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DENDRITE SPINES PLASTICITY IN BRAIN DISORDERS

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GENERAL INTRODUCTION TO SPECIAL ISSUE

Since the original description of dendritic spines using the Golgi impregnation method by Ramon y Cajal in the late 1800s, our knowledge of the importance of these neuronal structures in normal physiological processes and brain dysfunctions underwent tremendous advances. The development of sophisticated high resolution approaches to visualize dendritic spines, and assess their complex plastic properties and capabilities in rapid structural remodeling in response to physiological or pathophysiological changes in brain activity has led to a clear understanding that these neuronal elements are key substrates of synaptic transmission in the normal and diseased brain. Because of their abundance on dendrites of specific neuronal populations (i.e. cortical pyramidal neurons, cerebellar Purkinje cells, striatal medium spiny neurons, etc…), and the fact that they represent the main synaptic target of glutamatergic excitatory synapses in the central nervous system, dysregulation of their homeostatic properties can have dramatic influences upon normal synaptic communication, and lead to complex behavioral changes seen in neurological and neuropsychiatric disorders. At the cellular level, pruning, growth and morphological remodeling of dendritic spines are closely related to synaptic function and plasticity, thereby allowing synaptic phenomena such as long-term potentiation and long-term depression of excitatory transmission to occur and underlie complex cognitive processes associated with learning and memory. Understanding the molecular mechanisms that regulate dendritic spine plasticity and pathology is another area of rapid growth and tremendous relevance for our knowledge of the etiologies and the development of new therapeutics for brain disorders.

Taking into consideration the knowledge gained in the past decades about the importance of dendritic spine pathology in brain disorders, the main goal of this Special Issue is to provide a current overview of recent advances that have been made in our understanding of the morphological, functional and molecular underpinnings of dendritic spine alterations in various neurological and neuropsychiatric disorders (Fragile X syndrome, Schizophrenia, Depression, Huntington's disease, Aging, Drug addiction, Parkinson's disease, Alzheimer's disease, and Epilepsy). Because such advances are highly dependent on the continued development and refinement of methods that allow localizing, reconstructing, molecularly dissecting and functionally monitoring individual spines, manuscripts of this Special Issue

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are also devoted to technical breakthroughs in studies of dendritic spine architecture and dynamic regulation (3D EM reconstruction methods, Optical imaging techniques). In many reviews, authors provide a comprehensive assessment of the literature related to spine pathology in specific disorders, and discuss their current understanding of spine pathology as being the cause or consequences of brain diseases.

As is the case for most studies of the central nervous system, advances of our knowledge of the role of dendritic spines in normal and abnormal brain activity rely on the development of collaborative and multidisciplinary research programs that cut across a broad spectrum of genetic, molecular, anatomical and physiological approaches. The combination of these methods will allow dissecting out the complex substrates that mediate the unique properties of dendritic spine plasticity, and examine their relevance in the context of changes in neuronal circuits and complex brain networks that underlie neurological and neuropsychiatric disorders. Two other areas of research that warrant significant development in this field is the urgent need for more in-depth studies of spine pathologies in diseased human brains, and the development of animal models that more closely mimic the human diseased condition. These two areas are critical if one hopes to translate more efficiently knowledge gained about dendritic spine pathology in the laboratory to human brain disorders and therapeutics.