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CHAPTER 14

Sensory rehabilitation in the plastic brain

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Abstract: The purpose of this review is to consider new sensory rehabilitation avenues in the context of the brain's remarkable ability to reorganize itself following sensory deprivation. Here, deafness and blindness are taken as two illustrative models. Mainly, two promising rehabilitative strategies based on opposing theoretical principles will be considered: sensory substitution and neuroprostheses. Sensory substitution makes use of the remaining intact senses to provide blind or deaf individuals with coded information of the lost sensory system. This technique thus benefits from added neural resources in the processing of the remaining senses resulting from crossmodal plasticity, which is thought to be coupled with behavioral enhancements in the intact senses. On the other hand, neuroprostheses represent an invasive approach aimed at stimulating the deprived sensory system directly in order to restore, at least partially, its functioning. This technique therefore relies on the neuronal integrity of the brain areas normally dedicated to the deprived sense and is rather hindered by the compensatory reorganization observed in the deprived cortex. Here, we stress that our understanding of the neuroplastic changes that occur in sensory-deprived individuals may help guide the design and the implementation of such rehabilitative methods.

Keywords: blindness; deafness; neuroplasticity; rehabilitation; sensory substitution; neuroprosthesis.

Introduction

It has long been believed that the brain is hard-wired, in a predetermined manner mainly shaped by evolution. It is likely that the apparent regularity and homogeneity of cortical anatomy have prolonged this conception of an immutable brain. However, results acquired mainly in the past two decades have led to the recognition that the developing, and even adult, brain has a remarkable ability to remodel and restructure the different circuits within it, based on learning and experience. This concept, called

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neuroplasticity, is opening up exciting new fields of research based on the brain's ability to constantly adapt itself to its environment throughout life.

Recognizing the dynamic nature of cortical circuitry is important in understanding how the nervous system adapts after sensory deprivation. Pioneering studies of Wiesel and Hubel (1965, 1974) on the development of ocular dominance columns have compellingly demonstrated that alterations in visual experience can influence the normal development of the visual cortex. Other seminal experiments have also shown that cortical maps can change/expand with use; for example, the representation of the finger tips in the somatosensory cortex has been shown to expand after a period of intense stimulation (Kaas et al., 1983), as observed in proficient Braille blind readers (Pascual-Leone and Torres, 1993; Sterr et al., 1998). Similarly, the tonotopic map in the auditory cortex is larger in musicians (Pantev et al., 1998) and visually deprived individuals (Elbert et al., 2002). Aside from such *intramodal* plasticity, massive *crossmodal* changes have also been observed in sensory-deprived cortex (Bavelier and Neville, 2002; Pascual-Leone et al., 2005). Striking evidence that external inputs can determine the functional role of a sensory cortex has come from experiments on “rewired” animals. For instance, by making a series of brainstem lesions, researchers surgically rerouted visual input toward primary somatosensory or auditory areas (Frost and Metin, 1985; Frost et al., 2000; Roe et al., 1990; Sur et al., 1988). These experiments demonstrated that cells from the rewired regions shared some structural and functional similarities with cells recorded in the visual cortex of normally raised animals. Moreover, these authors demonstrated that these newly visual cells also mediated visually guided behavior (Frost et al., 2000; von Melchner et al., 2000). Taken together, these data suggest that primary cortical areas can change their functional specificity depending on which inputs they receive. Indeed, the observation that “visual” regions can be recruited for nonvisual processing in blind subjects (Sadato et al., 1996; Wanet-Defalque et al., 1988) and that auditory regions can be recruited by nonauditory inputs in deaf subjects (Bavelier et al., 2001; Finney et al., 2001) has led to a change in how we think about the brain and its development in relation to experience. Importantly, these findings also demonstrate that these plastic changes are compensatory in nature because they appear to underlie improved abilities in the remaining senses of sensory-deprived individuals (Amedi et al., 2003; Bavelier et al., 2000, 2006; Collignon et al., 2006, 2009b; Gougoux et al., 2005).

Overall, these results point to the important role of sensory experience in the development and the maintenance of sensory brain functions. This has major implications, given current developments in sensory rehabilitation technologies, whether they are of the invasive type or not (Veraart et al., 2004; see Fig. 1). Invasive interventions rely on the integrity of the deprived system. Plastic reorganization that occurs all along the sensory pathway after deprivation is therefore likely to interfere with the reacquisition of the initial function of the system (Merabet et al., 2005). Indeed, in addition to the technical and surgical challenge of sensory restoration, there exists a neuropsychological one: how will the restored sensory input be interpreted by the reorganized sensory cortex? In contrast, sensory substitution refers to the use of one sensory modality to supply information normally gathered from another sense (Bach-y-Rita and Kercel, 2003). In so doing, sensory substitution devices can take advantage of the crossmodal plasticity observed in deprived individuals whereby deafferented areas provide the neural basis for behavioral compensation reported in the preserved senses (Amedi et al., 2003; Gougoux et al., 2005). Indeed, studies on how the brain changes following sensory deprivation are not only central to our understanding of the development of brain function but are also crucial to the development of adequate and successful rehabilitation strategies in case of sensory alterations.

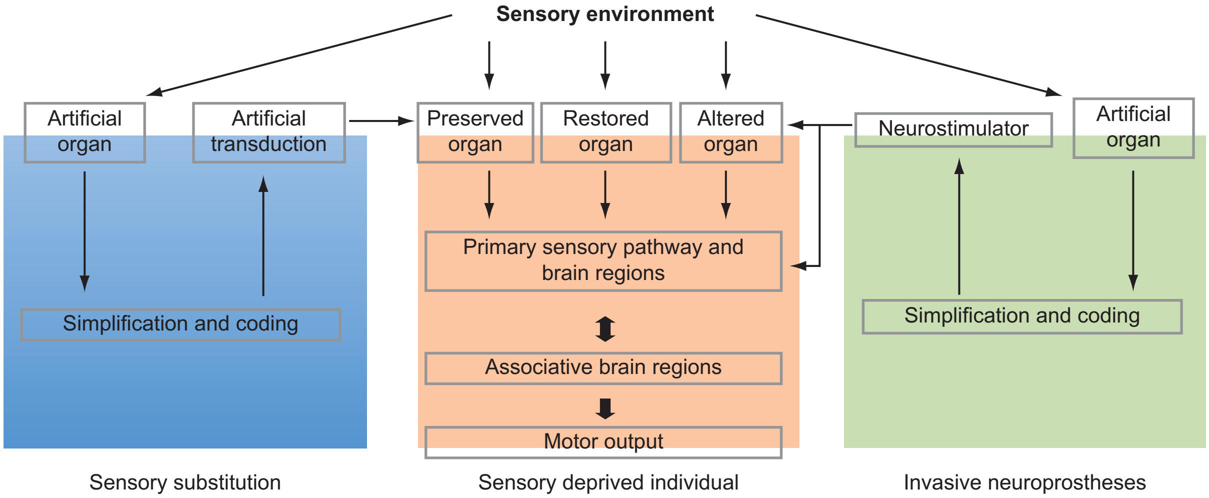

Fig. 1. Model of rehabilitation procedures for sensory-deprived individuals. The middle section represents a sensory-deprived person for whom environmental information can be transmitted to the brain by means of a remaining modality after sensory substitution (left panel), surgical restoration of the defective organ, or by the use of an implanted neuroprosthesis stimulating the deficient sensory system (right panel). With sensory substitution, the environmental inputs usually gathered by the defective sense is simplified and coded in order to be manipulated in a preserved remaining modality. With neuroprostheses, the lacking sensory information is simplified and coded into electrical impulses to stimulate the fully or partly preserved part of the deficient sense.

Rehabilitation in blindness

Early visual deprivation causes atrophy in the optic tracts and radiations as well as massive gray and white matter volume reduction in early visual areas (Noppeney et al., 2005; Pan et al., 2007; Park et al., 2009; Ptito et al., 2008b; Shu et al., 2009). Although increased cortical thickness of occipital cortex has also been reported in the blind (Jiang et al., 2009; Park et al., 2009), it is believed to reflect the reduced surface area of the primary and secondary visual cortices (Park et al., 2009). In addition to these structural changes, visual deprivation enables a new role for the visual cortex in that it becomes responsive to nonvisual inputs (Bavelier and Neville, 2002). Moreover, a growing number of studies show that the recruitment of the deafferented visual areas during nonvisual tasks is not simply an epiphenomenon. First, these changes are thought to underpin superior nonvisual abilities often observed in blind individuals as several studies have shown positive correlations between nonvisual performance and occipital activity: the most efficient blind participants are the ones who recruit occipital regions the most (Amedi et al., 2003; Gougoux et al., 2005). Second, transient disruption of occipital activity induced by transcranial magnetic stimulation (TMS) disrupts nonvisual abilities, further demonstrating the functional role of occipital regions of congenitally blind subjects in nonvisual processing (Amedi et al., 2004; Cohen et al., 1997; Collignon et al., 2007, 2009a). Finally, some aspects of the functional architecture present in the occipital cortex of sighted subjects appear to be preserved in the blind (Collignon et al., 2009b, Dormal et al., 2011). For example, the “visual” dorsal stream appears to maintain its preferential coding for spatial processing (Collignon et al., 2007, 2011; Renier et al., 2010; Fig. 2), the ventral stream for the processing of the identity of the input

