (Bob) Wright at that time); the team also worked with Feinstein on the stereotactic technology for therapeutic purposes.

I should note that my decision to commit a major research effort to this question was a risky one, in terms of my career. In such difficult and relatively unknown terrain there was every possibility of a complete failure to find out anything worthwhile. I would be working on an issue that was not popular at the time. Indeed, there was a fair amount of antagonism, especially by many positivists, psychologists, and philosophers, who held that studying subjective, introspective experience was not a fit scientific activity. That attitude has mellowed in recent years with the development of cognitive science and with demonstrations that subjective experience can be studied quantitatively and reliably.

As late as 1977, when we already had made some intriguing discoveries, a leading neurophysiologist urged me, as a good friend, to give up this brain research and concentrate fully on my studies of slow synaptic actions in ganglia. Fortunately, I had achieved tenure as an associate professor in 1952 and the chairman of my physiology department, Leslie Bennett, a scholar with broad interests, approved of my spending a large fraction of my research time with Feinstein at the Mt. Zion Hospital. With our first report of results in 1964 (Libet et al., 1964; Libet, 1966), I received interest and approval from a number of great neuroscientists (including John Eccles, Ragnar Granit, Frederic Bremer, Lord Edgar Adrian, Charles Phillips, Wilder Penfield, Herbert Jasper, Ralph Gerard, Anders Lundberg, and Robert Doty) and that helped to bolster my courage to carry on in this field.

I was confronted with the difficult question of how to begin such an investigation. I decided that the subjective side of the brain-mind study must be kept to the simplest possible so that my brain research group

could concentrate on the physiology. Because we were given access to electrodes in the cerebral somatosensory system, we adopted as our criterion of a conscious subjective experience the introspective report of a simple somatic sensation. Report of such a "raw feel" would be fairly immune to possible emotional distortions, and reliability of the reports could be established by the investigator's ability to manipulate production of this sensory experience, by changing stimulus intensities, etc. That ability also allowed us to design tests of causative, rather than merely correlative, factors in the relationship between brain processes and a conscious experience. The other principle was that we should study the *differences* in cerebral processes for the transition between unconscious (nonconscious) responses and just threshold conscious responses. That procedure would avoid having to deal with all the brain features that are necessary for, but not uniquely causative of, conscious experience.

Given these circumstances, we adopted a classical physiological approach. We started with the question, What kinds of activations of cortical somatosensory (SI) neurons lead to production of a conscious sensory experience? More specifically, what are the changes in electrical stimuli that are needed to go from below threshold to a just-threshold sensory experience? This formulation also opened the possibility for characterizing neuronal activities that may mediate *unconscious* mental functions, when these activities are insufficient to elicit awareness. Also, stimulating the SI cortex directly got us closer to the cerebral requirement for awareness than is the case for a peripheral sensory input; the latter can give rise to a multiplicity of ascending parallel actions at the cortex, actions that are difficult to specify or manipulate experimentally. Finally, the operational criterion for a conscious experience had to be an introspective report of it by the subject. Purely behavioral responses that did not directly represent the subject's introspective experience could not be valid criteria. To study the physiology of subjective experience, I thought it obvious that we must study the subject's report of it. I soon discovered that such a definition met with considerable opposition, but that has faded in recent years.

Delay in Awareness

The most interesting requirement for producing a just-threshold sensory experience turned out to be the duration of the train of repetitive stimulus pulses (Libet et al., 1964). With minimum effective stimulus intensity, a minimum train duration of around 0.5 seconds was required. My colleagues and I went on to show a similar requirement for stimulation of subcortical cerebral sites in the somatosensory pathway, e.g., in ventrobasal thalamus and medial lemniscus. Although stimuli to skin or sensory nerve can be effective even with one pulse, we developed several lines of evidence that strongly supported the view that cerebral responses to the single skin pulse also had to persist for 0.5 seconds or more to give a

threshold sensation (Libet et al., 1967; Libet et al., 1971; Libet, 1973; Libet et al., 1992; Libet, 1993a,b). All of the evidence, then, indicated that our awareness of the sensory world is delayed by about 0.5 seconds (or more) and is not synchronous with the actual events sensed.

