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Preference for binocular concordant visual input in early postnatal development remains despite prior monocular deprivation

Donald E. Mitchell *, Jan Kennie, Kevin R. Duffy

Department of Psychology, Dalhousie University, Halifax N.S., Canada B3H 4R2

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ABSTRACT

Short daily periods of binocular vision, if concordant and continuous, have been shown to outweigh or protect against much longer daily periods of monocular deprivation to allow the development of normal visual acuity in both eyes of kittens. The greater weight placed on binocular visual input could arise because of an inherent bias for binocular input within the visual pathway at all times during development (Binocular model), or else from a more passive process that follows from its match to a highly binocular template at the time mixed daily visual input began (Template model). To distinguish between the predictions of these two models, kittens were monocularly deprived from normal eye-opening until either 4, 5, or 6 weeks of age at which time they received mixed daily visual input for 4 weeks. According to the Template model, the preferred input for these animals would be monocular exposure (ME) because of its match to the monocular template produced by a period of preceding monocular deprivation. However, instead of short daily period of ME offsetting much longer periods of binocular exposure (BE) to perpetuate the dire effects of the prior deprivation, short daily periods of BE promoted significant recovery of vision in the deprived eye. The fit to the Binocular model implies the existence of a robust substrate for binocular vision that is highly resistant to disruption and which could form the substrate for binocular approaches to treatment of amblyopia.

1. Introduction

Recent experiments conducted on both cats (Mitchell, Kind, Sengpiel, & Murphy, 2003; Mitchell, Kind, Sengpiel, & Murphy, 2006) and monkeys (Sakai et al., 2006; Wensveen et al., 2006) provide new insight into the role of early visual experience in the development of vision and of the central visual pathways. As an alternative to one traditional approach that examines the consequences for development of rearing animals with exclusively abnormal visual input, new experiments have pitted daily periods of normal and abnormal vision against each other in order to determine if all visual input is equally effective (Mitchell et al., 2003). In these experiments, daily visual exposure early in life consisted of adjacent periods of normal and abnormal exposure in differing proportions. For the latter exposure, animals had one eye occluded by a mask so that they received only monocular input. Such exposure, when exclusive and extended, can virtually eliminate form vision in the deprived eye of both cats (Giffin & Mitchell, 1978; Mitchell, 1988) and monkeys (Harwerth, Crawford, Smith, & Boltz, 1981; Von Noorden, 1973; Von Noorden, Dowling, & Ferguson, 1970), and can cause a marked shift in cortical ocular dominance (Hubel, Wiesel, & LeVay, 1977; Hata et al., 2000; Schmidt, Stephan, Singer, & Lowel, 2002). Results from this work clearly showed that not all visual input was treated equally, and that short daily periods of normal concordant binocular exposure (BE) effectively offset much longer adjacent periods of abnormal monocular exposure (ME) to allow the normal development of spatial vision in both eyes. Not only did the daily period of binocular vision prevent the development of deprivation amblyopia in the (deprived) eye, but it also allowed the development of normal (i.e. similarly sized) cortical ocular dominance domains for the two eyes (Schwarzkopf, Vorobyov, Mitchell, & Sengpiel, 2007).

On the basis of experiments on kittens (Mitchell et al., 2006; Mitchell & Sengpiel, 2009; Mitchell, Sengpiel, Hamilton, Schwarzkopf, & Kennie, 2011) that manipulated the duration of daily visual exposure, the critical daily binocular exposure required to prevent the development of deprivation amblyopia was shown to be best expressed by the proportion of the total daily visual exposure that was binocular, as opposed to an absolute amount of such exposure. The critical proportion, approximately 30%, was very close to the value computed from experiments conducted on monkeys (Wensveen et al., 2006), which indicates a noteworthy convergence across species.

The greater influence of daily binocular vision over comparatively longer monocular visual input is at odds with models that postulate a strong instructive role for visual experience in visual

* Corresponding author.
E-mail address: d.e.mitchell@dal.ca (D.E. Mitchell).

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development. According to such a role, both daily exposures would be expected to inform development so that all non-trivial periods of ME would be expected to have a negative impact on the vision of the deprived eye. But no impact on spatial vision occurs when the ME is accompanied by a period of BE that accounts for at least 30% of the total visual exposure (Mitchell & Sengpiel, 2009; Mitchell et al., 2006). It is possible that binocular exposure is privileged because it is more closely matched than ME to the pre-existing neural template at the time that mixed daily visual exposure began. The visual cortex of kittens is known to be highly binocular at 4 weeks (Crair, Gillespie, & Stryker, 1998; Hubel & Wiesel, 1963; Olson & Freeman, 1980) so the enhanced weighting of binocular exposure could follow from a higher level of neural excitation during binocular exposure that could thereby override the influence on activity-dependent mechanisms of neural development during a period of ME on the same day. Although the preferential weighting of binocular visual input may arise for other as yet unknown reasons, the idea that it follows as a passive consequence of a pre-existing neural architecture is testable because it is possible, through early selected visual deprivation, to begin the experiment on animals with an abnormal neural template.

