Journal of Biological Engineering Research and Review, 2019; 6(1): 29-36
ISSN: 2349-3232 Online
DOI: 10.5281/zenodo.15355726

Review Article

Neuronal Remodeling and Dendritic Spines: A Review

Adarsh Kumar, Mamta Tamta, Hemlata, Ram C. Maurya*

Department of Zoology (DST-FIST Sponsored), Kumaun University, S.S.J. Campus, Almora, Uttarakhand, India

***Corresponding author. E-mail address: mauryarc@gmail.com (R C Maurya)**

ARTICLE INFO:

Article History:
Received: 31/12/2018
Revised: 22/02/2019
Accepted: 26/02/2019
Available Online: 06/04/2019

Keywords:
Dendritic spines; Enriched environment; Plasticity; Morphology; Learning; Memory

Citation: Kumar A, Tamta M, Hemlata, Maurya RC. Neuronal Remodeling and Dendritic Spines: A Review. Journal of Biological Engineering Research and Review. 2019, 6(1), 29-36

Abstract: The neurons show remodeling in their dendritic arbor and spine/synapse number in many brain regions including the hippocampus, amygdala and the prefrontal cortex. The dendritic spine density is reported to be changed due to experiences and stressful conditions. The dendritic spines are the small protrusions arising from the dendritic shaft of the neurons. They have basic shapes as large mushroom spines, short stubby spines and thin spines. The morphology of spines changes rapidly in response to various stimuli that may be internal such as hormones and external such as environmental changes. Dendritic spine density plays a major role in classification of principal neurons i.e. multipolar and pyramidal neurons. The principal neurons may be classified as sparsely spinous, moderately spinous and heavily spinous on the basis of density of spine over the dendritic branches. In response to environment dendritic remodeling takes place in the form of spine shapes, spine turnover and spine density etc. Synaptic plasticity primarily takes place in dendritic spines and enriched environment have positive effect while social isolation have negative effect on synapse formation. Exposure of animals to environmental complexity may improve the learning and memory by providing adaptive changes in the dendritic spine density.

INTRODUCTION

The adult brain is much more active and adaptable than previously believed, and neuronal remodeling involves growth and shrinkage of dendritic trees, turnover of synapses and neurogenesis in some areas of forebrain. Dendritic spines arise as small protrusions from the dendritic shaft of various types of neuron and receive inputs from excitatory axons. Dendritic spines on neurons were first described in the 1888 by the legendary neuroanatomist Ramon y Cajal [1, 2]. Dendritic spines have variety of shapes and sizes, suggesting a high degree of functional diversity. Spines occur at various densities depending on the neuronal type and are reported in all vertebrates [3] such as reptiles [4-14], birds [15-20] and mammals [21-23]. Most of the principal neurons are classified by taking spine density as one of the classification criteria. The morphology of spines is highly variable and they are commonly classified into three types: thin, mushroom and stubby (Fig. 1) [24]. The size of dendritic spines varies among brain areas, as well as between species according to their functional aspect [25].

The basic structure of synaptic spines was established early in evolution and appears to be roughly the same in all animal groups, but they have been studied best in mammals. Typical spines have a head and narrower neck region and project from the sides of dendrites [22, 26-30] (Fig. 1). They broadly come in three basic shapes: (a) large, mushroom spines with enlarged head regions, (b) short, stubby spines without a clearly defined neck, and (c) thin spines with a relatively slender head and neck [22, 31, 32]. Stubby spines are devoid of a neck [33] and are prominent between postnatal development [34].

Dendritic spines have been a source of fascination since long time and it is believed that these anatomical structures are involved in learning and memory. The capacity to learn and remember is undeniably critical for mammalian livelihood. It has long been assumed that changes in the structure and organization of synapses can be brought about by anatomical modifications of neurons [30, 35]. Dendritic spines, small protrusions found on the shaft of dendrites in the mammalian brain, are one aspect of cellular anatomy that may play a role in the expression of memory [35].

The majority of synapses in the brain are chemical synapses found on the synaptic specializations of dendrites. A chemical synapse consists of two membranes separated by a gap called the synaptic cleft. Neurotransmitters released from synaptic vesicles on the presynaptic side of the cleft diffuse across the cleft to activate receptors in the postsynaptic membrane. Because spines represent potential sites of postsynaptic excitatory input, an increase in their number can

translate into an increase in the number of excitatory synapses [30, 36]. Thus, changes in the density of spines can have a major impact on the amount of excitatory neurotransmission and processing of information in a particular brain region. In present review, we surveyed the morphological aspects of the dendritic spines that are used in neuronal classification. In addition to this we also discussed the changes in dendritic spine density due to external stimulus in the form of enriched environment, hormonal stress etc., that have effects on the learning and memory.

MORPHOLOGICAL DIVERSITY OF DENDRITIC SPINES

The morphology of a spine can change rapidly through activity-dependent and independent mechanisms [35, 37-40]. In addition, thin, hair-like protrusions called filopodia, which lack a bulbous head, are found on dendrites of developing neurons (Fig. 1). They are transient structures that might receive synaptic input and can develop into dendritic spines [41, 42]. The structures of spines are linked to high number of biochemical reactions taking place inside the spine [43]. Spine heads form an asymmetric excitatory synapse with a presynaptic axon [44]. Calcium dynamics in spines revealed a close relationship between spine morphology and function [40]. The spine–neck geometry is an important determinant of NMDA receptor-dependent calcium signaling in spine heads and dendritic shafts [45]. Furthermore, there is evidence that the induction of long-term potentiation (LTP) correlates with spine enlargement [46].

