Brain development- the critical 1000 days- what develops and when-

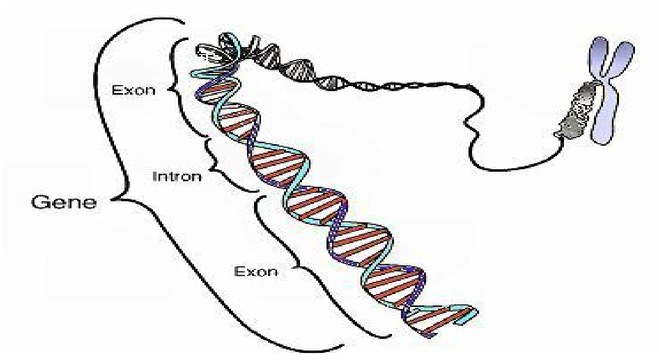
Right from conception upto about 3 years age (especially the first 2 years), there is very rapid growth and development of the human brain. The period in utero is a very critical period for brain development. By the age of two years, the brain has already reached about 80% of the adult brain weight. However, development and refinement continues for a long time well beyond 2 years of age. Brain development is influenced by interaction between nature (genes) and nurture (environment). Environment has a strong and even permanent influence on brain development. Evidence is now available that even the genetic influence can be altered (for better or worse) through nurture. Nurturing plays an important role but the first 1000 days (270 days in utero and 730 days during the first 2 years of life) are crucial for good nurturing to get the maximum returns from genetic endowment. The overwhelming scientific evidence and knowledge from biological sciences make a compelling case for greater attention to the fetal life and the first two years of life. This is also the critical time for all care givers and stakeholders to reduce the risks from ill effects of stress, neglect and trauma on the developing brain.

A lot more is now known about the human brain development that can guide the provision of best possible environment to maximize the gains in improving survival, thriving and transformation. This nurturing provides much greater returns for the investment through brain development if equity and quality of care at all levels of care provision and care giving is ensured.

Major milestones in brain development in utero

The central nervous system comprises of the brain, the spinal cord, and peripheral nerves. The brain and the spinal cord are protected by cerebro spinal fluid (CSF) and bones- skull and the vertebrae. The development progresses from below upwards i.e. spinal cord first followed by the brain stem (lower part of the brain) followed by cerebral cortex in a sequential manner.

The nervous system starts to develop even before the mother realizes that she is pregnant. At conception, the sperm and egg meet to form a single cell determining the genetic potential. About 60% of the genes are dedicated to brain development. Genetic makeup is the main driving force in the early phase of brain development. This is followed by the effect of an ongoing interaction of the environment and genes. The genes are left with imprints and these contribute to a long term impact. At the time of fertilization genes have their maximal influence but after that there is an ongoing interaction between the genes and the environment. The effect of environment or it can occur permanently.



