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Cortical plasticity and preserved function in early blindness

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Abstract

The “neural Darwinism” theory predicts that when one sensory modality is lacking, as in congenital blindness, the target structures are taken over by the afferent inputs from other senses that will promote and control their functional maturation (Edelman, 1993). This view receives support from both cross-modal plasticity experiments in animal models and functional imaging studies in man, which are presented here.

Keywords

cross-modal plasticity; functional neuroimaging; congenital blindness; cortical reorganization; visual deprivation

Introduction

The plasticity of the mammalian brain, that is, its ability to adapt to environmental situations by changing its connectivity, is one of its most outstanding properties. This plasticity is perhaps most striking in the sensory systems, which provide all input to the brain. The plasticity of sensory systems in higher centers of the brain, such as the cerebral cortex, is the basis for its adaptability to the environment. During individual development, neural plasticity is greater than during adulthood, which is necessitated by the growth of the organism and the need of the brain to get programmed. While sensory plasticity tapers off in adulthood, it does not cease completely.

The present paper deals with the behavioural, anatomical and physiological plasticity in animals and humans that grow up blind. Here we discuss plasticity in the sensory systems of visually deprived mice, cats and humans. Evidence for crossmodal plasticity was acquired

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using single-unit neurophysiology and neuroanatomy in animal models of early blindness and using imaging techniques in blind humans. The data support a concept of developmental plasticity whereby major sensory processing modules in the cortex are set up without the influence of sensory experience, but the sensory modality that drives them depends on sensory experience.

Expansion of the whisker-barrel system in early blind rodents

In rodents, the facial vibrissae or whiskers provide one of the most important sources of information to the brain. This is underscored by the fact that rodents possess a special representation in their somatosensory cortex that can be visualized with various anatomical and histochemical techniques (Van der Loos and Woolsey, 1973). The barrel cortex shows pronounced intramodal plasticity: When one of the whiskers is removed, the corresponding barrel shrinks. However, this plasticity of the whisker-barrel system is apparent even when sensory deprivation is exerted in a different sensory modality, such as the visual: Mice that are reared blind from birth by binocular enucleation, develop significantly longer vibrissae and, correspondingly, an expanded barrel field (Rauschecker, et al., 1992; Fig. 1). This may be interpreted by increased usage of the whiskers, which leads to use-dependent expansion of their central representation but also a hypertrophy of the peripheral sense organ itself.

Sound localization in the blind cat

Cats that are binocularly lid sutured from birth for several months do not show any signs of overt behavioral impairments in spatial behavior, as one would predict if vision was needed for its development. Quantitative measurements of sound localization behavior confirm this impression. Sound localization error was measured in a task that required the cats to walk towards a sound source that varied randomly in azimuth location in order to get a food reward. The error was consistently smaller in visually deprived cats as compared to sighted controls (Rauschecker and Kniepert, 1994). The improvement was largest for lateral positions of space, but even in straight-ahead positions, where the localization error is smallest in normal controls, no deterioration was found by any means (Fig. 2). Identical results have been described in visually deprived ferrets (King and Parsons, 1999; King and Semple, 1996) thus confirming the earlier cat studies. Similar findings have also been reported for blind humans (Lessard et al. 1998; Muchnik et al., 1991; Röder et al., 1999). The study by Röder et al. (1999) confirmed the animal studies even in quite specific detail in that it found the improvements to be most significant in lateral azimuth positions and no deterioration whatsoever in straight-ahead positions. These studies also fit extremely well with the classical findings by Rice and colleagues, who analyzed the echolocation abilities of blind humans and found them to be improved particularly in lateral positions of space (Rice, 1970; Rice et al., 1965). Head motion contributes to the localization of sounds with longer duration (Middlebrooks and Green, 1991). Cats deprived of vision from birth develop conspicuous scanning movements of head and pinnae in the vertical dimension (Rauschecker and Henning, 2001). These movements are triggered only by sound, are never found in sighted cats (even in the dark), but occur in blind cats regardless of ambient light conditions. One must assume, therefore, that vertical auditory scanning is part of the compensatory plasticity process in visually deprived cats (Rauschecker, 1995) and provides

an advantage for these animals in terms of improved sound perception in elevation (Rauschecker and Henning, 2001). In addition, scanning may also contribute to improving signal-to-noise ratio in auditory object recognition.

