Neural reorganization following sensory loss: the opportunity of change

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Abstract | There is growing evidence that sensory deprivation is associated with crossmodal neuroplastic changes in the brain. After visual or auditory deprivation, brain areas that are normally associated with the lost sense are recruited by spared sensory modalities. These changes underlie adaptive and compensatory behaviours in blind and deaf individuals. Although there are differences between these populations owing to the nature of the deprived sensory modality, there seem to be common principles regarding how the brain copes with sensory loss and the factors that influence neuroplastic changes. Here, we discuss crossmodal neuroplasticity with regards to behavioural adaptation after sensory deprivation and highlight the possibility of maladaptive consequences within the context of rehabilitation.

Cooperative advantage
With regards to multisensory integration, refers to the interaction of sensory information from the different sensory modalities that can lead to an enhanced perceptual experience.

Neuroplastic changes
The ability of the nervous system to change its functional and structural organization in response to development, experience, the environment, damage or insult.

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doi:10.1038/nrn2758
Published online
25 November 2009

Equipped with multiple senses and specialized sensory organs, we capture and interact with a rich multisensory world. The unified and salient nature of our sensory experiences is the product of extensive and dynamic neural connections, which in turn are highly influenced by our experiences and developmental constraints. Current evidence supports the notion that multisensory integration enhances overall perceptual accuracy and saliency through cooperative advantages[1,2] and provides the redundancy of cues that is necessary to fully characterize objects in our environment[3]. This integrative strategy and organization might also account for compensatory behaviours that follow the loss of a sensory modality.

Traditionally, life without a particular sense has been viewed as 'impoverished' and many early theories postulated that sensory deprivation would have devastating effects on development, learning and cognitive behavioural performance (for example, REFS 4,5). The 'deficiency' theory purports that a lack of perceptual sensory experience leads to an overall impairment in cognitive task performance given that proper multisensory integration can result only from the normal development of each sense. However, it is clear that blind and deaf individuals make striking adjustments to their sensory loss in order to operate effectively within their environment. Growing evidence from human and animal research indicates that these adaptations are inextricably linked to changes at multiple levels of the brain[6]. In particular, it seems that these changes involve not only areas of the brain that are responsible for the processing of the remaining senses but also areas normally associated with the processing of the sensory modality that is lost. Furthermore, these changes might translate into behavioural skills and task performance levels that are equal and in certain cases even superior to those of individuals with intact sensory function. In other situations, however, neuroplastic changes might be maladaptive, particularly in light of rehabilitative efforts that attempt to restore sensory function after it has been lost or fails to develop. Thus, at one extreme there seems to be an underestimation of the adaptive potential of the brain, whereas at the other there is an assumption that neuroplasticity always leads to positive and advantageous outcomes. Understanding the nature of these neuroplastic changes is important not just in terms of establishing the brain's true adaptive potential but also in elucidating intervening developmental constraints and guiding future rehabilitation strategies. The study of neuroplasticity is an extremely broad field that is investigated at multiple levels from molecules, to neural systems, to behaviour. Much of the seminal work regarding neuroplasticity has arisen from investigations of the somatosensory and motor systems. Here, we focus on behavioural and neurophysiological evidence in relation to visual and auditory deprivation (for reviews of sensorimotor plasticity, see REFS 7–9).

Adaptation to sensory loss

Blindness. There has long been anecdotal evidence that blind individuals compensate for the loss of vision through more effective use of their remaining senses[10,11]. A systematic review of this issue reveals that blind individuals (particularly if blind from birth or very early in life) show comparable, and in some cases even superior, behavioural skills to sighted subjects. This includes finer tactile-discrimination thresholds[12–15] and superior performance in auditory-pitch discrimination[16] and spatial sound localization[17–20]. Superior performance has also been shown in other behavioural and cognitive tasks including spatial navigation[21], speech discrimination[22] and verbal recall[23,24].

Given that the blind rely heavily on touch and hearing to interact with their environment, it would seem reasonable that neurophysiological changes would manifest themselves within regions of the brain responsible for somatosensory and auditory processing. Expansion and reorganization of the cortical finger representation have been reported in blind proficient Braille readers (detected by somatosensory evoked potentials[25] and magnetoencephalography (MEG)[26,27]). This reorganization has been interpreted to reflect an adaptation that might allow more enhanced processing and efficient reading skills in these individuals[26,27]. Changes at the level of auditory cortical areas in the blind have also been investigated. For example, responses to tone bursts and tonotopic mapping studies (using MEG) have revealed an expansion in areas that respond to auditory stimuli, and signal response latencies (specifically the N1 potential, which is associated with acuity in central auditory areas) are significantly shorter in blind individuals than in sighted controls[28]. In a recent functional MRI (fMRI) study, individuals who had been blind from an early age showed signal alterations in the auditory cortex that were consistent with more efficient processing of auditory stimuli as opposed to an altering of inherent patterns of tonotopic organization[29]. Structural changes outside somatosensory and auditory cortical areas have also been reported. For example, superior spatial navigation performance in the blind has been correlated with a larger volume of the hippocampus (assessed by morphometric MRI[21]), a structure with a well-established role in navigation and spatial memory[30].

