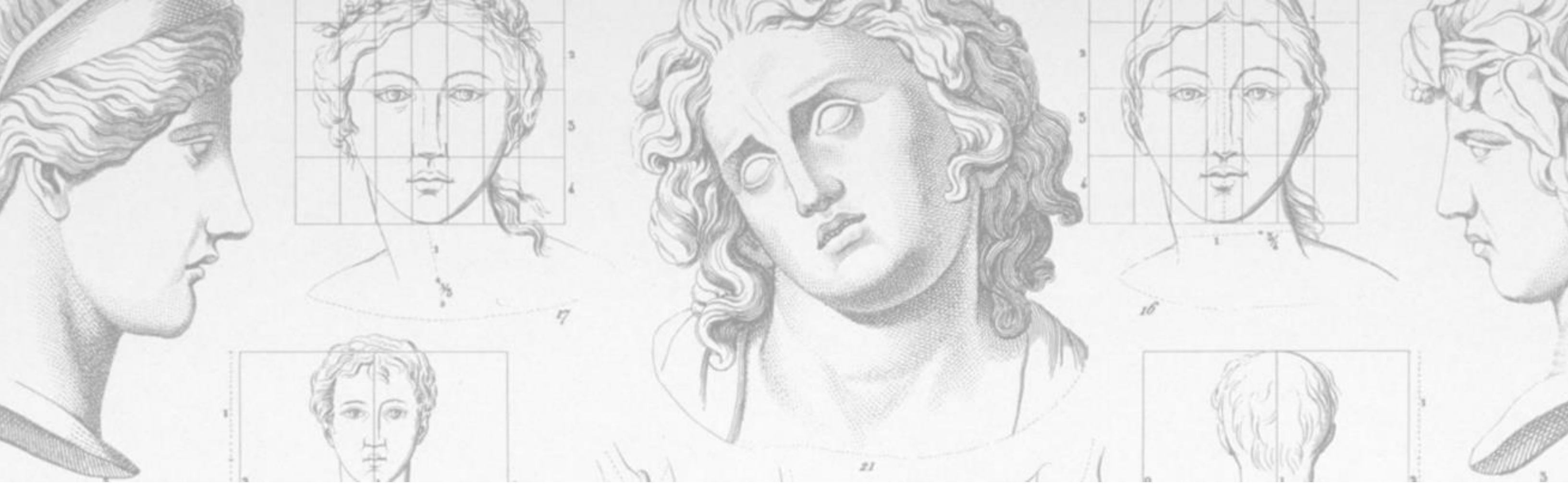

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## Robert W. Doty

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# Robert W. Doty

**BORN:**

New Rochelle, New York
January 10, 1920

**EDUCATION:**

University of Chicago, B.S. (1948)
University of Chicago, M.S. (1949)
University of Chicago, Ph.D. (Ralph W. Gerard, Mentor) (1950)

**APPOINTMENTS:**

Postdoctoral Fellow, Neuropsychiatric Institute, University of Illinois College of Medicine (1950; Warren S. McCulloch, Sponsor)
University of Utah (1951)
University of Michigan (1956)
University of Rochester (1961)

**HONORS AND AWARDS:**

Society for Neuroscience, President (1975–1976)

*Robert Doty began his research by carrying out detailed neurophysiological analyses of the coordination of swallowing. Subsequently, he carried out electrophysiological studies of visual cortex in cats and monkeys, elucidating the importance of nongeniculate inputs. He was the first to show (with Giurgea) that conditioned reflexes could be established by paired stimulation within the cerebral cortex. He also carried out studies of interhemispheric independence and cooperation during learning and remembering.*

# Robert W. Doty

To an immeasurable degree my life and character have been molded by two women, my mother and my wife. I have few firm recollections of my mother because she died of thyroid surgery, for "goiter," just before my seventh birthday. She lay within the palace of her domestic dreams that she and my father had just built with loving care in River Forest, Illinois. Taking me to her for a last farewell, he pressed a rose to her lifeless lips, folded it into her bible, and solemnly presented me with that melancholy remembrance, that I should merit the hopes she held for me. The thought still brings forth a tear as I recall it.

While sorrow undoubtedly wrought its effect, the thoughtless behavior of some of my less civilized schoolmates, taunting and teasing me—"Hah, hah, your mother's dead"—perhaps had similar consequences. A certain misanthropy and social aloofness may have resulted from such experience, subsequently reinforced by a somewhat nomadic childhood—nine different schools in the ensuing 9 years.

This anomalous background, however, did not leave me morose nor withdrawn. I was never "one of the crowd," yet I could have as much fun and foolishness as the next fellow. I suppose my pedigree, much and vacuously emphasized within the family, afforded some protection, at least subtly to the mind of a child, from any incipient sense of insecurity. My birth in 1920 had propitiously coincided with the tercentenary of the Pilgrim landing of Edward Doty, duly noted by my father's enclosing the commemorative half dollar in my "baby book." Thanksgiving Day thus always held special significance for family gatherings. I was the 10th of the Doty lineage. My mother's ancestry traced back to one of the eight children (with John Mack) of a daughter of the Earl of Montagu, Isabella Brown, who, blessedly, left Londonderry, Ireland, in 1732. My wife, whose parents arrived from the Tsar's Vilnius, Lithuania, in 1906–1908, would always deflate any pretense the Dotys might display as to who begot whom how long ago by asking why, if we had been here so long, were we still so poor? Pride of ancestry, of course, ignores mathematics, which quickly deflates the glory of the genetic pyramid. Choosing, for example, 1400 AD as a starting point, it is easily calculated that each today can claim descent from an army of a million or more (20 generations, $2^{20}$), illustrious or no.

My father remarried and we moved to Macomb, Illinois, for a year or two until the Depression seriously altered our financial condition. Then it was back to Chicago (and Cicero). Perhaps subconsciously, another feature of my outlook on life derived from these experiences—that money provides but an illusory, though pleasant, attainment in life's doings. Among other lessons I may have acquired, albeit again unconsciously, was the contrast offered between our straightened circumstances and the seemingly more comfortable life of Uncle Fred, who was a professor of education at the University of Chicago. My mother's two sisters had each married men who became university professors, and my father, with a hangover from his more affluent days but with considerable cause, always disparaged the level of wealth attainable by these academics. In later years, when I was well immersed in testing the vision of cats using what had become known as the "Yerkes box," my Aunt Jeanette evoked an astonishing moment of nostalgia and kinship when she sent me Uncle Fred's thesis (Breed, 1911), in which he had initiated use of this training "box," with Yerkes at Harvard, testing color vision in chickens. This, of course, remained wholly unknown to me as a child. I do remember that Uncle Fred had his dog (Trixie?) trained to balance a biscuit interminably on her nose until he gave the signal for the catch.

Yet another formative influence was the two summers I spent, probably in 1933 and 1934, on the farms of relatives in Plymouth, Indiana. This revealed the wholesome beauty of hard physical work and the lush fascination of the land and its creatures. Those were days when a dozen or more farm families pooled their labor and resources to get the grain threshed. The stacked sheaves were pitched to precarious heights upon horsedrawn wagons and then delivered into the devouring maw of the monster machine. It spat out a hurricane of straw and dust through one vent to make the haystack and a golden rain of grain at the other, which was shoveled vehemently into the bin, from which it then sustained the horses, cows, pigs, and chickens for another year. The threshers' dinner, prepared by the small battalion of wives and daughters, was a feast incomparable.

When I was 14 I came down with scarlet fever. That meant quarantine, and since the family could not afford any other solution I was sent to the Cook County Contagious Disease Unit, adult division. There my fellow patients, a ne'er-do-well drunk, a one-legged tramp, and a gangster, considerably advanced my education with fanciful tales, real or imagined, of their respective worlds. My vocabulary expanded so that when I acquired a paper route a year or so later, I was well prepared to profanely punctuate my speech, consistently in habit with my colleagues, as we folded our papers at 4 am, ready to hurl them onto third-story apartment porches at the crack of dawn.

