Dr. Eric Kandel M.D.

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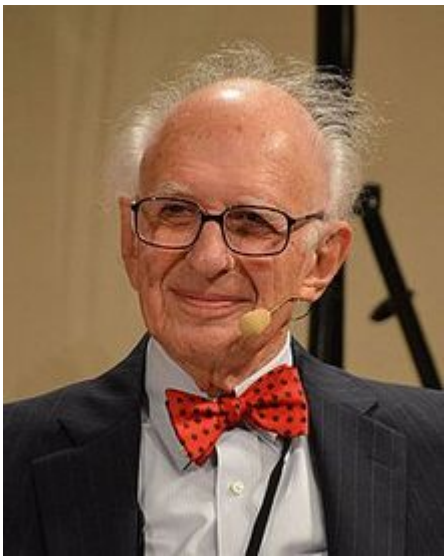


Dr. Eric Kandel's Notable Awards
Dickson Prize (1983)
Lasker Award (1983)
National Medal of Science (1988)[1]
Harvey Prize (1993)
Wolf Prize in Medicine (1999)
Nobel Prize in Physiology or Medicine (2000)

Eric Richard Kandel (German:; born November 7, 1929) is an American neuropsychiatrist. He was a recipient of the 2000 Nobel Prize in Physiology or Medicine for his research on the physiological basis of memory storage in neurons. He shared the prize with Arvid Carlsson and Paul Greengard.

Kandel, who had studied psychoanalysis, wanted to understand how memory works. His mentor, Harry Grundfest, said, "If you want to understand the brain you're going to have to take a reductionist approach, one cell at a time." So Kandel studied the neural system of the sea slug *Aplysia californica*, which has large nerve cells amenable to experimental manipulation and is a member of the simplest group of animals known to be capable of learning.[2]

Kandel is a professor of biochemistry and biophysics at the College of Physicians and Surgeons at Columbia University. He is a Senior Investigator in the Howard Hughes Medical Institute. He was also the founding director of the Center for Neurobiology and Behavior, which is now the Department of Neuroscience at Columbia University. Kandel's popularized account chronicling his life and research, *In Search of Memory: The*

Emergence of a New Science of Mind,[3] was awarded the 2006 Los Angeles Times Book Award for Science and Technology.

Early years

Eric's mother, Charlotte Zimels, was born in 1897 in Kolomyya, Pokuttya (modern Ukraine). She came from an educated Ashkenazi Jewish middle-class family. At that time Kolomyya was in Eastern Poland. His father, Hermann Kandel, was born in 1898 into a poor family in Olesko, Galicia (then part of Austria-Hungary). At the beginning of World War I, his parents moved to Vienna, Austria, where they met and married in 1923.

Eric Kandel was born in 1929 in Vienna. Shortly after, Eric's father established a toy store. But, although they were thoroughly assimilated and acculturated, they left Austria after the country had been annexed by Germany in March 1938. As a result of Aryanization (*Arisierung*), attacks on Jews had escalated and Jewish property was being confiscated. When Eric was 9, he and his brother Ludwig, 14, boarded the *Gerolstein* at Antwerp, Belgium, and joined their uncle in Brooklyn on May 11, 1939, to be followed later by his parents.

After arriving in the United States and settling in Brooklyn, Kandel was tutored by his grandfather in Judaic studies and was accepted at the Yeshiva of Flatbush, from which he graduated in 1944. He attended Brooklyn's Erasmus Hall High School in the New York City school system.[4]

Kandel's initial interests lay in the area of history. History and Literature was his undergraduate major at Harvard University. He wrote an honors dissertation on "The Attitude Toward National Socialism of Three German Writers: Carl Zuckmayer, Hans Carossa, and Ernst Jünger." While at Harvard, a place dominated by the work of B. F. Skinner, Kandel became interested in learning and memory. However, while Skinner championed a strict separation of psychology, as its own level of discourse, from biological considerations such as neurology, Kandel's work is essentially centered on an explication of the relationships between psychology and neurology.

The world of neuroscience was opened up to Kandel when he met Anna Kris, whose parents were psychoanalysts. Sigmund Freud, a pioneer in revealing the importance of unconscious neural processes, was at the root of Kandel's interest in the biology of motivation and unconscious and conscious memory.[*citation needed*]

Medical school and early research

In 1952 he started at the New York University Medical School. By graduation he was firmly interested in the biological basis of the mind. During this time he met his future wife, Denise Bystryn. Kandel was first exposed to research in Harry Grundfest's laboratory at Columbia University. Grundfest was known for using the oscilloscope to demonstrate that action potential conduction velocity depends on axon diameter. The researchers Kandel interacted with were contemplating the technically challenges of

intracellular recordings of the electrical activity of the relatively small neurons of the vertebrate brain.

