

Preface

Neuroplasticity is a key feature of adult brain function, enabling adaptation to a continuously changing environment. In the past, it was thought that this process was only significant during the developmental period, making the adult brain relatively inflexible. This idea became hard-wired in the scientific culture, as a dogma, despite evidence from 100 years ago showing that some brain cells are able to undergo mitosis. Proof that these proliferating cells become new neurons required more potent cellular imaging techniques such as confocal microscopy together with the ability to identify cells by double immunolabelling. The same applies to synaptogenesis, as evidence showing that new synapses are constantly being formed and eliminated in the brain required the development of specific novel methodologies. However, behavioral observations, showing that subjects continually learn new information and new procedures throughout their life, strongly suggested a requirement for plasticity and that neuronal changes might underlie such flexibility.

For more than 20 years, it has been recognized that these processes, while decreasing with age, occur in some specific areas of the adult brain, from early adulthood to senescence, and are necessary for behavioral and cognitive flexibility. This plasticity can be morphological, as in the generation of new synapses and new neurons or functional when the strength of synapses changes; as in long-term potentiation or long-term depression. While adult neurogenesis appears to be mainly restricted to the hippocampus and the olfactory system, synaptogenesis and its associated functional changes in plasticity occur in all cortical and subcortical areas. Thus relating these changes to a large number of divergent functions, associated with the brain areas in which this occurs. Synaptogenesis is a rapid process, as formation of new synapses or dendritic spines requires less than two hours. The functional importance of synaptogenesis is closely related to the function of the brain areas in which it takes place, and can thus provide increased flexibility when occurring in frontal or hippocampal areas, or decreased flexibility in the amygdala or some parts of the striatum. Alterations in adult neurogenesis can produce changes in cognition which might participate in the triggering of

pathological conditions such as psychiatric and neurological conditions. Some conditions such as aging or stress induce a decrease in neurogenesis and a remodelling of synaptogenesis (decreased in some regions, and increased in others).

This volume aims to provide a synthetic overview of current findings in neuroplasticity. The first part focuses on the characterization of these processes. While many aspects of memory formation and retrieval are still uncertain, it is now clear that changes in synaptic strength and the recruitment of newly formed neurons to form network units underlies many features of memory. The molecular mechanisms in the formation and regulation of these networks together with the generation of new neurons from stem cells are discussed in chapters by Mariana Carastore, Yan Gu, and Ilias Kazanis and their co authors. The chapter of Gilles Gheusi et al. investigates the characteristics of neurogenesis in the olfactory bulbs, focusing on the behavioral consequences of their functional integration. The chapter by Andrea Gómez-Palacio-Shjetnan and Martha Escobar concerns neurotrophins, particularly Brain-derived Neurotrophic Factor (BDNF) and neurotrophin-3 (NT3), and their role in the stabilization and maturation of already existing synapses, as well as in their ability to generate new synaptic contacts. This is crucial for learning and memory.

The external features of an individual's environment have a major impact on brain plasticity and this is covered in the second part of this book. The chapter by Timothy J. Schoenfeld and Elizabeth Gould provides a new view about the effects of stress and of stress hormones such as glucocorticoids on hippocampal neurogenesis. This chapter attempts to understand the paradoxical finding that certain situations, such as physical exercise or an enriched environment which induce a release of glucocorticoids actually increase neurogenesis in contrast to other stressful situations where these hormones have the opposite effect. The chapter by Michael J. Eckert and Wickliffe C. Abraham is more focused on functional plasticity; it shows how an early transient increase in cell activity might elicit long-term enhancements in cellular and network function necessary for hippocampus-dependent cognition. Subsequent chapters in this part by Peter Wigmore, Carmen Vivar and co-authors, cover the negative impact of chemotherapy on neurogenesis and memory, while physical exercise improves cognition and may in fact be a means to treat chemotherapy-induced memory decline.

The third part of the book describes alterations in brain plasticity occurring in pathological conditions including psychiatric disorders such as depression or addiction and neurological conditions such as neurodegeneration. The chapter by Francis Bambico and Catherine Belzung describes the synaptic reorganization and hippocampal neurogenesis in relation to depression and to the effects of antidepressants. It proposes a comprehensive view regarding the dynamic of these changes, suggesting that antidepressant therapy first increases synaptogenesis in frontal areas, which facilitates the initiation of recovery, and then stimulates neurogenesis, which enables the therapeutic effects to become long lasting, preventing recurrence. The chapter by Juan Canales provides evidence suggesting that hippocampal neurogenesis might be involved in the emergence and maintenance

of addictive behavior. Indeed, several components of the downward spiraling loop that characterizes addiction, including elevated sensitivity to drug-induced reward and reinforcement, enhanced neurohormonal responsiveness, emergence of a negative affective state, memory impairment, and inflexible behavior are all related to neurogenesis. Alzheimer's disease with its associated decline in cognition is a major medical concern with an increasingly aging population. The use of transgenic animal models which mimic aspects of the disease and can now be used to test potential treatments is discussed by Michael Marlatt and co-authors.

Finally, Aging and Repair are crucial processes related to neuroplasticity. The chapter by Sebastian Couillard-Despres reports studies showing a decline of hippocampal neurogenesis associated with normal aging. However, these changes probably do not underlie the decrease in cognitive function seen in older subjects, as current studies suggest a distinct role of hippocampal neurogenesis in young versus adult and old brain. Stem cell therapy offers the tantalizing prospect of repairing the damaged or degenerating brain. Rebecca Trueman and co-authors discuss the use of endogenous and transplanted stem cells to repair Parkinson's and Huntington's disease and stroke.

We have only started to understand the nature and importance of plasticity to the functioning of the brain. The ability to change and build new circuits in response to both internal and external stimuli makes the brain uniquely able to cope with the demands imposed upon it. This volume discusses recent work ranging from theoretical aspects of cognition, to the detailed cellular and molecular biology mechanisms which underlie the functional changes the brain can make. An understanding of these is now opening up avenues to influence these events in the treatment of a wide range of neurological and psychiatric conditions. These are indeed exciting times to be working on brain plasticity and neurogenesis and the authors gathered together here convey much of this excitement in what is becoming a rapidly expanding field.

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