

## Cross-modal plasticity for the spatial processing of sounds in visually deprived subjects

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**Abstract** Until only a few decades ago, researchers still considered sensory cortices to be fixed or “hardwired,” with specific cortical regions solely dedicated to the processing of selective sensory inputs. But recent evidences have shown that the brain can rewire itself, showing an impressive range of cross-modal plasticity. Visual deprivation is one of the rare human models that allow us to explore the role of experience-dependent plasticity of a sensory cortex deprived of its natural inputs. The objective of this paper is to describe recent results regarding the spatial processing of sounds in blind subjects. These studies suggest that blind individuals may demonstrate exceptional abilities in auditory spatial processing and that such enhanced performances may be intrinsically linked to the recruitment of occipital areas deprived of their normal visual inputs. Such results highlight the brain’s remarkable ability to rewire its components to compensate for the challenging neurological condition that is visual deprivation. Moreover, we shall dis-

cuss that such cross-modal recruitment may, to some extent, follow organizational principles similar to the functional topography of the region observed in the sighted. Even if such recruitment is especially present in individuals having lost their sight in early infancy, occipital regions also show impressive plastic properties when vision is lost at a later age. This observation will be related to recent results demonstrating that occipital regions play a more important role than previously expected in the spatial processing of sounds, even in sighted subjects. Putative physiological mechanisms underlying such cross-modal recruitment will then be discussed. All these results have important implications for understanding the role of visual experience in shaping the development of occipital regions and may guide the implementation of rehabilitative methods such as sensory substitution or neural implants.

**Keywords** Blindness · Plasticity · Cross-modal · Auditory · Spatial

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### Behavioral compensation for the spatial processing of sounds

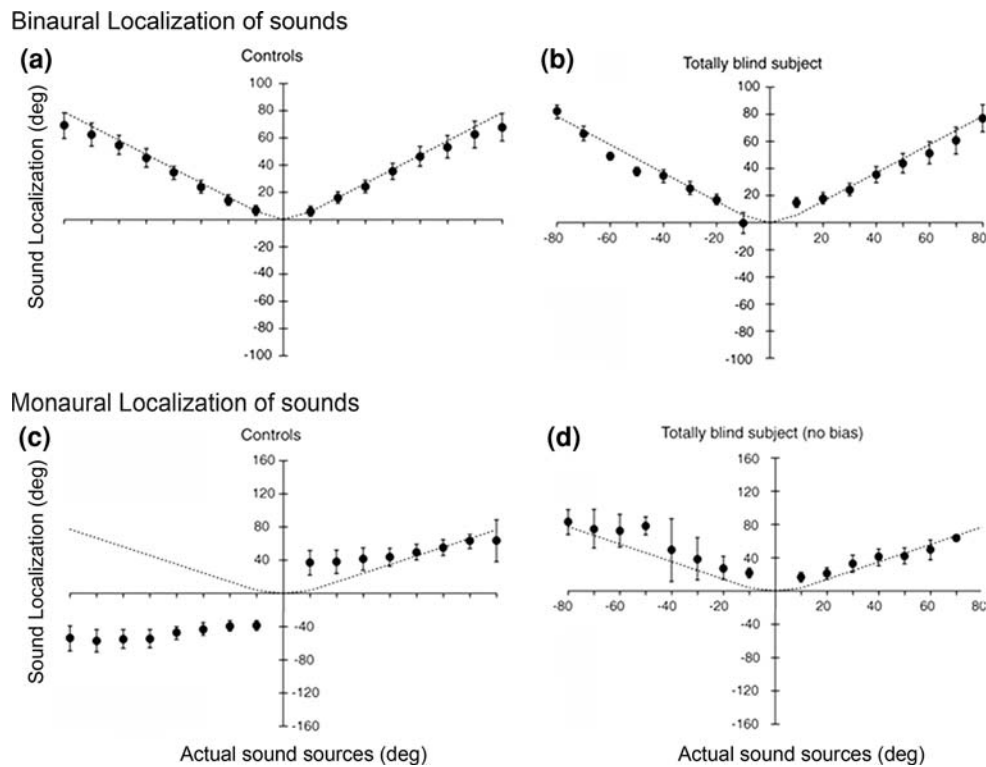
Evolution has provided several sensory modalities to humans in order to capture distinct forms of energies, opening different windows through which we can experience the world around us. The presence of these different sensory systems paves the way for considerable behavioral flexibility by allowing a system to supplement another following sensory deprivation (Stein and Meredith 1993). In this context, the notion that vision loss is partly offset by improved performance in the remaining modalities has become very popular and is often used to explain the development of some special abilities in blind people (Collignon et al. 2006).

The spatial processing of sounds has received considerable attention from researchers investigating putative sensory compensation resulting from blindness. This is certainly due to the fundamental role that this ability plays for blind people in navigating in their environment, which is a prerequisite to independent daily-life activities. This may also be related to the essential and dominant role that vision normally plays in the analysis of space in sighted subjects, which may lead to a greater susceptibility of reorganization for non-visual space processing in the case of visual deprivation. Indeed, it has long been debated whether blind individuals have perceptual advantages or disadvantages in processing auditory spatial information. The fundamental question has been whether the lack of vision disrupts the proper development of auditory spatial skills or if, on the contrary, blindness results in above-normal performance in the preserved modalities. It was first thought that visual deprivation might be detrimental to the development of spatial abilities in the remaining modalities since vision may be required to calibrate the other sensory systems (Axelrod 1959; Locke 1954; Rock and Halper 1969; Warren and Cleaves 1971). Even if a few studies gave some support to this notion (Lewald 2002a; Zwiers et al. 2001), a number of recent results, including the ones from our group, clearly demonstrate that vision is not essential for the calibration of auditory localization cues and that, under some circumstances, blind people show supra-normal abilities in auditory tasks.

In a seminal study, we investigated the auditory spatial localization abilities of early blind individuals under binaural and monaural listening conditions (Lessard et al. 1998). We 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 map of space (see Fig. 1a, b). Moreover, it was found that under monaural localization, performances of blind subjects can surpass those of sighted participants. In fact, in all sighted subjects and in half of the blind ones, the obstruction of one ear induced a strong localization bias towards the unobstructed ear (see Fig. 1c). However, half of the blind subjects were able to correctly localize sounds ipsilateral to the obstructed ear in almost 100% of the trials (Fig. 1d). This finding strongly suggests that some blind individuals can use subtle spatial cues more efficiently than sighted controls, particularly the spectral content of the sound, which is one of the principal remaining cues for localizing a source under a monaural listening condition (Van Wanrooij and Van Opstal 2004). In order to further test this hypothesis, we manipulated the spectral content of stimuli either by frequency filtering or by filling the cavities of the open ear pinna with acoustical paste and examined how performance under monaural testing was affected (Doucet et al. 2004). These manipulations induced a significant increase in

localization errors in blind subjects who previously performed well in the monaural task. This finding confirms the view that enhanced localization performance observed in some blind subjects may be related to a refined use of subtle auditory cues, such as the spectral content of sounds.

