Brain Plasticity 3 (2017/2018) 117–118
DOI 10.3233/BPL-189001
IOS Press

Introduction

The Role of Neurogenesis in Brain Disorders

Bryan W. Luikart

Embryonic and post-natal neurogenesis are necessary for the organization of neuronal connectivity and activity that underly all behaviors. It therefore is not surprising that mutations in genes or environmental insults that alter neurogenesis cause an abundance of neurological and psychiatric disorders. In this special issue of **Brain Plasticity** we have gathered review articles that focus on, **The Role of Neurogenesis in Brain Disorders**. In this issue authors discuss the function of neurogenesis in development and post development. Additionally, there is a focus on behavioral impact of post-natal neurogenesis and how insults to this system directly contributed to neuropsychiatric disorders. Finally, some articles highlight disorders where alteration of postnatal neurogenesis is not the sole, or even major, contributing factor to disease pathogenesis, yet can be used as a powerful system to study cellular changes that are generalizable across brain regions.

A basic understanding of the molecular mechanisms leading to embryonic cortical development has led to increased understanding of how mutations in genes contributing to this process contribute to diseases ranging from holoprosencephaly, developmental delay, epilepsy, and intellectual disability, to name a few. In the first article of this special issue Yabut and Pleasure review the process of embryonic neurogenesis. Specifically, they focus on the development of cortical projections neurons and the role of Sonic Hedgehog signaling in this process. Not only does this allow for an increased understanding of many neurodevelopmental disorders, it also uncovers pharmacological targets that may be leveraged to develop therapies.

The emerging field studying the interrelationship of vascular and neuronal development holds promise for understanding birth-related brain injuries such as neonatal hypoxic-ischemic encephalopathy and adult disorders such as diabetes, hypertension, and Alzheimer's disease. The article from Kirschen et al. reviews aspects of both perinatal and adult neurogenesis. They focus on the basic science of how regulation of vascular development and function impacts neurogenesis. Such work will lead to new strategies to decrease damage and increase regeneration in response to metabolic injury in the brain.

For some disorders including depression, anxiety, and addiction alteration of hippocampal neurogenesis may directly contribute to the pathophysiology of disease. Hollos et al, review the well-studied link between adult neurogenesis, depression, and anxiety. Regulation of JNK directly in newborn granule neurons alters anxiety and depression related behaviors. Takashima and Mandyam review the link of neurogenesis to addiction with a focus on methamphetamine. They discuss that neurogenesis may lead to alteration of hippocampal plasticity underlying methamphetamine relapse. Both articles discuss new drugs and drug targets that modulate neurogenesis and produce therapeutic gains in the respective disorders.

Hippocampal neurogenesis is exquisitely sensitive to alterations in neuronal activity. Danzer discusses how pathological activity, in the form of seizures, results in aberrant neurogenesis and development of newborn neurons with distinct morphological features. These abnormalities lead to alterations in circuit connectivity that favor further epileptogenesis. In support of this, Danzer discusses how mutations in genes such as Pten directly cause similar pathological changes in neurogenesis contributing to epilepsy. Thus, targeting neurogenesis directly is a promising treatment avenue for temporal lobe epilepsy.

ISSN 2213-6304/17/18/$35.00 © 2017/2018 – IOS Press and the authors. All rights reserved
This article is published online with Open Access and distributed under the terms of the Creative Commons Attribution Non-Commercial License (CC BY-NC 4.0).

Age-related decline in neurogenesis has begun to be linked to cognitive decline and neurodegenerative disorders. While cognitive decline and neurodegeneration clearly occur outside of the hippocampus, Vo et al., discuss that the protein Klotho affects adult neurogenesis and contributes to cognitive decline. The cellular effects exerted by Klotho during neurogenesis may serve as a proxy for the widespread effects of Klotho throughout the brain. In a similar line of reasoning Pircs et al. discuss the molecular influence of microRNAs on autophagy in both olfactory and hippocampal neurogenesis. This influence on autophagy regulating adult neurogenesis may directly contribute to cognitive decline and occur in other non-neurogenic areas of the brain in diseases such as Huntington's disease

In the closing article of the issue Patzlaff et al., review the basic biology of both fragile-x mental retardation (FMR) related proteins and adult neurogenesis. They then discuss evidence that FMRP and related proteins regulate adult neurogenesis and neuronal maturation contributing to the cognitive deficits observed in fragile x syndrome and more broadly to behavioral changes observed in autism spectrum disorder. Importantly, while fragile-x and autism are not considered to be specific deficits in adult neurogenesis, this work underscores the utility of this system to understand diseases effecting neural stem cells in general. Specifically, the hippocampus offers an easily accessible pool of neural stem cells in postnatal animals with an abundant toolkit for specific molecular manipulation. Mechanisms regulating adult neurogenesis are largely conserved in neurogenic niche's of the embryo thus, alterations in the more experimentally tractable adult dentate gyrus are applicable to development in general.

In conclusion, the collection of reviews in this issue of Brain Plasticity highlight the basic biology and molecular mechanisms regulating embryonic, post-natal, and adult neurogenesis. They demonstrate that perturbation of this process at any time in development can directly contribute to many neurological and psychiatric disorders. Finally, the study of neurogenesis can serve as a model system to study stem-cell and neuronal biology that is broadly applicable to understanding brain disorders that are not specifically considered deficits of neurogenesis per se.