I certainly was no star in school; it all came too easily, and much was rather boring. I graduated from Chicago's Austin High School in February 1937 with a diploma in history and went to work at nearby Hotpoint assembling electric ranges. The assembly line provided another immersion in the life of the common man, and I exulted in being uncommon, giving our drear hours relief by "demonstrating" ballet steps or singing Italian arias, all to our mutual amusement. The money gave me the freedom to leave home, which I promptly did, renting a room and carousing as much as I could afford. Ties with my family remained, however, and my father urged me to go to night school and become a certified public accountant, whereby in a relatively short time, he assured me, I might command $10,000/year, a princely sum at the time. I found Accounting and Business Law to be excruciatingly dull; so while I passed the courses, my more lively hours were spent with library books on chemistry and philosophy. (I particularly remember James Jeans' *Mysterious Universe*.) I also dabbled in German at the Berlitz school for a bit, but the cost was beyond my means.

It was about this time, thanks to my bosom pal Bill Beamish, who was an accomplished trumpet player, that I too began the endeavor to acquire that skill—the idea being that I would work my way through school playing the horn. That, fortunately, when the time arrived proved to be as unnecessary as it was unequivocally futile. Technique I ultimately mastered to considerable degree, but inherent musical skill was missing. The association with musicians, however, also led to more artistic inclinations, and I acquired some pretense as an aesthete and would-be Bohemian, 25-cent seats for the opera in the dizzying heights of the acoustically magnificent Auditorium Theater.

After a couple of fruitless years at the Walton School of Commerce, I finally found my niche at Austin Evening Junior College. It was superb, drawing heavily upon moonlighting grad students or junior faculty ("instructors") from the University of Chicago. My physics teacher, for instance (who was also briefly a suitor of my future wife), was Maurice Shapiro, who was to become a renowned astrophysicist. Happily, physics did not win out in courtship, for in a subsequent semester I shared biology and humanities classes with a woman so tantalizingly beautiful as to evoke an unaccustomed shyness in myself, so wondrously unattainable did she seem to be. Were not men who wore glasses unattractive to women? But oh, such hidden guile of destiny, for in her diary of Thursday, March 6 1941, Elizabeth Natalie Radzun-Jusewich wrote, "Out to school—Robert Doty—I shall have to get acquainted with him before long—He makes me very much aware of his presence." Clearly, we were both impelled, yet cautious; there was no hint foreseen of what was soon to follow when at last we came to recognize what fate had bestowed upon us. Opportunity for acquaintance came on May 30–15 hours together preparing for the humanities exam. Our destiny abruptly became manifest and irresistible. By our seventh meeting (Sunday June 15), I essentially proposed to her. Her diaried response: "Bob told me he was going to betray Doty and get married and, of course, the implication was unmistakable—and I felt another of those exquisitely poignant tugs on my heart. Oh, Betty, do try to keep your head, even though you're emotionally and spiritually beyond salvation." We were married in city hall 76 days later on August 30, 1941, culminating an intense romance replete with dilemmas timely (impending war) and timeless, surviving quarrels serious and trivial, as man and woman strove to mold their passion and their common sense into an unassailable unity of mind, heart, and purpose.

Our success was divine and remained so for 58 years. She restrained my would-be recklessness, and I provided confidence for her spirit of adventure. Thrift was reflexive, and we shared a self-sufficiency that made us independent of the crowd. However, 3 weeks after moving from my room to the long-awaited apartment came Pearl Harbor. We could feel the sword descending, but fate again was kind—we had a year of incomparable bliss together, despite the receding hours available for togetherness. She worked for the War Department, Corps of Engineers ("Manhattan Project") 6+ days/week, and I worked as foreman of a battery of automatic screw machines on the second shift, making hardened cores for armor-piercing, 50-calibre machine gun bullets. Then, with a certain malevolency of timing, to the year but a day of our marriage, I walked from telephone to mailbox and life's wheel spun out of control—from arrangements to take the entrance exam at the University of Chicago to "Greetings from the President." I was in the army. And so began a correspondence of monumental proportions. For 4 years we wrote each other daily whenever there was hope of mail delivery, and volumes that were otherwise delivered to uncertainty—letters wantonly adorned with extravagant professions of undying love, unstintingly fulfilled in the decades that followed.

> 9 PM Saturday January 9, 1943
>
> Woman memory my
> life joy always
>
> Have been wallowing in the delight of your letters, soaking up each precious word; as you say, a part of you. We are both black skies awaiting the glory of the coming morn; but the glittering stars of your letters must suffice for present promise.

Basic training at Camp Lee in Virginia, was almost fun; but then, nadir of my position in life, I was assigned to be a bugle boy. Having inevitably failed to make the Post orchestra, directed by an assistant to Eugene Ormandy and with trumpet played by the first chair from the Minneapolis symphony, I was given the next logical assignment. My trumpet pal, Beamish, was far more unlucky because he was already on Guadalcanal. Being a bugle boy, however, turned out to be a huge blessing. Already at least capable on the bugle, I repaired to the piney woods, read Joyce's *Ulysses* with avid admiration, and studied for an attempt at Officer Candidate School (OCS). Of the 300 applicants from our regiment, 50 were given a chance, but then from the much more severe examination by the Post Board there were only 6 survivors, I among them. I still relish the memory of the snappy salute and heel-clicking about-face that I could there bring forth, thanks to my high school participation in the Reserve Officers' Training Corps. However, I also knew what the three courts-martial were, who was head of the Office of War Information, questions of strategy and supply, etc. I was also buoyed by a 5-day visit from my beloved, braving a 33-hour train trip each way, her description of the trip reading like something from Dos Passos.

Upon graduating from OCS on April 2, 1943, I was assigned to training in refrigeration and air-conditioning (!) at Fort Warren, Wyoming, presumably because I might be capable of understanding the gas laws. Would I perhaps be held in the United State as an instructor? Uncertainty at best, but we had lived with that successfully for a year. Therefore, not without great misgiving, my ever-beloved surrendered the opportunity for a career in labor relations and, much more reluctantly, our lovingly furnished apartment, to join me, willy-nilly, as an army wife. The reunion was short-lived. First I was to take a refrigeration company to New Guinea, cadre already selected at Vancouver Barracks, but overnight the orders were changed—I was in the Transportation Corps. We were off to the New York Port of Embarkation (NYPOE), Brooklyn Army Base. We got a room in Brooklyn for a week or so, but then went to Baltimore to pick up my ship. There was a delay for convoy assembly and we had a few more days of "the sweet sorrow of parting" before I departed for North Africa on July 22, 1943, with 300 troops under my command.

She repaired to Brooklyn, where she got an apartment, a series of "Wall Street" jobs, and awaited my promised return. This I did within a couple of months, bringing 700 prisoners from Rommel's Afrika Korps to New York. With my smattering of German, and essential help from a former German officer, I was then able to write the NYPOE "Stehender Befehl" (standing orders) for Kriegsgefangenen (prisoners of war; POWs) being transported in the bowels of our Liberty ships. This did not keep me ashore for long, however; and I was off to the Mediterranean again on October 5. My beloved, now all too aware of the ephemeral nature of our future meetings, returned to Chicago and the greater stability of her parents' home.

First was cargo to Palermo, then a load of high-octane gas to Naples. While awaiting a load of ammunition for the Anzio invasion, I paid a thankfully brief visit to the "front" to experience the beauty of the Appenines and the devastation of war. I visited the "Winter Line" (Anonymous, 1945) that the Germans had so craftily constructed and so stubbornly defended, running through the mountains of central Italy. I arrived before the serene vista of the Liri valley just after the costly capture of San Pietro, carbine in tow but no necessity of using it and a dry bed to return to in Naples harbor. Our gutted tanks lined the road, like mythological monsters, derelicts, shadowed by ruins of the shattered town. At the aid station a Texas sergeant from the 142nd Regimental Combat Team, reported in to have slivers of shrapnel removed from his hand that he had acquired some days before as he pitched back the German grenades in the taking of Monte Maggiore. A rain of death gracefully ascended the German-held Mt. Trocchio, tiny puffs of white phosphorous in the distance, working systematically to the crest, The Abbe of Monte Cassino stood in the background, picturesquely awaiting its destruction.