After starting his neurobiological work in the difficult thicket of the electrophysiology of the cerebral cortex, Kandel was impressed by the progress that had been made by Stephen Kuffler using a much more experimentally accessible system: neurons isolated from marine invertebrates. After becoming aware of Kuffler's work in 1955, Kandel graduated from medical school and learned from Stanley Crain how to make microelectrodes that could be used for intracellular recordings of crayfish giant axons.

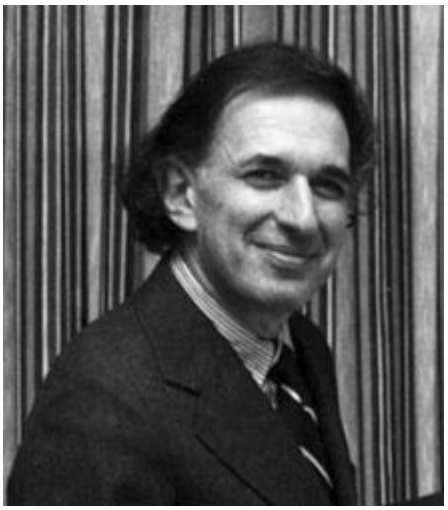
Karl Lashley, a well-known American neuropsychologist, had tried but failed to identify an anatomical locus for memory storage in the cortex of the brain. When Kandel joined the Laboratory of Neurophysiology at the US National Institutes of Health in 1957, William Beecher Scoville and Brenda Milner had recently described the patient HM, who had lost the ability to form new memories after removal of his hippocampus. Kandel took on the task of performing electrophysiological recordings from hippocampal pyramidal neurons. Working with Alden Spencer, he found electrophysiological evidence for action potentials in the dendritic trees of hippocampal neurons. The team also noticed the spontaneous pacemaker-like activity of these neurons and a robust recurrent inhibition in the hippocampus. They provided the first intracellular records of the electrical activity that underlies the epileptic spike (the intracellular paroxysmal depolarizing shift) and the epileptic runs of spikes (the intracellular sustained depolarization). But, with respect to memory, there was nothing in the general electrophysiological properties of hippocampal neurons that suggested why the hippocampus was special for explicit memory storage.

Kandel began to realize that memory storage must rely on modifications in the synaptic connections between neurons and that the complex connectivity of the hippocampus did not provide the best system for study of the detailed function of synapses. Kandel was aware that comparative studies of behavior, such as those by Konrad Lorenz, Niko Tinbergen, and Karl von Frisch had revealed that simple forms of learning were found even in very simple animals. Kandel felt it would be productive to select a simple animal model that would facilitate electrophysiological analysis of the synaptic changes involved in learning and memory storage. He believed that, ultimately, the results would be found to be applicable to humans. This decision was not without risk: many senior biologists and psychologists believed that nothing useful could be learned about human memory by studying invertebrate physiology.[*citation needed*]

In 1962, after completing his residency in psychiatry, Kandel went to Paris to learn about the marine mollusk *Aplysia californica* from Ladislav Tauc. Kandel had realized that simple forms of learning such as habituation, sensitization, classical conditioning, and operant conditioning could readily be studied with ganglia isolated from *Aplysia*. "While recording the behavior of a single cell in a ganglion, one nerve axon pathway to the ganglion could be stimulated weakly electrically as a conditioned [tactile] stimulus, while another pathway was stimulated as an unconditioned [pain] stimulus, following the exact protocol used for classical conditioning with natural stimuli in intact animals."[*citation needed*] Electrophysiological changes resulting from the combined stimuli could then be traced to

specific synapses. In 1965 Kandel published his initial results, including a form of presynaptic potentiation that seemed to correspond to a simple form of learning.

Faculty member at New York University Medical School


Kandel in 1978

Kandel took a position in the Departments of Physiology and Psychiatry at the New York University Medical School, eventually forming the Division of Neurobiology and Behavior. Working with Irving Kupferman and Harold Pinsker, he developed protocols for demonstrating simple forms of learning by intact *Aplysia*. In particular, the researchers showed that the now famous gill-withdrawal reflex, by which the slug protects its tender gill tissue from danger, was sensitive to both habituation and sensitization. By 1971 Tom Carew had joined the research group and helped extend the work from studies restricted to short-term memory to experiments that included physiological processes required for long-term memory.