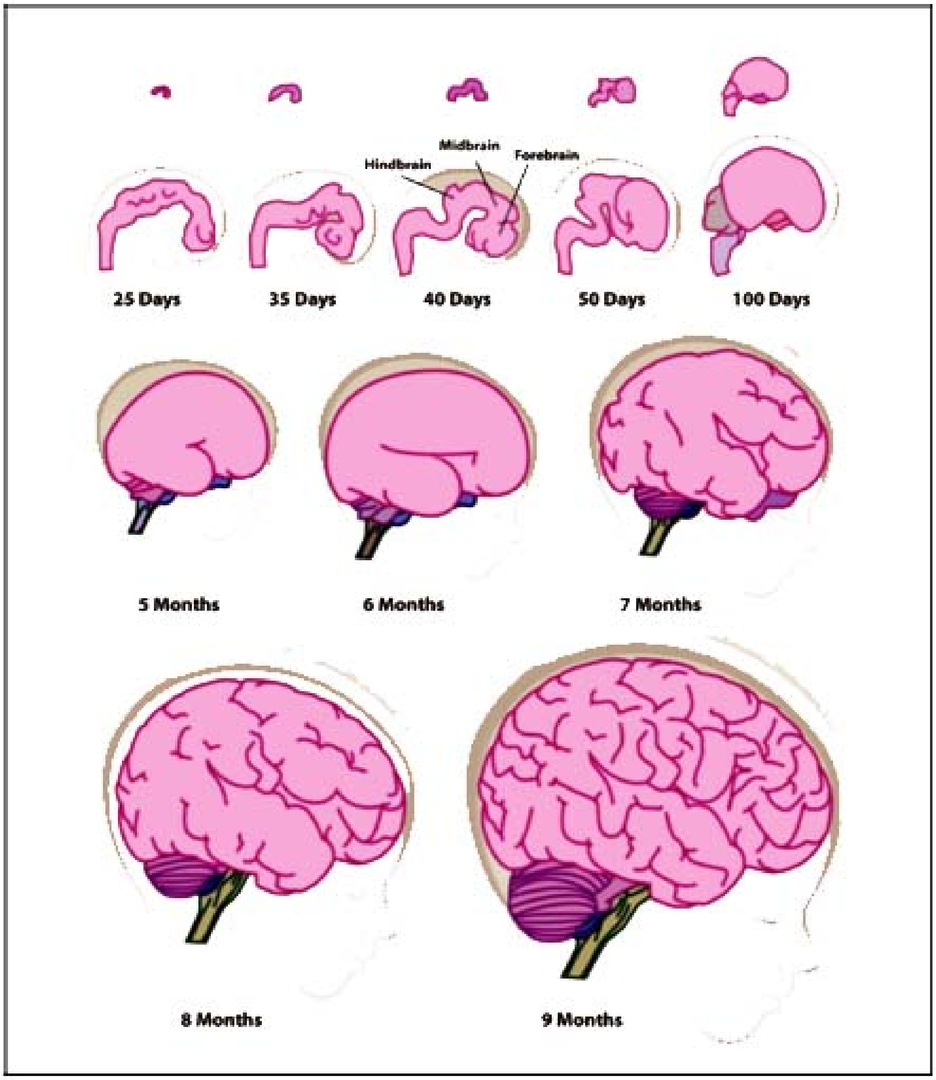
Source: The Science of Early Childhood Development - College of Education .
www.cehd.umn.edu/CEED/.../GunnarMNLegInst2-10-14.**pdf** **accessed October 2016**

Three to four weeks after conception, a thin layer of cells forms on the embryo. These cells fold and fuse to form a liquid filled tube. This neural plate appears by about 15-20 days and it closes by about 4 weeks. Nerve cells called neurons begin to form in this closed neural plate initiating the formation of spinal cord and the brain. If the neural tube fails to close on the side of the brain, the baby is born without cerebral cortex and an unfinished brain stem. This condition is called anencephaly which is incompatible with sustaining life after being born. If the neural tube fails to close at its lower end or somewhere in between, the brain stem and the end of the spine, a condition known as spina bifida occurs. There can be different severity of spina bifida. In this condition, the spinal cord may be damaged. This is a serious condition that requires repair after the baby is born. Although the cause (s) of these conditions is not known, some 70% can be prevented through prevention of folic acid insufficiency in pre and peri conceptional period. Food fortification of wheat flour is an effective public health strategy to prevent neural tube defects.

As stated earlier, neuron formation occurs very early at around the time of closure of the neural plate. At about 4-6 weeks after conception, neurons begin to develop connections in the fetal spinal cord. The connections between these neurons are called synapses. The simultaneous growth and development of neurons and synapses contribute to the beginning of fetal movements which are crude and not coordinated at this stage of human development. In the next few weeks, maturation occurs and this leads to more coordinated movements and fetal activities. At around 16-18 weeks, pregnant women begin to feel the fetal movements and this is very exciting to her since communication between the fetus and the mother has started.