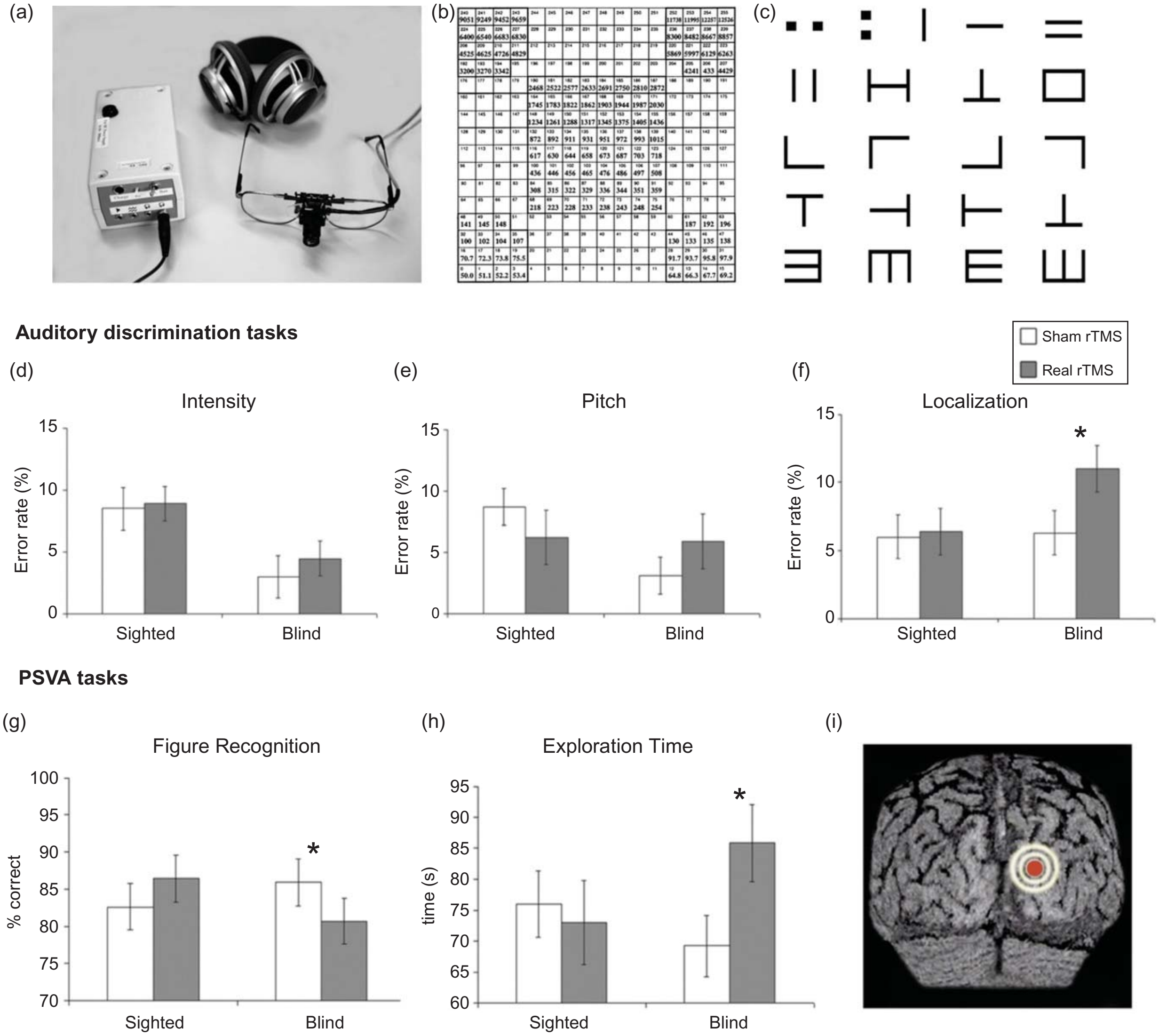

Fig. 2. Prosthesis substituting vision by audition (PSVA). (a) A head-worn video camera (fixed on glasses) allows online translation of visual patterns into sounds that are transmitted to the subject through headphones. (b) The artificial retina provided by the PSVA. The acquired image is divided into pixels according to a 2-resolution artificial retina scheme. The central part of the processed image or fovea has a four times higher resolution than the periphery. The coding scheme is based on a pixel–frequency association. Pixels in use are drawn with a bold border. Frequency is indicated in hertz in the lower part of the used pixels. A single sinusoidal tone is assigned to each pixel of the multiresolution image. The amplitude of each sine wave (the intensity of each sound) is modulated by the gray level of the corresponding pixel. The pattern moves on the grid according to the head movements of the subject, and the corresponding sounds of the activated pixels are transmitted to the subject in real time. (c) Examples of patterns used in the experiments. The second part of the figure denotes the average error rate in blind and sighted subjects after sham and real TMS targeting the dorsal occipital stream during auditory tasks involving discrimination of intensity (d), pitch (e), and spatial location (f). The data show a significant increase of the error rate after real rTMS only in the blind group and selectively for the sound location task. Also, the figure displays the average percentage of correct pattern recognition (g) and the mean exploration time (h) taken to recognize patterns with the PSVA. The data indicate a significant decrease of recognition score and a significant increase of exploration time after real compared to sham TMS in the blind group only. Panel (i) displays the projection of the site of TMS application. This area corresponds to the right dorsal extrastriate occipital cortex (BA 18). Adapted with permission from Collignon et al. (2007).

(Amedi et al., 2007; Gougoux et al., 2009), and hMT+/V5 for processing movement (Bedny et al., 2010; Poirier et *al.*, 2004; Ricciardi et al., 2007). Taken together, these structural and functional changes in "visual" areas of early-blind individuals are thought to induce permanent changes in visual capabilities (Maurer et al., 2005). For example, the ability to elicit phosphenes with application of TMS over the occipital cortex (a measure of visual cortex excitability) is dramatically reduced in congenitally blind individuals (Gothe et al., 2002).

Sight restoration with surgery

The study of adult sight-recovery patients after early-onset blindness, even if extremely rare, has served as an important testing ground for hypotheses about the role of experience in shaping the functional architecture of the brain. These studies have demonstrated that early visual deprivation permanently and deeply affects visual functions (Fine et al., 2003; Gregory, 2003; Levin et al., 2010). Probably the most famous case report concerns patient SB, studied by Richard Gregory (Gregory and Wallace, 1963). SB lost his sight at 10 months of age before regaining it at 52 years of age, by means of a corneal graft. Despite the fact that the visual world now mapped correctly on his retina, SB had severe problems interpreting what he saw. Perception of depth was notably problematic (i.e., Necker's cube appeared flat) and he was only able to recognize faces when they moved. SB continued to rely on audition and touch to interact with his environment and situations that he managed very well while blind, like crossing a street in traffic, suddenly became problematic for him because of the presence of concurrent confusing visual information. Shortly after implantation, he became clinically depressed, probably due to his change of status from a successful blind to an unsuccessful sighted person (Gregory and Wallace, 1963). Another fascinating case was documented more recently in the literature, patient MM, who was blind since the age of 3 years and who had his sight restored at 43 years of age, thanks to stem cell transplant (Fine et al., 2003). MM also had considerable difficulty perceiving depth and perceiving the specific details of objects, including faces. Even 7 years after the intervention, MM still had poor spatial resolution and limited visual abilities that did not allow him to rely on his vision in day-to-day activities (Levin et al., 2010). Imaging studies of MM showed extensive cortical reorganization, even after implantation, which may play a role in his visual difficulties (Fine et al., 2003; Levin et al., 2010; Saenz et al., 2008; Fig. 3). This is hypothesized to be due to an absence of mature cells coding for "fine" details because these cells were still not tuned at 3 years of age when MM lost his sight (Levin et al., 2010). In contrast to visual acuity and form or face perception, visual motion ability appeared relatively preserved after vision restoration in both SB and MM, with robust and specific brain activations for visual motion stimuli having been observed in subject MM (Fine et al., 2003; Levin et al., 2010; Sacks, 1995; Saenz et al., 2008). This is thought to be due to the fact that motion processing develops very early in infancy compared to form processing and might therefore have been more established and robust, allowing its preservation despite many years of visual deprivation (Fine et al., 2003).

It was also shown that robust and specific crossmodal auditory motion responses coexist with regained visual motion responses in area hMT+/V5 after sight restoration in subject MM (Saenz et al., 2008). However, it was not ascertained if the presence of such crossmodal auditory motion responses competes with or improves visual motion perception after recovery, nor whether the interaction between these two senses is enhanced or decreased due to interference (see our related discussion in the cochlear implant (CI) section below). This question is of major importance because the challenge for MM is to use the strong nonvisual skills he developed

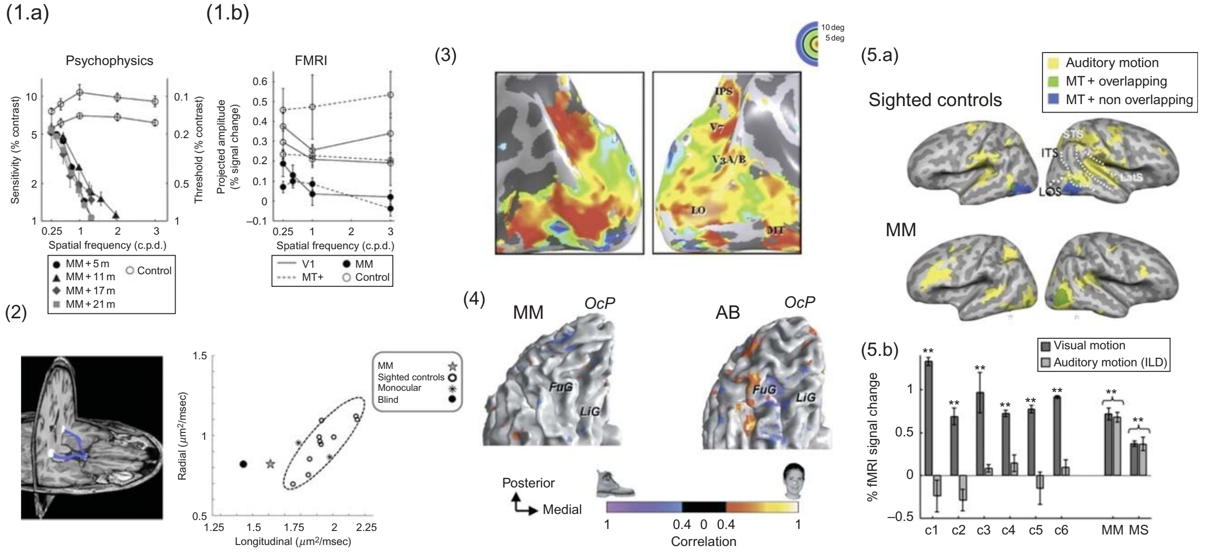

Fig. 3. Patchwork of different studies carried out with MM, an early-blind person who recovered sight at 43 years. Altogether, the results show major alteration in visual processing in this subject. (1.a) MM's sensitivity as a function of spatial frequency measured psychophysically 5–21 months after surgery. (1.b) Neural responses as a function of spatial frequency measured using fMRI in MT+ (dashed line) and V1 (solid line). (2) Comparison of radial and longitudinal diffusivities in the optic tracts and optic radiations (a) Three-dimensional rendering of the optic tract fibers (blue) shown superimposed on axial and coronal slices of MM's brain. The optic tracts connect the optic chiasm and the LGN (white sphere). Scatter plot of the radial and longitudinal diffusivities for the average of the right and left optic tracts. Data are from MM (gray star), 10 normal controls (black open circles), two seeing monocular subjects (black asterisks), and one blind subject (black closed circle). The 2 standard deviation covariance ellipsoid (dashed) is shown. (3) Visual field eccentricity representations in medial-ventral and dorsal-lateral cortex visual field eccentricity maps in lateral-occipital surface of MM's left (left panel) and right (right panel) hemispheres. Several extrastriate regions respond unusually to foveal stimuli. The right hemisphere shows some regions and a color map defining the visual field eccentricity representations.(4) Left hemisphere activation in response to faces versus objects with red–orange regions that responded more to faces and green–blue regions that responded more to objects. A control subject (AB) showed a typical pattern of activation, with large contiguous regions that responded more either to faces or objects near the fusiform gyrus (FuG) and lingual gyrus (LiG). In contrast, MM showed little activity to objects, and almost no activity to faces. (5.a) Surface maps of auditory and visual motion responses in MT for MM and sighted controls. Yellow regions responded more to moving versus stationary auditory white noise. Green and blue regions show MT location as determined by a visual MT localizer scans run in the same subjects (green, MT overlapped by auditory ILD motion responses; blue, MT not overlapped by auditory ILD motion responses). Note the near-complete overlap (very little blue) in subject MM indicating colocalization of MT for auditory motion processing. Adapted with permission from Fine et al. (2003; parts 1 and 4), Levin et al. (2010; parts 2 and 3), and Saenz et al. (2008; part 5).

as a proficient blind subject (sensory compensation in the remaining senses) in conjunction with his rudimentary vision in order to improve his use of visual functions. Indeed, knowledge of how visual and auditory responses interact in sight-recovery patients is important for optimizing patients' use of their restored vision (Saenz et al., 2008).