The final determinant of spine morphology is the cytoskeleton. Spine heads contain actin filaments that interact with the plasma membrane and the PSD at their barbed ends (Fig. 1). In spine necks, actin filaments form long bundles (Fig. 1) [47]. It was shown that actin polymerization occurs within seconds of LTP, underlying the enlargement of dendritic spines [48]. Thus, there is good evidence that, at least for hippocampal synapses, the reorganization of the actin cytoskeleton is tightly linked to synaptic efficacy [35, 49].

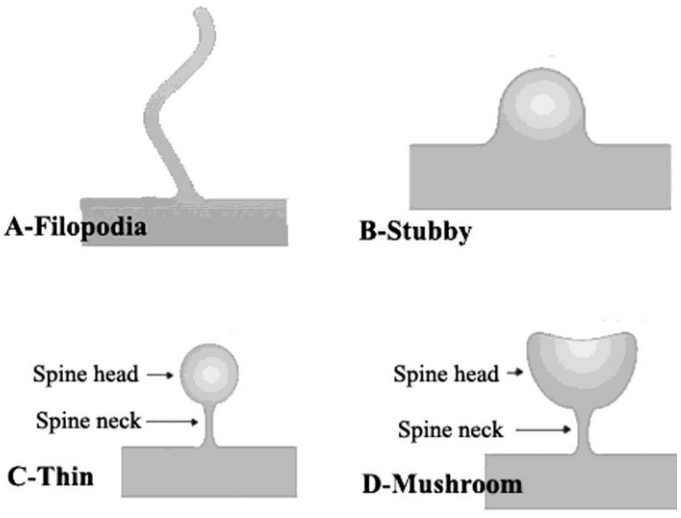

Fig 1. Structural and molecular organization of spine; Schematic drawings of spine morphologies based on the most common four-category classification

DENDRITIC SPINES AND NEURONAL CLASSIFICATION

Distribution of dendritic spines over the dendritic shaft have important role in the classification of neurons. The neurons are classified on the basis of the density of the dendritic spines present on the dendritic branches of the neuron. Neurons are sub-classified as highly spinous, moderately spinous and sparsely spinous on the basis of number of spines present in 10μm or 25 μm distance of the dendritic shaft [3, 5] (Fig. 2).

While describing medial cortex neurons in different reptiles various authors have taken the spine density as major criteria. In medial cortex of *L. pityusensis* Sparsely spinous horizontal neurons; Spinous pyramidal neurons; Spinous bitufted neurons; Small, sparsely spinous pyramidal neurons; Spinous multipolar neurons have been described [10]. In medial cortex of *P. hispanica* Heavily spiny granular monotufted, Heavily spiny bitufted neurons; Spiny bitufted neurons; Sparsely spiny bitufted neurons; Superficial multipolar neurons have been described [9]. Recent study in *M. carinata* and *H. flaviviridis*, describes the aspinous bipolar neurons; aspinous monotufted monopolar neurons; aspinous monotufted bipolar neurons; spinous monotufted monopolar neurons; spinous monotufted bipolar neurons; spinous bitufted bipolar neurons (heavily spinous bitufted bipolar neurons; spinous bitufted bipolar neurons; sparsely spinous bitufted bipolar neurons) and spinous multipolar neurons [3, 4, 6].

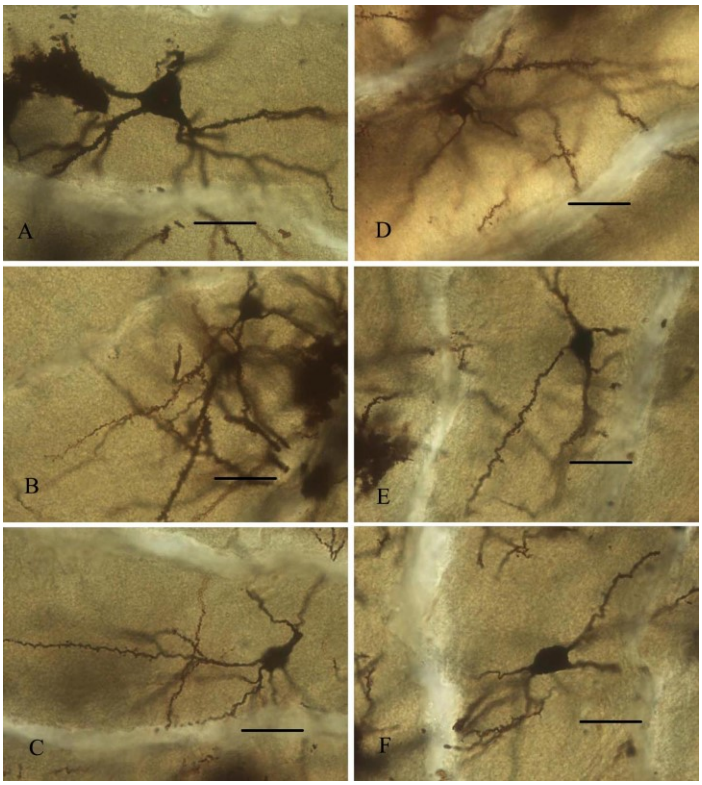

Fig. 2. Photomicrographs showing the Golgi impregnated pyramidal and multipolar neurons of the hippocampal complex of chick brain. (A) heavily spinous pyramidal neuron, (B) moderately spinous pyramidal neuron, (C) sparsely spinous pyramidal neuron, (D) heavily spinous multipolar neuron, (E) moderately spinous multipolar neuron, (F) sparsely spinous multipolar neuron, (Scale bar = 20μm)

