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## BOOK REVIEWS

IN SEARCH OF MEMORY: THE EMERGENCE OF A NEW SCIENCE OF MIND. By Eric R. Kandel. New York/London: W. W. Norton and Company, 2006. 510 pp.

This book is about many things. Foremost, it is an autobiography of a smart, hardworking, and principled man. It is also all of the following: a historical account of some of the most important developments in neuroscience over the last one hundred years; an account of how science is done in the modern era, revealing a long, complex, and distinctively collaborative process; in small part, the story of how one of the worst horrors of humankind affected some of its victims and their families throughout their lifetimes; and a commentary on what happened to psychoanalysis as well as, to a lesser extent, to psychiatry, in the latter part of the twentieth century. And, finally, it suggests ways to explore exceptionally intriguing questions about the human mind.

I enjoyed this book tremendously, notwithstanding the pain it sometimes evoked. I am grateful to have been provided with the information it included and to have felt the kinship its stories provided.

The author, Eric R. Kandel, was born on November 7, 1929, in Vienna, Austria. The first memory he chooses to tell us is of his ninth birthday, which began happily with the gift of a shiny blue, remote-controlled car. He played with it inside his family's apartment for the better part of two days, until the Nazis came banging on the door. They took him, his mother, and his brother out of their home, returning them a few days later to find his father missing, the apartment ransacked, and their valuables stolen. Kandel's father was eventually released—one of few Jewish men to be let go after the roundup on Kristallnacht. The author recounts: "Although my family and I lived under the Nazi regime for only a year, the bewilder-

ment, poverty, humiliation, and fear I experienced that last year in Vienna made it a defining period of my life" (p. 5).

In fact, throughout this book, Kandel substantiates how "defining" this period was. He and his brother were able to escape to relatives in Brooklyn, New York, and his parents managed to join them several months later. He was educated at the Yeshiva of Flatbush, Erasmus Hall High School, and then Harvard University. His attempt to understand the civilization that had caused him such distress led him to the study of Austrian and German history at Harvard. *In Search of Memory* reflects this work in its substantive descriptions of those countries. The author documents the enthusiasm with which so many Austrians welcomed the Nazis, and the barbarism, sadism, and irrationality with which those same Austrians treated Jews. His inclusion of photographs from his own collection, and those of various institutional archives, gives powerful support to his text. Also, his heartfelt recognition of his good fortune in escaping, while others did not, makes him a more compelling person and writer.

Kandel explains unabashedly that, while at Harvard, he met and "fell in love with Anna Kris" (p. 18). This led to his association with her parents, Ernst and Marianne Kris, and thus a much fuller exposure to psychoanalysis and Freud than his studies at Harvard alone provided. His plans to do graduate work in European intellectual history were somewhat compromised by the death of an important mentor. That and his exposure to this new field, as exemplified by the work of Hartmann, Kris, and Lowenstein, changed Kandel's career direction.

I was converted to their view that psychoanalysis offered a fascinating approach, perhaps the only approach, to understanding mind. Psychoanalysis opened an unsurpassed view not only into the rational and irrational aspects of motivation and unconscious and conscious memory, but also into the orderly nature of cognitive development, the development of perception and thought. This area of study began to seem much more exciting to me than European literature and intellectual history. [p. 43]

Since Kandel perceived that the best route to psychoanalysis was through medical school, he fulfilled the necessary requirements and was admitted to the New York University Medical School in 1952. His description of the course he took in brain anatomy, taught by Louis Hausman, is compelling. It was much more enlivening and creative than the courses many of us experienced in our medical training, and facilitated Kandel's thinking about the biological correlates of mental phenomena. Encouraged by forward-thinking psychoanalysts such as Lawrence Kubie, Sidney Margolin, and Mortimer Ostow, he began an elective in neurophysiology with Harry Grundfest. He and Anna Kris "parted ways" in 1953, and in 1955, he met his future wife, Denise Bystryn, with whom he had in common a European childhood—both having been persecuted by the Nazis. In addition, the two shared a strong identification with Judaism and a love of things artistic and intellectual.

