BIOGRAPHICAL MEMOIRS

Harvey J. Karten

July 13, 1935–July 15, 2024
Elected to the NAS, 2015

A Biographical Memoir by Anton Reiner and Thomas E. Finger

Harvey J. Karten was the preeminent comparative neuroscientist of this era. "Harvey," as friends, students, and colleagues alike knew him, was recognized for his landmark studies that fundamentally reshaped the understanding of brain organization and intelligence in birds and other non-mammalian vertebrates. Although his groundbreaking work in avian neuroscience stands as his most recognized achievement, his contributions to the field of systems neuroscience were far-reaching, including seminal findings on the visual, auditory, trigeminal, and viscerosensory modalities, as well as on the organization and evolution of the basal ganglia. The impact of his work was acknowledged at the highest levels, earning Harvey election to the American Academy of Arts and Sciences in 2008 and to the National Academy of Sciences in 2015.

Figure 1 Harvey J. Karten, 2013. *Used with permission of Fernando García-Moreno.*

Harvey was born on July 13, 1935, in the Bronx, New York City, and his earliest years were spent on the Grand Concourse in a neighborhood of European Jewish immigrants. His parents, Ernest Karten and Esther Wacks Karten, had separately immigrated to the United States in the mid-1920s from a small town called Molodechno, Galicia, then part of Poland. They married in New York City and settled in the Bronx, where daughter Deborah was born in 1929. Soon after Harvey was born, the family moved to Jersey City, New Jersey, and Ernest became the shopkeeper of a candy store there and later in nearby Bayonne. When Harvey reached school age, he attended and boarded at the Rabbi Jacob Joseph School, an elite private Jewish school (yeshiva) on the Lower East Side of Manhattan, where students studied a rigorous Talmudic curriculum. Although it was a financial strain to send Harvey to a private school, the family wanted to provide him with an opportunity to succeed in America, and they saw education as the path to that goal. For high school, Harvey attended, as a boarder, Yeshiva University's Preparatory School for Boys, also known as the Manhattan Talmudical Academy (MTA), located in Washington Heights in northern Manhattan. The MTA, a renowned orthodox Jewish private school, combined religious instruction with excellent education in science and mathematics. Many years later, Harvey noted that one of the teachers, Samuel Greitzer, changed his life by introducing him to the rigors and wonders of mathematics. Greitzer went on to a notable career in academia as the founding chairman of the committee running the United States of America Mathematical Olympiad. Living in Manhattan, Harvey often went to the American Museum of Natural History, where he was especially drawn to the bird exhibits. He also dabbled in electronics and read avidly any unsold *Science Illustrated* magazines that his mother brought him from the family candy store. He additionally developed an interest in classical music by listening to the Metropolitan Opera Saturday Matinee radio broadcast and eventually learned to read music and play the flute. Notably, Harvey spent summer breaks at Camp Mechaneh, an overnight camp in the Catskills where he discovered a love of the great outdoors.

After graduating from MTA in 1951, Harvey attended Yeshiva University, a private Orthodox Jewish university in New York City. He graduated with a bachelor of arts in chemistry in 1955 and was admitted to the inaugural class of the Albert Einstein College of Medicine in the Bronx. Although Harvey had considered graduate school in chemistry, he felt the weight of family obligations and believed that becoming a physician seemed a better way to fulfill them. After completing medical school in 1959, Harvey interned for one year in psychiatry at hospitals affiliated with the University of Utah in Salt Lake City, and in 1960 began what was intended to be a two-year residency in psychiatry at the Colorado Psychopathic Hospital of the University of Colorado in Denver. Harvey soon became convinced that he was a poor fit for psychiatry, so during his first year, he applied for and was awarded a Public Health Service training grant in psychiatry from the National Institutes of Health (NIH) to do an eighteen-month research stint at the Walter Reed Army Institute of Research in Washington, D.C. Although Harvey was expected to return to finish his residency, the allure of neuroscience and his emergent talent for it led him to abandon clinical psychiatry. His first day at Walter Reed, Harvey was given a microscope and slides of cat brain sections to examine; he was transfixed by the beauty of the brain. Harvey was to remain there until 1965, making discoveries during that four-year period that began to establish his scientific legacy.