The study of children treated for congenital bilateral cataracts after varying periods of visual deprivation presents the opportunity to examine the fundamental role of visual inputs for the normal development of specific aspects of vision. Particular studies on this topic have shed light on the fact that different visual abilities have various sensitive periods during which the absence of visual inputs permanently impairs the investigated process. For example, even when treated for congenital bilateral cataracts before the first 6 months of age, permanent deficits in sensitivity to global motion have been shown to develop (Ellemberg et al., 2002; Lewis and Maurer, 2005), as well as for holistic face processing (Le Grand et al., 2001, 2004). However, the loss of sight after 6 months of age preserves the global detection of motion even if the period of blindness is extended as shown in patients MM and SB (Fine et al., 2003; Gregory and Wallace, 1963) but still can dramatically impair acuity, peripheral light sensitivity, and object and face processing (Fine et al., 2003; Levin et al., 2010; Lewis and Maurer, 2005; Gregory and Wallace, 1963). Strikingly, in some visual domains, visual input is necessary throughout the period of normal development and even after the age when performance reaches adult levels (Maurer et al., 2005). For instance, a short period of visual deprivation beginning any time before the age of 10 years causes permanent deficits in letter visual acuity, which normally reaches adult levels by the age of 6 years (Lewis and Maurer, 2005). Similarly, short periods of deprivation beginning even in early adolescence cause permanent deficits in peripheral light sensitivity, which normally reaches adult functional levels by 7 years of age (Bowering et al., 1993). It thus appears that visual input is necessary not only for the development but also for the consolidation of some visual connections (Lewis and Maurer, 2005). Regarding multisensory integration abilities, recent studies conducted in bilateral congenital cataract patients treated within the first two years of life demonstrated that visual input in early infancy is also a prerequisite for the normal development of multisensory functions (Putzar et al., 2007, 2010). Even if some studies demonstrated that the human brain retains an impressive capacity for visual learning well into late childhood (Ostrovsky et al., 2006, 2009), an important point raised by these studies in sight-restored patients is that early intervention is often a good predictor of visual abilities in adults. In the particular case of congenital blindness, sight restoration in adults may be less miraculous than intuitively expected, probably because of the deterioration of visual tracts and massive crossmodal plasticity observed in the visual cortex of these persons (Noppeney, 2007).

Sensory substitution in the blind

The fact that the crossmodal recruitment of visually deafferented occipital areas effectively contributes to the processing of nonvisual inputs offers a real opportunity for rehabilitation via sensory substitution. Indeed, this fact has been intuitively exploited in numerous rehabilitation programs aimed at promoting nonvisual skills. Since it was discovered that the enrichment of the environment is an effective means of dramatically enhancing crossmodal plasticity associated with blindness (Piche et al., 2004), and because such reorganization mechanisms are thought to underlie enhanced perceptual skills in the blind (Amedi et al., 2003; Gougoux et al., 2005), orientation and mobility programs assume that they can help develop enhanced skills in the remaining senses of blind subjects though rehabilitation. These rehabilitation programs rely on the concept of sensory substitution, which refers to the use of one sensory modality to supply information normally gathered from another sense (Bach-y-Rita et al., 1969). The use of the long-cane as an extension of the body (Serino et al., 2007), the development of refined tactile discrimination in order to fluently read Braille dots (Van Boven et al., 2000; Wong et al., 2011), or the use of the reverberation of sounds to locate obstacles and discriminate object size (Dufour et al., 2005; Rice, 1967; Rice and Feinstein, 1965; Strelow and Brabyn, 1982) are excellent examples of such abilities that appear “supranormal” for a naïve sighted person but which are mastered by blind individuals due to a combination of extensive training programs and neuroplastic mechanisms. The Braille reading system is probably the best example of these effects and massive involvement of the occipital cortex has been demonstrated in blind individuals when reading (Buchel, 1998; Burton et al., 2002; Sadato et al., 1996, 1998). Moreover, it has been shown that TMS over the occipital cortex of early-blind subjects disrupts Braille reading and even induces tactile sensations on the tip of the reading fingers in experienced users (Cohen et al., 1997; Kupers et al., 2007; Ptito et al., 2008a). Such findings demonstrate the functional involvement of the reorganized occipital cortex of blind subjects in Braille reading. This notion is even further supported by the reported case study of an expert blind Braille reader who lost her ability (Braille alexia) following an ischemic stroke which caused bilateral lesions to her occipital cortex (Hamilton et al., 2000).

Aside from these classical rehabilitative programs, researchers have also considered providing blind people with new sensory-motor interactions with their environment in order to lower the impact of visual deprivation. Bach-y-Rita can arguably be seen as a visionary in the field since he had the idea in 1969 to design the first sensory substitution devices for the blind by using the preserved sense of touch to supply information usually gathered from vision (Bach-y-Rita et al., 1969). Since this seminal work, and partly due to subsequent technological improvements, several laboratories have been engaged in developing and testing new sensory substitution prosthesis (Bach-y-Rita et al., 1998; Capelle et al., 1998; Cronly-Dillon et al., 1999; Kaczmarek et al., 1985; Meijer, 1992). All these systems are designed to make use of the residual intact senses, mainly audition or touch, to provide blind people with a sample of the visual world that has been coded into another modality via specific algorithms that can be learned through practice (Veraart et al., 2004). These systems have proven their efficiency for the recognition of quite complex two-dimensional shapes (Arno et al., 1999, 2001b), to localize objects (Proulx et al., 2008; Renier and De Volder, 2010) or to navigate in a "virtual" environment (Segond et al., 2005) and were found to massively and crossmodally recruit the occipital cortex of blind subjects (Amedi et al., 2007; De Volder et al., 1999; Kupers et al., 2010; Merabet et al., 2009; Poirier et al., 2007; Ptito et al., 2005). In our group, we investigated one such system, a prosthesis for substitution of vision by audition (PSVA) (Capelle et al., 1998). Early-blind participants were found to be more accurate when using the PSVA (Arno et al., 2001b) and their occipital cortex was more strongly activated than in the sighted in a pattern recognition task (Arno et al., 2001a). We also demonstrated that TMS interfered with the use of the PSVA when applied over the right dorsal extrastriate cortex of blind participants, probably due to the spatial cognitive components associated with the use of the prosthesis (Collignon et al., 2007). By contrast, TMS targeting the same cortical area had no effect on performance in sighted subjects (Fig. 2). As stated previously, we postulate that occipital regions are recruited in a compensatory crossmodal manner that may account for the superior abilities seen when using the prosthesis.

The sensory substitution devices, therefore, constitute interesting noninvasive techniques, in great part because their working principles follow the natural tendency of the brain to reorganize itself in favor of the remaining sensory modalities. That being said, their principal drawback is that they are currently mainly dedicated to fundamental research on crossmodal reorganization; in their present form, there are no realistic opportunities for their introduction into the blind community. This is generally related to the poor ergonomic quality of such human–machine interfaces. In addition, the coding scheme may appear quite difficult, and the visual information gathered by the camera is generally too complex to be entirely recorded in the substitutive modality without creating a "noisy" percept. Indeed, laboratory settings where such systems are tested are extremely impoverished in order to avoid an excessive sensory and cognitive load when using such devices. These experimental situations are usually composed of few target elements having a high figure-ground contrast (i.e., white shape on a black background). In the case of auditory devices, the technology appropriates a sensory channel that blind people already use in a skilful way for their daily-life activities. Modern tactile devices have mainly used the tongue to deliver the substituted information. This body part has been preferred because its sensitivity, spatial acuity, and discrimination abilities are better than other parts of the body (Bach-y-Rita et al., 1998). However, this choice probably adds aesthetic and hygienic problems, which may impact on the willingness of the blind community to introduce the system as a standard aid. Moreover, in order to become a real option for the blind in guiding their navigation, such systems should be complementary and thus provide new information to existing aids like the guide-dog and the white cane. Consequently, it appears evident that more consideration is needed in the design of more ergonometric sensory substitution systems for visual rehabilitation purposes. However, because sensory substitution greatly benefit from the crossmodal changes that occur in the brain of blind individuals they constitute a promising solution especially for early-blind individuals for whom surgical intervention is not possible, particularly if introduced in early infancy when the plasticity of the brain is the highest.

Neuroprostheses in the blind

Visual prosthetic implants aim to electrically stimulate the remaining functional parts of the previously fully developed visual system in order to restore some visual-like perception, mainly by inducing the perception of patterned spots of light called phosphenes (Merabet et al., 2005; Zrenner, 2002). Such implants would connect a digital camera to a signal processor that would convert visual information into patterned electrical signals (Fig. 1). Several approaches are currently under investigation and involve subretinal (Pardue et al., 2006a,b; Zrenner et al., 1999), epiretinal (Humayun et al., 2003; Rizzo et al., 2003a,b), optic nerve (Veraart et al., 1998, 2003), or occipital (Schiller and Tehovnik, 2008; Schmidt et al., 1996; Tehovnik et al., 2005) stimulation. Aside from the major issues of electrical safety and biocompatibility of the material (Veraart et al., 2004), knowledge about the selectivity and diffusivity of the stimulation is an essential problem in evaluating the behavioral effects of the stimulated area itself. As a result, researchers are currently trying to combine microstimulation of neural tissue with fMRI in order to provide the unique opportunity to visualize the networks underlying electrostimulation-induced perceptions (Logothetis et al., 2010).

In contrast to sensory substitution systems, the visual prostheses do not take advantage of the natural reorganization of the cortex of the blind since such invasive approaches attempt to stimulate the deficient sensory system directly. As such, these prostheses are mainly dedicated to blindness acquired at a later age since the development of the visual system and previous visual experience would be a prerequisite to trigger and interpret the visual percept induced by the stimulation of neural tissues. For example, one study demonstrated that the ability to elicit phosphenes with application of TMS over the occipital area is dramatically reduced in subjects with an early onset of visual deafferentation, especially in those without history of visual experience (Gothe et al., 2002). Indeed, the structural (deterioration of visual tracks) and functional (crossmodal plasticity) changes following early visual deprivation might hamper the reacquisition of the original visual function of a given structure via the prosthetic implant. There are reasons to believe, however, that such devices might work with late-blind individuals since far less alterations in the visual tracks and areas (Jiang et al., 2009; Noppeney et al., 2005; Park et al., 2009) and less-crossmodal recruitment of occipital regions by nonvisual stimuli (Burton et al., 2003; Cohen et al., 1999; Voss et al., 2008) have been observed in subjects who developed late-onset blindness. Moreover, studies of sustained blindfolding in sighted subjects suggest that the crossmodal recruitment of occipital cortex that appears after visual deprivation later in life may be more reversible after the reintroduction of vision (Merabet et al., 2008; Pascual-Leone et al., 2005). In fact, the mechanisms underlying crossmodal occipital recruitment in early- and late-blind individuals may differ considerably (Collignon et al., 2009b). Early deprivation could favor the maintenance of intermodal connections between cortical areas that are normally pruned in infancy, thus preventing the strengthening of typical visual cortical networks. In late blindness, however, these extrinsic connections would not escape the normal developmental synaptic pruning due to the presence of stabilizing visual input. Indeed, crossmodal recruitment of occipital regions observed in late blindness may reflect the strengthening, probably via Hebbian mechanisms[1] (Hebb, 1949), of existing intermodal connections also present in sighted subjects. In line with such an assumption, an elegant study combining PET-scan and TMS showed that the application of TMS over the primary somatosensory cortex induced significant activation of the primary visual cortex only in an early-blind group but not in late-blind or sighted subjects (Wittenberg et al., 2004). These results are consistent with the hypothesis of reinforced cortico-cortical connections between primary sensory cortices in early- but not in late-blind subjects (Collignon et al., 2009b).

These results place late-blind individuals as the candidate of choice for visual prosthetic implantation, especially because blindness acquired later in life may prevent the development of all the compensatory mechanisms observed in the early blind; this is also true because in the absence of enhanced abilities in the remaining senses, the late blind may encounter greater difficulty in coping with the handicap (Wan et al., 2010).