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. The question remained, however, whether normal or supra-normal abilities would also be observed for sounds originating in far space, where no such calibration is possible. In a recent experiment using distal (3–4 m) sound sources, we showed that blind individuals properly map auditory space beyond their peri-personal environment but also demonstrate supra-normal performance when subtle acoustic cues for target location and distance discrimination are needed to carry out the task (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). The latter result of enhanced auditory spatial abilities in subjects with late onset blindness was confirmed in another recent study (Fieger et al. 2006). It is worth noting that in both cases (Voss et al. 2004; Fieger et al. 2006) the superiority of late blind subjects was only present when sounds were presented in peripheral space straddling the inter-aural plane. These results precisely reproduce what was observed with early blind subjects, whose supra-normal performances were mainly observed in the periphery, where more subtle auditory cues (i.e., spectral) have to be exploited to efficiently resolve the task (Roder et al. 1999; Voss et al. 2004; Fieger et al. 2006; Simon et al. 2002). Interestingly, when behavioral compensations are observed for the processing of visuo-spatial stimuli in deaf subjects, they also mainly concern inputs originating in the peripheral visual-field (Neville and Lawson 1987; Bavelier et al. 2000). These compensations observed specifically for peripheral stimuli may be related to the fact that they occur preferentially in conditions where the task is difficult. If the processing at play is already extremely precise in sighted subjects, as during binaural processing of central stimuli, the condition generally leads to ceiling effects in both groups, and thus renders it difficult to observe differences between groups (Lessard et al. 1998; Voss et al. 2008; Roder et al. 1999). However, if the task requiring the processing of a central source is sufficiently difficult, one may also observe differences between the two groups. This hypothesis is partially supported by studies demonstrating superior spatial hearing abilities in blind subjects in complex tasks not relying on eccentricity, such as



**Fig. 1** Sound localization performances in the study of Lessard et al. (1998). **a** Sighted control subjects in the binaural condition of listening; **b** one representative early blind subject in the binaural condition of listening; **c** sighted control subjects in the monaural condition of listening; **d** one totally blind subject who correctly localized the sound with no directional bias. The *dashed lines* indicate the actual sound sources, whereas the dots refer to the perceived target locations with their respective standard deviations. Results are shown for one monaural

condition only (left ear-obstructed) as the other condition (right ear-obstructed) yielded identical results. The figure illustrates that in binaural condition of listening, early blind subjects localize sounds as well as sighted subjects. However, in monaural conditions, whereas all sighted subjects localized sounds presented on the side of the obstructed ear to the opposite side, half of the blind group did not show such a bias and thus showing supra-normal performance for spatial hearing. Adapted with permission from Lessard et al. (1998)

inter-aural time difference discrimination (Yabe and Kaga 2005) or the use of echo-location cues (Dufour et al. 2005; Rice et al. 1965; Rice and Feinstein 1965; Strelow and Brabyn 1982). Interestingly, in one of these echo-location studies, researchers demonstrated improved processing of echo information even in myopic (near-sighted) subjects (Despres et al. 2005; Dufour and Gerard 2000), suggesting that an increase in spatial acuity of the intact auditory system can not only occur when the visual system undergoes a total deprivation but also in the case of only partial deficits.

All these studies point to the fact that visually deprived listeners are fully able to use auditory cues for spatial hearing and that vision is not a mandatory prerequisite for the calibration of space. It seems likely that this calibration in blind subjects comes from experiencing changes in sound-localization cues arising from self-motion, such as turning of the head, the body, or walking in the environment toward the sound sources (Ashmead et al. 1989, 1998). However, the assumption that vision is not necessary for the adequate development of auditory spatial representation has also been challenged. Zwiers and collaborators (2001) and Lewald (2002a, b) found that blind subjects were inferior to

sighted ones in localizing sounds in the vertical plane (elevation). These findings led to the conclusion that visual feedback might be necessary to calibrate the vertical auditory space in front of the subject. Such results may be related to the work of Knudsen (1988) who demonstrated that the optic tectum of the barn owls raised without sight, but with normal hearing, develop auditory space maps with degraded precision and with aspects of topography that are abnormal (Knudsen 1988). These data put into question previous report of the representation of space and auditory hyperacuity in the blind. Since our study reporting supra-normal abilities have used constant sound intensity regardless of the location of the sound source (Lessard et al. 1998), Zwiers et al. (2001) argued that monaural intensity judgement may explain the better performance of blind individuals. Lewald (2002b) proposes an alternative interpretation by suggesting that the compensatory abilities that could be observed in some conditions in blind subjects may be attributable to the enhanced processing of proprioceptive information (i.e., body position) rather than superior auditory capabilities per se. Evidently, further research is necessary to disentangle which auditory localization cues are

better processed by the blind while others are less well calibrated in the absence of vision during development.

### Cross-modal processing of spatial sounds in the occipital cortex

The visual system has served as a model for studies dealing with neuronal development and plasticity for a long time. Since the seminal studies of Wiesel and Hubel on the development of ocular dominance, we know that alterations in visual experience can influence the normal development of the visual cortex (Wiesel and Hubel 1965, 1974). In fact, extensive neuroplastic changes have been demonstrated in intact sensory systems following different training regimens (Elbert et al. 2002; Pascual-Leone and Torres 1993; Sterr et al. 1998). It was further postulated that the functioning of visual structures would be influenced in a dramatic fashion following visual deprivation, and increasing evidence points to extensive cross-modal reorganizations in the deprived system.

Rauschecker and collaborators were among the first to clearly establish that early visual deprivation in cats leads to cross-modal compensation at both the behavioral and neurophysiological levels (Rauschecker 1995). As was the case for the human subjects described above, they found that visually deprived animals showed superior sound localization abilities (Rauschecker and Kniepert 1994; see also King and Parsons 1999). They also studied the physiological mechanisms underlying this superior performance. They recorded neurons of the anterior ectosylvian area, which is normally a multi-modal area, and found not only that the sub-area responsive to auditory stimuli was significantly expanded in the deprived animals (Rauschecker and Korte 1993) but also that the neurons were more sharply tuned to auditory spatial location (Korte and Rauschecker 1993). Similarly, in humans, a number of laboratories have attempted to examine whether occipital areas deprived of their normal input could adapt to process inputs from the remaining senses. In a pioneering study using positron emission tomography (PET), Veraart and collaborators demonstrated abnormally elevated metabolic activity in occipital areas of early blind individuals at rest, which was at about the same level as in sighted subjects involved in a constraining visual task (Veraart et al. 1990; Wanet-Defalque et al. 1988). A further study showed that this elevated metabolic activity was not due to gliosis, but indeed related to neural activity (De Volder et al. 1997). Since these preliminary works, a number of neuroimaging studies using various paradigms have now demonstrated task-dependent activations of the occipital cortex (OC) during tactile (Buchel 1998; Burton et al. 2002a; Pietrini et al. 2004; Sadato et al. 1996), auditory (Kujala et al. 1995; Leclerc et al. 2000; Roder et al. 1999; Weeks et al. 2000),

