

Missing sights: consequences for visual cognitive development

Daphne Maurer^{1,2}, Terri L. Lewis^{1,2,3} and Catherine J. Mondloch^{1,4}

¹Department of Psychology, McMaster University, Hamilton, ON, Canada L8S 4K1

²Department of Ophthalmology, The Hospital for Sick Children, Toronto, Ontario, Canada M5G 1X8

³Department of Ophthalmology & Vision Sciences, University of Toronto, Toronto, Ontario, Canada M5S 1A8

⁴Department of Psychology, Brock University, St. Catharines, ON, Canada

Corresponding author: Maurer, Daphne (maurer@mcmaster.ca).

The effects of early-onset blindness on the development of the visual system have been explained traditionally by the stabilization of transient connections through Hebbian competition. Although many of the findings from congenital cataract and congenital blindness are consistent with that view, there is inconsistent evidence from studies of visual cognition in children treated for visual deprivation from cataract, case reports of recovery of vision in adults, and studies of visual reorganization after late-onset blindness. Collectively, the data from congenital cataract and congenital blindness indicate that early visual experience sets up the infrastructure for later learning involving both the dorsal ('where') and ventral ('what') streams. Nevertheless, there is surprising residual plasticity in adulthood that can be revealed if vision is lost either temporarily or permanently. This has important implications for understanding the role of early visual experience in shaping visual cognitive development.

Introduction

Human visual acuity improves fivefold in the first 6 months after birth and continues to improve over the next 6 years [1]. The final acuity is abnormal if early visual input was blocked by cataracts, with a larger impairment in the affected eye(s) if the deprivation was monocular rather than binocular and if the deprivation occurred earlier in life [2]. As in animal studies [3,4], these results suggest that early visual deprivation during a sensitive period causes permanent damage to the visual cortex and presumably the higher visual areas to which it projects, with a worse outcome if there was also uneven competition for cortical synapses between a non-deprived eye and a treated eye. Recent studies indicate that when visual input is missing permanently because of congenital blindness, the visual cortex becomes specialized for the processing of touch and sound instead of vision. These findings can be explained by a shaping of otherwise transient connections through a process of Hebbian competition in which stronger input signals win out and unused connections are pruned permanently. However, the generality of these patterns and their interpretation by Hebbian competition has been called into question: (i) by recent studies of children treated for cataract that followed patients longitudinally and that included measures of higher visual functions; (ii) by case reports of surprising recovery of vision under some circumstances in adulthood; and (iii) by studies of visual re-organization after late-onset blindness. This review considers the

implications of these findings for understanding the role of early visual input in shaping normal visual cognitive development.

Cataract-reversal patients

Children born with bilateral or unilateral cataracts provide a natural experiment to assess the effects on human development of early deprivation and of uneven competition between the eyes for cortical connections. A cataract is an opacity in the lens of the eye which, if large and dense, allows only diffuse light to reach the retina. Pattern deprivation continues until the defective natural lens of the eye is removed surgically and the eye is fitted with a compensatory optical correction (e.g. a contact lens). When the final outcome is measured, some visual capabilities are normal despite early visual deprivation, while others seem permanently impaired (see Table 1 for examples). For example, children born with dense bilateral cataracts and then treated during the first year of life later develop normal sensitivity to high rates of flicker, are normal at discriminating between large shapes including facial features, and are normal at detecting direction of eye gaze [5–7]. Because these skills exceed those present at birth in the visually normal child [8–10], the normal performance of cataract-reversal patients implies that the neural circuits underlying these capabilities can develop in the absence of patterned visual input or more likely, can recover completely from a period of earlier visual deprivation. (Another possibility is that alternative networks are recruited). Longitudinal studies have documented that such recovery occurs for some visual capabilities: patients treated for bilateral congenital cataracts reduce the size of an initial acuity deficit by improving at faster-than-normal rates in the first month after treatment, and they overcome later deficits by contrast sensitivity for low spatial frequencies (the minimum contrast at which wide stripes can be seen) by improving more-than-normal between 4 and 7 years of age [11,12].

By contrast, children treated for bilateral congenital cataracts later have reduced visual acuity (except in some cases when the deprivation lasted less than 10 days [13,14]) and impairments in some aspects of higher visual cognition: reduced capability to integrate local elements into a global form or global direction of motion, and impaired face processing [7,15–19]. Without special training, these deficits persist into adulthood. Nevertheless, in almost all patients, the sensitivity

achieved is better than that of visually normal newborns, a result indicating that there was some visual plasticity despite the early deprivation.

Congenital blindness

Another natural experiment for studying visual plasticity is children who were born with non-reversible blindness, such that the visual cortex never receives input from external visual stimuli. Recent imaging studies of adults who were blind from an early age indicate that the visual cortex can be recruited for processing tactile and auditory input [20]. For example, tactile input from reading Braille or discriminating between complex tactile patterns activates the visual cortex almost as much as it activates sensorimotor cortex (Figure 1) [21–23]. When the visual cortical activity is disrupted temporarily by transcranial magnetic stimulation (TMS), adults blind from an early age report that Braille dots do not make sense, that some are missing, and that they feel extraneous phantom dots; their error rates also increase significantly [24]. Auditory input also activates the visual cortex after early blindness: spoken sentences cause fMRI activation of primary and higher visual cortical areas [25] and deviant sounds such as an incongruous word or unexpected pitch elicit a response over the visual cortex [26–28], although some of these effects may reflect higher-order language processing rather than auditory processing *per se* [29,30]. In the cat, the removal of the eyes at birth is sufficient to induce neurons in the primary visual cortex to respond to auditory stimuli [31].