In the visual wulst region of bird, *Estrilda amandava* Pyramidal neurons are classified as moderately spinous and sparsely spinous; Multipolar neurons as highly spinous, moderately spinous, and sparsely spinous; Local circuit neurons (small and medium sized) as aspinous; stellate, sparsely spinous neurons [17]. However, in *Taenopygea guttata*, the multipolar type neurons which were small and medium sized with few spines, has been described as Local circuit neurons [50]. Spine density is significantly different among interlaminar basal dendrites of Indian bat. Spine density on the apical and basal dendrites of atypical pyramidal neurons is reported to be relatively higher than of typical pyramidal neurons in Indian bat [21].

ADAPTIVE CHANGES AND SPINE FLUCTUATIONS

Spine density in layer V pyramidal neurons of the primary visual cortex was found to be decreased in Golgi-stained material in mice when raised in total darkness from birth [51]. It is also shown that spine density can recover in some dendrites after few days of life in normal light conditions [52]. The spine density of dentate granule cells in the rat hippocampus, after an initial decrease due to entorhinal cortex lesions, subsequently returned to normal levels as a result of re-afferentation by sprouting of nearby axons [53]. These findings demonstrated the bidirectional nature of these morphological changes and indicated that the initial decrease in spine density was an adaptive response to changes in afferent input instead of a sign of injury to the postsynaptic neuron.

It has been shown that, at early postnatal ages, dendritic spines of cortical neurons of rat brain are highly plastic and spine turnover decreases with age [54, 55]. The total spine number is found to be stable in adults over time due to comparable rates of spine elimination and their formation [56-58]. However, experience has tremendous effect on spine density and spine remodeling occurs in the adult brain due to induction of experience [58].

NEURONAL REMODELING TO CHANGING ENVIRONMENT

The adult brain possesses a remarkable ability to adapt and the minute structural changes in the brain due to the response to the environment can be noted in the form of neuronal replacement, dendritic remodeling (dendritic spine shapes) and synapse turnover (dendritic spine density) [59]. The brain is capable of rewiring after brain damage [53] and also able to grow and change as seen by spine turnover, dendritic branching, angiogenesis and glial cell proliferation during cumulated experience [60]. More specific physiological changes in synaptic connectivity have been recognized in relation to environmentally directed plasticity of the adult songbird brain, showing seasonally varying neurogenesis in restricted areas of the brain [61-63].

Stress hormones have major effect on the function of the brain by changing the structure of neurons. The hippocampus is one of the most sensitive region of the brain which shows the effect of the stress hormones. Within the hippocampus, the input from the entorhinal cortex to the dentate gyrus is ramified by the connections between the dentate gyrus and the CA3 pyramidal neurons [64]. There is adaptive structural plasticity in dentate gyrus, where the new neurons produced continuously throughout adult life, and CA3 pyramidal cells show a reversible dendritic remodeling during hibernation and chronic stress [64-67]. This type of plasticity may be protective against permanent damage and the hippocampus undergoes a number of changes in response to acute and chronic stress to adapt new environmental conditions.

The hippocampus involves replacement of neurons such as the subgranular layer of the dentate gyrus contains cells that have some properties of astrocytes which give rise to granule neurons [68, 69]. These cells appear as clusters in the inner part of the granule cell layer, where some of them will go on to differentiate into granule neurons within few days. There are many hormonal, neurochemical and behavioral modulators of neurogenesis in the dentate gyrus, including estradiol, antidepressants, IGF-1, voluntary exercise and hippocampal-dependent learning [70-72].

Remodeling of dendrites and synapses in the hippocampus, amygdala and prefrontal cortex is also a type of structural plasticity. In hippocampus, chronic restraint stress CRS; daily for 21 days causes retraction and simplification of dendrites in the CA3 region of the hippocampus [64, 73]. Such dendritic reorganization is independent of adrenal size and found in both dominant and subordinate rats undergoing adaptation to psychosocial stress in the visible burrow system [74].

In species of hibernating mammals, dendritic remodeling is a reversible process and occurs within hours of the onset of hibernation and it is also reversible within hours of wakening of the animals from torpor [65-67, 75]. This shows that changes in dendrite length and branching are a form of structural plasticity not “damage” and the reorganization of the cytoskeleton is taking place rapidly and reversibly [59].

ENVIRONMENTAL ENRICHMENT AND NEURONAL PLASTICITY

Postischemic housing in an enriched environment significantly improves the functional outcome after permanent focal brain ischemia in the rat [76-78]. Different mechanisms may contribute to the environmental effects in the postischemic brain. Dendritic spines are the primary postsynaptic targets of excitatory glutamatergic synapses [79-81]. Dendritic spines, as bridges between axons and dendrites, were proposed as primary sites of synaptic plasticity [82]. The spine cytoskeleton consists of actin filaments, and it has been shown that the shape of spines can change rapidly [83, 84]. Spines are calcium compartments with a constantly changing ability to compartmentalize calcium [40, 85]. Housing intact animals in an enriched environment can increase dendritic branching and number of synapses and dendritic spines [86-89], whereas rearing animals in social isolation has the opposite effect [90, 91].