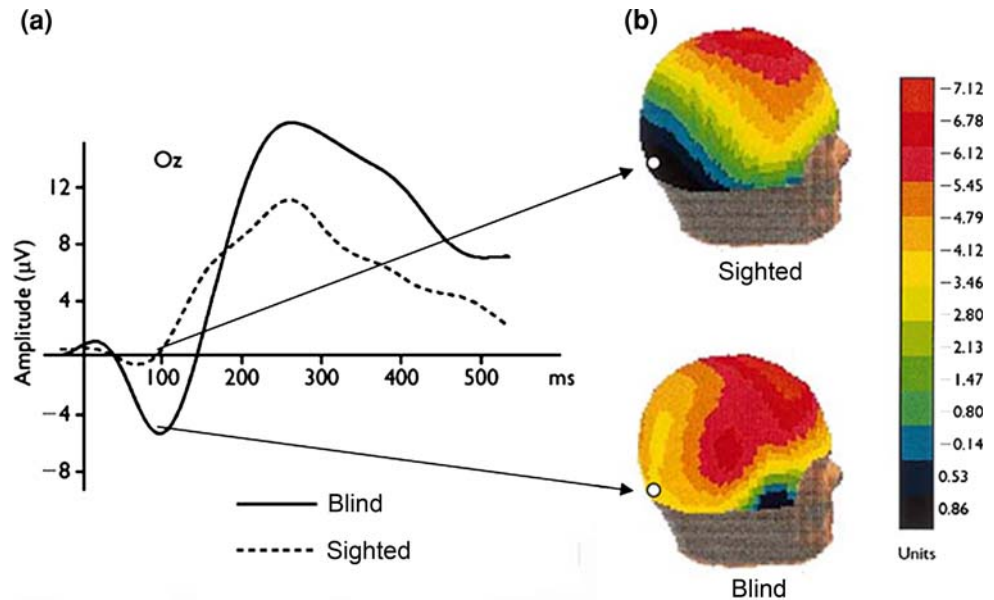
memory (Amedi et al. 2003; Roder et al. 2001; Roder and Rosler 2003) and language-related (Burton et al. 2002b; Roder et al. 2000) processing in early blind subjects.

Of great relevance for the arguments advanced in the present paper, Kujala et al. were among the first to show that event-related potentials (ERPs) triggered by a change in the locus of origin of a repetitive sound was more posteriorly distributed on the scalp in early blind subjects as compared to sighted controls (Kujala et al. 1992). This suggested that the blind might use occipital brain areas to a larger extent than sighted individuals in sound localization. In our laboratory, we also recorded auditory ERPs in blind participants during a free-field sound localization paradigm (Leclerc et al. 2000). The participants were the same congenitally blind subjects who had previously shown a supra-normal performance in the sound localization task of Lesnard et al. (1998). The results revealed that the N1 and the P3 components peaked at their usual positions in both groups but were also found to be robust over occipital regions in blind individuals only. The presence of a steeper N1 deflection over the occipital pole of blind persons (Fig. 2) suggests that their occipital cortex may be involved in early stages of auditory processing (at around 100 ms after sound presentation). To further explore the relevance of the N1 as a marker of cross-modal compensation, Leclerc et al. (2005) analyzed these data for EEG coherence in a wide range of frequency bands to determine whether blind individuals would show enhanced coherence reflecting increased connectivity between the central auditory and posterior cortical regions. It was found that oscillations in the theta, alpha, and beta frequency bands in fronto-central and occipital electrodes were linked during the task to a larger extent in early blind subjects compared to sighted controls. This finding can be seen as an indicator of enhanced connectivity between auditory and visual brain regions in the former group (Leclerc et al. 2005). Another previous ERP study also demonstrated a posterior distribution of the N1 during the spatial processing of laterally presented sounds in early blind subjects (Roder et al. 1999), supporting the hypothesis that early aspects of auditory processing are involved in the cross-modal recruitment of occipital regions in the blind.

As a complement to these electrophysiological techniques and their powerful temporal resolution, functional neuroimaging tools, like PET or functional magnetic resonance imaging (fMRI), provide much better spatial precision regarding the localization of cortical regions involved in cross-modal processing in the blind. Weeks and collaborators (Weeks et al. 2000) used PET and reported that blind but not sighted subjects strongly activated association areas in the right dorsal occipital cortex. This region was also highly activated in early blind subjects using a sensory substitution prosthesis translating visual information into



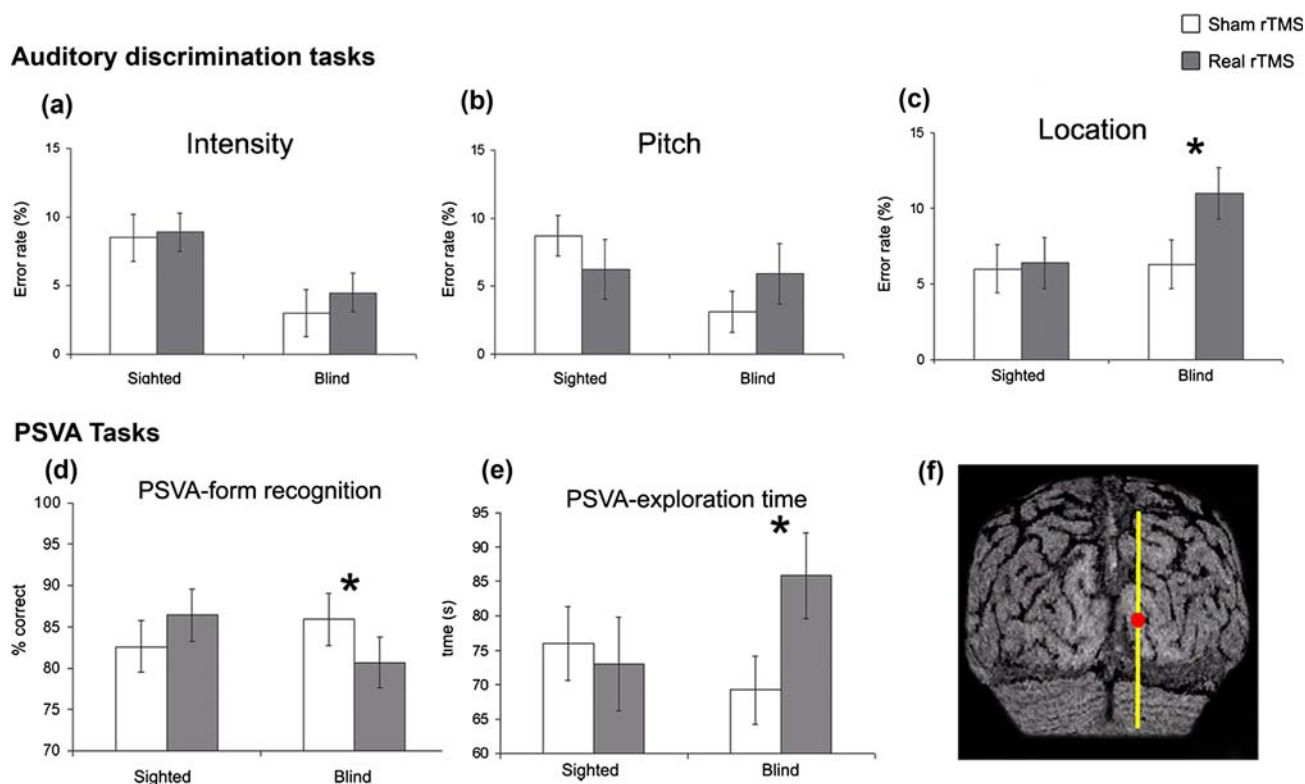
**Fig. 2** **a** Grand average ERPs to auditory stimuli recorded over Oz site in four blind subjects with supra-normal auditory localization abilities and in 12 sighted controls subjects. **b** Scalp distribution of the N1 with topographical maps of the mean voltage amplitudes ( $\mu\text{V}$ ) in the sighted (*top*) and blind (*bottom*) groups. The *rightmost bar* presents negative activation in graduated fashion. The figure illustrates that the early auditory component N1 is prominent in blind subjects but almost absent in sighted ones. Adapted with permissions from Leclerc et al. (2000)