It was Grundfest who helped operationalize Kandel's aspirations by telling him that, in order to understand the mind, one would first need to "look at the brain one cell at a time" (p. 55). Remembering Freud's journey in which he began by studying single nerve cells and had some prescience about what would be discovered later, Kandel recognized the value of this advice (pp. 55-56). For those reluctant to read *In Search of Memory* because they "can't understand the science," be assured that Kandel is able to explain it in clear prose that makes it understandable to a lay audience, while it remains nonetheless engaging to a professional one. He begins with what Grundfest taught him about the biology of nerve cells: (1) the neuron doctrine: that the nerve cell "is the fundamental building block and elementary signaling unit of the brain" (p. 59); (2) the ionic hypothesis: that information is transmitted via an electric signal or action potential within a nerve cell; and (3) the chemical theory of synaptic transmission: that information is passed between cells via a chemical neurotransmitter.

Kandel continues by elucidating the work of Cajal, Sherrington, Adrian, Hodgekin, Huxley, and Katz in easily understandable terms with the use of clarifying diagrams. In a way that keeps the reader engaged, the author explains the relevance of the questions asked by these researchers to the developing body of neuroscien-

tific knowledge. He offers information about these men's lives as well as their work, in order to expand our understanding of how science can be advanced and how it can be delayed. When he gets to the debate over whether the transmission between nerve cells is electric or chemical, he enlivens the discussion by explaining how Karl Popper influenced Eccles. Eccles had grown despondent as his position about the electric hypothesis became increasingly in doubt, while the quality of his research continued to be excellent. He was enabled to handle with pride and equanimity the refutation of his original position. True science, after all, is the refutation of hypotheses, not the gamble on one argument versus another.

Kandel next describes the contributions, both scientific and personal, of Wade Marshall, his chief at the National Institute of Health, who allowed him the opportunity to pursue his own interests. By this time, Kandel had

. . . progressed from the naive notion of trying to find the ego, id, and superego in the brain to the slightly less vague idea that finding the biological basis of memory might be an effective approach to understanding higher mental processes. [p. 116]

The author brings us up to date about what was known at that time concerning *where* memory is stored in the brain, which enabled him to proceed in addressing the question of *how* it is stored. His summary of the research that brought us to an understanding of working memory, long-term memory, explicit and implicit memory, and the geographical correlates of each is elegant and straightforward. He heartens us by making two points: (1) this work validated Freud's theory about the existence of the unconscious; and (2) much can be learned from "the careful study of clinical cases" (p. 131).

Kandel decided to examine "the simplest instance of memory storage . . . in an animal with the simplest possible nervous system, . . . [in order to] trace the flow of information from sensory input to motor output" (p. 143). This decision ran against the tide of much thinking at the time, even that of Kandel's collaborator. Many biological scientists, psychologists, and psychoanalysts felt that the

mammalian mind—and, specifically, the human one—was so different from that of lower organisms that we could not learn about learning from an examination of simpler forms of life. Kandel had good reason to believe the contrary and continued his pursuit, eventually settling on *Aplysia* as his experimental animal of choice—a large snail whose brain has a relatively small number of cells and whose neurons are some of the largest in the animal kingdom.

The author explains his initial reasoning that “different forms of learning give rise to different patterns of neural activity, and that each of these patterns of activity changes the strength of synaptic connections in a particular way. When such changes persist, the result is memory storage” (pp. 159-160). Kandel and his colleagues studied the gill-withdrawal reflex in *Aplysia* and learned that both non-associative as well as associative learning could modify it. In the first condition, they gently touched the snail near its breathing apparatus. Initially, this induced a reflex withdrawal, but with subsequent gentle touches, there was no withdrawal (habituation). However, when the gentle touch was paired with a strong shock to the head or tail, the snail became sensitized and thus produced a strong gill-withdrawal reflex after only a gentle touch. The snail had demonstrated associative learning. One might reasonably conclude that a gentle touch had come to mean danger.

Next, researchers were able to identify the specific sensory and modulatory interneurons that mediated these processes:

Moreover, the same neurons were involved in the gill-withdrawal reflex in every snail studied, and the same cells always formed the same connections with one another. Thus, the neural architecture of at least one behavior of *Aplysia* was amazingly precise. In time, . . . the same specificity and invariance [was found] in the neural circuitry of other behaviors. [p. 196]

Here, Kandel pauses to indicate how similar his discoveries were to what Freud had predicted in his “Project for a Scientific Psychology.”<sup>1</sup>

<sup>1</sup> Freud, S. (1895). Project for a scientific psychology. *S. E.*, 1.