The major milestone in the development of central nervous system is the connection that develops between the brain and the spinal cord through brain stem. The development of brain stem leads to development of reflexes that mature progressively i.e. control over heartbeat, rhythmic contractions of the diaphragm and chest muscles in preparation for breathing and sucking as well as swallowing. Once these functions appear, the fetus becomes viable. This is the main reason for providing good quality antenatal care to prevent premature delivery. In the fourth month of pregnancy, the eyes and ears have already connected to the developing brain and the fetus begins to react to sounds and bright lights.

For the next 4 months, brain cells (neurons) form at an astonishing rate, up to around 250,000 every minute. In the fetus at about 14 weeks some of these nerve cells are sparked off to begin functioning. After this phase, new cell formation slows, while vast numbers of axon interconnections among the neurons are made. By four to five months of gestation, the fetus has about 100 billion neurons.



Source: Goldowitz, D., "How do you make a brain and keep it working?" University of Tennessee Health Science Center quoted in [www.urbanchildinstitute.org/...TUCI accessed October 2016](www.urbanchildinstitute.org/...TUCI)

During pregnancy, the neurons begin their migration to critical areas of the brain in a programmed and systematic manner for development of vital functions of the brain. Most of the neurons arrive at the right areas at the right time. However, this migration can be disturbed. Those that are damaged or move inappropriately die. In very rare situations, some do reach the wrong location and form the wrong connections. The brain produces many more cells than it will ultimately need. By the time the fetus is twenty weeks old, about half of these cells are deliberately shed. The remaining cells are organized into forty different physical areas that will broadly govern senses and skills such as vision, language and muscle movement. The process of migration occurs in layers from inside to outside much like the layering of a cake.

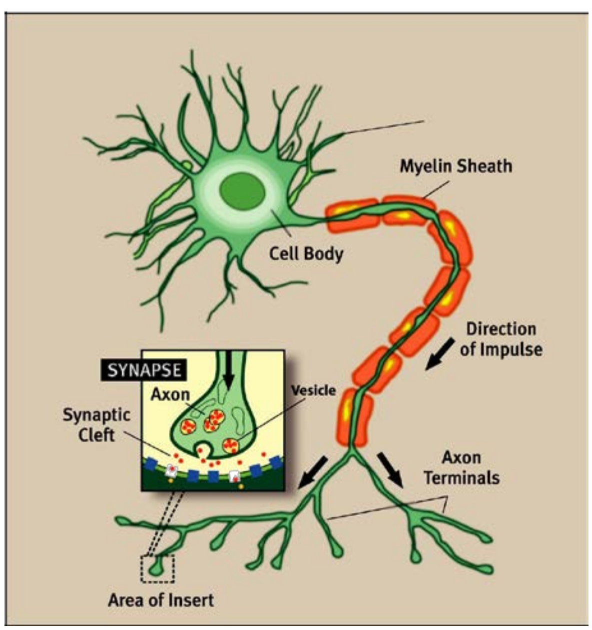
By the sixth month, new neuron growth has greatly reduced, while many more connections among neurons are being established through multiple dendrites (like many and complex branches of a tree) forming on the axons. Electrical activity of the fetal brain can be detected by 7 months in pregnancy. During this period of very rapid growth mother's diet, activity are important as also the intake of essential micro nutrients (folic acid, vitamin B 12 etc.). Exposure to toxins and maternal stress that is persistent can interrupt the structure and functioning of rapidly developing brain. Consumption of alcohol and the use of tobacco should be avoided since this can be harmful for the brain of the fetus. During the final stages of pregnancy, the number of neurons begins to decline as cell death eliminates those that are not actively involved in the developing brain pathways and systems. Even though almost all the neurons have been formed by the time the baby is born, brain development is still work in progress. Besides neurons, the major white matter pathways that make up the brain's information processing networks are also present at the time of birth. Yet, brain development is far from complete in the newborn.

Dendritic Development

Two processes occur during development of the dendrite: dendritic arborization and spine growth. The dendrites begin as individual processes protruding from the cell body of the neuron. Later, they develop increasingly complex extensions, looking much like the branches of trees in winter. Spines are little appendages, resembling thorns that begin to appear in the seventh intrauterine month (Dendrites spine development). Before birth, dendrites are observed only on the biggest neurons. Afterbirth, they can also be found on other neurons where they spread and densely cover the dendritic surface. Although dendritic development begins prenatally in the human, much of dendritic development takes place after the birth of the baby. The synapses present at birth are primarily those that govern our bodily functions such as heart rate, breathing, eating, and sleeping.