sounds, in a task that mainly targeted auditory spatial processing (Arno et al. 2001a). It is worth noting that this region corresponds to regions that have previously been shown to be involved in visuo-spatial processing in sighted subjects (Haxby et al. 1991, 1994). The similarity in the foci of activation between visuo-spatial 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. Reinforcing this notion, some of us recently observed that auditory motion processing in congenitally blind individuals activated the brain network for auditory and visual motion processing classically observed in sighted subjects (Poirier et al. 2006b). Accordingly, brain areas previously considered to be involved in visual motion processing were specifically recruited in blind people by motion stimuli presented through the auditory modality. In the same vein, a recent fMRI study showed that region MT+/V5, that normally processes visual motion in the sighted, selectively responded to both moving sounds and moving visual stimuli in two individuals who had been blind since early childhood and whose vision had been partially recovered in adulthood (Saenz et al. 2008).

It is, on the other hand, possible that these results may simply reflect an association between stimulus presentation and cortical activation, without actually proving that occipital areas of the blind are functionally involved in non-visual processing. These co-activations may simply result from non-functionally related connections between these cortices. Transcranial magnetic stimulation (TMS), which induces a focal and transient disruption of the proper functioning of a targeted area, is therefore a useful approach to determine whether and to what extent a specific brain

region is critical for a particular behavior. This method has thus been used to prove the necessity of the occipital cortex 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 interfered with the use of a prosthesis substituting vision by audition (PSVA) and with the localization of sounds in blind subjects when applied over the right dorsal extrastriate cortex (Collignon et al. 2007), a region that was shown in PET to be highly activated by these tasks in the blind (Arno et al. 2001a; Weeks et al. 2000). 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 (see Fig. 3). We thus concluded that early visual deprivation leads to functional cerebral reorganization such that the right dorsal stream is recruited for the spatial processing of sounds, a result which is in clear agreement with previous neuroimaging studies on non-visual space processing in this population (Arno et al. 2001a; Poirier et al. 2006b; Saenz et al. 2008; Vanlierde et al. 2003). Here again, these results suggest that spatial hearing in the blind maps onto specialized sub-regions of the occipital cortex known to be involved in the spatial processing of visual input in sighted people. Interestingly, a recent study reported activation of a sub-region of the lateral-occipital complex (LOtv) 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, neuroimaging studies showed that mental imagery of object shape recruited more ventral occipital areas (De Volder et al. 2001), whereas mental imagery of object position



**Fig. 3** Influence of TMS over the occipital cortex on performance in three auditory discrimination tasks and in a pattern recognition task using PSVA. The first 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 (a), pitch (b) and spatial location (c). 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. The second part of the

figure displays the average percentage of correct pattern recognition (d) and the mean exploration time (e) taken to recognize patterns. 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 f displays the projection of the site of TMS application on a 3-D reconstruction of a blind subject's brain. This area corresponds to the right dorsal extrastriate occipital cortex (BA 18). Adapted with permissions from Collignon et al. (2007)

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 also exists for auditory stimuli treated in the occipital cortex of blind subjects.

The demonstration that transient perturbation of occipital area with TMS selectively disrupted auditory spatial processing in the blind compared to sighted subjects illustrates that this “visual” area is functionally involved in the neural network that underlies auditory ability (Collignon et al. 2007). This functional relevance of occipital recruitment thus explains how visual cortex activation may contribute to superior hearing abilities observed in blind people. We therefore examined whether occipital activity levels would predict differences in behavioral performances. We used a speaker array that permitted pseudo-free-field presentations of sounds during PET-scanning (Gougoux et al. 2005; Voss et al. 2006, 2008) (see Fig. 4a). In a first study conducted in early blind individuals, we 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 (Gougoux et al. 2005) (see Fig. 4b). Among these foci, we found that a region of the right dorsal extrastriate cortex highly correlated with performance, thus confirming the implication of this region in spatial hearing in early blind subjects (Collignon et al. 2007; Weeks et al. 2000). Moreover, we found a correlation between performance and the right lingual gyrus, a region known to form part of the ventral visual pathway, which is important for identifying visual objects, such as contour or texture (Kastner et al. 2000; Mendola et al. 1999), it is possible that the same area is used in the blind to process analogous features for auditory stimuli such as spectral contour, as elicited by the monaural localization task. This result not only confirms an enhanced recruitment of occipital region in auditory spatial processing in blind subjects but also suggests that such restructuring of the auditory circuit may underlie their superior abilities.