Rehabilitation in deafness

While crossmodal plasticity has been less extensively studied in deaf than in blind individuals, research in deaf subjects again leads to the conclusion that crossmodal reorganization occurs, such that cortical territories from the unused auditory modality can be recruited by other senses, in particular vision (Bavelier et al., 2006).

Sensory substitution in the deaf

These functional changes in the network dedicated to visual processing in the deaf appear to be accompanied by behavioral enhancements in visual attention and visual localization in peripheral visual space (Bavelier et al., 2000; Bosworth and Dobkins, 2002; Neville, 1990; Neville and Lawson, 1987a,b; Proksch and Bavelier, 2002; Rettenbach et al., 1999). Along with these low-level processing enhancements (i.e., devoid of phonetics), extensive visual-to-auditory reorganization has also been demonstrated with the presentation of visual stimuli activating the auditory cortex of deaf individuals. Indeed, activation of primary, secondary, and association auditory regions has been observed in early-deaf subjects during the observation of moving dot patterns (Armstrong et al., 2002; Finney et al., 2001) or moving sinusoidal luminance gratings (Finney et al., 2003). Crossmodal changes have also been related to cognitive functions. In normally hearing individuals, speech comprehension is achieved in a multisensory mode that combines auditory and visual (e.g., movement of the lips) speech information. To improve speech recognition or discrimination capabilities, this multisensory process is substituted to favor more exclusively the visual strategies in profoundly

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[1] "When the axon of cell A excites cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells so that A's efficiency as one of the cells firing B is increased."

deaf individuals. These communication strategies consist mainly of lipreading (Kaiser et al., 2003; Tyler et al., 1997) and sign language reading capabilities (Brozinsky and Bavelier, 2004; Neville et al., 1997; Proksch and Bavelier, 2002). Again, activity in traditionally considered auditory regions has been reported in the deaf during the observation of visual lip motion in the left planum temporale and during the visual presentation of sign language in the superior temporal gyrus and association auditory cortex (Hirano et al., 2000; MacSweeney et al., 2002; Nishimura et al., 1999; Petitto et al., 2000; Sadato et al., 2005). As in the literature on blind subjects, it is believed that the crossmodal plasticity observed in deaf subjects directly leads to a behavioral advantage and improved communication strategies (Bavelier et al., 2006). In those individuals who are trying to achieve some recovery of hearing function, however, such extensive reorganization may represent a challenge that may, in some case, hinder their rehabilitation.

Cochlear implant

While the visual takeover of the normally auditory cortices represents an impressive cerebral ability to adapt to changes in environment, it begs an important question relative to the recovery of the hearing function. Indeed, once responsive to a new input modality, can the auditory cortices respond to their original auditory input? This question bears special importance given that profound deafness can sometimes be reversed by auditory stimulation via a cochlear implant (CI) (Ponton et al., 1996). Put simply, the device replaces normal cochlear function by converting auditory signals into electrical impulses delivered to the auditory nerve (see Mens, 2007 for a more detailed description). Over the past decade, advances in engineering and surgical implantation techniques have begun to make the CI a standard part of the treatment for hearing loss (Clark, 2006; Fallon et al., 2008). Such success has allowed researchers to ascertain the consequences of crossmodal plasticity in the deaf population on the success rate of CIs.

In deaf individuals, activity in auditory cortical regions is increased following cochlear implantation (Lee et al., 2001; Naito et al., 1995; Wong et al., 1999), as soon as the implant is turned on (Giraud et al., 2001). In their longitudinal electrophysiological investigation, Pantev et al. (2006) showed that the cortical activity in auditory regions had normal component configurations and localizations, confirming that the input from the CI stimulation may be transmitted adequately to auditory structures as soon as the implant is made active in postlingually deaf individuals. The authors also showed that brain activity increased progressively over several months following implantation (Pantev et al., 2006).

However, the general outcome of the hearing proficiency following implantation is still highly unpredictable (Green et al., 2007). It has been argued that the level of crossmodal plasticity occurring as a consequence of early deprivation can predict the performance with an auditory prosthesis, with less reorganization leading to greater proficiency with the implant and vice versa (Giraud and Lee, 2007). For instance, it was shown that speech perception performance was positively associated with preoperative activity in frontoparietal networks and negatively associated with activity in occipito-temporal networks (Lee et al., 2005), even when factoring out the confounding effect of age of implantation (Lee et al., 2007). Indeed, the hindering effect of preoperative activity in temporal areas might be a sign that auditory areas may have been taken over by the visual modality, suggesting that crossmodal recruitment can serve as a predictor of the outcome of implantation. Similarly, a recent study compared cortical evoked potentials involved in the processing of visual stimuli between implanted (at least 1 year post-op) and hearing subjects (Doucet et al., 2006). After evaluation of speech perception abilities of the implanted subjects, they were subsequently divided into two groups based on their performance. The results showed that implanted individuals with broader and more anterior scalp distributions (i.e., showing signs of visual processing in the temporal cortices) in response to visual stimuli were those who performed more poorly in the speech perception task and vice versa.

In fact, several factors interact and influence crossmodal reorganization in deaf individuals, which in turn impacts auditory perception following implantation. The most influential factors are most likely the duration of deafness, the deafness onset, the time of implantation, and the communication strategy used before implantation.

(i) *Duration of deafness.* Straightforward correlations have been reported between postimplantation auditory-word recognition performance, cortical activity in response to auditory stimulation, and the duration of deafness. Indeed, it appears that implanted deaf individuals who had a longer period of deprivation show less cortical activity in response to auditory stimulation and poorer auditory performance (Lee et al., 2001). The results of this neuroimaging study suggest that a long duration of deafness might lead the higher visual cognitive functions to invade the underutilized areas of the auditory cortex. However, in a retrospective case review, Green et al. (2007) showed that the duration of deprivation only accounted for 9% of the variability in implant outcome, which is substantially less than first thought. In fact, Lee et al. (2001) had already suggested that other factors, such as the onset of deafness or the preimplantation communication strategies, could also have a dramatic impact on auditory perception following implantation.

(ii) *Onset of deafness.* It is in fact commonly acknowledged that postlingually deafened candidates perform better following cochlear implantation in adulthood in all auditory tasks compared to prelingually deaf individuals implanted in later life (Giraud et al., 2001). Supporting this behavioral evidence, imaging data also suggest more extensive plastic changes in the early-deafened individuals. Indeed, auditory stimuli have been shown to activate both the primary and secondary auditory cortices in postlingually deafened individuals, whereas they merely activate the primary auditory cortex in the prelingually deafened ones following implantation (Naito et al., 1997). Also illustrative of the importance of the age of onset of deafness, Sadato et al. (2004) demonstrated that both early- and late-onset deaf groups showed similar activation of the planum temporale in a visual sentence comprehension task whereas early-deaf subjects showed more prominent activation in the middle superior temporal sulcus (STS), a region thought to be important for the processing of vocalizations (Belin et al., 2000).

(iii) *Time of implantation.* Several studies have shown that if implanted before the age of 2, implanted children can acquire spoken language in a comparable time frame to normal hearing children (Hammes et al., 2002; Waltzman and Cohen, 1998). However, this time window for the recovery of auditory function following deprivation is generally limited to the first few years of life, with the chances of recovery rapidly decreasing afterward (Kral et al., 2005).

(iv) *Communication strategy before implantation.* Hirano et al. (2000) have suggested that crossmodal plasticity may be influenced by the communication strategies (i.e., familiarity with lipreading or sign language ability) used before implantation. Indeed, the authors showed that patients trained to communicate with visual modes of communication are more prone to extensive crossmodal changes compared to individuals trained in a more exclusive auditory mode (i.e., with conventional auditory amplification strategies based on the residual hearing). This last rehabilitation technique seems to prevent visual

> information from invading the relatively unused cortical regions (Hirano et al., 2000). However, it is worth noting here that the use of this technique in patients with very little or no residual hearing may have a dramatic impact on the communication capabilities of these persons.

Although difficult to assess, it is commonly acknowledged that these features (duration of deafness, onset of deafness, time of implantation, and communication strategy before implantation) might also interact in determining the degree to which crossmodal changes might occur, and so, in defining the level of proficiency reached by each participant following cochlear implantation.

Multisensory interactions in CI users

Since the world around us is made up of events that stimulate several senses simultaneously, it begs the question of how the regained auditory modality might interact with other sensory information during multisensory perception in CI users, especially with regard to speech perception.

The integration of congruent cues. Greater visual activity during speech recognition tasks has been reported in deaf individuals with a CI (Giraud et al., 2001). Some evidence even suggests that such visual activity increases progressively with the use of the auditory device (Desai et al., 2008). Indeed, Giraud et al. (2001) suggested that cochlear implantation might result in a mutual reinforcement between vision and hearing. In accordance with this belief of reciprocal enhancement, there seems to be a consensus surrounding the notion that accessing simultaneous visual and auditory information, when both cues are related, is beneficial in CI users (Bergeson and Pisoni, 2004; Geers, 2004; Kaiser et al., 2003; Moody-Antonio et al., 2005; Tyler et al., 1997). Some have even argued that CI users might be better at integrating congruent auditory and visual information when compared to normally hearing individuals (Rouger et al., 2007).

The fusion of incongruent cues. The ability to fuse incongruent audiovisual information has also been studied recently. Schorr et al. (2005) used McGurk-like stimuli, where incongruent lip movements can induce the misperception of spoken syllables (McGurk and MacDonald, 1976), to investigate the ability to integrate incongruent multisensory cues in children with a CI, as a function of experience with spoken language (Schorr et al., 2005). In children aged two and a half years or younger, the authors found normal-like results in the audiovisual task. In contrast, the fusion capability in children implanted later in life was significantly reduced. This is consistent with the notion that an extended duration of deafness might be detrimental to the use of a CI. In addition, typical McGurk-like effects have recently been showed in postlingually deafened candidates (Rouger et al., 2007; Tremblay et al., 2010), in accordance with the idea that crossmodal changes depend of the onset of sensory deprivation.