During the third trimester some development of cerebral cortex occurs and some learning begins at this stage of fetal development. The implication is that fetus can be affected positively by music, positivity of the mother and negatively by persistent stress, loud sound, noise, trauma, violence etc.

In summary, human brain development is preparing the fetus to be fully equipped for independent existence (though some dependence continues even after birth). If the gestation for any reason is cut short, the chances of survival and intact survival are compromised. The more the immaturity, the greater is the risk to the newborn survival and brain growth.



Source: http://www.educarer.com The world of infants (quoted in www.urbanchildinstitute.org/...TUCI accessed October 2016).

Newborn upto 2 years of life - a critical part in human brain development

Babies are born fully equipped with basic instincts, and reflexes for its survival and use of key senses viz. vision, hearing, touch, smell, and taste. Its body temperature control mechanism is not fully mature. The newborn can reach out for food (rooting), suck and swallow. At birth, the infant is prepared to start the key vital functions of the body (breathing, heartbeat, temperature maintenance etc.). The brainstem controls most of the earliest activities of a newborn to ensure survival.

Post-natal growth is characterized by rapid formation of synapses and synaptic connections. The other key important developments are myelination, glial cell formation, dendrites and functioning of synapses through electro and chemical neuro transmitters. This is the beginning of establishing solid foundations for brain functioning for a life time.

Synapses and synaptogenesis

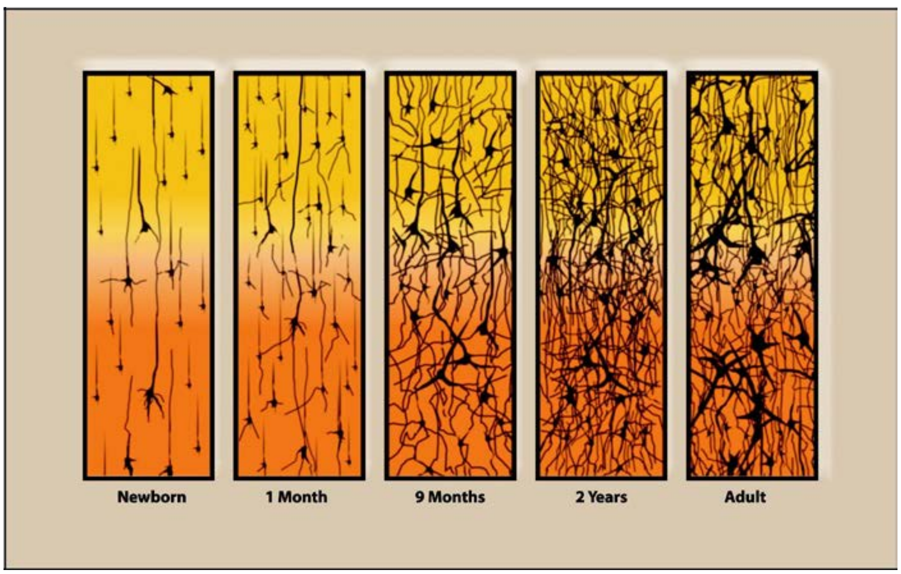
The onset of synaptogenesis is abrupt, and the appearance of synapses in any particular area is remarkably rapid. Neurons may be together for days before they actually make synaptic connections. Synapses usually form between the axons and the dendrites, cell body, axons, or synapses of other cells. Early embryonic life is characterized by the generation of low density synapses. After birth synaptic connections are formed rapidly at the rate of about 70-100/second. This is followed by rapid growth of synapses with a peak of about 40,000/second and sometimes much higher rates. This phase begins before birth and continues until nearly 2 years of age in humans. The next phase is characterized by an initial plateau in synapse number followed by a rapid elimination of synapses that continues through puberty. The last phase is characterized by another plateau in synapse number through middle age followed by a drop.

