Brain Research Bulletin 129 (2017) 3–11

Contents lists available at ScienceDirect

Brain Research Bulletin

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

Review

Insights into age-old questions of new dendritic spines: From form to function

Laxmi Kumar Parajuli, Shinji Tanaka, Shigeo Okabe*

Department of Cellular Neurobiology, Graduate School of Medicine, The University of Tokyo, Bunkyo-ku, Tokyo 113-0033, Japan

ARTICLE INFO

Article history:
Received 8 June 2016
Received in revised form 18 July 2016
Accepted 31 July 2016
Available online 1 August 2016

Keywords:
Glutamate receptors
Live imaging
Nascent spines
Neocortex
Spinogenesis
Synapse

ABSTRACT

Principal neurons in multiple brain regions receive a vast majority of excitatory synaptic contacts on the tiny dendritic appendages called dendritic spines. These structures are believed to be the locus of memory storage in the brain. Indeed, neurological diseases leading to impairment in memory and cognitive capabilities are often associated with structural alteration of dendritic spines. While several landmark studies in the past have provided a great deal of information on the structure, function and molecular composition of prototypical mature dendritic spines, we still have a limited knowledge of nascent spines. In recent years there has been a surge of interest to understand the nascent spines and the increasing technical advances in the genetic, molecular and imaging methods have opened avenues for systematic and thorough investigation. In this review, by discussing studies from several labs including ours, we provide a systematic summary of the development, structure, molecular expression and function of nascent spines and highlight some of the potentially important and interesting research questions that remain to be answered.

Contents

1. Introduction 3
2. Formation of nascent spines: structural and molecular substrates 5
3. Structure and molecular content of nascent spines 7
   3.1. Structure of new spines 7
   3.2. Molecules (ionotropic glutamate receptors) in nascent spines 8
4. Stability of nascent spines 8
5. Perspectives and future challenges 9
   Acknowledgements 9
   References 10

1. Introduction

One of the fundamental challenges of modern neuroscience is to understand the structural, molecular and functional changes in the brain underpinning learning and memory. Our brain is constantly exposed to the novel sensory stimuli from our surroundings. The vast amount of information that can be handled by a mass of tissue weighing a mere 3 pounds is extraordinary. Unlike other parts of our body, the neurons in most part of our brain are neither formed after birth, nor undergo cell division to increase in number. Indeed, this raises the question as to why the capacity of information storage in this seemingly rigid, hard-wired structure does not saturate over time. How can the relatively constant number of neurons accommodate the volume of novel information that they encounter every millisecond over the course of a lifetime?

It is widely believed that this ability is conferred to neurons by microscopic structures called dendritic spines- femtoliter sized, actin-rich protrusions that serve as the primary locus of excitatory synaptic contacts onto neuronal dendrites. Dendritic spines are highly plastic and are constantly remodeled both morphologically and functionally in response to experience. New dendritic spines are formed upon learning (Moser et al., 1994; Xu et al., 2009; Fu et al., 2012) and the retention of the learned skill correlates well with their survival (Yang et al., 2014), suggesting that the nascent

* Corresponding author at: 7-3-1 Hongo, Bunkyo-ku, Tokyo, 113-0033, Japan.
E-mail address: okabe@m.u-tokyo.ac.jp (S. Okabe).