The segregation of incongruent cues. In our laboratory, we investigated the ability of CI users to segregate conflicting auditory and visual inputs (Champoux et al., 2009; see Fig. 4). An auditory speech recognition task was used in the presence of three different incongruent visual stimuli (color-shift, random-dot motion, and lip movement). We showed that the presentation of visual stimuli significantly impairs auditory-word recognition in nonproficient CI users (individuals with poor performance in the speech task without any concurrent visual presentation) while not affecting the performance of proficient CI users and normal hearing subjects. Moreover, this effect was not specific to the presence of linguistic cues (lip movement condition) but was also present during the random-dot motion stimuli. These results are consistent with the notion of extensive changes for the motion-processing dorsal pathway in the deaf (Armstrong et al., 2002) and with our idea that the level of plastic changes consequent to deafferentation might be a crucial factor for auditory rehabilitation through the use of a CI (Doucet et al., 2006). Most

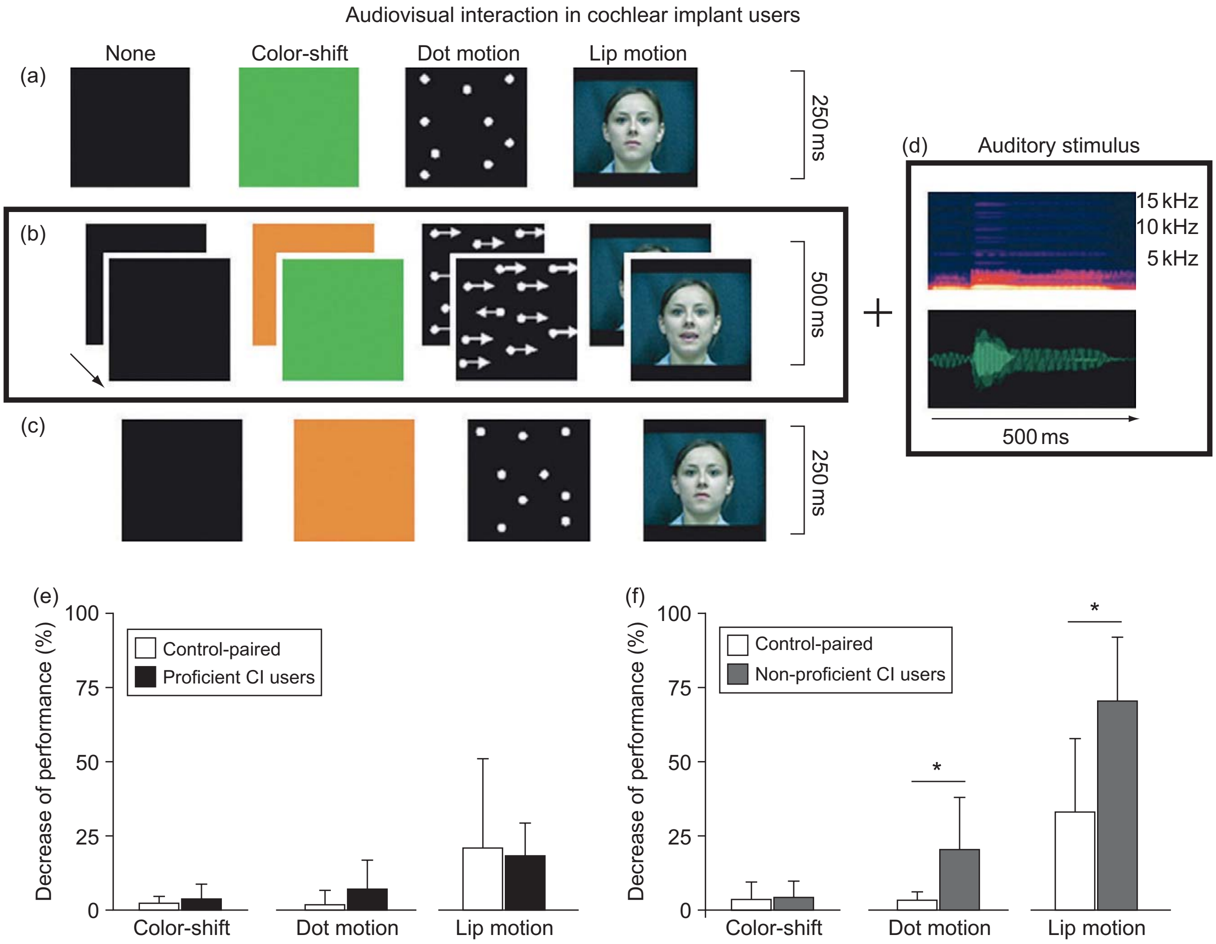

Fig. 4. Audiovisual interaction in CI users. In the top panel is the illustration of the experimental procedure. Each condition began (a) and ended (c) in a static neutral position. In all audiovisual conditions (b), auditory stimuli (d) were simultaneously presented with a visual stimulus change (color, movement, or video sequence). In the bottom panel are plotted the decreases in performance (%) for each audiovisual condition for both proficient (e) and nonproficient (f) CI users. Adapted with permission from Champoux et al. (2009).

important, these data suggest that although visual signals can facilitate speech perception in CI users in congruent audiovisual conditions, they might also hinder speech discrimination performance in some CI users when audiovisual inputs need to be segregated.

Conclusion

The immaturity of the human brain at birth is a valuable trait. Delaying the maturation and growth of brain circuits allows initial confrontations with the environment to shape the developing neural architecture in order to create the most adapted circuitry to cope with the external world (Meltzoff et al., 2009). Over the first few years of life, the brain grows rapidly, with each neuron having ~2500 synapses at birth and going to ~15,000 synapses per neuron after 2–3 years (Gopnik et al., 1999). As we age, experience will drive a process called synaptic pruning, which eliminates or strengthens connections based on the frequency of their use. Indeed, in the same way a gardener would prune a tree in order to give it a desired shape, ineffective connections are pruned in order to adapt the brain to its environment. Even if experience-dependent plasticity appears to be far more pronounced in children, synaptic connection efficiency changes based on experience are also present at more advanced ages.

As discussed at length in this chapter, sensory deprivation at early and, to a lesser extent, later ages will induce plastic changes in the structural and functional architecture of sensory cortices. Any severe sensory deafferentation precipitates unexpected sensory access to the affected cortex by the remaining senses. Such crossmodal plasticity is thought to be intrinsically linked to behavioral compensation mechanisms observed in sensory-deprived individuals (Amedi et al., 2003; Gougoux et al., 2005). Indeed, we have argued that rehabilitation based on sensory substitution systems, among which the two most well known are probably the Braille reading system for the blind and the sign language system for the deaf, spontaneously benefit from the natural tendency of the sensory-deprived brain to reorganize itself to optimize the processing of nonvisual inputs. In contrast, rehabilitation techniques aimed at restoring the deprived sense, like neuroprostheses, are based on an opposite principle of rehabilitation and rely on the integrity of the original function of sensory-deprived cortex. In both cases, we strongly believe that a better understanding of the mechanisms underlying experience-dependent crossmodal plasticity is a necessary prerequisite to properly develop new rehabilitation avenues. The task is obviously not an easy one because the full impact of sensory deprivation is always the result of a complex interaction between the specific etiology, the age of onset, the length of the deprivation, as well as the strategy that has been put in place in order to cope with the handicap. However, some lessons can be learned from the studies described above. For instance, if an invasive intervention for restoring the deprived sense is chosen in the case of congenital or early childhood deprivation, the “the earlier, the better” adage holds true based on the principle that it is easier to build than to rebuild, meaning that when neural circuitry has reached maturity, the possibility of rewiring it by the introduction of a novel input is more limited.

The rapid development of neuroimaging tools over the past few decades has allowed us to probe the brain's functioning and anatomy in a noninvasive manner and thus may serve as a standard procedure in order to evaluate the suitability of specific rehabilitation procedures in the future (Merabet et al., 2005). For example, the observation of massive crossmodal recruitment of the deafferented cortex could alert us that the restoration of the deprived function with new rehabilitative interventions may be more problematic than first thought (Gregory and Wallace, 1963). This is reminiscent of a quote from the philosopher Jean-Jacques Rousseau: “With progress, we know what we gain but not what we lose.” We again stress that a better basic comprehension of the underlying mechanisms of crossmodal plasticity will help us better understand and predict the outcome of sensory restoration based on increasingly complex biotechnologies.

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CHAPTER 15

Crossmodal plasticity in sensory loss

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Abstract: In this review, we describe crossmodal plasticity following sensory loss in three parts, with each section focusing on one sensory system. We summarize a wide range of studies showing that sensory loss may lead, depending of the affected sensory system, to functional changes in other, primarily not affected senses, which range from heightened to lowered abilities. In the first part, the effects of blindness on mainly audition and touch are described. The latest findings on brain reorganization in blindness are reported, with a particular emphasis on imaging studies illustrating how nonvisual inputs recruit the visually deafferented occipital cortex. The second part covers crossmodal processing in deafness, with a special focus on the effects of deafness on visual processing. In the last portion of this review, we present the effects that the loss of a chemical sense have on the sensitivity of the other chemical senses, that is, smell, taste, and trigeminal chemosensation. We outline how the convergence of the chemical senses to the same central processing areas may lead to the observed reduction in sensitivity of the primarily not affected senses. Altogether, the studies reviewed herein illustrate the fascinating plasticity of the brain when coping with sensory deprivation.

Keywords: blindness; deafness; anosmia; crossmodal plasticity.

Introduction

While most humans can rely on several sensory systems to appropriately interact with the environment, some individuals are born without one or more senses while others may lose one or more senses during their lifetime. Still, persons with sensory loss are often able to live independently and can achieve an impressive degree of accomplishments. In fact, there is a plethora of reports (though often anecdotic) of persons with a sensory loss demonstrating extraordinary abilities with one or several of their remaining senses, with the large number of successful blind musicians being the most prominent example. Going back several decades, Diderot, in his "Lettre

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sur les aveugles" (Diderot, 1749), reported the famous case of a blind mathematician who could recognize fake from real money coins just by touching them. Similarly, William James explained blind individuals' remarkable ability to navigate through their environment without colliding with obstacles as resulting from a form of "facial perception" (James, 1890). At first glance, such performance may seem somewhat "supranormal." However, over the past decades, we have acquired extensive knowledge on compensatory and adaptive changes in primarily unaffected senses occurring after sensory loss and have a better understanding as to how and why they occur.

The substantial literature on such compensatory mechanisms that are observed in the blind has often attributed these enhancements to some form of "crossmodal plasticity." Crossmodal plasticity generally refers to the adaptive reorganization of neurons to integrate the function of a new sensory modality following the loss of another. In fact, such crossmodal plasticity appears to at least partly explain many extraordinary abilities observed in persons with sensory loss.

In the following sections, we provide an overview of crossmodal plastic changes that follow sensory loss. We specifically focus on three major topics, that is, blindness, deafness, and loss of chemical senses and how these states affect the other sensory systems.

Blindness

Behavioral reorganization in blindness

It has long been debated whether blind individuals have perceptual advantages or disadvantages in processing information received via the intact modalities. The fundamental question has been whether the lack of vision disrupts the proper development of nonvisual skills or if, in contrast, blindness enables above-normal performance in the preserved modalities. Even if several studies support the notion that vision may be required to adequately calibrate other sensory modalities (Axelrod, 1959; Lewald, 2002; Zwiers et al., 2001), a substantial number of recent experiments have demonstrated that blind people are able to compensate for their lack of vision through efficient use of their remaining senses. In studies exploring sharpened nonvisual skills in blind people, spatial processing has been extensively investigated (Collignon et al., 2009c). This observation is probably due to the predominant role of vision in this cognitive ability and the importance for blind people to efficiently extract spatial information from the remaining senses in order to properly and safely navigate in their environment.

In a seminal study, Lessard et al. (1998) investigated the auditory localization abilities of early blind individuals under binaural and monaural listening conditions. They first demonstrated that blind subjects can localize binaurally presented sounds as well as sighted individuals, suggesting that vision is not necessary for the construction of a three-dimensional auditory map of space. Moreover, half of the blind subjects significantly outperformed the sighted ones when they had to localize the sounds with one ear occluded (monaural localization). This finding strongly suggests that some blind individuals can use subtle spatial cues (i.e., spectral cues) more efficiently than sighted controls. Another consistent finding is that blind individuals typically outperform sighted ones in binaural localization tasks when the sound sources are located in more peripheral positions as opposed to when they are presented centrally (Roder et al., 1999; Simon et al., 2002, Voss et al., 2004).

In recent experiments, we investigated the ability of blind participants to sharply focus their attention and quickly react to auditory or tactile spatial targets (Collignon and De Volder, 2009; Collignon et al., 2006). These studies demonstrated that blind subjects reacted faster than sighted controls to non visual spatial targets in selective and divided attention tasks further extending the view that blind individuals are able to compensate their lack of vision by developing capacities in their remaining senses that exceed those of sighted individuals.