I was all too glad to leave that beauty and excitement, although the sentiment was not entirely shared by several of my new front-line friends. They were happy to be free of the threatened ships. Their landlubber instincts proved strangely prophetic. Back in Naples, it was the opera, *La Bohème*, that saved my life. The theater was heated only by the breath of its GI audience, with helmets occasionally clattering to the floor, "*Che gelida manina*" all too credible. Intermission offered that delectable Italian temptation, cannoli, perhaps not surprisingly laced with *salmonella*. I do not remember just when I became ill the following day but, thankfully, I did. While I lay sick, topside in my bunk, strong offshore wind, roaring down the slopes of erupting Vesuvius, had driven our empty ship out of the harbor, dragging both anchors. The first torpedo struck squarely in the middle of my tween deck office, where I would normally have been, still crazily practicing my trumpet. The second explosion was aft, shy of the engine room, the kindly submarine captain, and good marksman, thus leaving the boilers intact. It took almost an hour to sink; but scrambling down the listing Jacobs ladder to the bobbing boats, our concern was whether the boilers, too, might explode. The S.S. Wm. S. Rosecrans settled into history between Capri and Ischia on January 6, 1944.

I managed to cadge rides on returning cargo planes—Algiers, Casablanca, a glorious view of the snow-capped Atlas mountains, Dakar, Fortaleza, San Juan, and home. Together again after 4 months, my Elizabeth and I had 39 days in the fullness of life, and the rich offerings of New York, before I was off once more with a platoon of meteorologists for Egypt, with 36 B-47 aircraft aboard bound for Karachi. Then across the Indian Ocean to Perth, through Bass Straits and the sullen Tasman Sea, on long leaden swells that rolled the ship like a toy. Landfall finally in Los Angeles to find that orders had changed—no transcontinental travel; however, my orders read "return to NYPOE," and with a bit of wile I found a transportation officer to honor them. While home in Chicago wiring NYPOE requesting leave, I was informed that I was AWOL.

However, they took me back, put a letter in my 201 file,[1] and sent me to Scotland on a rusting, roach-ridden hulk from World War I, a "Hog Islander" as they were called, which was ultimately sunk as a breakwater for ships still unloading at Normandy—I reveled in the drowning of the roaches.

Returning, thanks to the navy, there was another trip to England; then fortune smiled again. I was promoted to 1st Lt and joined the office at NYPOE, supervising the loading of troops and cargo; Elizabeth secured a transfer from the Chicago to the New York office of the Manhattan Project. This was November 1944. We rented a basement apartment in Flatbush and reestablished domestic life. By the following spring the end of the war was sufficiently in sight that we could accede to my darling's fervent wish for motherhood. She left for home, conspicuously pregnant, and with a commendation from the Corps of Engineers for the work she had resumed in the Manhattan District. It was dated August 6, 1945, the day of Hiroshima's atomic destruction, to which her Medal of Merit details the significance of her contribution. I went back to sea: grain from New Orleans to Antwerp, then 700 troops in prisoner conditions but happy to be going home. The course was supposed to be to New York, but the sea dictated otherwise. In one of the most violent North Atlantic storms in decades, we were forced to point to Portugal to keep from capsizing. From the flying bridge I took, and still have, a photograph of waves towering above me, a good 50 feet above the Plimsol line. Dangerously low on fuel, we hove into the Azores, where I had one of the greater challenges of my career as Transport Commander—giving 700 troops shore leave on Christmas Eve. I think there were approximately 30 Portuguese in the jail of Punta Delgado on Christmas Day, but only a half dozen GIs—nothing serious. We soon had them returned for military discipline.

It took several radiograms to pry fuel out of the Naval reserve, and as a result the *New York Times* announcement of our arrival at NYPOE was fallacious. My poor wife gave birth to Robert Jr. on December 27, thinking my obvious absence might signify that I was lost at sea. The fierce storm had been duly reported, with approximately 25 sailors being swept away from the forward turret of the cruiser Augusta.

There was one last trip, now as a captain, on the beautiful hospital ship, Jarrett M. Huddleston, to bring back 362 "war brides" and their 108 children from Southampton. I was not relieved of active duty until August 9, 1946, but terminal leave had given time for us to buy a bungalow in the Marquette Park section on the south side of Chicago a week after I returned home. As we were to do again 15 years later in Rochester, Elizabeth and I completely repainted and papered and otherwise restored

[1] This constituted the personal record of each army officer, dates and locations of service, commendations, or criticisms by superiors, disciplinary action, etc.

this sturdy house, and domestic bliss was complete. We had carefully conserved our funds to that end, and now she was free to be the creative Hausfrau, as had always been her keen desire.

With the "GI Bill" my tuition was paid at the University of Chicago where, after the 4-year interruption, I was now about to begin. As a result of their rational policy of allowing students to pass courses simply by examination, I was able to enter at the junior year. It was a unique time, with mature and extraordinarily eager students, and Chicago was a super school. I had physics from Enrico Fermi, P chemistry from Willard Libby, Biochemistry from Konrad Bloch and Albert Lehninger, embryology from Viktor Hamburger, and intimate courses with Heinrich Klüver, Austin Riesen, Ward Halstead, and Eckhard Hess; Stefan Polyak was also there, and Roger Sperry was the "outside" reader for my Ph.D. thesis. I opted for physiology, particularly attracted by Nathaniel Kleitman's lectures on the nervous system. I did a "lab rotation" with him. Unfortunately, it was rather dull—measuring my body temperature throughout the waking hours. He was, of course, very interested in circadian rhythm, as he had named it, and since I was working the third shift I was an interesting subject. Having a family to support, I had returned to work at Hotpoint where, counting my army years, I now had 9 years seniority. I became the night fireman for the plant, i.e., twice a night I had to remove the clinkers from the boiler and shovel 4 tons of coal into the automatic feed; and then do my homework betimes. Kleitman was not overly impressed with my lack of enthusiasm for body temperature, and as a result I missed making the discovery of REM sleep. That distinct, and well-deserved, honor fell to Eugene Aserinsky, the next graduate student to work with Kleitman.

It was an easy passage from Kleitman to Ralph Gerard, whose lectures were each small jewels. I remember once interrupting him early in the morning before lecture, and to my surprise I found him busily preparing. It had all seemed so effortless and, indeed, he was a master at extemporaneity; but shooing me away at the time, he counseled that preparation still made for the better presentation, and that if one was not a bit nervous about a lecture, it was likely to be detrimental to performance. So, I joined Gerard's large group. Thanks to the support he received from Orr Reynolds and the Office of Naval Research, this ultimately relieved me of my duties at Hotpoint, and I terminated my "blue-collar" days with 11 years seniority. The group with Gerard was attractively versatile: Ben Libet as chef de travaux, Lou Boyarsky, who had just made the first demonstration of axoplasmic transport (Samuels *et al.*, 1951), and Gilbert Ling, Karl Frank, Sid Ochs, and E. Roy John, were fellow graduate students.

Using my machinist skills, I milled a multichambered respirometer from Plexiglas and installed electrodes for stimulating and recording action potentials from frog sciatic nerves. Calibrated movement of a low-viscosity fluid in capillaries, read via a microscope mounted on a milling attachment, measured the oxygen consumption of each of the nerves in the presence and absence of stimulation (Doty and Gerard, 1950). By differential poisoning we were able to show that the metabolic support for the increase in respiration consequent to activity was qualitatively distinct from that at rest. One agent could greatly diminish resting metabolism without affecting that accruing with activity, and leaving the concomitant action potential unchanged; whereas another could leave resting metabolic rate unaffected while blocking the increase consequent to activity—again leaving the action potential unaffected for a considerable time. This work constituted my master's thesis.

I was accepted to the University of Chicago medical school. However, faced with the decision, it was quite easy to see that studying the brain was more interesting than delivering babies and not as costly to my familial responsibilities. The next step then was the PhD. Another nadir in my life was reached, briefly, in the oral portion of my qualifying exam. I was asked some penetrating questions about the basis of the osmotic behavior of erythrocytes. Since I was a teaching assistant in the course in which all this was currently being examined, it was perhaps assumed that such questions were kindness toward me. I fumbled foolishly and irretrievably, getting things hopelessly confused. That evening my precious one and I carefully pondered whether I should accept the teaching position already offered in the Chicago Evening College system, so sure was I that I had failed. Mercifully, the faculty weighed other factors besides the negative in my performance, and I was accepted.

