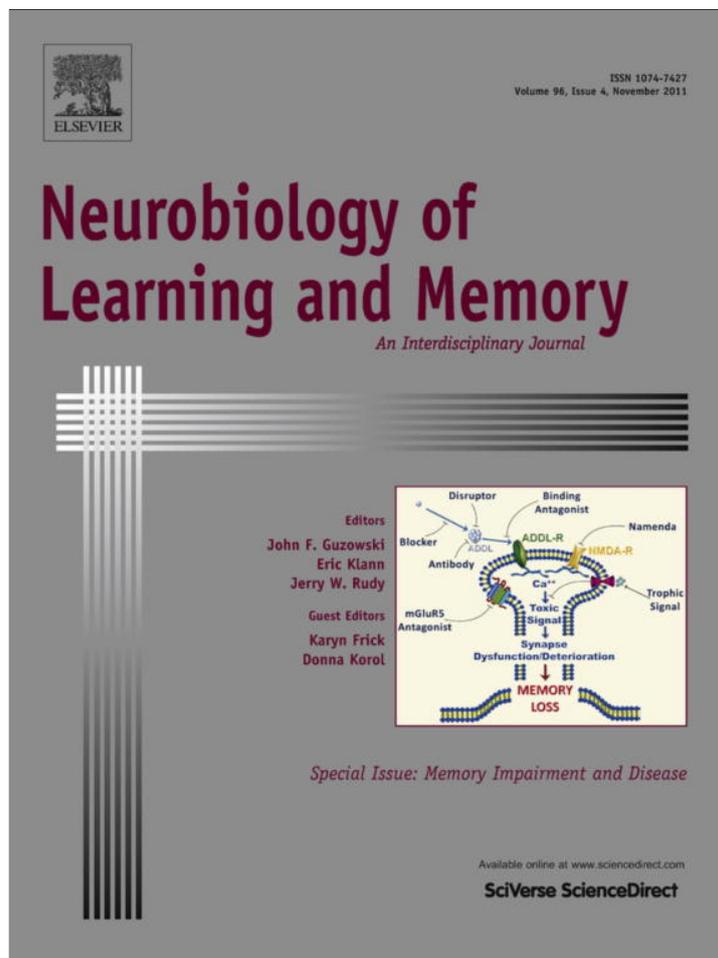


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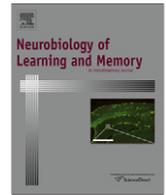
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Neurobiology of Learning and Memory

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Editorial

Introduction to the special issue of *Neurobiology of Learning and Memory* on memory impairment and disease [☆]

This special issue of *Neurobiology of Learning and Memory* highlights current research into how various diseases impair memory in humans and animal models. Our goal for this issue was to appeal to investigators from a variety of fields that have a common interest in memory disorders. Although the issue reviews diseases for which memory dysfunction is well established (e.g., Alzheimer's, chronic stress, sleep disorders), we intentionally solicited reviews on a wide range of diseases and conditions that have not historically been associated with memory loss (e.g., diabetes, metabolic disorders, Rett's syndrome) to encourage a broader consideration of how disease states affect learning and memory. Authors with expertise in disease processes were asked to provide an overview of the disease's effects on memory processes and brain function in humans and/or non-human animal models. Although the scope of this overview was determined by the authors, the articles were intended for a diverse audience of scientists interested in neural mechanisms of learning and memory. All manuscripts were peer reviewed by experts in each field and revised prior to publication. The resulting collection of papers provides readers with specific information about how each disease affects learning and memory processes, as well as a more general overview of the many ways in which disease states can affect learning and memory.