Neural mechanisms of visual cortical reorganization: Hebbian competition?

The traditional explanation of the effects of congenital blindness is the stabilization of transient connections among sensory cortical areas that are present in early infancy [20]. There is anatomical evidence for such exuberant connections in humans [32], as in animals [33], and some indication that they are functional during infancy: spoken language elicits a large event-related potential (ERP) over the temporal cortex in infants, as it does in adults, but in infants it also elicits a large response over the visual cortex, as if the infant is 'hearing' with the visual cortex [34]. The postnatal pruning of the exuberant connections is driven, at least in part, by Hebbian competition among sensory inputs: the input from the eyes to the visual cortex is stronger, faster, and more coherent than the input arriving via the auditory and somatosensory cortices and hence it is strengthened to the detriment of the other inputs [28]. The most striking evidence that external input determines what is pruned and what remains comes from studies in which retinal axons in the infant ferret were induced to replace the normal auditory innervation of the medial geniculate nucleus (MGN) and its input to the auditory cortex. Neurons in the auditory cortex became sensitive to visual orientation, direction of motion, and velocity and mediated *visual* percepts [35]. A similar explanation is given for the worse outcome after unilateral than after bilateral congenital cataracts: when a child is born with a cataract in only one eye, connections from the deprived eye to

visual cortical neurons lose out in favour of the connections from the normal eye [3]. In other words, Hebbian competition works during normal early development to tune the connections to visual cortical neurons, eliminating non-visual inputs and balancing the input from the two eyes.

Beyond Hebbian competition

The pruning effected by Hebbian competition is believed to leave the visual nervous system more-or-less permanently rewired and to ramify through to higher cortical areas that receive their main input from primary sensory cortical areas. However, recent studies indicate that some exuberant connections are inhibited rather than pruned and that, for some visual functions, there is visual plasticity even in adolescence and adulthood – well beyond the period of synaptic pruning. Furthermore, the effects of uneven competition between the eyes for cortical connections vary across visual functions, in ways that are not consistent with an explanation based entirely on Hebbian competition.

Crystallization of visual connections by visual input long after the end of pruning

Studies of children who had normal visual input at birth but developed cataracts postnatally allow an assessment of the role of visual input at various times during postnatal development. For some visual capabilities, these studies indicate that visual input is necessary throughout the period of normal functional development and even after the age when performance reaches adult levels – that is, visual input is necessary to induce changes and to crystallize connections after they are formed. Thus, a short period of visual deprivation beginning any time before about age 10 causes permanent deficits in letter acuity, which reaches adult functional levels by age 6 [2]. Similarly, short periods of deprivation beginning even in early adolescence cause permanent deficits in peripheral light sensitivity, which reaches adult functional levels by age 7 [36], although the deficits are smaller with later onset for both aspects of vision. These effects are beyond the period of anatomical pruning of visual cortical connections [32]. Visual input is not necessary for the crystallization of all visual connections. For example, sensitivity to the overall direction of motion of a stimulus (a capability called global motion which implicates higher visual cortical area V5 in the dorsal stream) is normal even when deprivation begins as early as 4 months of age (Figure 2) [17], despite the fact that visually normal 4-month-olds are much worse (7 times less sensitive) than adults at detecting the global direction of motion [37]. Striking evidence for the resilience of sensitivity to global motion is the case of an adult who suffered visual deprivation after the loss of one eye and corneal damage to the other eye at age 3.5 years. After a corneal transplant at age 43, he had severe deficits in acuity, form identification, and face processing, and abnormal activation of the primary visual cortex V1 and higher visual cortical areas (V2, V3, fusiform and lingual gyri). By contrast, the fMRI activation of area v5 was normal

both in strength and area and he performed normally on many motion tasks [38].

Residual plasticity in adulthood

The visual system is assumed to be hard-wired long before adolescence, such that short-term perturbations (e.g. patching an eye during an infection or a short period of deprivation from senile cataract) cause no permanent damage. Conversely, it is assumed to be too late to offset the effects of early visual deprivation from cataract – either by patching the good eye in monocular cases or active training in either monocular or binocular cases – after about age 6 yrs, the age when acuity is adult-like [40]. Yet surprising plasticity after age 6 has been shown in individuals with impaired visual function (amblyopia) resulting from visual problems during early development such as partial cataracts, misaligned eyes, or misfocus in one eye. There are anecdotal reports of improved vision in an adult's amblyopic eye after vision in the fellow 'good' eye was lost, with changes occurring so rapidly in some cases that new connections are unlikely to have formed [40–42]. These reports suggest that the amblyopic eye is capable of functioning well, but is inhibited by the fellow eye. Similarly, full-time patching or blurring of the good eye for 6 months to 1 year beginning between 7 and 10 years of age can induce a dramatic improvement in the acuity of the amblyopic eye and improved binocular function: acuity improved from a median value of 20/134 (almost 3 times worse than normal) to a median value of 20/25, or almost normal [43]. As well, concentrated training of the amblyopic eye by providing feedback in the laboratory or by doing close work at home is successful in inducing improvements in the specific trained abilities, as well as in letter acuity [44–46]. Collectively, these results suggest that there is considerable visual plasticity in the adult brain.

