Marian C. Diamond

Marian Cleeves Diamond

Born:

Glendale, California, USA
November 11, 1926

Education:

University of California at Berkeley, B.A. (1948), M.A. (1949), Ph.D. (1953)
University of Oslo, Norway, Certificate of Courses (1948)

Appointments:

Research Assistant, Harvard University (1952–1953)
Instructor, Cornell University, (1955–1958)
Lecturer, University of California School of Medicine at San Francisco, (1958–1960)
Lecturer, University of California at Berkeley, (1960–1965)
Assistant Professor–Professor, University of California at Berkeley, (1965–)
Assistant Dean–Associate Dean of College of Letters and Science, University of California at Berkeley (1967–1972)
Director of Lawrence Hall of Science, University of California at Berkeley, (1990–1996)
Governor's Board Rand Graduate School (1985–1996)

Honors and Awards (Selected):

Fellow, American Association for the Advancement of Science Fellow, California Academy of Sciences
Council for Advancement & Support of Education. Wash. D.C. award for California Professor of the Year and National Gold Medalist
California Biomedical Research Association Distinguished Service Award
Alumna of the Year—California Alumni Association
San Francisco Chronicle Hall of Fame
University Medal, La Universidad del Zulia, Maracaibo, Venezuela
Brazilian Gold Medal of Honor
Benjamin Ide Wheeler Service Award
The Distinguished Senior Woman Scholar in America awarded by the American Association of University Women

Major scientific contributions from Marian Diamond's laboratory are threefold: One, the structural components of the cerebral cortex can be altered by either enriched or impoverished environments at any age, from prenatal to extremely old age. An enriched cortex shows greater learning capacity, an impoverished, the opposite. Two, the structural arrangement of the male and female cortices is significantly different and can be altered in the absence of sex steroid hormones. Three, the dorsal lateral frontal cerebral cortex is bilaterally deficient in the immune deficient mouse and can be reversed with thymic transplants. In humans, cognitive stimulation increases circulating CD4-positive T lymphocytes, supporting the idea that immunity can be voluntarily modulated.

Marian Cleeves Diamond

Growing up: What Constitutes an Enriched Environment?

I was born in Glendale, California, on November 11, Armistice Day, 1926, the youngest of six children. A large uterine tumor accompanied me during my growth process in my 42-year-old mother's uterus. My 47-year-old father brought all my brothers and sisters to say good-bye to my mother because he was told the doctor could save one but not both. How wrong he was! My mother lived to be 75, and I am now 80.

Because most of my biological research efforts have dealt with the effects of the environment on the development of the anatomy of the brain, I thought it might be appropriate to describe the environment that played a role in developing my young postnatal brain during its most rapid growth period.

In the early 1920s the area north of Los Angeles appeared to be mostly sagebrush, buck wheat, and poison oak. The landscape extended through the narrow valley between the Sierra Madres to the north, rising to 5000 feet, and the Verdugo Hills to the south, but not quite as high. This southern California area was home to black widow spiders, rattlesnakes, and tarantulas. But it was also the home of dragonflies, scrub and stellar jays, humming birds, deer, opossums, coyotes, and rabbits. The air was pure and crystal clear, a delight to breathe; yet one took it for granted.

What attracted an Englishman from the green moors of Northern England to California's dry climate? I will never know for certain, but I think he, as a physician, wanted to set up a sanitarium to cure those with respiratory problems. He saw so much suffering from the miners with lung disease acquired from working in the depths of the coal mines. Father was the only one of his large family to leave the comforts of his fine residence in England and make his home in the United States. There is no one left to ask why.

The home father carved out of the rugged brush and rocks in La Crescenta left little to be desired. First, he hired Mexican laborers to clear his 20 acres and make a stone wall completely surrounding his land, similar to the ones around the fields in Tasmania. He continued to take advantage of all the rocks of every conceivable size and shape to make his house. In front of the house he erected a rock pergola that was eventually covered with delicate, lavender wisteria, providing lunch for thousands of noisy honey bees. The rock terraces were later filled with roses for his formal garden and vegetables for the dinner table. The little rock-covered "study," as we called it, where he wrote letters and conducted some of his medical practice, was separate from the house. Rock-lined paths led through the citrus trees to rock walls that supported the swimming pool where we spent most of our days with our friends during the hot southern California summer months. A rock semicircular alcove for sitting adjacent to the tennis court was surrounded by a low rock wall that supported a high wire fence. (Once a deer, trapped on the tennis court, dove against the wire fence with such force that she left a well-circumscribed hole.) We used the tennis court not only for learning to play tennis but for roller skating as well, often until dark.

Our orchard appeared blanketed with rocks. As my brother plowed between the trees, it seemed that all the tractor did was turn over rocks. But the soil beneath those rocks nourished every kind of fruit imaginable, such as, quince, plums—Santa Rosa and Green Gage—apricots, peaches, and nectarines. The orchard also provided black and white figs that Mother preserved or candied for our dinner table. Rows and rows of grape vines supplied plump, juicy red tokay grapes that made delightfully fresh gifts when placed on a grape-leaf, lined plate. (We used to deliver such a gift to Mrs. Beach, a Carter Ink heiress, who lived in the light pink, Italian villa across Briggs Avenue where we lived.) Father often experimented in making wine from the Concord grapes that grew over a rock wall. Blackberries flavored our favorite ice cream. Orange and lemon blossoms lent their fragrance to the whole ambience. Almond trees added their lovely delicate, white-pink blossoms in the spring, and walnuts stained our hands dark brown as we hulled them in autumn. (We ate Mother's blanched almonds by the hand full while still warm.)

The almond trees were interspersed with carob trees. We had to pick the carob beans up off the ground after my father had knocked them down with a long stick. It seemed to us he had the easier job, as we stooped over the beans and our boxes. On the street side of the rock wall was the row of olive trees where people would come on Sunday afternoon and fill their buckets without permission. My father would send us out to ask them to leave.

Father fed the carobs we grew in our orchard to the goats, which he kept because he believed goat's milk was healthier for children than was cow's milk. Next to the goat shed was the chicken coop. He would stop by the side of the road on his way home from Los Angeles, where he practiced medicine, to pick mustard greens for the chickens to eat. My sister used a stick to keep the head of the chicken turned away from my arm, as I slid my hand under the hen to steal her egg. We raised Rhode Island reds, Plymouth rocks, black Manorcas, and white Leghorns. English walnut trees shaded the chicken yard below which was next to the horse stable with an adjacent house for the cooing pigeons. On warm summer afternoons we often climbed onto the roof of the horse stable to play in the shade of the over-hanging pepper tree.

Father also built us swings that sailed us up to view over the roof of the house, as well as a bar for going around and around 100 times on one knee, a see-saw, and a teeter-totter. Many a summer afternoon we picked pomegranates and ate them on the wall surrounding our property, covering our shorts, faces, legs and hands with the sweet, sticky, red juice.

Yes, my Episcopalian-raised father, Dr. Montague Cleeves, was a many talented man speaking several foreign languages, versatile with Shakespeare and the Bible and many other literary classics. He later left the Episcopal Church in favor of the Unitarian. At his memorial service in 1973, Reverend Stephen Fritchman from the First Unitarian Church in Los Angeles stated that "Today teachers and psychologists call such persons models. In my day, they were, in more elegant Tennysonian language, called exemplars." "He was proud of his children, grandchildren, and great grandchildren, a gracious patriarch, a witty one, a keen-minded and loving patriarch indeed, far more so than some of the more celebrated ones found in the Old Testament or in Browning's *The Barretts of Wimpole Street*.

To summarize all of this, down the long driveway in front of our home, Father posted a large sign, which was almost a public statement of why he left England to live in "Rock Crescenta," SUNNYSLOPE: A PLACE IN THE SUN RESERVED FOR CHILDREN. I might add that this short description is only the tip of the iceberg of the kind of enrichment we enjoyed during the period of most rapid growth of our cerebral cortices.

Carol McLaughlin once asked when interviewing me for Women's Forum West, "What kind of a child was I during this period?" I answered in two words: very independent. My father was an extremely strict, strong minded, yet kind, Englishman who frightened all my siblings but me. If they wanted something, I was elected to go to my father to ask permission. At an early age I learned not to be afraid of strong, dominant men. This characteristic served me well when I faced difficulties during my professional life.

It is important to point out that my father did not produce our enrichment and sculpting by himself. My Presbyterian-raised mother, Rosa Marian Wamphler Cleeves, carried a good deal of the domestic responsibilities. She was of Swiss parentage, though born in upstate New York. Her "education genes" must have been inherited from both parents, her father being a university professor in Bern and her mother a high school teacher in Interlocken, Switzerland. As a girl, she was trained to play the piano, not casually, but seriously, practicing nine hours a day. In high school and college she was a classics scholar, studying Greek and Latin for about 8 years. Later she taught Latin in Berkeley High School and in Vacaville north of Berkeley. At University of California at Berkeley (CAL) she enjoyed German literature, especially Goethe and Schiller when she could read their texts in German. At the university she worked with Monroe Deutsch, the Vice President, as she was accumulating data for her Ph.D. After she married my father, she left her home in Berkeley and her studies for her advanced degree to set up a new home to raise six children in the sagebrush of isolated La Crescenta. La Crescenta was rich with nature's treasures, but was not, needless to say, a university town rich in academia, as was Berkeley. In her later life she regretted not having a profession and told me to work half-time while raising the children so that when they were gone, I could continue full-time with my professional interests.