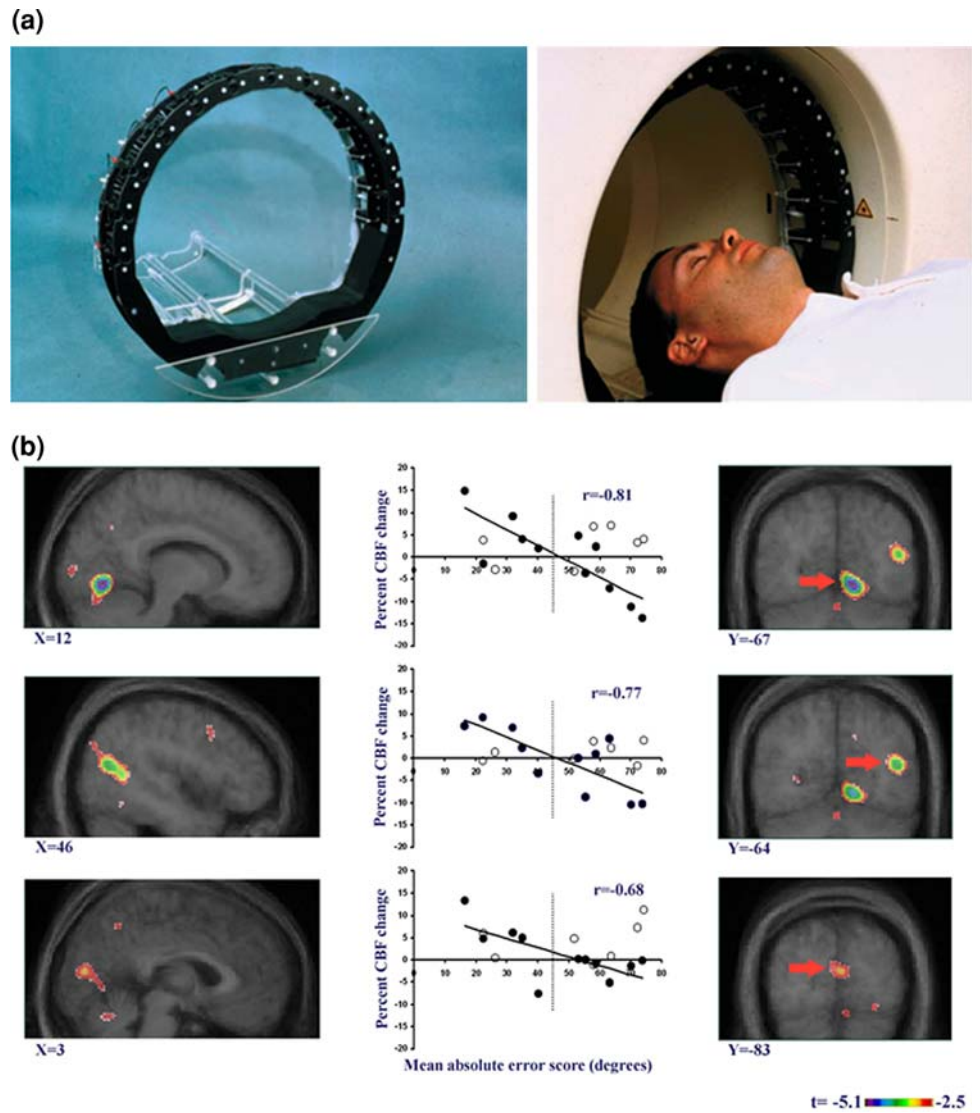
Although most researchers now agree that early blind individuals benefit from plastic changes involving the occipital cortex, the debate is still open as to whether or not the same is true for late blind ones.<sup>1</sup> Some studies have shown that plastic changes can occur in the latter (Buchel et al. 1998; Kujala et al. 1997), whereas others have suggested the existence of a critical period beyond which little or no cerebral reorganization is possible (Cohen et al. 1999; Sadato et al. 2002). We thus designed two PET studies using the same material described above (see Fig. 4a) to assess the effects of the age of onset of blindness on auditory localization. In two separate studies (Voss et al. 2006, 2008), we observed altered functioning of the deprived visual cortices of late blind subjects. In a first study using a sound localization task, we observed occipital activations in late blind subjects but not in sighted ones, without any behavioral advantage of late blind participants over sighted ones during both monaural and binaural conditions (Voss et al. 2006) (see Fig. 5). A second experiment (Voss et al. 2008) was designed to use a less demanding spatial auditory task while sharing similarities with the one used in our previous behavioral study (Voss et al. 2004). The similarities with the tasks, however, did not produce similar results. One subgroup of early blind subjects excelled in the monaural task, whereas the late blinds (along with a second group of early blind subjects) were no different than sighted individuals. While behavioral enhancements in the late blinds were not observed within the context of the current experiment, clear and novel plastic changes were on the other hand observed. Ventral visual areas of the occipito-temporal cortices were recruited during the monaural task. This contrasts with both what was observed in sighted individuals (no activation in visual areas) and in early blind participants with superior performance (widespread activa-

tion in striate and extrastriate cortices of the left hemisphere). Overall, the current results indicate that the late blind do show altered functioning of their deafferented visual cortices. However, the age of onset appears to play an important role regarding the extent of plasticity and in determining the specific regions recruited by auditory tasks. Similarly, the ERP paradigm used by Roder and collaborators (1999) to demonstrate a posterior distribution of the N1 component in the early blind was recently used to test late blind subjects (Fieger et al. 2006). It was found that the latter, like the former, demonstrate an enhanced capability for focusing auditory attention in the periphery. However, these supra-normal abilities seem to depend on different mechanisms, since the early blind demonstrate a more sharply tuned early attentional filtering, manifested in the N1 ERP component, whereas the late blind show reorganization in the later stages of target discrimination, indexed by the P3 (Fieger et al. 2006). Similarly, Munte and collaborators (2001) carried out the same ERP paradigm and found that experienced professional conductors displayed a sharper slope of the N1 gradient compared to pianists and non-musicians when spatially processing sounds in the periphery. However, in contrast to the results of early blind subjects (Roder et al. 1999), the scalp distribution of the N1 for conductors did not differ from that of other musicians. This distributional similarity of the two groups may be compared to the finding that the N1 distributions of sighted and late blind adults did not differ in the study of Fieger et al. (2006). Taken together, all these results reinforce the hypothesis that improved sound localization is mediated by different reorganization mechanisms in developing and adult brains. More generally, they suggest that the human brain retains a high level of plasticity into adulthood, though not necessarily identical to that of the young brain, making it possible for adaptive changes which can possibly partially compensate for the visual handicap throughout the lifetime. However, the exact mechanisms underlying these differential takeovers with respect to the age of onset of blindness remain unclear.

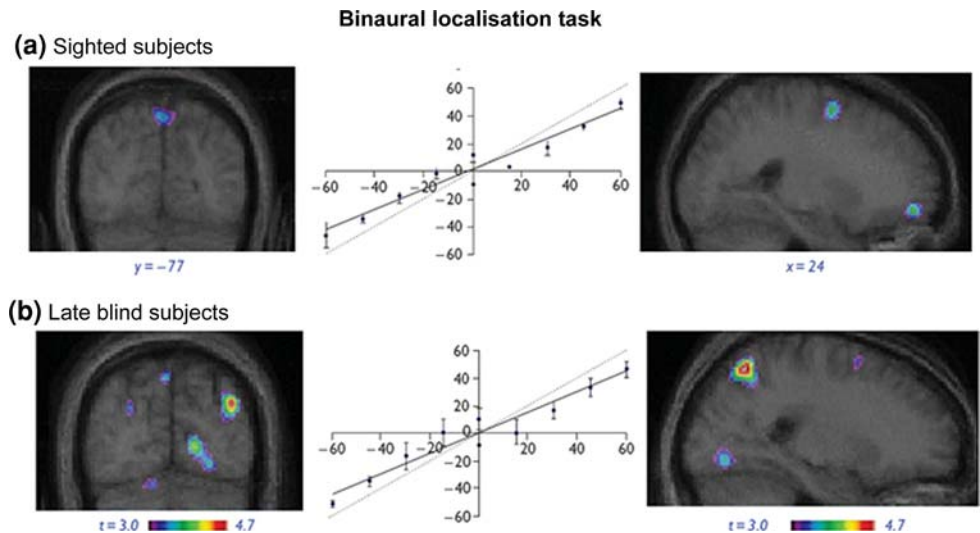
Support for the existence of behavioral and cerebral reorganization and behavioral compensation in the adult resulting from visual deprivation can also be seen in studies with sighted subjects blindfolded for short periods of time. For example Boroojerdi and collaborators (2000) elegantly showed using TMS and fMRI that short-term visual deprivation can induce substantial changes in the visual cortex's excitability (see also Pitskel et al. 2007). These results are compatible with the report of a significant increase in occipital responses to sounds in sighted subjects blindfolded for 5 days (Pascual-Leone et al. 2005). Other studies have also shown enhanced perceptual acuity in sighted subjects after a short period of visual deprivation (Facchini and Aglioti 2003; Kauffman et al. 2002). For example, simply