Plasticity after permanent blindness with late onset

Imaging studies of adults who became permanently blind during early adolescence, long after the transient connections from auditory and somatosensory cortex to the visual cortex would have been pruned by Hebbian competition, show robust activation of the primary visual cortex during tactile discrimination [23,24]. In higher visual areas, there is some activity during tactile discrimination even when the onset of blindness occurred in adulthood [21] – as if tactile responses from visual cortical neurons were released after the abolition of visual signals. Consistent with that interpretation is evidence that normally sighted adults improve in discriminating Braille characters after 5 days of training while blindfolded and begin to show fMRI activation of the visual cortex in response to tactile stimulation of the fingertips, activation that disappears within a day of sight being restored [47]. Collectively, these data suggest that some of the transient connections may not be pruned but rather may be silenced because of their relatively low signal strength and/or because they are actively inhibited, such that they retain the potential to be activated and influence perception if the normal visual input is removed [20]. Evidence for active inhibition comes from studies of

monocularly deprived kittens: input through the previously deprived eye that is insufficient to drive a neuron can, nevertheless, modulate the neuron's response to input from the good eye ([48]; and see [49] for more general evidence of inhibition, rather than pruning, of unused connections).

Sparing of some higher visual functions after monocular deprivation

Consistent with anatomical and physiological studies in animal models [2], children treated for unilateral congenital cataract show deficits in grating acuity during infancy, in asymptotic acuity, by contrast sensitivity, and in peripheral sensitivity to a dim light [14,50–54]. As predicted by Hebbian competition, the deficits are larger than those after binocular deprivation unless the non-deprived eye had been patched regularly [1–4]. However, this pattern does not hold for some higher-order visual functions. After early binocular deprivation, there are severe impairments in sensitivity to the overall direction of motion of a stimulus (global motion). Surprisingly, after early monocular deprivation, the impairment in the deprived eye is three times *smaller* than after binocular deprivation (Figure 2) [17]. There is a similar pattern for global form, which requires integration of local pattern elements into a global percept of form and implicates higher visual cortical area V4 in the ventral stream. The impairment is significantly smaller in the deprived eye after early monocular deprivation than after early binocular deprivation, although the difference between unilateral and bilateral cases is not as marked as for global motion (Figure 3) [16]. In these same patients, there was no sparing of acuity, for which higher visual cortical areas do not play an essential role: acuity after monocular deprivation was equal to that after bilateral deprivation, if there had been regular patching of the good eye to force usage of the previously deprived eye, and worse than that of bilaterally deprived patients, if there had been no such patching. Thus, competitive interactions compatible with Hebbian competition which are evident at lower levels of the visual system co-occur with collaborative interactions in some higher visual cortical areas that enable a relative sparing of some aspects of vision after early monocular deprivation

Lessons for understanding visual cognitive development

Early experience can be important to preserve the infrastructure for later learning, without any learning taking place at the earlier time

Children treated for bilateral congenital cataracts as early as 2–3 months of age fail to develop normal holistic face processing and normal sensitivity to the spacing of facial features ([15,19]; see Table 1). Yet the first signs of these capabilities do not appear in the visually normal infant until later during infancy [55] and sensitivity to the spacing of facial features is not adult-like until after 14 years of age [56]. There is a similar pattern for visual acuity: by the first birthday, children treated during early infancy for bilateral congenital cataract have overcome their initial deficit in acuity and perform within normal limits. However, their acuity hits an asymptote by age 4

ys, while that of visually normal children continues to improve until about age 6 yrs, leaving the patients with the permanent deficit in acuity described above ([2,12]; see Table 1). Like the results for face processing, this sleeper effect indicates that early visual input may set up the neural architecture that will be refined by later experience. Without visual input, that hardware may be recruited for other functions like touch or hearing. Similarly, the visual cortex of the congenitally blind is preserved for tactile processing of Braille characters by connections that normally are transient, even though the child does not learn Braille until much later in development. When there is normal visual input, the infrastructure is preserved because visual connections are not pruned or are strongly inhibited.

Early experience has a large impact on slowly developing abilities but can also affect abilities that mature rapidly

Early binocular deprivation leads to large, permanent deficits in some aspects of vision, but spares other aspects or causes only small deficits. One unifying developmental principle is the Detroit model: 'last hired, first fired' or 'last to develop, most damaged' [44]. Thus, after early deprivation, there are bigger deficits in sensitivity to slow than to fast rates of flicker (Table 1) [5,50], in the far temporal field (e.g. the far left visual field for the left eye) than in other parts of the visual field [52], and to the direction of local motion defined by contrast rather than luminance [57]. In each case, the greater deficit is for the aspect of vision that is slower to mature in visually normal children [8,52,58,59].

However, the effects of early binocular deprivation do not always follow the Detroit principle. Visually normal children and monkeys achieve adult levels of sensitivity earlier for sensitivity to the direction of global motion than the perception of global form defined by dot patterns, and brain areas necessary for perceiving global motion mature exceptionally early in the monkey [17,60–62]. However, early binocular deprivation in humans causes much larger deficits in the motion task than in the form task (Figures 2,3) [16,17]. The Detroit principle also does not hold for comparisons of the sensitive period for damage: grating acuity and sensitivity to global motion are similarly immature during infancy and take about 6 years to reach adult levels [1,17,37], but postnatal visual deprivation causes large impairments in acuity if the onset is before about age 10, but has no effect on global motion if the onset is after the first few months of life. Similarly, the use of the visual cortex for tactile and auditory processing in the congenitally blind occurs for both capabilities that develop rapidly during infancy (e.g. auditory localization, processing of relative pitch) and those that develop slowly in the visually normal child (e.g. word learning).