Education

Being the youngest of six children, a good deal of informal education or enrichment came directly and indirectly from my five, bright, older siblings. All of us received our formal education in California public schools beginning in La Crescenta grammar school 2 miles down the hill from our home. Clark Junior High was not much farther, but Glendale High school was 7 miles away on the other side of the Verdugo Mountains. I remember most of my teachers, the good and the bad. Both provided useful learning experiences.

Then in one moment of time when I was about 15 years old, I saw my first human brain, while walking down the corridor at the Los Angeles County Hospital behind my father as he was visiting his patients. A door was slightly ajar, and in that room on a small table was a whole human brain with four men clothed in white coats standing around the table. I have no idea what they were doing, but the sight of that brain, which formerly had the potential to create ideas, was embedded in my brain forever, as clearly as if it were yesterday. The thought was mesmerizing that that brain represented the most complex mass of protoplasm on this earth and, perhaps, in our galaxy. Someday I knew an opportunity would arise for me to learn more about it. Now it was essential to continue my general education.

About the same time I had written an essay saying that when I grew up I would go to the CAL "because those who didn't wish they did." Though I had an appropriate academic record to go directly from high school to CAL, I chose to go to nearby Glendale Community College because I thought my parents would be depressed without some of the large family at home.

As I look back at my university education, I do appreciate several of the classes I took at the community college. Without such small classes with excellent qualified teachers, one a physician on a health leave, I might not have found my calling in anatomy, especially the esthetic side of anatomy including neurohistology with the varied structures highlighted with multicolored stains. A particular picture in *Gray's Anatomy* of a beautiful profile of a head with the vascular system showing clearly was indeed attractive to me. I enjoyed the small classes in chemistry, physics, and math at Glendale College, some of them being taught by University of California at Los Angeles (UCLA) professors during the summer. (To confirm the level of my enjoyment, in my second year I became president of the student body.)

After 2 years, I was eager to attend CAL and soon majored in general biology, especially concentrating on vertebrate embryology and comparative anatomy. The first-year medical courses dealing with human material were in the same Life Sciences Building as my undergraduate biology courses. I could see the use of human material by the medical students but had no access to it, only to animals. I thought if I went to graduate school at CAL I could then study human material with the medical students. (But before graduate school I might mention that as an undergraduate, I played on the CAL women's tennis team, earning my Big "C" at the same time I was president of my dorm, Stern Hall.)

Having graduated from CAL in June of 1948 at 21 years of age, I applied for a scholarship to attend a summer school program at the University of Oslo, Norway, established by the Norwegians to repay the Americans for their assistance during World War II. (My father could not understand why I had to go so far away from California.) I also needed to supplement my scholarship so I used the money I earned when I was 16 or 17 during summers while in high school working in the vineyards in 125-degree sunshine near Bakersfield, as a member of the Women's Land Army during World War II. There were few men to pick the crops.

What a marvelous assortment of subjects we experienced in Oslo, including polar research, reconstruction of Norway, marine biology with field trips on the Oslo Fjord, interspersed with lectures by leading politicians and musical performances by talented Norwegians. Our trans-Atlantic ship, the *Marine Jumper*, a converted troop ship, provided the time and space to become acquainted with U.S. students attending other summer schools. By consensus, our Norwegian program was top of the list.

At the end of summer of 1948 I was excited, focused, and full of energy to enter graduate school in the Department of Anatomy at CAL and begin my studies of the nervous system. What a heterogeneous assortment of major professors assisted us. Herbert M. Evans and Miriam Simpson were leading histologists and endocrinologists; John B. de C.M. Saunders and William Reinhardt were the gross anatomists and Bill Garoutte and Bert Feinstein were the neuroanatomists. (Dr. Feinstein was the husband of our now U.S. Senator, Diane Feinstein.) I enrolled in the medical school courses in Neuroanatomy, Gross Anatomy, and Histology to gain the fundamentals of human anatomy, a subject that truly fascinated me. To earn my way through graduate school, I became a teaching assistant the year after I completed these courses with A grades.

How did I ever know I could teach! The first time a medical student asked me a question and I knew the answer, I felt a deep, warm glow of satisfaction radiate through my body. This is where I belong. That night I had time to recall that my Swiss grandmother, grandfather, and mother were teachers; I had possibly inherited their "teaching genes." What a blessing to be at CAL studying the nervous system and enjoying imparting useful knowledge to eager medical students! I later discovered that having a life including teaching and research was extremely satisfying. Trying to achieve excellence in both was a difficult but desirable challenge.

Being the only woman graduate student in the department, the first "job" I was given was to sew a plastic cover for a huge, long, sliding, magnifying contraption. This I quickly did because I had learned from watching my older siblings wait for the right opportunity and sometimes they waited too long. I did "that which was present and not that which lay dimly in the distance" from Thomas Carlyle.

Because World War II had recently terminated in 1945, many of the young men were returning with missing limbs and suffering from referred pain and phantom limb sensations. A Professor Jameson asked if I would like to study referred pain induced by the injection of hypertonic saline into various muscle groups in the upper extremity and mapping the resulting pain patterns. Admittedly, this was a far cry from studying the human brain and its higher cognitive functions as I had envisioned upon coming to graduate school, but again I did that which was present. (No one was studying the anatomy of higher cognitive functions in those days.) I certainly learned a good deal about different resulting pain patterns as well as sensitivity to pain. This project culminated in my earning my master's degree in anatomy in 1949.

Being in a department mainly interested in hormones, and again not in higher cerebral cortical functions, by now I had become fascinated with a part of the brain called the hypothalamus. How could 4 grams of nerve tissue carry out such diverse functions? For example, regulate body temperature, appetite and thirst, mating behavior, anterior pituitary hormones, form posterior pituitary hormones, sympathetic and parasympathetic functions, memory, and circadian rhythm. What an intriguing, complex little mass of tissue to study!

For my doctoral dissertation that was eventually titled "Functional Interrelationships of the Hypothalamus and the Neurohypophysis" (1953), I was interested in learning about the amount of antidiuretic hormone (ADH) in the supraoptic area of the hypothalamus and posterior pituitary after various experimental conditions including normal control rats, saline controls, hypophysectomy, posterior lobectomy, dehydration, hydration, adrenalectomy, adrenalcorticotrophic hormone (ACTH) treatment, and desoxycorticosterone acetate (DOCA) treatment.

From these experiments there are far too much data to present here, but a few examples can be offered. Histological and physiological measures using assay techniques were determined. From histological studies, Gomori positive substance demonstrating granules in the supraoptic nuclei was extremely sparse under any of the above conditions; yet large quantities were demonstrated in the normal posterior pituitary. With toluidin blue stain the Nissl substance in the neurons in the supraoptic nucleus of dehydrated rats was peripherally dispersed due to an increase in the size of the neuron. As might be expected, with hypophysectomy there was a decrease in the number of cells in the supraoptic nucleus. The amount of ADH left in the supraoptic area after posterior lobectomy was decreased in an amount comparable with that after complete hypophysectomy. The administration of a 5% NaCl solution reduced the antidiuretic activity in the hypothalamus and hypophysis.

Injection of DOCA and ACTH into normal animals did affect the ADH content of the hypothalamic-hypophyseal system. The evidence that ADH in the hypothalamus and neurohypophysis is not altered several days after adrenalectomy, and yet has been reported to increase in the circulatory system, supports the suggestion that there may be decreased destruction of the substance (by the liver) rather than increased production by the hypothalamic-hypophyseal system. These examples indicated that a good deal of information was gathered from these experiments, but it would take another lifetime to integrate them into a functional whole. That being said I now wish to continue with the personal side of my life that I was trying continuously to integrate with my biological interests.

While in graduate school, I first lived in an old house we called the "Ritz" close to the university with four other young ladies, Marian Melrose, Jean Cline, Florence Bevis, and Peggy Shedd, who lived with me in Stern Hall during our undergraduate days. I later moved to International House that as the name implies was a wonderful establishment for men and women from everywhere in the world who were mostly graduate students. It was here that I met a man, kind, extremely brilliant and well educated, in addition to being a very superb athlete. I loved sports, having grown up with two older brothers who were very adept with many kinds of sports. We all played tennis, skied, swam, dived, and hiked. Who is to say which I liked best. I know I liked them all as did Dick. Consequently taking many of Dick's fine traits into consideration, on December 20, 1950, I married Richard Martin Diamond who received his Ph.D. in nuclear physics/chemistry at CAL under the direction of Professor Glen Seaborg. Dick's first academic appointment was in the Chemistry Department at Harvard University where he taught for a year before I could join him.

Family

The greatest thrill in my life up to that moment was when I held my first newborn child in my arms against my breast. I knew why I existed. This experience was beyond any other I had ever contemplated and was repeated with each of my next three children. I loved being a new mom just as much as I presently love being an older grandmother or "muti," as I like to be called.

Catherine Theresa Diamond was born May 6, 1953, in Boston, Massachusetts. At CAL, she majored in cross-cultural aesthetics, concentrating in Chinese and European art. After receiving a masters degree in creative writing, she wrote three works of fiction based in Asia. She obtained her doctorate in comparative drama at the University of Washington, and is currently a

Professor of Theatre in Taipei, Taiwan. She has published extensively on the contemporary theater of Southeast Asia and is the director of an English-language troupe in Taipei, Phoenix Theater.