In parallel to these reported physiological and morphological changes, areas within the occipital cortex (normally attributed to visual processing) are functionally recruited in blind persons to process non-visual information obtained from intact sensory modalities (FIG. 1a). This form of crossmodal plasticity has been demonstrated repeatedly using various neuroimaging methods[31,32] and numerous subsequent reports have demonstrated task-specific activation related to tactile processing tasks such as Braille reading[33–36], haptic object identification[37] and the use of visual-to-tactile sensory substitutive devices (SSDs)[38]. Occipital visual cortical areas also seem to be recruited in response to auditory stimuli. Neuroimaging studies have demonstrated crossmodal activation of occipital cortical areas by sound-processing tasks, including sound-source discrimination[39], auditory motion perception[40], auditory change detection[41] and sound localization[17,42]. Occipital cortex activation has also been reported in conjunction with auditory linguistic tasks such as speech processing[43], semantic judgment[44], auditory verb generation[45] and verbal-memory tasks[23]. Finally, similar to observations in the tactile domain, the use of visual-to-auditory SSDs is also associated with activation in occipital cortical areas[46–49].

The specific cortical areas implicated in this form of crossmodal plasticity (for example, primary versus higher-order visual areas) vary across studies and are likely to relate to the behavioural tasks being performed. It is also important to note that there is considerable variability in terms of the spatial and temporal resolution of the methodologies used, the nature of the tasks and analyses performed and the types of patients investigated, making comparisons across studies difficult. However, there is direct experimental and clinical evidence that the recruitment of occipital areas is causally related to compensatory behaviours in the blind. The experimental evidence comes from a series of studies demonstrating impairments in crossmodal behavioural tasks following the transient and localized disruption of occipital cortex function with transcranial magnetic stimulation (TMS)[50]. For example, TMS delivered to the occipital cortex impairs Braille reading performance in proficient Braille readers[51–53]. Using a similar approach, TMS delivered to occipital cortical targets has been shown to disrupt verb generation performance[54] and also the use of auditory SSD systems[48,55]. In the clinical setting, there is also a case report of a congenitally blind patient rendered alexic for Braille after suffering a bilateral occipital stroke[56]. Although the patient could discriminate everyday objects by touch, she was no longer able to read Braille and showed striking deficits in tasks requiring fine tactile spatial discrimination[56,57]. The deficits described in this case are in line with the functional impairments described following reversible cortical disruption using TMS. Together, these findings support the idea that the recruitment of occipital cortex in high-level cognitive processing and within the context of visual deprivation is functionally relevant.

Deafness. Like blind individuals, deaf people rely strongly on their intact senses to interact with their surroundings. For example, deaf individuals use visual or tactile stimuli to alert attention and many use visuospatial forms of linguistic communication such as sign language. As a corollary to the findings described in the blind, deaf individuals show superior skills in certain perceptual tasks compared with hearing control subjects (FIG. 1b). For example, enhanced tactile sensitivity (using vibrotactile stimuli) has been reported[58]. In the visual domain, deaf subjects perform better than hearing controls in distinguishing emotional expression and local facial features[59,60]. Deaf individuals are also better than hearing controls at performing peripheral visual tasks and distributing attention to the visual periphery[61–64]. This augmentation of attentional resources towards the periphery might be adaptive and serve as a compensatory means to direct attention or

N1 potential
A large negative-direction evoked potential (measured by electroencephalography) detected over the fronto-central region of the scalp and peaking between 80 and 120 ms after the onset of a stimulus (typically auditory). This potential has been found to be sensitive to features of sounds associated with speech.

Sensory substitution device
(SSD). A device that transforms the characteristics of one sensory modality (for example, vision) into stimuli that can be perceived by another sensory modality (for example, touch or hearing). This strategy is often used in assistive technology to access sensory information normally perceived by an impaired sensory modality by using the remaining intact senses.

Alexia
A neurological disorder characterized by the loss of the ability to read. Alexia typically occurs following damage to specific language-relevant areas of the brain (particularly within the left hemisphere) as well as the occipital and parietal lobes.

