



# Can Adult Neurogenesis Be Considered as Neuroplasticity?

Hamidreza Famitafreshi<sup>1</sup> and Morteza Karimian<sup>2,\*</sup>

<sup>1</sup>Physiology Department, Tehran University of Medical Sciences-International Campus, Tehran, Iran

<sup>2</sup>Physiology Department, Tehran University of Medical Sciences, Tehran, Iran

\*Corresponding author: Physiology Department, Tehran University of Medical Sciences, Tehran, Iran. Fax: +98-2166419484, Email: karimian@tums.ac.ir

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## Abstract

Neuroplasticity is defined as adaptive changes in the sub-structures of synapses. Neuroplasticity is an important capability of the brain to respond to new stress. Stress can range from environmental changes to organic damages. Neurogenesis defined as the generation of new neurons in some parts of brain regions, especially the dentate gyrus of the hippocampus and sub-ventricular zone, can be considered as neuroplasticity. Neurogenesis facilitates the brain's adaptive response to new stress by integrating new neurons into related areas. In this review, we recall some aspects of neurogenesis that may be considered as neuroplasticity.

**Keywords:** Neuroplasticity, Neurogenesis, Stress, Memory, Hippocampus, Stroke

## 1. Context

Neuroplasticity refers to changes in the neuronal function as the consequence of the ever-changing environment (1). It means that as long as environmental changes persist, the changes in neuronal function persist (2). Therefore, the adaptation to the alteration of the environment causes neurons to change their functions as the consequence of synaptic changes (3). The changes in synapses can alter neuronal function in such a way that they adapt to the new condition (4). Since this phenomenon is present in all parts of the nervous system, it causes a wide variety of outcomes in different parts of the central nervous system (CNS) (4-6). Neurogenesis defined as the production of new neurons is associated with the alteration of brain function; thus, neurogenesis can be considered as neuroplasticity that changes in accordance with some conditions (7).

## 2. Neurogenesis

Neurogenesis is defined as the production of new neurons in some parts of brain regions (8-10). Neurogenesis occurs in some parts of brain regions including the sub-ventricular zone (7), dentate gyrus (7), striatum (11), and substantia nigra (12). Neurogenesis in the olfactory bulb is considered a very quiescent phenomenon (13). Neurogenesis reduces with increasing age (9). One of the important aspects of neurogenesis that might be considered as neuroplasticity is the continuous generation of new neurons accompanied by behavioral changes. We know that neuroplasticity is defined as changes in synaptic structures (14)

and the addition of new neurons to previous existing neurons is a less specific definition. However, based on new experiments that considered a function for all neuronal subtypes including neurons in all stages of maturation, neurogenesis can be considered as neuroplasticity (15). From this view, a newly born immature neuron has a specific function that is different from the function of mature neurons (16). Moreover, if we consider that adaptation to the environment that is one of the most striking features of neuroplasticity (17) also occurs in neurogenesis, neurogenesis in this regard can be considered as neuroplasticity.

## 3. About the Generation of New Neurons

The concept of neurogenesis is derived from Altman studies that proposed for the first time that new neurons in later adulthood are generated in some parts of the brain region (18). Later on, many studies were performed to find out the nature of this phenomenon. The origin of newly born neurons in the CNS is thought glial-derived cells. Experiments have shown that a glial-like cell is a primary cell in this regard. This glial-like cell will eventually be differentiated into both glial cells and mature neurons (19). However, an important point in this regard is to answer the question that what are the characteristics of new neurons that are integrated into pre-existing circuits. There is an important question about the direction of migration that is an important determinant of fates of newly born neurons. For example, radially directed migrating neurons eventually show interneuron characteristics (20). The ma-

jority of these cells will show GABAergic, dopaminergic, and glutamatergic neurons (21). Immature neurons will be integrated into the pre-existing circuit and become mature. There is a difference in the fate of newly born neurons in different parts of the CNS. In dentate gyrus of the hippocampus, immature neurons will develop new processes such as dendrites and axons that are necessary for integrating into new circuits (22). GABAergic interneurons have a critical role in activating the quiescent neurons (23). Of course for the generation of new neurons, efficient neurogenic niches are necessary (7). They are composed of various cells such as endothelial cells, different types of glial neurons, and ependymal cells. These niches must be efficacious for neurogenesis.