Just as synapses can be formed very rapidly during development, they may be lost at a rate of as many as 100,000 per second during adolescence. The development (and elimination) of synapses is influenced by sensitivity and responsiveness mechanisms. Sensitivity means that the synaptic development depends on the presence of certain sensory experiences. Responsiveness refers to the generation of synapses that are unique to the individual. This is a crucial process in brain development and functioning and it continues throughout life in the form of 'serve and return' much like the game of tennis. Synaptic density has no relationship to the functioning of the brain.

Synaptic development, pruning, plasticity

The connections are formed by each neuron putting out a long tentacle like fiber called an axon. The neuron uses the axon to send messages to other neurons. The messages are sent as electrical signals and picked up by thousands of short, hair like fibers called dendrites (also produced by the neurons). Each neuron is able to connect up with thousands of other neurons. Repeated experiences causes the connections to become strong, efficient and well tested pathways, permanently etched into the brain. Infrequent experiences result in the loss of developing pathways. This development is responsible for learning by the young infant and master the learning. By eight months of age the average infant, living in a stimulating, secure and loving environment, will have sparked 500 trillion of these connections and by the age of two, an infant has developed around 1000 trillion of these connections. Although the connections continue to form throughout life they have reached their highest density (about 15,000 synapses per neuron).

There are many short-lived pathways that form throughout the infant's brain, creating connections among brain areas that are not observed in adults. This overabundance of connections and pathways gradually declines during childhood as many of them are 'pruned' and disappear. The activity of a neural pathway, which is driven by experience, affects whether a particular connection weakens or stabilizes as part of a permanent network. The pruning process works on the basis of the principle 'use it or lose it' which is determined predominantly on the basis of serve and return. This is a key factor in supporting the developing brain's 'plasticity' – its adaptability to experience, which confers great survival value. The brain's plasticity is strongest in the first few years after birth. Thus, it is easier and less costly to form strong brain circuits during the early years than it is to intervene or "fix" them later. The plasticity is determined by support, positive relationships, sensitivity and responsiveness and negatively influenced by persistent stress and neglect trauma and deprivation. Plasticity and pruning contributes richly to resilience of the brain.



Source: Corel, J.L.(1975): The postnatal development of the human cerebral cortex. Cambridge, MA: Harvard University Press

Glial Development

There are two types of cells in the brain, **neurons** and **glial** cells (glia - Greek word for glue).The functioning of neurons depends on the support and the housekeeping that they get. Basically this is done by glial cells. The differentiation and growth of neurons, which are generally produced before their associated glia, appear to play some role in stimulating the growth and proliferation of glial cells, but the mechanisms are unknown. In contrast to neurons, which only relatively recently have been shown to continue to be born in very restricted brain areas, glial cells continue to proliferate throughout life. Glial cells perform the following key functions:

Support: Glia cells act as a physical support and protection for neurons. They also help keep the blood-brain barrier which prevents toxic chemicals in the blood from entering the brain.

Nutrition: Glia cells help keep the environment around neurons in balance and make sure the right nutrients are available for neurons.

Insulation: Glia cells can create myelin, a fatty substance that helps insulate the axons of neurons. This helps keep electrical signals inside the neuron and helps them move faster.

Housekeeping: Glia cells can prevent the buildup of toxic chemicals, help destroy viruses and bacteria, and get rid of dead neurons.