The course to the Ph.D. seemed to be well in hand. Gerard had assembled a solid team of experts in biochemistry, and the ingenious experiments were up and running. An abstract had already been published (Gerard and Tschirgi, 1949) in a Festschrift for Hans Winterstein (who had been forced from Germany to Istanbul during the Nazi era). The idea was to record, from the artificially perfused spinal cord of the rat, the action potential evoked in the ventral root by electrical pulses applied to the dorsal root and then determine what artificial perfusate material would sustain this response. Thus, the metabolic substrate required for synaptic transmission could be defined. Clever, except that fellow grad student, Howard Jenerick, and I spent 6 months showing that it never could have worked! We tried every reasonable perfusate, including, of course, multiple variations on the one that had presumably been successful previously. When normal blood flow was replaced with any and all perfusates, the vivid postsynaptic response was quickly lost, with the same time course as obtained when the etherized rat breathed only nitrogen. It became obvious that perfusates were causing severe vascular insufficiency, carried inadequate $O_2$, or both to sustain the activity. The washed erythrocytes previously used seemed particularly prone to produce the former. Two mysteries remain: Was the first team somehow confused by stimulus artifact or stimulated the ventral root directly, and how were Yamamoto and McIlwain (1966) then able to invent the highly successful "slice" preparation that survives famously in artificial media (though not ***perfused***)?

In any event, I gradually found myself without a thesis problem. Ralph Gerard, however, always technically inventive, had set Michael Davis to building what was certainly one of the first pulse generators capable of producing neurophysiologically relevant *patterns* of stimuli. In our class exercise on swallowing, using dogs, we were supposed to find that stimulation of the superior laryngeal nerve elicited the act, whereas stimulation of the glossopharyngeal inhibited it. My idea was to measure the timing by which pulses applied to the glossopharyngeal could inhibit the effect of the pulses applied to the superior laryngeal, thus revealing something of the nature of neural inhibition. Again, the basic phenomenon turned out to be either untrue or unreliable, but the pulse generator was a beauty. It allowed me to demonstrate that the "swallowing center" was highly sensitive to the temporal *pattern* of stimulus input, presumably reflecting a mechanism by which inputs from a single reflexogenic area could be sorted as to what action would be produced (e.g., swallowing, coughing, or gagging)—i.e., distinct temporal codes to trigger particular reflexes. Although using a cutting-edge electronic device, my records were obtained via mechanical recording on the smoked drum kymograph. It must be one of the last theses published using this clever but antiquated procedure, shellac coating and all (Doty, 1951).

We contemplated joining Eccles in Dunedin, but selling house and car and transporting our little family abroad seemed a high price, especially since we could stay put and join Warren McCulloch at the Illinois Neuropsychiatric Institute. This was a good decision. My ego was sufficient to withstand Warren's role as genius, though not that of Walter Pitts (Smalheiser, 2000). The incipient mathematical approach of McCulloch, and of Rashevsky, to clarifying neuronal processes was the initial attraction, although I have subsequently become less impressed with its utility. There was also the excitement of Jerry Lettvin, Arnold and Madge Scheibel, and Paul Dell to broaden my perspective and Percival Bailey and the weekly neurosurgical conferences to add to the fascination. It was here that I began my work with extirpation of visual cortex in newborn kittens, and I continued the work on swallowing. One morning, the latter produced an almost uncanny experience. Alone in the deserted lab at 2 am, and barely a mile from the hospital in which my mother had died 25 years before, I discovered that stimulation of the recurrent laryngeal nerve could stop the heart, a manipulation clearly relevant in the area of thyroid surgery. Of course, the true connection of this phenomenon to her death is wildly speculative, and I never pursued the matter; however, the drama of that moment has stayed with me as one of life's strange coincidences.

The time had come to get a job. There was what Davenport called the "gold-plated centrifuge" at the Philadelphia Naval Yard, which involved studying vestibular and other consequences of high *g*, and a position at the Kirksville Osteopathic College. Horace Davenport, however, rescued us with an assistant professorship in physiology at the University of Utah College of Medicine. We bought a lovely house with a view of Mt. Olympus from our picture window. We now also had daughter, Mary, and soon another equally wonderful daughter, Cheryl, during our idyllic Utah days.

Edward C. (Ted) Beck was my first graduate student. Using cats and my previously futile skills in spinal cord surgery, I was able to crush the ventral roots prior to Ted's "training" of the paralyzed limb. Furthermore, training proceeded while the animal was in a cataleptic state induced with bulbocapnine, thus eliminating other, nonspecific movement. The presence of the conditional reflex in the normal state once movement had returned showed that feedback from the movement per se, or other movement, was dispensable in the learning (Beck and Doty, 1957). Les Rutledge and I also began studies that were to play a prominent role in my future endeavors, establishing conditional reflexes to electrical excitation of the cerebral cortex as the conditional stimulus (Doty *et al.*, 1956). Our very first experiment forcefully instructed us in the necessity for strict controls because although we readily established the desired CRs, we found that the plastic we had used to construct our implant had dissolved, leaving bare wires subcutaneously! Les Rutledge was also responsible for getting me to join him in the army, in the reserves of the 328th General Hospital. We did two tours of active duty, one at the Presidio in San Francisco, and a fabulous 2 weeks in February 1956 with the group that David Rioch had assembled at the Walter Reed Armed Forces Institute (e.g., Walle Nauta, Bob Galambos, Victor Wilson, Joe Brady, and Dave Hubel, the latter demonstrating how his newly contrived tungsten microelectrode could penetrate his fingernail). These victims of my name dropping scarcely need further comment in these pages. Finally, in April 1964, I retired as a major in the Medical Service Corps.

We had spent 5 years in Chicago and 5 years in Utah and another 5-year stint was to be spent at the University of Michigan, when Davenport became chairman of physiology. We lived a year as transients, survived the frustrations of building a new house, and settled into a productive life in Ann Arbor. Baby Richard came in 1958, completing our family. Research proceeded along all too many lines; but the chore of grading >200 exams for the huge class of medical students and of teaching laboratory courses in respiratory and renal physiology, about which the students soon came to know more than I, began to test my patience. Thus, in a time of financial stress for the state of Michigan, when an offer came from an old colleague, E. Roy John, and the University of Rochester to found a Center for Brain Research, with a 50% increase in pay, we took the plunge again. We experienced another move and all its attendant stresses and organizational challenges, with my poor wife, as ever, bearing the brunt of selling a house so dear to us, so unaffordable or unattractive to the world. However, at Rochester Doty luck held again. We purchased a small, although somewhat decrepit mansion, spent long days and nights refurbishing it, and settled in for life, with nomadic days behind us. School years finished for the children, we did move again, but only into more rustic surroundings—a paradise, comprising 90 acres of rolling forest, stream, swamp, and farmland on which to garden, hunt, and ponder the vast inventiveness and resilience of the earth. We had 20 more years there to revel in our good fortune. Spring welcomes almost a kilometer of daffodils, each planted with a joy for the future, a golden tracery of renewal; however, they and the ensuing poppies, peonies, iris, roses, and chrysanthemums must now serve sad duty, an enduring memorial to the beauty that was the life of Elizabeth. She left me in April 1999, quietly entering the messiness that is death, cheerful and hopeful until her final day. I cannot rationally mourn one so graced with 84 years of joy and fulfilment. Death is but the ineluctable price for being, and for us both it has been a bounteous bargain. Yet bereft of my companion of a lifetime, I cannot deny a gnawing loneliness, a dull pointlessness to all ambition, that must, it seems, forevermore intrude upon the serenity of each day.

The story of my life now completed, I turn to the story of the science.

## Swallowing

Jim Bosma was my great blessing at Utah. He had acquired a taste for electrophysiology working with Ernst Gellhorn, was a first-class anatomist, and as a young pediatrician had witnessed the devastation wrought by bulbar polio on the coordination of deglutition. We set about studying the neuromuscular pattern evoked in this most complex of all reflexly elicited motor acts. Between mysterious bouts of hearing Utah football games on our audio monitor, we recorded from approximately 22 different muscles (most then wholly unknown to me) in the mouth, pharynx, and larynx of cat, dog, and macaque, effectively defining the spatiotemporal pattern of activity emanating from motoneurons scattered from trigeminal through hypoglossal nuclei. Our paper (Doty and Bosma, 1956) is graced with the elegant drawings of some of Jim's dissections and with an oft requested diagram illustrating the comings and goings of excitation and inhibition, commandeered by some still undefined medullary circuitry for approximately 500 msec.

