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Obituary

Patricia Goldman-Rakic, 1937–2003

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When Patricia Goldman-Rakic died on July 31 at the age of 66, she was at the zenith of her career as a world-renowned neuroscientist, whose ground breaking discoveries about the frontal cortex of the brain helped scientists to probe into the neurobiological basis of normal behavior and such complex disorders as schizophrenia and Alzheimer's disease. She died of injuries sustained after being struck by a car as she was crossing a heavily trafficked street in Hamden, near her New Haven, Connecticut home. While she did not go gentle into that good night, we, in the scientific community, her friends, and colleagues, alternately rage, and grieve, and remain in stunned disbelief that this vibrant and brilliant woman was taken from us by a freak accident that revealed the cruel menace of impartial chance.

Trained as a psychologist, she became one of the most innovative and sophisticated neuroscientists in the modern era of brain explorations. A principal thrust of her work probed the structure and function of the brain's frontal lobes, once regarded as inaccessible to rigorous scientific analysis. She was the first to discover and describe the delicate order of this brain region, which is implicated in high level cognitive functioning. At the time of her death, she held appointments as Professor in the Departments of Neurobiology, Psychiatry, Neurology, and Psychology at Yale. For over three decades, she had worked closely with her husband, Pasko Rakic on major issues in neuroscience.

Paul Greengard, Professor at Rockefeller University and Nobel Laureate in Physiology and Medicine, said, 'Patricia Goldman-Rakic raised the quality of multidisciplinary brain research to a new level. She utilized biochemical, electrophysiological, pharmacological, anatomical, and behavioral techniques to elucidate much of what we know about memory, behavior, and the actions of antipsychotic drugs.'

Dr Herbert Pardes, President and CEO of New York Presbyterian Hospital and former Dean of Columbia University College of Physicians and Surgeons, said, 'Pat Goldman-Rakic was one of the most outstanding neuroscientists. She linked important issues in behavior and clinical psychiatry to basic science. She was truly a pioneer and a leader of our time,'

'The world of neuroscience has lost a formidable ally in the search for a deeper understanding of the human brain. Not only was she a dedicated and brilliant researcher, she was also a great and beloved mentor to many junior researchers. Her discoveries and insights into brain function have forever changed our understanding of the mind and brain,' commented Susan Hockfield, Provost of Yale University.

Richard C Levin, the President of Yale, said, 'Pat Goldman-Rakic was one of the most distinguished neuroscientists of her generation. We grieve at her tragic loss in the knowledge that her important contributions will live on.'

In her beginning studies, she found that the brain was rather fluid in its early development, that injuries could be compensated for, and later function could be spared from being lost, as they might have been if they had occurred later in life. The capacity of the nervous system to repair itself early in life impressed her, and stimulated an examination of ontogenetic development of cortical connections in nonhuman primates. She was one of the first to take advantage of new techniques such as radioactive tracers to follow the activity of cells. With the use of a variety of techniques, she became aware of many influences on brain development, including gender and age. She, of course, also discovered that regeneration and compensation for injury had limits.

In the course of her studies on developmental neuroanatomy, she rediscovered the delayed response task, which had been used early in the 20th century to study retention in lower primates and very young children. Pat saw that this method could provide a way to examine the biology of short-term retention. Show an animal a bit of food; then hide the food in one of two containers; for varying periods of time, prevent the animal from seeing the field where the food had been hidden. Now, represent the field and note whether the animal goes to the container in which the food

had been placed. Rhesus monkeys with lesions in the prefrontal cortex are impaired on this task, although they are quite able to find the food if their behavior is guided by what they are able to see, that is, they will find the food if they are not required to rely on their memory for where the food had been placed. Prior to Pat's studies, little was known about the prefrontal cortex, and received wisdom had it that this area of the brain was too complex to study. Rather, areas of the visual system, like the primary visual cortex, were more accessible to behavioral and anatomical study. Pat persisted, and found that the prefrontal cortex had a modular architecture just as was characteristic of other parts of the brain. One could, therefore, study the functioning of different parts of the frontal cortex.

