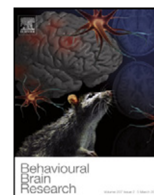
Behavioural Brain Research 227 (2012) 459–463

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr



Review

The role of neurogenesis in olfaction-dependent behaviors

Ryoichiro Kageyama[a,b,*], Itaru Imayoshi[a,c], Masayuki Sakamoto[a,b,d]

[a] Institute for Virus Research, Kyoto University, Kyoto 606-8507, Japan
[b] Japan Science and Technology Agency, CREST, Kyoto 606-8507, Japan
[c] Japan Science and Technology Agency, PRESTO, Kyoto 606-8507, Japan
[d] Kyoto University Graduate School of Biostudies, Kyoto 606-8502, Japan

ARTICLE INFO

Article history:
Received 1 October 2010
Received in revised form 5 April 2011
Accepted 24 April 2011
Available online 3 May 2011

Keywords:
Adult neurogenesis
Main olfactory bulb
Accessory olfactory bulb

ABSTRACT

Newly born neurons continuously migrate into the main and accessory olfactory bulbs and modulate the output of projection neurons. Despite some contradictory results, it is becoming clear that these newly born neurons play an important role in the response to some odorant cues. In this minireview, we discuss the recent findings surrounding the functional significance of adult neurogenesis in olfaction-dependent behaviors.

© 2011 Elsevier B.V. All rights reserved.

Contents

1. Introduction 459
2. Approaches for ablating newly born neurons 460
3. Behavioral tests for the response to chemical cues 461
4. Behavioral tests for the response to pheromonal cues 462
5. Concluding remarks 462
References 462

1. Introduction

There are many neural stem cells in two brain regions of adult mammals, the subventricular zone (SVZ) of the lateral ventricles and the subgranular zone (SGZ) of the hippocampal formation [23,36,38]. These neural stem cells are mostly quiescent under the control of Notch, Shh and BMP signaling [1,3,6,8,16,24,28] but occasionally divide to give rise to transit-amplifying cells, which proliferate and generate many neurons. Neurons born in the SVZ migrate via the rostral migratory stream into the olfactory bulb (Fig. 1), while neurons born in the SGZ migrate into the hippocampal dentate gyrus [23,38]. The functional significance of adult neurogenesis in hippocampal-dependent learning and memory has been well documented [9,38], but the role of such neurogenesis in olfactory activity is rather obscure.

The olfactory bulb consists of two structures, the main olfactory bulb and the accessory olfactory bulb (Fig. 1). The main olfactory bulb is involved in the cognitive response to chemical cues detected by the main olfactory epithelium, while the accessory olfactory bulb is involved in the instinctive response to pheromonal cues detected by the vomeronasal organ, although this functional difference between the main and accessory olfactory bulbs is not absolute [4,10]. The vast majority of neurons born in the SVZ differentiate into granule cells while others become periglomerular cells in the main olfactory bulb [23,36,38]. Some neurons born in the SVZ migrate into the accessory olfactory bulb (Fig. 1) [29]. All these neurons are local interneurons that modulate the output of projection neurons (mitral and tufted cells) [36]. Interestingly, newly born neurons exhibit different synaptic plasticity from that of mature neurons: theta-burst stimulation induces long-term potentiation in newly born neurons but not in mature neurons [27]. Furthermore, aged mice, which have more mature neurons and fewer newly born neurons than young adult mice, are impaired at fine olfactory discrimination [11,25]. These data suggest that newly born neurons might be required for optimal olfactory activity. However, the pre-

* Corresponding author at: Institute for Virus Research, Kyoto University, Shogoin-Kawahara, Sakyo-ku, Kyoto 606-8507, Japan. Tel.: +81 75 751 4011; fax: +81 75 751 4807.
E-mail address: rkageyam@virus.kyoto-u.ac.jp (R. Kageyama).

