Complete Restoration of Visual Cortical Responses is Possible Late in Development. Focus on “Recovery of Cortical Binocularity and Orientation Selectivity After the Critical Period for Ocular Dominance Plasticity”

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This story began about 40 years ago when Wiesel and Hubel (1963, 1965) first reported that closing one eye early in development (by monocular lid suturing) produced devastating consequences later in life on the ability of the deprived eye to activate cells in the visual cortex. In the intervening decades, a voluminous literature that continues largely unabated to this day has dealt with virtually every conceivable aspect of how this simple manipulation can impact the developing visual system (Chapman 2004). One of the factors that made this phenomenon so intriguing is the ability to define a relatively clear-cut developmental period during which the visual system is susceptible to monocular deprivation. Such studies have provided a compelling case for critical periods during early brain development. While most effort in this field has focused on the consequences of monocular deprivation, the prospect of recovery of function after a period of early monocular deprivation has also been of considerable interest, driven in no small measure by the clinical implications of such studies. It has been generally assumed that substantial recovery of function can occur, provided that the deprived eye is opened during the critical period. This has led to the tacit assumption that the factors underlying the plasticity of the developing visual system, as defined by the consequences of early monocular deprivation, and the recovery process could be regulated by related, if not entirely equivalent, cellular and molecular mechanisms.

In this issue, Liao et al. (p. 2113–2121) offer compelling evidence challenging this prevalent viewpoint. These investigators examined two key properties of the visual cortex: binocularity and orientation selectivity in ferrets that were allowed to recover from different periods of monocular deprivation. In ferrets, the critical period, during which the visual system is susceptible to the effects of monocular deprivation, has been established as lasting from about 35 to 70 days after birth (Issa et al. 1999). Liao and colleagues studied three groups of animals. One group of ferrets was monocularly deprived for a brief period of time during the peak of the critical period and then allowed normal binocular vision for a short time during the critical period before recordings were made from single neurons in the visual cortex. Within a few days, the ocular dominance profile (ability of both eyes to drive cortical cells) and the orientation selectivity of these neurons were indistinguishable from those of normal animals. This is no surprise since this result confirms the prevalent viewpoint. A second group of ferrets was deprived of patterned vision in one eye from shortly after birth until the critical period had commenced. These animals were then permitted normal vision for the remainder of the critical period. Electrophysiological recordings showed that, in this case, the deprived eye was largely incapable of driving the normal contingent of cells, and virtually all of these neurons were broadly tuned for bars of light at different orientations. Again, this result is in line with the results of earlier studies (Chapman and Stryker 1993). The third group of ferrets was monocularly deprived later in development (in comparison with the second group), with the deprivation period extending well beyond the end of the critical period. Recordings from the visual cortex of these animals yielded an unexpected outcome. Following a relatively brief period of normal vision, binocularity, and orientation selectivity, the two hallmark properties of neurons in the primary visual cortex, were fully restored.

These findings are important for several reasons. First, they provide evidence that the developmental events underlying the functional consequences of monocular deprivation are distinct from those regulating recovery of function. This is in line with the results of studies showing that, while CREB function is essential for ocular dominance plasticity during monocular deprivation (Mower et al. 2002; Pham et al. 1999), this factor is not required for recovery of visual function in visually deprived animals (Liao et al. 2002). Second, the findings suggest that success of amblyopia treatment may be related to the existence of a relatively narrow and early window of normal vision prior to the onset of the amblyopia-inducing condition. Given the potential clinical significance of these results and the obvious differences between the visual system of the ferret and primate, it would now be important to carry out related work on monocularly deprived monkeys. Unlike what has been found in the ferret and other carnivores (Kind et al. 2002; Olson and Freeman 1978), reopening the deprived eye during the critical period in the monkey has been reported to result in little if any recovery of function unless the nondeprived eye is closed (Blakemore et al. 1981). Third, the findings raise questions about the widely accepted Hebbian model as an explanation for the development and plasticity of neuronal circuits in the developing visual system. Since the projections of the nondeprived eye presumably dominate synaptic contacts in layer 4 of the visual cortex, the retraction of these inputs during the recovery period at the expense of the much weaker projections of the deprived eye seems contrary to the widely accepted Hebbian model. In this respect, this study is in broad agreement with the results of other recent studies on the formation of connections in the developing retino-geniculo-cortical system that have challenged the prevalent notion that normal patterns of activity play an essential role in this process.

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(Crowley and Katz 2000; Huberman et al. 2003). On the other hand, the results of Liao et al. do point to some sort of role for visual activity, since recovery was only observed in the group of animals that was permitted normal visual experience prior to the period of monocular deprivation. Perhaps the normal competitive interactions that were allowed early in development, prior to the onset of the deprivation period, left some sort of remnant or marker that the deprived eye projections could reactivate during the subsequent recovery period.

After 40 years of effort, we have learned a great deal about the importance of normal experience on the development and recovery of the visual system from early monocular deprivation. The results of Liao et al. add to this body of literature. However, these results also serve to underscore that much remains to be learned before we can offer a reasonably complete explanation of why monocular deprivation causes a loss of visual function and how visual experience, even after the critical period, can restore such function.

REFERENCES