It was in this way that, in the 1970s, at first in Haldor Rosvold's laboratory, and then in her own, Pat staked out a program of research into the nature of the prefrontal cortex, and discovered regional differences in the concentration of dopamine. In 1979, she published a landmark paper demonstrating the role of dopamine within the prefrontal cortex as a key modulator of the spatial delayed response task. She found that depletion of dopamine in the prefrontal cortex resulted in memory deficits similar to those produced by surgical lesions of this area. After her arrival at Yale, in 1979, Pat's laboratory began a daring program of research that continued her exploration of the prefrontal cortex's activity. She continued her behavioral research and pursued studies on the intrinsic anatomical and histochemical organization of the prefrontal cortex and its major afferent and efferent systems, including dopaminergic and other monoaminergic systems. Later in the 1990s, the use of single-cell recordings in monkeys to investigate the prefrontal activity during performance of the delayed response task came to the fore. In a series of papers, beginning in 1993, she and her colleagues showed that sustained activity of single prefrontal cortical neurons in alert monkeys served as a neuronal code for working memory. She and her colleagues were thus able to show that the prefrontal cortex had memory fields that could be mapped as modules and arrayed in columns. Pat conjectured that the activation of prefrontal cells in the absence of any concrete presence of a stimulus suggested that there was an active memory system in the prefrontal cortex. This idea was somewhat at cross-purposes with the prevailing view in neuroscience and in psychiatry that memory was a unitary process, with a single locus in the brain.

These basic studies, moreover, had a profound influence on our understanding of disease processes, and that influence was not lost on Pat. Parkinson's disease and schizophrenia both involve dynamics in dopamine-containing cells in the brain. Pat's lab showed that one could produce deficits in the performance of this delayed response task by depleting the prefrontal cortex of dopamine. Other investigators then showed that schizophrenic patients perform poorly on a spatial delayed response task. She approached these issues behaviorally, neurochemically, and anatomically.

It is noteworthy that in over three decades of research Patricia Goldman-Rakic kept a clear focus on specific phenomena, which she pursued with a fierce determination that permitted no deviation and distraction from the essential target of her scientific scrutiny. Her odyssey was not without obstacles, especially during the early years of her career. As a young woman making her way though an essentially man's world, she had to wait until 1975 before being promoted to the tenure track at the NIMH, which was 8 years after joining the intramural program.

Patricia Goldman-Rakic was born in Salem, Massachusetts on April 22, 1937 one of three sisters, all of whom obtained PhD's in science. Like many young woman of the time, she never expected to become a scientist. However, after graduating from Vassar College magna cum laude with a BA degree in science, she entered the PhD program in experimental psychology at UCLA. Somewhat later (1974), while she was visiting the neuroanatomist Walle Nauta at MIT, she met Pasko Rakic, then on the faculty of the Harvard Medical School. Eventually they married (1979), and she joined Pasko at Yale where he had become head of the newly created Section of Neurobiology. From that point on, their academic and scientific careers merged and they became a team in which great synergies emerged. For her work, Pat received many prestigious honors, among which are election to the National Academy of Sciences (1990), the American Academy of Arts and Sciences (1991), the Institute of Medicine of the National Academy of Sciences (1994), and the American Philosophical Society (1996). She was awarded the Lieber Prize of the National Association for Research in Schizophrenia and Depression (NARSAD) in 1991, France's Fyssen Prize in Neuroscience (1990), the Gold Medal for Distinguished Scientific Contributions from the American Psychological Association. Pat was also a member of the Scientific Council of NARSAD and a member of the ACNP since 1997. In 2000, she received an honorary degree from the University of Utrecht and only 2 months ago, received an honorary degree from St Andrew's University in Scotland.

It is true that Pat devoted an extraordinary amount of energy and passion to her work – her dream of understanding the intricacies of brain function and dysfunction. She believed not so much in herself, but in her ideas, her vision. Petite in stature and soft spoken, she was tenacious, incisively logical, and defended her positions with strength and conviction. It has been said that Pat was uncommonly multidisciplinary in her research. This may have stemmed, in part, from her youth. As a teenager, she took on many tasks and responsibilities, playing the piano for a local dance studio in the afternoons and moving on in the evenings to wait on tables at a local seafood restaurant. All this while studying piano, violin, and even mastering calligraphy.

Although assertive and strong minded in her scientific work, Pat was very feminine in her demeanor and gentle in her human relationships. She was a loving and devoted daughter, sister and wife providing unconditional love and affection not only to her family, but also to those with whom she formed academic, collegial, and domestic relationships. Pat brought an artistic flair not only to her work, but also to her private life – adorning her home with beautiful objects of art and creating culinary delights in her kitchen. She enjoyed nothing more than preparing lavish dinners for her family and diverse groups of friends. The extraordinary number of truly deeply sorrowful and loving messages of condolence received by her family from all over the world is testimony not only of her pivotal scientific contributions,

but also of her humanity. Despite her many accolades and hard won success, she was very humble and unassuming. Surely, she has left a deep chasm in the lives of so many individuals who were fortunate enough to have crossed her path.

Pat's career was in continued full bloom. She attracted a steady stream of new graduate students and postdoctoral fellows who came to study with her. Besides her husband Pasko Rakic, with whom she worked closely for three decades, she is survived by a sister, Ruth Rappaport, of Radnor Pa., as well as by countless others who owe her uncounted debts.

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