The next task, given the invariance of the found circuitry, was to discover how behaviors could be changed. It was demonstrated that:

The number of synapses in the brain is not fixed . . . but changes with learning . . . . Short-term memory produces a change in the function of the synapse, strengthening or weakening pre-existing connections; long-term memory requires anatomical changes. Repeated sensitization training (practice) causes neurons to grow new terminals, giving rise to long-term memory, whereas habituation causes neurons to retract existing terminals. Thus, by producing profound structural changes, learning can make inactive synapses active or active synapses inactive. [pp. 214-215]

Now the molecular basis of these processes needed explication. It would turn out that in habituation, the sensory neuron released less neurotransmitter into the synapse and more with sensitization. The sensory neurons release the transmitter glutamate, and modulatory interneurons release the transmitter serotonin. With the understanding that glutamate and serotonin were the relevant transmitters, they proceeded to a biochemical analysis of these processes, and worked out the steps described in the caption to the figure shown on the opposite page (excerpted from the book, p. 229), labeled here as Figure 1.<sup>2</sup>

Arvid Carlsson, Paul Greengard, and Eric Kandel were awarded the Nobel Prize in Physiology or Medicine in 2000, for their groundbreaking studies on signal transformations in the nervous system. They had worked out the biological processes that correlate with the phenomenon of implicit short-term memory. Later work with other organisms led them to believe that “the cellular mechanisms underlying simple forms of implicit memory are likely to be the same in many animal species, including people, and in many different forms of learning because those mechanisms have been conserved through evolution” (p. 234).

<sup>2</sup> Reprinted from *In Search of Memory: The Emergence of a New Science of Mind*, by Eric R. Kandel. Copyright © 2006 by Eric R. Kandel. Courtesy of Eric R. Kandel, M.D., and used by permission of the publisher, W. W. Norton & Company, Inc.