Richard Cleeves Diamond was born on October 10, 1955, in Ithaca, New York. He came into the world a month early, possibly because I was mowing the lawn on a nice Fall afternoon. He asked to play the violin when he was only 4 years old and began taking lessons when he was 6. He joined the Berkeley Symphony Orchestra in 1973 soon after it was established and is still playing there. He majored in visual and environmental studies as an undergraduate at Harvard, completed his Ph.D. in architecture at CAL in 1986, and enjoyed a postdoc at Princeton, before accepting a position as a staff scientist at the Lawrence Berkeley National Laboratory. His research at the lab presently is on energy, behavior, and buildings, when he is not looking after his 4-year-old twin sons, Aaron and Paul, with his wife, Alice Kaswan, a Professor of Law at the University of San Francisco.

Jeff Barja Diamond was born on March 20, 1958, in Ithaca, New York. Jeff's unusual middle name came from Professor Caesar Barja who, with his wife, Jean, at UCLA, were guardians of the two little boys, Dick and Phil Diamond, after their parents unfortunately died when the boys were very young. We are extremely grateful to the Barjas. As a young boy, Jeff enjoyed exploring and looking for birds and other animals, becoming an avid amateur bird guide. In the late 1960s and 1970s he was a political activist and went by himself to Central America during political unrest. Needless to say, we were not too comfortable with that move. Jeff completed his M.A. in political science at Amherst College in Massachusetts, and his Ph.D. in political theory at McGill University in Montreal, Canada. After that time he became an assistant professor in the Department of Social Sciences at Boston University. He now teaches political science at Skyline College in San Bruno, California, and has an 11-year-old son, Will, who plays soccer and video games.

Ann Diamond was born on May 1, 1962, in Berkeley, the easiest of the four C-sections. In those days there was no ultrasound. Determining the sex before birth was not routine, so we took to the hospital the application for the University Day Care Center to note the sex immediately after birth to reserve a place at the Center. Ann always loved her sports, playing varsity soccer at Harvard College in Massachusetts while studying geology and botany. Ann did not want a conventional urban family medical practice. After completing her medical degree at the University of California at San Francisco, she now has her own County Clinic in Winthrop, Washington, where she lives on a meadow surrounded by pine trees with her partner, Jerry Laverty, a superb contractor. With Ann's assistance, he has built their family home and clinic, with company from son, Cory, and the family dog, Poi. Because Ann has practiced and traveled widely, she brings a world of experience to her patients.

Family Rearrangement

In the 1970s CAL had an arrangement with other UC campuses to pay transportation for UC faculty to give lectures on other UC campuses. In 1979 I had a seminar that followed my graduate neuroanatomy class with more complex, in-depth topics given by invited speakers who were suggested by the class. One of these was Professor Arnold Scheibel, a neuroanatomist from UCLA. I had heard of Professor Scheibel but had never seen or met him. When I went to pick him up at the airport, I took Ruth Johnson with me because I had heard he was a rather formidable, intimidating man who always wore a bowtie. I soon learned he was quite the opposite, a quiet spoken, highly intelligent, witty, innately intense, caring man with a winning smile and calm demeanor. Coming to Berkeley from his southern California home, where for decades he had taken care of his now-deceased wife, Mila, was rather like a caged bird flying through an open door for the first time and finding the outside life refreshing, stimulating, and challenging. I had never met a man so exuberant about his environment, one who could spontaneously express his emotions so warmly, clearly, and deeply about nearly everything.

That afternoon his lecture was about consciousness and the reticular formation. When he described how the nucleus reticularis thalami "opened the gates to the cerebral cortex," I was completely enchanted. In the months that followed after this first encounter, we found we had a great deal in common to share professionally and personally as well as a great deal not so common to share, he having lived and trained mostly in public schools in New York City and I having lived essentially in open countryside, with highly educated parents, and trained in public schools in California.

We continued to see one another at professional conferences, and I all the time considering my personal family situation with my husband and children. Fortunately, the children, who already were quite independent since I had been working professionally half-time, were each on their way with their desired educational paths. Dick was completely consumed with his profession, and I was caught in a stressful, difficult void. It was by chance I had met Professor Arne Scheibel at this time. Considering my personal circumstances, our relationship slowly blossomed. Our varied combination of positive commonalities provided a possible reason to consider our spending our lives together permanently so I made a decision to end my marriage to Dick. Arne and I were married in 1982. His broad, yet in-depth range of academic and cultural topics and my broad range of firsthand experiences in various parts of the world provided growth for each in many directions. For example, he loved learning about airplanes and flight, and I loved climbing mountains, both finding means to extend ourselves to great heights. At present I feel the whole family has integrated smoothly in a most congenial manner. At family gatherings Dick and Arne can be seen sitting together and talking about problems in physics!

A few months after I had completed the preceding paragraph, Dick, a nuclear chemist and senior staff scientist emeritus with the Lawrence

Berkeley National Laboratory, passed away on September 14, 2007, following a brief illness. He was 83. Colleagues say that he and his partner at the Lab, Frank Stephens, pioneered and then revolutionized the field of high-spin physics with their work building the High-Energy Resolution Array (HERA) and, later, contributing to the "gammasphere" at the 88-inch cyclotron. In 1981 he and Frank won the Bonner Prize of the American Physical Society for their contributions to the understanding of high-spin states of nuclei. According some, this work had a profound impact on all of nuclear structure physics, particularly in the area of gamma-ray spectroscopy. In 1993, he received the Seaborg Award in Nuclear Chemistry from the American Chemical Society, being one of the few recipients of major prizes from the American Physical Society and the American Chemical Society.

James Symons, Division Director for Nuclear Science, said that "Dick had a long and distinguished career (37 years) at the laboratory." "He was also one of the nicest men one could ever hope to meet, and will be much missed by all who knew him." On this his family can concur.

In Transition

In May 1953 I received my Ph.D. the same month I gave birth to my first child, Catherine, as mentioned previously. Unfortunately, due to a mishap in the hospital, phlebitis occurred after this birth, culminating in bifemoral ligations that necessitated a home-bound recovery with limited outside activities. During this period I had a delightful encounter with Mrs. James Conant, the wife of the President of Harvard. She later asked if I would consider becoming the Hospitality Chairman for the wife of the new President of Harvard, Nathan Pusey. I accepted only to learn after several months that such a role was not one I wished to continue because I didn't get the deep pleasure that I found with teaching and doing research.

At this time, Harvard decided that biochemistry with F. H. Westheimer and K. E. Bloch, and not nuclear chemistry with R. M. Diamond and G. Wilkinson (later a Nobelist), was the appropriate direction to develop science in the future. Fortunately, Dick was quickly hired at Cornell University where many distinguished nuclear scientists were working after World War II. I was pleased with this move because Marcus Singer, a neuroanatomist formerly at Harvard Medical School, was now a professor in the Zoology Department at Cornell. Because I did not have an academic appointment there, I hired a babysitter for my now two children and began a research project part time with Singer in the Zoology Department when an extremely unusual event took place.

An Unexpected Turn of Events

In 1954 Singer was indicted for contempt of Congress during the McCarthy era because he would not state which other Harvard students had accompanied him to some communist meetings to learn what communism was all about. The President of Cornell stated that he could not maintain someone on his faculty who had been associated with communists and dismissed Singer in the middle of the semester. At this time Singer was teaching a course for 250 students in Human Growth and Development. Who could continue to teach his course? Singer turned in my name, and I began the next day, the initiation of 3 years of rich experiences as an instructor teaching one new course after another in Comparative Anatomy, Histology, and Embryology. Actually each course was repeated each morning, one at 8:00 and one an hour later at 9:00.

As I looked back years later, I realized what a marvelous type of postdoctoral experiences I had. Giving these lectures while raising two small children, Cath and Rick, provided a wide intellectual base for future teaching and research. Also while living in Ithaca, I became vice president of the Tompkins County Democrats and resigned after my first assignment when I was asked to sign something I did not agree with. I knew then I was not meant for this role.

One afternoon while at Cornell when the children were sleeping I was reading an article in *Science* magazine by three researchers at CAL who had been studying the brain chemistry of maze-smart and -dull rats. David Krech, Edward Bennett, and Mark Rosenzweig used one strain of “maze-bright” rats that ran the maze quickly and another strain of “maze-dull” rats that ran the maze more slowly and laboriously. The team compared the amount of acetylcholinesterase in the brains of the two different strains of rats. The maze-bright animals had significantly more of this chemical than the maze dull animals. They showed for the first time a link between the chemistry in an animal’s brain and its ability to learn.

What a thrill I had when my mind jumped immediately to the question, “I wonder if the anatomy of these brains would also show a difference in learning ability?” This is exactly the kind of problem I would like to solve. When a few months later Dick Diamond received an invitation to return to Berkeley to continue his research, I could not have been happier to pack up the children and all our possessions.

Upon returning to the San Francisco Bay Area in 1959 with our now three children, having added Jeff, my first teaching job was at the University of California in San Francisco. I began in the School of Pharmacy giving the lectures in Gross Anatomy and sharing the teaching load in the gross lab. The next year I was promoted to teaching anatomy to the dental students, and by the third year I was teaching Neuroanatomy to the medical students.