Early experience has an impact on both the dorsal (where) and ventral (what) streams

To a large extent, visual stimuli are processed in parallel by the dorsal visual stream, which is specialized for processing information about motion and space and which favors the peripheral visual field, and by the ventral visual stream, which is specialized for processing

information about form and colour and which favors the central visual field [34]. Some have hypothesized that the dorsal pathway is more plastic than the ventral pathway both for possible enhancement (as in the congenitally deaf, where the absence of competitive auditory inputs promotes supranormal development) and for deficits (as in children with dyslexia, Williams syndrome, or hemiplegic cerebral palsy), possibly because the dorsal pathway has a more protracted period of development [34,63,64]. This hypothesis leads to the prediction that the deficits after early binocular deprivation and the adverse effects of uneven competition between the eyes should be greater for tasks tapping mainly the dorsal stream (e.g. peripheral, moving) than for tasks tapping mainly the ventral stream (e.g. central, colour, form). It also leads to the prediction that the visual cortex of the congenitally blind should be recruited for tasks involving the dorsal rather than the ventral stream. Consistent with these predictions, children treated for bilateral congenital cataract have larger deficits in integrating local signals to perceive global motion (dorsal) than to perceive global form (ventral) (Figures 2,3) [16,17].

However, contrary to the expectation of larger deficits in peripheral (dorsal) than central (ventral) vision, children treated for bilateral congenital cataract have deficits by contrast sensitivity that are of constant magnitude from the centre of the visual field to 30° in the periphery, and children treated for unilateral cataract have their largest deficit in the central visual field [53]. Moreover, children treated for unilateral cataract have a relative sparing of sensitivity to global motion (dorsal), such that their deficit is of similarly small size for global motion and global form (Figures 2,3) [16,17]. Deficits in configural processing of faces after early binocular deprivation [15,19,56] also indicate that the ventral pathway is not spared. Overall, the results suggest that early visual input plays a large role in the development of both the dorsal and ventral streams, perhaps by preventing pruning of connections to be refined later or protection of them from inhibitory silencing. The predictions are complicated by recent evidence that the two pathways are not well segregated in infants [65] and that parts of the dorsal stream mature relatively early [17,60–62]. Analogously, the visual cortex of the congenitally blind is recruited both for spatial localization of auditory stimuli (dorsal) and for recognition of word form (ventral) [29,30,69].

Conclusions

Studies of adults with a history of early visual deprivation from cataract or permanent blindness indicate that early sensory input plays an important role in setting up the infrastructure for later tuning of the visual cortex. When visual input is delayed until cataracts are removed, there is only partial recovery of visual capabilities. When visual input is missing permanently because of blindness, the visual cortex becomes specialized for touch and hearing. To a large extent, these changes represent the expected outcome of Hebbian competition among transient connections to the visual cortex, a competition that determines which connections are strengthened and which

are pruned. However, evidence of rapid plastic changes under some circumstances in adolescence and adulthood suggests that some of those connections are silenced rather than pruned. Future studies investigating the details of the developmental trajectory after early visual deprivation at both the functional and neural levels will allow a better understanding of the limits to plasticity and may suggest new approaches to rehabilitation (see Box 1).