Having defined what to expect, the next logical step was to define from whence it was put together. It took a few years to get to this. Starting at Michigan and continuing at Rochester, with neurologist Bill Richmond and dental scientist Art Storey (Doty, *et al.*, 1967), and taking a clue from my mentor Roger Sperry, I began my "split-brain" phase, at the nether end. We studied how the two halves of the medullary, and pontine and mesencephalic components of swallowing were coordinated. The brain stem was split stepwise longitudinally throughout its course and/or hemisected at various levels. Surprisingly, we had had a predecessor, Ishihara (1906). We confirmed and extended his observations and predicted (a bit erroneously it turns out) where the coordinating "center" lay. Perhaps the most unexpected finding was that, although all of the earlier components of the act were controlled ipsilaterally, there was decussating control of the series of later firing, constrictor muscles. This certainly has broad implication for theorizing as to the meaning of such mammalian decussations as the corticospinal tract. The common interpretation is that decussation is related to the inversion produced by ocular refraction (a thesis disproven by the insect facet eye, in which the inversion is immediately reversed by spiraling nerve fibers, but decussation from ocular ganglia to ventral cord still occurs). Finding decussating control for pharyngeal musculature, an arrangement also seen in the input of the medullary respiratory system onto phrenic motoneurons (Merrill, 1974), suggests that the decussation arises consequent to some, still unspecified, principle of neuronal organization but one unrelated to optical inversion.

I subsequently abandoned the field to the very competent group at Marseille: Claude Roman, André Jean, and Alexandre Car (Zoungrana *et al.*, 1997). However, first I wrote a review (Doty, 1968) in which I extensively quoted (from translation) my illustrious predecessor, William Harvey's (1628) almost poetic description of the wondrous, "harmonious" action, as he called it, that constitutes such a constant but unattended part of our lives. I have always regretted that that review is largely lost from neuroscience, being stored in the intricacies of the alimentary canal. I did, however, go on to use swallowing as an example of how motor control in general could be achieved (Doty, 1976a) as an ensemble of neurons stirred into action by a specific spatiotemporal pattern of afferent input (by no means merely from peripheral sources) and, once so triggered, proceeding through a reliable sequence of controlling discharge that defines the neuromuscular coordination as commonly observed. It is unfortunate that the term "center" is so easily applied to such an ensemble, connoting anatomical confinement, when in fact the operative constituents of such an ensemble may be widely distributed within the neuraxis.

## Cat Visual Cortex

For Labor Day, September 4, 1950, the diary of my beloved notes that our cat, Tcherina, gave birth to four kittens, and that "RW took them to UoI to remove occipital lobes." That was the beginning of my many endeavors with the visual system. The idea was that if one removed striate cortex prior to its full development, i.e., on the day of birth and long before eye opening in kittens, surrounding cortical areas might be induced to assume some of the lost function and one could then test electrophysiologically and anatomically to determine what degree of reorganization occurred to support whatever visual recovery might be behaviorally demonstrable. The idea was certainly driven by the claim of Margaret Kennard that remarkable recovery followed removal of "motor" cortex in infant macaques. I probably also knew of the work of Gudden; at least I have a clear recollection of psychiatrist Arnie Scheibel at the time asking me if this were not the same Gudden who was murdered by his patient, the mad king Ludwig II of Bavaria—indeed it was. Subsequently, in reviewing the effects of ablating portions of the visual system, I republished von Gudden's dramatic drawing, taken from his ***hinterlassene Abhandlungen***, of the rabbit brain with visual cortex removed at birth without much detriment to vision (Doty, 1973).

This was to be an arduous undertaking. First, it was difficult to predict from the neonatal brain just what portion of the incipient adult cortex one was removing. Most kittens survived the surgery only to die later from "distemper" in the vivarium. In an effort to side step that disaster I kept approximately 20 kittens at our Utah home until my dear wife understandably rebelled. Paul Cornwell, my student who, with Bert Payne and Steve Lomber (Lomber *et al.*, 1993), finally followed these experiments to a successful conclusion, was better situated in that he had a barn on his Pennsylvania property. Finally, my inexperience and impatience as an anatomist failed to identify fully just what the histology was revealing, and it was only when Jim Sprague straightened out the geniculocortical relations of the cat that I was able to begin making some sense of my results.

The major result, of course, was that the kittens could, indeed, see quite well, sans all of those simple, complex, and other cells and columns that Hubel and Wiesel so elegantly revealed. The trouble was that ultimately I came to find that the neonatal extirpation conferred rather minimal if any advantage over simply removing the corresponding tissue from adult animals (Doty, 1971; but see Cornwell *et al.*, 1989). Where I really got in trouble, however, was in claiming, from my electrophysiology, that the famous "topographical retinocortical projection" was something of an illusion so far as function was concerned (Doty, 1958, 1961). My bête noire in this regard was Henschen, and at Richard Jung's exhilarating symposium at Freiburg im Breisgau I endeavored the demolition of Henschen's anatomical claims. A delightful challenge followed afterward when another attendee cordially introduced himself, as David **Henschen** Ingvar, who generously admitted that his grandfather had been a bit irascible. I had previously benefitted from the generosity of Sam Talbot and Wade Marshall in their discussions with me about my trouble with their original electrophysiological definition of this projection onto visual cortex of the cat. Still, when I submitted my 1958 paper, Clint Woolsey, in reviewing it, objected, properly, to its "polemical tone." To some degree I was able to change the tone, but I could not hide the clear discrepancy between my findings that the largest amplitude photically evoked potentials lay outside area striata and the geniculocortical projection, and that the distribution of responses even to the lowest intensity stimulus far exceeded any "point-to-point" representation. After the Freiburg conference, David Whitteridge took me under his wing, and I spent two wonderful days as his house and laboratory guest. Together we thoroughly examined two cats with his apparatus and technique, and he forced me to concede that it was possible to demonstrate the point-to-point projection; but it was also readily apparent that within a few more milliseconds widely distributed responses are apparent (Doty, 1961). The cat/elephant has many manifestations to the blind.

In all my "punctate" photic stimuli I had never thought of directing stimuli at the cat's "blind spot" (optic disk) as a means of addressing how far the diffuseness of the responses I obtained might be attributable to light scattering in the optic media. Had I been clinically trained in assessing visual fields I would never have been guilty of such an egregious oversight. However, Frances Ross Grimm and I (1962) were able largely to refute the scattered light argument by using direct, electrical stimulation of the retina. Widely distributed "late" responses could still be evoked, even ipsilaterally to stimulation of nasal retina; however, since activity continued in the optic tract for >100 msec after a 1-msec retinal stimulus, such elaboration could have been intraretinal. Subsequent sophisticated analysis, however, by Takuji Kasamatsu and colleagues (Kitano *et al.*, 1994) using an ingenious means of avoiding light scattering, confirmed the reality of these "nonretinotopic" effects, extending as much as 35° across the visual field.

## Visual System in Primates

In the transition to working on the visual system of macaques and squirrel monkeys, Doug Kimura and I (1963) demonstrated the remarkable series of oscillatory potentials, found as a common feature of recordings from the optic tract and, in primates, transmitted to the striate cortex, in response to diffuse flashes. In cats lower frequency oscillations were evident even at rest in darkness. Thus, complex circuits of the retina are rather strongly rhythmogenic, and similar properties of the cerebral cortex are now attracting wide attention as evidencing momentary coupling of neuronal ensembles. What, if anything, such oscillatory behavior at cortex owes to retinal initiation is a question yet to be asked.

We then went on, with Gordon Mogenson (Doty, *et al.*, 1964), to establish the conduction velocities and latencies, particularly for squirrel monkeys, and showed the severe depression wrought by anesthesia on cortical responses to visual input. Another interesting feature was the demonstration of a doubling of conduction velocity in passing from optic tract to optic radiation. One can reason that, in the eye, the small cell size plays to an advantage of mobility; however, once within the brain, size, and hence conduction velocity, is not subject to quite as much selective pressure.