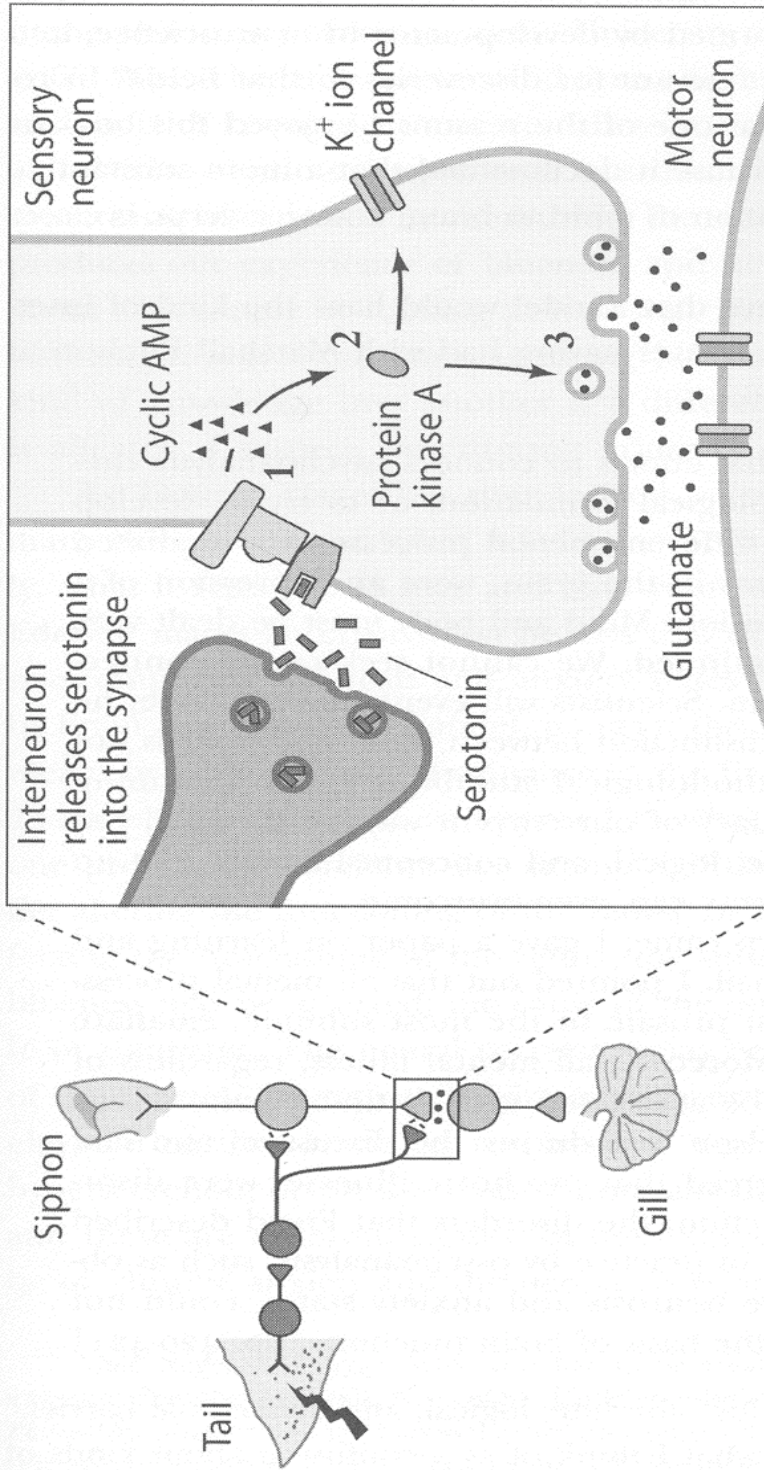


FIGURE 1: BIOCHEMICAL STEPS IN SHORT-TERM MEMORY

Figure 1 shows the following process: A shock to the tail of *Aplysia* activates an interneuron that releases the chemical messenger serotonin into the synapse. After crossing the synaptic cleft, serotonin binds to a receptor on the sensory neuron, leading to production of cyclic AMP (1). Cyclic AMP frees the catalytic unit of protein kinase A (2). The catalytic unit of protein kinase A enhances the release of the neurotransmitter glutamate (3).

“So what?” you may ask. “I’m a therapist, a psychoanalyst—what do I care about the biological correlates of my patients felt experience? How am I informed by developments in neuroscience, and how can my work be relevant for discoveries in that field?” In response, I will note that one of the reasons I enjoyed this book as much as I did was because it documented that a more substantive explication of the relation of mind to brain, and vice versa, is closer than ever before.

It is hard to believe that Kandel would have the kind of interchange today that he relates having had with Marshall Edelson at Yale University in 1986:

Edelson argued that efforts to connect psychoanalytic theory to a neurobiological foundation, or to try to develop ideas about how different mental processes are mediated by different systems in the brain, were an expression of a deep logical confusion. Mind and body must be dealt with separately, he continued. We cannot seek causal connections between them. Scientists will eventually conclude, he argued, that the distinction between mind and body is not a temporary methodological stumbling block stemming from the inadequacy of our current ways of thought, but rather an absolute, logical, and conceptual barrier that no future developments can ever overcome.

When my turn came, I gave a paper on learning and memory in the snail. I pointed out that all mental processes, from the most prosaic to the most sublime, emanate from the brain. Moreover, all mental illness, regardless of symptoms, must be associated with distinctive alterations in the brain. Edelson rose during the discussion and said that, while he agreed that psychotic illnesses were disorders of brain function, the disorders that Freud described and that are seen in practice by psychoanalysts, such as obsessive-compulsive neurosis and anxiety states, could not be explained on the basis of brain function. [pp. 420-421]

Let me speak to this “absolute, logical, and conceptual barrier.” There remains today what I think of as a confusion about kinds of knowledge and how one kind can inform the other. I do not claim

that what I am about to describe originated in my own thinking; rather, it reflects what I learned from Nicolas Maxwell in a course in the philosophy of science at the University of Manchester in 1965-1966. What I began to understand then was that there are two different kinds of knowledge: one we call *scientific* and the other *experiential*. The classic example used was that of color: we can know something about *blue* by measuring the wavelength of whatever produces our experience of blueness, and we can know something about *blue* simply by looking at it as well. Knowledge about blue's wavelength is not the same as seeing it. Whether one values one kind of knowledge over another is a different question—one that is affected, I suspect, by differing priorities.

As Thomas Nagel has popularized, science can tell us about many things, but not “what it is like to be a bat”<sup>3</sup>—or, analogously, what it feels like to love and hate your mother simultaneously. Edelson makes an error when he says that disorders such as obsessive-compulsive neurosis and anxiety states cannot be “explained by brain function” (see Kandel, p. 421); this depends on what one means by *explained*. The dissonance in the field seems to have been about what is causative as opposed to what is correlative—or, if one prefers, concomitant. For example, if there is a genetic disorder altering the functioning of the retina, or if there is a trauma affecting the functioning of the retina, the subsequent experience of blueness may be affected; the cause of the difficulty is either genetic or traumatic. The neural correlates may be found in the biology of the functioning retina. To give another example, a boy may have elevated cortisol levels on the basis of a genetically determined hypersecretion, or on the basis of constant threats from his father, and these are different causes. In both cases, the experience may be of chronic anxiety and the neural correlate excess cortisol.

