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Neurosciences

Neurogenesis in the adult central nervous system

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Abstract

Contrary to the long-held dogma, neurogenesis occurs throughout adulthood, and neural stem cells reside in the adult central nervous system (CNS) in mammals. The developmental process of the brain may thus never end, and the brain may be amenable to repair. Neurogenesis is modulated in a wide variety of physiological and pathological conditions, and is involved in processes such as learning and memory and depression. However, the relative contribution of newly generated neuronal cells to these processes, as well as to CNS plasticity, remains to be determined. Thus, not only neurogenesis contributes to reshaping the adult brain, it will ultimately lead us to redefine our knowledge and understanding of the nervous system. ***To cite this article: P. Taupin, C. R. Biologies 329 (2006).***

Résumé

Neurogenèse dans le système nerveux central adulte. Contrairement au dogme, la neurogenèse se déroule tout au long de la vie dans le cerveau, et des cellules souches neuronales résident dans le système nerveux central (SNC) chez les mammifères adultes. Le processus de développement du cerveau ne s'arrêterait donc pas, et le cerveau serait capable de se réparer. La neurogenèse est modulée dans une grande variété de conditions physiologiques et pathologiques, et est impliquée dans les processus d'apprentissage et de la mémoire et la dépression. Cependant, la contribution relative des cellules nouvellement générées dans ces processus, mais aussi dans la plasticité du SNC, reste à déterminer. Ainsi, non seulement la neurogenèse contribue à remodeler le cerveau adulte, mais aussi elle nous amènera à redéfinir nos connaissances et compréhension du système nerveux. ***Pour citer cet article : P. Taupin, C. R. Biologies 329 (2006).***

Keywords: Neurogenesis; Neural stem cells; Hippocampus; Development; Regeneration; Cellular therapy; Transplantation

Mots-clés : Neurogenèse ; Cellules souches neurales ; Hippocampus ; Développement ; Régénération ; Thérapie cellulaire ; Transplantation

1. Introduction

Neural stem cells (NSCs) are the self-renewing, multipotent cells that generate the main phenotypes of the nervous system (Fig. 1). During development, NSCs

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participate to the formation of the nervous system. It was believed that the generation of neuronal cells in mammals was mostly limited to the pre-natal phase of development, and that the adult brain was devoid of stem cells, and thus of the ability to make new nerve cells and regenerate after injuries [1]. Seminal studies in the 1960s, that were substantiated in the 1970s and 1980s, reported that neurogenesis occurs in discrete areas of the adult brain in rodents [2–6]. With the advent of new methods for labelling dividing cells, such as 5-bromo-2′-deoxyuridine (BrdU, Fig. 1) labelling, retroviral labelling and confocal microscopy, investigators have confirmed that neurogenesis occurs in discrete areas of the rodent brain throughout adulthood [7–12], and reassessed and presented evidences that adult neurogenesis also occurs in primates, humans and non-humans [13–15]. BrdU is a thymidine analogue used for birth-dating and monitoring cell proliferation [16]. BrdU is generally administered intraperitoneally; it inserts into the DNA of dividing cells, including in the central nervous system (CNS), as it crosses the blood–brain barrier [17]. It is hypothesized that newly generated neuronal cells originate from stem cells in the adult brain. A hypothesis further supported by the recent isolation and characterization of neural progenitor and stem cells from the adult brain [18,19]. The confirmation that neurogenesis occurs in the adult brain and NSCs reside in the adult CNS have profound implications for our understanding of brain development and functioning, as well as for cellular therapy in the CNS.

