

Adult Neurogenesis: Potential and Challenges for Therapy

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Introduction

Neural stem cells (NSCs) in the adult brain are fundamental to cognitive processes, primarily residing in the subgranular zone of the hippocampus and the subventricular zone of the lateral ventricles. These cells are in a constant state of proliferation, differentiation, and integration, leading to the generation of new neurons. This phenomenon, known as adult neurogenesis, is critical for learning, memory, and mood regulation. Various factors, including physical activity, enriched environments, and specific neurotransmitters, can positively influence neurogenesis. Conversely, detrimental factors such as stress and aging can impair this vital process. Understanding the intricate mechanisms governing adult neurogenesis is paramount for devising effective therapeutic strategies for a range of neurological disorders. [1]

The plasticity of the adult brain's neurogenic niches is profoundly shaped by external stimuli and internal physiological states. For example, engaging in learning experiences can foster the survival and integration of new neurons, vividly demonstrating the dynamic nature of adult neurogenesis. Ongoing research endeavors are actively exploring methods to manipulate these endogenous repair mechanisms for the treatment of debilitating conditions like Alzheimer's disease and depression. [2]

Aging is a significant factor that contributes to a decline in the proliferation and survival rates of neural stem cells. This age-related decline is a key contributor to the cognitive deficits observed in older adults. Consequently, investigating the molecular pathways that underlie this age-related deterioration, including alterations in growth factor signaling and inflammatory processes, is of utmost importance for developing interventions aimed at preserving cognitive function in aging populations. [3]

Physical exercise emerges as a potent stimulus for adult neurogenesis. It demonstrably influences the proliferation of neural stem cells and enhances the survival of newly generated neurons. This augmentation is believed to underlie the significant cognitive benefits associated with physical activity, such as improved learning and memory capabilities. Current research is focused on elucidating the specific types and intensities of exercise that yield the most significant positive effects. [4]

The subventricular zone (SVZ) stands out as a crucial niche for adult neurogenesis, serving as the origin of interneurons that subsequently migrate to the olfactory bulb. A comprehensive understanding of the regulatory signals operative within the SVZ is indispensable for effectively harnessing its regenerative potential for conditions that impact olfaction and other brain functions. [5]

The intricate signaling pathways that govern the fate of neural stem cells, encompassing pathways such as Wnt, Notch, and BMP, are central to the regulation of neurogenesis. Aberrations in these signaling pathways have been implicated in the pathogenesis of numerous neurological disorders, thus positioning them as

critical targets for therapeutic intervention. [6]

Neuroinflammation exerts a substantial influence on adult neurogenesis, frequently leading to its suppression. Comprehending the mechanisms by which inflammatory mediators impact neural stem cell proliferation and survival is essential for the development of strategies to counteract the detrimental effects of chronic inflammation on overall brain health. [7]

The differentiation of neural stem cells into specific neuronal subtypes represents a complex biological process that is meticulously regulated by both intrinsic cellular factors and extrinsic environmental cues. Current scientific research is dedicated to achieving precise control over this differentiation process for potential regenerative applications in diseases characterized by significant neuronal loss. [8]

Adult neurogenesis has been identified as playing a role in the pathophysiology of major depressive disorder (MDD). It is understood that antidepressant treatments, particularly selective serotonin reuptake inhibitors (SSRIs), appear to mediate their therapeutic effects, at least in part, through the promotion of neurogenesis within the hippocampus. This observation underscores the therapeutic potential of targeting neural stem cell activity for the management of mood disorders. [9]

Stem cell-based therapies offer considerable promise for the treatment of neurodegenerative diseases, including Parkinson's and Huntington's. These strategies typically involve the transplantation of neural stem cells or the stimulation of endogenous NSC proliferation with the objective of replacing lost neurons and restoring impaired brain function. However, significant challenges persist in achieving efficient engraftment, functional integration, and overall recovery. [10]

Description

Neural stem cells (NSCs) within the adult brain, predominantly situated in the subgranular zone of the hippocampus and the subventricular zone of the lateral ventricles, are characterized by continuous proliferation, differentiation, and integration to give rise to new neurons. This process, termed adult neurogenesis, holds significant importance for cognitive functions such as learning and memory, as well as for the regulation of mood. The extent of neurogenesis can be influenced by various factors; exercise, enriched environments, and certain neurotransmitters are known to enhance it, while stress and aging can lead to its impairment. A thorough understanding of these underlying mechanisms is crucial for the development of therapeutic interventions for neurological disorders. [1]