Subjective Referral Backwards in Time; Antedating of Sensory Experience

If awareness is delayed, my research group and many others were concerned about how to account for the fact that sensory experiences seem subjectively to appear with no delay from the real time of the events. It took us a while to realize we must distinguish subjective timing from neural timing, the latter being the time at which neuronal activations became sufficient or adequate for eliciting the awareness. That distinction led us to the hypothesis that, after the actually delayed appearance of the experience, subjective timing is automatically antedated; and that the primary evoked response (of the SI cortex to the earliest signal arriving, within 10 to 20 msec of a peripheral stimulus) serves as a timing signal to which the experience is subjectively referred. Fortunately, we were able to devise and carry out a convincing, crucial experimental test of the hypothesis (Libet et al., 1979). One of my thrills in research occurred when I observed the astonishing confirmatory results of that test as they came out of the subjects' reports during the experiment.

Subjective referral in the *spatial* dimension was already well known. The simplest example of that is seen when the subject reports feeling something in a hand and not in the contralateral SI cortex that is stimulated to produce the sensation. But spatial referral is evident also in all peripheral sensory inputs, in which the pattern of neuronal responses in the cortex are spatially quite distorted in relation to the original sensory configuration. We had now discovered that there is also subjective referral in the *temporal* dimension. Both forms of subjective referral serve to "correct" the sensory experience so that it appears to coincide with the actual sensory event despite spatial and temporal distortions imposed by the way the brain represents it. There is no known neural mechanism that could have predicted such subjective referrals. The question of why such subjective referrals appear may be in the same metaphysical category as one that asks why or how certain cerebral activities give rise to any conscious subjective experience at all. What we can do, scientifically, is study how the neural and subjective events are related, especially if we can discover causative relationships.

Cerebral Initiation of a Voluntary Act vs. Conscious Will

Kornhuber and Deecke (1965) had reported that a slowly rising negative potential was recordable at the scalp preceding a "self-paced" act by a human subject. The "Bereitshaft Potential" or "readiness potential" (RP) began about 0.8 seconds or more before the act. However, the authors made

no attempt to relate this interesting finding to the operation of conscious will. In a symposium discussion some years later, I heard Eccles say that, in view of the RP finding, the conscious will to act must obviously be appearing almost a second before the act. I realized that Eccles had no direct evidence for making that assertion, and such an alleged advance appearance of conscious will seemed to me to be unlikely. However, to devise an experimental test of the question seemed impossible, as one would have to find a way to measure the time of appearance of the subject's conscious intention to act, in conjunction with recording the RP in a voluntary act.

It was during my stay as a Scholar in Residence in the Bellagio Center for Advanced Study, on Lake Como in Italy, that a seemingly simple way of determining the time of a subjective intention to act occurred to me. This was in the fall of 1977, and I was there working on the paper on antedating (Libet et al., 1979), and so the question about voluntary action was floating about in a mostly subconscious fashion. The method, in principle, was simply to have the subject observe the equivalent of a "clock-time" at which he/she first became aware of an intention to "act now," and then to report that "clock-time" later to the observer. We tried this out in 1978 and found, to our surprise, that subjects could report these timings with a reliability of ±20 msec (S.E.). We also addressed a number of other issues, especially that of validity.

In the experimental series, RPs were recorded for the same voluntary acts for which subjects reported the times of the first awareness of intending to act (Libet et al., 1983). In studies of self-paced movements, by Kornhuber and Deecke and by others, there were some limitations on volition, but we eliminated those. The resulting freely volitional self-initiated acts showed RPs beginning an average of –550 msec (before the act), well *before* the –200 msec for the appearance of the reported conscious intention to act. The 350 msec difference between these values had a strong statistical significance. I discussed this finding and important implications of it for free will and individual responsibility in a paper in *Behavioral and Brain Sciences,* accompanied by 25 critical commentaries (Libet, 1985). Our basic experiment (Libet et al., 1983) has been repeated and the results confirmed by several groups (e.g., Keller and Heckhausen, 1990). On the other hand, our experimental studies of conscious *sensory* experience employed intracranial electrodes, and that radically restricts opportunities for others to repeat them. There have, however, been at least several confirmations of the requirement of repetition of inputs to somatosensory cortex (e.g., Amassian et al., 1991).