At Walter Reed, Harvey trained with the famed neuroanatomist Walle J. H. Nauta, who had developed the Nauta-Gygax silver-stain method for visualizing degenerating axons, thereby facilitating tracing of connections within the brain. This method was a major breakthrough because it enabled researchers to determine the wiring of the brain, essential for understanding function. Nauta advised Harvey to use the Nauta-Gygax method to develop his own research program. Driven by his interest in brain evolution, Harvey chose to study brain organization in pigeons. This relatively unspecialized avian species was an ideal choice, given how extensively it had already been studied behaviorally by Burrhus "B. F." Skinner and others. Because the Nauta-Gygax technique required accurate placement of electrodes for recording or for making lesions in the brain, one of his first tasks was to create a stereotaxic atlas of the pigeon brain. Together with Bill Hodos, a young colleague with expertise in behavioral analysis, Harvey set about doing so. This endeavor required developing both a high-quality and stable head-holder as well as a high-resolution imaging system to allow adequate documentation of the cell groups in a relatively small brain. In keeping with his lifelong pursuit of high-quality imaging, Harvey used a six-foot-long horizontal optical bench system from Bausch & Lomb that allowed for flat-field magnification factors of 12x to 25x across an entire pigeon brain section while maintaining a physical resolution roughly equivalent to 100 megapixels in today's terms.

With this tool in hand, Harvey and Bill, together with electrophysiologist Alan Revzin, set about studying the visual system in pigeons. They found that the optic tectum had a major projection to a prominent round nucleus in the thalamus aptly called nucleus rotundus, and that nucleus rotundus projected to a circumscribed nucleus in the telencephalon, then called the ectostriatum (subsequently renamed entopallium). Using behavioral approaches, Bill and Harvey further showed that damage to either rotundus or the ectostriatum impaired visual ability.

During this time, Harvey also traced auditory pathways, finding an ascending projection from the auditory midbrain (the inferior colliculus) that ends in a circumscribed rounded thalamic nucleus called ovoidalis, which projected in turn to a crescent-shaped field in the telencephalon called Field L. Their discoveries posed a problem, however, for what was then the conventional understanding of avian brain organization. Both the visual target in the ectostriatum and the auditory target in Field L are parts of a larger telencephalic area then named the neostriatum (now called the nidopallium; see Figure 2). Lying above the neostriatum is another field then named the hyperstriatum ventrale (now called the mesopallium), and lying above that is a series of additional zones (with hyperstriatum in their name at that time) collectively called the Wulst. Because they are constituents of a large dorsal territory that bulges into the lateral ventricle, the hyperstriatum ventrale and neostriatum together are referred to as the dorsal ventricular ridge (DVR). The canonical interpretation at that time was that the avian and mammalian telencephalons were fundamentally different.[1] In particular, whereas the mammalian telencephalon was known to consist of a nonlaminated core region termed the basal ganglia (that is, the striatum and pallidum), with an overlying laminated region called the neocortex, the non-laminated avian telencephalon was considered to consist almost exclusively of a greatly enlarged basal ganglia—giving rise to the root suffix