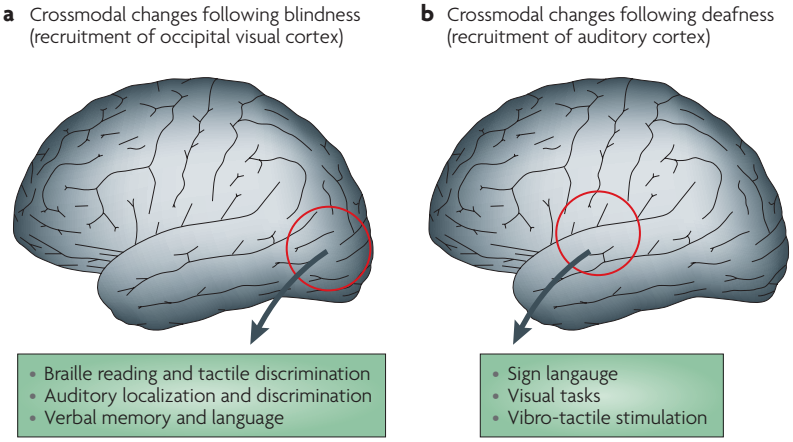

Figure 1 | **Summary of crossmodal neuroplasticity following sensory loss.** Crossmodal recruitment of occipital visual cortex in the blind and auditory cortex in the deaf have been reported. **a** | Occipital recruitment for tactile processing such as Braille reading, sound localization and verbal memory. **b** | Recruitment of auditory and language-related areas for viewing sign language, peripheral visual processing and vibro-tactile stimulation.

orient towards objects of interest outside the central field of view[62]. Superior performance in visual motion detection and discrimination has been described in the deaf, particularly with respect to the right visual field[65,66]. This right visual field advantage might be related to the lateralization of language function, which is typically ascribed to the left hemisphere. Thus, there might be a preferential association regarding the processing of motion information within the right visual field and the left (that is, the contralateral) hemisphere, which is normally associated with language processing[65,66].

In deaf humans, there is less evidence for large morphological changes in brain areas that process intact sensory modalities. One study found no differences in responsivity or in the size of early visual cortical areas (assessed with fMRI) in deaf subjects compared with hearing controls[67]. However, this lack of observed changes does not rule out the possibility of potential morphological differences in higher-order visual areas or even other sensory cortices. Thus, further investigation of this issue seems necessary. As in blind individuals, there is evidence that auditory cortical areas are recruited by tactile, language and visual processing tasks. For example, activity in the auditory cortex has been detected by MEG in response to vibrotactile stimulation in congenitally deaf subjects[68]. Also, fMRI has detected activity in the auditory cortex of subjects deaf from an early age in response to vibration stimuli derived from speech and fixed frequencies[69]. Several studies have shown crossmodal recruitment of auditory areas in deaf individuals viewing sign language[70–72]. Crossmodal activation of auditory cortex by non-linguistic visual stimuli (for example, moving dot patterns) has also been demonstrated using MEG[73] and fMRI[74]. Interestingly, this pattern of activation was not found in hearing signers (specifically, the children of deaf parents), indicating that auditory deprivation (as opposed to sign language experience) might be crucial for this form of crossmodal recruitment (see also REF. 67 and BOX 1). Finally, a series of neuroimaging studies combined with visual peripheral tasks have also reported evidence that deaf individuals show greater recruitment of occipital-parietal cortical areas related to attention processing than hearing controls[61,63,75,76].

It has been difficult to demonstrate experimentally the causal role of crossmodal recruitment of auditory cortex in non-auditory tasks. This might relate to technical issues with the experimental methodologies used. For example, TMS must be delivered close to the ear to transiently disrupt the function of auditory temporal regions, and the audible click generated by a discharging TMS coil could interfere with task performance. Furthermore, apart from such stimulation being quite uncomfortable (owing to stimulation of the overlying temporalis muscle), the sulcal geometry and orientation of auditory cortical areas make them difficult to stimulate optimally.

Although these technical issues might have limited controlled experimental investigations, several case reports describing deaf patients with circumscribed brain lesions have provided clinical evidence regarding sign language production and comprehension. For example, lesions of the left temporal cortex lead to impairments in sign language comprehension, consistent with the notion that sign language comprehension depends primarily on the left hemispheric structures that mediate language function in hearing subjects[77,78]. There have also been reports of 'sign blindness' in a deaf signer following damage to the left occipital cortex[79]. This patient exhibited severe impairments in comprehension but not in the production of signs, analogous to alexia. Similarly, a left occipital lesion in a deaf signer caused acquired sign language aphasia with severe impairment in word production as well as comprehension, reading and writing[80]. Thus, consistent with neuroimaging data, it seems that temporal-auditory and occipital-visual cortical areas have specialized functions that are crucial for language abilities in deaf signers.