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References

- 1 Maurer, D. and Lewis, T.L. (2001) Visual acuity: the role of visual input in inducing postnatal change. *Clin. Neurosci. Res.* 1, 239–247
- 2 Lewis, T.L. and Maurer, D. Multiple sensitive periods in human visual development: Evidence from visually deprived children. *Dev. Psychobiol.* (in press)
- 3 Mitchell, D.E. and MacKinnon, S. (2002) The present and potential impact of research in animal models for clinical treatment of deprivation amblyopia. *Clin. Exp. Optom.* 85, 5–18
- 4 Daw, N.W. (2003) Critical periods in the visual system. In *Neurobiology of Infant Vision* (Hopkins, B. and Johnson, S.P., eds), pp. 43–103, Praeger
- 5 Ellemberg, D. *et al.* (1999) Spatial and temporal vision in patients treated for bilateral congenital cataracts. *Vision Res.* 39, 3480–3489
- 6 Maurer, D. *et al.* (1989) The effects of deprivation on human visual development: Studies of children treated for cataracts. In *Applied Developmental Psychology* (Vol. 3): *Psychological Development in Infancy*, pp. 139–227, Academic Press
- 7 Geldart, S. *et al.* (2002) The effects of early visual deprivation on the development of face processing. *Dev. Sci.* 5, 490–501
- 8 Ellemberg, D. *et al.* (1999) The development of spatial and temporal vision during childhood. *Vision Res.* 39, 2325–2333
- 9 Mondloch, C.J. *et al.* (2002) Configural face processing develops more slowly than featural face processing. *Perception* 31, 553–566
- 10 Mondloch, C. *et al.* (2003) Developmental changes in face processing skills. *J. Exp. Child Psychol.* 86, 67–84
- 11 Maurer, D. *et al.* (1999) Rapid improvement in the acuity of infants after visual input. *Science* 286, 108–110
- 12 Ellemberg, D. *et al.* (2001) The role of visual input in setting up spatial filters in the human visual system. *Proceedings of The Society for Imaging Science and Technology: Image Processing, Image Quality, Image Capture Systems Conference, Imaging Science and Technology*, pp. 421–425, PICS
- 13 Magnusson, G. *et al.* (2002) Changes in visual acuity from 4 to 12 years of age in children operated for bilateral congenital cataracts. *Br. J. Ophthalmol.* 86, 1385–1398
- 14 Lundvall, A. and Kugelberg, U. (2002) Outcome after treatment for congenital bilateral cataract. *Acta Ophthalmol. Scand.* 80, 593–597
- 15 Le Grand, R. *et al.* (2001) Early visual experience and face processing. *Nature* 410, 890; Correction. 412, 786
- 16 Lewis, T.L. *et al.* (2002) Sensitivity to global form in glass patterns after early visual deprivation in humans. *Vision Res.* 42, 939–948
- 17 Ellemberg, D. *et al.* (2002) Better perception of global motion after monocular than after binocular deprivation. *Vision Res.* 42, 169–179
- 18 Jeffrey, B.G. *et al.* (2004) Altered global shape discrimination in deprivation amblyopia. *Vision Res.* 44, 167–177
- 19 Le Grand, R. *et al.* (2004) Impairment in holistic face processing following early visual deprivation. *Psychol. Sci.* 15, 762–768
- 20 Théoret, H. *et al.* (2004) Behavioral and neuroplastic changes in the blind: evidence for functionally relevant cross-modal interactions. *J. Physiol. (Paris)* 98, 221–233
- 21 Burton, H. *et al.* (2002) Adaptive changes in early and late blind: a fMRI study of Braille reading. *J. Neurophysiol.* 87, 589–607
- 22 Gizewski, E. *et al.* (2003) Cross-modal plasticity for sensory and motor activation patterns in blind subjects. *Neuroimage* 19, 968–975
- 23 Sadato, N. *et al.* (2002) Critical period for cross-modal plasticity in blind humans: A functional MRI study. *Neuroimage* 16, 389–400
- 24 Cohen, L. *et al.* (1999) Period of susceptibility for cross-modal plasticity in the blind. *Ann. Neurol.* 45, 451–460
- 25 Röder, B. *et al.* (2002) Speech processing activates visual cortex in congenitally blind humans. *Eur. J. Neurosci.* 16, 930–936
- 26 Kujala, T. *et al.* (1995) Visual cortex activation in blind humans during sound discrimination. *Neurosci. Lett.* 183, 143–146
- 27 Röder, B. *et al.* (2000) Event-related potentials during auditory language processing in congenitally blind and sighted people. *Neuropsychologia* 38, 1482–1502
- 28 Bavelier, D. and Neville, H. (2002) Cross-modal plasticity: Where and how? *Nat. Rev. Neurosci.* 3, 443–452
- 29 Amedi, A. *et al.* (2003) Early 'visual' cortex activation correlates with superior verbal memory performance in the blind. *Nat. Neurosci.* 6, 758–766
- 30 Burton, H. *et al.* (2003) Dissociating cortical regions activated by semantic and phonological tasks: a fMRI studying blind and sighted people. *J. Neurophysiol.* 90, 1965–1982
- 31 Yaka, R. *et al.* (1999) Auditory activation of cortical visual areas in cats after early visual deprivation. *Eur. J. Neurosci.* 11, 1301–1312
- 32 Huttenlocher, P. (1994) Synaptogenesis in human cerebral cortex. In *Human Behaviour and the Developing Brain* (Dawson, G. and Fischer, K., eds), pp. 137–152, Guilford Press
- 33 Kennedy, H. *et al.* (1997) Synaesthesia: implications for developmental neurobiology. In *Synaesthesia: Classic and contemporary readings* (Baron-Cohen, S. and Harrison, J., eds), pp. 243–256, Blackwell
- 34 Neville, H. (2005) Variability in human brain plasticity. In *Attention and Performance XXI: Processes of Change in Brain and Cognitive Development* (Munakata, Y. and Johnson, M.H., eds), pp. 000–000, (in press)
- 35 Sur, M. and Leamey, C. (2001) Development and plasticity of cortical areas and networks. *Nat. Rev. Neurosci.* 2, 251–262
- 36 Bowering, E.R. *et al.* (1993) Sensitivity in the nasal and temporal hemifields in children treated for cataract. *Invest. Ophthalmol. Vis. Sci.* 34, 3501–3509
- 37 Wattam-Bell, J. (1994) Coherence thresholds for discrimination of motion direction in infants. *Vision Res.* 34, 877–883
- 38 Fine, I. *et al.* (2003) Long-term deprivation affects visual perception and cortex. *Nat. Neurosci.* 6, 915–916
- 39 Birnbaum, M. *et al.* (1977) Success in amblyopia therapy as a function of age: a literature review. *Am. J. Optom. Physiol. Opt.* 54, 269–275
- 40 Vereecken, E. and Brabant, P. (1984) Prognosis for vision in amblyopia after the loss of the good eye. *Arch. Ophthalmol.* 102, 220–224
- 41 Mallach, M. *et al.* (2000) Amblyopia: is visual loss permanent? *Br. J. Ophthalmol.* 84, 952–956
- 42 Tsuchiya, S. (1986) Changes in the contrast sensitivity of an amblyopic eye after losing the other normal eye. *Tokai J. Exp. Clin. Med.* 11, 145–150
- 43 Mintz-Hittner, H. and Fernandez, K. (2000) Successful amblyopia therapy initiated after age 7 years. *Arch. Ophthalmol.* 118, 1535–1541
- 44 Levi, D. Perceptual learning in adults with amblyopia: A re-evaluation of critical periods in human vision. *Dev. Psychobiol.* (in press)
- 45 Li, R. and Levi, D. (2004) Characterizing the mechanisms of improvement for position discrimination in adult amblyopia. *J. Vis.* 4, 476–487
- 46 Simmers, A. and Gray, L. (1999) Improvement of visual function in an adult amblyope. *Optom. Vis. Sci.* 76, 82–87