Being in San Francisco while my family was in Berkeley created a strong pull. Specifically, the heavy bridge traffic between Berkeley and San Francisco warned me of a problem that might occur in case of an emergency. How could I ever arrive home quickly in such a stressful situation. I soon turned in my resignation.

The new research direction that happened afterward back in Berkeley has been reported in our book *Magic Trees of Mind* by Diamond and Hopson in 1998 written so everyone could learn to appreciate their brains and their potential. We had reason to believe many people might be interested in our book when it was first published because I had sent a copy to Professor Xie Xide, a physics professor and former President of Fudan University in Shanghai, as well as a personal friend who had scraped carrots with me in my kitchen in Berkeley. She had given *Magic Trees* to a publisher who asked permission to copy many specific pages from the book to distribute to pregnant women presently in China and in the future. We were told these messages from our book would affect the lives of 10 million babies and more!

First Anatomical Enrichment Experiment

Now I wish to quote directly from our book to give an introduction to our first experimental results showing the plasticity of the anatomy of the mammalian cerebral cortex, an important finding which opened the doors for our experiments to follow for the next 37 years.

> By the time I got settled in, taught a few courses, and went down to their offices to see Krech, Rosenzweig and Bennett, they had moved on to an even more exciting project. Their new work was inspired by a man named Donald Hebb at McGill University. It turns out that the Hebbs allowed their children's pet rats to run freely around the house, and this gave Hebb an inspiration. After a few weeks of free roaming, Hebb took the rats to his lab to run mazes and compared the results with maze-running by rats living in laboratory cages. Interestingly, the free-ranging rodents ran a better maze than the locked-up rats. Hebb speculated that rats confined to small unstimulating cages would develop brains worse at solving problems than animals growing up in a stimulating environment like a large house with hallways, staircases and human playmates.
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> From Hebb's observation the Berkeley team got the idea of deliberately raising baby rats in two kinds of cages: a large "enrichment cage," filled with toys and housing a colony of twelve rats; and a small "impoverished cage," housing a solitary rat with no toys. Indeed, the rats growing up in a deliberately enriched environment ran better mazes than the "impoverished rats" raised in unstimulating confinement. And like the bright and dull rats that Krech and his colleagues had already tested, the deliberately enriched rats had more of that particular brain chemical, acetylcholinesterse, than the impoverished rats. This time, however, it was apparently nurture at work, not nature.

When I showed up at the Krech, Bennett and Rosenzweig lab, full of enthusiasm for their work and anxious to look at the rats' brains, they were surprised but accepting In those days, money was readily accessible to add new people to scientific projects. So within days, my wish was coming true.

The research process involved removing the brain of a laboratory rat, chemically fixing, or preserving, the brain tissue and making thin slices of it (20 micra thick), viewing the slices under a microscope, then very carefully measuring the thickness of the cerebral cortex from the rats raised in both kinds of cages, enriched and impoverished. I did see variations: The enriched rats had a thicker cerebral cortex than the impoverished rats, but the difference was not the sort you could observe casually. You had to compare the brain tissue under the microscope, and the cerebral cortex of the enriched rats was only 6 percent thicker than the cortex of the impoverished rats. Nevertheless, it was highly statistically significant; nine cases out of nine showed a 6 percent difference. This was the first time anyone had ever seen a structural change in an animal's brain based on different kinds of early life experiences. Could it really be true?

I took another year and repeated the experiment with nine more animals. Then I started to get excited. It was about 1963 by then, and my life was really hectic. I now had four children, Catherine, Rick, Jeff, and Ann and was only at the university half time, doing demanding, pioneering work in the lab. In some ways, that period is hard to recall. But I do remember very clearly the day I took the results over to show David Krech. I ran across campus with the papers in my hand and laid them out on his desk. He stared at them, then at me, and immediately said, "This is unique. This will change scientific thought about the brain." it was a great thrill—truly an emotional high—to sit with him and share that moment.

In 1964, we published the results in a paper by Diamond, Krech, and Rosenzweig called "Effect of Enriched Environments on the Histology of the Cerebral Cortex." And a year after that I found myself standing in front of a session on the brain at the annual meeting of the American Association of Anatomists.

We were at a hotel conference room in Washington, D.C., and I was truly scared. There were hundreds of people in the room—very few of them women—and this was the first scientific paper I had presented at a big conference. I explained the projects as calmly as I could, people applauded politely, and then—I'll always remember this—a man stood up in the back of the room and said in a loud voice, "Young lady, that brain cannot change!"

It was an uphill battle for women scientists then—even more than now—and people at scientific conferences are often terribly critical. But I felt good about the work, and I simply replied, "I'm sorry, sir, but we have the initial experiment and the replication experiment that shows it can." That confidence is the beauty of doing anatomy. Ed Bennett used to say to me, "Marian, your data will be good from here to eternity, because it's based on anatomical structure." Eternity is a long time, of course. But so far—and it's been thirty-four years—Bennett has been right. And the man in the back row? My entire research career and some of the many scientific findings that stemmed from it will continue to show how wrong he was in the pages ahead.

Excerpts from Later Research

Normal Cortical Development

Before we could make sense of our measurements of the cerebral cortex from enriched and impoverished rats, we first had to map the normal developing and aging pattern of the cerebral cortex to serve as a standard for comparison. The cerebral cortex was of greatest interest to me because it is not only the seat of higher cognitive functions, but also one of the last structures to develop embryologically and is one of the most recent phylogenetically. No baseline for the dimensions of the rat cortex, for example, was available for the young, adult, and old-aged animal. Roger Sperry, the Nobel laureate from California Institute of Technology, once said, "Marian, all you are doing with your enriched environments is stimulating the maturation of the cortex." We did not know whether he was right or not. You will shortly see he was half-right.

Were the stimulating environmental conditions increasing a growing, maturing cortex, or a cortex that had reached a plateau, or a decreasing, shrinking cortex? When does the cortex stop growing, and how does it age under "normal" laboratory conditions?

To answer these questions, we accumulated, over a 7-year span, information on the patterns of development and aging in the male and female cortex (Diamond, 1988b). Not only was it important to examine the cortex as a whole, but we wondered whether the right and left cortices followed similar patterns during development and aging because new information was accumulating about functional differences in the two hemispheres of human beings. Would structural differences help us to understand the basis of the functional aspects?

First, I mention the results of growth curves of cortical depths of the combined right and left cerebral cortex from histological sections of the frontal, somatosensory, and occipital cortex. In the male and female, we have two basic slopes: a positive rapidly growing cortex for the first month after birth and then a gradual negative slope throughout life. However, though the direction of the slopes of the curves was similar, we found a different developmental pattern at birth when the female was initially more highly developed than the male but the male became thicker by 3 weeks after birth.

When comparing the right and left cortical thickness differences there was no doubt there were significant sex differences in general (Diamond, 1984). In general, the male cortex was significantly thicker on the right side, and the female cortex was not significantly asymmetrical. There were exceptions, however, with the area 2 of the male cortex being symmetrical early in life, and the very old male cortex became symmetrical like the female younger cortex, possibly explaining why many older males prefer either to stay at home or let their wives drive the cars while they relax beside her.

Anatomical Brain Changes with Varied Environmental Input

Having presented the initial experimental data showing that the enriched and impoverished environments could alter the structure of the rat cerebral cortex, now I might expand upon what is considered to be an enriched environment for a rat. At Berkeley, an enriched environment contained 12 rats in a large cage with a variety of novel objects for the rats to explore; whereas, the impoverished animals were caged singly in small cages and had neither the objects, nor companions, nor the large living space. All rats had free access to food and water.

For many reasons, the feral condition, the natural outdoor environment for the rat, could not be duplicated. I admit that the laboratory conditions were sterile, controlled, and protective by comparison, and even at the very best, not like living in the rat's natural habitat. Therefore, all types of our laboratory environments had to be considered relative to the natural one. Nonetheless, the results from the experimental conditions in the laboratory can be validly compared to each other; one condition is more enriched than the other.

With the magnitude of new experiments requiring much more work, additional help was needed. Over time, six new technicians worked in the lab: Ruth Johnson, Bernice Lindner, Carole Ingham, Fay Law, Lennis Lyon, and Alma Raymond. All were extremely capable, intelligent, and became lifetime friends.

After the initial anatomical experiment, published in 1964, when the rats were in their respective environments for 80 days (from 25 days at weaning until 105 days of age), and showed a 6% ($p < 0.001$) cortical depth change in initial and replication experiments, I wondered if we could find differences in the brains of preweaned rats before 25 days of age, rats who lived in the experimental conditions along with their mothers?

The thought of this project stimulated the imagination of a very bright, new graduate student, Dennis Malkasian (Ph.D. in 1969 and now an M.D., a neurosurgeon and Associate Clinical Professor of Neurology at UCLA). His experiment included an enriched cage with three mothers with three pups each (multifamily) and an impoverished cage with one mother and three pups (unifamily). All pups were 6 days old when they entered their conditions and were removed from these conditions at 14 days of age. (Before 6 days of age, the mothers destroyed the pups in the multifamily condition.)

Because the eyes had only opened in the preweaned enriched babies at 13 days of age and at 14 days in the impoverished babies, no visual cortical depth changes were found. However, the largest change that we have ever seen in the cerebral cortex of enriched versus impoverished rats was a 16% difference in an association area 39 in this group of 6- to 14-day-old experimental animals! (Malkasian and Diamond, 1971)

Here I wish to repeat that the cortex in our developmental study, presented earlier, was rapidly increasing during these first 26 days. Thus, these new preweaned data indicated that enrichment could increase the rate of maturation, as previously suggested by Roger Sperry.