We had noted how "attention" in the unanesthetized animal dramatically augmented the response in striate cortex to single pulses applied to the optic radiation. These modulations of geniculocortical excitability were both tonic and phasic. Using electrical pulses to optic tract and radiation (Bartlett, *et al.*, 1973) we then showed that during slow-wave sleep in macaques transmission through the lateral geniculate nucleus is almost "shut off" and correspondingly the response at the striate cortex (to stimulation of optic radiation) is greatly augmented. This change in state of striate cortex with sleep was even more dramatically demonstrated by Hisatoshi Sakakura (Sakakura and Doty, 1976). In the total absence of retinal input (i.e., blindness), in squirrel monkeys the EEG of striate cortex became isoelectric save for its punctuation by spikes signaling each saccadic eye movement. However, when the animal passed into the REM stage of sleep, the EEG assumed an essentially normal pattern! Perhaps this astonishing control of primary visual cortex in the total absence of visual input is truly the stuff of which dreams are made.

In an attempt to explore the possible basis of these remarkable modulations, I loaded striate cortex with horseradish peroxidase in several macaques to trace the available input paths (Doty, 1983). Even without counting input from immediately adjacent extrastriate cortex, which makes a rather substantial contribution, it could be seen that approximately 30% of the afferents to area striata arose from nongeniculate sources. Most intriguing were the large cells, probably mostly cholinergic, of the nucleus basalis at the level of the anterior commissure and optic chiasm, the cells of locus coeruleus, and the dorsal and median raphé. The latter two had the unique characteristic that a substantial proportion of them arose contralaterally, i.e., the input of these brain stem groups to striate cortex arose bilaterally.

Other studies showed strong, phasic control of transmission through the lateral geniculate nucleus from the mesencephalon (Bartlett, *et al.*, 1973), probably in association with saccadic eye movements (Bartlett, *et al.*, 1976).

Thus, the geniculocortical system in primates is under powerful control from brain stem systems expressing cholinergic, serotonergic, and adrenergic transmission, and its excitability is strongly affected by attention, eye movements, and various stages of sleep. These facts remain to be integrated into how this intricately organized net of neurons produces the miracles of vision (Doty, 1995).

There were two last bits in the puzzle: John Bartlett discovered that many neurons in striate cortex of alert squirrel monkeys and macaques respond steadily, merely to the presence of diffuse illumination or its opposite, darkness. He named these "luxotonic" units and their two types as "photergic" and "scotergic." The luxotonic signal can be found in roughly one-fourth of the units in striate cortex (Kayama, *et al.*, 1979), units that otherwise display a wide range of properties. We reason that this signal provides something of a "veridical" baseline of ambient illumination to provide scaling for the intensity of phasic inputs, otherwise uninterpretable as to strength in the absence of a level to which they can be compared. As something of a corollary to this finding of the photergic system, Sandy Bolanowski and I (1987) showed, contrary to the idea that stabilized retinal images disappear, that in viewing a binocular Ganzfeld (uniform, featureless illumination) the sensation endures indefinitely. On the other hand, if the Ganzfeld is viewed only with one eye, just as with the monocularly stabilized images, sensation lapses within approximately 15 sec. Thus, the condition for disappearance, with either the Ganzfeld or the stabilized images, is monocular viewing; evidencing a strong rivalry such that steady input from one eye is suppressed by the other. Binocular photergic input, however, can sustain sensation. Rozhkova, Nickolayev, and Shchadrin (1982) from Yarbus' laboratory similarly showed that stabilized retinal images remain visible as long as they are also binocular.

## Electrical Excitation of Cortex as a Conditional Stimulus

As noted previously, Les Rutledge and I began these experiments with a technical disaster so that when we did publish our authentic results (Doty, *et al.*, 1956), we held forth at length about the need for careful controls. This annoyed our most important predecessor, Roger Loucks, who in Horsley Gantt's laboratory at Johns Hopkins had pioneered the technique. He believed that we were questioning the validity of his findings. I had no doubt, however, that our inspiration derived primarily from Loucks, so I was wholly unprepared when Ralph Gerard congratulated us for doing the experiments "that we had all talked about"! I haven't the slightest recollection of any such discussion, but I am equally convinced that Ralph did not imagine it. The answer is probably that in Gerard's weekly meetings from 1948 to 1950, Wendell Krieg's proposal had been discussed that an array of stimulating electrodes on striate cortex could provide a modicum of vision for the blind. I may never have been present at such discussions, but neither would I be the first failing to remember the true source of a good idea.

Later, at Rochester, John Bartlett and I were to pursue Krieg's theme for many years, delineating measures to avoid deleterious effects from protracted stimulation and demonstrating that macaques could reliably detect microstimulation of as little as 2–4 μA in layers V and VI of striate cortex (Bartlett and Doty, 1980; Doty and Bartlett, 1981). There are two other highlights from this work with electrical stimulation: the Kupalov "shortened conditional reflex" and the unilateral engram. Both have a bit of a story.

I had read a German abstract of the work of Cornel Giurgea in which he paired conditional and unconditional stimuli by applying them directly to the cerebral cortex to form conditional reflexes. This suggested that by this technique one should theoretically be able to effect relatively permanent, functional connections between any two cortical loci, a thesis that I held to be dubious. Giurgea had done this work in Pavlov's famous "tower of silence" in Leningrad with one of Pavlov's most brilliant students, Pyotr Kupalov, and then had returned to his native Bucharest. Kupalov's idea was that perhaps most conditional reflexes naturally arose not from pairing of peripheral stimuli but from stimuli within the brain; hence, they were "shortened." Giurgea and I met in Brussels at a Neurological Congress, and we were subsequently able to work together for 3 months in Michigan. There, his thesis was fully substantiated (Doty and Giurgea, 1961). In dogs and macaques we applied electrical excitation to a cortical area that initially had little or no effect upon the animal. We then selected a unique movement, or combination of movements, elicited by electrical excitation of a "motor" area. A daily series of 6–10 pairings was then begun, preceding the motor excitation (as unconditional stimulus; US) by a couple of seconds of excitation applied to the "ineffective" area (as conditional stimulus; CS). After several days the CS elicited responses often remarkably similar to those elicited by the US. Subsequent examination, by pairing either stimulus with the animal's pressing of a lever, showed that the animals were quite indifferent to the stimulation, thus demonstrating the absence of a "motivational factor" in establishing these conditional connections.

The communist government of Rumania subsequently sold (!) Giurgea and his family to the West. He settled in Belgium and became the discoverer of the behavioral effects of a new class of drugs (e.g., piracetam), that he named "nootropic."

The other highlight was equally international. Nubio Negrão had come from São Paulo to work with me to stimulate neocortex in macaques. Consequent to this Brazilian connection I became the proud recipient of a lecture tour there, and one of my side trips took me to Manaus, far up the Amazon. Traversing a boardwalk along the river, my attention was directed more to preserving my Hasselblad[2] from the Amazonian flood than to seeing where I was going. I thus had the good luck to impale my forehead on a house decoration. Being stitched up at the local hospital that evening, it dawned on me that this minor surgery, producing little excitement in myself, should be similarly benign for our macaques. Thus, when I returned, we set things up so that the forebrain commissures were all cut save for the splenium, about which I passed a ligature and closed the incision. We then trained the animals to respond to electrical excitation of striate cortex in one hemisphere and tested the other side. The animals unhesitantly responded to excitation of the new locus in the other hemisphere, i.e., the "engram" was accessible. That the access proceeded via the splenium was then confirmed using the trick of local anesthesia I had learned in Manaus. The ensnaring ligature was retrieved and pulled, severing the 10+ million fibers of the splenium and causing the animals to blink once at that instant. Stimulation of the "untrained" hemisphere was henceforth without effect, while stimulation on the original side continued to give unaltered conditional responses, even to stimulation at "new," previously untested loci in ipsilateral striate cortex (Doty, *et al.*, 1973). Thus, we advanced the hypothesis that one feature of the corpus callosum was to ensure that memory traces were formed unilaterally, avoiding redundancy, and thus doubling the mnemonic storage capacity of the brain (Doty and Negrão, 1973).