The studies described above examined spatial hearing in near space, a region where auditory representations can be calibrated through sensory-motor feedback in blind subjects, such as touching the source of the sound or through the use of a cane, for example. In a later study, we evaluated sound localization in far space, a region of space where sensori-motor feedback could not contribute to the calibration of auditory spatial maps. We showed not only that blind individuals properly mapped their auditory distant space, but actually outperformed their sighted counterparts under specific conditions (Voss et al., 2004). Moreover, we examined whether late-onset blind subjects can manifest sensory compensation, since only a few studies have investigated this point. We thus carried out the task in late-blind subjects and showed that this group could also develop above-normal spatial abilities (Voss et al., 2004), as confirmed in another study (Fieger et al., 2006). However, a recent experiment showed that early but not late-blind participants showed better performance than that of sighted participants on a range of auditory perception tasks (Wan et al., 2010). Interestingly, in the above-mentioned studies, the superiority of early- and late-blind subjects was only present when sounds were presented in the periphery, where more subtle (e.g., spectral) auditory cues have to be exploited to efficiently resolve the task (Fieger et al., 2006; Roder et al., 1999; Simon et al., 2002; Voss et al., 2004). Similarly, when behavioral compensations are observed for the processing of visuospatial stimuli in deaf subjects, they also mainly concern inputs originating in the peripheral visual field (Bavelier et al., 2000; Neville and Lawson, 1987). These compensations observed specifically for peripheral stimuli may be related to the fact that differences in performance may emerge preferentially in conditions where the task is difficult (i.e., the sighted subjects are not performing at near perfect levels).

Recent studies have also pointed out that visual deprivation during early development results in important qualitative changes in nonvisual spatial perception (Eimer, 2004). Other experiments with blind people have suggested that the default localization of touch and proprioception in external space is in fact dependent on early visual experience (Hotting and Roder, 2009; Roder et al., 2004, 2008). For example, Roder et al. (2004) asked participants to judge the temporal order in which two tactile stimuli were delivered to their left and right hands. As expected, they found that temporal order judgments of sighted participants were less accurate with crossed than with uncrossed hands, which would result from the conflict between external and somatotopic spatial codes. By contrast, a congenitally blind group was completely unaffected by crossing the hands. Thus, it seems that sighted persons always use a visually defined reference frame to localize tactile events in external space (Kitazawa, 2002), and are impaired by conflicting external and somatotopic spatial information. By contrast, congenitally blind subjects do not use external spatial coordinates and thus remain unaffected by this conflict. Moreover, the fact that there is no need, in the case of early blindness, to make a correspondence between a nonvisual frame of reference and a visual one would contribute to a faster processing of nonvisual spatial information (Roder et al., 2004). This explanation was supported by an electroencephalographic study showing that the detection of deviant tactile stimuli at the hand induced event-related potentials that varied in crossed when compared to uncrossed postural conditions in sighted subjects, whereas changing the posture of the hand had no influence on the early blind subjects' brain activity (Roder et al., 2008). In a recent study, we extended this finding by demonstrating that the use of an anatomically anchored reference system for touch and proprioception in subjects visually deprived since birth impaired their ability to integrate audio-tactile information across postural changes (Collignon et al., 2009a). Altogether, these results thus demonstrate that the default remapping of touch/proprioception into external coordinates is acquired during early development as a consequence of visual input.

It is, however, important to note that compensatory mechanisms following visual deprivation could extend beyond the auditory spatial domain. For example, enhanced performance in blind participants was also observed in auditory tasks involving pitch (Gougoux et al., 2004; Wan et al., 2010), echoes (Rice and Feinstein, 1965; Rice et al., 1965), or verbal (Amedi et al., 2003) discrimination. The tactile modality has also been studied in blind individuals and is especially interesting given its importance in Braille reading. Compared to sighted controls, blind subjects showed superior abilities in some tactile tasks, such as a haptic angle discrimination task (Alary et al., 2008) and a texture discrimination task, but exhibited similar grating orientation thresholds and vibrotactile frequency discrimination thresholds as the sighted subjects (Alary et al., 2009). A carefully designed study demonstrated that when age and sex of the two groups were carefully matched, the average blind subject had the acuity of an average sighted person of the same gender but 23 years younger (Goldreich and Kanics, 2003). A recent study by Wong and collaborators (2011) observed this heightened tactile acuity in blind subjects to depend on braille readings skills suggesting the sensory compensation to be a direct consequence of the practice of the blind subjects with the braille system. With regard to the chemical senses, several studies suggest that blind subjects outperform sighted subjects in difficult higher-order olfactory tasks, such as free odor identification and odor labeling (Murphy and Cain, 1986; Rosenbluth et al., 2000; Wakefield et al., 2004), but not in simpler and more basic olfactory tasks such as odor threshold or odor discrimination (Diekmann et al., 1994; Schwenn et al., 2002; Smith et al., 1993; Wakefield et al., 2004).

Brain reorganization in blindness

Researchers have hypothesized for a long time that brain reorganization could underlie the changes in behavior observed in blind individuals. In particular, it was postulated that the functioning of visual structures changed dramatically following visual deprivation, and increasing evidence points now to the extensive colonization of the occipital cortex (OC)—traditionally considered as visual—by nonvisual inputs in blind individuals (Collignon et al., 2009c). In pioneering studies using positron emission tomography (PET), Veraart and collaborators demonstrated elevated metabolic activity in OC of early blind individuals at rest, which was at about the same level as in sighted subjects involved in a visual task (Veraart et al., 1990; Wanet-Defalque et al., 1988). Following the advent of more powerful neuroimaging techniques, a plethora of studies have demonstrated task-dependent activations of the OC during auditory (Kujala et al., 1997; Roder et al., 1999; Weeks et al., 2000), olfactory (Kupers et al., 2011) and tactile (Buchel et al., 1998; Burton et al., 2004; Gizewski et al., 2003) processing in early blind subjects.

It is, however, possible that these results simply reflect an association between stimulus presentation and cortical activation, without there being any functional involvement of occipital areas in nonvisual processing. Transcranial magnetic stimulation (TMS), which induces a focal and transient disruption of the proper functioning of a targeted area, has been used to demonstrate the necessity of the OC of the blind for Braille reading (Cohen et al., 1997; Kupers et al., 2007) and verbal (Amedi et al., 2004) processing. We also demonstrated that TMS applied over the right dorsal extrastriate cortex interfered with the use of a prosthesis substituting vision by audition and with the localization of sounds in blind subjects (Collignon et al., 2007). By contrast, TMS targeting the same cortical area had no effect on any auditory performance in sighted subjects and did not interfere with pitch and intensity discriminations in the blind. The demonstration that transient perturbation of OC with TMS selectively disrupted specific auditory processing in the blind compared to sighted subjects illustrates that this “visual” area is functionally linked to the neural network that underlies this auditory ability. We thus concluded that early visual deprivation leads to functional cerebral reorganization such that the right dorsal visual stream is recruited for the spatial processing of sounds, a result which is in clear agreement with previous neuroimaging studies on nonvisual space processing in this population (Arno et al., 2001; Poirier et al., 2006; Ricciardi et al., 2007; Vanlierde et al., 2003; Weeks et al., 2000). In a recent fMRI study we compared brain activity of congenitally blind and sighted participants processing either the spatial or the pitch properties of sounds carrying information in both domains (the same sounds were used in both tasks), using an adaptive procedure specifically designed to adjust for performance level. In addition to showing a substantial recruitment of the occipital cortex for sound processing in the blind, we also demonstrated that auditory-spatial processing mainly recruited regions of the dorsal occipital stream. Moreover, functional connectivity analyses revealed that these reorganized occipital regions are part of an extensive brain network including regions known to underlie audio-visual spatial abilities in sighted subjects (Collignon et al., 2011). It is worth noting that dorsal occipital regions have previously been shown to be involved in visuospatial processing in sighted subjects (Haxby et al., 1991). The similarity in the activation foci between visuospatial processing in the sighted and auditory spatial processing in the blind suggests that these areas may retain their functional and neuronal coding ability, which would enable them to process input from a different sensory modality. These results suggest that spatial processing in the blind maps onto specialized subregions of the OC known to be involved in the spatial processing of visual input in sighted people (Haxby et al., 1991). Interestingly, a recent study reported activation of a subregion of the lateral-occipital complex normally responsive to visual and tactile object-related processing when blind subjects extracted shape information from visual-to-auditory sensory substitution soundscapes (Amedi et al., 2007; see also Pietrini et al., 2004 for ventral activations in tactile shape recognition in the blind). In a similar manner, mental imagery of object shape recruited more ventral occipital areas (De Volder et al., 2001), whereas mental imagery of object position recruited more dorsal occipital regions (Vanlierde et al., 2003) in the blind. It thus appears that a functional dissociation between a ventral “what?” stream for the processing of object shape and a dorsal “where?” stream for the processing of space may also exist for nonvisual stimuli processed in the OC of blind subjects (Collignon et al., 2009c; Dormal and Collignon, 2011).

In order to further understand whether occipital activity levels leads to differences in behavioral performance, several studies correlated individual levels of occipital activity in blind participants with performance in nonvisual tasks. In a study conducted in early blind individuals using a speaker array that permitted pseudo-free-field presentations of sounds during PET scanning, Gougoux and collaborators (Gougoux et al., 2005) observed that during monaural sound localization (one ear plugged), the degree of activation of several foci in the striate and extrastriate cortex correlated with sound localization accuracy (Fig. 1). This result not only confirms an enhanced recruitment of occipital regions in auditory spatial processing in blind subjects but also suggests that such restructuring of the auditory circuit may underlie their superior abilities.

The above-mentioned studies undoubtedly demonstrate the presence of crossmodal plasticity in blind individuals, as cortical territories normally involved in visual processing are recruited for nonvisual functions. Still, questions remain about the nature of the mechanisms mediating such massive reorganizations. Top-down processing from associative cortices, feed-forward connections between primary sensory regions, or subcortical reorganizations are putative pathways that could explain how nonvisual inputs enter occipital areas of visually deprived subjects (Bavelier and Neville, 2002; Pascual-Leone et al., 2005). In order to further understand such