Adaptation to multiple sensory loss

Deaf-blindness. Few studies have examined the behavioural and physiological consequences of multiple sensory loss, particularly in humans. The development of language function and communication skills in deaf-blind individuals provides an interesting opportunity to investigate this issue. Deaf-blind individuals communicate using tactile-based languages, including Braille and various haptic forms of sign language. In a study of one late-blind, post-lingual deaf-blind subject, MEG and positron emission tomography (PET) imaging were used to investigate the neural activity associated with identifying Japanese words using a tactile mode of letter spelling (that is, by touching and stroking the fingertips representing different consonants and vowels)[80]. In line with the crossmodal changes described in blind and deaf individuals, the identification of tactile words was associated with activation of visual and auditory language cortical areas. These results indicate that in the case of dual sensory deprivation, dramatic crossmodal recruitment of cortical areas associated with visual, auditory

Aphasia
A neurological disorder characterized by impaired expression and understanding of language, as well as reading and writing. It is usually the result of damage to areas of the brain involved with language processing.

Usher syndrome
A relatively rare genetic disorder with clinical subtypes characterizing the degree of severity and a leading cause of combined deafness and blindness. Hearing loss is associated with a defective inner ear whereas the visual loss is associated with degeneration of retinal cell function.

and language processing is possible. However, the subject's late-blind and post-lingual deaf status makes it difficult to disentangle the contribution of prior sensory experience with regards to the pattern of crossmodal cortical recruitment observed. Indeed, visual imagery[81] and inner speech and auditory verbal imagery[82] activate corresponding occipital, auditory and language processing areas. To rule out this possible confound, the neural correlates of language processing in a congenitally deaf and early-blind individual who is highly proficient in communicating through a haptic form of American Sign Language (ASL) were explored[83]. By placing his hand over a signer's hand, he could capture the meaning of word signs and gestures. Functional MRI showed that word identification (compared with non-words) activated areas of occipital cortex (including calcarine-striate and extrastriate regions), left posterior superior-temporal areas (including Wernicke's area and the superior temporal gyrus (Brodmann area 22)) and inferior frontal cortical areas (including Broca's area (Brodmann area 44)) (FIG. 2a). To further distinguish between activation related to haptic language processing and areas related to combined early onset deprivation, a control experiment used the same word identification task in a normally hearing and sighted interpreter for the deaf-blind. As with the deaf-blind subject, the identification of words through haptic ASL was associated with left-lateralized activation of inferior frontal language areas (including Broca's area). However, robust occipital cortex activation was not observed[83] (FIG. 2b). The crossmodal recruitment observed in this deaf-blind individual is striking, given that he never developed articulated speech or, unlike deaf signers, learned ASL through visual associations. Furthermore, these results suggest that following early onset visual and auditory deprivation, tactile communication is associated with the recruitment of occipital and auditory cortical areas, further demonstrating the remarkable neuroplastic changes that follow sensory loss.

Box 1 | **The heterogeneity of sensory loss: a potential confound**

The World Health Organization (WHO) defines legal blindness as a best-corrected visual acuity worse than 20/200 (Snellen equivalent) or a visual field less than 20° (note that legal blindness does not necessarily imply profound blindness). Current estimates suggest that blindness afflicts 45 million individuals worldwide, with cataracts, age-related macular degeneration and glaucoma being leading causes[135]. In terms of hearing impairment, the WHO has estimated that 278 million individuals worldwide have moderate to profound hearing loss in both ears (profound hearing loss being defined as not being able to detect a tone of 90 dB or greater), and causes are typically associated with sensorineural deficits of the auditory nerve[136]. As with visual impairment, the aetiology is highly variable and includes hereditary causes as well as acquired causes including infections and trauma. Combined vision and hearing loss (or dual sensory loss) is more prevalent with increasing age. However, certain hereditary conditions such as Usher syndrome[137] can also lead to combined, early-onset visual and auditory impairment.

When interpreting the experimental evidence, it is important to underscore the tremendous degree of heterogeneity with regards to sensory impairment in both blind and deaf populations. Important factors include the aetiology, severity, onset and developmental time course of the sensory loss. Furthermore, many of the human studies demonstrating superior performance abilities in blind and deaf persons have been carried out in highly specific population subsamples, such as in congenitally blind individuals or deaf native signers (that is, children who have had early exposure to sign language and achieve language development milestones similar to hearing individuals[127]). In addition, many of these studies have been carried out under very controlled experimental conditions and/or high task demands (for example, monaural testing[18]) or by comparing performance against control subjects but under acute sensory deprivation conditions (for example, by blindfolding sighted participants[12]). Finally, it is important to disentangle evidence of brain activation related to long-term skill training (for example, Braille and ASL) from activation due to the sensory deprivation itself[56,67,73,138].

At the other extreme, studying specialized population subgroups and highly controlled experimental conditions might allow 'cleaner' interpretation of data but potentially at the expense of a loss in generalizability across the entire population. Finally, vision and hearing loss typically occur progressively, later in adult life, and individuals often maintain some degree of residual sensory function. Future studies might benefit from considering variables beyond simply the aetiology and strict age cut-offs for acquiring total sensory deprivation. For example, functional (such as language experience and travel independence), personal (such as confidence and motivation) and behavioural (such as degree of instruction and level of proficiency) criteria may prove helpful in grouping and comparing study subjects in terms of underlying neuroplastic change (see also REFS 62,127,139 for related discussion).