<sup>1</sup> In all the cited papers, the upper limit for total blindness acquisition in the early blind group vary between 2 and 10 years and the lower limit for total blindness acquisition for the late blind group vary from 9 to 16 years. Although some authors have suggested the existence of a precise critical period (i.e., 14 years) beyond which little or no behavioral compensation and no crossmodal recruitment of primary visual cortex is possible (Cohen et al. 1999; Sadato et al. 2002), we think that the determination of an exact age cut-off between “early” and “late” blind subject is a difficult exercise since it is influenced by the history of deficit acquisition. Indeed, it is quite rare that blind subjects suffer from sudden and total blindness. Usually, blind subjects experience progressive visual impairment prior to the onset of complete blindness. We thus think that functional criteria should also be added when separating early and late blind subjects. Indeed, it is fundamental that early blind subjects, if not totally blind at birth, never had functional vision during the first years of life which would have led to the normal development of the visual system. At the contrary, late blind subjects only represent a good model for the observation of plasticity in adult if they had an intact visual system before the apparition of visual deficits. For example, in our studies, all late blind subjects had been able to read print, travel by themselves, etc., to be included in our sample.

**Fig. 4** **a** Stimulus array used to present spatial sounds into the PET-scan, shown outside the scanner (*left*) and inside the scanner (*right*). **b** Data of the correlational analysis between performance (mean absolute error) in pointing task to monaurally presented sounds and CBF in a group of blind subjects. The two columns of brain images (left image series, sagittal sections; right image series, coronal sections) illustrate regions in the ventral extrastriate (**a**), in the dorsal extrastriate (**b**) and striate (**c**) cortices that correlate with monaural sound location performance in early blind subjects. The *red arrows* in the coronal slices indicate the focus selected for the respective sagittal slices. The *scattergram* shows the individual values extracted from each of these regions; *closed circles* indicate blind subjects; *open circles* indicate sighted controls. X and Y coordinates refer to standardized stereotaxic space. Adapted with permissions from Gougoux et al. (2005)



**Fig. 5** In the central portion of the figure are presented the behavioral results in a binaural localization task. The *dashed lines* indicate ideal performance and the *solid lines* represent the real localization performance. To the left and right of the graph are shown coronal and sagittal slices, respectively, of activated cortices in the binaural localization task. Despite identical behavioral performance, significant activation is observed in the visual cortex of the late-onset blind group (*Panel b*) but not in the sighted group (*panel a*)





blindfolding participants for 90 min resulted in a reversible improvement in accuracy during sound localization (Lewald 2007), similar, though smaller in magnitude, to the previously observed effect in blind subjects (Lewald 2002b). These findings indicate that short-term visual deprivation may reveal highly dynamic plastic interactions between visual and auditory systems. It thus follows that visual deprivation at a later age may influence existing neuronal circuits involved in processing auditory information in visual areas of normal subjects. In fact, a number of studies, both in animals and humans, have demonstrated the involvement of occipital cortex in the processing of spatial sounds. In adult cats, Morrell (1972) found that up to 41% of recorded neurons in extrastriate occipital areas could be modulated by both visual and auditory stimuli and that the receptive fields for both responses typically overlapped in space (Morrell 1972; see also Fishman and Michael 1973 for comparable results). Recent studies in humans have also brought forth evidence of an occipital activation (Allman and Meredith 2007; Giard and Peronnet 1999; Molholm et al. 2002; Poirier et al. 2005; Zimmer et al. 2004) or involvement (Lewald et al. 2004; Collignon et al. 2008) in auditory processing. Along these lines, recent anatomical studies have provided evidence for direct projections from the auditory cortex to the visual cortex in normal adult monkeys (Falchier et al. 2002; Rockland and Ojima 2003). These data suggest that sound localization cues may be processed in the occipital cortex of sighted subjects, putatively for multisensory purposes, such as the remapping of space across changes in posture to keep the external auditory and visual maps spatially aligned (Collignon et al. 2008). It is thus plausible that the processing of sounds in occipital cortex of sighted subjects increases in the absence of the dominant visual inputs, even after a short period of light deprivation. This mechanism of reinforcing pre-existing auditory afferents to occipital regions may also underlie at least in part the cross-modal plasticity in late blindness. As will be discussed below, this mechanism probably differs from the one at play in early blind subjects because of the absence of developmental and competitive visual inputs in the latter population.

### **Putative mechanisms and anatomical substrates underlying cross-modal plasticity**

While studies focusing on visual deprivation in animals and humans have undoubtedly demonstrated cross-modal recruitment of occipital regions, the mechanisms mediating such a reorganization are still elusive. We know from neuro-developmental studies in humans and primates that after a first period of exuberant proliferation of synapses, their numbers are gradually reduced (Bourgeois and Rakic

1993, 1996; Huttenlocher 1966; Huttenlocher and de Court 1987; Huttenlocher and Dabholkar 1997; Rakic et al. 1986). It was postulated that early synaptic contacts are largely random and it is the elimination of weaker, unused or redundant synapses that mediates the specification of functional and modular neuronal networks (Changeux et al. 1973; Changeux and Danchin 1976). The human occipital cortex undergoes such changes in synaptic density during its normal development (Huttenlocher and de Courten 1987). After a peak of development ending approximately at the age of 8 months, about 40% of the synapses of the visual cortex are gradually removed to achieve a stable synaptic density at approximately the age of 11 years (Huttenlocher and de Court 1987). Experiments with cats have shown that during the synaptic pruning phase, projections from the auditory cortex towards the occipital cortex are eliminated either through cell death or retraction of exuberant collaterals (Dehay et al. 1988; Innocenti and Clarke 1984; Innocenti et al. 1988; Kennedy et al. 1989), probably through Hebbian competition (synapses that participate in driving a postsynaptic cell strengthen, while synapses that fail to drive a postsynaptic cell weaken; Hebb 1949). However, in kittens deprived of vision at birth, these extrinsic connections to the occipital cortex seem to remain (Berman 1991; Yaka et al. 1999).