Neural basis of improved sound localization in blind animals

Neurophysiological recordings were undertaken in visually deprived cats to find the neural basis of the improved sound localization abilities in blind animals and humans. At first an involvement of the superior colliculus (SC) in the midbrain tectum, a pivotal structure for orienting behavior, was suspected. Indeed, increased numbers of neurons responsive to auditory (and somatosensory) stimuli were found, whereas the proportion of generally unresponsive neurons stayed the same (Rauschecker and Harris, 1983). Later, attention turned to the cerebral cortex: it was found on the basis of retrograde tracer experiments that the projection from visual cortex to the SC was impoverished, whereas the projection from association areas such as the anterior ectosylvian sulcus (AES) was preserved at the same strength as in normal animals (Rauschecker, 2006). The AES region quickly moved into focus, as it is also the main source of auditory cortical input to the SC (Meredith and Clemo, 1989). Visual responses of the anterior ectosylvian visual (AEV) area in the fundus of the AES (a possible homolog, for reasons of connectivity, of posterior parietal cortex in primates (Rauschecker, 1995)) virtually disappeared. Neurons in this region, however, did not become unresponsive, but were replaced by neurons with brisk responses to auditory and tactile stimuli. Apparently, auditory and somatosensory areas within the AES had expanded at the expense of formerly visual territory (Rauschecker and Korte, 1993). The response properties of the expanded auditory ectosylvian area (AEA) and those of neighboring auditory fields in the AES region were homogeneous. Auditory spatial tuning (the tuning for the location of a sound source in free field) was significantly sharper in the whole AES region when compared to sighted controls. Visually deprived cats had close to 90% spatially tuned cells (with a spatial tuning ratio of better than 2:1 between responses to best and worst location). In addition, neurons with spatial tuning ratios of 10:1 or better were more abundant in blind cats (Korte and Rauschecker, 1993). The improvement of spatial tuning was independent of the best frequency of the neurons. The increased number of auditory cortical neurons, together with their sharpened spatial filtering characteristics, is likely to improve the sampling density of auditory space and provide the neural basis for the improved spatial abilities of early blind cats and ferrets (Fig. 2; Rauschecker, 1995, 2002).

Neuroimaging of auditory spatial functions in blind humans

How do the changes in visually deprived animals translate into compensation of early blindness in man? Apart from behavioral studies, modern neuroimaging has contributed to a better understanding of these processes. One of the first imaging studies in the blind was performed over 20 years ago by Veraart and colleagues, who found that the early visually deprived cortex displayed metabolic activity that was actually higher, on average, than in sighted controls studied blindfolded (Wanet-Defalque et al., 1988; see also Uhl et al., 1993). In early blind adults, affected by pregeniculate (ocular or optic nerve) lesions from birth or in the first years of life, rates of glucose metabolism measured in primary and association visual cortex by means of positron emission tomography (PET) reached a level similar to

