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# Novel application of principal component analysis to understanding visual cortical development

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Visual experience has a profound effect on cortical development and function. Monocular deprivation early in life leads to anatomical and physiological changes in visual cortex that result in poor visual acuity in the deprived eye. Multiple mechanisms mediate this synaptic plasticity in developing visual cortex, including excitatory (NMDA, AMPA) and inhibitory ($GABA_A$) receptors and their subunit composition. However, as the number of mechanisms under consideration increases beyond 2 or 3, it becomes difficult to understand the multidimensional nature of the data and to identify the significant combinations and interactions. We overcame this complexity by applying Principal Components Analysis.

We conducted a comprehensive study of changes in excitatory and inhibitory receptors in visual cortex of cats reared with either normal vision, monocular deprivation, or monocular deprivation followed by a short period of binocular vision. Using Western blot analysis of samples from different regions of visual cortex, we examined changes in excitatory (NR1, NR2A, NR2B, GluR2) and inhibitory ($GABA_A\alpha1$, $GABA_A\alpha3$) receptor subunit expression. Monocular deprivation promoted a complex pattern of changes that were most severe in regions of visual cortex where the central visual field is represented.

To understand the complex nature of these changes, we applied a neuroinformatics approach using Principal Component Analysis (PCA) to address the global pattern of change in these plasticity mechanisms. The biological significance of the principal components was determined by correlating them with the ratios of various synaptic proteins. Principal components reflected the overall receptor expression, the balance between excitation and inhibition, and the maturational shift in receptor subunit composition. PCA showed that monocular deprivation causes a significant shift of the developmental trajectory, bypassing a large proportion of the normal developmental path, and accelerating maturation of the receptor subunit expression. This analysis suggests that monocularly deprived animals have less developmental plasticity and lack the molecular machinery needed for functional maturation of cortical circuits. A brief 4 day period of binocular vision was sufficient to restore these important plasticity mechanisms towards that of normal animals.

The application of Principal Components Analysis allows us to understand the overall changes in this multidimensional data and the correlation analysis enables us to understand their biological significance. These results provide insights into molecular mechanisms underlying amblyopia, why binocular vision is crucial for optimal recovery, and why recovery of vision is so poor when deprivation extends beyond 6 weeks of age.