<sup>3</sup> See Nagel, T. (1974). What it is like to be a bat. *Philosophical Rev.*, 83(4): 435-450. See also Maxwell, N. (1968). Understanding Sensations. *Australasian J. Philosophy*, 46(2):127-145. Maxwell ([www.nick-maxwell.demon.co.uk](http://www.nick-maxwell.demon.co.uk)) claims that this article presaged Thomas Nagel's; in fact, his lectures during the year that I studied with him (1965-1966) seemed to me to do so as well.

In other words, postnatal psychosocial determinants may be more “causative” of certain difficulties, and genetic inheritance more “causative” of others. This does not negate the fact that both have neural correlates. Further, it does not negate the possibility that one type of knowing may facilitate an increase in the other and vice versa. We have good reason to believe that genetic factors play a significant role in the development of bipolar illness, and that life events have more to do with the development of Post-Traumatic Stress Disorder and Dissociative Identity Disorder, as well as the anxiety that results from neurotic conflict. Nonetheless, identifiable neural correlates are being worked out for each.

While he recounts some unfortunate personal experiences with psychoanalysts, Kandel also gives the people and the field much credit, both for the intellectual inspiration they have engendered and the help his personal analysis provided. In the latter sections of the book, Kandel describes his more recent work and that of others. He maintains that psychoanalysis is in a unique position to aid our understanding of both mind and brain, and that, if it is to regain its preeminence, it must work to make its hypotheses falsifiable. Advances in many fields have made it possible to entertain interesting questions that can be cast as falsifiable hypotheses related directly to topics of psychoanalytic interest.

The author’s optimism made me ponder questions I have wondered about for some time. For example, what are the neural concomitants of the altered states of consciousness that occur during an analysis? I was reminded of a patient of mine who, in his third year of analysis, was able to recall a time in his life when his father, due to a sudden change of jobs, was away from home a great deal. The patient recalled watching television when out of the corner of his eye, he saw his mother—wearing a rather transparent nightgown—pass by. The rush of mixed feelings of excitement, fear, guilt, and confusion that he felt at the time became available to the patient, as did the connection to his subsequent preferred place in life of being “number two,” as well as his characteristic lack of confidence. Is the notion of studying the ambience in which insight occurs so far out of reach?

I also thought about another patient, one with a very different diagnosis, who in his third year of psychotherapy had a relapse and was rehospitalized. When I came to the hospital for his psychotherapy session, he began by telling me that he was Jesus Christ, and that Gerald Ford had instructed the CIA to kill him because he had just caused the president's favorite football team to lose its game. Twenty minutes into his hour, the patient suddenly stopped talking, looked at me, and said that none of this was true. He then proceeded to tell me his real name, the name of the hospital he was in, and his current realistic situation. I asked him how it was that he now knew what he had not known moments before. He said he did not know the answer to this, but that, twenty minutes after I left, he would again start believing what he had when I first entered. I have long wondered about the relevant relational determinants of this shift, as well as its biological correlates.

Kandel's book integrates autobiography with an elegant didactic exposition of a scientific enterprise spanning a lifetime. He generously shares not only how the trauma he experienced at the hands of the Nazis motivated his scientific and intellectual pursuits, but also how it influenced his social and interpersonal behavior. These influences are revealed most clearly when he recounts his trips to France, Austria, and Stockholm as an adult. In Austria, for example, he took the opportunity granted by his winning the Nobel Prize to "suggest we organize a symposium" that he hoped

. . . would serve three functions: first, to help acknowledge Austria's role in the Nazi effort to destroy the Jews during World War II; second, to try to come to grips with Austria's implicit denial of its role during the Nazi period; and third, to evaluate the significance for scholarship of the disappearance of the Jewish community of Vienna. [p. 405]

With more personal and emotionally powerful descriptions, Kandel recounts the trips that he and his wife took to visit the people and places of their wartime past.

One aspect of the kinship I felt in reading this book, to which I referred in the beginning of this review, has to do with shared mo-

tivations. Many of us became psychoanalysts, in part, as our response to that dark chapter in human history—trying to understand how humans could behave as they did, and perhaps what might prevent such behavior in the future. *In Search of Memory* makes clear some of the challenges ahead if we are to better address the questions that drew many of us to the study of the human mind. Can we cast our clinical experience into falsifiable hypotheses? Based on that clinical experience, can we offer helpful suggestions to the burgeoning field of neuroscience?

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