ROSTRAL MIGRATORY STREAM: HIGHWAY NEUROGENESIS

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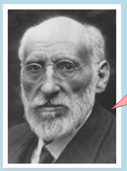
Santiago Ramón y Cajal [1]



There is no ability to generate new neurons in adults

1. INTRODUCTION

Neurogenesis is defined as a process of generating functional neurons from neural stem cells. Traditionally it is thought to occur only during embryonic and perinatal stages. Altman's pioneered studies provided the firsts evidence for the presence of newly generated neurons in adults. This discovery denied the main dogma of neuroscience, since from Ramón y Cajal it was kept that the central nervous system was unable to generate new neurons in adult stages.

The aim of this study is to provide a current view of neurogenesis, the factors that modulate it, focusing on the subventricular zone (SVZ) and the migration that occurs to the olfactory bulb (OB) via a single path in the brain: the rostral migratory stream (RMS) (Figure 4).

Thanks to experiments in adult rats it has been shown that there is generation of new neurons in adults.

Joseph Altman [2]

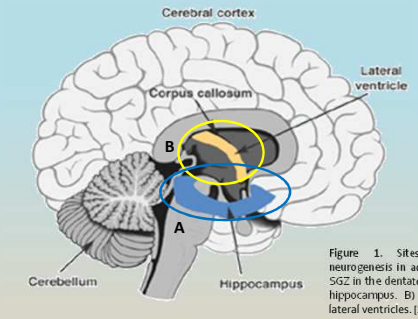


Figure 1. Sites of adult neurogenesis in adult brain. A) SGZ in the dentate gyrus of the hippocampus. B) ZSV of the lateral ventricles. [3]

2. NEUROGENIC ZONES

Two neurogenic zones persist in the adult brain (Figure 1):

A. **Subgranular zone** (SGZ) in the dentate gyrus of the hippocampus → generate dentate granule neurons.
B. **Subventricular zone** (SVZ) of the lateral ventricles → generate periglomerular and granule interneurons.

We also find **neurogenic niche**: a specialized microenvironment that regulate neural stem cells activity such as maturation and formation of the neural network. It is a highly dynamic center for complex biochemical signalling and cellular interaction.

The new neurons are produced by progenitor cells which are derived from stem cells. These are self-renewing and multipotent cells (Figure 2).

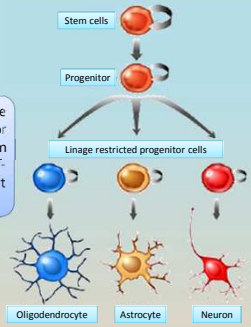


Figure 2. Production of neurons from stem cells. [4]

3. SUBVENTRICULAR ZONE

SVZ is situated throughout the lateral walls of the lateral ventricles. Different cell types are described in this zone (Figure 3):

- Type B cells or radial glia-like slow proliferating cells.
- Type C cells or transit amplifying cells.
- Type A cells or neuroblasts.
- Type E cells or ciliated ependymal cells . These cells lining the ventricular wall.

B → C → A

Type B cells are the stem cells with astrocytic properties. These cells are in close association with ciliated ependymal cells. Type B cells generate type C cells.

Transit amplifying cells (type C cells) divide quickly and give rise to type A cells.

Neuroblasts (type A cells) originated from type C cells ,migrate through the RMS to OB.

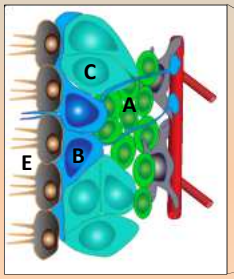
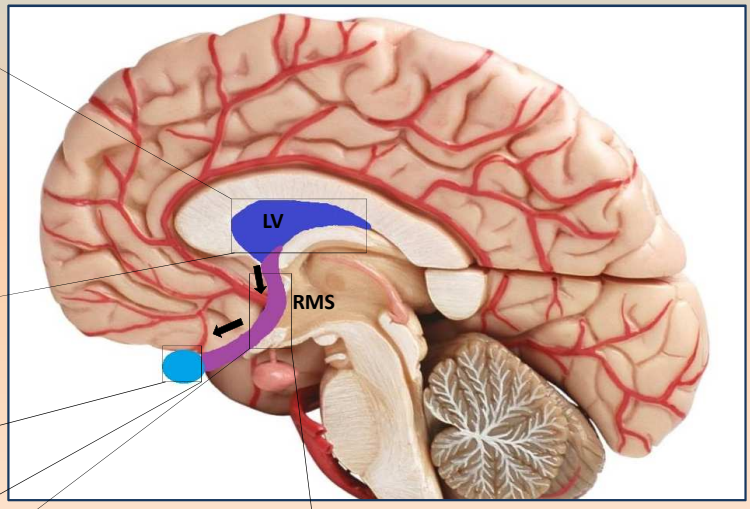


Figure 3. Neural stem cells niche in the SVZ. There are stem cells with astrocytic properties (B) that express GFAP, transit amplifying cells (C) that express Nestina, neuroblasts (A) that express PSA-NCAM and ciliated ependymal cells (E). Type B cells are in contact with blood vessels (red) through cytoplasmic projections. [5]



5. OLFACTORY BULB

Once neuroblasts reach the OB, stop their tangential migration, they separate from the chains and start to descend radially into the different bulbar layers where they differentiate into interneurons (Figure 6).