that of control subjects who were studied with their eyes open (Veraart et al., 1990). These results were later substantiated by a number of studies from several laboratories that showed specific activation of occipital cortex in the blind by nonvisual stimuli, including Braille, tactile shapes, spoken words and sounds (Sadato et al., 1996; Büchel et al., 1998; De Volder et al., 1999; Weeks et al., 2000; Arno et al., 2001; Burton et al., 2002; Röder et al., 2002). Among these studies in early blind subjects, some reported an involvement of the occipital cortex during sound localization (Weeks et al., 2000; Gougoux et al., 2005; Renier et al., 2010). In the study by Weeks et al. (2000), congenitally blind and sighted subjects (who were studied blindfolded) were tested in a virtual auditory space environment (simulating quasi-free-field sound with standardized head-related transfer functions (HRTFs) and headphones), and their relative cerebral blood flow was measured in a whole-head PET scanner. The task was (a) to decide whether two subsequent sounds were coming from the same or from different azimuth positions in space, or (b) to move a joystick into the presumed direction. Both tasks yielded similar results. In all subjects (sighted or blind) the inferior parietal lobule (IPL) was activated, which provides clear evidence for an involvement of this region in auditory spatial processing. It was confirmed by independent studies that this parietal region (possibly the human analog of the ventral intraparietal area [VIP] in the rhesus monkey) contains in fact a unimodal auditory area (Bushara et al., 1999; Weeks et al., 1999). This area is part and parcel of a dorsal auditory processing stream (Rauschecker and Scott, 2009; Rauschecker and Tian, 2000). Area VIP receives its input from auditory belt and parabelt cortex in the posterior superior temporal gyrus (STG) (Lewis and Van Essen, 2000). Both sighted and blind subjects also activated frontal areas, owing to the delayed-matching task involving working memory, which are also part of the auditory dorsal stream (Romanski et al., 1999). In blind subjects, occipital cortex was activated in addition to the above areas. Activation zones originated in posterior parietal cortex and extended all the way into Brodmann areas 18 and 19, as determined on the basis of Talairach coordinates (Talairach and Tournoux, 1988). The expansion was most extensive in the right hemisphere, which testifies to its special involvement in spatial processes (Mesulam, 1999). So, this PET imaging study provided evidence in blind humans that representation of sound localization was expanded into areas of cortex normally devoted to vision, resulting in a massive increase of activation in occipital cortex in these subjects when compared to sighted controls. Similar results of auditory activation in the occipital cortex of blind subjects were obtained using event-related potentials (Kujala et al., 1992; Kujala et al., 1995) and fMRI (Fig. 3, Renier et al., 2010). Furthermore, recruitment of occipital cortex during auditory processing in the blind was shown to be related to successful behavioral performance, since the degree of occipital cortex activation correlated positively with sound localization accuracy (Gougoux et al., 2005; Renier et al., 2010). This constitutes a strong argument in favor of the hypothesis according to which the occipital cortex of the blind would be the neural basis of the improved perceptual abilities usually observed in these persons (Goldreich et al., 2003; Collignon et al., 2006). The functional role of the occipital cortex in the processing of non visual stimuli was also confirmed using transcranial magnetic stimulation (TMS) to transiently disrupt the brain activity of the occipital cortex in the blind (Cohen et al., 1997; Amedi et al., 2004; Merabet et al. 2009). In particular, Collignon and colleagues (2007) showed that applying repetitive TMS on the occipital part of the dorsal visual stream to induce virtual lesions in this region affected selectively the performance in

sound localization by the blind whereas it did not affect pitch or intensity discrimination. By contrast, rTMS targeting the same cortical areas in sighted subjects did not affect performance on any auditory tasks (Collignon et al., 2007).

The activation of occipital, normally visual, cortical areas in blind humans raises a fundamental question: Is the auditory activation of occipital areas in the blind due to feedforward, bottom-up activation from auditory areas, or is it due to feedback input from higher-order, parietal cortical regions, homologous to the AES in cats? It should be noted that some earlier studies reported auditory activation of visual cortex even in normal cats (Fishman and Michael, 1973; Spinelli, Starr, and Barrett, 1968). Initially, such reports were not taken seriously, because the activation was sparse and was generally attributed to unspecific effects of anesthesia or arousal. However, auditory projections to visual cortex were later demonstrated in very young kittens (Innocenti and Clarke, 1984), and more recent anatomical data with more sensitive tracers showed that a direct projection from auditory to visual cortex also exists in adult rhesus monkeys (Falchier et al., 2002; Rockland and Ojima, 2003). Robust multisensory activation was later found in the dorsal stream, supported by anatomical projections (Smiley et al., 2007). Similar connections between the somatosensory cortex and the visual cortex were also described in monkeys and humans (Wittenberg et al., 2004; Négyessi et al., 2006). Prefrontal area 46 and parietal areas VIP and 7a seem to occupy a central position in the visuo-tactile network (Négyessi et al., 2006). More generally, an increasing number of studies show that populations of neurons in most sensory cortices, including the visual one, are multisensory and respond to stimulation from several sensory modalities (Wallace et al., 2004). In humans, various visual cortical areas were found to be activated in sighted subjects during tactile processing (Amedi et al., 2002; Amedi et al., 2001; Peltier et al., 2006; Pietrini et al., 2004; Prather et al., 2004; Sathian and Zangaladze, 2002; Sathian et al., 1997; Zangaladze et al., 1999; Zhang et al., 2005; Zhang et al., 2004; Ptito et al., 2005) and auditory processing (Poirier et al., 2005; Wallace et al., 1996; Weeks et al., 1999; Zimmer et al., 2004). Moreover, several specialized visual brain areas that were for long considered as modality-specific have been recently found to be involved in the processing of non visual information in sighted subjects. For instance, the visual motion area v5/hMT was activated by auditory and tactile motion perception (Poirier et al., 2005; Matteau et al., 2010). The lateral occipital complex (LOC) was involved in haptic shape processing (Amedi et al., 2001, 2002) or using a visual-to-auditory sensory substitution device to extract shape information from soundscapes (Amedi et al., 2007). All these reports indicate that non-visual inputs naturally reached the visual cortex and were processed in visual brain areas in sighted subjects. In this perspective, the cross-modal plasticity of the occipital cortex observed in visually deprived humans and animals could be an exacerbation and expansion of multisensory properties of these regions to neighbouring neurons or visual brain areas that are normally modality-specific. It has also been proposed that these multisensory areas could be the entering points of non-visual information to the occipital cortex of the blind (e.g. Pascual-Leone et al., 2005). In accordance with this hypothesis, these results in sighted subjects may be interpreted in favor of a metamodal organization of the brain (Pascual-Leone and Hamilton, 2001), which could be utilized for compensatory plasticity; normally latent cortical connections that participate in multisensory percepts in sighted subjects might be unmasked and may be potentiated in the event of