Underlying mechanisms

The exact mechanisms that underlie crossmodal plasticity and the neural basis of behavioural compensation remain largely unknown. However, animal studies have provided important insights based on physiological, behavioural and anatomical data (for reviews, see REFS 2,6,84,85). Similar to the behavioural results described in blind humans, animal models of visual deprivation also show evidence of crossmodal compensatory changes. For example, experimentally visually deprived cats[6,86] and ferrets[87] possess superior sound localization abilities to normal animals. At a neurophysiological level, single-unit recordings from a multisensory region called the anterior ectosylvian cortex (AES; FIG. 3a) show that in visually deprived cats, cortical areas that respond to auditory stimuli expand significantly[88] and neurons in this region are more sharply tuned to auditory spatial location[89]. Investigations of the development and maturation of multisensory circuits within the cat AES confirm that the capacity for multisensory integration is rudimentary during early postnatal life, that it gradually develops over time and that it is highly influenced by timing and the animal's overall sensory experience[90,91]. To investigate the contribution of early visual sensory experience to cortical multisensory development, further work was carried out on dark-reared cats[92]. In these experiments, semichronic single-unit recordings in the AES (in anesthetized animals) were made at weekly intervals from birth until adulthood. The results confirmed that visual deprivation (and non-visual multisensory experiences) had a striking effect on the integrative capabilities of multisensory neurons in the AES. Specifically, there was a significant increase in the proportion of multisensory neurons modulated by a second sensory modality (FIG. 3b). These results confirm that early deprivation has a significant impact on crossmodal function and show how the senses interact to reflect specific features of an animal's environment and ultimately optimize adaptation to that environment[91].

Parallel studies of auditory cortical plasticity have also been carried out. These are not as extensive as those carried out within the visual and somatosensory systems, possibly owing to technical challenges in developing

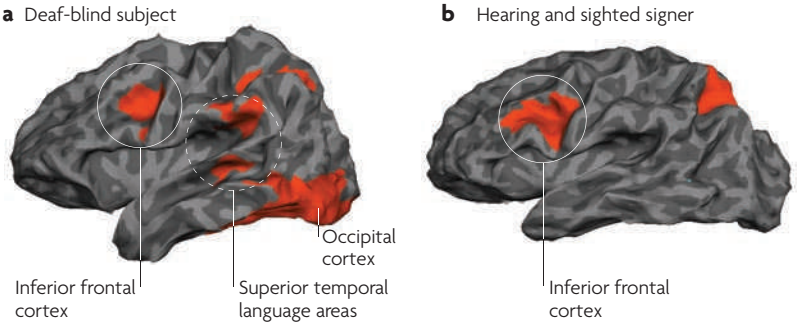

Figure 2 | **Crossmodal neuroplasticity in dual sensory loss (vision and hearing).** Localization of activation (revealed by functional MRI) associated with identifying words through haptically presented American Sign Language (ASL) in both a pre-lingually deaf and early-blind individual (**a**) and a hearing and sighted control (**b**) subject (for simplicity, only the left hemisphere is shown). Crossmodal networks associated with the identification of words (as opposed to non-words) include the inferior frontal cortex in the left hemisphere (corresponding to Broca's area (Brodmann area 44)) in both subjects. The white dashed circle identifies activation in superior temporal language areas (including Wernicke's area and the superior temporal gyrus). Occipital cortex activation is also labelled. Activation in occipital and temporal cortical areas seems to be specific to the combined loss of vision and hearing. Data from REF. 83.

appropriate animal models and controlled restricted environments (see REF. 93 for a review). The organization of auditory receptive fields and cortical mapping have been actively studied using various electrophysiological techniques (reviewed in REF. 94). The extent of crossmodal reorganization has been investigated in congenitally deaf cats. Electrophysiological recordings from the primary auditory cortex (A1) of congenitally deaf cats failed to find crossmodal responses to visual or somatosensory stimuli[95] (although it is unclear whether such responses exist in higher-order, associative auditory areas). The investigators proposed that in the case of congenital deafness, the ability to learn and develop higher-order auditory representations is substantially affected in the absence of auditory experience and that very early onset auditory deprivation cannot be compensated for by top-down influences arising from higher-tier auditory and associative areas[96]. Thus, the degree of crossmodal plasticity might be related not only to the timing and profoundness of sensory deprivation but also to whether one considers primary or associative areas. Along these lines, there has been speculation that A1 might represent higher processing complexity than V1 (that is, processing stimuli beyond simple feature detection) and would therefore be more analogous to higher-order areas along the visual processing stream[97]. In other words, differences in the functional contribution of primary auditory and visual areas within the context of sensory deprivation might be based on their inherent abilities to retain their intrinsic processing in response to crossmodal influences from other sensory modalities.