- 47 Kauffman, T. *et al.* (2002) Braille character discrimination in blindfolded human subjects. *Neuroreport* 13, 571–574
- 48 Freeman, R.D. and Ohzawa, I. (1988) Monocularly deprived cats: binocular tests of cortical cells reveal functional connections from deprived eye. *J. Neurosci.* 8, 2491–2506
- 49 Maurer, D. and Mondloch, C. (2005) The infant as synaesthete. In *Attention and Performance XXI: Processes of Change in Brain and Cognitive Development* (Munakata, Y. and Johnson, M.H., eds), pp. 000–000, (in press)
- 50 Elleberg, D. *et al.* (2000) Influence of monocular deprivation during infancy on the later development of spatial and temporal vision. *Vision Res.* 40, 3283–3295
- 51 Birch, E.E. *et al.* (1998) Early treatment of congenital unilateral cataract minimizes unequal competition. *Invest. Ophthalmol. Vis. Sci.* 39, 1560–1566
- 52 Bowering, E. *et al.* (1997) Constriction of the visual field of children after early visual deprivation. *J. Pediatr. Ophthalmol. Strabismus* 34, 347–356
- 53 Maurer, D. and Lewis, T.L. (1998) Overt orienting toward peripheral stimuli: Normal development and underlying mechanisms. In *Eye movements, Attention and Development*. (Richards, J., ed.), pp. 51–102, Erlbaum
- 54 Lewis, T.L. *et al.* (1995) The development of grating acuity in children treated for unilateral or bilateral congenital cataract. *Invest. Ophthalmol. Vis. Sci.* 36, 2080–20
- 55 Cashion, C. and Cohen, L. (2003) Beyond U-shaped development in infants' processing of faces: an information-processing account. *J. Cognition Develop.* 5, 59–80
- 56 Mondloch, C. *et al.* (2003) Early visual experience is necessary for the development of some – but not all – aspects of face processing. In *The Development of Face Processing in Infancy and Early Childhood: Current Perspectives* (Pascalis, O. and Slater, A, eds), pp. 99–117, Nova Science
- 57 Elleberg, D. *et al.* (2003) Greater losses in sensitivity to second-order local motion than to first-order local motion after early visual deprivation in humans. *Vision Res.* (in press)
- 58 Elleberg, D. *et al.* (2003) Comparison of sensitivity to first- and second-order local motion in 5-year-olds and adults. *Spat. Vis.* 16, 419–428
- 59 Bowering, E.R. *et al.* (1996) The visual field in childhood: Normal development and the influence of deprivation. *Dev. Cogn. Neurosci. Technical Report* No. 96.1
- 60 Lewis, T.L. *et al.* (2004) A window on the normal development of sensitivity to global form in Glass patterns. *Perception* 33, 409–418
- 61 Bourne, J. *et al.* (2004) Topographic and laminar maturation of striate cortex in early postnatal marmoset monkeys, as revealed by neurofilament immunohistochemistry. *Cereb. Cortex* (e-publication ahead of print)
- 62 Price, T.A. *et al.* (2004) Differential development of form and motion perception in macaque monkeys. Program No. 66.13. *Abstract Viewer/Itinerary Planner*, Society for Neuroscience
- 63 Atkinson, J. (2000) *The Developing Visual Brain*, Oxford University Press
- 64 Gunn, A. *et al.* (2002) Dorsal and ventral stream sensitivity in normal development and hemiplegia. *Neuroreport* 13, 843–847
- 65 Dobkins, K. (2005) Enhanced red/green color input to motion processing in infancy: Evidence for increasing dissociation of color and motion information during development. In *Attention and Performance XXI: Processes of Change in Brain and Cognitive Development* (Munakata, Y. and Johnson, M.H., eds), pp. 000–000, (in press)
- 66 Kugelberg, U. (1992) Visual acuity following treatment of bilateral congenital cataracts. *Doc. Ophthalmol.* 82, 211–215
- 67 Maurer, D. and Lewis, T. (1993) Visual outcomes after infantile cataract. In *Early Visual Development: Normal and Abnormal* (Simons, K., ed.), pp. 454–484, Oxford University Press
- 68 Mioche, L. and Perenin, M. (1986) Central and peripheral residual vision in humans with bilateral deprivation amblyopia. *Exp. Brain Res.* 62, 259–272
- 69 Leclerc, C. *et al.* (2000) Brain functional reorganization in early blind humans revealed by auditory event-related potentials. *Neuroreport* 11, 545–550