Now to return to the first group of postweaned rats in our original study published in 1964, who were in their experimental conditions for 80 days from 25 to 105 days of age. At this period in our developmental study the thickness of the cortex was slowly decreasing. Now we found by measuring cortical thickness that enrichment could counteract this downward slope

A logical next question was "What does cortical thickness mean?" "What constitutes cortical thickness?" We counted nerve cells and glial cells in each microscopic field, reading vertically from the pial surface to the underlying white matter. Nerve cells were significantly 7% fewer per field in the enriched than in the impoverished occipital cortex, suggesting that further development of dendritic branching had occurred. We also found that the soma of the nerve cells was significantly larger in enriched animals (Diamond, 1967; Diamond et al., 1975) and the dendrites increased in length and number as shown by several investigators, (Holloway, 1966; Uylings et al., 1978), and (Connor et al., 1981). In addition, the glial to neuron ratio was greater with enrichment (Diamond et al. 1966); dendritic spine increases were noted (Globus et al., 1973); synaptic junctions were larger in the enriched brains (Diamond et al., 1975) as were the capillaries (Diamond et al., 1964) In summary (Diamond, 1988b), all the constituents that we measured which play a role in cortical thickness showed increases in dimensions as a consequence of enriched environments.

The fact that the glial cells increased with enrichment led to my hypothesis that Albert Einstein might have more glial cells in his enriched cortex, specifically right and left association areas 9 and 39, when compared to the cortical average in these areas from 11 other males. We found all four regions had more glial cells than the other males, but only the left 39 had statistically significantly more (Diamond et al., 1985).

Another question to be asked was, "Does it really take 80 days for cortical nerve cells to create measurable changes in their structures? How about reducing the experimental days to 30 days or 15 days or 7 days or 4 days or just one day?"

Designing similar experimental conditions to the initial ones, but using these various new time frames, we learned that we could create significant experimental differences in the cortical thickness between enriched and impoverished rats at every time period except in the brains of rats exposed for only one day. (Yet we know that one good moment can last a lifetime; some kind of changes must occur.)

As might be expected, fewer cortical thickness changes were noted in those rats exposed to their respective conditions for the shorter periods of time. A 30-day experimental period from 60 to 90 days of age proved to show the thickness increases in more cortical areas than did the other time periods. Therefore, this time period was consistently adopted for additional studies.

Another most competent, considerate, graduate student, James Connor (Ph.D. now Chairman of Neurosurgery and a professor at Penn State University Medical School) found cortical differences in their 630-day-old rats after being exposed to enrichment or impoverishment for a 30-day period. However, in this old age group a few of the enriched animals died shortly thereafter.

How could we get our enriched rats to live longer? When I would speak to folks in retirement homes, I noted that something was missing. In the early 1970s, where in their lives was the genuine, warm caring for others? (I was told that now retirement homes have introduced much more enrichment and loving care.) Perhaps, by adding some "tender loving care" (TLC) to the daily routine of our enriched rats would prove to be beneficial to their longevity.

Now we planned a new experiment where our rats lived three to a cage until 766 days of age and then they were separated into the enriched or impoverished conditions. For TLC we held the enriched rats against our chest covered by our lab coats and petted them for a few minutes as their cages were cleaned each day. Such TLC was added to the daily routine by Ruth Johnson, my faithful technician, and me. At 904 days of age when we lost an animal, we stopped the behavioral aspect of the experiment and measured the cerebral cortex for cortical thickness. Three conscientious undergraduates, Ann Marie Protti, Carol Ott, and Linda Kajisa (Linda is now an MD, an oral surgeon with her own practice) assisted with the measurements which showed that the enriched rat cortices were significantly thicker by as much as 10% ($p < 0.05$) compared with the impoverished rat's cortex (Diamond, Johnson, Protti, Ott, and Kajisa, 1985). This finding provided us with immediate joy!

To our knowledge no one had ever shown plasticity in such very old rat brains or in any other comparably aged animals. These were indeed welcome results.

With our ever-increasing aging population, this result was considered to be a most optimistic finding, to know the cortex could still show plasticity in very old age! This finding gave us another reason to continue to include "love" along with enrichment into our daily human encounters. Under normal circumstances why do we wait until a valued friend dies before we say how much we loved that friend.

Crowding, Super Enrichment, and Enrichment Following Brain Injury

Even though factors affecting responses to crowding are complex, we sought to illuminate at least some of them by examining the effects of crowding on brain development in our enriched rats. All rats were in their enriched or super enriched conditions for 30 days, from 60 to 90 days. We found no significant difference in cortical thickness growth, 4% to 6% with either 12 rats or 36 rats in the enrichment cages with toys when compared with controls, 3 rats per small cage with no toys. We hypothesized that interaction with the toys might be diverting the rats' attention or entertaining them sufficiently to mitigate the stress of the crowded condition.

With an overabundance of children's enrichment toys these days, pediatricians have asked me, "What is the effect on the cerebral cortex of too much stimulation provided by playing with too many toys?" To find an answer to this question, in the enrichment cage the toys were changed every hour for three consecutive hours, 8, 9, 10 at night for 4 weeks instead of changing toys daily or a few times each week for 4 weeks.

We did not find excessive growth with additional input. Instead we found the cortex changed less with this super enrichment than with our routine enrichment. Other investigators have shown that stress-related adrenal cortical hormones, such as cortisone, will reduce the size of the cerebral cortex. When the adrenals were removed in young animals, we saw the greatest growth in cortical thickness developed in any of our experimental conditions, indicating once more that adrenal hormones can inhibit cerebral cortical growth.

A practicing physical therapist, Alison Mckenzie, was interested in learning if she could find significant neurological changes in the injured rat cerebral cortex after 30 days exposure to an enriched environment. She found a significant increase in dendritic growth around the lesion in the left motor cortex, as well as in the right unlesioned motor cortex. Unexpectedly the somatosensory cortex adjacent to the right and left motor cortices also showed increases in dendritic growth as a consequence of an enriched environment. Indeed compensatory hypertrophy of the dendrites was evident with enrichment following injury to the motor cortex and somatosensory cortex.

In summary, our results have shown at least five factors which are important for a healthy brain according to our research.

1. Diet
2. Exercise
3. Challenge
4. Newness
5. Love

Gender Differences in the Anatomy of the Cerebral Cortex

We first noted cortical asymmetry in the Long-Evans male rat in a developmental and aging study. Using rats 6, 10, 14, 20, 41, 55, 77, 90, 185, 300, 400, and 650 days of age, we observed in coronal sections that the right cerebral cortex was thicker than the left in 92 out of 98 areas. Later 900-day-old male rats showed no statistical differences between the right and left hemispheres, indicating that the very old male cortex had become very much like the younger females, as seen in the next study (Diamond, 1984).

In considering the right–left differences in the cortex of the female Long-Evans rat, out of 54 areas 50 showed a nonsignificant right–left difference, using rats at 7, 14, 21, 90, 180, 390, and 800 days of age. Although nonsignificant, in 36 locations, the female left cortex was thicker than the right (Diamond, 1984). (The fact that the male and female cortex showed such striking cortical depth differences actually made me feel good. There was a reason why I approached my scientific studies differently from my male colleagues.)

It has been reported that male rats are superior to females in visual spatial ability and that spatial laterality may be important for territoriality in the male. Right structural dominance in the visual spatial region of the cortex fits these male roles.

One might offer the following hypothesis for the fact that symmetry in the female cortex might prove advantageous in allowing her to respond in any behavioral mode when protecting her young. An asymmetrical cortical pattern might prove a hindrance. Many further studies were carried out to determine the role of sex hormones on laterality. For one example, if the testes were removed at one day of age and the rats were autopsied at 90 days of age, the right greater than left cortical thickness was reversed everywhere in the cortex except in the visual cortex where significant right–left differences were retained.

An example showing that female sex steroid hormones might influence the dimensions of her cortex appeared quite by accident. Upon comparing the cortical thickness of enriched postpartum females with the impoverished postpartum females, we unexpectedly found no significant differences in initial and replication experiments. The reason was that both the enriched and impoverished postpartum females had increased their cortical thickness during pregnancy. In essence, the impoverished cortex had caught up with the enriched. Should we try to benefit from this knowledge and apply more educational lessons during this enhanced period?

Immune Regulation and the Cerebral Cortex

With genes for the disease of Lupus Erythematosus rampant in my family, I promised my sister when she was dying at 26 years of age and I was 19 that someday I would try to shed light on the role of the cerebral cortex with the immune system. I have since lost a brother, a niece, and a nephew because of this horrible disease, lupus. In the early 1980s I read a publication by some French scientists (Renoux et al., 1980) showing that lesions in the cerebral cortex resulted in enhancing or inhibiting effects on the immune system. Inspired by these initial investigations, we studied the congenitally athymic nude mouse to identify areas of the cerebral cortex that might be affected by the T cell-deficient state.