One possible explanation for the recruitment of cortical areas following sensory deprivation is through direct neural connections with intact sensory areas. Anatomical studies in cats[98] and non-human adult primates have demonstrated direct connections between auditory and visual cortical areas[99,100]. The patterns of these connections seem to differ between primary and associative areas, and also to depend on whether the cortical representations are central or peripheral[98]. A more recent anatomical tracing study (using marmosets) found that unimodal sensory areas were linked by multiple heteromodal connections including visuo-somatosensory, visuo-auditory and somatosensory-auditory projections[101]. Furthermore, electrophysiological evidence in monkeys confirms multisensory convergence at the neuronal level and in early stages of cortical sensory processing, including auditory-visual convergence within V1 (REF. 102) and somatosensory-auditory interactions within a region caudal-medial to primary auditory cortex[103]. As these connections exist in the intact adult brain, one possibility is that sensory deprivation leads to more pronounced changes in relative connectivity between cortical areas.

It is unclear whether these connections and mechanisms underlie crossmodal neuroplastic changes in humans. However, there is evidence consistent with the notion of enhanced cortico-cortical inter-sensory interactions. Specifically, effective connectivity between somatosensory and visual cortical areas was demonstrated in early-blind humans using a combination of TMS (to stimulate primary somatosensory areas) and PET imaging (to visualize the effect of somatosensory stimulation in early visual cortical areas)[104]. Furthermore, evidence of functional crossmodal sensory processing in the occipital visual cortex in adult sighted subjects[57,105] and rapid and reversible crossmodal recruitment of the occipital cortex in response to sudden and complete visual deprivation (prolonged blindfolding and sensory training) in adult humans with intact senses are consistent with the notion that existing connections can be unmasked as a response to sensory processing and afferent demand[106]. Thus, it is possible that the unmasking of pre-existing connections and shifts in connectivity might underlie rapid, early plastic changes that can lead, if sustained and reinforced, to slower but more permanent structural changes, such as dendritic arborization, sprouting and growth with rewiring of connections[107].

Critical periods and adult plasticity

Pioneering work in sensory deprivation (for example, REF. 108) showed that the brain is most receptive to change during an early period of postnatal life referred to as the critical period[109]. Critical periods are specific to sensory modality, function and species[109]. Furthermore, experimental evidence is consistent with the notion that the earlier the sensory loss, the more striking the neuroplastic effects[109]. In fact, many of the studies reporting superior behavioural performance and crossmodal neuroplastic changes have been carried out in subjects who have been blind from birth or early in life (BOX 1). In the case of blindness, this idea has led some authors to suggest the existence of a precise critical period (around 14 (REF. 110) to 16 (REF. 111) years of age) beyond which functionally relevant crossmodal recruitment of occipital cortex (particularly V1) does not occur, theoretically limiting the extent of potential adaptive compensatory behaviour. However, the current view regarding plasticity is not one of a finite window of opportunity,

Top-down
Pertaining to information processing strategies, a top-down approach describes the flow of sensory information from higher-order cortical areas to lower-order processing levels. This is opposite to 'bottom-up' processing, in which information being processed from lower-order regions flows to higher-order areas of sensory cortex.