Box 1. Questions for future research

- What developmental trajectory underlies the spared aspects of vision in cataract-reversal patients? Does it represent normal functioning throughout development; recovery from an earlier deficit, with the developmental timetable simply delayed; or is there a qualitative change in the developmental trajectory? How do the visual deficits themselves (e.g. reduced visual input from the periphery) contribute to the alterations of the subsequent developmental trajectory?
- What are the neural substrates of the spared visual abilities and of the permanent deficits after cataract-reversal? Do they represent recovery and damage, respectively, to the normal neural substrates and/or the recruitment of alternative networks?
- Is there a topographic arrangement of the auditory, somatosensory, and language abilities mediated by the visual cortex after congenital blindness? What types of networks do they form with other sensory cortical areas, higher association cortex, and subcortical structures?
- What is the optimal patching regimen to promote recovery from unilateral deprivation? Given the evidence of some plasticity even in adulthood, is continued patching advantageous past its typical stopping point of 5–6 years of age?
- To what extent, if any, can the deficits after cataract-reversal be overcome by training or other types of rehabilitation? Is the optimal form of rehabilitation the same for unilateral and bilateral cases? For early- and late-onset cases? When, if ever, is it too late to induce improvement?
- Do cataract-reversal patients, like the congenitally blind, show enhanced sensitivity in other modalities? Can training increase this sensitivity in either population?
- To what extent, and under what circumstances, do the lessons derived from cataract-reversal and congenital blindness apply to other sensory modalities (such as deaf children who receive cochlear implants)?
- Can prostheses be developed to restore vision to the congenitally blind? If so, how will the pattern of spared visual abilities and permanent deficits compare to those from cataract-reversal patients?

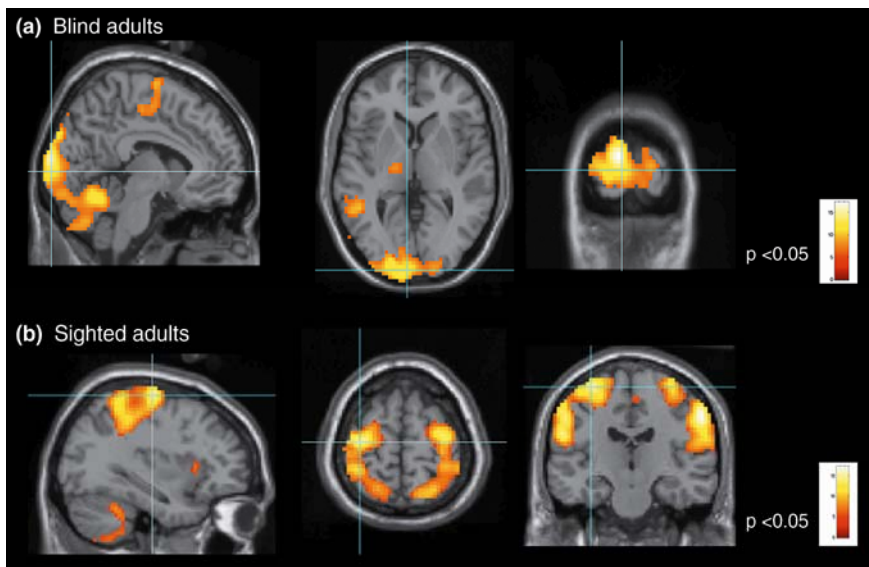


Figure 1. Activation of visual cortex during Braille reading in adults blind from an early age. Measurements based on fMRI are shown for (a) 12 blind adults and (b) 12 sighted adults given the same tactile stimulation. Both groups show the expected activation of sensorimotor cortex, but only the blind show activation of the primary, secondary, and higher visual cortices. Results were similar for the tactile discrimination of nonsense dots. Shown are statistical maps of task-related activation (Braille versus rest) on three orthogonal sections of a T-1 weighted standard brain, using a statistical corrected threshold of $p < 0.05$. Reproduced with permission from Ref [22].

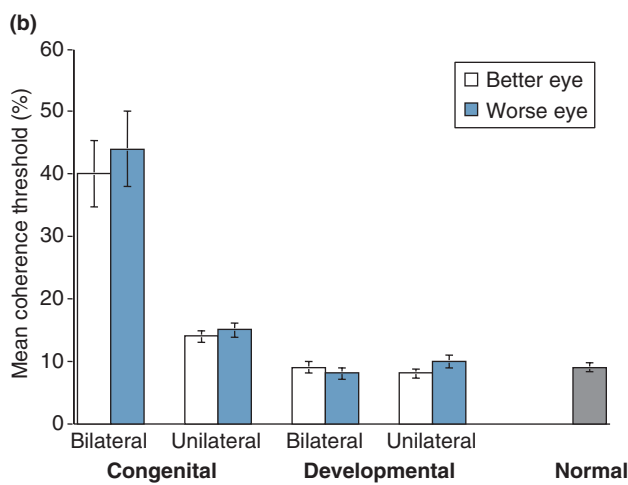
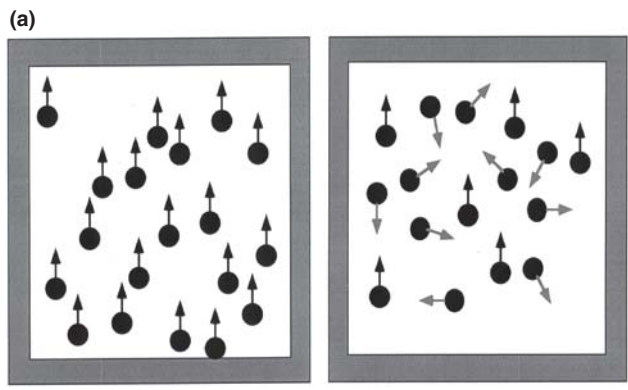