In 1986, we published our first research project dealing with the cerebral cortex and the immune system (Diamond et al., 1986). Essentially this project demonstrated that the dorsal lateral frontal cortex was bilaterally deficient, as measured by microscopic thickness, in the female, immune incompetent, nude mouse when compared with the cortical thickness of an immune competent mouse from the BALB/c strain. In 1996 and 1997, two more studies of ours confirmed this cortical deficiency. In addition, Gary Gaufo, a talented and reliable graduate student (now an assistant professor at the University of Texas, San Antonio) learned to transplant the thymus and reverse the cerebral cortical and blood immune deficiencies in the nude mouse (Gaufo and Diamond, 1996, 1997).

Other findings with rodents suggest that cortical immune responses can be generalized across both sexes and in different species and possibly in human beings. With this information, I was ready to take this project to human subjects instead of rats.

The functions of the dorsal lateral frontal cortex in humans include working memory, changing set, judgment, initiative, planning ahead, sequencing data, etc. Some investigators have utilized the xenon dynamic single photon emission-computed tomography (SPECT) during the performance of the Wisconsin Card Sorting Test (WCST) to demonstrate activation of the dorsal lateral frontal cortex in humans. Individuals with dorsal lateral prefrontal lesions do poorly on the WCST. Instead of using the WCST we chose the well-known card game of contract bridge.

We hypothesized that while individuals played bridge, this area of the cortex might be stimulated and possibly influence the production of T lymphocytes. Therefore, we planned to take blood samples before and after adult women played 1½ hours of contract bridge and to quantify the number of

T lymphocytes in the blood samples, including CD3, CD4, CD8, and CD56 cells types. In 2001 (Diamond et al.) we published our results obtained by comparing the venous blood sample before and after playing bridge, showing a significant increase in CD-4 positive T lymphocytes as measured by the Wilcoxon signed rank test and the sign test. No significant increases were found in CD3, CD8, or CD56 cells. Also no significant CD4 cell increases were found between the two samples of blood drawn from each of three women who did not play bridge but only sat quietly listening to gentle music at the same time the other women played cards.

Our data suggest that people might be able to improve their immune functions with more purposeful demanding activities related to frontal lobe tasks. For example, because CD4 cells are decreased in AIDS, might it be possible for people with this devastating disease to learn to play bridge or a comparable mental stimulating activity?

Overseas Enriched Experiences

Australia

In 1977 during a 6-month stay, Professor Richard Mark from the Biology Department at the Australia National University in Canberra, asked if I would present a seminar on my enriched and impoverished research at Berkeley. I was delighted because I had some new data on the environmental influences on the female brain when previously we only worked with male brains.

I submitted my title stating, “Environmental Influences on the Female Brain.” On the day of the seminar, the folks from Richard’s lab were present, but that was all. Only three people came. Little did I realize how chauvinistic the Australian men were in those days. There were no women professors at their university, I was told. When asked by Professor Mark a year or so later to give another seminar, I offered the title, “The Effects of the Environment on the Mammalian Brain” and had a full house. We had found gender differences in response to identical environments. The male showed greater growth in the occipital cortex and the female in the somatosensory cortex.

I had another unusual experience with brains in Canberra. Keith Crowley, the Principal of Village Creek primary school in Kumbah, Canberra, agreed to allow me to teach an anatomy class to his children after I had successfully given a course to the parents. First, I needed a real human brain and gathered courage to go to the main Health Center in Canberra and spoke with an administrative official. When I asked to have a real human brain to use for teaching in the schools, his reply was the following: “If I gave you a brain and if you stored it in a classroom closet, then a child might decide to take it home. The child might leave it out so the dog could eat it. The headlines of the *Canberra Times* would read 'Dog eats Mr. Jones's Brain'." Needless to say, I obtained no brain from him. But the nurses at the Health Center had heard of my plea and brought me a brain!!!

I later had a World Health Fellowship from The World Health Organization in Geneva, Switzerland, to continue with the teaching I had started. Each morning a car and driver awaited to take me to the different schools. A possible indication that the Australian officials approved of my teaching human anatomy to their children is shown by the following example. One morning an unusually fine car arrived, and the driver informed me that the car belonged to the Prime Minister's wife; no other car was available that day. They could have said no car was available.

China

I had originally visited The People's Republic of China in 1978, as the wife of Richard Diamond and his colleague, Professor John Rasmussen, both of whom were invited by professors in the Department of Physics at Fudan University in Shanghai. Our daughter, Catherine, a professor in Taiwan, and Louise Rasmussen also accompanied us.

At this time I had the privilege of witnessing several surgeries on the nervous system performed with acupuncture anesthesia. In one laboratory the investigators had learned they could reduce pain by stimulating two thalamic nuclei, the centromedial and parafascicularis. I asked if they knew the level of endorphins in these nuclei. They had not heard of endorphins. When arriving home, I looked up this subject and found indeed both nuclei were rich in endorphins. I also witnessed surgery removing schwannomas on the VIII nerve within the skull; three such operations were occurring simultaneously in that one surgical room.

In 1985 I returned to China for 6 weeks with my second husband, Arne Scheibel, in response to an invitation from two professors I had met during my previous trip. This time scientific lectures were in order. In the Biology Department in Fudan University on the hottest days of the year, Professor Bo, a leading biologist, introduced me to speak about our work with enriched and impoverished environmental effects on the brain. My next lecture covered my experiments on increased glial cells in Albert Einstein's brain with students sitting in the windowsills in an overcrowded auditorium. Professor Bo kindly paid back us a visit in Berkeley after our return.

One particularly memorable enrichment/impoverishment talk took place in a Naval Research Institute with a huge, tiered amphitheater filled with uniformed attendants complete with formal white military hats. We were told we were the first foreign visitors invited to speak at this Institute whose specialty dealt with submarines. Our experimental results showing the detrimental effects on brains of isolated rats may have been one reason for their interest in our work. Since our visit, other foreigners have enjoyed visits as well.

Before leaving Shanghai, we made arrangements to obtain small blocks of cerebral cortex including Broca's area from the brains of Chinese who had recently died. We studied these brain tissues in comparison with English-speaking Americans and have yet to decipher the results.

In 1998 I returned to Shanghai to present a keynote address in the hotel Pudong Shangri La, with Jane Goodall and Robert Haas, the poet laureate for the year. The administrators of Independent Schools in South East Asia asked me to speak on plasticity of the brain induced by the environment, experiential and nutritional. The data of one of our graduate students, Arianna Carughi (Carughi et al., 1989), was of particular interest, showing the detrimental effects on rat brains caused by low-protein diets during pregnancy. However, if low protein was maintained during pregnancy, but after birth, a high-protein diet was provided during lactation and for the first month following weaning, the dendrites in the cerebral cortex showed growth but not as complete as normal. Nonetheless, these dendrites did show a response to an enriched environment; whereas the protein-deprived ones did not.

Nairobi, Kenya, Africa

In 1988 Professor James Kimani, the Chairman of Anatomy at the medical school in Nairobi, invited Arne and me to spend 6 weeks lecturing about the brain, both environmental influences, and a theory on the biological basis of schizophrenia and aging. Dr. Kimani's wife, a practicing obstetrician, was the one who informed us that the women in Nairobi did not like to eat protein while they were pregnant because they delivered too large a baby. I wonder if our lectures on the importance of protein during pregnancy and thereafter had any effect on turning this practice around in hopes of developing better brains.

We delivered lectures on basic neurohistology as well as our research data from our enriched and impoverished studies with rats. We asked for a round table discussion with the medical students as we have done in other countries with success, but here our request was refused because we think they were afraid of our political ideas coming from the United States. However, the last day of our visit, we were granted permission to have our round table discussion. The amphitheater was filled with doctors and medical students. The very first question: "How did Arne and I meet?" I answered satisfactorily evidently. Needless to say, we were surprised after all of our lectures about the brain. Another question: "Are people north of the equator more intelligent that those south of the equator?" I answered, "What is your definition of intelligence?" Then I continued that I am certain in relation to your society you are much more intelligent than I and vice versa. We learned the girls did not want to become doctors because the boys would not be attracted to them.

The two nonprofessional highlights in Africa were spending a few days in the Masai Mara in Kenya with the marvelous wild animals in their natural habitat and climbing to 12,000 feet on Mount Kilimanjaro in adjacent Tanzania where I had a fireside chat with two men, one of whom was former President of the United States, Jimmy Carter.

Cambodia

After successfully working on the effects of enriched and impoverished environments on the structure of rat brains for many decades, I developed a project to apply any successes and benefits from those results. My new project, Enrichment In Action (EIA), is funded by private donations. The main goal of EIA is to enrich the lives of very impoverished children, mentally and physically, in order for them to find meaningful employment while living healthy, productive lives.

In December 2001, a friend, Carole Miller, a former research associate at CAL, and I worked for 5 weeks with orphans living in a Buddhist compound in the forest adjacent to the famous Angkor Wat temples in Siem Reap, Cambodia. We began our project with three objectives: (1) enrich their diet of fish and rice with supplementary vitamins and minerals in addition to education about a more balanced diet, (2) enrich their knowledge and mental capabilities with English and computer lessons for them to obtain good jobs in the future, and (3) enrich their interactions with foreigners by playing physical and mental games. We wanted the children to know we sincerely cared about them by providing as much interaction, kindness, consideration, and love as we knew how.

