



Eric Kandel, who planned to become a psychoanalyst before choosing a career in research, says modern psychiatry would benefit from a more biological outlook.
Photo: Christopher Denney

THE FUTURE OF PSYCHIATRY

ERIC KANDEL SAYS IT LIES WITH BIOLOGY

By **Steve Mirsky**

Some five miles north of Manhattan's trendy and misnamed Upper West Side lies a grittier part of town, just as westerly and even more upper, known as Washington Heights. Traveling to this tough, working-class neighborhood on Duke Ellington's A train is like moving from the city's id to its ego, to a region dealing squarely with life's realities. Fittingly, West 168th street is the home of the Center for Neurobiology and Behavior and of the Howard Hughes Medical Institute at Columbia University. Eric Kandel works here.

Kandel's is a household name to students of the brain. His textbook, *Principles of Neural Science*, coauthored with Columbia colleagues James Schwartz and fellow HHMI investigator Thomas Jessell, is in its fourth edition. Kandel's research on the biology of memory has won him the National Medal of Science, the Lasker Award, the Wolf Prize and membership in the National Academy of Sciences. After a half-century contemplating behavior, mind and brain, he has also won a hard-fought perspective: The time has come for psychiatry, once his training ground and long an art more than a science, to reinvigorate itself by embracing biology.

Kandel first outlined his thoughts in a 1996 talk commemorating the 100th anniversary of Columbia's New York State Psychiatric Institute. That talk became a 1998 article, "A New Intellectual Framework for Psychiatry," for the *American Journal of Psychiatry*. "I don't consider this my science," Kandel says of his prescriptions. "This is my avocation. But that avocation has been completely influenced by my science." For example, the humble snail *Aplysia* and the common fruit fly *Drosophila* showed Kandel that memory storage depends on the coordinated

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expression of specific genes. These genes code for proteins that actually alter the structural elements in the brain. "In *Aplysia*," he says, "you can see in front of your eyes that the connections change. When the animal remembers something for the long term, it grows new synaptic connections." Biology thus reflected and revealed mental functioning.

These findings were part revelation and part confirmation for Kandel, who long believed that biology could inform psychiatry. "I went into the biology of memory because I was looking for a problem that was at once deep and yet amenable to a reductionist approach relevant to psychiatry," he says. Healthy behavioral changes rely on memory and learning. "What happens in psychotherapy in part is a learning experience," he notes. "You relearn old ways of behaving and take on new degrees of freedom."

Born in Vienna, Kandel would connect to that city's psychiatric roots, but in a circuitous fashion. His family came to the United States in 1939 and he eventually enrolled as an undergraduate at Harvard. There he met the children of other Viennese, some of whose parents had been psychoanalysts. "Through them I got extremely interested in psychoanalysis," he recalls, "and changed my career interests from history and literature to psychoanalysis." He went to medical school at New York University with the idea of becoming a psychoanalyst, but his growing interest in biology led him also to study neuroscience. "I thought I should learn something about the brain, because an analyst should know something about what's between the ears." He would eventually learn that this seemingly reasonable notion was not necessarily common wisdom.

After his internship ended in 1957, Kandel trained in neuroscience at the NIH, studying the cell biology of the hippocampus, a region of the brain that had just been shown to be involved in memory formation. When he returned to Harvard in 1960 for residency training in psychiatry, Kandel found a climate that he perceived as highly intelligent but anti-intellectual. "There were no required or even recommended readings," he recounts in his 1998 paper. "We were assigned no textbook; rarely was there a reference to scientific papers—Even Freud's papers were not recommended reading." The assumption was that residents unburdened by too much theory had a better chance to connect to each patient as a unique individual—the patient was the textbook.

Kandel laughs heartily—as he does often—when he remembers this attitude, but then quickly points out some of its benefits. "I must tell you that even though it sounds humorous, there is a component of truth in it," he admits. "You can intellectualize too much. If you read about schizophrenia and depression in a textbook, you'll never get a feeling of what they're about. And there is a tendency for medical students to substitute the book for the patient."

Kandel pointed out in his 1998 article that Freud himself

originally sought "a neural model of behavior in an attempt to develop a scientific psychology." But the backward state of brain science in Freud's day convinced him to abandon that search and rely on an abstract model of the mind, to be found in the verbal accounts of subjective experience. This reliance eventually became codified, in some camps, into a dogmatic exclusion of material, physical processes.

The advent of effective psychiatric drugs in the last three decades forced psychiatry to confront neuroscience to some degree, "if only to understand how specific pharmacological treatments were working," Kandel writes. He argues that the input from biology, to both psychiatry and psychoanalysis, can be even more profound. "The idea right now is to take advantage of the enormous increase in knowledge in the biological basis of behavior, such as imaging methodology and the human genome," he says. "Psychiatry, in principle, is going to be in a wonderful position to profit from this."

Imaging technology, for example, has the potential to do away with the differentiation between "organic" conditions, marked by obvious brain lesions, and "functional" ones, which so far are reflected solely in behavior. "Insofar as psychotherapy works," Kandel explains, it's got to be doing something [in the brain]. And if it does, one should be able to detect it with various imaging techniques. To me it's really a question of time and resolution in finding it." The ability to detect the subtlest physical response means that the effects of therapy could, in theory, be objectively observed. Kandel exclaims, "We'll see whether you do better psychotherapy than I do!"

Similarly, behavioral modifications should be reducible to modulations in the levels of the various proteins crucial for memory and learning, and attendant structural changes. If so, then pharmacology and psychotherapy must finally converge at the end point of gene expression. "So then the question is what is most effective for a particular patient," Kandel says. Cognitive neuroscience and molecular biology thus may be able to identify the physical structures and biochemical signaling systems of the brain that are associated with the various components of the classical psychoanalytical model of the mind. Psychiatrists would then have access to that most crucial scientific gift—something material to measure.

Kandel's article provoked a large number of responses, both positive and negative, including many from psychoanalysts. (He answered them in detail with a second article, published in 1999, titled "Biology and the Future of Psychoanalysis.") Some of the objections seemed to note that Kandel's kind of data merely move the mystery of the mind back another step. "Fuller knowledge about how genes function does not account for how a thought, feeling or choice becomes a physical thing," wrote one correspondent. Nevertheless, fuller knowledge, even if still incomplete, may be informative. "Of course, we are extremely far away from grasping, even in outline, the

nature of human thought processes, of motivation, aspiration, conflict, social interaction," he notes. And to those who fear he is reducing the psychiatric patient to a set of biological functions, Kandel replies, "The patient is a set of biological functions," and then laughs again. "But I think one has to realize," he continues, "that the whole is more than the sum of the parts. There is something wonderful and special about each person as a unique individual—a unique set of biological functions, if you will. The ultimate aim is to use reductionism, not only to take things apart, but to put them together again. You have to be a reductionist and a holist at the same time."

Two additional benefits may accrue from the incorporation of a more biological outlook in psychiatry. Kandel believes that the specialty, which has become less popular over the years, could once again attract increasing numbers of talented medical students. And there could be feedback in the opposite direction—as psychiatrists and neuroscientists find more common ground, the former could help define for the latter the mental functions that should be most closely studied. Such study might complete Kandel's quest for "a meaningful and sophisticated understanding of the biology of the human mind."

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