#### 4. Neurogenesis and Stress

Stress is defined as any issue that causes hemostasis to alter and this, in turn, causes the body to respond in several manners to keep hemostasis in equilibrium (24). In this regard, allostatic is the reaction of the body to stress to keep the body in a steady-state (25). In this sense, adaptation occurs to combat unwanted stress (26, 27). One of the main responses of the body to stress is changes in neurogenesis to neutralize the stress (28-30). In different paradigms of behavioral experiment, it has been shown that stress will influence neurogenesis and causes psychiatric symptom development and in many others, the symptoms will not develop (31, 32). The hippocampus is a brain region known to be important to combat the negative effects of stress (31, 33). Neurogenesis that occurs in the hippocampus plays an important role in this regard. Neurogenesis in the hippocampus has shown to be important for the regulation of many stress response phenomena (34). The evidence that supports this theory is that many stress-exposed animals will eventually develop anxiety-related disorders (35). However, many of them will not develop anxiety-related responses (36, 37). This is probably because molecular mechanisms that regulate neurogenesis interfere with the severity of the response to stress (38).

#### 5. Neurogenesis and Psychiatric Disorders

Psychiatric disorders encompass a great proportion of human diseases (39). Neurogenesis can control the development of psychiatric disorders and this may offer neurogenesis a regulator function (40). It may be considered as neuroplasticity. Neurogenesis alteration can alleviate many psychiatric disorders (41-44). Depression as one of the most common diseases has shown to be alleviated with increasing neurogenesis (45). However, other psychiatric diseases may benefit by increasing neurogenesis.

For example, schizophrenic patients may benefit from antipsychotic drugs by increasing neurogenesis (46). Post-traumatic stress disorder (PTSD), uncontrollable expression of fear in neutral and safe environments may benefit from the improvement of neurogenesis (47). An important concept in this regard is that hippocampal neurogenesis can modulate emotional responses (48). Other anxiety-related disorders can be influenced by hippocampal neurogenesis (49). An important point in this regard is that many psychiatric diseases co-morbid with another one (50-52). Thus, there is strong evidence that neurogenesis is a modulator or at least can alleviate psychiatric comorbidities. Also, drug addiction is another reflection of this issue. Overall, drugs are the most potent modulators of neurogenesis to suppress it (53, 54). The suppression of neurogenesis, in turn, may cause various psychiatric comorbidities such as depression and anxiety disorders (55, 56).

#### 6. Neurogenesis and Cognition

Memory and cognition as essential functions of the brain that are necessary for life are regulated by neurogenesis (57, 58). Memory formation involves some parts of brain regions (59). Neurogenesis in the hippocampus is a dynamic process that improves memory with the addition of new neurons (60). It has been shown that the improvement of memory with various drugs is accompanied by an increase in neurogenesis (61, 62). The complex nature of memory formation inside the hippocampus offers neurogenesis a neuroplasticity function. Memory formation inside the hippocampus involves all parts of the hippocampus encompassing the dentate gyrus of the hippocampus, CA1, CA2, CA3, and CA4 (63-65). The integration of new neurons to all parts of this circuit will improve memory (66). Memory is an important brain function that is needed for adaption to the new environment probably by avoiding unwanted stressors (67-69). Memory is necessary for various functions and neurogenesis has an important adaptive function in memory regulation. The flexibility of cognition is an important concept that offers the hippocampus an important ability to cope with various situations (70, 71). A common issue in this regard is the pattern separation (72, 73).

#### 7. Neurogenesis and Stroke

Besides the hippocampus, neurogenesis occurs in other parts of the brain such as the sub-ventricular zone (74). Experiments have shown that the improvement of neurogenesis in the sub-ventricular zone (75) and striatum (76) in the infarcted area significantly reduces the infarct

size. However, the improvement of stroke with improving neurogenesis through various mechanisms may signify the role of mediators that confer neuronal maturation and alternation in peri-infarcted areas (77-79). Stroke as the second leading cause of death (80) is an important issue to be studied and the sub-ventricular zone and striatal neurogenesis derive many defensive mechanisms in this regard.

## 8. Neurogenesis in Other Areas

In addition to the dentate gyrus of the hippocampus and sub-ventricular zone, neurogenesis also occurs in the striatum (11) and substantia nigra (12). The occurrence of neurogenesis in other areas besides the two mentioned areas may signify the importance of this phenomenon for the brain to show a great potential to regenerate the injured and impaired areas. Other places besides the mentioned areas are plausible for neurogenesis. This reflects the adaptive function capabilities of the brain to stress and unwanted injuries.

## 9. Conclusions

Overall, the importance of neurogenesis in brain function was discussed. Neurogenesis plays an important role in regenerating the injured areas of the brain. It may give the brain an additional function and may strengthen its existing functions. It should be noted that when there is no stress, neurogenesis is a quiescent phenomenon with no definite function. Therefore, it cannot be considered as neuroplasticity to help the brain overcome the stress. Neuroplasticity defined as the alternation of the brain in response to new stress can be used for neurogenesis since neurogenesis prepares the brain to face new stress that may be opposed to life.

## Footnotes

**Authors' Contribution:** This manuscript was written in collaboration between two authors. Hamidreza Famitafreshi selected the subject, collected the references, and wrote the first draft of the manuscript with the assistance of Morteza Karimian. Both authors read and approved the final draft of the manuscript.

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