Neuroplasticity in Children

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Abstract. Research in the field of neurosciences and genetics has given us great insight into the understanding of learning and behavior and changes in the brain in resonse to experience. It is seen that brain is dynamically changing throughout life and is capable of learing at any time. Critical periods of neuroplasticity for various streams of development are also beter understood. Technological advances in non invasive imaging techniques and advances in moleculoar genetics have helped us understand the basis of many developmental disorders which may help in planning effective intervention strategies.
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The brain is an amazing organ. As the secrets of the brain are unraveled one after another, one cannot but marvel at its development, organization, efficiency and abilities. In the embryo, where it all begins, the neural plate forms the neural tube which subsequently becomes the Central Nervous System. Few cells separate from the tube to become the neural crest, which is the future Peripheral nervous system.

The development of the brain goes in an orderly, sequential manner. Neurogenesis is followed by neuronal proliferation, migration and aggregation. This is followed by axonal growth and formation of synapses. These events begin in the first trimester of pregnancy and occur in overlapping stages. Much of these activities occur in the prenatal period. After birth, synaptogenesis and myelination continue at a rapid pace until the end of 2nd year. Thereafter, the processes of neurogenesis, synaptogenesis and myelination are reduced to a large extent; but it may continue at reduced rate throughout life. Most postnatal changes in neurons involve increase in size, volume, development of processes and establishment of mature synaptic connections.[1]

Neuroplasticity

In this context, it is important to understand the plasticity of the brain. The term neuroplasticity is derived from the Greek word "plastikos" meaning "to form". Neuroplasticity refers to structural and functional changes in the brain that are brought about by training and experience. The brain is the organ that is designed to change in response to experience.[2]

Vast amount of research in neuroscience and psychology over the past decade has led to new insights about the many ways in which the brain and behavior change in response to experience. This basic issue is being studied at many different levels, in different species, and on different time scales. All of the work invariably leads to the conclusion that the brain is not static but rather is dynamically changing and undergoes such changes throughout one's entire life

At birth, each neuron has 7500 connections. These increase rapidly in the first 2 years of life until the synaptic connections are double that of adult brain. This is followed by pruning of synapses through the process of apoptosis or programmed cell death.[3,4]

What determines pruning? Which synapses are preserved and which are pruned?

The Hebb Rule

The answer to this question was hypothesized by the Canadian neurophysiologist Donald Hebb as early as the 1950s. He postulated that "neurons that fire together wire together." When an axon of cell A is near enough to excite cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells, such that A's efficiency as one of the cells firing B is increased.[5]

To put it simply, when cells are active together synapses are strengthened and preserved. This strengthening and preservation of neurons are very much activity dependent. The neurons and synapses that are activated repeatedly are preserved while those that are not activated are pruned. Early experience has an enormous impact on brain development, behavior, learning and memory. This process of pruning of excessive synapses continues till the age of 16 years.

This postulate is substantiated by the phenomenon of long term potentiation or LTP which has been studied at a variety of synapses in the mammalian central nervous system. In an LTP experiment, a brief period of intense high frequency stimulation enhances the subsequent response of post synaptic neurons to low intensity

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stimulation of presynaptic neurons. This enhancement can last for weeks, depending on the number, duration, frequency and intensity of the inducing stimulations. Co-occurrence of activity in presynaptic and postsynaptic neurons is necessary for LTP. Research on LTP suggests that synaptic facilitation is capable of storing experiences for relatively long period

It is this neuroplastic principle which forms the basis for early stimulation.[6,7] Programs and environment that provide enriched activities that stimulate various sensory, motor and language development will enhance synaptogenesis and bring about a change in the brains of infants.[3]

Cellular and Molecular Basis of Plasticity

The process of neuroplasticity is now being studied at the cellular and molecular levels. The excitatory neurotransmitter glutamate has a vital role in this. The post synaptic neuron has the AMPA (alpha – amino-3-hydroxy-5 methyl-4 isoxazole propionate) receptors and the NMDA (N Methyl-D-Aspartate) receptors. The AMPA receptor is activated by glutamate, which then opens up the Na ionic channel linked to it and causes localized depolarization. This depolarization is essential for the glutamate to bind with the NMDA receptor which is kept closed by Mg ions. The depolarization causes the entry of Ca ions through the NMDA receptors which then starts a signaling cascade and release of trophic factors and activation of gene transcription in the nucleus that support synaptic connections. Persistent and coincident firing of neurons is essential for the entry of Ca ions and the signaling cascade activation.[8,9]

The function of the immature NMDA receptor is enhanced in the postnatal period which explains the greater plasticity of the brain in this period. Thus with every new experience, the brain slightly rewires its physical structure and this rewiring is mediated through the signaling cascade. Studies at the molecular level reveal that the chemistry of DNA can be changed by experience in ways that affect the expression of our genes. Moreover, such effects on the chemistry of DNA can be produced by social experience, which in turn modifies gene expression in ways that can persist for the duration of a lifetime.[7]

Experience alters neural development in at least 3 different ways: 1) by influencing gene expression; 2) by influencing the release of neurotrophins; and 3) by influencing the release of neurotransmitters like norepinephrine that play a role in normal development[10]

These findings have radical implications for conceptualizing the dynamic interplay between nature and nurture. At more macro levels of brain systems, research demonstrates how sensory, perceptual and language functions are modified by experience and how the neural systems that underlie these complex behaviors are transformed through experiential alterations that occur early in life.