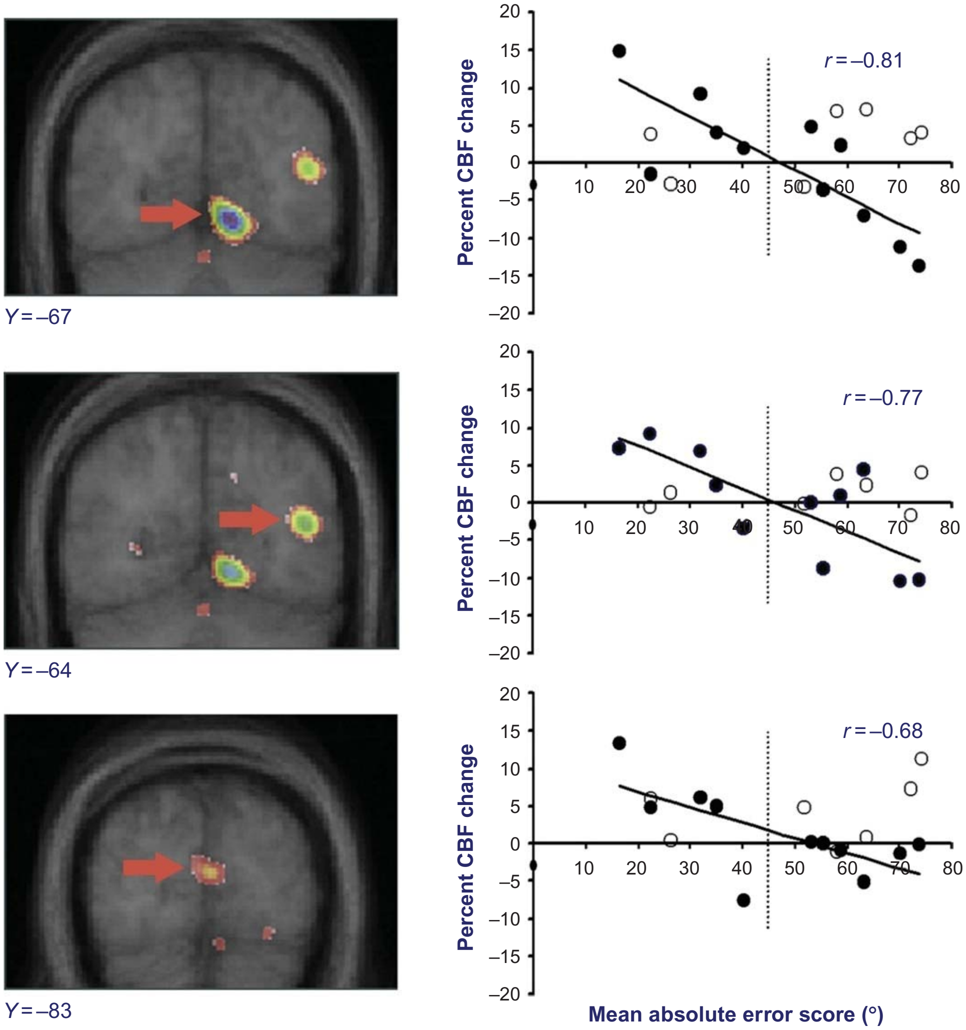

Fig. 1. Data of a correlational analysis between performance (mean absolute error) in a pointing task to monaurally presented sounds and cerebral blood flow (as measured by PET) in a group of blind subjects. The column of brain images illustrates regions in the ventral extrastriate (top), in the dorsal extrastriate (middle), and striate (bottom) cortices that correlate with monaural sound location performance in early blind subjects. Arrows point to the regions of interest. The scattergram shows the individual values extracted from each of these regions; closed circles indicate blind subjects; open circles indicate sighted controls; regression lines were fitted to data from blind subjects. Y coordinates refer to standardized stereotaxic space. With permission from Gougoux et al. (2005).

mechanisms, we used event-related TMS to disclose the time course of the spatial processing of sounds in the dorsolateral "where" stream of blind and sighted individuals (Collignon et al., 2008, 2009b). To address this issue, we induced a virtual lesion of either the right intraparietal sulcus (rIPS) or the right dorsal extrastriate occipital cortex (rOC) at different delays in blind and sighted subjects performing a sound lateralization task. We observed that TMS applied over rIPS 100–150 ms after sound onset disrupted the spatial processing of sound in sighted subjects but surprisingly had no influence on the task performance in blind individuals at any timing. In contrast, TMS applied over rOC 50 ms after sound onset disrupted the spatial processing of sounds in blind and in sighted participants. These studies suggest an early contribution of rOC in the spatial processing of sound in blind but also, to some extent, in sighted participants and also point to a lesser involvement of rIPS in this ability in blind participants. Given the very short latency of the disruptive effect of TMS applied over rOC on auditory spatial processing and considering the absence of rIPS contribution to this function in the blind, we suggested that sounds may reach the OC in blind subjects either via subcortical connections (Piche et al., 2007) or direct "feed-forward" afferent projections arising from the auditory cortex (Falchier et al., 2002). However, further studies are needed to better understand how these mechanisms combine together and the influence of age of onset of blindness on the installation of such mechanisms.

Deafness

The previous section provided evidence as to why the study of blind individuals constitutes an excellent model of the adaptability of the human brain, and how its plastic properties can in turn influence behavior and often improve sensory and cognitive abilities in these individuals. While crossmodal plasticity has been less extensively studied in the deaf, with the advent of small and efficient cochlear implants, it will become more and more important to understand crossmodal plasticity in deafness in order to comprehend the brain's ability to reverse the changes that followed sensory loss. Here, we will briefly review some of the main findings in the literature regarding crossmodal processing and plasticity in the deaf.

Behavioral reorganization in deafness

Deaf individuals must rely more heavily on their remaining senses to carry out their everyday activities. The fine input they receive from the outside world is essentially limited to the binocular visual field, whereas precious information obtained from the auditory system can capture precepts from all directions in space covering 360° along any axis. Given this loss of information, do deaf individuals compensate for their deficit via heightened visual abilities? In other words, do they "see better" than hearing individuals?

While some of the earlier studies produced very conflicting results, recent findings suggesting improved visual skills in the deaf tend to be more homogenous, in part because the individuals studied were themselves more homogenous as groups than in the past (see Bavelier et al., 2006). In recent studies, these groups were generally composed exclusively of deaf native signers, a subsample of the deaf population known to not suffer from comorbidity confounds related to language and communication deficits often associated with deafness (Meier, 1991). The heightened visual abilities in deaf native signers do not appear to be widespread, however, but rather seem limited to specific areas of visual cognition. For instance, basic sensory thresholds, such as contrast sensitivity (Finney and Dobkins, 2001), motion velocity (Brozinsky and Bavelier, 2004), motion sensitivity (Bosworth and Dobkins, 1999), brightness discrimination (Bross, 1979), and temporal resolution (Nava et al., 2008; Poizner and Tallal, 1987), do not appear to be enhanced in deaf individuals. Enhanced visual skills have rather revealed themselves in more complex tasks, where visual attention and/or processing of the peripheral visual field are manipulated (Bavelier et al., 2001; Dye et al., 2007; Loke and Song, 1991; Neville and Lawson, 1987; Neville et al., 1983; Proksch and Bavelier, 2002; Sladen et al., 2005; Stevens and Neville, 2006). It has thus been proposed that the loss of hearing leads to changes in higher-level attentional processing, with a redistribution of attentional resources to the periphery (see Bavelier et al., 2006). However, this hypothesis has been challenged by the results of a recent study showing faster reactivity to visual events in the deaf compared to hearing individuals, regardless of spatial location (both peripheral and central; Bottari et al., 2010). Moreover, while hearing subjects were substantially slower for peripheral targets (in relation to central ones), deaf subjects were equally efficient across all spatial locations, suggesting functional enhancements for the peripheral visual field that cannot be explained by different attentional gradients alone.

Brain reorganization in deafness

When considering the above-highlighted changes in visual processing, it naturally follows to ask whether we can observe an associated neuronal substrate to these improvements. There is now a substantial body of work looking at compensatory changes in the brain following early auditory deprivation; several studies have focused their attention on the middle temporal (MT) and middle superior temporal (MST) areas known to be not only involved in visual motion processing but also known to be heavily modulated by attentional processes. Consistent with the behavioral data, neuroimaging has revealed that differences in MT/MST between deaf and hearing individuals in response to motion stimuli only emerge when they are attended to in the peripheral field (Bavelier et al., 2001; Fine et al., 2005). However, one could argue that given the substantial role of motion in sign language, this difference could be due to the acquisition of this visuospatial language rather than to auditory deprivation *per se*. Bavelier et al. (2001) addressed this issue by including a second control group, one composed of hearing native signers, and showed that only early deafness and not early exposure to sign language lead to an increase of MT/MST activation.

Other notable areas of interest are the auditory cortices that are deprived of their normal input following deafness. Early animal studies showed that neurons in the primary auditory cortex could reorganize themselves to process visual information in the absence of auditory input (Pallas et al., 1990; Roe et al., 1992). More recently, several groups have shown BOLD changes in the auditory cortex of deaf individuals in response to visual motion (Finney and Dobkins, 2001; Finney et al., 2003; Sadato et al., 2004; Shibata, 2007). We have also recently investigated BOLD signal changes in both deaf and sighted individuals using global motion and forms defined by motion stimuli previously validated in healthy hearing individuals (see Vachon et al., 2009). Our preliminary results with deaf individuals are consistent with the current literature and show the involvement of higher-order auditory areas in the processing of the stimuli, most notably the right supratemporal gyrus (P. Vachon et al., unpublished). Similarly, several other groups have shown recruitment of the auditory cortex by visually presented sign language in deaf subjects (Nishimura et al., 1999; Petitto et al., 2000), and importantly, it was also shown that this crossmodal recruitment is not a by-product of signing, but rather of being auditorily deafferented (Fine et al., 2005).

There are several potential ways in which crossmodal reorganization could lead to the observed functional changes in the deaf. First, anatomical support for visual processing in the auditory cortex comes from animal studies showing direct connections between both primary cortices (Falchier et al., 2002; Rockland and Ojima, 2003). However, corresponding pathways have yet to be identified in humans. Other anatomical findings have focused on the auditory cortex and the superior temporal gyrus, where morphometry and diffusion tensor imaging studies have shown a reduction in white matter as well as reduced diffusion anisotropy within remaining white matter in deaf individuals compared to hearing individuals (Emmorey et al., 2003; Kim et al., 2009; Shibata, 2007). While finding no differences within the auditory cortices, Penhune et al. (2003) did reveal an increase in gray matter density within the left motor hand area, possibly related to more active use of the dominant hand in sign language.

Finally, an important point worth discussing is the impact of the age of onset of deafness on crossmodal processing and plasticity. While studies with blind individuals have clearly shown the age of acquisition of blindness to modulate the observed plastic changes, only one study, to our knowledge, has specifically attempted to address this important issue in the deaf (Sadato et al., 2004). Both early and late-onset deaf groups showed similar activation of the planum temporale, but differed with respect to the activation in the middle superior temporal sulcus (STS), which was more prominent in the early deaf. Given that the middle STS corresponds to the main voice sensitive area, the authors argued that exposure to voices had hindered the region's ability to ultimately process sign language in the late deaf.

Anosmia, ageusia, loss of trigeminal chemosensation

The chemical senses, that is, smell, taste, and the chemosensory trigeminal system, have obtained considerably less attention when compared to vision or audition. As opposed to physical senses, such as vision, audition, and touch, they allow us to experience our chemical environment via the interaction of substances with sensory organs, mostly, but not exclusively (Lindemann, 1996), via ligand–receptor interactions (Alimohammadi and Silver, 2000; Buck and Axel, 1991). Together, the three chemical senses constitute the main components of flavor perception (Small et al., 1997b). In the following paragraph, we will briefly outline the physiology of the chemical senses, in order to better understand the adaptive changes that occur when one of these senses is impaired or lost.

Gustation, better known as the sense of taste, allows us to perceive five distinct taste qualities. In addition to the four classical ones (bitterness, sourness, saltiness, and sweetness; Lindemann, 2000), a fifth taste quality, umami, allows for the perception of the savory aspects of protein-rich food (Chaudhari et al., 2000). Taste receptors are located mostly on the tongue, although elsewhere in the oral cavity as well. In contrast to the sense of taste, the sense of smell allows us to perceive a virtually unlimited number of different odors. Volatile substances reach the olfactory receptor neurons, which are located in the upper portions of the nasal cavity, either orthonasally via the nostrils (while sniffing) or retronasally via the nasopharynx (Burdach et al., 1984). The latter is of utmost importance when perceiving the olfactory components of flavors from the oral cavity (Frasnelli et al., 2005). The chemosensory trigeminal system, finally, allows for the perception of burning, cooling, stinging, and other sensations originating from chemical substances (Laska et al., 1997). Here, trigeminal stimuli interact with receptors and free nerve endings of the trigeminal nerve throughout the oral and the nasal cavities. Since the chemical senses are perceptually interconnected so tightly (Small et al., 1997b), some have put forward the idea of a unique flavor sense (Auvray and Spence, 2008). In fact, a major complaint of individuals who lose one of their chemical senses relates to their reduced ability to appreciate foods.