Although seemingly disparate diseases are discussed in this issue, common themes emerged. One theme that ties together the first four papers is metabolic dysfunction. Although not a unitary central nervous system disease per se, alterations in metabolism have emerged as critically important in the etiology of several neurodegenerative diseases, particularly those that present with memory dysfunction. The issue starts quite generally with a discussion by Stranahan and Mattson of memory decline in the context of impaired energy metabolism associated with diabetes and obesity. Importantly from a public health perspective, these authors focus not only on the detrimental effects of dysfunctional metabolism, but also on the potential benefits of increasing metabolism through exercise and dietary restriction. The next article by McNay and Recknagel focuses on deficiencies in insulin signaling, with a specific emphasis on type 2 diabetes. The authors synthesize the literature demonstrating that insulin, particularly intrahippocampal insulin, is a critical modulator of learning and memory processes, and argue that impaired brain insulin signaling causes cognitive impairments, including those observed in type 2 diabetes. Interestingly, insulin dysregulation has recently been implicated in the

incidence of two classic neuropathological diseases, Alzheimer's disease and schizophrenia. McNay and Recknagel's detailed discussion of diabetes sets the stage for the article by Ferreira and Klein, whose review of the literature leads them to suggest that Alzheimer's may be a form of brain-specific diabetes. Although Ferreira and Klein also provide historical background on the traditional amyloid hypothesis of Alzheimer's, they focus primarily on evidence supporting an oligomeric hypothesis positing that the disease is caused by small soluble oligomers of the amyloid beta peptide. The authors detail the pathological effects of amyloid beta oligomers and link these pathologies to those present in other diseases such as Fragile X Syndrome. The next article, by Stone and His, ties metabolic dysfunction, including diabetes and impaired glucose regulation, to the etiology and expression of schizophrenia. This article comprehensively summarizes the literature documenting verbal declarative memory deficits and hippocampal pathology in schizophrenia. Although these articles each have their own distinct focus on a different aspect of memory decline, they provide a consensus view of the importance of insulin signaling in regulating memory processes, particularly those mediated by the hippocampus, and highlight the need to better understand how insulin signaling may interact with other aspects of hippocampal function to influence the risks of cognitive decline and dementia. The work on exercise and dietary restriction discussed by Stranahan and Mattson provides avenues for lifestyle change that could significantly alter an individual's trajectory for cognitive aging.

Another theme common to several articles is sex differences in the susceptibility to or severity of diseases related to stress, depression, and addiction. The next three articles highlight emotion regulation. Murrough and colleagues discuss the cognitive biases and deficits produced by major depressive disorder, as well as recent neuroimaging data that probe the neural circuitry underlying this cognitive dysfunction. Next, McCoy and Strecker systematically delineate the detrimental effects of various types of sleep disturbances on cognitive and neural function in rodent models of human sleep loss. Marin and colleagues then describe the effects of chronic stress on hippocampal function and cognition throughout the lifespan, including discussions of early life adversity, workplace stress and burnout, and post-traumatic stress disorder. Chronic stress, depression, and lack of sleep often lead to substance abuse, and the next two articles deal with these issues. First, Vetreno, Hall, and Savage review the literature on memory impairment and pathological alterations in the hippocampus and frontal cortex induced by chronic alcohol intake in humans and animal models, differentiating between the effects of alcohol and the nutritional deficiencies that often accompany alcoholism. Next, Torregrossa, Corlett, and Taylor examine more generally the

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molecular and biochemical effects of drugs of abuse on learning and memory systems, and argue that addiction results from aberrant learning and memory processes induced by drug exposure. In search of effective therapies for addictive disorders, the authors suggest updating past treatment models focused more singly on extinction to include recent research highlighting the role and clinical relevance of reconsolidation mechanisms.

The remaining two articles focus specifically on diseases that are lesser known in terms of memory dysfunction, and serve to conclude the issue with a broader view of neuropathology. First, Foerde and Shohamy detail learning and memory deficits in patients with Parkinson's disease, using these deficits to illustrate both the unique contributions of the basal ganglia to learning and memory processes and the interactions between the basal ganglia and other memory systems. Next, Berger-Sweeney describes how a mutation in the transcription factor MeCP2 is thought to produce Rett's syndrome, an autism spectrum disorder that is a

leading cause of severe mental retardation in girls. This final review provides an overview of the cognitive impairments and neural pathologies inherent to this syndrome.

We gratefully thank the authors and reviewers who contributed to this issue and hope that readers will find it a useful reference.

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