Myelin Development

Myelin is a fatty material made up of water (40 per cent), lipids (45 per cent) and proteins (15 per cent) and is white in color; it is part of the 'white matter' of the brain. It forms into sheaths around nerve fibers (axons), insulating them in a similar way to the plastic or rubber insulation on electricity cables. During early fetal life, axons are formed without any sheaths, but myelination starts during the later months of pregnancy and continues rapidly after birth and then at a slower rate through childhood and adolescence. Without myelin covering them, the majority of axons transmit electrical impulses relatively slowly, as a series of waves, but once the myelin sheaths form, impulses are able to leap from one sheathed section to the next, transmitting the signal faster and ensuring that they travel with less diffusion or interference from signals travelling along other axons. The sheaths do this by preventing electric charges from 'leaking' out of the axon. Brain growth, and hence the growth of white matter, is fastest during the first 2 years of life, particularly in the frontal part of the brain, the part that is actively involved in working memory, thinking and planning. It is likely that the improvements in these cognitive functions that we see in early development are in part due to myelination reducing the diffusion of axon signals while increasing their speed. A diet with sufficient protein and micronutrients (World Health Organization, 2008), for mothers during pregnancy and for children after they are born, is crucial for myelin production to proceed without disruption. There is some evidence that vitamin B12 deficiency during these two potentially sensitive periods may inhibit axon myelination and it is known that disorders where myelination is disrupted are also associated with impairments in cognitive functions.

Cell Death

One of the most intriguing stages in brain development is cell death. Cell death is a necessity to control over crowding. The growth of brain comprises of block building and sculpting. The brain creates the blocks to be sculpted, by generating an overabundance of neurons and connections. The ''chisel'' in the brain could be in the form of genetic signals, stress, environmental stimulation, gonadal hormones, stress, etc. Similarly, the same processes are likely to affect the development of dendrites, axons, and synapses. Cell death does not end in infancy but continues well into adulthood. The brain adapts to the environment through an ongoing process of creating strengthening and discarding This is influenced by nurture and environment.

Early brain messages are critical

A stimulated neuron sends a message electrochemically down its long tail (known as an axon). Dendrites branch off of the neurons and allow communication among neurons. Signals are sent across synapses (synaptic clefts) through chemical neuro-transmitters. When a dendrite receives these signals it translates them into electrochemical messages, and the entire process is repeated through multiple neurons.

The earliest messages that the infant brain receives have an enormous impact. Parents and other care-givers therefore play critical roles in helping to stimulate these infant brains with the right messages. Loving, the young infant, looking into a baby's eyes, touching, stroking, talking, singing and repeating the sounds and facial expressions of the infant all provide an ideal stimulus for an infant's growing brain.

Key points for consideration

1. Both nature and nurture contribute to brain development enormously throughout life. Genes determine when where and how many brain circuits are formed. Environment influence the stimulation and ongoing use of the circuits. The most impressive impact of interventions is on children at the highest risk. The central role of family and the support that is provided should be well understood.
2. Adequate nutrition supports brain development throughout early childhood. Exclusive breast feeding not only provides optimal nutrition it also helps in bonding, attachment and happiness of the mother and the infant. How breast feeding stimulates brain development may not be clear but the relationship is well established. Micronutrients in the infant's diet is critical for brain development.
3. There are window periods in life when brain is most sensitive to the experiences, and if they are suitably utilized it helps in brain development. However, if for reason the opportunities are missed, the plasticity of the brain helps to make up for deficiencies. Repeated experience helps in creating memory which is implicit (unconscious memory) in young age and explicit (conscious memory) as the person grows above the age of 2 years. Implicit memory cannot be recalled while explicit memory can be recalled. The pathways get encoded and this contributes to permanence in the memory.
4. Childhood is a period of increasing specialization when redundancy is progressively reduced to make the brain a very efficient organ of the body. This is helped by pruning and increased plasticity of the brain. The efficiency is rapidly increased during adolescence.
5. During resting and while asleep, there is continuing activity of the brain. Resting and sleeping states in childhood are important in early childhood development and its functions perhaps as important as during the time when the child is active awake and playful.
6. Brain is social soon after the birth. The most important for the development of the social brain are the human face, voice of caregiver, human movement, eye to eye contact with a loved one, singing a song, soft touch, loving hugs, soft massage, or repeatedly calling the child's name. These are important objects of attention right from early infancy. These are replaced by other prominent objects of attention later in life. Attention modulates our learning. The ongoing interaction is important.
7. Feelings memories and thoughts are the highest function of the brain that are progressively improved and mastered with age. These are organized in the cerebral cortex.

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