THE FACULTY OF MEDICINE
Harvard University

Seymour Solomon Kety

Seymour S. Kety, who applied the basic sciences to the study of human behavior in health and disease, died at his home in a suburb of Boston on May 25, 2000. More than any other single individual, Kety was responsible for the emergence of modern psychiatry as a rigorous and heuristic branch of medicine. He discovered a method for measuring blood flow in the brain, was the first Scientific Director of the National Institutes of Mental Health and Neurological Diseases, and produced the most definitive evidence for the major role of genetic factors in schizophrenia.

Born in Philadelphia, Kety received his MD from the University of Pennsylvania, but his interest in science burgeoned when, at the age of 10, an aunt bought him a chemistry set. Thus, chemistry became his hobby, and, during college, Kety obtained a job with a toxicologist, who was a consultant to several lead manufacturing companies. He had Kety analyze the urine of the workers at those sites. The standard procedure was to precipitate the lead as an insoluble salt, and then to redissolve it with sodium citrate, which formed a chelate with lead. On the basis of this experiment, he deduced that one could treat lead poisoning by administering sodium citrate to increase the excretion of lead, a hypothesis he later confirmed while a medical student, and then published the results in 1942.

Kety obtained a fellowship at Harvard with Joseph Aub, M.D., a world authority on lead poisoning, but World War II had broken out, and Aub was now working on the problem of traumatic shock. Kety recognized that the reflexes triggered in shock preserved the circulation of the blood to the brain and the heart at the expense of the circulation in other organs. His interest then turned to cerebral circulation, and after completing his fellowship with Aub, he returned to Pennsylvania to work on cerebral circulation in Dr. Carl Schmidt's laboratory. There he developed a highly original technique for quantitative measurements of blood flow and energy metabolism in the human brain.

In tribute to their dedicated efforts to science and medicine, deceased members of the Harvard Faculty of Medicine (those at the rank of full or emeritus professor) receive a review of their life and contributions with a complete reflection, ***a Memorial Minute****.*

The technique was based on his insight that the brain would absorb an inert diffusible gas (inhaled nitrous oxide) from arterial blood, its accumulation being independent of the brain's metabolic activity and dependent only on physical parameters such as diffusion, solubility, and perfusion. In a classic paper published in 1951, he presented his mathematical treatment, according to the Fick principle, of the exchange of diffusible substances between capillaries and tissue in the lung and other organs, and opened a new chapter in physiology and medicine. He examined cerebral blood flow in conditions such as essential hypertension, diabetic acidosis, schizophrenia, normal sleep, and clinical anesthesia, and elucidated many of the underlying physiological processes. By combining his equations with autoradiography, he could measure the circulation in different regions of the brain. When used with positron emission tomography, his principles made the measurement of local blood flow and the visualization of functional activity in the living human brain possible. Kety can be said to have ushered in the field of functional brain imaging, revolutionizing the study of mental, cognitive, and emotional processes.

Although he was not a psychiatrist, Kety was offered the scientific directorship of the newly established National Institute of Mental Health in 1951, and was given the opportunity to create a research program of unprecedented magnitude and quality. The laboratories under his direction formed the first comprehensive research program in the neurosciences, ranging from brain biochemistry and physiology to experimental psychology. Under his mentorship, Julius Axelrod carried out his Nobel Prize winning work on catecholamine metabolism. Louis Sokoloff developed his spectacularly successful deoxyglucose method for measuring local cerebral metabolism and Marcus Raichle applied these techniques to the study of cognitive function by positron emission tomography. More than 20 of those persons he appointed to NIMH were elected to the National Academy of Sciences. Kety's contributions continue to influence the field of neuroscience, not only because his discoveries have been seamlessly integrated into the *Zeitgeist* – PET scanning no longer amazes us nor do biological probes on mental disorders seem strange –, but also because those he trained have themselves trained so many other to see science as he did: as an absorbing process of elegant simplification.

Equally important contributions arose from Kety's use of a national sample of adopted children who had become schizophrenic. This was to parse out genetic and environmental variables by comparing the biological with the adoptive families of these patients. When these studies began, parenting and sociocultural factors were widely regarded as the causes of schizophrenia. With David Rosenthal and Paul Wender at NIMH and Fini Schulsinger in Copenhagen, Kety used the Danish Case Register as his source of families. Because mental illness was more frequent in the biological families than in controls, but there was no difference between controls and the adoptive families, the study laid a genetic foundation for the current era of biological investigation in schizophrenia.

Kety had a broad comprehension of the genesis of mental disorders. In an era when psychiatry was being polarized between "brainlessness" and "mindlessness", he wrote a remarkable paper entitled "A Biologist Examines Mind and Behavior" (*Science* 1960; 132:1861). To highlight the need for multiple

levels of inquiry, he invoked a powerful metaphor. "Imagine", he asked the reader, "a civilization of high intelligence whose inhabitants had never seen a book. On discovering a library, they establish a scientific institute for its investigation, employing anatomists, physical chemists, molecular biologists, behavioral scientists and psychoanalysts. Each discipline discovers important facts (the structure of cellulose, the frequency of collections of letters of varying length, etc.). But the meaning of a "book" continues to escape them." As he put it: "We do not always get closer to the truth as we slice and homogenize and isolate – what we gain in precision and in the rigorous control of variables we sometimes lose in relevance…a truer picture of the nervous system and behavior will emerge only from its study by a variety of disciplines and techniques, each with its own virtues and its own particular limitations."

In 1967 Kety accepted an appointment at Harvard University, where he became chief of the Laboratories of Psychiatric Research, first at Massachusetts General Hospital and then at McLean Hospital. There, as he had at the NIMH, he built strong research programs that emphasized basic research in the sciences pertinent to psychiatry. The MGH/McLean laboratories made fundamental contributions to the exploration of schizophrenia through the pharmacology of antipsychotic drugs, the integration of experimental psychopathology and brain physiology, and the anatomy of modulating pathways in animal and human brains.

At every stage of his career, Kety's work evinced a rare gift for discerning a single hypothesis and designing an elegant experiment to test it. His scientific contributions earned him election to the National Academy of Sciences, the American Philosophical Society, the American Academy of Arts and Sciences, 10 honorary degrees, and many awards. In the year before his death, he received an Award for Special Achievement in Medical Science from the Lasker Foundation for a lifetime of contribution to neuroscience and for providing "visionary leadership in mental health that ushered psychiatry into the molecular era." How apt a citation! The psychiatric careers of our contemporaries were changed fundamentally by the research he set in motion.

Seymour Kety was a warm, thoughtful, reflective, and gentle man, a connoisseur of music, food and wine, as he was of science. Few could match his ability to tell a sidesplitting joke. He treasured family life, and was devoted to Josephine, his wife of 60 years, his two children, Roberta and Lawrence, and two grandchildren. They survive him, as do several generations of scientists who were his students, colleagues, and grateful admirers. All are richer for having been touched by his presence and poorer for having lost him.

Respectfully submitted,

Leon Eisenberg, *Chairperson*
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