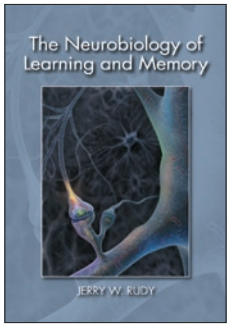
From eIF2alpha to Ebbinghaus



The Neurobiology of Learning and Memory

by Jerry W Rudy

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Reviewed by Paul W Frankland & Karim Nader

Many of the concepts and methodologies that dominate contemporary studies of learning and memory were developed around the turn of the twentieth century. It was in this 'golden age' that German psychologist Hermann Ebbinghaus developed the first empirical approaches for studying human memory, and, around the same time, the Russian physiologist Ivan Pavlov and the American psychologist Edward Thorndike developed the behavioral frameworks for studying these processes in nonhuman experimental subjects. In bringing scientific rigor to the study of learning and memory, Ebbinghaus, Thorndike, Pavlov and others provided the impetus for twentieth and twenty-first century scientists to begin to look inside the 'black box' of learning and memory and to ultimately develop neurobiological accounts of these processes. In his new book, *The Neurobiology of Learning and Memory*, Jerry Rudy takes us on a journey from the work of these pioneers to contemporary neurobiological studies where, armed with a plethora of imaging and molecular tools, today's neurobiologists are getting unprecedented views inside of this black box. The challenge for this book, and for the field in general, is to bring together such diverse observations into coherent models of how experience modifies the brain.

In taking this journey, Rudy chooses to start at the bottom and work his way up. Accordingly, the chapters are organized around three major themes: the synaptic basis of memory, memories and molecules, and neural systems and memories. He begins with synaptic plasticity, ably describing how experience alters existing synaptic connections via long-term potentiation– or long-term depression–type mechanisms. The emphasis here is on the molecular machinery underlying these changes and includes detailed discussion of post-translational modification of existing synaptic proteins, receptor trafficking and the transcriptional mechanisms underlying the stabilization of synaptic changes. Although this first section describes experiments using reduced preparations (such as brain slices), the focus shifts in the second part of the book to the whole animal. Here Rudy evaluates whether the molecular machinery required for synaptic plasticity is also required for behavioral plasticity or learning and memory. Picking up on parallel themes in the first section, we follow the well-trodden path from NMDA and AMPA receptors through CaMKII to a final destination of CREB, the putative gateway to long-term memory. In the third section, Rudy turns his attention to the different neural systems that support memory, with a particular emphasis on the hippocampus. This is Rudy's bedrock and he expertly guides readers through different theories of hippocampal function.

In many textbooks, scientific progress is presented as a staid, logical process, inevitably converging on some set of scientific truths or facts. As many of us are quick to recognize, progress is more typically characterized by an unremitting series of claims and counter-claims, with unexpected observations leading to paradigmatic shifts. It is shaped not only by data but also by fashions, personalities and the ensuing, often emotionally laden, debates between rival factions. The study of learning and memory is no exception and, straying from standard textbook convention, Rudy highlights current areas of controversy and debate. He casts his most critical eye over debates to which he himself has contributed, questioning, for example, the specificity of widely used translational inhibitors such as anisomycin, the generality of graded retrograde amnesia following hippocampal damage and emphasizing the difficulties in interpreting behavioral data from conventional knockout mice. Although some may quibble with Rudy's presentation (and occasional attempted resolution) of some of these debates, it is nonetheless a refreshingly nuanced view of the current state of affairs. This dynamic view of the scientific process is further brought to life by pictures of many of the main protagonists throughout the book. From Tulving to Tonegawa and Squire to Svoboda, the reader is treated to mug shots of the famous and influential.

Given the current diversity of approaches, it is undoubtedly a daunting task to bring together contemporary studies of the neurobiology of learning and memory into a single tome. Rudy readily acknowledges that he covers this expansive field with relatively broad brushstrokes, hesitant to become bogged down in technical detail. The advantage of this strategy is that it makes the material readily accessible for both undergraduate- and graduate-level students. Unavoidably, however, there are some notable omissions. Most notably, the book is nearly exclusively focused on rodent studies. Although we unquestionably benefit from Rudy's extensive knowledge of this literature, this narrows the focus somewhat (especially at the expense of more molecular analyses in flies, sea slugs and worms). Furthermore, several very active subfields in learning and memory are conspicuous in their absence. For example, when outlining the types of computations carried out by medial temporal lobe structures such as the hippocampus and entorhinal cortex, there is surprisingly no discussion of place cells or grid cells. Likewise, aficionados of adult neurogenesis might be disappointed that this major form of structural plasticity is not discussed in the book.

These omissions aside, there is still more than enough here for students of learning and memory. The real strength of this book is in placing contemporary, molecular-centric studies of learning and memory in a broader historical context, that is, tracing a path from eIF2alpha to Ebbinghaus. ■

Paul Frankland is in the Program in Neurosciences and Mental Health at The Hospital for Sick Children, 555 University Avenue, Toronto, ON, M5G 1X8, Canada. Karim Nader is at the Department of Psychology, McGill University, 1205 Dr. Penfield, Montreal, QC, H2A1B1, Canada.
e-mail: karim.nader@mcgill.ca