Figure 2. Effect of visual deprivation from cataract on the later development of sensitivity to the direction of global motion. (a) Examples of stimuli used to test sensitivity to the direction of global motion. The pattern on the left has 100% coherent motion (all the dots are moving upwards); the pattern on the right has 37% coherent signal (6 of 16 dots are moving upward and the remaining dots are moving in random directions). The subject's task was to say whether the overall direction of motion was

upward or downward. Threshold was defined as the minimum percentage coherence necessary to discriminate accurately whether the predominant direction was upward or downward. **(b)** Mean coherence thresholds (± 1 SE) for the perception of the direction of global motion in children treated for cataract and visually normal controls (grey bar). The children treated for cataract had either deprivation from birth (congenital cases) or deprivation that developed postnatally after a period of normal visual input (developmental cases). Shown are the data for each eye (better eye, white bars; worse eye, blue bars) for each patient, where the better eye in bilateral cases is the eye with a better clinical history of ocular alignment and acuity and the better eye in unilateral case is the non-deprived eye. Children treated for bilateral congenital cataracts had highly elevated thresholds, whereas children treated for unilateral congenital cataract had slightly elevated thresholds in both the deprived and non-deprived eyes. Children treated for developmental cataract performed normally, even in the six cases when the onset of deprivation was between 4 and 10 months of age.

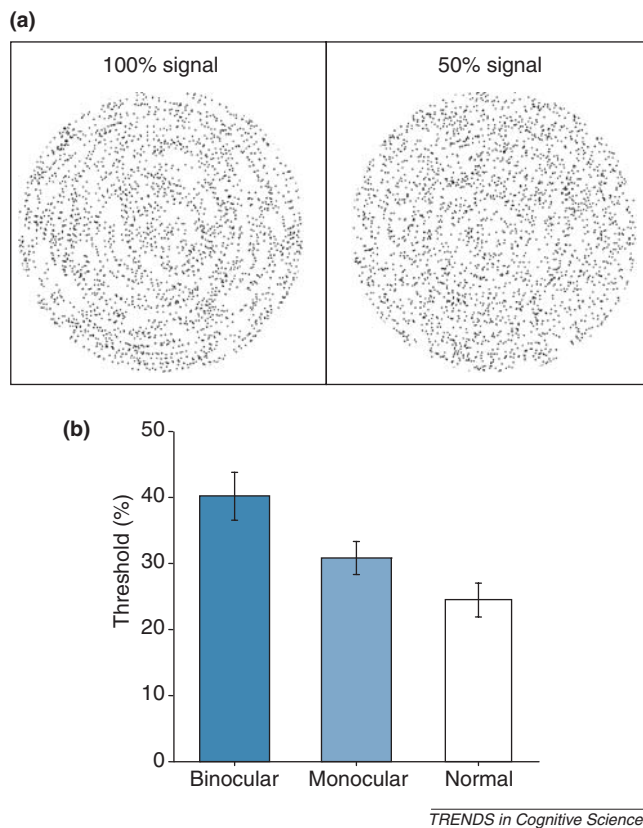


Figure 3. Effect of visual deprivation from birth in one or both eyes on the development of the ability to integrate elements into a global percept of form. **(a)** Examples of patterns used to test sensitivity to global form. The pattern on the left has 100% of the dots paired to form a global swirl, whereas the pattern on the right has 50% paired signal dots and 50% randomly placed noise dots (the original stimuli contained white dots on a grey background). Subjects saw two stimuli sequentially: one with the paired dots (signal) embedded in randomly placed dots (noise) and one with just noise. Their task was to say whether the signal appeared in Interval 1 or Interval 2. Threshold was defined as the minimum percentage signal necessary to discriminate accurately which interval contained the signal dots defining the global structure of swirls. **(b)** Mean threshold (± 1 SE). Blue bars represent the results for patients treated for bilateral or unilateral congenital cataract and white bars represent the results for comparably aged visually normal controls. Both patient groups had abnormal thresholds, but thresholds in bilateral congenital cases were significantly worse than in the deprived eye of unilateral congenital cases. Reproduced with permission from Ref. [16].

Table 1. Normal and impaired visual capabilities following early binocular deprivation from cataracts^a

Aspect of vision	Normal	Impaired	Refs
Spatial vision	Acuity for letters and stripes if deprivation < 10 days	Acuity for letters and stripes if deprivation > 10 days	[1,2,13,14,66]
	Detection of wide stripes of low contrast	Detection of medium width stripes of low contrast	[5]
Temporal vision	Detection of high rates of flicker	Detection of narrow stripes	[36,52,53,67,68]
		Sensitivity to stimuli in the periphery	
Object perception	Discrimination of large, high-contrast shapes (e.g., triangle versus cross)	Detection of flicker in low contrast stimuli	[5]
Face perception	Discrimination between individual faces differing in the shape of the internal features or the external contour	Sensitivity to small differences in global form (see Figure 3)	[6,16,17]
		Discrimination of a face from a scrambled image	[15,19,56]
	Recognition of direction of eye gaze, emotional expression, and vowel being mouthed	Binding together facial features into a holistic Gestalt	
Motion perception		Recognition of a face from different points of view	[7]
		Sensitivity to direction of locally defined and globally defined motion (see Figure 2)	[17,57]

^aTable indicates the final outcome for each aspect of vision after treatment and many years of visual input to allow recovery from the initial deprivation