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Review article

Activity-dependent synaptic plasticity modulates the critical phase of brain development

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Abstract

Plasticity or neuronal plasticity is a unique and adaptive feature of nervous system which allows neurons to reorganize their interactions in response to an intrinsic or extrinsic stimulation and shapes the formation and maintenance of a functional neuronal circuit. Synaptic plasticity is the most important form of neural plasticity and plays critical role during the development allowing the formation of precise neural connectivity via the process of pruning. In the sensory systems-auditory and visual, this process is heavily dependent on the external cues perceived during the development. Environmental enrichment paradigms in an activity-dependent manner result in early maturation of the synapses and more efficient trans-synaptic signaling or communication flow. This has been extensively observed in the avian auditory system. On the other hand, stimuli results in negative effect can cause alterations in the synaptic connectivity and strength resulting in various developmental brain disorders including autism, fragile X syndrome and rett syndrome. In this review we discuss the role of different forms of activity (spontaneous or environmental) during the development of the nervous system in modifying synaptic plasticity necessary for shaping the adult brain. Also, we try to explore various factors (molecular, genetic and epigenetic) involved in altering the synaptic plasticity in positive and negative way.

Keywords: Synaptic plasticity; Stimulation; Development

1. Introduction

The nervous system is highly active during the process of its development. The wiring of neurons in the early stage of development shapes the various brain circuitry required for the particular brain functioning. During development of the nervous system, there is interplay of various events like neurogenesis, migration, differentiation, circuit formation by axogenesis and synaptogenesis to produce physiologically active circuits [1]. Classic developmental events of neuronal birth, migration, circuit refinement and plasticity appear to be influenced significantly by both spontaneous and experience-dependent activities. Spontaneous activities are dependent on many factors including calcium-mediated mechanisms [2]. There are number of studies which elucidate the mechanisms of activity-driven changes in synaptic strength to understand its

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physiological significance during learning and memory [3]. An appropriate number and strength of synaptic connections are necessary for proper wiring of neural circuits during development. Auditory and visual modalities are two predominant external sensory stimuli which modify synaptic efficacy positively and alter experience-dependent plasticity during development for early maturation. However, changes in the synaptic plasticity can cause number of developmental abnormalities which leads to brain disorders. Therefore, it is important to understand how these synaptic connections are established, refined and modified to perform various cognitive functions including learning, memory, consolidation as well as responses to the external environment. It is further relevant to comprehend the influence of various conditions (external and internal stimuli) through which the brain circuitry undergoes refinement during development to affect the activity-dependent synaptic plasticity.

2. Normal process of spontaneous activity influencing synaptic plasticity during development

Spontaneous activity during neural development is important for regulating necessary functions such as the proliferation of precursor cells [4], neuronal survival [5], migration [6] and growth as well as branching of axon and dendrite [7]. Endogenous or spontaneous stimulation for a neuron is one which originates in the sensory organs or peripheral nerves of brain without external stimulation. For example in the auditory system, cell-to-cell connection by axonal growth is promoted by spontaneous firing of spiral ganglion cells and cochlear nuclei [8]. In the human, this starts before the 20WG and continues until the endogenous stimuli reach the temporal cortex by 28 to 29 WG [8]. The innate activity is also thought to play a crucial role in synaptic plasticity, learning and memory [9] as well as in pathophysiology [10]. The developing nervous system internally generates patterned spontaneous activity as stimuli, which regulates the formation of synapse and later its refinement through pruning resulting in modifying synaptic plasticity. There are several mechanisms through which spontaneous activity is processed in the developing nervous system. It is mediated by synchronized Ca^{2+} oscillations in small groups of newborn neurons and maintained by gap junctions. These Ca^{2+} oscillations facilitated by gap junctions have been shown in the proliferative ventricular zones of the neocortex and the retina [11].

Another process through which spontaneous activity is driven is via extra synaptic neurotransmission. This type of neurotransmission involves non-synaptic release of a transmitter or leakage from the synaptic cleft. Both of these processes are associated with the generation and propagation of spontaneous activity in neural networks with immature synaptic connections [12] seen in the cochlea [13,14], spinal cord [15] as well as in the retina [16]. In addition to the above mentioned process, spontaneous synaptic activity also generates and propagates via transient cells, e.g., the support cells in Kölliker's organ of the cochlea [13], inner hair cells [14], cortical neurons [17]. Further, developing cerebellar Purkinje cells have also been shown to fire spontaneous bursts of action potentials [18].

3. Environmental stimulation impels synaptic plasticity during development

Sensory experience or neuronal stimuli forms the basis of activity dependent processes [19] and studies have shown that the ultimate patterns of connections can be disrupted by blockade of such neuronal activity [20]. More recently developmental disorders like autism are also being investigated as examples of error in activity dependent processes [21]. Activity-dependent processes can originate/trigger from either endogenous or exogenous stimuli. For example, exogenous stimulation or external acoustic stimuli includes species specific communication sound (e.g. voice and language in humans and avian vocalization), music, and meaningful environmental sounds. There are number of studies conducted in avian system regarding prenatal sound stimulation and its effect on auditory pathway and other connected areas. Studies have shown that prenatal sound stimulation with maternal sound and complex music results in increased volume, neuronal area, total number of neurons and glia as well as expression of synaptic proteins (synaptophysin and syntaxin), c-fos and are also responsible for the survival of neurons in the two auditory nuclei, nucleus magnocellularis and nucleus laminaris in the chick [22–25]. Further, the neuronal size as well as the proportion of neurons containing calcium-binding proteins (Calbindin D-28K and Parvalbumin) in the chick mediorostral nidopallium/hyperpallium ventrale, an auditory imprinting area [26], and hippocampus was increased [27,28]. In the same study, both types of prenatal sound stimulation enhanced the postnatal auditory response and preference of the chicks to only the species-specific maternal calls [29]. In mice, enhancement of learning performance was observed following music in the perinatal period [30]. In another study, an increased neurogenesis and spatial learning was observed in rat pups following prenatal music exposure [31]. In humans, music was shown to play a critical role in the performance of higher brain areas even at birth [32,33]. All these studies explain the role of sound stimulation in modifying the neural circuit during pre