Utilizing the theme Each One Teach One where those who know teach those who do not, our Cambodian children have progressed very well from many perspectives. (I have used this theme in Berkeley schools for about 30 years.) Initially the age range of the Cambodian children was between 10 to 19 years of age, with one 19-year-old having completed the second grade. We soon learned age alone was not adequate criteria from which to judge these children. Since 2001, I have returned for 2 weeks each year to provide new directions and ideas for their education. Some have become quite proficient with the computer and with their English lessons. At present I have requested Mr. Som Chamroeun, who manages the project most of the year when I am here in Berkeley, to provide me with papers written in English by the children. I wish to evaluate their progress to see how much they have learned to date. A few of those papers have already arrived and are quite impressive, not only in terms of their English but also in terms of their sensitive content.

Teaching at Berkeley

Here I wish to highlight only four courses, which include the nervous system, and which I have designed or taught for decades; others have not been offered as frequently. In the Fall semester I have two courses, General

Human Anatomy dealing with both gross and microscopic anatomy, and Applied Anatomy. In General Human Anatomy, though the nervous system is covered by twice the number of lectures as the other systems, I want the students to realize all systems work together. In the Applied Anatomy lectures, the range of topics includes Neurosurgery, Neuropathology, Neurology, Pediatrics, Healthy Environments, Neuroradiology. What is Applied Anatomy? This is a course where former anatomy students return after they have applied their anatomy to become professionally successful in their chosen, medically related fields. These young professionals give lectures to the present Berkeley students to indicate how basic anatomy and neuroanatomy are fundamental to their disciplines.

Why do I continue to present these courses? Because I believe if more people understood the structure and function of their bodies, influenced so intricately by the nervous system, and took care of themselves early in life, then the period of their lives after 50 would be more healthy and enjoyable. At present, look at the cost of health care for the disabled elderly. Many are not even aware that the simple phrase "Use It or Lose It" applies to their brains, bones, and muscles! In the Fall of 2006 alone, I had 736 students, including mostly undergraduate students, with some graduate students as well, taking Human Anatomy, a kernel that could eventually make a difference in health education.

In the Spring I offer two courses: Human Neuroanatomy and Anatomy Enrichment. The graduate Human Neuroanatomy course for about 50 students covers gross and microscopic anatomy of the nervous system and the associated structures. To aid in the study of the structure and function of the brain and the spinal cord, their protective coverings and vascular supply, we designed and wrote an unconventional book, *The Human Brain Coloring Book* (Diamond et al., 1985.) Arne and I use this book for our classes: he at UCLA, and I at Berkeley. Learning neuroanatomy is not conceptually difficult but is rich in detail and is essential to remember as a foundation for research as well as clinical practice. For these reasons when we were invited to write a *Brain Coloring Book* by Larry Elson, Ph.D., the author of the *Anatomy Coloring Book*, we accepted wholeheartedly. Using one's kinesthetic sense in coloring enhances the learning and memory processes. What a pleasure knowing we have a resource to offer students of all ages to enhance their learning challenge. *The Human Brain Coloring Book* has been continuously in print since 1985 and has been translated into German and Spanish.

The Anatomy Enrichment course was established in 1977, 30 years ago, but under a different title. This course includes those Berkeley students who earn an A or B in the undergraduate Human Anatomy course. They are then eligible to use their anatomy notes to design lessons to teach gross and neuroanatomy in the Berkeley and Albany public schools, K through 7th grade. The children see their first human brain in first grade. One little boy was wise enough to say it was "awesome." The nervous system is taught more thoroughly in the seventh grade when the schoolchildren are advanced enough to comprehend a bit more detail.

New Horizons

In 1980 Dee Dickinson in Seattle, Washington, established New Horizons for learning, a very successful international educational network and on-line resource for educators. She had the foresight before the field became popular to value the role that the brain plays in education. As logical as it seemed, this relationship was not accepted as fact when we first showed that anatomical brain changes could be measured microscopically in response to enriched or impoverished experiential conditions, in other words, with different levels of education. Dee was very supportive by including these findings on her Website at www.newhorizons.org that now receives around eight million hits a month. Over decades we constantly added new data, providing examples of brain plasticity to a wider audience on the Web. At one time a national senior organization used our article, "Successful Aging of the Brain," for a topic for their Website interaction conference. Thanks you, Dee, for this means of sharing neuroscience and education with a greater audience.

Administration Roles

Now, I wish to mention some of the administrative positions I carried out at the same time I was raising my family, teaching, and running a research laboratory.

In 1967 Dean Walter Knight asked if I would like to become an Assistant Dean in the College of Letters and Science at CAL. I had previously criticized the quality of academic advising for our undergraduate students so I responded positively to his invitation to serve this administrative position. The major role, in addition to everyday commitments, I accomplished in my opinion, was to survey about 20 or more universities in the United States to inquire about their best academic advising programs. When all were evaluated, I learned that a most effective system was having senior, honor students serve as major advisers because they knew the quality of the present faculty and their courses, the present requirements of the college, appropriate work loads, and so on. After a 5-year term, I resigned thinking I had set up a good path for the new dean to follow, only to learn he had taken the job to earn money for his golf lessons!

In 1970 I accepted the position to be the first woman Associate Dean of the College of Letters & Science. I served for many years before I was invited to be the Dean of the College. I knew I loved my family, teaching, and research too much to attempt taking on this demanding responsibility. I declined. When I returned to my academic department, Physiology and Anatomy, the

Chairman, Nello Pace, told me that the faculty had voted to invite me to become chairman of the department. Once again I declined. Later on former President Clark Kerr asked if I would like to be Chancellor of the University of California at Santa Cruz campus, and I declined for the same reasons as mentioned previously. I honestly felt I could serve our CAL students and the health of our society better by teaching anatomy and neuroanatomy and at the same time contributing new information from my research on how to develop and maintain a healthy brain and body throughout our lives. Without a doubt, I still gained most satisfaction from following these roles for many decades.

Being invited to take on such demanding roles within our great University of California system, inspired me to write my 4 **P**s.

1. **P**ersonal priority. . . . Family and friends
2. **P**rofessional priority. . . . Brains, friendly colleagues and students
3. **P**erseverance. . . . Essential for everything
4. **P**ositive attitude. . . . Look at the alternative

One year I took a survey of nine CAL Nobelists who had earned their prize in science. I asked each of them, “What or who inspired you to go into science?” All but one replied, “a great high school teacher.” What inspired the “missing” one? His parents had hired a young woman directly out of teacher’s college to live in their home and teach their child as much as she could about everything. This Nobelist kept track of this special teacher until she was 90 years old!

If good teachers were responsible for producing so many Nobel Laureates, such an accomplishment should inspire generations of teachers new and old!

In the 1980s I was asked if I would like to become the Director of the Lawrence Hall of Science (LHS) up in the hills overlooking the campus. After inquiring about various aspects of the administrative role of this position, I learned there was a large debt lurking in the background, convincing me that I did not wish to become entangled in such a large, negative, financial web and declined. When I was asked again in 1990, my primary responsibilities on campus were in a manageable condition. I knew of no major problems at the Hall so I accepted and held the position for 5½ years.

What major accomplishments at the science hall brought me satisfaction? Working with Dr. Jenny White and Cathy Barrett we designed and set up exhibits about brains. At first I provided an assortment of animal brains from a whale, a dolphin, a monkey, a sheep, a bird, a cat, a mouse, and a rat for the visitors to compare the broad spectrum of their sizes and shapes. (One science museum on the East Coast had a cockroach brain!) We displayed a cocaine addict's brain compared to a normal with a label saying that "the choice is yours." Many concerned mothers alerted their children to this exhibit. We developed a large, interactive exhibit based on the optimistic data we had collected from our laboratory rat experiments on campus with enriched and impoverished environments. Thousands of visitors to the Science Center learned how their brains could "grow with use" and "decrease with disuse." This exhibit was sent to at least seven other science centers in the United States. In addition, on many weekends each year we held 2-day Brain Conferences for hundreds of California public school teachers to benefit from ours and other scientific investigator's new, brain research. Using the LHS vans, the staff took brain materials around to the Bay Area public schools to accompany the brain skits they had created.

One other original creative effort at the Hall was a "jungle gym" in the shape of a deoxyribonucleic acid (DNA) molecule 60 feet long and 5 feet high. I wanted children to associate fun with solid science. This 60-foot molecule was constructed in Michigan and carried in three parts on a flatbed truck across the country to LHS. Now when young people encounter DNA in their textbooks they will recall playing on it at LHS. I am deeply indebted to Ken Hofmann, a successful local contractor, for financing this structure.

When I finished my 5½-year term at the Hall, I hoped that most of the LHS staff knew what dendrites were, that the local public knew their brains could change favorably with use or unfavorably with disuse and that children were familiar with DNA!

Special Berkeley Colleagues

I might begin this section with an obvious statement indicating how nearly impossible it is to write an autobiography about my neuroscience career of 60 years upon the required 30-plus pages during 3 summer months between my teaching classes in the Fall and Spring semesters. Undoubtedly, many worthwhile experiments and lovable, long-term colleagues have been omitted, definitely not willingly. I offer my deepest apologies. Maybe some day I will tackle a more extensive creative effort.