I must add a note about my stay in Bellagio. My wife Fay and I were given a large airy room plus a study in the villa, formerly a ducal palace. This was the first and only time we experienced the aristocratic lifestyle. For the roughly 12 resident scholars and their spouses there was a butler and about 10 assistants, and a chef with several assistants. The servants

told Fay and me that our room had been occupied by President John Kennedy during a trip to Italy. One of the servants was named Amilcar, a name associated with Hannibal's march through northern Italy some 2,000 years earlier. Amilcar could make remarkably accurate weather forecasts by simply looking at the sky and putting up a wet finger. That ability fascinated one of the other resident scholars who happened to be a world renowned meteorologist. The opportunity to interact with the other scholars, who were all eminent in their fields (sciences, humanities, literature, etc.), was a great benefit. On one Saturday evening gathering, I sang classical lieder (by Schubert and Scarlatti), accompanied very capably on the piano by the wife of a scholar from England.

Cerebral Transition Between Unconscious Detection and the Conscious Awareness of a Signal

Even when stimulations of the somatosensory system were too brief to elicit a conscious sensation, substantial neural activities were recordable. I proposed that these shorter-lasting activations may mediate unconscious mental functions, whereas longer-lasting similar activations produce awareness; I called this proposal the "time-on" hypothesis. My brain research team was able to carry out an experimental series that directly tested this hypothesis (Libet et al., 1991). This research study (during 1987 to 1990) was made possible by the availability of patients with stimulating electrodes permanently implanted in ventrobasal thalamus (by UCSF neurosurgeons Yoshio Hosobuchi and Nicholas Barbaro, for treatment of intractable pain). Also, a room and computer facility were loaned to me at UCSF by my colleague and good friend, Michael Merzenich; I had already achieved emeritus status and had no facility of my own for this work. My good friend and colleague, neurosurgeon Bert Feinstein, had unfortunately died prematurely in 1978. Subsequently we lost not only his supply of research subjects and collaborative efforts, but also the splendid research facility and research team that had functioned so fruitfully at the Mt. Zion Hospital. I had been intending, on my retirement from the University of California, and after giving up my animal lab and the work on sympathetic ganglia, to move to the Mt. Zion facility and continue with the brain research. That plan fell through with Feinstein's death.

The experimental test of the "time-on" hypothesis for explaining the cerebral difference between unconscious and conscious functions involved the following: Stimuli of varying train durations (0 to 750 msec) to ventrobasal thalamus were delivered in different trials, and the subjects were asked (1) to report on the presence or absence of a stimulus, even when nothing was felt (a forced choice) and (2) to report whether they felt any sensation or even anything different, in each trial. Stimuli in a given series were all at the same near-threshold intensity that was required for eliciting a conscious sensation when such pretested stimuli had a train duration

of 400 msec. The results, from hundreds of trials with each subject, showed (1) that subjects detected the presence of a stimulus even when they felt nothing and were guessing, with accuracies well above the 50 percent expected on pure chance; and (2) to go *from* detection-without-awareness *to* detection-with-awareness (even of the most minimal and uncertain level) required an *additional* almost 400 msec of stimulus duration.

The transition between an unconscious mental function and a conscious one could thus be controlled by or be a function of the duration of the appropriate neuronal activations. Such a relationship raised the possibility that unconscious mental functions in general may be mediated by neuronal activities too brief to elicit awareness; and that awareness may arise from those same kinds of neuronal activities if they simply persist long enough.