0166-4328/$ – see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.bbr.2011.04.038

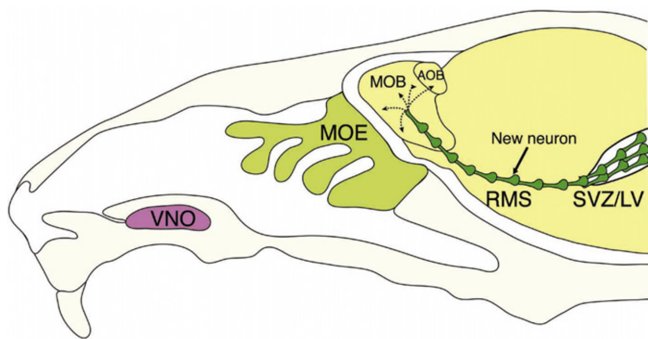


Fig. 1. Adult neurogenesis and the olfactory system. Neurons born in the subventricular zone (SVZ) of the lateral ventricles (LV) migrate via the rostral migratory stream (RMS) into the olfactory bulb. The olfactory bulb consists of two structures, the main olfactory bulb (MOB) and the accessory olfactory bulb (AOB). The main and accessory olfactory bulbs receive signals from the main olfactory epithelium (MOE) and the vomeronasal organ (VNO), respectively.

cise roles of adult neurogenesis in odor processing remain to be determined.

To understand the functional significance of adult neurogenesis in olfactory activity, researchers have used many methods to ablate newly born neurons in animals, and these animals have been used for behavioral analyses [9]. However, there are some discrepancies among the published reports of neurogenesis-dependent odor-associated behaviors, complicating the interpretation of the significance of neurogenesis. These discrepancies may be due to different ablation methods and different behavioral tests. In this minireview, we discuss the recent data about the functional significance of adult neurogenesis in olfactory activity.

2. Approaches for ablating newly born neurons

Ablation of newly born neurons has been attempted to understand their functions in the adult brain [9]. The most common ablation methods are treatments with γ-ray irradiation or anti-mitotic drugs, such as methylazoxymethanol acetate (MAM), to kill dividing neural stem/progenitor cells. For γ-ray treatment, a brain area encompassing the SVZ or SGZ is exposed to irradiation while the other brain region is protected with lead shields (Fig. 2a). This method allows region-specific inhibition of neurogenesis, although the long-term effect on the SGZ neurogenesis by the SVZ irradiation was not analyzed. For anti-mitotic drug treatment, an appropriate dose is injected subcutaneously or intraperitoneally. This method inhibits neurogenesis in both the SVZ and SGZ. Drug can be also specifically applied to the SVZ by implanting an osmotic minipump into the lateral ventricle (Fig. 2b), although neurogenesis in the SGZ is also affected to a lesser extent [5,34]. It was reported that about 60–90% of neurogenesis in the SVZ is reduced by γ-ray treatment or anti-mitotic drugs [5,12,20,34,35]. Although these methods are effective, the efficiency for inhibition of neurogenesis could be variable depending on treatment protocols, and neurogenesis could recover later because quiescent neural stem cells are rather resistant to γ-ray irradiation and anti-mitotic drugs. In addition, these treatments also cause severe side effects, such as inflammation, on mature neurons, which might affect the mood and behavior of the animals. These disadvantages may lead to inconsistency in behavior defects observed after such treatments.

To overcome such disadvantages, genetic methods for ablating newly born neurons have been developed. One such method uses Nestin-CreER^{T2} mice, which express tamoxifen-inducible Cre in neural stem/progenitor cells under the control of the Nestin promoter/enhancer (Fig. 2c). These mice were crossed with NSE-loxP-Stop-loxP-DTA (NSE-DTA) mice, in which Cre induces