2. Neurogenesis in the adult brain

Neurogenesis occurs in two forebrain regions of the adult brain: the subventricular zone (SVZ) and the dentate gyrus (DG) in various species [20]. Of these two regions, the SVZ harbours the largest pool of dividing neuronal progenitor cells in the adult rodent brain [21,22]. Newly generated neuronal cells in the SVZ migrate to the olfactory bulb (OB) through the rostro-migratory stream (RMS), where they differentiate into granule and periglomerular neurons of the OB,

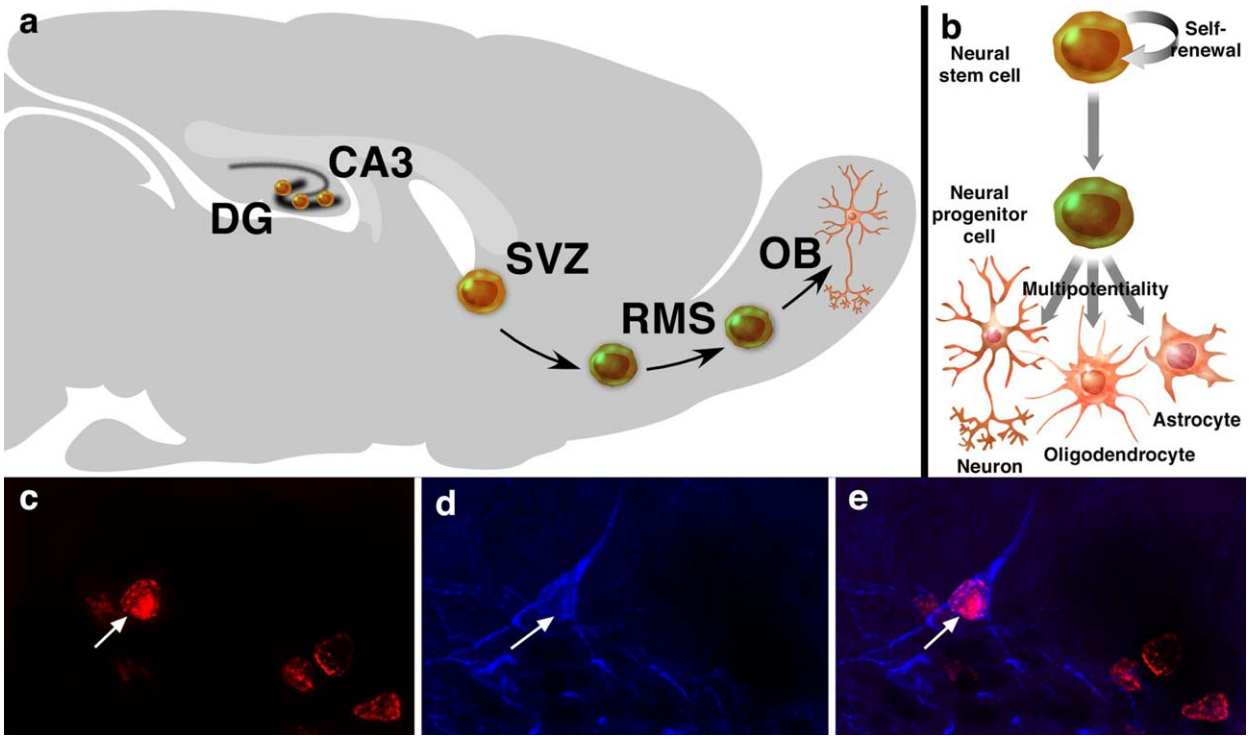

Fig. 1. Neurogenesis and neural stem cells in the adult brain. Neurogenesis occurs mainly in two areas of the adult brain, the DG and the SVZ. In the DG, new neuronal cells are generated in the subgranular zone. In the SVZ, newly generated neuronal cells migrate to the OB, through the RMS, where they differentiate into interneurons of the OB (**a**). NSCs are the self-renewing, multipotent cells that generate the neuronal and glial cells of the nervous system. Neural progenitor cells are multipotent cells with limited proliferative capacity (**b**). 5-Bromo-2′-deoxyuridine-labelling is the standard for studying neurogenesis and its regulation. Co-labelling of a BrdU-positive cell (**c**, red, arrow) with class III β-tubulin isotype (**d**, blue) in the DG. Tuj-1 is a marker of immature neuronal cells. The merge picture shows a BrdU-positive cell also positive for Tuj-1 (arrow, **e**) in the DG, representative of a newly generated neuronal cell.