# Guest Editorial

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## Amblyopia Decoded

*Amblyopia is a developmental cortical disorder, secondary to abnormal visual experience occurring during the early post natal period of life (from 4 months to 36 months).[1] Usually unilateral, but may be bilateral, and if diagnosed and treated early, is reversible. The amblyopic eye has many deficits besides reduced visual acuity (like contrast sensitivity, stereo acuity, motion deficits, spatial localization deficits) and these deficits in the amblyopic eye cannot be explained by lesion in visual cortex V 1 alone. Abnormal binocular interaction is the root cause of Amblyopia.*

*A simple definition of Amblyopia, that it is reduced vision in one eye, for which, there are no ophthalmoscopically visible changes, does not reveal the underlying complexity of this condition. Animal experiments have revealed a vast amount of information about the vision and its complexity. Interested readers are referred to go through this exhaustive list.[2,3]*

*Knowledge of the normal retinocerebral apparatus is necessary to comprehend Amblyopia. A brief review of the anatomy and physiology of the visual pathway, from ganglion to cortical area V 1 and beyond, is very much needed, for a better understanding of pathophysiology of Amblyopia.*

***Anatomy and Physiology of Normal Visual Pathway***

*Vision has many dichotomous, parallel, bottom up and top down impulses going up to striate cortex (primary visual area or V 1) from the retina. These parallel streams (top down and bottom up impulses) have interconnections too at various levels. The first conversion of light energy to neural impulse happens at the ganglion cell level in the retina. There are many different types of ganglion cells, but briefly there are P cells (Parvocellular) and Magnocellular M cell types. This classification is based on both structural and functional differences between the two types of ganglion cells.[4] P cells are concentrated in the central 10° of retina and M cells are beyond that.[4,5] The P cells are involved in fine stereopsis and color vision and have a high resolution capacity owing to their rich cortical connection. The P cells have a much larger representation in V1, compared to M cells. M cells are involved in gross stereopsis and motion and spatial localization.*

*The first dichotomy starts at ganglion cell level in to M cells and P cells. There is nasal and temporal dichotomy of the axons of the ganglion cells. Nasal fibres cross over to the contra lateral side at chiasma, in a specific pattern, and temporal fibres stay on the ipsilateral side. This crossing of fibres was necessitated by the moving of the two eyes from lateral position to more frontal position.[4,7] LGB (Lateral Geniculate body) has a distinctly stratified structure. The right and left retinal fibres discharge on to the lateral geniculate body separately, M cells and P cells discharge on to different layers in LGB as well. Nearly 90% of the retinogeniculate fibres are concerned with vision. The topographical representation of the fibres in the LGB reflects that in retina. Fibres from adjacent retinal ganglion cells in the retina discharge on to adjacent LGB cells. LGB modifies the retinal impulses, before passing it on to the V1 area, and is influenced by the descending corticogeniculate impulses. LGB passes on to the V 1 area only about 30% of the retinal impulses that it receives.[4,6,7]*

*The geniculo cortical fibres, Optic radiations discharge on to V1, the primary visual cortex. The V 1 has many layers from I to VI. The Geniculocortical afferents discharge in layer IV C of the V1 cortex. 80% of the cortical neurons are binocularly responsive.[4] Above and below layer IV, the cortical cells are binocular. At Layer IV, the right and left fibres are still separate and myelinated and are called ocular dominance columns. Many of the changes in amblyopia have been noted in this cortical layer.*

*The M cells and P cells discharge separately in layer IV C. M cells discharge on to Layer IV C alfa and P cells on to Layer IV C beta.*

*These M and P fibres then go to different cortical areas. M fibres go to supero parietal area (dorsal stream) and is involved in where of vision and P cells go on to mid temporal cortex (what of vision) or ventral stream. Both these are affected in Amblyopia.*

***Cortical Development***

*A brief discussion of the cortical development is essential. The questions that are being investigated are*

1. *What makes the ganglional axons grow and find the respective cell bodies in the LGB to discharge,*
2. *What makes the LGB axons to discharge precisely on to the respective cortical soma?*
3. *There are genetic factors involved and spontaneous discharge of electrical impulses from the retinal ganglion cells, in utero, that guides these axons.[8] Both these are necessary in the proper development of the visual pathway.*