DENDRITIC SPINES IN LEARNING AND MEMORY

Dendritic branching patterns and spine density determine which populations of afferent axons terminate upon a population of neurons and the relative weighting of each type

of input. The vast majority of synaptic inputs onto neurons are on dendrites or dendritic spines, and the amount of synaptic input, cells receive, varies with the amount of dendritic surface available [29]. Most of the excitatory synapses are on dendritic spines, and changes in the number of dendritic spines are associated with experiences like learning or environmental complexity [92-95]. Thus, changes in dendritic morphology in the form of spine density are reliably associated with functional alterations induced by neuroendocrine changes [96-99].

There are numerous evidences in literature that behavioral training can alter different aspects of dendritic anatomy, such as length and branching of dendrites, dendritic spine density [92, 100]. There is a relationship between the presence of dendritic spines and the formation and expression of new memories due to new experiences in the life.

Environmental complexity can alter the presence of dendritic spines and these complex experiences can affect learning ability on a variety of tasks [101-103]. Moreover, animals exposed to the complex environment showed faster acquisition in the water maze task [102, 104] and spine density analysis showed that the enriched animals possessed a higher density of dendritic spines on pyramidal cells in the CA1 region of the hippocampus. Similarly, Rampon et al. [103] reported a 20% increase in hippocampal dendritic spine density as well as enhanced performance on both object recognition and fear conditioning tasks following environmental enrichment. These results suggest that experience leading to increased spine density can also improve new learning. It should be noted that enrichment also induces changes in spine number in cortical regions [87].

CONCLUSIONS

A hundred years after Ramon y Cajal, the relationship between structure and function in neurons are still being discovered. The dendritic spine morphology have major role in neuronal classification in various animal groups [3, 4, 6, 9, 10, 17, 18, 50]. The pattern of dendritic arborization is clearly related to connectivity. Similarly, the synaptic specializations extended by dendrites contribute significantly to connectivity. They allow thin dendrites to reach multiple axons such that larger numbers of synapses interdigitate in a relatively small brain volume [105]. The enormous diversity in the structure, composition, and plasticity of dendrites and their synaptic specializations suggests that the functional contributions of these structures to mind and brain are enormously diverse.

Hormonal influences in the form of stress may also be considered along with the effects of experience in understanding how the brain adapts to challenges. Stress affects brain circuits in ways that promote adaptive plasticity by remodeling dendrites. Although repeated stress can cause deleterious effects on the brain neurons, but the primary role of the stress response is to promote adaptation [106].

There are individual differences in the adaptive management in response to stress, based upon the individual experiences, early in life and in adult life. Early life experiences, positive or negative, in school, at work or in family relationships, have greater role in terms of how an individual reacts to new situations [107]. Depression and anxiety are a natural reaction to major life events and when the individual fails to "bounce back", they need treatment. Most of these effects are seen on brain structure and function [108-111].

Throughout the life span, the external environment and internal body conditions can modify dendritic form and other aspects of neural circuitry [93]. How changes in spine density would alter processes involved in learning and memory remains to be undetermined question for future researchers [112]. The presence of spines may enhance synaptic efficacy and thereby enhances the excitability of the network involved in the learning process. Thus, learning is not necessarily dependent on spine density changes, but rather changes in the presence of dendritic spines provide anatomical support for the processing of novel environmental information that will be helpful in memory formation.

ACKNOWLEDGEMENTS

The authors would like to thank the Head, Department of Zoology (DST-FIST Sponsored), Kumaun University, Soban Singh Jeena Campus, Almora, for providing infrastructural support during the preparation of this manuscript. The author Ram Chandra Maurya thanks the UGC-Startup grant for financial support.

CONFLICT OF INTEREST: None

REFERENCES

1. Garcia-Lopez P, Garcia-Marin V, Freire M. The discovery of dendritic spines by Cajal in 1888 and its relevance in the present neuroscience. Prog Neurobiol 2007;83(2):110-130.
2. Lambert KG, Buckelew SK, Staffiso-Sandoz G, Gaffga S, Carpenter W, Fisher J, et al. Activity-stress induces atrophy of apical dendrites of hippocampal pyramidal neurons in male rats. Physiol Behav 1998;65(1):43-49.
3. Srivastava UC, Maurya RC. Evolution of the cerebral cortex in amniotes: Anatomical consideration of neuronal types. In: Sharma VP, editor. Nature at work: Ongoing saga of evolution: Springer; 2009. p. 329-354.
4. Srivastava UC, Maurya RC, Shishodiya U. Cyto-architecture and morphology of the different neuronal types of the cerebral cortex of an Indian lizard, *Mabouia carinata*. Proc. Nat. Acad. Sci., India 2007;77 (B)(IV):331-347.
5. Maurya RC, Sakal ID, Srivastava UC. Cyto-architecture and morphology of neuronal types of the cerebral cortex of reptiles. In: Srivastava UC, Kumar S, editors. Emerging trends in Zoology. Delhi: Narendra Publishing House; 2011. p. 51-79.
6. Maurya RC, Srivastava UC. Morphological diversity of the Medial Cortex Neurons in the Common Indian Wall Lizard, *Hemidactylus flaviviridis*. Nat. Acad. Sci. Lett. 2006;29 (9 & 10):375-383.
7. Maurya RC, Srivastava UC. Cyto-architecture of the cerebral hemisphere of Indian Wall Lizard, *Hemidactylus*