http://dx.doi.org/10.1016/j.brainresbull.2016.07.014
0361-9230/

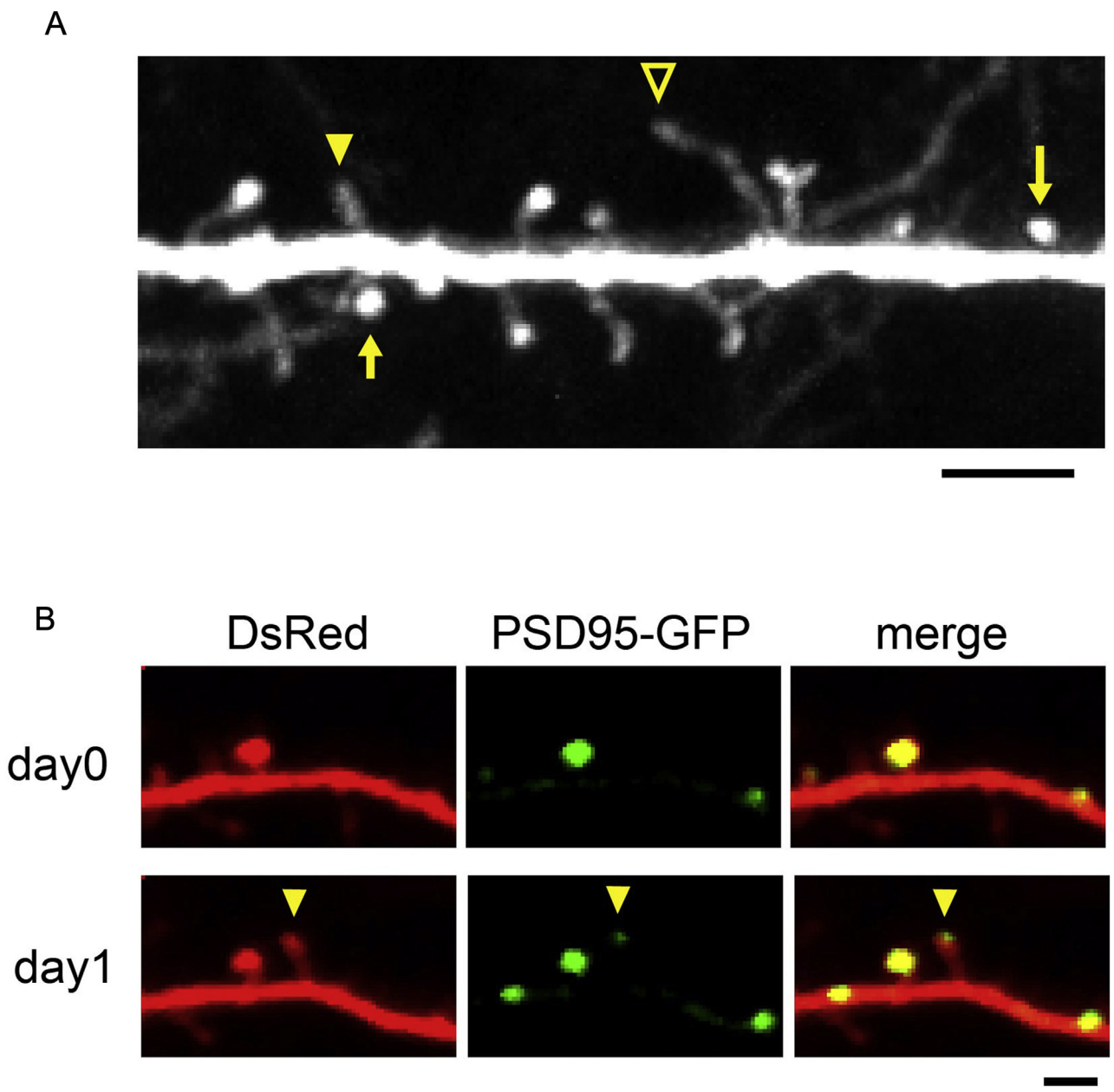

Fig. 1. (A) *In vivo* two-photon image showing a dendritic segment of a layer 2/3 pyramidal neuron from somatosensory cortex. Spines of different morphologies are seen (arrows; mushroom-type spines, filled arrowhead; thin-type spine, open arrowhead; filopodium). The neuron was visualized by transfection of dsRed plasmid by *in utero* electroporation. (B) *In vivo* two-photon time-lapse images of a dendritic segment showing the appearance of a new spine (arrowhead). The newly formed spine acquires PSD within a day of its appearance. Scale bars; 5 um in A and 2 um in B.

dendritic spines are the structural substrate for novel information storage in the brain.

Despite the crucial role of nascent spines in neuronal networks, our current understanding of nascent spines is scant and fragmentary. In contrast to the wealth of information on the structural, molecular and functional details of prototypical mature spines, only limited information can be gleaned from the literature on nascent spines. Understanding the structure and molecular composition of nascent spines, however, is essential to infer their functional capabilities. The number of ion channels, receptors and signaling molecules in dendritic spines governs the efficacy of synaptic transmission, which in turn shapes the duration and patterns of activation of downstream signaling pathways in response to a given synaptic input. Importantly, revealing the identity of the molecules recruited at various developmental stages of a nascent spine will provide mechanistic insight into how mere physical contact between a motile axonal growth cone and a nascent dendritic protrusion evolves into a highly complicated synaptic structure to eventually stabilize and integrate into a functional neural circuit.

The mechanisms that regulate the structure and the molecular composition of a nascent spine are likely to be highly complex and dynamically controlled by neuronal activity. It is overly simplistic and incomplete to infer the structure and the molecular content of nascent spines based on our current knowledge of prototypical mature spines. Individual spines differ in terms of their age, history of plasticity, origin of the presynaptic input, and the path length between their parent dendrite and the soma. Intriguingly, even the dendritic spines located in the same branch do not look alike morphologically (Fig. 1A), and are broadly categorized into thin, stubby and mushroom-types (Peters and Kaiserman-Abramof,