*So every child is born with binocular connection or it may be absent due to many disruptive influences during intrauterine phase of growth. Nativity theory. What is role of the normal visual experience during the post natal period? What does it do to these already existing cortical connections? Is it very essential for solidifying these circuits and strengthening the connections?*

*Animal experiments have given us a lot of information and answered these questions with great clarity. For our understanding of Amblyopia, it is sufficient for us to know that normal visual experience means equal and similar neural impulses from both the eyes, reaching the cortex at the same time. If there is a discrepancy in this process, the eye sending a lower quality of impulse to the cortex is suppressed by the other eye, due to interocular suppression. Callosal fibres are involved in this process.*

*The first effects of Amblyopia are seen at level IV of V 1. The earlier the disruptive visual experience starts in postnatal life, the denser is the amblyopia. The first changes of Amblyopia are seen in level II and III of V 1 cortex in the inhibitory interneurons. The gabaergic neurons are important for the plasticity of the cortex. The Gabaergic inhibitory interneurons are responsible for maturity of the cortex.[8] An immature cortical circuitry during the growth phase of an infant allows for adjustments needed for the varying visual experience, due to separation of the eyes and mature cortex is resistant. Delayed maturation or precocious maturation of the cortical circuitry are well balanced in normal cortex. Plasticity is a developmental necessity and loss of this plasticity happens over a period of time. It does not stop abruptly and there are molecular and biochemical processes involved in the cortical maturation process.[9] Any Amblyopia therapy has to look at how to regain some plasticity and prolong the plasticity of the cortex.[10]*

*In Amblyopia, the lower visual pathways are almost normal and higher pathways are abnormal. During the plasticity period (up to 8 years of age), strabismus, high refractive error, anisometropia and cataract are most amblyopiogenic, and it is important to treat these conditions aggressively to prevent the loss of visual acuity and stereopsis and deficits of visuomotor tasks.*

*In Amblyopia, though the changes occur in cortical area V 1 first, the amplified changes occur in V 2 /V 5 and beyond like in MT area and parietal area and this is what causes many deficits in amblyopia apart from just loss of visual acuity. Patching can improve the acuity, but may leave the other deficits unaltered.*

*The earlier the disruptive influence starts, and longer the influence persists, the denser the Amblyopia and more difficult to reverse the changes.*

*In order to prevent the disruptive influences of abnormal visual experience, during the cortical plasticity stage, we have to diagnose these conditions of Strabismus, Refractive error, Cataract and Anisometropia very early and treat them adequately. This is the only way to prevent Amblyopia. For this, we need to have a structured preschool screening program of all the children. This is very expensive and logistical nightmare. But we have to take steps as the long term financial burden is too much.[11]*

*The mainstay of treatment of Amblyopia has been patching of the sound eye for a few hours a day to all waking hours.[12] The patching of the sound eye during the plasticity period does improve the visual acuity of the Amblyopic eye. The patching works by reducing the competition from the normal eye for the cortical binocular cells and removing the inter ocular suppression. But what the patching does to the binocular cells and stereo acuity is debatable. Patching of the normal eye,*

*though it helps to improve visual acuity of the amblyopic eye, leaves many of the behavioral deficits of vision unaltered. Hence the need to look at binocular forms of therapy. Patching works better when the Amblyopia is not very dense.*

*The alternative methods of therapy of Amblyopia like Dichoptic training methods, perceptual training and more recently, Trans cranial Magnetic stimulation have been tried and shown significant gains in not only visual acuity but also in behavioral aspects of vision.*

***Conclusion:***

*Amblyopia is a developmental cortical disorder secondary to visual disruptive influence occurring early in post natal life. If diagnosed and treated during the plasticity stage, it is reversible. Though the primary cortical changes in Amblyopia are seen in V 1, the other areas like V 2 and MT and parietal areas are also affected and can explain the behavioral deficits in amblyopic eye.*

*Patching remains the mainstay of treatment, and is known to improve the visual acuity in the amblyopic eye but leaves the behavioral deficits of vision unaltered. Hence alternative forms of therapy are needed. The alternative therapy, besides Patching, like Video games, Dichoptic stimulation, Perceptual exercises and Trans cranial Magnetic stimulation all seem to go the root of amblyopia and may be the future of therapy of Amblyopia.*

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