complete loss of visual input (Theoret et al., 2004). The balance of activation by experienced versus deprived sensory modalities would be tipped in favor of experienced modalities by strengthening them at the expense of the deprived modalities.

As to the question of bottom-up versus top-down input, interregional analysis of the PET imaging data by Weeks et al. (2000) suggests that feedback connections from the IPL region could provide a stronger auditory signal in blind than in sighted individuals and perhaps be responsible for the auditory activation in the occipital lobe. Whereas auditory cortex in the superior temporal region was negatively correlated with the right IPL in sighted subjects, it showed strongly positive correlation with the IPL in blind subjects. In addition, IPL activation was strongly correlated with occipital regions. This brought support to the view according to which the IPL region is dominated by auditory input in the blind, which is then carried into occipital cortex by a strengthened back-projection from IPL. Similarly, to explain the increased functional coupling between the primary visual cortex (V1) and the primary somatosensory cortex (SI) in early blind human subjects (Wittenberg et al., 2004), it has been proposed that somatosensory inputs from SI to V1 passed through parietal areas VIP and 7a and then reached V1 via MT (Négyessy et al., 2006).

Effect of early sensory loss on the development of the visual cortex

Studies in animals suggest that cortical connections with and within the visual cortex are genetically programmed as they appear before birth and continue to develop after birth even in animals reared in the dark or with binocular enucleation, though some differences in the precision or density of these connections can however be observed in these animals (Howard, 2002). For instance, interlayer cortical connections are present in V1 with a rather high degree of specificity in prenatal macaque monkeys (Callaway, 1998). The clustering of cortical cells displaying similar functional preferences (characteristics) or intercolumn connections (also called horizontal or lateral connections) are set as in adult cats by the seventh postnatal week in all cats (Hata et al., 1993), even though the pattern of clustering is less precise in cats binocularly deprived from birth (Callaway and Katz, 1991). The clustering pattern that occurs during the first weeks of life would involve growth and elimination of synaptic connections that would be overproduced before birth (Callaway and Katz, 1990). It is worth noting that binocular enucleation did not prevent the development of the initial crude clustering (Ruthazer and Stryker, 1996). However, binocular deprivation and blockage of afferents from the LGN reduced the density and precision of projections from area 17 to area 18 (Caric and Price, 1999, see also Blakemore and Price, 1987; Caric and Price, 1999). Therefore it seems that the initial clustering depends on spontaneous neural activity at the level of the Lateral geniculate nucleus (LGN) or cortex while the fine tuning of the clustering depends on sensory experience (Howard, 2002, see also Innocenti and Frost 1979; Innocenti et al., 1985). In non human primates, it has been shown that the absence of retinal input via the lateral geniculate nucleus did not affect the schedule and magnitude of synaptogenesis in the visual cortex (Bourgeois and Rakic, 1996). Indeed, in monkeys enucleated at early embryonic stages, atrophy of geniculocortical pathways was observed (Rakic et al., 1988) and the striate cortex had a smaller surface area than in control animals (Bourgeois and Rakic, 1996) but a normal thickness and complement of layers, although the details of the synaptic circuits did not mature properly: the ratio of synapses