Even if auditory inputs to occipital regions are maintained in visually deprived subjects, is it possible that this area normally dedicated to visual inputs reverts to processing auditory stimuli in a functional way? Experiments on “rewired” animals may help answer the question. By making a series of brainstem lesions, it is possible to surgically re-route visual input toward primary somatosensory or auditory areas (Frost and Metin 1985; Roe et al. 1992, 1990; Sur et al. 1988). Such experiments not only demonstrated that these rewired regions share some structural and functional similarities with cells recorded in the visual cortex of normally raised animals, but they also mediate some visually-guided behavior (Frost et al. 2000; von Melchner et al. 2000). These data therefore suggest that primary cortical areas can change their functional specificity depending on which inputs they receive. It is thus possible that in the absence of competitive visual inputs during the synaptic stabilization phase, a significant number of auditory connections to the occipital cortex persist due to their activity, which could explain the massive and functional intervention of this region for the processing of sounds in blind subjects.

It is worth noting that besides changes in cortico-cortical connections from auditory to visual cortex, reorganization of subcortical pathways has also been proposed to drive auditory information in the visual cortex of the blind. Indeed, neuronal tracing studies in blind animals have revealed that the inferior colliculus (an auditory relay) may

project to thalamic structures normally occupied by the visual system (i.e., the lateral geniculate nucleus) (Chabot et al. 2008; Doron and Wollberg 1994; Izraeli et al. 2002; Piche et al. 2004, 2007). It is possible that a combination of both cortical and subcortical connectivity changes explain how the visually deprived occipital cortex receives auditory inputs in cases of early blindness (Karlen et al. 2006).

While the maintenance of normally transient intermodal connections may underlie, at least in part, the plastic changes observed with congenital loss of sight, this could not account for the cerebral reorganization in the case of late blindness since visual deprivation arises in a brain already wired for visual processing. Consequently, differences in the mechanisms mediating cross-modal plasticity in early and late blind subjects must explain the different patterns of occipital recruitment observed between these populations. For example, Veraart and collaborators (1990) showed, using PET-scan, that glucose utilization in the occipital cortex of early blind is elevated and comparable to the one of sighted subjects with eyes open. However, metabolic activity in late blind was significantly lower and comparable to sighted subjects with eyes closed. This was thought to reflect the persistence, in early blindness, of normally transient connections between auditory and visual centers. In late blindness, however, these extrinsic inputs would not escape the normal developmental synaptic pruning due to the presence of stabilizing visual input. In line with such an assumption, an elegant study combining PET-scan and TMS was carried out to probe the connection between primary somatosensory cortex (S1) and early visual cortex (V1) in early blind, late blind and sighted subjects (Wittenberg et al. 2004). They showed that the application of TMS over S1 induced significant activation of V1 only in the early blind group. These results are again consistent with the hypothesis of reinforced cortico-cortical connection in early- but not in late blind subjects, possibly due to a lack of synaptic pruning in early blindness.

However, even though it was assumed that cross-modal reorganization was absent in the late blind subjects due to the fact that it occurred after a “critical period” for plastic changes (Cohen et al. 1999), a number of studies do point to functional changes in how their occipital cortex processes non-visual inputs (Buchel et al. 1998; Burton et al. 2002a, b; Burton and McLaren 2006; Voss et al. 2006, 2008; see also Ghazanfar and Schroeder 2006 for a review). Moreover, these findings are supported by anatomical studies showing direct connections between auditory and visual cortical regions in adult sighted monkeys (Cappe and Barone 2005; Clavagnier et al. 2004; Falchier et al. 2002; Rockland and Ojima 2003), suggesting that some exuberant intermodal connections might not be pruned in early infancy, even if their functional purpose remains elusive. The absence of a systematic observation of such auditory

inputs in visual cortex when comparing blind to sighted subjects might be due to a masking effect of the dominant visual modality in this region. The cross-modal plasticity in the case of late blindness may in fact rely on the strengthening of normally present subtle auditory connections within the occipital visual areas following the loss of vision. This idea receives further support from studies using short-term visual deprivation where the speed at which changes in occipital activity occur is not commensurate with the creation of new connections (Pascual-Leone and Hamilton 2001; Pascual-Leone et al. 2005). In summary, these data suggest that some of the transient auditory connections might not be pruned but rather silenced because of their relatively low signal strength in a context of visual dominance, but may gain greater functional relevance when the visual cortex is challenged by visual deprivation.

Taken together, the results obtained in early and late blind subjects clearly demonstrate the presence of cross-modal plasticity, as cortical territories normally involved in visual processing are recruited for auditory functions. However, questions remain about the nature of the organization of the visual cortex in blind people. Does the recruited occipital cortex process different stimuli in a global manner or does it do so using some functional modularity similar to that observed in sighted subjects, with precise regions involved in specific cognitive functions? As pointed in the last section, such cortical reorganization does not occur randomly and formidable constraints are imposed on the way non-visual inputs are processed. An important characteristic of visual cortex in sighted people is domain specialization wherein specific functional activity has been found in anatomically identifiable regions (Grill-Spector and Malach 2004). If a specific domain dedicated to visual features, such as color or retinal disparity, is unlikely to function as such in blindness, it appears more probable that the functional specialization described for “object”-selective regions in the ventral occipito-temporal region—and for “position in space”-selective regions in the dorsal occipito-parietal region—may persist in blind people. As described above, certain results seem to indicate that the occipital cortex of blind people could be organized in a modular way similar to the one in sighted people. Adapting the neuronal “recycling” hypothesis (Dehaene and Cohen 2007) for cross-modal plasticity in the blind, we postulate that recruitments of occipital regions in the blind must find their “neuronal niche” into a set of circuits that are sufficiently close to the required function and sufficiently plastic as to reorient a significant fraction of their neural resources for this novel use. This is eloquently illustrated by the fact that moving sounds seem to preferentially recruit area MT+/V5 in blind subjects (Poirier et al. 2006a; Saenz et al. 2008), a region dedicated to the processing of visual movement in the sighted (Tootell et al. 1995). Similarly, Ricciardi and

collaborators (2007) have found that tactile flow perception activates MT+/V5 region in blind subjects. In summary, these results suggest that cross-modal recruitment of visually deprived occipital regions might depend on the computational contribution that a given region normally makes to visual inputs in sighted subjects.

It is however also important to note that verbal-memory tasks generate robust activations in the visual cortex of congenitally blind subjects, even in the absence of any sensory stimulation (Amedi et al. 2003). Accordingly, language task activate the same occipital regions in the blind, regardless of the input modality (Amedi et al. 2003; Burton et al., 2002a). These results confirm the presence of adaptation in the visual cortex and suggest that some recruitment of occipital region in blind subjects can be more likely explained in terms of particular cognitive operations rather than due to basic sensory processing. To associate these results to the present topic of the paper, we also consider that the take-over of dorsal occipital areas of the blinds for spatial processing is done regardless of the input modality. In fact, we know that the spatial processing of tactile stimuli (Ricciardi et al. 2007) or even spatial imagery without sensory stimulation recruits the same dorsal occipital areas in the blind (Vanlierde et al. 2003). Moreover, studies exploring language-related activation in the occipital cortex of the blind found a strong left lateralization in blind subjects (Amedi et al. 2003; Burton et al. 2002b), in agreement with the left lateralization of language processing in sighted subjects. Again, this result suggests that the recruitment of occipital regions in blind subjects may be constrained by the normal functional organization of the brain observed in sighted subjects. It is thus likely that visual cortex of the blinds may participate in linguistic (Amedi et al. 2003; Burton et al. 2002a, b; Roder et al. 2002), memory (Amedi 2003) or attentional (Stevens et al. 2007; Weaver et al. 2007) tasks as well as in more basic sensory processing. Whether these various functions are subserved by the same or segregated sets of neurons, as well as the neural mechanisms that mediate such plasticity (top-down processing from associative cortices or feed-forward connections between primary sensory cortices), are still however elusive and must be subjects for future research (Sathian 2005).