More recently, I proposed the existence of a hypothetical "conscious mental field" that would have the attributes of a unified subjective experience and the ability to effectuate conscious will by modulating appropriate neuronal activities (Libet, 1993b, 1994). I had, by design, previously not proposed any hypotheses or theories of mind-brain relationships without subjecting them first to some experimental testing. That was also my intention for this field theory; the hypothesis and an experimental design to test it had occurred to me more than 30 years earlier, but I was not able to muster the appropriate patients suitable for the test or the collaboration of the few neurosurgeons who did have access to such subjects. The saving grace in my present proposal is, at least, that it is accompanied by a description of an experimental design to test it. The experiment is a difficult one and would benefit from preliminary testing with monkeys before going to the human subject, but it is in principle workable. I suspect this proposal is getting a cool reception from my neuroscience peers. I found it interesting, however, that the young people (graduate students and young postdocs) generally have found the proposal not only an acceptable idea but even an attractive one. I was recently pleased to find that Karl Popper was proposing existence of a "conscious force field" that has much in common with my proposal (Popper et al., 1993; Lindahl and Arhem, 1994).

Some Concluding Remarks

My approach to research has been predominantly one of seeking for or being attuned to fundamental questions of broad significance and staying with an experimental program to answer these questions. Of course, the questions and hypotheses to answer them had to be formulated in ways that permitted experimental designs that were practicable and potentially fruitful; as we know, that skill is an essential ingredient for experimental research. On the other hand, if such experimental qualifications were met by me, I was ready to commit my efforts to them, even if the research topics were not in the mainstream of neuroscience research.

Indeed, I liked working on issues that were not being pursued competitively, giving me the opportunity to explore such issues patiently without external pressures (except for those from the granting agencies).

That style of research was begun with my initial efforts as Gerard's pupil, as it also characterized much of Gerard's pioneering research activities. The style is clearly evident in my two major lines of research during the last 35 years, especially so in the one on brain processes in conscious experience. I was told a number of times, in the responses from granting agencies (the National Institutes of Health and the National Science Foundation) and by some leading neuroscientists, especially by behavioristic psychologists, that I was not working on a properly fruitful subject. On the other hand, a large number of the internationally prominent figures in neuroscience expressed strong interest in and approval of my work on the physiology of subjective experience. I also received antagonism from some philosophers; but, again, the interest and appreciation from others (including Stephen Pepper, Karl Popper, Thomas Nagel, and Martin Edman) served as a comforting counterbalance. Actually, I was surprised at the degree and nature of the opposition to this experimental plunge into the fundamental problem of mind-brain interaction. Happily, there has been in recent years a growing and widespread interest in the nature of consciousness. This interest has been accompanied by a wider recognition that our work provided one of the few direct and fruitful experimental attacks on the problem.

I am delighted with the growth of interest in the issues of brain and conscious experience. I would still like to continue with some experimental research in this fascinating area, but that will be contingent on my own energy levels and on the availability of facilities, collaborators, and suitable subjects. I had indeed begun, in 1992 to 1993, to try for a study that might provide a rigorous test of my hypothesis that unconscious and conscious functions can be mediated in the same cerebral areas. That effort was abruptly stopped by my having to undergo major surgery in late 1993, but I hope to get back to that experimental program. I am, however, currently attempting to write a book that will be addressed to a general audience about my work on conscious experience.

Of course, research, writing, and lecturing are not all there is to living. I have been fortunate to have a loving interaction with my family and warm relations with friends, both scientific and other. Music has been important in my family and continues to be a major source of pleasure. My four children play stringed instruments, with a high level of musicality. We have a cellist (Julian), violist (Moreen), and two violinists (Ralph and Gayla). My wife Fay is an accomplished pianist, and I have been a singer. Indeed, it was through her piano and my singing that we first met, in 1936. When we were in Australia in 1957 with Eccles, our cellist son Julian (then 15), my wife, and I entered an audition by the Australian Broadcasting Commission. We were selected to perform on the national radio network; I

appeared in three programs, Julian in two of these, and Fay also in the third, billed as a Libet family recital. My wife Fay has, by her example, helped to expand my appreciation of the artistry in music to that in paintings, sculpture, and ceramics. I have always felt that my scientific research involved a strong element of artistic creativity, especially in the intuitive nature of the hypotheses and experimental designs; such feelings have also been expressed by some other scientists about their work.

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