situated on dendritic spines and shafts in sublayers IVAB and IVC were not reversed during late maturation in the enucleates (Bourgeois and Rakic, 1996). In humans, lateral connections first emerged at 37 weeks of gestation and reached their adult form at the 15th month (postnatal) (Burkhalter et al., 1993) but the effect of early blindness on synaptogenesis and synaptic revision during neuronal activity driven by sensory experience (Changeux and Danchin, 1976) remains unknown. In accordance with the observations in animal studies, studies that used diffusion tensor imaging (DTI) to identify changes in the neuronal connections or tracts in adult humans that are affected by early visual deprivation reported an atrophy of the geniculocortical tracts with relative sparing of cortico-cortical tracts such as those connecting visual cortex to orbital frontal and temporal cortices (Shimony et al., 2005). They did not detect any additional tracts or any apparent strengthening of connections in the blind subjects. However, we cannot exclude that cortical changes occurring in case of sensory deprivation are too subtil to be detected by this method for the moment. Further examination of the mean fractional anisotropy (FA) along three major tracts (corticospinal, optical radiation, and corpus callosum) in early blind and sighted control subjects revealed a significant increase along the corticospinal tract (Liu et al., 2007). The existence of genetically determined connections that took place independently of visual experience is consistent with the reports made from studies of sight recovering patients who had a congenital cataract removed at adult age. Although these patients experienced difficulties with the interpretation of their visual perception and a relatively low visual acuity, their visual system was noneless functional, suggesting that most connections were present despite early and extended visual deprivation (Von Senden, 1960; Gregory and Wallace, 1963; Ackroyd et al., 1974; Ostrovsky et al., 2006; Fine et al., 2003).

Meanwhile, with the advent of functional magnetic resonance imaging (fMRI), brain activation results with even finer spatial resolution have been obtained. Several groups have demonstrated that specific functions performed by the blind using the auditory or somatosensory modalities correlate with activation in specific regions of the occipital cortex (e.g. Amedi et al., 2003; Prather et al., 2004). This preserved specialization of the occipital cortex in early blind humans is particularly highlighted in recent studies (e.g. Renier et al., 2010; Collignon et al., 2011; Striem-Amit et al., 2012a, see also Ptito et al., 2008).

Preserved “what and where” dichotomy in early blind humans

The study by Renier et al. (2010) provided demonstration that the functional specialization of the dorsal stream was preserved in the “visual” cortex of the blind but changes its sensory modality. In this study, we used fMRI in early-blind individuals and sighted controls to compare brain activation patterns elicited by the processing of spatial and nonspatial attributes of equivalent auditory and vibrotactile stimuli. The main experiment was done in two groups of 12 early-blind (EB) volunteers and 12 sighted controls (SCs). Both auditory and vibrotactile stimuli varied in two dimensions: frequency and spatial location. The subjects were instructed to either detect the stimuli (Detection condition) or perform a one-back comparison task where they had to determine whether each stimulus was the same or different from the preceding one regarding either its frequency (Identification condition) or its location (Localization condition). When probing the blind volunteers with these auditory and tactile stimuli (Fig. 4), a specialized region was found in the right middle occipital gyrus

(MOG), which responded preferentially during localization of sensory stimuli (in both the auditory and tactile domain) as opposed to their identification. Results also indicated that medial parietal areas showed a preference for spatial processing in both modalities in the two groups. Furthermore, in the auditory domain, the right MOG region showed a strong correlation between individual BOLD response and behavioral sound localization. As the MOG is part of the visual dorsal stream in sighted individuals (Dumoulin et al., 2000; Wandell et al., 2007), and considering that this region was recruited by similar tasks in vision in a control experiment in a separate group, it follows that specialized brain regions develop their computational functions independently of experience. However, the allegiance to a particular sensory modality driving them can change depending on early postnatal experience. So, while visual deprivation leads to a replacement of visual by nonvisual input (“compensatory plasticity”; Rauschecker, 1995), each structure retains its designated functional role. Recent studies brought support to an analogous hypothesis in congenital deafness (Lomber et al., 2010; Meredith et al., 2011). In both congenitally deaf (Lomber et al., 2010) and early deafened adult cats reversible deactivation posterior auditory cortex selectively eliminated superior visual localization abilities, indicating that enhanced visual performance in the deaf is caused by cross-modal reorganization of deaf auditory cortex (Meredith et al., 2011). This suggests that the preserved functional specialization may be a general principle in the brain and could be generalized to most sensory modalities.