The neurogenic niches within the adult brain exhibit considerable plasticity, being significantly influenced by both external stimuli and internal physiological states. For instance, the experience of learning can actively promote the survival and integration of newly generated neurons, highlighting the dynamic and responsive nature of adult neurogenesis. Current research is actively investigating avenues

for manipulating these endogenous repair mechanisms, particularly for conditions such as Alzheimer's disease and depression. [2]

Aging is associated with a discernible decline in the proliferation and survival capabilities of neural stem cells, a phenomenon that significantly contributes to the onset of age-related cognitive deficits. Therefore, rigorous investigation into the specific molecular pathways responsible for this age-related decline, including changes in growth factor signaling and inflammatory processes, is considered critical for the formulation of interventions designed to preserve cognitive function in older individuals. [3]

Physical exercise has been recognized as a potent enhancer of adult neurogenesis. It exerts its effects by promoting the proliferation of neural stem cells and improving the survival rate of newly generated neurons. This enhancement is hypothesized to be a primary contributor to the cognitive benefits observed with regular physical activity, such as improvements in learning and memory. Research efforts are currently focused on identifying the precise types and intensities of exercise that maximize these beneficial outcomes. [4]

The subventricular zone (SVZ) represents a highly significant niche for adult neurogenesis, responsible for generating interneurons that subsequently embark on a migratory path to the olfactory bulb. A deep comprehension of the specific regulatory signals within the SVZ is deemed essential for effectively harnessing its inherent regenerative capacity, not only for conditions affecting olfaction but also for a broader spectrum of neurological issues. [5]

The complex network of signaling pathways that orchestrate neural stem cell fate, including critical pathways like Wnt, Notch, and BMP, are central regulators of neurogenesis. Disruptions or dysregulation within these pathways have been implicated in the etiology of a variety of neurological disorders, thereby establishing them as prime targets for the development of novel therapeutic strategies. [6]

Neuroinflammation plays a pivotal role in modulating adult neurogenesis, often resulting in a significant suppression of this process. Gaining a comprehensive understanding of how inflammatory mediators interact with and affect neural stem cell proliferation and survival is fundamental to devising effective strategies aimed at mitigating the adverse consequences of chronic inflammation on brain health. [7]

The differentiation of neural stem cells into distinct neuronal subtypes is an intricate biological process governed by a combination of intrinsic cellular properties and extrinsic environmental signals. Current scientific endeavors are directed towards achieving precise control over this differentiation process, with the ultimate goal of applying it for regenerative purposes in diseases characterized by substantial neuronal loss. [8]

Adult neurogenesis is increasingly recognized for its involvement in the pathophysiology of major depressive disorder (MDD). Evidence suggests that antidepressant medications, such as selective serotonin reuptake inhibitors (SSRIs), exert their therapeutic effects, at least in part, by fostering neurogenesis within the hippocampus. This linkage highlights the potential therapeutic avenues that target neural stem cell activity for managing mood-related disorders. [9]

Therapies based on stem cells hold significant promise for the effective treatment of neurodegenerative diseases like Parkinson's and Huntington's. Current strategies involve either the transplantation of neural stem cells or the stimulation of endogenous NSC proliferation to replace neurons that have been lost and to restore normal brain function. Nonetheless, substantial challenges remain concerning the achievement of efficient engraftment, successful integration, and comprehensive functional recovery. [10]

Conclusion

Adult neurogenesis, the generation of new neurons in the adult brain, occurs primarily in the hippocampus and subventricular zone. This process is vital for learning, memory, and mood regulation. It is influenced by factors like exercise and enriched environments, while stress and aging can hinder it. Research is exploring how to manipulate neurogenesis for therapeutic purposes in neurological disorders such as Alzheimer's, depression, and neurodegenerative diseases. Key signaling pathways, including Wnt, Notch, and BMP, control stem cell fate. Neuroinflammation can suppress neurogenesis, and understanding this interaction is crucial. Aging leads to reduced neurogenesis and cognitive decline. Stem cell-based therapies offer potential for treating neurodegenerative conditions, though challenges in engraftment and integration persist. Targeted differentiation of neural stem cells is also an area of active research.

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Conflict of Interest

None.

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