## Rehabilitation

When multifunctional visual rehabilitation is desired as a treatment for blindness, invasive and non-invasive solutions can be investigated. Invasive neuroprostheses rely on the integrity of visual cortex function for the generation of visual phosphenes through electrical stimulation. In contrast, in sensory substitution, information acquired with one

sensory modality is used to accomplish a task, which is normally subserved primarily by another sensory modality. In both cases, our understanding of neuroplastic changes in the blind, and in particular cross-modal plasticity, may guide the design of these methods which are currently under experimental consideration, but are based on opposing principles of rehabilitation.

The use of the plastic capacity of the brain is intuitively exploited in numerous rehabilitation programs aiming at promoting non-visual skills (i.e., echo-location). Since it was recently discovered that enrichment of the environment is an effective means of dramatically enhancing cross-modal plasticity associated with blindness (Piche et al. 2004), and because such reorganization mechanisms may underlie enhanced perceptual skills in the blind (Gougoux et al. 2005), orientation and mobility programs assume that they can trigger supra-normal skills in blind subjects through rehabilitation. Hence, an increasing number of laboratories are currently engaged in developing and testing new *sensory substitution prostheses* to attenuate the effects of visual deprivation (Amedi et al. 2007; Bach-y-Rita et al. 1969; Capelle et al. 1998; Collignon et al. 2007; Meijer 1992; Proulx et al. 2008; Poirier et al. 2007; Ptito et al. 2005; Renier et al. 2005). All these systems are designed to make use of the residual intact senses to provide blind people with coded information related to lost perception in a rehabilitation paradigm (Veraart et al. 2004). Our group has experimented one such system, namely a prosthesis for substitution of vision by audition (PSVA) (Capelle et al. 1998). This system has proven its efficiency in blind individuals for the recognition of quite complex 2-dimensional shapes (Arno et al. 1999). Moreover, the latter were found to be more accurate when using the PSVA (Arno et al. 2001b) and they recruited more the occipital cortex than the sighted when using the device in a pattern recognition task (Arno et al. 2001a; Collignon et al. 2007). As stated previously, we postulate that occipital regions are recruited in a compensatory cross-modal manner that may account for the superior abilities seen when using the prosthesis. The sensory substitution devices, therefore, constitute interesting new techniques that are non-invasive, and their working principles follow the natural tendency of the brain to reorganize itself through the other modalities. However, their principal drawbacks are that they are mainly dedicated to the fundamental study of cross-modal reorganization and do not yet constitute, in their present form, realistic opportunities for their introduction in the blind community. This is generally related to the poor ergonomic quality of such human-machine interface. The coding scheme is quite complex, inducing an excessive cognitive load when using the device outside of laboratory settings, 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. Moreover, these devices require the use of a remaining modality (most often audition) that blind people already dedicate in a skilful way for their daily-life activities. As a good example that sometimes “less is more”, and aside from the guide-dog, the only substitutive systems widely in use in the blind community is the Braille reading system and the white cane, both relying on a direct and “simple” coding scheme of information. Consequently, it appears evident that more consideration needs to be dedicated in the designing of more ergonomic sensory substitution systems for visual rehabilitation purposes.

*Visual prosthetic implants* (see Merabet et al. 2005 or Veraart et al. 2004 for reviews), contrary to sensory substitution systems 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, a study demonstrated that the ability to elicit phosphenes with application of TMS over the occipital area is dramatically reduced in subjects with a high degree of visual deafferentation, especially in those without history of visual experience (Gothe et al. 2002). Similarly, studies exploring visual skills in individuals who have recovered their sight after prolonged blindness (Fine et al. 2003; Gregory 1963) have shown that they presented marked visual deficiencies, especially when interpreting complex visual inputs or scenes, even if more basic visual functions appeared to be intact (i.e., motion detection). Indeed, the loss of visual abilities following early visual deprivation and consequent recruitment of occipital regions by non-visual inputs might in fact hinder the reacquisition of the original visual function via the prosthetic implant. For example, it was recently demonstrated that individuals who had recovered their sight still had robust responses to auditory stimulation in their visual cortex many years after sight-recovery (Saenz et al. 2008). It thus seems that the cross-modal rewiring that follows visual deprivation can be detrimental to the preservation of visual processing capabilities in the regions. A similar phenomenon can be observed in deaf individuals. It was demonstrated that because of cross-modal plasticity, resulting in visual activation of the auditory cortex, impaired the chances of a successful outcome to cochlear implantation (Doucet et al. 2006; Lee et al. 2001). These results suggest that pre-implantation neuroimaging assessments could guide implementation of neuroprostheses, such as cochlear or visual implants, by allowing the prediction of the outcome of such interven-

tions based on the extent to which the deprived cortex is now reorganized.

## Conclusion

Sensory deprivation often leads to reorganization of certain neural networks in order to develop the most effective possible adaptation in the remaining senses to cope with the deficit. In this review, we explored recent views on cross-modal plastic changes occurring in the occipital areas of blind subjects, with a special emphasis on the spatial processing of sounds. We have seen that the absence of visual inputs in the blind may lead to improved perceptual skills and dramatic changes in the functional properties of the occipital cortex. Moreover, it seems that these behavioral and cerebral adaptations are intrinsically linked. We also pointed out that the mechanisms underlying occipital recruitment could considerably differ in early and late blind. We postulated that early deprivation could favor the maintenance of normally pruned intermodal connections between cortices while late blindness may induce the strengthening of existing intermodal connections already present in sighted subjects. Moreover, we hypothesize that the recruitment of occipital regions by non-visual processing in blind subjects may be constrained by the normal functional specialization of this region. For example, the spatial processing of sounds seems to recruit more extensively the dorsal occipital stream in blind subjects, a region known to be involved in the processing of visuo-spatial information in the sighted (Haxby et al. 1991). We have now reached a point where it is no longer sufficient to simply show that the occipital cortex can be recruited by non-visual processing in the blind. Rather, the challenge we now face is to unravel how this process could be related to normal development in sighted subjects and to what extent occipital colonization by a novel modality in the blind follow organizational principles present in sighted subjects. Moreover, future studies will have to investigate how differences in cross-modal plasticity in congenitally and late blind people may be related to activation of the occipital cortex by non-visual input already present in sighted people. The aim should be to provide a unified framework to understand cross-modal processing in the occipital cortex of normal and visually deprived people, and reveal the mechanisms that may facilitate network dynamics in order to improve the functional outcome.

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