In the medial parietal cortex, the precuneus has previously been described as a multisensory operator that is specialized for spatial processing in sighted subjects (Renier et al., 2009). Studies in visually deprived cats and monkeys have suggested that cross-modal plasticity could in fact originate in multisensory parietal regions, where the opportunity for cross-modal competition may be greatest (Hyvärinen et al., 1981; Rauschecker & Korte, 1993). Prior imaging data from blind humans using inter-regional correlation techniques have been compatible with this proposition (Weeks et al., 2000; see above). Other possible mechanisms include a strengthening of cortico-cortical input from other sensory modalities (Hamilton & Pascual-Leone, 1998; Sadato et al., 1998; Bavelier & Neville, 2002; Falchier et al., 2002; Rockland and Ojima, 2003) or of nonvisual thalamocortical connections (Hackett and Schroeder, 2009).

The segregation between cortical pathways for the identification and localization of objects is thought of as a general organizational principle in the brain: the functional specialization into a ventral/identification (“what”) and a dorsal/localization (“where”) stream has been demonstrated in vision (Zeki, 1978; Ungerleider and Mishkin, 1982; Haxby et al., 1991) in hearing (Rauschecker, 1998; Romanski et al., 1999; Kaas & Hackett, 2000; Rauschecker and Tian, 2000; Tian et al., 2001; Alain et al., 2001; Maeder et al., 2001; Lomber and Malhotra, 2008) and, to a lesser extent, for touch (Deibert et al., 1999; Zangaladze et al., 1999; Stoez et al., 2003; Prather et al., 2004; Van Boven et al., 2005; Renier et al., 2009). In case of visual deprivation, the tactile and auditory streams would expand to the “visual” streams that would maintain their original functional role (Renier et al., 2010). Earlier studies in animals also brought results that are consistent with this hypothesis. Although the cells in the visual areas 17 and 18 come to maturation during the first months of life (Buisseret and Imbert, 1976; Buisseret et al., 1978; Milleret et al., 1988), a significant proportion of cells already display characteristics of functional specialization early in the

development. For instance, about 40% of the cells in area 17 showed tuning to stimulus orientation at eight days in kitten (Braastad and Heggelund, 1985). In one to four-week old dark-reared kitten, specialized cells were found in visual areas 17 and 18 for direction (Pettigrew, 1974), orientation (Blakemore and Van Sluyters, 1975; Buisseret and Imbert, 1976; Frégnac and Imbert, 1978), spatial frequency and binocular disparity (Freeman and Ohzawa, 1992), although the responses of these cells were weaker, less stable and the proportion of these specialized cells was lower than in experienced animals. One may conclude that the development of the basic physiological apparatus for processing visual stimuli in the cat predates visual experience and its function must therefore be genetically determined, even though visual experience makes it finer.

Visuo-spatial imagery in early blind humans

A specific recruitment of dorsal-stream occipital and parietal areas has been repeatedly observed in blind subjects during tasks involving either spatial features or spatial analyses, e.g. distance estimation using an ultrasonic device (De Volder et al., 1999), tactile imagery (Uhl et al., 1994; Zangaladze et al., 1999; Weisser et al., 2005; Stilla et al., 2008), sound localization (Weeks et al., 2000; Gougoux et al., 2005; Collignon et al., 2011), spatial working memory (Bonino et al., 2008), motion perception (Poirier et al., 2006a; Ricciardi et al., 2007; Saenz et al., 2008; Ptito et al., 2009; Kuper et al., 2011), and also in visuo-spatial imagery (Vanlierde et al., 2003). In the study by Vanlierde et al. (2003), regional cerebral blood flow was assessed in early blind subjects and in sighted control volunteers who were studied blindfolded during a complex spatial imagery task (to mentally generate a matrix organized like a crossword grid). Subjects were required to build up a bidimensional pattern that was verbally described as a 6×6 square grid depicted line by line, with some squares filled and others left empty. Subjects were asked to memorize the precise location of filled-in squares inside the grid in order to assess pattern symmetry in relation to a given grid axis. This condition was contrasted with a verbal memory task to subtract the brain activation related to the verbal and memory aspects and to isolate the brain activation specific to spatial imagery. Results showed a selective activation of parieto-occipital areas during visuo-spatial imagery in both groups, involving the precuneus, superior parietal lobule, and occipital gyrus (Brodmann areas 7, 19). In accordance with previous studies conducted in sighted subjects, which indicated that the same parieto-occipital areas are involved in visual perception as in mental imagery dealing with spatial components, the dorsal visual pathway was critically involved in visuo-spatial imagery in early blind individuals in a similar way as in sighted controls. This indicates further that the inputs from auditory and tactile modalities are capable of promoting efficient functional development of the dorsal visual pathway in the absence of vision.