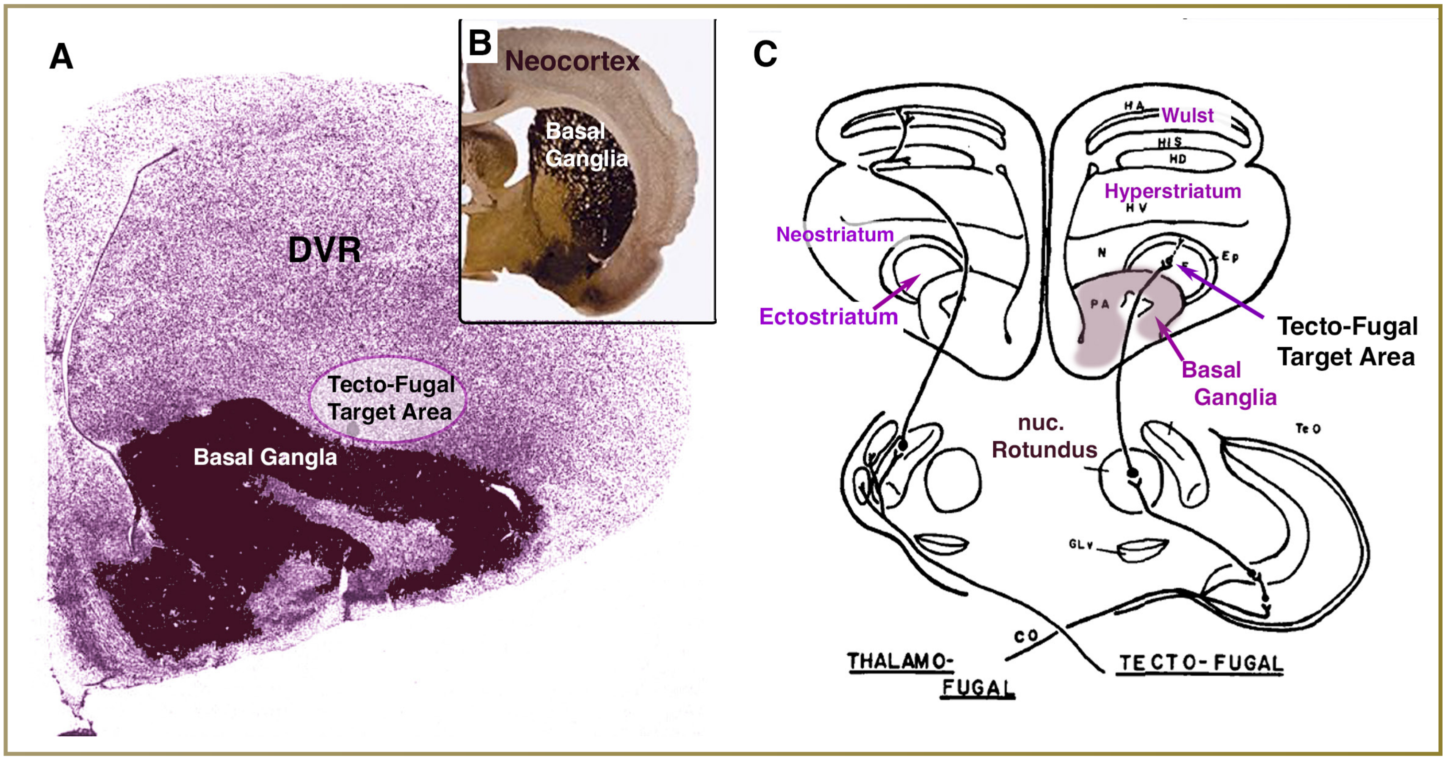

Figure 2 Composite figures adapted from the works of H. J. Karten. A Cholinesterase-stained section from the brain of a pigeon showing high activity (black) in the limited part of the forebrain equivalent to mammalian caudoputamen, part of the basal ganglia. Image colorized and adapted from (Karten 1969). B Insert of a rodent brain stained for cholinesterase. As in the pigeon, the basal ganglia sit deep to a relatively unstained cortex. *Image used with permission from Neuroscience Associates.* C Adapted image (Karten 1969) showing the dual visual pathways targeting the forebrain in a pigeon. Both the thalamo-fugal and tecto-fugal pathways target discrete portions of the forebrain, which relay in turn to overlying regions. *Figs A & C reproduced with permission from the New York Academy of Sciences.*

-striatum in many telencephalic regional names in birds at that time. This neuroanatomical interpretation was in concordance with the prevalent view that mammals exhibit flexible intelligent behavior, whereas birds exhibit only stereotyped behavior. The mammalian neocortex was considered necessary for intelligent behavior, and the basal ganglia served as the seat of stereotyped, behavioral routines. Harvey and Bill recognized that ectostriatum and Field L were anatomically similar to regions of neocortex in that they received specific visual and auditory thalamic inputs comparable to those to the visual and auditory cortices in mammals. When Harvey applied histochemical staining methods to pigeon telencephalon, he further found that only a ventral territory below the DVR had the characteristic staining pattern of the basal ganglia in mammals. Harvey concluded that the avian basal ganglia was this ventral territory and occupied no greater proportion of the telencephalon than it did in mammals. Harvey further concluded that the DVR lying above the avian basal ganglia, along with its overlying Wulst, were akin to mammalian neocortex in connectivity, function, and neurochemistry.