Behavioral reorganization in chemosensory loss

Olfactory dysfunctions can be categorized into quantitative dysfunctions (reduced sense of smell—hyposmia; loss of sense of smell—anosmia) and qualitative dysfunctions (altered perception of existing odors—parosmia; perception of inexistent odors—phantosmia; Leopold, 2002). These are relatively common conditions as up to 5% and 15% of the population are thought to exhibit anosmia and hyposmia, respectively (Bramerson et al., 2004; Landis and Hummel, 2006; Landis et al., 2004). Next to the physiological age related decline of olfactory function, the major etiologies of olfactory dysfunction are sinunasal diseases (polyps, chronic rhino-sinusitis), viral infections (persisting dysfunction after upper respiratory tract infection), traumatic brain injury, neurodegenerative diseases (Parkinson's and Alzheimer's disease, etc.), and others. Up to 1% of the anosmic individuals exhibit congenital anosmia (Kallmann's syndrome, isolated congenital anosmia; Temmel et al., 2002).

There are several reports on crossmodal effects of olfactory dysfunctions, mainly on other chemosensory systems. There is an established detrimental effect of olfactory dysfunction on trigeminal perception. When compared to controls, individuals with reduced olfactory function can perceive trigeminal stimuli only at higher concentrations (Frasnelli et al., 2010; Gudziol et al., 2001) and perceive suprathreshold stimuli as less intense (Frasnelli et al., 2007a). This reduced trigeminal sensitivity is, however, restricted to chemosensory trigeminal fibers (Frasnelli et al., 2006). A specific method to test trigeminal sensitivity is the odor lateralization task. In this test, subjects have to determine which of their two nostrils had been stimulated by an odorant in a monorhinal stimulation paradigm. We are only able to do so if the odorant also stimulates the trigeminal system (Kobal et al., 1989). Anosmic individuals have been shown to perform worse than healthy controls in the odor localization task (Hummel et al., 2003).

With regard to effects of olfactory dysfunction on taste perception, it is important to note that most of the individuals suffering from an olfactory dysfunction complain about a taste disturbance (Deems et al., 1991). This is because they mainly experience the reduced retronasal olfactory sensation during flavor perception (Deems et al., 1991). This phenomenon can be very impressive as some persons with olfactory dysfunction do not believe their olfactory system to be disturbed at all. However, when referring specifically to gustation, that is, the perception of the five taste qualities, effects of olfactory loss on gustation are more debated. Some studies have reported that, in analogy to trigeminal function, gustatory function is also reduced in individuals with olfactory dysfunction (Gudziol et al., 2007; Landis et al., 2010), while a recent report failed to confirm this finding (Stinton et al., 2010).

As opposed to the commonly observed olfactory dysfunctions, a loss of trigeminal chemosensation is a very rare condition. In a case report, olfactory function was assessed in a woman who suffered from unilateral loss of trigeminal function on the left side resulting from a meningeoma. She also exhibited reduced olfactory function, as assessed with a behavioral test and the measurement of olfactory event-related potentials, but only ipsilaterally to the affected side. Her gustatory function was, however, similar on both sides of the tongue (Husner et al., 2006).

While patients seeking help with a medical specialist often complain about a qualitatively altered taste perception (dysgeusia), a complete loss of gustatory sensation (ageusia) is a very rare condition (Deems et al., 1991). No reports of crossmodal effects of loss of gustatory function are known.

In summary, a dysfunction or loss of one of the chemical senses is a relatively common finding. Olfaction is by far the most affected sensory system. However, no compensatory mechanisms appear to take place, where another (chemical) sense becomes more sensitive. Rather, the loss of a chemical sense (which in most cases is the loss of olfactory function) is usually accompanied by a reduced sensitivity in the other chemical senses. This is in sharp contrast to blindness and deafness, as described above. A possible explanation for this may be the tight connection of the different chemical senses, an expression of which is the perception of flavor. As stated above, some researchers have in fact put forward the idea of a unique "flavor sense," consisting of inputs of all different contributing sensory channels (Auvray and Spence, 2008). The loss of one sense would therefore lead to a breakdown of the whole flavor system.

There is indeed also evidence from imaging studies for such a flavor sense. The chemical senses share important central processing areas. For example, it has been shown that the orbitofrontal cortex (OFC) and its different subdivisions are activated by olfactory (e.g., Gottfried and Zald, 2005; Savic and Gulyas, 2000; Zatorre et al., 1992), gustatory (e.g., Hummel et al., 2007; Small et al., 1997a, 2003; Veldhuizen et al., 2007), and trigeminal (e.g., Albrecht et al., 2010; Boyle et al., 2007b) stimulation. Similarly, the insula is activated following olfactory (e.g., Bengtsson et al., 2001; Cerf-Ducastel and Murphy, 2003; Savic and Gulyas, 2000), gustatory (e.g., Small et al., 1999, 2003; Veldhuizen et al., 2007), and trigeminal (e.g., Albrecht et al., 2010; Boyle et al., 2007b; Iannilli et al., 2008) stimulation. More importantly, combined stimuli consisting of mixtures of gustatory, olfactory, and/or trigeminal stimuli have been shown to activate "chemosensory" brain regions to a higher degree than their single constituents. In their seminal paper, Small and collaborators (1997b) showed that the administration of matching gustatory and olfactory stimuli together evoked different changes in cerebral blood flow in the insula, the opercula, and the OFC than the administration of both kinds of stimuli on their own. Similarly, using the trigeminal stimulus CO_2 together with the pure olfactory stimulus phenyl ethanol, we showed that a mixture of both activated chemosensory centers (left OFC) and integration areas (left STS, rIPS) to a higher degree than the mathematical sum of the single components (Boyle et al., 2007a). Cerf-Ducastel et al. (2001) finally showed that both gustatory and lingual trigeminal stimuli showed a striking overlap in their activation of the insula as well as the rolandic, frontal, and temporal opercula. Again, these studies support the existence of a cerebral network for flavor consisting mainly of the OFC as well as the insula and surrounding cortex.

Brain reorganization in chemosensory loss

Unfortunately, only few reports are available on changes in brain activations due to chemosensory loss. In accordance with the behavioral findings, anosmic and hyposmic individuals exhibit smaller trigeminal event-related potentials (Frasnelli et al., 2007a; Hummel et al., 1996). Similarly, following trigeminal stimulation with the trigeminal stimulus carbon dioxide, persons suffering from anosmia were described to exhibit smaller activations in "chemosensory" brain regions when compared to controls with a normal sense of smell. The anosmia group, however, exhibited larger responses in other regions in the frontal and temporal lobe, which usually are not involved in chemosensory perception (Iannilli et al., 2007).

However, there appears to be a dissociation between peripheral and central levels of trigeminal processing. When the negative mucosal potential (NMP)—a measure of peripheral responsiveness—is assessed, individuals with anosmia or hyposmia exhibit larger responses than healthy controls, which is in striking contrast to the findings in central responses (Frasnelli et al., 2007a,b). Thus, a model of mixed sensory adaptation/compensation in the interaction between the olfactory and the trigeminal system has been put forward. In normal functioning systems, peripheral trigeminal responsiveness is constantly inhibited; consequently, the periphery of the trigeminal system is functionally downregulated. On central levels, trigeminal input is increased by olfactory costimulation resulting in larger signals. In olfactory loss, however, a release of peripheral inhibition occurs, resulting in increased peripheral susceptibility. However, there is no olfactory costimulation to be integrated, resulting in relatively smaller central signals (Frasnelli et al., 2007a,b; Fig. 2).

These data therefore suggest the mechanisms in chemosensory loss to be different from other sensory systems. A first difference is that the chemical senses converge, at least partly, to the same processing areas. Second, sensory loss leads to a reduction in sensitivity in the other senses as well, in addition to the loss in the primarily affected sense. More studies are needed to confirm a causal connection between these consistent observations and to deepen our understanding of crossmodal effects of a loss in the chemical senses.

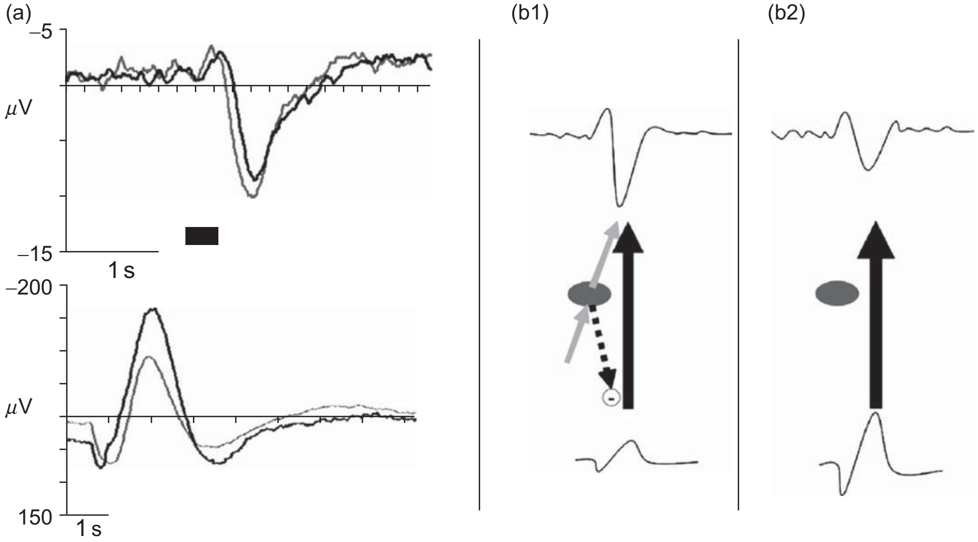

Fig. 2. Effects of loss of olfactory function on the trigeminal chemosensory system. (A) Grand means of trigeminal event-related potentials (central measure; top) and negative mucosal potential (NMP; peripheral measure; bottom) following stimuli of 60% (v/v) CO_2 in subjects with acquired anosmia (black) and controls (gray). The black horizontal bars indicate the onset and duration of the CO_2 stimulus. (B) Model of the interaction between olfactory (gray arrows) and trigeminal (black arrows) systems. (B1) Normal conditions. Peripheral responsiveness is decreased due to constant activation of intrabulbar trigeminal collaterals and consequent functional downregulation in the periphery of the trigeminal system. Functional integration of olfactory and trigeminal processes leads to augmented cortical signal. (B2) Olfactory loss. Increased NMP due to top downregulation; decreased event-related potential due to missing olfactory augmentation. With permission from Frasnelli et al. (2007b).

Conclusion

Loss of a sensory system has vast consequences for the affected person and his interactions with environment. Here, we have outlined how sensory loss leads to changes in primarily unaffected sensory systems. This crossmodal plasticity shows in a fascinating way how the brain copes with sensory deprivation. Only the proper understanding of the mechanisms of crossmodal plasticity will allow us to develop tools to help persons with sensory loss to better experience the world with the unaffected senses and thus enable them to live more independently.

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