That being said, I have one colleague who has been directly involved in my neuroscience contributions here at Berkeley so I would like to expand on this relationship. Over a 23-year period Professor Robert Knight M.D. repeatedly came to Berkeley from Davis to help teach in my graduate, neuroanatomy laboratory course. Now he gives a lecture each year to my Applied Anatomy class, bringing us up to date on his research dealing with electrophysiological techniques to study cognitive processing. What a pleasure to have a competent, friendly, practicing neurologist work with our students! More recently he has become the Director of the Helen Wills Neuroscience Institute at Berkeley. In my opinion to have him fill such a position at Berkeley is the wisest choice our administration could make as shown by the growth of the budget, number of faculty with their varied research projects and quality students, and so on under his direction.

Two other colleagues, Professors George Brooks and Steve Lehman, have combined their teaching efforts with mine to make two successful, popular, undergraduate courses in Human Anatomy and Human Physiology. I definitely value their long-time friendship and effective scholarship. Thank you, Bob, George, and Steve as well as many others for making my professional life at Berkeley an incomparable, enriched experience!

In Closing

At this time I wish to express my sincerest gratitude to Larry Squire and the Society of Neuroscience for inviting me to join my colleagues in presenting a collection of thoughts and facts about my professional and personal life as a neuroscientist. I am deeply indebted to my family, administrators, colleagues, students at all levels, technicians, and other friends for their contributions of time, valued assistance, and support. To have spent decades investigating and teaching about brains has provided incomparable satisfaction.

Finally, let me share something of precious significance to me from one of my children. About a year ago in the evening, I walked into my bedroom and saw lying on my pillow a note containing just three words; MOM, DOC, EXTRORDINAIRE . . . Who could ask for more when I was doing what I loved best!

Selected Bibliography

Bennett EL, Diamond MC, Krech D, Rosenzweig MR. Chemical and anatomical plasticity of the brain. *Science* 1964;146:610–619.

Carughi A, Carpenter KJ, Diamond MC. Effect of environmental enrichment during nutritional rehabilitation on body growth, blood parameters and cerebral cortical development in rats. *J Nutr* 1989;119:2005–2026.

Connor JR, Melone JH, Yuen AR, Diamond MC. Dendritic length in aged rats' occipital cocrtex: An environmentally-induced response. *Exp Neurol* 1981;73: 827–830.

Connor JR, Diamond MC. A comparison of dendritic spine number and type of pyramidal neurons in the visual cortex of old adult rats from social and isolated environments. *J Comp Neurol* 1982;210:99–106.

Diamond MC. Functional Interrationships of the Hypothalamus and the Neurohypophysis. PhD Thesis 1953; University of California at Berkeley.

Diamond MC, Law F, Rhodes H, Lindner B, Rosenzweig MR, Krech D, Bennett EL. Increases in cortical depth and glia numbers in rats subjected to enriched environments. *J Comp Neurol* 1966;128;117–126.

Diamond MC. Extensive cortical depth measurements and neuron size increases in the cortex of environmentally enriched rats. *J Comp Neurol* 1967;131:357–364.

Diamond MC, Lindner B, Johnson R, Bennett EL. Differences in occipital cortical synapses from environmentally-enriched, impoverished, and standard colony rats. *J Neurosci Res* 1975;1:109–119.

Diamond MC. The aging brain-some enlightening and optimistic results. *Am Sci* 1978;Jan-Feb:66–71.

Diamond MC, Connor JR, Orenberg EK, Bissell M, Yost M, Krueger A. Environmental influences on serotonin and cyclic nucleotides in rat cerebral cortex. *Science* 1980;210:652–654.

Diamond M. Age, sex and environmental influences. In Geschwind N,& Galaburda AM, eds. *Cerebral dominance-The biological foundations*. Cambridge, MA: Harvard University Press, 1984;134–146.

Diamond MC. Sex differences in the brain. *Brain Res Rev* 1988a;12:235–240.

Diamond MC. *Enriching heredity*. New York: Free Press, 1988b.

Diamond MC. Hormonal effects on the development of cerebral lateralization. *Psychoneuroendocrinology* 1991;16:121–129.

Diamond MC. Enrichment, response of the brain. *Encyclopedia of neuroscience 3rd edition*. Elsevier Science, 2001a.

Diamond MC. Response of the brain to enrichment. *Annals of the Brazilian Academy of Sciences* 2001b;73:211–222.

Diamond MC, Dowling GA, Johnson RE. Morphologic cerebral cortical asymmetry in male and female rats. *Exp Neurol* 1981;71:261–268.

Diamond MC, Hopson J. *Magic trees of the mind*. New York: Dutton, 1998.

Diamond MC, Johnson RE, Gold MW. Changes in neuron and glia number in the young, adult, and aging rat occipital cortex. *Behav Biol* 1977;20:409–418.

Diamond MC, Johnson RE, Ingham C. Brain plasticity induced by environment and pregnancy. *Neuroscience* 1971;2:171–178.

Diamond MC, Johnson RE, Ingham CA. Morphological changes in the young, adult and aging rat cerebral cortex, hippocampus and diencephalon. *Behav Biol* 1975;14:163–174.

Diamond MC, Johnson RE, Mizono G, Ip S, Lee CL, Wells M. Effect of aging and environment on the pyriform cortex, the occipital cortex and the hippocampus. *Behav Bio* 1977;20:325–336.

Diamond MC, Korenbrot CC. Eds. *Hormonal contraceptives, estrogens, and human welfare*. New York: Academic Press, 1978.

Diamond MC, Krech D, Rosenzweig MR. The effects of an enriched environment on the histology of the rat cerebral cortex. *J Comp Neurol* 1964;123:111–120.

Diamond MC, Law F, Rhodes H, Lindner B, Rosenzweig MR, Krech D, Bennett EL. Increases in cortical depth and glia numbers in rats subjected to enriched environment. *J Comp Neurol* 1966;128:117–126.

Diamond MC, Lindner B, Johnson R, Bennett EL, Rosenzweig MR. Differences in occipital cortical synapses from environmentally enriched, impoverished and standard colony rats. *J Neurosci Res* 1975;2:109–119.

Diamond MC, Johnson RE, Protti AM, Ott C, Kajisa L. Plasticity in the 904-day-old male rat cerebral cortex. *Exp Neurol* 1985;87:309–317.

Diamond MC, Rainbolt RD, Guzman R, Greer ER, Teitelbaum S. Regional cortical deficits in the immune deficient nude mouse: a preliminary study. *Exp Neurol* 1986;92:311–322.

Diamond MC, Scheibel AB, Elson LM. *The human brain coloring book*. New York: Harper and Row, 1985.

Diamond MC, Scheibel AB, Murphy GM Jr, Harvey T. On the brain of a scientist: Albert Einstein. *Exp Neurol* 1985;88:198–204.

Diamond MC, Weidner J, Schow P, Grell S, Everett M. Mental stimulation increases circulating CD4-positive T lymphocytes: a preliminary study. *Cognitive Brain Research* 2001;12:329–331.

Gaufo GO, Diamond MC. Prolactin increases CD4/CD8 cell ratio in thymus-grafted congenitally athymic nude mouse. *Proc Natl Acad Sci* 1996;93:4165–4169.

Gaufo GO, Diamond MC. Thymus graft reverses morphological deficits in dorsolateral frontal cortex of congenitally athymic nude mice. *Brain Res* 1997;756: 191–199.

Globus A, Rosenzweig MR, Bennett EL, Diamond MC. Effects of differential experience on dendritic spine counts in rat cerebral cortex. *J Comp Physiol Psychol* 1973;82:175–181.

Greer ER, Diamond MC, Murphy G Jr. Increased branching of basal dendrites on pyramidal neurons in the occipital cortex of homozygous Brattleboro rats in standard and enriched environmental conditions: a Golgi study. *Exp Neurol* 1982;76:254–262.

Holloway RL. Dendritic branching: some preliminary results of training and complexity in rat visual cortex. *Brain Res* 1966;2:393–396

Malkasian D, Diamond MC. The effects of environmental manipulation on the morphology of the neonatal rat brain. *Intern J Neurosci* 1971;2:161–170.

Mohammed AH, Zhu SW, Darmopil S, Hjerling-Leffler J, Ernfrs P, Winblad BK, Diamond MC, Eriksson PS, Bogdanovic N. Environmental enrichment and the brain. *Prog Brain Res* 2002;138:109–133.

Renoux G, Biziere K, Renoux M, Guillaumin GM. The cerebral cortex regulates immune responses in the mouse. *CR Acad Sci D (Paris)* 1980;290:719–722.

Rosenzweig MR, Bennett EL, Diamond MC. Cerebral effects of differential environments occur in hypophysectomized rats. *J Comp Physiol Psychol* 1972;79:56–66.

Rosenzweig MR, Bennett EL, Diamond MC. Modifying brain chemistry and anatomy by enrichment or impoverishment of experience. In Newton G, Levine S, eds. *Early experience and behavior*. Springfield, IL:Charles C Thomas, 1968;258–298.

Rosenzweig MR, Krech D, Bennett EL, Diamond MC. Effects of environmental complexity and training on brain chemistry and anatomy: A replication and extension. *J Comp Physiol Psychol* 1962;55:429–437.

Uylings HBM, Kuypers K, Diamond MC, Veltman WAM. The effects of differential environments on plasticity of cortical pyramidal neurons in adult rats. *Exp Neurol* 1978;62:658–677.

York AD, Breedlove SM, Diamond MC, Greer ER. Housing adult male rats in enriched conditions increases neurogenesis in the dentate gyrus. *Soc Neurosci Abstracts* 1989;15(383.11):962.

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