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Review Article

Neurogenesis- An Overview

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Abstract

Neurogenesis is a phenomenon that involves the formation of new neurons in the brain by neural stem cells (NSCs). Investigators have confirmed that neurogenesis occurs in discrete parts of the adult brain as opposed to the embryos [1]. However, this was not the case long time back. Researchers have always been interested in learning if humans or other large organisms could show regenerative properties like the one seen in specific small organisms which can regrow different parts of their own bodies [2]. If possible, this would lead to a new avenue in therapeutics as more scientists would try to stimulate regeneration to deal with injury or any harmful stimuli. Like mentioned previously, researchers were not convinced with this approach and deemed that there is no possibility of adult neurogenesis [3].

Keywords: Neurogenesis; Degenerative diseases; Progenitor cells; Alzheimer disease.

Introduction

Researchers demonstrated that there are undifferentiated and differentiating cells in the hippocampus region of rats [4]. This finding debunked the previous hypothesis that no neurogenesis takes place in the adult rodent brain. This finding also motivated other researchers to look deeper in the aspect of adult neurogenesis to determine whether it would have any potential for repair or regeneration of neurons, astrocytes, or oligodendrocytes in some of the most common neurodegenerative disorders.

Research further demonstrated that neurogenesis develops primarily in the dentate gyrus (sub-granular zone) and the sub-ventricular zone of the lateral ventricle. The major regulators of adult neurogenesis are growth factors, neurotrophins, cytokines and hormones [5]. In vivo studies have shown that folate plays a critical role in DNA methylation and epigenetic phenomenon

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with the CNS together with vitamins B-6 and B-12, which is critical for the upkeep of adult neurogenesis [6]. Neural stem cells within the embryonic and early postnatal murine brain produce neurons and glia, including astrocytes and oligodendrocytes [7]. The transformation of multipotent and proliferative NSCs to fully differentiated nerve cells is tagged "neurogenesis" [8]. Neurogenesis in humans begins from gestational week 10 and ends around gestational week 25 [9].

Discussion

Compared to humans, researchers also reported that adult neurogenesis also takes place in monkeys, specifically in marmosets and macaques [10,11]. But when the rate of neurogenesis between adult monkeys and adult mice were compared, it was seen that the rate of neurogenesis in adult monkeys was a lot lower than that in mice. Some researchers also went ahead and stated that in adult monkeys, the rate of neurogenesis keeps on declining as the monkeys get older [12]. Same group of researchers also reported that the rate of neurogenesis in adult mice also keeps reducing as they get older.

Neurogenesis in the adult hippocampus declines with age, a process that has been compromised in cognitive and emotional impairments [13]. However, the mechanisms underlying this decline have stayed elusive [14]. Disruption of neurogenesis and origination of aging-associated behavioral behaviors occurs due to deletion of the nuclear envelope proteins in neural stem or progenitor cells [15], as well as altered nuclear shape and size [16,17]. It is shown that the age-related downregulation of Lamins in ANSPCs (adult neural stem or progenitor cells), underlies growth-related alterations in adult hippocampal neurogenesis [13]. Results relate the excessive levels of Lamins in ANSPCs and untimely differentiation and controlling the maintenance of ANSPCs in the brain. Advanced loss of Lamins in ANSPCs progressively promotes neurogenesis but eventually depletes it [18,19]. Altogether, results indicate that the reduction in Lamins buttresses stem cell aging; this influences the homeostasis of neurogenesis in adults and mood synchronization [20].

Due to such advances, researchers started looking at the rate or potential of neurogenesis in different diseases. They wondered if it is possible to enhance or improve neurogenesis in diseases where the neurons die due to various reasons. Different studies showed that the results are variable in terms of whether neurogenesis increases or decreases in different diseases. For example, researchers have shown that rate of neurogenesis decrease in some cultures representing Alzheimer disease (AD) pathology, whereas some mouse models mirroring AD pathology showed increased rate of neurogenesis [21,22]. In another culture system of AD, it was shown that the rate of neurogenesis increases based on the genetic makeup of the cultured neurons [23].

Similar contradictory reports are present when rate of adult neurogenesis is determined in Parkinson's disease (PD). Two papers showed that the rate of neurogenesis is reduced or there is no change in PD [24].

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Neuronal differentiation is also observed to be altered in human induced pluripotent stem cells (iPSC) derived dopaminergic neurons in the context of PD [25,26] also observed when glutamatergic neurons were transdifferentiated into dopaminergic neurons [27,28]. Mouse models of PD showed there is less amount of neurogenesis in older mice [29], as well as different protein accumulation was significantly toxic to the neurons [30]. It is, however, clear if this strategy is to be considered as a therapy approach, more work needs to be performed to determine whether adult neurogenesis is affected in neurodegenerative disorders, till then more emphasis needs to be given to identifying biomarkers to predict the disease at an earlier stage [31] or use the differentiated neurons as tools to test different drug candidates [32], as it has been demonstrated that neurons are affected differently [33].

Conclusion

Till then, neurogenesis can be boosted in various conditions such as fasting and physical exercise. Exercises, especially aerobic activity, have been proven to have a hands-down profound effect on neurogenesis [34]. Intermittent fasting boosts the development of brain stem cells to mature neurons [35]. This theory, however, contributes to the aspect of adult neurogenesis in the human brain. Therefore, understanding this process on a physiological level will be critically important in reducing the rate of degenerative diseases.

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