

to investigate the basis of memory — something beyond the ken of psychiatry of the 1950s, which largely ignored brain neurophysiology. One can only speculate as to whether Freud, if he had lived during the same era as Kandel, would have explained the id, ego, and superego in terms of genes and the regulation of genetic expression.

The key element in Kandel's quest for understanding memory was his realization that to probe the basis of memory, he would need a model organism that was less complex than the human brain and its billions of neurons. With wisdom and brilliance, he recognized that the solution of such a complex problem required a reductionist approach. He chose for his model the aplysia, a marine snail with only 20,000 neurons that was nonetheless capable of simulating many of the conditions of memory in higher forms. Kandel's major breakthrough arose when he found that memory could be associated with the relation of the strength of neuronal connections to a universal signaling molecule, cyclic adenosine monophosphate (cAMP). He and his colleagues were able to show that short-term memory was related to cAMP-mediated protein kinase A activity, which catalyzed cytosolic protein phosphorylation and thereby led to changes in potassium channels. Long-term memory also involved cAMP and protein kinase A, but in this case a transcription factor, cAMP responsive element-binding (CREB) protein, was phosphorylated and bound to nuclear DNA to activate genes, resulting in the synthesis of proteins that potentiated long-term memory. Over the years, Kandel has extended these observations to mice. CREB protein has now been shown to play a major role in brain physiology and continues to be an exciting area of investigation. This work, for which Kandel, along with Arvid Carlsson and Paul Greengard, was awarded the Nobel Prize in Physiology or Medicine in 2000, laid down some universal principles that govern memory and other dynamics of neurobiology.

Kandel intersperses autobiography with the development of molecular neuroscience in a seamless and lucid fashion. In addition, *In Search of Memory* serves as a handbook of advice for both beginning and mature scientists. Its message is that for a successful life in science, the selection of scientific problems must parallel one's inter-

ests and become one's passion. It also conveys that in the practice of science, hypotheses guide scientific accomplishment; the choice of experimental system and design is critical to progress; and a learning community of exciting, creative, and interactive colleagues is optimal for success. Kandel demonstrates an extraordinary ability to communicate scientific theory, experimental design, and progression of understanding, together with a passion for life and a gift for understanding people and events. These qualities make this multidimensional book an inspiring and valuable resource for both students and practitioners of science, for historians, and for the scientifically minded general reader. I have given copies to all of the trainees in my own laboratory. It is likely that *In Search of Memory* will become a classic scientific memoir.

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CORRECTIONS

Prevalence and Correlates of Accelerated Atherosclerosis in Systemic Lupus Erythematosus (December 18, 2003;349:2399-2406). On page 2403, in Table 2, the 12th entry should have read "Homocysteine ($\mu\text{mol/liter}$)," not "Homocysteine (mg/dl)," as printed.

A Randomized Trial of Exemestane after Two to Three Years of Tamoxifen Therapy in Postmenopausal Women with Primary Breast Cancer (March 11, 2004;350:1081-92). On page 1081, the list of authors should have included "Cornelius van de Velde, M.D., Department of Surgery, Leiden University Medical Center, Leiden, the Netherlands." On page 1083, the legend for Figure 1 should have read "The percentage of patients who continue to receive treatment represents the percentage who are not known to have discontinued their randomized treatment and who began initial tamoxifen therapy less than five years before March 31, 2004," not "December 31, 2004," as printed. On page 1089, in Figure 3, the upper limit of the 95 percent confidence interval for the previous-chemotherapy subgroup should have been 0.92 and should not have crossed 1.0, as printed. On page 1090, the P values listed in Table 4 were incorrect.

The table has been corrected on the *Journal's* Web site at www.nejm.org.

Erlotinib in Lung Cancer — Molecular and Clinical Predictors of Outcome (July 14, 2005;353:133-44). On page 139, the second line from the bottom of the right-hand column should have read "95 percent confidence interval, 0.40 to 1.50; P=0.45)," not "P=0.54," as printed.