Object imagery in early blind humans

Numerous studies in early blind subjects also showed that brain areas in the ventral “visual” stream develop and retain their designated role regardless of visual experience (Arno et al., 2001; De Volder et al., 2001; 2005; Amedi et al., 2007; Reich et al., 2011; Striem-Amit et al., 2012a). In the study by De Volder et al. (2001), regional cerebral blood flow was examined using PET in six right-handed early blind and six age-matched control volunteers

during an object imagery task. The brain activity was assessed during three conditions: resting state, passive listening to noise sounds (control task) and a mental imagery task (imagery of object shape) triggered by the sound of familiar objects. During a training session, blind subjects were required to explore a series of objects one by one, by touching them for 1 min, while receiving the corresponding sound through earphones, and to build up a precise mental representation of the object. The same instructions were provided to sighted controls who explored the objects visually and auditorily. During the PET session, the mental imagery task required silent identification of each individual meaningful sound, provided by earphones, followed by mental retrieval of the internal representation of the related object. In all subjects, the PET results showed a selective activation of the ventral visual pathway during mental imagery of object shape, as contrasted to the control condition. Activation foci were found in occipito-temporal and visual association areas, particularly in the left fusiform gyrus (Brodmann areas 19–37) during mental imagery of object shape by both groups (Fig. 5). Since shape imagery by early blind subjects does involve similar visual structures as in controls at an adult age, it indicates developmental crossmodal reorganization to allow perceptual representation in the absence of vision, i.e. in individuals with early-onset blindness, in whom internal representations of shape are attainable only through tactile and auditory experience. Interestingly, Reich et al. (2011) recently showed that a specific module in the “visual” ventral stream specialized in word reading, the reading center, was also specifically recruited when congenitally blind subjects were reading Braille words. This convergence of results indicates that auditory and tactile senses, at least partly, did act as a natural substitutive system for vision during brain maturation. Other studies, using a visual-to-auditory sensory substitution device, demonstrated that the lateral occipital complex (LOC) developed its role in shape processing in early blind subjects (Arno et al., 2001; Amedi et al., 2007).

Sensory substitution and cross-modal plasticity in early blindness

Sensory substitution (SS) refers to the use of a sensory modality to provide environmental information normally gathered by another sense (Bach-y-Rita et al., 1969), while still preserving some of the key functions of the original senses. For example, the use of auditory signal might give information about visual scenes. Most electronic vision substitution systems were developed to provide visual information either through the tactile (e.g. Bach-y-Rita et al., 1998; White, 1970) or the auditory modality (e.g. Capelle et al., 1998; Cronly-Dillon et al., 1999; Meijer, 1992). This kind of devices device allows online translation of visual images into electrotactile stimuli or into sounds and offers the rare opportunity to convey information via another sense than the one usually devoted to its processing. In this perspective, sensory substitution in blindness presents a unique venue for understanding how the brain adapts itself when it processes visual-like information after an extended period of sensory deprivation, or the complete absence of such since birth (see Renier and De Volder, 2005 for a detailed review of this question). Sensory substitution enables blind persons to recognize 2D shapes (Arno et al., 2001b; Sampaio et al., 2001; Auvray et al., 2005) and to locate objects in space (Renier et al., 2005b; Renier and De Volder, 2010) and the neural structures involved in these tasks included several regions of the visual cortex that

were usually not recruited for sound processing (Renier et al., 2005a; Poirier et al., 2006b; Amedi et al., 2007).

Brain imaging studies provided clear demonstration of a recruitment of occipito-parietal brain areas in early blind subjects during the processing of auditory or tactually encoded visual information (Arno et al. 2001a; Ptito et al. 2005) and further indicated that specialized “visual” brain areas within the ventral and the dorsal visual streams were selectively recruited using a sensory substitution device (Arno et al., 2001; Ptito et al., 2009; Amedi et al., 2007; Ptito et al., 2012; Striem-Amit et al., 2012a). For instance, Amedi et al. (2007) reported activation of the LOC during object shape processing, Striem-Amit et al. (2012b) showed that the visual word form area was recruited when reading letters with a visual-to auditory sensory substitution device. All together, these studies further demonstrated that the functional specialization of parts of the “visual” cortex is maintained in early blind subjects but switch of sensory modality.