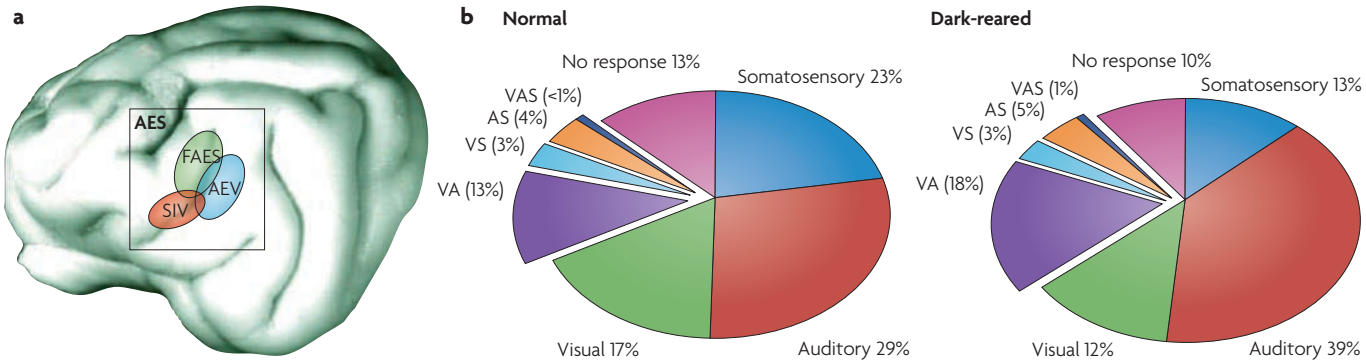

Figure 3 | **Effects of early visual deprivation in cats.** Dark rearing alters the distribution of sensory responsive neurons in the anterior ectosylvian sulcus (AES). **a** | The lateral surface of the adult cat cortex, with the location of the AES and the relative positions of its three major subdivisions: SIV (fourth somatosensory area), FAES (auditory field of the AES) and AEV (anterior ectosylvian visual area). **b** | The distribution of sensory unresponsive, unisensory and multisensory mature AES neurons in normally reared and dark-reared animals. Values are rounded to the nearest percent. AS, auditory-somatosensory; VA, visual-auditory; VAS, visual-auditory-somatosensory; VS, visual-somatosensory. Part **a** is modified, with permission, from REF. 2 © (2008) Macmillan Publishers Ltd. All rights reserved. Data in part **b** from REF. 92.

but rather one in which the brain retains a high level of neuroplasticity well into adulthood, although not to the same extent as in the young developing brain[107]. Admittedly, neuroplastic changes and associated behavioural gains in the case of late-onset sensory deprivation are less clear and relatively few studies have addressed this issue. In one study, the occipital activation related to a verb generation task (using a Braille-presented cue) in congenitally and late-blind subjects was compared. The occipital cortex (including early visual areas) was activated in both study groups[34]. However, congenitally blind individuals showed greater activity (in terms of magnitude and spatial extent) than late-blind participants[34]. In terms of compensatory behaviours in the auditory domain, enhanced auditory spatial abilities (for example, peripheral sound localization) have also been reported in subjects with late-onset blindness compared with sighted controls[20,112]. With regards to auditory deprivation, the effect of timing on the acquisition of language function through the use of a cochlear implant provides parallel insight. Traditionally, language acquisition following implantation has been approached with the mantra of 'the earlier the better'[113] and was once considered to be feasible only in post-lingual deaf patients. More recently, the indications for cochlear implantation have expanded to include pre-lingual deaf patients. With very intensive and rigorous training, improved language performance has been reported in these patients[114].

Work in animal models might help to uncover the potential underlying neuroplastic mechanisms and their relationship to critical periods, learning and developmental experience. Analogous to the visual deprivation studies mentioned earlier, it has been shown that rearing infant rats in a low-frequency-modulated noise environment leads to profound deficits in primary auditory cortex that endure throughout adulthood (specifically, with regards to the spatial and temporal selectivity of neurons)[115]. Intriguingly, these deficits incurred during the critical period of development can be reversed in the adult through intensive training (for example, using perceptual learning tasks)[116]. Thus, the possibility of 'reopening' critical periods in the adult animal through intensive behavioural and perceptual training has important implications for regaining function in adults even after early-onset sensory deprivation. Furthermore, given that typical ageing trends suggest that individuals are more likely to acquire sensory loss with increasing age as opposed to early in life (BOX 1), the issue of neuroplasticity in the context of late-onset sensory deprivation also deserves careful investigation.

Cochlear implant
A surgically implanted electronic device that provides the sense of sound in individuals with profound hearing loss. The device works by electrically stimulating nerve fibres of the cochlea to transmit sensory information provided by external components including a microphone and speech processor.

Restoring sensory function

Although crossmodal plasticity following sensory deprivation can translate into compensatory behavioural gains, it cannot be viewed as universally adaptive, and unintended consequences are possible. In fact, neuroplastic changes might undermine the ability of reorganized cortex to perform its primary function, particularly in the context of rehabilitative training (for example, learning to read Braille proficiently or other forms of language training). Take, for example, crossmodal changes in the case of blindness. Proficient Braille readers who use multiple fingers to read text can mis-identify fingers and mis-localize tactile stimuli[117]. As another example, TMS delivered to the occipital cortex of blind proficient Braille readers can induce phantom tactile sensations at the finger tips[51,118] as well as at the tongue in users of certain tactile SSDs[119]. Perhaps the most striking examples come from historic case studies of surgical sight restoration following long-term visual deprivation[120,121]. In the case of patients with treatable early-onset blindness (treated by cataract removal or corneal transplantation), restoring vision in adulthood reportedly leads to profound difficulties in visual tasks, particularly those requiring the visual identification and recognition of objects. These outcomes have largely been attributed to the idea that early visual deprivation has striking effects on the development of the visual cortex and its ability to process complex visual information. However, more comprehensive behavioural and neuroimaging

studies have revealed a different potential explanation (for example REFS 122–125). Specifically, results from adults with early-onset blindness whose sight has been surgically restored suggest that visual areas that process different visual attributes might vary in their susceptibility to visual deprivation and in their recovery rates. Furthermore, although patients might not show a striking improvement in measured visual acuity following surgery, other aspects of their visual perception can improve, disproving the assumption that if acuity does not progress then neither do other aspects of visual function[126]. These studies also reveal that after years of blindness from an early age the brain retains an impressive capacity for visual learning. Furthermore, these observations might lead to new strategies of visual rehabilitation that take advantage of the crossmodal transfer of sensory information (for example, registering the direction of motion signalled through touch with what is perceived through vision) or using one visual attribute to 'bootstrap' and enhance the development of another (for example, learning to perceive object form as defined by its motion)[124].