## The Split Brain and Memory

This shift to interest in interhemispheric transfer, as per the foregoing, was more fully pursued once I had learned, from Jack Downer, how to perform the demanding transphenoidal cutting of the optic chiasm in macaques. I had learned the approach on cats from Roger Sperry's lab and had used it in some of our work on the visual system; however, the chiasm seemed completely out of reach via that route in macaques. The dorsal approach, while possible, held considerable hazard of compromising the preoptic area as well as the anterior commissure. Downer not only had discovered otological burs, which could reach the distance, but also had figured out how to get through the extremely bloody bone that lay in the way to the sphenoid. During a brief stay I had in London, he carefully schooled me in surmounting these difficulties.

Prior work had studied the capabilities of the forebrain commissures to interhemispheric transfer of stimulus discriminations, usually learned

[2] The Hasselblad is a very expensive and versatile camera, the kind used by the astronauts to take pictures from space—an association particularly relevant here since my "accident" occurred on July 20, 1969, the day of the moon landing, to which we listened as we navigated the Amazon.

over a period of several days. Now, using normal visual stimuli (i.e., not electrical excitation), we extended the paradigm to show that, in macaques, either of the forebrain commissures supported moment-to-moment transfer of visual information from one to the other hemisphere, in different tasks and with different types of material (Doty, *et al.*, 1988). Lewine, in his doctoral thesis, then took the demonstration a step further, using the Sternberg task to illustrate how the commissures unify mnemonic information in the two hemispheres (Lewine, *et al.*, 1994). For distinguishing remembered from novel stimuli, Sternberg had found that reaction time increased linearly depending on the number of to-be-remembered stimuli. Lewine's trick was to put some stimuli into one hemisphere and some into the other. Regardless of how the stimuli were distributed interhemispherically in our macaques, the Sternberg function held, even when only the splenium or the anterior commissure provided the surviving interhemispheric connections.

A fascinating ancillary observation was made when the hemispheres were separated by total section of the forebrain commissures. As expected, each hemisphere then gave a reaction time corresponding only to the stimuli that it had been given to remember; however, remarkably, the ***accuracy*** of the response from either hemisphere alone reflected the ***total*** of the number of target stimuli held by the two hemispheres together (Lewine et al., 1994). Thus, there must be some limited, presumably brain stem, resource that the two separated hemispheres are required to share in this mnemonic task, and it is not reflected in the reaction time, which remains hemisphere specific.

Voyko Kavcic *et al.*, (2000) have since gone on to explore more fully the nature of the hemispheric interchange possible in the absence of the forebrain commissures. Again, there was a surprising indication of subcortical participation in the memory trace(s) established in fully split-brain macaques, i.e., with animals incapable of recognizing with one hemisphere items seen by the other. The animals were required to report whether a colored visual pattern was being seen for the first time (new) in the test session or had been seen previously (old) in that session. Interleaved with trials in which the new and old items were matched in single presentations to one or the other eye/hemisphere were trials in which new items were presented to ***both*** hemispheres simultaneously. The subsequent, old (matching) stimulus was then presented ***to only one*** hemisphere to determine whether both of the isolated hemispheres had been capable of forming an engram of the simultaneously presented item(s), i.e., parallel processing. In 9 of 12 different comparisons across two animals, there was a significant diminution in subsequent recognition by either hemisphere alone for old items that had been viewed simultaneously by the two hemispheres as new compared with trials in which the items had been presented only to a single hemisphere on each occasion. The effect was particularly striking when the two hemispheres simultaneously viewed ***entirely different*** images compared with their viewing the same image. This effect of presenting ***different*** images to the two hemispheres also added greatly to the confusion that ensued when trials were inserted in which the hemispheres were provided with conflicting information, one hemisphere viewing a new item and the other an old item.

Lacking ***inter***hemispheric recognition mnemonic performance was thus nevertheless impaired for either hemisphere when each had simultaneously viewed ***different*** items compared with simultaneously viewing the ***same item***. We reason that the two hemispheres communicate with some subcortical process that endeavors to unify the inputs concurrently received from the two eyes. Failure of such unification, perhaps related to but anatomically entirely distinct from binocular rivalry, produces some degree of confusion. "Unification," if such it is, presumably proceeds directly (e.g., via retinocollicular paths), indirectly via cortico subcortical projections, or both (Kavcic *et al.*, 2000). Indeed, such subcortical unification, to produce a conscious percept, has been demonstrated in a human patient (Marcel, 1998). The critical portion of an illusory image was presented in the visual field lacking projection to striate cortex, yet this subcortical component induced the sensation of the full image.

In all of this work with interhemispheric mnemonic transfer, any indication of hemispheric differences in our macaques was essentially absent (Doty *et al.*, 1988; Lewine *et al.*, 1994). However, following the lead of Vermeire, Hamilton, and Erdmann (1998), after extensive training and a long postoperative period we succeeded in demonstrating a consistently better performance of the right hemisphere for remembering macaque faces (Doty, *et al.*, 1999). It was surprising that after an hiatus of 7 months in one animal this functional asymmetry of the hemispheres was completely reversed. The factors responsible for either the initial hemispheric asymmetry in facial recognition or its subsequent reversal remain entirely unknown. We suspect, however, that the answer is related to the still inadequately explored rivalry between the hemispheres, as to which will assume control for any given behavior, i.e., the expression of "metacontrol" (Levy and Trevarthen, 1976).

Ringo, *et al.*, (1994) proposed that because of the longer pathway across the commissures as compared to intracortical projections, sharing of processing by crossed interactions between the two hemispheres will take significantly longer than if the processing is confined to one hemisphere. Such limitation will promote specialization of each hemisphere as being more efficient than would redundant intrahemispheric calculations by each hemisphere for every type of stimulus. The pressure becomes greater the larger the brain (i.e., longer conduction distances), and since increasing the size of commissural fibers to gain conduction velocity would increase brain size (Ringo, 1991) there is no simple solution to the temporal cost. Güntürkün (1993) made a similar proposal and pointed out that even in smaller brains (e.g., birds), the complexity of processing may still make intrahemispheric specialization more advantageous than engaging both hemispheres in the calculations. Again, it remains undefined as to how the issue is decided between the hemispheres in relation to metacontrol.

## Time Course of Establishing a Memory Trace

Ray Kesner and I made an interesting, and still unexploited, discovery on the "consolidation" of memory traces. First, using highly palatable food, we trained cats to eat repeatedly and unhesitantly from a metal dish while standing on a copper floor. Once thoroughly accommodated to this routine, the animals one day received a strong electrical shock from the metal dish. Following such an experience none of the animals would ever return voluntarily to the feeding chamber. If, however, within 4 sec of receiving the first mouth-shock they experienced an electroconvulsive seizure, triggered by current applied bilaterally to electrodes over ectosylvian or postcruciate gyri, on the following days they continued eating as though nothing had happened (Kesner and Doty, 1968). Thus, the seizure seemingly had "erased" all memory of the experience. The seizure per se (i.e., unaccompanied by the mouth shock), was without effect. Remarkably, however, if on subsequent days the animals had a second experience with the mouth shock followed within 4 sec by a second seizure, full retention of the aversive experience was established (i.e., they henceforth refused to enter the feeding chamber) (Kesner *et al.*, 1970). In other words, an incipient trace must actually have survived the first seizure and was available for consolidation with the second experience ***despite the second seizure***; that is, ***two*** experiences ***a day or more apart*** could be amalgamated into an effective trace even though each had only 4 sec to act before disruption by the seizure activity. On day 1 up to 6 min could transpire between receipt of the mouth shock and onset of the seizure, and yet there was no evidence of "consolidation" on the following day (i.e., the seizure still produced amnesia). However, if the delay was 15 min, the aversive experience was remembered. Thus, even when 6 min are available for registering the aversive experience, whatever trace there is remains ineffective following a seizure. However, only a 4-sec interval is enough for a trace to be formed that can sum with a second, similarly induced trace, also allowed to form for 4 sec, with the two together yielding a permanent and highly effective record of the event. This would seem to suggest that the first few seconds in trace formation are far more effective than continued development since 6 min of unperturbed existence fails to withstand the disruption of the seizure.

## Schizophrenia

My results with retrograde transport from striate cortex (Doty, 1983), noted previously, and its revelation of the bilaterality of pontomesencephalic projections to neocortex got me to thinking about schizophrenia (Doty, 1989). The very name of this affliction suggests perturbation of the manner in which the two cerebral hemispheres interact, as they must, to produce the unity of conscious experience. Since each alone, as shown by hemispherectomy and split-brain patients, is capable of individual consciousness, there needs normally be some fundamental interchange to preclude their pathological duality. Failure of that mechanism could well produce the confusion as to origin of thoughts so characteristic of this multifarious disease.