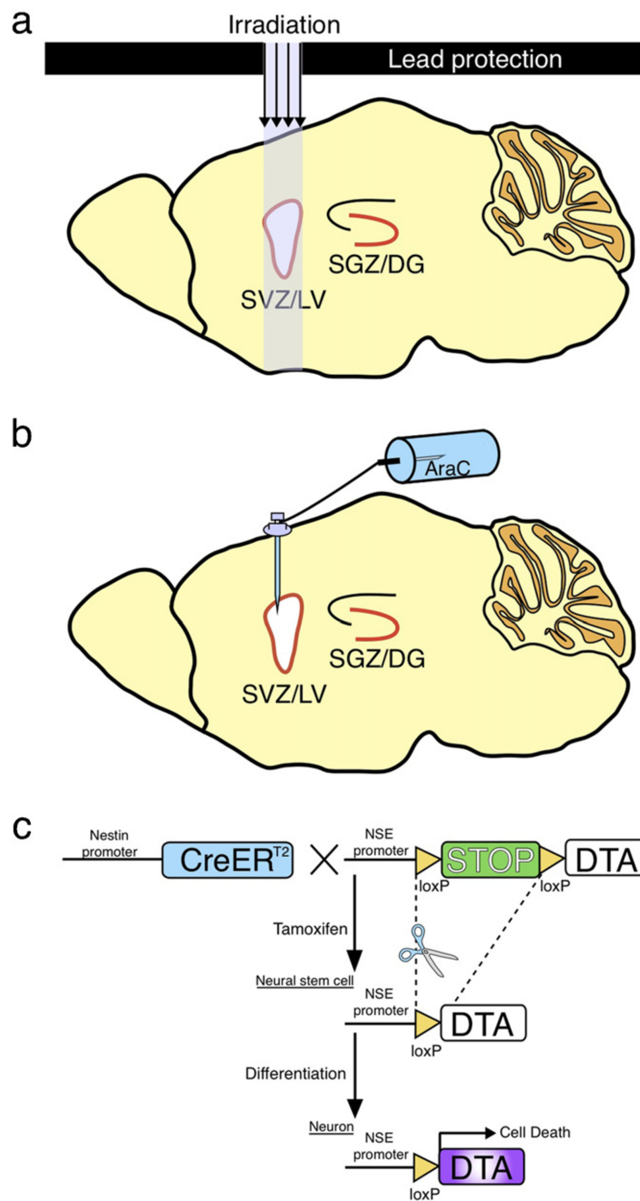


Fig. 2. Methods for inhibition of adult neurogenesis. (a) Inhibition of neurogenesis by γ-ray irradiation. A brain area encompassing the SVZ or SGZ is exposed to irradiation while the other brain region is protected with lead shields. (b) Inhibition of neurogenesis by administration of anti-mitotic drugs with an osmotic minipump. (c) Genetic ablation of newly born neurons. In Nestin-CreER^{T2};NSE-loxP-Stop-loxP-DTA mice, Cre is activated in neural stem/progenitor cells after tamoxifen administration, but DTA is not expressed in neural stem/progenitor cells because the NSE promoter is inactive in these cells. However, when these cells start neuronal differentiation, the NSE promoter becomes active and induces expression of DTA, which kills cells. Thus, in these mice, only newborn neurons are efficiently ablated after tamoxifen treatment. DTA, diphtheria toxin fragment A; NSE, neuron-specific enolase.

loxP-mediated deletion of a stop cassette and allows the neuron-specific enolase (NSE) promoter to drive expression of diphtheria toxin fragment A (DTA, Fig. 2b) [14,15]. In Nestin-CreER^{T2};NSE-DTA nice, Cre becomes active in neural stem/progenitor cells after tamoxifen administration, but DTA is not expressed in these cells because the NSE promoter is inactive (Fig. 2c). However, when the cells begin neuronal differentiation, the NSE promoter becomes active and induces expression of DTA, which kills the cells (Fig. 2c). Thus, in these mice, neural stem cells in the SVZ and SGZ do not die, but only newly born neurons are efficiently ablated after tamoxifen treatment without any noticeable side effects on mature neurons: this method achieved about 96% reduction of neurogenesis in the

Download English Version:

https://daneshyari.com/en/article/4313245

Download Persian Version:

https://daneshyari.com/article/4313245

Daneshyari.com