In 1964, Nauta became a professor of neuroanatomy in the Department of Psychology at the Massachusetts Institute of Technology (MIT). Harvey joined Nauta there a year later, as did Lennart Heimer, who developed the Fink-Heimer method, a modification of the Nauta technique that improved staining of degenerating terminals. Nauta, Harvey, and Heimer occupied contiguous lab space, and this formidable trio were among the foremost neuroanatomists in the world. The studies that Harvey started in the early 1960s took years to complete. For example, the pigeon brain atlas completed at Walter Reed was not published until 1967. In the years following the move to MIT, Harvey produced a series of papers describing his findings on the sensory pathways in the brain of the pigeon, detailing seminal discoveries related to a new conceptualization on the organization of the telencephalon of non-mammalian vertebrates. At that time, the orthodox view was that the six-layered neocortex was a mammalian invention that had accreted onto the pre-existing, primitive, non-laminated basal ganglia-like DVR present in reptilian ancestors. By the late 1960s, Harvey recognized that the DVR contained subregions organized into separate nuclear groups that were akin to the layers of neocortex and that had interconnections similar to those interconnecting the layers of cortex. For example, Field L was like the fourth layer of primary auditory cortex, in that they both receive auditory thalamic input. Field L then projected to nearby DVR regions akin to the second and third layers of primary auditory cortex; these in turn projected to a region like the fifth and sixth layers of cortex. Thus, the essential circuitry and processing capabilities of neocortex were present within the avian forebrain, but, unlike neocortex, this area in the avian telencephalon was not organized into overt layers.

This discovery upended the traditional view that the lateral wall of the ancestral forebrain mainly consisted of basal ganglia, with mammals adding a neocortex during their evolution. In recognition of this work, Harvey received the 1968 C. J. Herrick Award in Neuroanatomy from the American Association of Anatomists as the outstanding young comparative neuroanatomist of that year. In 1969, Harvey published a paper in the *Annals of the New York Academy of Sciences* in which he presented his evidence that DVR and Wulst in birds contain the same neuron types and patterns of connectivity as mammalian neocortex, despite being organized in birds into separate nuclei rather than into separate layers.[2,3] This conclusion shifted the paradigm on the organization and function of the avian telencephalon and set the stage for a large body of subsequent work further detailing comparisons between avian DVR and Wulst on one hand and neocortex on the other. These crucial insights spurred investigations into the cognitive abilities of birds, which we now know to rival those of mammals. The six-layered organization of mammalian neocortex was proven unnecessary for computational capabilities as long as the underlying connectivity and computational units were present. In 2002, in recognition of Harvey's insights into the nature of these non-laminated but cortex-like nuclei in the brains of birds, the Avian Brain Nomenclature Forum, organized by Anton Reiner and Erich D. Jarvis, generated a new nomenclature for avian forebrain structures, often replacing the root term *-striatum* in instances when *-striatum* had been misapplied; for example, *hyperstriatum* became *hyperpallium*.[4]

Harvey's broad interests in nature and many professional friendships led him to undertake diverse projects outside of his main focus on birds. For example, his first two graduate students at MIT, Len Maler and Tom Finger, studied the brains in teleost fishes. Despite this shift of vertebrate clade, Harvey was immensely supportive of each. Len had started out with a bird project but then became intrigued by a lecture by Michael V. L. Bennet in which he described the active electrosense of the elephant-nosed mormyrid fish, *Gnathonemus petersii*. Once the new project Len envisioned was described to Harvey, along with the requisite images of the huge cerebellum (proportionately the largest of any vertebrate!) and beautifully layered lateral line lobe, Harvey was all in. In fact, he became so enthusiastic about electric fish that he arranged to take Len and Tom on his six-month sabbatical with Theodore H. Bullock at the Scripps Institute of Oceanography in San Diego in 1972.