Plasticity and Critical Periods

At birth the brain is very immature. In fact, the human brain is not fully mature until at least twenty years after birth. Moreover, during this long development the human brain is highly dependent on and is modified and shaped by experience. For example, in people born blind, the parts of the brain that normally process visual information are rewired and come to process sounds, including language. In those born deaf, the areas of the brain that normally process sounds come to process vision.

This plasticity of the brain is also maximal during the critical periods. Critical period is a maturational time period during which some crucial experience will have its peak effect on development or learning resulting in normal behavior attuned to the particular environment to which the organism has been exposed. If the organism is not exposed to this experience until after this time period, the same experience will have only a reduced effect or in extreme cases may have no effect at all. After the critical period, the brain may never again show the same ability to make big changes in neuronal connectivity. For eg. the critical period for the development of the visual cortex in children with acquired amblyopia is up to 7 yr, and similarly, a cochlear implant for early deafness has maximal effectiveness within the first 7 yr of life. The critical period for natural language acquisition is the first 6 yrs of life and thereafter, the innate ability to acquire language declines gradually and after 12 yrs, it slows down dramatically. Children whose caregivers talk to them regularly display good language skills and well organized language brain systems. However, children who are rarely spoken to have stunted language development and immature language brain systems. In older individuals, the end of the critical period does not mean total loss of experience modified synaptic plasticity in the brain. It becomes restricted to more local synaptic modifications, and perhaps, it is more difficult to accomplish.[11,12]

Plasticity of the brain is maximal in the first few years of life, but continues at a reduced rate throughout life. It is more in certain parts of the brain compared to other parts and more in certain periods of life than in others. This explains the fact that children are able to recover from head injury much better than adults and recovery of functions is more complete. For *eg.* if the entire left hemisphere is removed in a 4-yr-old child, the child may still develop normal language functions whereas the same in an adult will lead to permanent loss of all language functions.[3]

The advocates of early intervention have always argued on the importance of the first 3 years of life and the critical periods in a child's life. The sensory experiences, stimulation and language exposure during this period may determine synaptogenesis, myelination and neuronal connectivity. The principles "use it or lose

it" and use it and grow it" are based on the principles of plasticity of the brain. Another fact of relevance is that as myelination increases, plasticity of the brain decreases.

The ability of the neurons to change, proliferate and synapse is not limited to the immature neurons at their developmental stage. The implications of neuroplasticity are being studied extensively in adults, such as its role in recovery from stroke, drug addiction and several psychiatric disorders. Several disorders of the signaling cascade and genetic transcription have been identified as the basis of disorders such as Neurofibromatosis, Tuberous sclerosis and Rhett's disease transcription have been identified as the basis of disorders such as Neurofibromatosis, Tuberous sclerosis and Rhett's disease.[13,14]

Types of Plasticity in Children

There are four major types of plasticity in children. These four types are adaptive, impaired, excessive and plasticity which make the brain vulnerable to injury or becomes the 'Achilles heel' of the developing brain. Adaptive plasticity refers to changes in neuronal circuitry that enhances a special skill with practice allowing the brain to adapt or compensate for injuries or changes in sensory output. One of the known examples of this type is the reorganization of connection in the visual cortex with acquired amblyopia due to strabismus. Selection of visual input in one eye leads to the loss of cortical synaptic connection in the other eye. The therapy of patching the opposite eye leads to improvement of vision if it is done during the period of visual plasticity which is the first decade of life. A similar period of maximum plasticity for recovery of auditory cortex is within the first seven years of life. It is for this reason that cochlear implants is most effective if it is done before this period.

Impaired plasticity refers to situation in which genetic or acquired disorders disrupt molecular plasticity pathways. One of the examples of this is Fragile X syndrome which is due to defect Fragile Mental retardation protein which binds the RNA within synapses and regulates activity dependent protein translation. Similarly disorders of transcription are seen in Rhett's, Coffin-Lowry and other syndrome[15]

Excessive plasticity in the developing brain can lead to disability through reorganization of new maladaptive neuronal circuits that cause neurological disorders as partial seizures following mesial temporal sclerosis or focal dystonia. Plasticity becomes the brain's Achilles heel in situations like status epilepticus when excitatory mechanism becomes over stimulated resulting in excitotoxic neuronal damage.[7]

CONCLUSION

To conclude, neuroplasticity refers to a range of neural responses, from cellular and molecular mechanisms of synapse formation to cellular realignment or organization of neural networks, or learning, memory and behavior.[16] Neuronal plasticity can be evaluated with transcranial magnetic stimulation technique, mapping EEG, and functional Magnetic resonance imaging, currently used mainly for research purposes.

New strategies are being developed to identify drugs, cells, or genes that will induce structural reorganization or repair damaged neurons, and to determine the kind of stimulation or training of newly forming synapses that is most likely to ensure functional recovery.

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