- Granule cell layer → granule cells
- Glomerular layer → periglomerular cells

Interneurons integrate into the existing neuronal circuitry perfectly maintaining homeostasis in the region.

It is thought that the functions of new neurons are:
- Maintenance of structural integrity of the OB.
- Olfactory discrimination.
- Modification of sexual behavior.

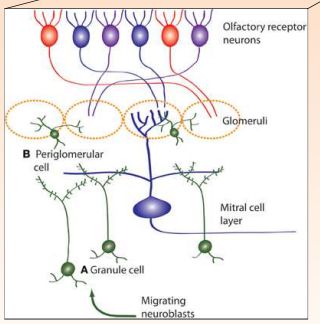


Figure 6. Neuroblasts migrate to the OB from the SVZ, then differentiate and integrate into the OB circuitry. Newborn neurons in the OB become granule cells (A) and periglomerular cells (B). [7]

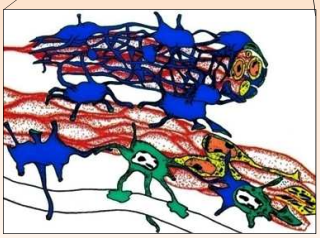


Figure 5. RMS chain migration. Neuroblasts migrate along each other to form long chains. Chains of migrating cells (red) are ensheathed by glial cells (blue) that have astrocytic characteristics. It can see a blood vessel (white) parallel to the path. Astrocytes with his endfeet encircling endothelial cells. They may serve as an interface to modulate influences of endothelial and circulation-derived factors as well as the availability of cytokines and growth factors in the basal lamina and aid to maintenance the blood–brain barrier. [8]

4. ROSTRAL MIGRATORY STREAM

One of the major neuronal migration pathway is the one used by neuroblasts to reach the OB. Neuroblasts migrate tangencially along each other to form long chains to facilitate locomotion (Figure 5).

RMS is set of:
- Neuroblasts
- Parallel blood vessels to the path
- Astrocytes that configure glial tubes

Beating of the cilia of ependymal cells of the SVZ appears to set up concentration gradients of guidance molecules to lead migration of neuroblasts to the OB.
Interaction between endothelial cells of blood vessels and glial tubes of RMS → form neurovascular niche.
Endothelial cells play an outstanding role in regulating proliferation, survival and migration of neuroblasts.

6. MOLECULAR MECHANISMS REGULATING ADULT NEUROGENESIS

Extracellular players	Intracellular players	Environmental players
• Genetic factors: morphogens • Growth factors • Neurotransmitters • Age	• Cell cycle regulators • Transcription factors • Epigenetic regulators	• Brain injuries • Neurological diseases

7. CONCLUDING REMARKS

Thanks to the early studies conducted by Joseph Altman in the 1960s was confirmed the **existence of neurogenesis** throughout life of adult stages of mammals, including humans.

The new neurons generated in SVZ must carry out one of the **biggest migrations** that take place in the brain. Therefore, they are introduced to the RMS and together with the blood vessels will set up an integration that directs the migration.

Once the new neurons arrive in OB are **integrated perfectly** in the predetermined circuit respecting the homeostasis of the area.

Despite the proven existence of neurogenesis in humans, it is still in doubt the **functions of the new neurons** integrated in the OB. It has to be taken into account that the OB suffers a regression in humans.

The neurogenesis is a potential **therapeutic target** to treat both neurodegenerative and other neurological diseases.

REFERENCES

[1] http://cvc.cervantes.es/ciencia/cajal/cajal_recuerdos/introduccion_18.htm

[2] http://www.diariodemallorca.es/ultima/2011/10/19/triste-abandonar-curiosidad-aprender/712860.html

[3] Crews, FT. and Nixon, K. Alcohol, neural stem cells, and adult neurogenesis. *Alcohol Research and Health* 27.2 (2003): 197-203.

[4] http://neurogenesis101.weebly.com/what-is-neurogenesis.html

[5] Ming, G. and Song, H. Adult neurogenesis in the mammalian brain: significant answers and significant questions. *Neuron* 70.4 (2011): 687-702.

[6] http://curiosidades.batanga.com/4262/mitos-sobre-el-cerebro-humano

[7] Konefal, S., Elliot, M. and Crespi, B. The adaptive significance of adult neurogenesis: an integrative approach. *Frontiers in neuroanatomy* 7 (2013).

[8] Alvarez-Buylla, A. and García-Verdugo, JM. Neurogenesis in adult subventricular zone. *The Journal of neuroscience* 22.3 (2002): 629-634.