flaviviridis (Rüppell). Nat. Acad. Sci. Lett. 2011;34(11 & 12):431-436.
8. Maurya RC, Srivastava UC. Neuronal morphology of dorsal cerebral cortex of the Indian wall lizard, *H. flaviviridis* (Rüppell). Asian J. Exp. Sci. 2012;26(2):83-88.
9. Luis de la Iglesia JA, Lopez-Garcia C. A Golgi study of the principal projection neurons of the medial cortex of the lizard *Podarcis hispanica*. J Comp Neurol 1997;385(4):528-564.
10. Berbel PJ, Martinez-Guijarro FJ, Lopez-Garcia C. Intrinsic organization of the medial cerebral cortex of the lizard *Lacerta pityusensis*: A golgi study. J Morphol 1987;194(3):275-286.
11. Srivastava UC, Maurya RC. Neuronal morphology of lateral cerebral cortex of the Indian wall lizard, *H. flaviviridis*. Nat. Acad. Sci. Lett. 2009;32(9 & 10):291-295.
12. Srivastava UC, Maurya RC, Chand P. Cyto-architecture and neuronal types of the dorsomedial cerebral cortex of the common Indian wall lizard, *Hemidactylus flaviviridis*. Arch Ital Biol 2009;147(1-2):21-35.
13. Srivastava UC, Maurya RC, Sakal ID. Quantitative neuronal diversity in the cerebral cortex of *Calotes versicolor* (Daudin, 1802). Nat. Acad. Sci. Lett. 2010;33(5 & 6):171-176.
14. Srivastava UC, Sakal ID, Maurya RC. Differences between spines of neurons of different regions of the cerebral cortex of the garden lizard, *C. versicolor* (Daudin). Proc. Natl. Acad. Sci., India 2012;82 (B)(2):307-316.
15. Srivastava UC, Gaur P. Naturally occurring neuronal plasticity in visual wulst of the Baya weaver, *Ploceus philippinus* (Linnaeus, 1766). Cell and tissue research 2013;352(3):445-467.
16. Srivastava UC, Chand P, Maurya RC. Neuronal Morphology and Spine Density of the Visual Wulst of the Strawberry Finch, *Estrilda amandava*. Proc. Natl. Acad. Sci., India 2013;83 (B)(4):627-642.
17. Srivastava UC, Chand P, Maurya RC. Neuronal classes in the corticoid complex of the telencephalon of the strawberry finch, *Estrilda amandava*. Cell Tissue Res 2009;336(3):393-409.
18. Srivastava UC, Chand P, Maurya RC. Cytoarchitectonic organization and morphology of the cells of hippocampal complex in strawberry finch, *Estrilda amandava*. Cell Mol Biol (Noisy-le-grand) 2007;53(5):103-120.
19. Maurya RC. The neuronal morphology of the chick (*Gallus domesticus*) hippocampus: A Golgi study. J. Biol. Sci. Med. 2015;1(1):1-10.
20. Srivastava UC, Singh S, Singh D. Seasonal fluctuation in the neuronal classes of parahippocampal area of *P. krameri* (Scopoli, 1769) and *E. scolopaceus* (Linnaeus, 1758). Cellular and molecular biology (Noisy-le-Grand, France) 2012:OL1768-79.
21. Srivastava UC, Pathak SV. Interlaminar differences in the pyramidal cell phenotype in parietal cortex of an Indian bat, *Cynopterus sphinx*. Cellular and molecular biology (Noisy-le-Grand, France) 2010;56:OL1410-1426.
22. Harris KM, Weinberg RJ. Ultrastructure of synapses in the mammalian brain. Cold Spring Harb Perspect Biol 2012;4(5).
23. Srivastava UC, Chauhan P. Morphological differences among pyramidal neurons in parietal lobe of a carnivore, Indian mongoose, *Herpestes edwardsii*. Nat. Acad. Sci. Lett. 2010;33(3-4):89-94.
24. Peters A, Kaiserman-Abramof IR. The small pyramidal neuron of the rat cerebral cortex. The perikaryon, dendrites and spines. Am J Anat 1970;127(4):321-355.
25. Benavides-Piccione R, Ballesteros-Yáñez I, DeFelipe J, Yuste R. Cortical area and species differences in dendritic spine morphology. J Neurocytol 2002;31:337-346.
26. Frotscher M, Studer D, Graber W, Chai X, Nestel S, Zhao S. Fine structure of synapses on dendritic spines. Front Neuroanat 2014;8:94.
27. Gray EG. Axo-somatic and axo-dendritic synapses of the cerebral cortex: an electron microscope study. J Anat 1959;93:420-433.
28. Coss RG, Perkel DH. The function of dendritic spines: a review of theoretical issues. Behav Neural Biol 1985;44(2):151-185.
29. Harris KM, Kater SB. Dendritic spines: cellular specializations imparting both stability and flexibility to synaptic function. Annual Review of Neuroscience 1994;17:341-371.
30. Sorra KE, Harris KM. Overview on the structure, composition, function, development, and plasticity of hippocampal dendritic spines. Hippocampus 2000;10(5):501-511.
31. Hering H, Sheng M. Dendritic spines: structure, dynamics and regulation. Nat Rev Neurosci 2001;2(12):880-888.
32. Bourne JN, Harris KM. Balancing structure and function at hippocampal dendritic spines. Annu Rev Neurosci 2008;31:47-67.
33. Jones EG, Powell TP. Morphological variations in the dendritic spines of the neocortex. J Cell Sci 1969;5(2):509-529.
34. Harris KM, Jensen FE, Tsao B. Three-dimensional structure of dendritic spines and synapses in rat hippocampus (CA1) at postnatal day 15 and adult ages: implications for the maturation of synaptic physiology and long-term potentiation. J Neurosci 1992;12(7):2685-2705.
35. Kasai H, Fukuda M, Watanabe S, Hayashi-Takagi A, Noguchi J. Structural dynamics of dendritic spines in memory and cognition. Trends Neurosci 2010;33(3):121-129.
36. Andersen P, Blackstad TW, Lomo T. Location and identification of excitatory synapses on hippocampal pyramidal cells. Exp Brain Res 1966;1(3):236-248.
37. Harris KM, Stevens JK. Dendritic spines of rat cerebellar Purkinje cells: serial electron microscopy with reference to their biophysical characteristics. J Neurosci 1988;8(12):4455-4469.
38. Harris KM, Stevens JK. Dendritic spines of CA 1 pyramidal cells in the rat hippocampus: serial electron microscopy with reference to their biophysical characteristics. J Neurosci 1989;9(8):2982-2997.
39. Schikorski T, Stevens CF. Quantitative fine-structural analysis of olfactory cortical synapses. Proc Natl Acad Sci U S A 1999;96(7):4107-4112.