Deaf individuals have often been characterized as more easily distracted by irrelevant information in the visual periphery than their hearing peers (see REFS 62,127 for further discussion). As in the blind, there might be trade-offs in terms of adaptive gains and maladaptive outcomes resulting from underlying crossmodal neuroplasticity following auditory deprivation. Detailed work on this issue has also been carried out with regards to hearing and language development in patients with cochlear implants. For example, in profoundly deaf cochlear implant recipients, speech performance outcomes are worse in those patients who showed near-normal resting levels of metabolic activity in auditory cortical areas (assessed with PET imaging)[128,129]. This sustained metabolic activity (attributed to evolved crossmodal neuroplastic changes) can ultimately interfere with the ability to recover auditory processing function after implantation of a cochlear implant. The duration of auditory deprivation remains an important factor, but the results of this study highlight the importance of investigating underlying neuroplastic changes directly as potential predictors of rehabilitative and functional outcomes[128]. As with the case of sight restoration, these results raise questions as to how restored and intact sensory modalities interact following the restitution of sensory afferents. There is evidence that crossmodal interactions between auditory and visual cortical areas tend to increase following cochlear implantation and that these interactions might even mutually reinforce one another[130]. Such language-related crossmodal changes could allow visual sign language to exploit existing connectivity between auditory cortex and neighbouring semantic and language processing areas. Interestingly, there is evidence that some cochlear implant users can integrate congruent auditory and visual information better than hearing control subjects[131]. However, these beneficial effects cannot be considered universal and there remains the possibility that, under certain circumstances, these crossmodal sensory interactions might be intrusive. A recent study investigated this issue by assessing the ability to segregate conflicting auditory and visual information in an auditory speech recognition task[132]. Key to the study design was the fact that hearing control subjects were matched to patients with cochlear implants for gender, age and hearing performance. Impaired task performance was particularly evident when comparing non-proficient cochlear-implant users with their hearing-matched controls[132]. These findings highlight how functional reorganization following auditory reafferentation might be beneficial in certain cases but detrimental to audiovisual performance in others, and could help to explain the striking variability in performance outcomes observed following cochlear implantation.

In summary, these reports of sensory restoration in both the blind and the deaf highlight how evolving plastic changes might lead to a gradual deterioration in the ability to process the missing sense and potentially render an individual a poor candidate for procedures aimed at restoring the lost sensory function. Thus, the decision to implant a prosthetic device or implement a given rehabilitative strategy needs to consider not only its effects on residual sensory function but also the potential to interfere with evolving crossmodal processing in response to sensory loss[133].

Conclusions and the implications for rehabilitation

In light of the striking neuroplastic changes that follow sensory deprivation, it seems that compensatory behaviour is not so much the result of sensory deprivation alone, but rather the consequence of how the entire brain maintains function in the context of sensory deprivation[107].

As a result of sensory deprivation, some of these plastic changes lead to crucial functional advantages, such as enhanced localization of sound sources and improved verbal memory in the blind, and enhanced visual peripheral sensitivity in the deaf. However, not all neuroplastic changes represent behavioural gains and the restoration of a deprived sense does not automatically translate to its eventual functional restitution. Neuroplasticity clearly affects an individual's rehabilitative outcome and new strategies are needed to leverage crossmodal interactions in a manner that promotes functional adaptation in parallel to rehabilitative and restorative approaches. These will require a careful consideration of brain plasticity mechanisms, perhaps even modulating brain activity (such as with non-invasive brain stimulation combined with rehabilitation) on an individual basis to therapeutically guide synaptic plasticity mechanisms and enhance those that promote behavioural gains and suppress those that may be maladaptive[107,134].

In conclusion, it is not possible to understand normal physiological function, the manifestations or consequences of sensory loss, or the possibility of restoring sensory function without incorporating the concept of brain plasticity. In considering the rehabilitation of an individual following sensory loss, it is crucial to consider each individual's specific needs and goals in the context of how his or her plastic brain interacts with a multisensory world.

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Acknowledgements
L.B.M. is supported by a K 23 EY016131 award from the National Eye Institute.

Competing interests statement
The authors declare no competing financial interests.

FURTHER INFORMATION
Berenson-Allen Center for Noninvasive Brain Stimulation: http://www.tmslab.org/

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