By 1981, laboratory members including Terry Walters, Tom Abrams, and Robert Hawkins had been able to extend the *Aplysia* system into the study of classical conditioning, a finding that helped close the apparent gap between the simple forms of learning often associated with invertebrates and more complex types of learning more often recognized in vertebrates. Along with the fundamental behavioral studies, other work in the lab traced the neuronal circuits of sensory neurons, interneurons, and motor neurons involved in the learned behaviors. This allowed analysis of the specific synaptic connections that are modified by learning in the intact animals. The results from Kandel's laboratory provided solid evidence for the mechanistic basis of learning as "a change in the functional effectiveness of previously existing excitatory connections."[*citation needed*]

Molecular changes during learning

Starting in 1966 James Schwartz collaborated with Kandel on a biochemical analysis of changes in neurons associated with learning and memory storage. By this time it was known that long-term memory, unlike short-term memory, involved the synthesis of new proteins. By 1972 they had evidence that the second messenger molecule cyclic AMP (cAMP) was produced in *Aplysia* ganglia under conditions that cause short-term memory formation (sensitization). In 1974 Kandel moved his lab to Columbia University and became founding director of the Center for Neurobiology and Behavior. It was soon found that the neurotransmitter serotonin, acting to produce the second messenger cAMP, is involved in the molecular basis of sensitization of the gill-withdrawal reflex. By 1980, collaboration with Paul Greengard resulted in demonstration that cAMP-dependent protein kinase, also known as protein kinase A (PKA), acted in this biochemical pathway in response to elevated levels of cAMP. Steven Siegelbaum identified a potassium channel that could be regulated by PKA, coupling serotonin's effects to altered synaptic electrophysiology.

In 1983 Kandel helped form the Howard Hughes Medical Research Institute at Columbia devoted to molecular neural science. The Kandel lab then sought to identify proteins that had to be synthesized to convert short-term memories into long-lasting memories. One of the nuclear targets for PKA is the transcriptional control protein CREB (cAMP response element binding protein). In collaboration with David Glanzman and Craig Bailey, Kandel identified CREB as being a protein involved in long-term memory storage. One result of CREB activation is an increase in the number of synaptic connections. Thus, short-term memory had been linked to functional changes in existing synapses, while long-term memory was associated with a change in the number of synaptic connections.

Experimental support for Hebbian learning

Some of the synaptic changes observed by Kandel's laboratory provide examples of Hebbian theory. One article describes the role of Hebbian learning in the *Aplysia* siphon-withdrawal reflex.[5]

The Kandel lab has also performed important experiments using transgenic mice as a system for investigating the molecular basis of memory storage in the vertebrate hippocampus.[6][7][8] Kandel's original idea that learning mechanisms would be conserved between all animals has been confirmed. Neurotransmitters, second messenger systems, protein kinases, ion channels, and transcription factors like CREB have been confirmed to function in both vertebrate and invertebrate learning and memory storage.[9][10]

Continuing work at Columbia University

Since 1974, Kandel actively contributes to science as a member of the Division of Neurobiology and Behavior at the Department of Psychiatry at Columbia University. In 2008, he and Daniela Pollak discovered that conditioning mice to associate a specific

noise with protection from harm, a behavior called “learned safety,” produces a behavioral antidepressant effect comparable to that of medications. This finding, reported in *Neuron*,[11] may inform further studies of the cellular interactions between antidepressants and behavioral treatments.

Kandel is also well known for the textbooks he has helped write, such as *Principles of Neural Science*.[12] First published in 1981 and now in its fifth edition, *Principles of Neural Science* is often used as a teaching and reference text in medical schools and undergraduate and graduate programs. Kandel has been a member of the United States National Academy of Sciences since 1974. He has also been at Columbia University since 1974 and lives in New York City.

Notable former members of his lab

- James H. Schwartz 1964–1972: Coauthor of the influential textbook *Principles of Neural Science*.[13]
- John H. (Jack) Byrne 1970–1975: Professor and Director of the Neuroscience Research Center at Texas A&M University; founder and editor of the research journal *Learning and Memory*.[14]
- Tom Carew 1970–1983: Professor and Dean of the Faculty of Arts and Sciences at New York University, Center for Neural Science. Past President of the Society for Neuroscience.[15]
- Edgar T. Walters 1974–1980: Professor at the Medical School of the University of Texas Health Science Center at Houston.[16]

Current views about Vienna

When Kandel won the Nobel Prize in 2000, it was claimed in Vienna that he was an "Austrian" Nobel, something he found "typically Viennese: very opportunistic, very disingenuous, somewhat hypocritical." He also said it was "... certainly not an Austrian Nobel, it was a Jewish-American Nobel." After that, he got a call from then Austrian president Thomas Klestil asking him, "How can we make things right?" Kandel said that first, Doktor-Karl-Lueger-Ring should be renamed; Karl Lueger was an anti-Semitic mayor of Vienna, cited by Hitler in *Mein Kampf*. The street was ultimately renamed in 2012.[17] Second, he wanted the Jewish intellectual community to be brought back to Vienna, with scholarships for Jewish students and researchers.[18] He also proposed a symposium on the response of Austria to National Socialism.[19] Kandel has since accepted an honorary citizenship of Vienna and participates in the academic and cultural life of his native city,[20] similar to Carl Djerassi. His 2012 book, *The Age of Insight*—as expressed in its subtitle, "The Quest to Understand the Unconscious in Art, Mind, and Brain, from Vienna 1900 to the Present"[21]—represents a wide-ranging historical attempt to place Vienna at the root of cultural modernism.