40. Yuste R, Majewska A, Holthoff K. From form to function: calcium compartmentalization in dendritic spines. Nat Neurosci 2000;3(7):653-659.
41. Miller M, Peters A. Maturation of rat visual cortex. II. A combined Golgi-electron microscope study of pyramidal neurons. J Comp Neurol 1981;203(4):555-573.
42. Fiala JC, Feinberg M, Popov V, Harris KM. Synaptogenesis via dendritic filopodia in developing hippocampal area CA1. J Neurosci 1998;18(21):8900-8911.
43. Tashiro A, Yuste R. Structure and molecular organization of dendritic spines. Histol Histopathol 2003;18(2):617-634.
44. Gray EG. Electron microscopy of synaptic contacts on dendrite spines of the cerebral cortex. Nature 1959;183(4675):1592-1593.
45. Noguchi J, Matsuzaki M, Ellis-Davies GC, Kasai H. Spine-neck geometry determines NMDA receptor-dependent Ca2+ signaling in dendrites. Neuron 2005;46(4):609-622.
46. Matsuzaki M, Honkura N, Ellis-Davies GC, Kasai H. Structural basis of long-term potentiation in single dendritic spines. Nature 2004;429(6993):761-766.
47. Fifkova E, Delay RJ. Cytoplasmic actin in neuronal processes as a possible mediator of synaptic plasticity. J Cell Biol 1982;95(1):345-350.
48. Honkura N, Matsuzaki M, Noguchi J, Ellis-Davies GC, Kasai H. The subspine organization of actin fibers regulates the structure and plasticity of dendritic spines. Neuron 2008;57(5):719-729.
49. Cingolani LA, Goda Y. Actin in action: the interplay between the actin cytoskeleton and synaptic efficacy. Nat Rev Neurosci 2008;9(5):344-356.
50. Montagnese CM, Krebs JR, Meyer G. The dorsomedial and dorsolateral forebrain of the zebra finch, *Taeniopygia guttata*: a Golgi study. Cell Tissue Res 1996;283(2):263-282.
51. Valverde F. Apical dendritic spines of the visual cortex and light deprivation in the mouse. Exp Brain Res 1967;3(4):337-352.
52. Valverde F. Rate and extent of recovery from dark rearing in the visual cortex of the mouse. Brain Res 1971;33(1):1-11.
53. Parnavelas JG, Lynch G, Brecha N, Cotman CW, Globus A. Spine loss and regrowth in hippocampus following deafferentation. Nature 1974;248(5443):71-73.
54. Lendvai B, Stern EA, Chen B, Svoboda K. Experience-dependent plasticity of dendritic spines in the developing rat barrel cortex in vivo. Nature 2000;404(6780):876-881.
55. Zuo Y, Lin A, Chang P, Gan WB. Development of long-term dendritic spine stability in diverse regions of cerebral cortex. Neuron 2005;46(2):181-189.
56. Xu T, Yu X, Perlik AJ, Tobin WF, Zweig JA, Tennant K, et al. Rapid formation and selective stabilization of synapses for enduring motor memories. Nature 2009;462(7275):915-919.
57. Zuo Y, Yang G, Kwon E, Gan WB. Long-term sensory deprivation prevents dendritic spine loss in primary somatosensory cortex. Nature 2005;436(7048):261-265.
58. Hofer SB, Mrsic-Flogel TD, Bonhoeffer T, Hubener M. Experience leaves a lasting structural trace in cortical circuits. Nature 2009;457(7227):313-317.
59. McEwen BS. Stress, sex, and neural adaptation to a changing environment: mechanisms of neuronal remodeling. Ann N Y Acad Sci 2010;1204 Suppl:E38-59.
60. Bennett EL, Diamond MC, Krech D, Rosenzweig MR. Chemical and Anatomical Plasticity of Brain. Science 1964;146(3644):610-619.
61. DeVoogd T, Nottebohm F. Gonadal hormones induce dendritic growth in the adult avian brain. Science 1981;214(4517):202-4.
62. Rasika S, Nottebohm F, Alvarez-Buylla A. Testosterone increases the recruitment and/or survival of new high vocal center neurons in adult female canaries. Proc Natl Acad Sci U S A 1994;91(17):7854-8.
63. Rasika S, Alvarez-Buylla A, Nottebohm F. BDNF mediates the effects of testosterone on the survival of new neurons in an adult brain. Neuron 1999;22(1):53-62.
64. McEwen BS. Stress and hippocampal plasticity. Annu Rev Neurosci 1999;22:105-122.
65. Popov VI, Bocharova LS. Hibernation-induced structural changes in synaptic contacts between mossy fibres and hippocampal pyramidal neurons. Neuroscience 1992;48(1):53-62.
66. Magarinos AM, McEwen BS, Saboureau M, Pevet P. Rapid and reversible changes in intrahippocampal connectivity during the course of hibernation in European hamsters. Proc Natl Acad Sci U S A 2006;103(49):18775-18780.
67. Popov VI, Bocharova LS, Bragin AG. Repeated changes of dendritic morphology in the hippocampus of ground squirrels in the course of hibernation. Neuroscience 1992;48(1):45-51.
68. Seri B, Garcia-Verdugo JM, McEwen BS, Alvarez-Buylla A. Astrocytes give rise to new neurons in the adult mammalian hippocampus. J Neurosci 2001;21(18):7153-7160.
69. Kempermann G, Gage FH. New nerve cells for the adult brain. Sci Am 1999;280(5):48-53.
70. Czeh B, Michaelis T, Watanabe T, Frahm J, de Biurrun G, van Kampen M, et al. Stress-induced changes in cerebral metabolites, hippocampal volume, and cell proliferation are prevented by antidepressant treatment with tianeptine. Proc Natl Acad Sci U S A 2001;98(22):12796-12801.
71. Trejo JL, Carro E, Torres-Aleman I. Circulating insulin-like growth factor I mediates exercise-induced increases in the number of new neurons in the adult hippocampus. J Neurosci 2001;21(5):1628-1634.
72. Aberg MA, Aberg ND, Hedbacker H, Oscarsson J, Eriksson PS. Peripheral infusion of IGF-I selectively induces neurogenesis in the adult rat hippocampus. J Neurosci 2000;20(8):2896-2903.
73. Sousa N, Lukoyanov NV, Madeira MD, Almeida OF, Paula-Barbosa MM. Reorganization of the morphology of hippocampal neurites and synapses after stress-induced damage correlates with behavioral improvement. Neuroscience 2000;97(2):253-266.
74. McKittrick CR, Magarinos AM, Blanchard DC, Blanchard RJ, McEwen BS, Sakai RR. Chronic social stress reduces