One clearly should not expect the situation to be simple. My point of entry was the bilaterality expressed in the putative serotonergic projection (dorsal raphé) I had found to neocortex (Doty, 1989). This thought was soon dramatically expanded by the findings of Mohammed *et al.* (1991). They demonstrated that a droplet of stomatitis virus (an RNA virus) nasally administered to neonatal rats produced a drastic reduction in adult levels of cortical serotonin, loss of two-thirds of the neurons in dorsal and median raphé, and deficiency in learning the Morris water maze. This is not the place to review the 100 references I have now accumulated to support the thesis (Doty, 2000), but the outline is relatively straightforward. That is, schizophrenia is a consequence of an agent, or agents (most likely viral, for which there is extensive if not conclusive evidence), that enters via the olfactory epithelium, either *in utero* or subsequently, and, as is well established for a number of neurotropic viruses, is retrogradely transported to the olfactory bulbs and thence to brain stem modulatory systems. The extraordinary genetic diversity of the olfactory receptors fits comfortably with the genetic predilection found for schizophrenia. The modulatory, brain stem systems, as widely shown by psychopharmacology, are intimately related to schizophrenia as well as to "attention." Also, their perturbation, asymmetrical or otherwise, is fundamental to the pathology. This explanation of the illness falters at elucidating the 30% remission rate (although possibly supported thereby in cases of nonuterine etiology). Also, if the etiology includes events *in utero*, why the ***seeming*** latency to adolesence (when the corpus callosum finally reaches its mature condition)? Such shortcomings, unfortunately, are shared by all efforts to understand this devastating illness.

## Miscellany

I have benefitted greatly from the more than 50 graduate students and postdoctoral fellows with whom I have shared my laboratory throughout the years. They have had free rein to choose and do projects of their liking. However, since in essentially every case the endeavor was of mutual interest, I usually joined in the trials and triumphs. This habit, in part, accounts for much of the diversity of interests manifest previously; however, discussing the endeavors of each and all would strain the patience of publisher and reader alike, so I merely mention, with gratitude, some of those whose artful work otherwise goes here unnoted: Keith Bignall, Will DeHart, Neal Barmack, David Lee Robinson, Brian Lamishaw, John Fentress, Robert Glassman, Harvey Swadlow, William Overman, Alan Cowey of Oxford, Wanda Wyrwicka and Bogusław Żernicki of the Nencki Institute, Hector Brust-Carmona of Mexico, Boris Tolkunov of Sankt Petersburg, Tetsuro Ogawa from Akita, Vakhtang Mosidze from the Beritashvili Institute in Tbilisi, Bishnu Choudhury of Cardiff, and Tsai-Hsin Yin of Taipeh.

My poor but serviceable Russian prompted many connections with Eastern Europe (e.g., Giurgea!). For several years, particularly as editor of *Neuroscience Translations*, I endeavored to bring some of the best work of Russian neuroscientists to the attention of the Anglophone West. Elizabeth had entered school in Chicago embarrassed at speaking only Russian, Lithuanian, and Polish, but she became by far the more reliable critic of English usage in our family. She retained considerable comprehension of these languages as an adult, however, far beyond my book-learned capability, but she was inhibited in speech, being often uncertain as to which word belonged to which language. Her background served as stimulus for me to while away some of the many hours at sea, mastering Cyrillic orthography and struggling with a multitude of unfamiliar tenses. When subsequently touring in the Soviet Union, my imperfect Russian, plus my ever-present camera, set me up for recognition as a hated (East) German, and people would spit in derision, or deny us entrance to restaurants. Elizabeth, however, was taken for a native, even to the point, in Rostov na Donu, of being asked to do brief "baby-sitting" of children as their mothers shopped.

Probably my most interesting Russian paper is the one I submitted to the Festschrift for M. N. Livanov (Doty, 1970), playfully entitled *On Butterflies in the Brain*. This was taken from observations that Nubio Negrão and I made when applying stimulation for 4 sec just posterior to the lunate sulcus (probably area 18) in an alert macaque. The animal's eyes moved steadily downward, as though tracking something. A quick, capturing movement ensued with the contralateral hand, which was then slowly and carefully opened. The animal intently examined its opening first, clearly expecting to find a captured object therein. This startling sequence was evoked on each of several occasions of stimulation over a period of days but gradually weakened, perhaps consequent to the animal's persistent failure to capture the hallucinated object. The "butterfly" connection derived from Ottfrid Foerster's (1936) description of an essentially identical response elicited from an alert patient when stimulation was applied to occipital cortex. The patient reached out from the operating table to catch the butterfly that he had seen, surprised that the surgeon had not noted it. Such complex stereotypy, similar to the "hand to mouth with mouth opening" (Doty, 1976a), also elicitable by cortical stimuli and sometimes as components of epileptic seizures, provide further examples of neuronal ensembles dedicated to coordinated movement. However, we subsequently found the butterfly phenomenon to be elicited only in macaques in whom the forebrain commissures had been severed. Perhaps, in the intact animal, unilateral evocation of this "hallucination" is countermanded from the unstimulated side, which "fails to confirm" the existence of the moving object. On the other hand, for the patient at least, the phenomenon provides a dramatic example of how neuronal circuitry, regardless of how it is activated, is able to create creatures existent only in the mind.

An invitation from Julian Tobias to write a celebratory piece for Ralph Gerard's 65th birthday got me started in expressing my opinions on matters philosophical (Doty, 1965, 1976b, 1990, 1998). The main thesis has been decidedly materialistic—that brain alone provides the wherewithal of mind; and that society, afflicted with fantasies, dangerous in their certitude, comforting though they be, is in dire need of rationality. Lately, however, I have tempered this message by also recognizing the degree to which science, too, has become dogmatic in its certitude that consciousness can be explained—that free will is an illusion, constructed of neurophysiological imperatives, a robotic unfurling of the molecular past. There is, indeed, a deeply mysterious problem as to how neurons might intercede with other matter, to move it beyond the molecular mean free path that energy surely dictates. However, is it not equally "scientific" to observe one's own capacity in this regard? Every keystroke is a choice! Thus, I have joined my ever-insightful mentor, Roger Sperry, in calling for a bit more humility in neuroscience. We need have no fantasies, indeed counter them with fact; but neither should minds, scientific or otherwise that can only describe, not comprehend, the duality, virtual particles, entanglement, and nonlocality of quantum mechanics, blithely insist that the ineffable nature of that neuronal product, consciousness, is understood. We remain primitive of decisive insight, Neanderthals contemplating the mystery of the seasons; we are captives in Plato's famous cave, viewing shadows as reality.

One of the high points of my career came in 1976 when I was president for the meeting of the Society for Neuroscience in Montréal. Not only did I have the future laureates, David Hubel and Torsten Wiesel, as Grass Lecturers, but also I was able to indulge some of the thoughts previously discussed by having Roger Sperry and Benjamin Libet as part of my presidential symposium on consciousness. These two individuals exemplify in their ingenious work what, and how, neuroscience can contribute to clarifying the nature of our experimential being, as basically mysterious to us as to Alkmaeon and Hippocrates. Of course, I took the opportunity to make a few introductory remarks and held forth a bit on the experiment of a young, blind French girl. Unobserved, she dressed herself in her Sunday best and soon discovered that her attire could be instantly perceived without physical contact by whomever entered the room. Thus, there existed some arrangement of nature that was previously beyond her ken—as, I was endeavoring to illustrate, might also be true of some still hidden feature of consciousness vis-á-vis neurons.

My wife was in the audience during this oration, sitting next to someone who shall remain nameless but who, perhaps unlike my wife, was wearing her name tag. Unwittingly, the neighbor turned to my darling and vehemently expressed her impatience at the delay in starting the main event: "When is that old windbag going to shut up!?" My beloved, ever an astute critic of my attainments, though inwardly bemused, held her peace. Were she but able now to review the many pages offered here, the perception would no doubt be similar: It is time to stop.

In perusing this outline of two lives, I can but hope that you have experienced at least an atom of the wondrous fascination and delight that unfailingly enveloped those who lived them.

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