This paper describes the result of application of mixed daily visual exposure in kittens with an abnormal neural template produced by a prior period of monocular deprivation beginning at around the time of normal eye-opening and extending to the time at which daily mixed visual input was initiated. A rich body of prior experimentation indicates that when daily mixed visual experience began after a period of monocular deprivation, the cortical neural substrate would have been highly monocular with ocular dominance skewed strongly toward the non-deprived eye (e.g. Mitchell & Timney, 1984; Movshon & Kiorpes, 1990). If the eventual outcome of mixed exposure followed passively from the functional anatomy of the cortical template, the predicted preferred input would be monocular due to its congruence with the strongly monocular neural template. Short daily periods of ME that duplicate the prior early deprivation would therefore be expected to offset much longer periods of binocular exposure to perpetuate apparent form blindness of the deprived eye. We demonstrate in this study that the results were inconsistent with this prediction as this outcome was observed only with long daily periods of ME and furthermore, that substantial improvement of the vision of the deprived eye occurred with just short daily periods of BE. Thus, just like normally reared kittens, binocular visual experience was weighted more than monocular experience despite the fact that the latter matched the animal's prior visual input and was congruent with the neural template.

2. Materials and methods

2.1. Experimental design and predictions

The experimental design builds upon the finding reproduced in Fig. 1 that displays the effects of different regimens of mixed daily visual exposure imposed for 4 weeks on kittens beginning at 4 weeks of age. This particular data set (Mitchell et al., in preparation) was obtained from kittens that received just 3.5 h visual experience each day divided between intervals of BE and ME of varying amounts. For the remaining 20.5 each day the animals were housed in complete darkness with their mother. The visual history of the animals is illustrated in schematic form at the top of Fig. 1. The graph shows the grating acuity of the eye that was occluded each day during the period of ME, as a function of the length of the daily period of BE. The acuity of the deprived eye has been plotted relative to the acuity of the other eye as measured the day before on the last day of mixed daily visual experience.

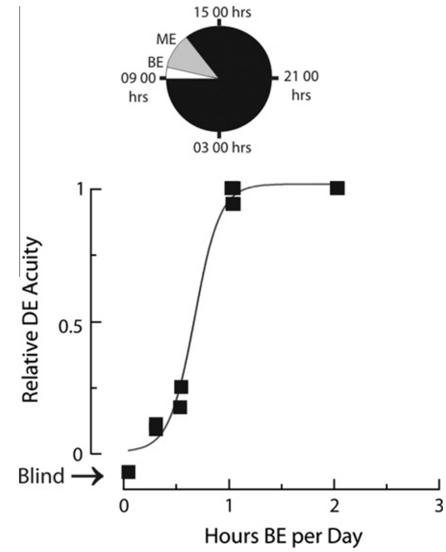

Fig. 1. Grating acuity of the deprived eye of 16 kittens that received 4 weeks of mixed daily visual experience starting at 4 weeks of age as a function of the amount of daily binocular visual exposure. The deprived eye acuity was measured on the day following the last episode of mixed daily exposure and has been plotted relative to that of the fellow eye measured on the previous day. The number of data points appears limited many animals had identical acuities (see Table 1). The daily visual history is illustrated schematically above the graph; the period of darkness is shown in black and the episodes of binocular and monocular exposure are depicted respectively, by the white and hatched (gray in my version) sectors. For simplicity the period of binocular exposure has been shown to occur first but for some animals it occurred after monocular exposure. The curve fitted to the data is the logistic function.

$$Y = 1.01 + \exp(-5.35 - 8.22X)$$

where Y is the normalized acuity of the deprived eye and X is the number of hours of daily BE.

Remarkably, 1 h of BE was sufficient to outweigh or protect against 2.5 h of ME each day to permit the development of equal and normal grating acuity in the two eyes.

For animals that received normal visual input prior to the 4 week period of daily mixed visual input, it is not possible to distinguish between explanations for the result in terms of the amount of daily visual input that was binocular (Binocular model) versus the amount of daily exposure matched to the pre-existing cortical template (Template model), as both scenarios predict the same outcome (Fig. 2A). However, for animals that were monocularly deprived prior to the initiation of mixed daily visual exposure (see Fig. 2B), the two predictions are very different because the length of the daily cortical template match and the amount of binocular exposure move in opposite directions to each other. According to the Template model and the results of Fig. 1, daily periods of ME that perpetuate the exposure during the prior period of MD (depicted by the eye icons) of 1 h or more might be expected to maintain apparent form blindness of the deprived eye as indicated by the dashed curve. Only when the daily periods of ME were short (<1 h) and the daily BE correspondingly long, would the deprived eye be expected to show any visual recovery. Projected data for the 3.5 h BE (zero ME) condition were derived from previously obtained results (Giffin & Mitchell, 1978; Mitchell, 1988) on the recovery of vision of the deprived eye that occurs in monocularly deprived kittens that experience exclusive BE during recovery. On the other hand, the Binocular model (continuous curve) would predict that the deprived eye acuity would be better than the expectation of the Template model as even short daily periods of BE would be expected to promote some recovery of the vision of