dendritic arbors in CA3 of hippocampus and decreases binding to serotonin transporter sites. Synapse 2000;36(2):85-94.
75. Arendt T, Stieler J, Strijkstra AM, Hut RA, Rudiger J, Van der Zee EA, et al. Reversible paired helical filament-like phosphorylation of tau is an adaptive process associated with neuronal plasticity in hibernating animals. J Neurosci 2003;23(18):6972-6981.
76. Grabowski M, Sorensen JC, Mattsson B, Zimmer J, Johansson BB. Influence of an enriched environment and cortical grafting on functional outcome in brain infarcts of adult rats. Exp Neurol 1995;133(1):96-102.
77. Ohlsson AL, Johansson BB. Environment influences functional outcome of cerebral infarction in rats. Stroke 1995;26(4):644-649.
78. Johansson BB, Ohlsson AL. Environment, social interaction, and physical activity as determinants of functional outcome after cerebral infarction in the rat. Exp Neurol 1996;139(2):322-327.
79. Eilers J, Konnerth A. Dendritic signal integration. Curr Opin Neurobiol 1997;7(3):385-390.
80. Boyer C, Schikorski T, Stevens CF. Comparison of hippocampal dendritic spines in culture and in brain. J Neurosci 1998;18(14):5294-3500.
81. Harris KM. Structure, development, and plasticity of dendritic spines. Curr Opin Neurobiol 1999;9(3):343-348.
82. Eccles JC. Synaptic plasticity. Naturwissenschaften 1979;66(3):147-153.
83. Fischer M, Kaech S, Knutti D, Matus A. Rapid actin-based plasticity in dendritic spines. Neuron 1998;20(5):847-854.
84. Matus A. Postsynaptic actin and neuronal plasticity. Curr Opin Neurobiol 1999;9(5):561-565.
85. Majewska A, Tashiro A, Yuste R. Regulation of spine calcium dynamics by rapid spine motility. J Neurosci 2000;20(22):8262-8268.
86. Volkmar FR, Greenough WT. Rearing complexity affects branching of dendrites in the visual cortex of the rat. Science 1972;176(4042):1445-1447.
87. Globus A, Rosenzweig MR, Bennett EL, Diamond MC. Effects of differential experience on dendritic spine counts in rat cerebral cortex. J Comp Physiol Psychol 1973;82(2):175-181.
88. Greenough WT, Volkmar FR, Juraska JM. Effects of rearing complexity on dendritic branching in frontolateral and temporal cortex of the rat. Exp Neurol 1973;41(2):371-378.
89. Comery TA, Stamoudis CX, Irwin SA, Greenough WT. Increased density of multiple-head dendritic spines on medium-sized spiny neurons of the striatum in rats reared in a complex environment. Neurobiol Learn Mem 1996;66(2):93-96.
90. Johansson BB, Belichenko PV. Neuronal plasticity and dendritic spines: effect of environmental enrichment on intact and postischemic rat brain. J Cereb Blood Flow Metab 2002;22(1):89-96.
91. Bryan GK, Riesen AH. Deprived somatosensory-motor experience in stumptailed monkey neocortex: dendritic spine density and dendritic branching of layer IIIB pyramidal cells. J Comp Neurol 1989;286(2):208-217.
92. Greenough WT, Juraska JM, Volkmar FR. Maze training effects on dendritic branching in occipital cortex of adult rats. Behav Neural Biol 1979;26(3):287-297.
93. Kolb B, Forgie M, Gibb R, Gorny G, Rowntree S. Age, experience and the changing brain. Neurosci Biobehav Rev 1998;22(2):143-159.
94. Rampon C, Jiang CH, Dong H, Tang YP, Lockhart DJ, Schultz PG, et al. Effects of environmental enrichment on gene expression in the brain. Proc Natl Acad Sci U S A 2000;97(23):12880-12884.
95. Woolley CS. Electrophysiological and cellular effects of estrogen on neuronal function. Crit Rev Neurobiol 1999;13(1):1-20.
