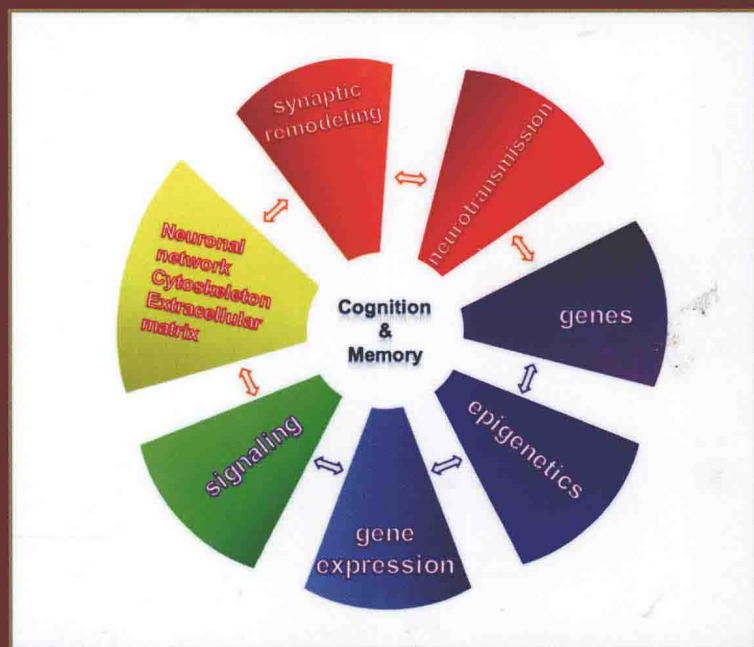


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VOLUME 122

MOLECULAR BASIS OF MEMORY

EDITED BY
ZAFAR U. KHAN
E. CHRIS MULY



VOLUME ONE HUNDRED AND TWENTY TWO

PROGRESS IN MOLECULAR BIOLOGY AND TRANSLATIONAL SCIENCE

Molecular Basis of Memory

Edited by

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MOLECULAR BIOLOGY
AND TRANSLATIONAL
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Molecular Basis of Memory

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PREFACE

Life is all memory, except for the one present moment that goes by you so quickly you hardly catch it going.

Tennessee Williams

Memory is central to our conceptualization of who we are as individuals. Memories of our childhood, of our experiences, and of our accomplishments are, for all intents and purposes, our identity. Memory allows us to place ourselves in the context of a family and society, and without a memory of our past, we could not effectively navigate our present nor plan for our future. Modern society places increased demands on memory as people are now called upon to have more information memorized than in centuries past. Furthermore, modern hygiene and health care have dramatically lengthened life expectancy over the past century, resulting in an increase in the number of people with memory impairment. Thus, there is a pressing and increasing need to identify strategies to optimize and preserve memory function.

In this volume, recent research is presented and reviewed which has pushed our understanding of memory processes beyond circuit activity to the underlying molecular mechanisms. It begins with a review of memory impairment in aging and disease (Chapter 1) and then examines the role of individual kinases and transcription factors shown to play a role in memory processes (Chapters 2–4). The molecular mechanisms of synaptic plasticity and its role in memory are then considered (Chapters 5–6). The next section considers the interface between molecules and circuits in different types of memory processes (Chapters 7–10). The volume concludes with considerations of the contributions of epigenetic studies and optogenetic approaches to the study of memory and a proposed hypothesis to link molecular synaptic changes to changes integrated into complex neural circuits (Chapters 11–13). It is our hope that this volume will provide a useful overview to the current state of knowledge in a rapidly evolving field with tremendous potential to translate into clinical benefits.

E. Chris Muly and Zafar U. Khan

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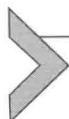
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Memory Deficits in Aging and Neurological Diseases

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Abstract

Memory is central to our ability to perform daily life activities and correctly function in society. Improvements in public health and medical treatment for a variety of diseases have resulted in longer life spans; however, age-related memory impairments have been significant sources of morbidity. Loss in memory function is not only associated with aging population but is also a feature of neurodegenerative diseases such as Alzheimer's disease and other psychiatric and neurological disorders. Here, we focus

on current understanding of the impact of normal aging on memory and what is known about its mechanisms, and further review pathological mechanisms behind the cause of dementia in Alzheimer's disease. Finally, we discuss schizophrenia and look into abnormalities in circuit function and neurotransmitter systems that contribute to memory impairment in this illness.

1. INTRODUCTION

Intact memory function is critical to carry out daily life activities, such as managing finances, remembering to take medications, driving, remembering a grandchild's birthday, and learning to use a new computer. Deficits in memory function are seen in aging and Alzheimer's disease but are also features of other psychiatric and neurological disorders. Mental retardation, autism, attention deficit disorder, learning disability, schizophrenia, and depression all have memory components, as do Parkinson's, Huntington's, and other neurodegenerative diseases. It is believed that memory deficits arise from aberrant activity in neuronal networks and diminished synaptic activity.¹ Active synaptic remodeling is essential for the formation of memories and is thought to be regulated by many biological events. These include gene expression, protein translation, protein degradation, cytoskeletal dynamics, extracellular matrix interactions, second-messenger signaling, and neurotransmitter receptor trafficking and function² (Fig. 1.1). Compromise of one or more of these interrelated biological events can hamper cognitive performance and produce memory loss.

2. MEMORY LOSS IN AGING

Aging differentially affects cognitive and neurological functioning.^{3,4} In particular, abilities reliant on processing speed such as problem solving, inhibitory function, working memory, long-term memory, and spatial ability decline with age.⁵ Aging can also affect the encoding of new information, particularly when effortful or strategic processes are required.⁶ For example, younger adults benefit from a higher degree of detailed information processing than older adults, suggesting that older individuals encode the detail of new information less thoroughly.⁷ Neuroimaging studies have shown an age-related decrease in functional activity in the medial temporal lobes and the prefrontal cortex while encoding new information and that has subsequently been linked to poorer memory performance.⁸⁻¹⁰ In general,