Conclusions

Thirty years of animal research have shown that early visual deprivation leads to a crossmodal expansion of brain regions in the auditory or somatosensory domain and a corresponding improvement of function. This has been demonstrated in the superior colliculus and, most prominently, in the cerebral cortex. Similarly, blindness from birth in humans can cause reassignment of cortical regions from one modality to another, as functional imaging studies have shown. This crossmodal plasticity, however, maintains the function of part of these cortical regions, which are presumably determined by experience-independent mechanisms, presumably during prenatal development. The most exciting consequence of these recent studies is that sensory substitution in the blind may become a practical reality, allowing blind individuals to harness the power of crossmodal plasticity to perceive, localize and recognize objects with their auditory (Renier et al., 2005; Amedi et al., 2007) and tactile senses (Bach-y-Rita, 2004; Kupers et al., 2010; Renier et al., 2010).

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Highlights

The visual cortex is activated by sound and touch in early blind subjects.

In the early blind, the occipital cortex is largely multisensory.

Cortical development seems to overlay modal responses on “visual” structures.

Visual brain areas assume their original role for nonvisual senses in the blind.

Figure 1.

Expansion of whisker-barrel system in blind mice. The size of barrels in the somatosensory cortex was compared in mouse pups that were reared with normal vision or with eyes surgically removed immediately after birth. The graph displays the size distribution of all barrels in the two groups. In the blind littermates barrel size was enlarged by up to 20%. The largest barrels were even larger in the binocularly deprived animals, which causes their distribution to be shifted to the right ($P < 0.0001$; t test). Comparisons within and between litters of the same group did not show any significant differences (adapted from Rauschecker et al., 1992).

Figure 2.

Sound localization in binocularly deprived (BD) and normal cats. The experimental setup is shown in (a) with azimuth positions 1 to 8 in clockwise fashion, with sham speakers in between. The bottom panel (b) displays the precision of sound localization at the eight positions in terms of mean variance (precision is related inversely to the width of the distribution of sound localization error). The results demonstrate that all cats were more precise in localizing straight ahead than rear positions, but blind cats were more precise than sighted cats at practically every position ($p < 0.002$, two-way ANOVA) (adapted from Rauschecker, 1995 and Rauschecker and Kniepert, 1994). (c) Schematic display of crossmodal plasticity determined by electrophysiological mapping in binocularly deprived and normal cats. The extent of sensory cortical representations in the cat is shown after normal development (a, b) and after extended periods of binocular visual deprivation (c, « blind »). The schematic displays are based on track reconstructions from single-unit recordings in both normal and blind cats, in which the sensory modality of the neurons was determined (from Rauschecker and Korte; 1993). Significant expansion of auditory and somatosensory cortical regions is seen in visually deprived cats (adapted from Rauschecker, 1995).

Figure 3.

Between-group comparison for the auditory modality. In orange-yellow the brain areas that were activated more in early blind subjects than in blindfolded sighted controls during auditory identification and localization tasks, whereas the blue-green zones are those that are more recruited in sighted subjects performing the same auditory processing tasks on the same stimuli. Activation maps are resulting from a random-effects (RFX) between-group comparison with a threshold of $p < 0.05$ corrected for multiple comparisons. The color-gradient scale codes the t value (adapted from Renier et al., 2010).

Figure 4.

In subjects who are blind from birth, the brain adapts itself and « re-uses » cortical areas that are normally devoted to visual abilities, in order to develop auditory and tactile abilities. During fMRI, subjects were provided with sounds or vibrotactile stimuli and were requested to identify, to localize, or simply detect them. The task comparison shows that the occipital cortex of blind subjects, devoid of visual function from birth, does reorganize itself to process these stimuli and the cortical reorganization follows the same architecture as the one of sighted subjects. In particular, the right middle occipital gyrus (MOG) is recruited to localize the stimuli, whether auditory or tactile, in early blind subjects, whereas the same region is only recruited to localize visual stimuli in sighted subjects, as shown by the activity profiles (adapted from Renier et al., 2010).

Figure 5.

PET imaging evidence in blind humans that auditory-triggered mental imagery of shape (IMAG) contrasted to a control auditory task (CONT) recruits the ventral “visual” pathway in these subjects. The statistical parametric map for this comparison is superimposed on an individual normalized MRI displaying the anterior, right and medial surfaces (first row), and the posterior, left and medial surfaces (second row). The results show bilateral activation of occipito-temporal brain areas in early blind subjects. The cursor lines indicate a voxel in the left fusiform gyrus with a Z-value of 5.0 ($p < 0.05$ corrected for multiple comparisons, coordinates with reference to the Talairach system). (adapted from De Volder et al., 2001).