96. Li C, Brake WG, Romeo RD, Dunlop JC, Gordon M, Buzescu R, et al. Estrogen alters hippocampal dendritic spine shape and enhances synaptic protein immunoreactivity and spatial memory in female mice. Proc Natl Acad Sci U S A 2004;101(7):2185-2190.
97. Rudick CN, Woolley CS. Estrogen regulates functional inhibition of hippocampal CA1 pyramidal cells in the adult female rat. J Neurosci 2001;21(17):6532-6543.
98. Woolley CS. Effects of oestradiol on hippocampal circuitry. Novartis Found Symp 2000;230:173-180; discussion 181-187.
99. Yankova M, Hart SA, Woolley CS. Estrogen increases synaptic connectivity between single presynaptic inputs and multiple postsynaptic CA1 pyramidal cells: a serial electron-microscopic study. Proc Natl Acad Sci U S A 2001;98(6):3525-3530.
100. Bailey CH, Kandel ER. Structural changes accompanying memory storage. Annu Rev Physiol 1993;55:397-426.
101. Greenough WT, Wood WE, Madden TC. Possible memory storage differences among mice reared in environments varying in complexity. Behav Biol 1972;7(5):717-722.
102. Moser MB, Trommald M, Andersen P. An increase in dendritic spine density on hippocampal CA1 pyramidal cells following spatial learning in adult rats suggests the formation of new synapses. Proc Natl Acad Sci U S A 1994;91(26):12673-12675.
103. Rampon C, Tang YP, Goodhouse J, Shimizu E, Kyin M, Tsien JZ. Enrichment induces structural changes and recovery from nonspatial memory deficits in CA1 NMDAR1-knockout mice. Nat Neurosci 2000;3(3):238-244.
104. Moser MB, Trommald M, Egeland T, Andersen P. Spatial training in a complex environment and isolation alter the spine distribution differently in rat CA1 pyramidal cells. J Comp Neurol 1997;380(3):373-381.
105. Shepherd GM. The dendritic spine: a multifunctional integrative unit. J Neurophysiol 1996;75(6):2197-2210.
106. McEwen BS. Protective and damaging effects of stress mediators. N Engl J Med 1998;338(3):171-179.
107. Heim C, Nemeroff CB. The role of childhood trauma in the neurobiology of mood and anxiety disorders: preclinical and clinical studies. Biol Psychiatry 2001;49(12):1023-1039.
108. Kaufman J, Charney DS. Neurobiological correlates of child abuse. Biol Psychiatry 1999;45(10):1235-1236.
109. Repetti RL, Taylor SE, Seeman TE. Risky families: family social environments and the mental and physical health of offspring. Psychol Bull 2002;128(2):330-366.

110. Kaufman J, Plotsky PM, Nemeroff CB, Charney DS. Effects of early adverse experiences on brain structure and function: clinical implications. Biol Psychiatry 2000;48(8):778-790.
111. Vermetten E, Schmahl C, Lindner S, Loewenstein RJ, Bremner JD. Hippocampal and amygdalar volumes in dissociative identity disorder. Am J Psychiatry 2006;163(4):630-636.
112. Lamprecht R, LeDoux J. Structural plasticity and memory. Nat Rev Neurosci 2004;5(1):45-54.

About Author

Dr. Ram Chandra Maurya have obtained his M.Sc. from University of Allahabad, qualified JRF-NET (CSIR) and joined Prof. U. C. Srivastava lab to complete his D.Phil. in neuroanatomy of lizard. Then after, he worked as Guest Faculty at the University of Allahabad. During 2012 to 2013, he worked as Assistant Professor (Ad-hoc) at GGU Bilaspur, Chhattisgarh. And, since May, 2013, he joined Department of Zoology, Kumaun University as Assistant Professor. He has received UGC startup project in 2014. He is highly interested to understand the role of environment and various stresses in remodeling of brain neurons.