After nine years at MIT, Harvey moved to the State University of New York (SUNY) at Stony Brook (which was in the process of investing in their neuroscience program) in 1974. Harvey had made a name for himself by then, and a stream of graduate students and postdoctoral fellows joined his lab. A second, long-term major research interest of Harvey's was visual processing, and it became a focus during his Stony Brook years. Harvey had found a visual system pathway in pigeons and owls like the geniculostriate system in mammals, targeting dorsal thalamus and, ultimately, the visual Wulst, an area comparable to the primary visual cortex (see Figure 2). Following up on this at Stony Brook, Harvey noted a multiplicity of retinal targets within the diencephalon and midbrain, leading to a series of papers describing the then little known basal optic nuclei and their role in directing eye movement. These seminal studies revealed a unique subset of retinal ganglion cells—displaced ganglion cells—that projected uniquely to basal optic nuclei and that were presynaptic to cerebellar areas involved in gaze stabilization. These studies led Harvey to the retina, one of his favorite laminated structures. His adoption of the relatively new immunocytochemical techniques then allowed for rigorous anatomical dissection of numerous retinal subcircuits and cell types. These studies on visual systems carried an undercurrent in Harvey's work—a fascination with laminated structures of the brain.

Continuing with his challenge to orthodoxy that was evident in his work on avian forebrain, Harvey's work with Phil Zeigler on trigeminal pathways and feeding behavior in pigeons led to uncovering a fallacy in the then-current formulation of the "lateral hypothalamic syndrome." This phenomenon, which appeared following large lesions of the lateral hypothalamus, included a component of ipsilateral orosensory neglect that resulted in dysphagia, adipsia, and weight loss. Phil and Harvey noticed that lesions of the central trigeminal nuclei and their pathways in pigeons recapitulated the orosensory neglect, adipsia, and aphagia of the lateral hypothalamic syndrome. They subsequently showed that similar deficits occur with lesions of the trigeminal pathways conveying orosensory information toward the forebrain in rats.[5] Harvey's interest in orosensory systems continued throughout his publishing career, including a series of studies in rodents undertaken with David Kleinfeld during Harvey's years in "retirement."

During his time at SUNY, Harvey spent 1979-80 as a visiting scientist at the Salk Institute in La Jolla, California, and this trip convinced him that he yearned to live and work in the San Diego area. Thus, he was very pleased to be recruited to the Department of Neurosciences at the University of California at San Diego (UCSD) and moved there with a number of lab members in 1986. Much of his research at UCSD continued to focus on retinal organization and neurochemistry, but the lab also worked on aspects of avian brain organization that harkened back to his research at Walter Reed and MIT. With Toru Shimizu, Harvey wrote several papers expanding on his earlier ideas on neocortex evolution vis-à-vis avian brain organization.[6] Work with Harald Luksch revealed that circuits of the visual midbrain involved in visual tracking were similar in birds and mammals in terms of both connectivity and cellular architecture. Shortly after a festschrift honoring him and Bill Hodos in 2004, Harvey officially retired but maintained an active research presence at UCSD.

Throughout his life, Harvey was an avid outdoorsman, enjoying skiing, hiking, and sailing. In his UCSD years, he went hiking in the Sierra Nevada and Cascade Mountains on a regular basis. Moreover, Harvey purchased a thirty-seven-foot sailboat, a Tayana 37, that he named the *Night Heron*. In his retirement years, Harvey also combined his passion for photography and birds and took his digital mirrorless camera to the nearby marshes to photograph his beloved birds. His photos were striking in composition and detail and typified his approach to photography, whether it be scientific or personal. Harvey continued sailing his cherished *Night Heron* into his eighty-eighth year, but he finally had to sell it because his Parkinson's disease had progressed to the point that he could no longer handle the boat. During his last years, Harvey took satisfaction that the pejorative "birdbrain" had faded from everyday speech, in part a result of the accretion of evidence that many types of birds, such as parrots and crows, possess a behavioral repertoire and complex brain structure rivaling primates. Harvey remained vital and mentally alert until his stroke. He died on July 15 of 2024, two days after his eighty-ninth birthday. He lived a full life that engaged his abilities and passions, and he enriched science by his research, and all who knew him by the person he was.

Note

This memorial tribute is an expansion of two prior memorial tributes to Harvey J. Karten published as obituaries in the *Journal of Comparative Neurology* and *Current Biology*.[7,8]

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