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REVIEW

REVISITING THE ADAPTIVE AND MALADAPTIVE EFFECTS OF CROSSMODAL PLASTICITY

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Abstract—One of the most striking demonstrations of experience-dependent plasticity comes from studies of sensory-deprived individuals (e.g., blind or deaf), showing that brain regions deprived of their natural inputs change their sensory tuning to support the processing of inputs coming from the spared senses. These mechanisms of crossmodal plasticity have been traditionally conceptualized as having a double-edged sword effect on behavior. On one side, crossmodal plasticity is conceived as adaptive for the development of enhanced behavioral skills in the remaining senses of early-deaf or blind individuals. On the other side, crossmodal plasticity raises crucial challenges for sensory restoration and is typically conceived as maladaptive since its presence may prevent optimal recovery in sensory-re-afferented individuals. In the present review we stress that this dichotomic vision is oversimplified and we emphasize that the notions of the unavoidable adaptive/maladaptive effects of crossmodal reorganization for sensory compensation/restoration may actually be misleading. For this purpose we critically review the findings from the blind and deaf literatures, highlighting the complementary nature of these two fields of research. The integrated framework we propose here has the potential to impact on the way rehabilitation programs for sensory recovery are carried out, with the promising prospect of eventually improving their final outcomes.

This article is part of a Special Issue entitled: Brain compensation. For good?

Key words: crossmodal plasticity, deafness, blindness, adaptive, maladaptive, behavior.

Contents

INTRODUCTION

One important translational objective of the research focusing on brain plasticity as a consequence of sensory loss (e.g., deafness or blindness) is to disclose the impact of the observed reorganizations on rehabilitation outcomes. During the last two decades, the recruitment of the deafferented sensory cortex by the spared sensory modalities has been repeatedly and consistently documented in blind and deaf adults (see for recent reviews Collignon et al., 2009a; Merabet and Pascual-Leone, 2010; Dormal and Collignon, 2011; Pavani and Röder, 2012; Voss and Zatorre, 2012a; Ricciardi et al., 2013). The noticeable phenomenon of experience-dependent plasticity is generally referred to

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Abbreviations: CIs, cochlear implants; DCM, dynamic causal modeling; fMRI, functional magnetic resonance imaging; LOC/LOtv, lateral occipital cortex; STS, superior temporal sulcus; TSM, Transcranial Magnetic Stimulation; V1, primary visual cortex; vMMN, visual Mismatch Negativity.

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as *crossmodal plasticity* (Bavelier and Neville, 2002). In describing the crucial relationship between the documented crossmodal reorganizations and behavioral outcomes, two main principles have been promoted, often conceptualizing this relationship as a double-edged sword effect (Merabet et al., 2005).

On one side, crossmodal plasticity is conceived as *adaptive* or *compensatory* for behavior. This conception stems from a series of studies that had successfully linked crossmodal recruitment to behavioral advantages documented in the remaining senses as a consequence of sensory loss (e.g., Amedi et al., 2003; Gougoux et al., 2005; Collignon et al., 2007; Karns et al., 2012; Voss et al., 2014; see for a review Voss et al., 2010).

On the other side, when it comes to sensory restoration outcomes (e.g., cochlear implants (CIs); interventions for bilateral cataract removal), crossmodal plasticity is ultimately considered as a negative predictor for efficient sensory recovery; in other words, it is conceived as *maladaptive* for optimal recovery of the previously missing sensory information. This notion mainly emerges from studies conducted with auditory-restored individuals, which documented a correlation between poor language recovery and persistent crossmodal activations elicited by visual or somatosensory inputs (e.g., Doucet et al., 2006; Buckley and Tobey, 2011; Rouger et al., 2012; Sandmann et al., 2012; Sharma et al., 2014; see for reviews Sharma et al., 2009; Collignon et al., 2011a; Kral and Sharma, 2012; Voss, 2013).

In the present review, we stress the limitations of adopting such an oversimplified dichotomic view of the double-edged sword effect of crossmodal plasticity. In particular we emphasize the possibility that the notion of its unavoidable maladaptive effect for sensory restoration outcomes may be misleading. To this final aim, we will review findings coming from two highly intertwined fields of research, namely, the literature on blindness and deafness. As will emerge in the following sections, the majority of the evidence documenting the *adaptive* effects of crossmodal plasticity in cases of sensory deprivation comes from studies carried out with early-blind people (i.e., individuals born with visual impairment and acquiring total blindness very early in life). Much less evidence is available from studies carried out with early bilateral deaf people (i.e., individuals born deaf and acquiring deafness before language acquisition). Evidence regarding the *maladaptive* effects of crossmodal plasticity for sensory restoration outcomes mainly arises from the literature on deafness and auditory restoration. In this domain, evidence coming from blindness and visual restoration is scarcer. Therefore, merging results acquired from these two distinct sensory-deprived populations is fundamental to extract general principles of crossmodal plasticity phenomena and to develop a common framework regarding the effects of crossmodal reorganization for behavior. In other words, such an integrated framework may provide general principles, which may hold true independently of the sensory modality that is absent (i.e., either vision or audition;

[Crossmodal Plasticity for Auditory Processing in the Blind]

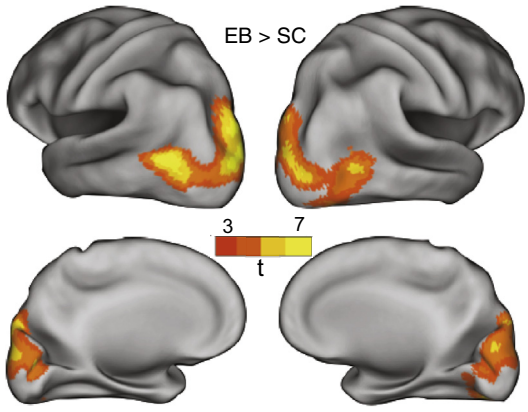

Fig. 1. Example of the massive activation elicited by sounds in the occipital cortex of blind adults. We created this figure using data from Collignon et al. (2011b): it depicts the activation obtained when contrasting early-blind individuals (EB) versus sighted controls (SC) when both groups of participants were exposed to auditory stimuli only.

Bavelier and Neville, 2002). We will first concisely review the evidence in favor of the adaptive effect of crossmodal plasticity in cases of sensory deprivation. We will then question the notion of the unavoidable maladaptive effects of crossmodal reorganization in cases of sensory restoration, starting with findings from auditory restoration and then moving to initial findings and considerations arising from research on sight restoration.

CROSS-MODAL PLASTICITY IN CASES OF SENSORY DEPRIVATION

Blindness

The occipital cortex of early-blind individuals is massively activated by non-visual inputs (e.g., Collignon et al., 2009a; see Fig. 1). In order to interpret the nature of these crossmodal activations, it was crucial to disambiguate whether they were the effect of a functional remapping of sensory/cognitive functions in the deprived regions, or the product of epiphenomenal or stochastic brain reorganization mechanisms. By now, several pieces of evidence strongly support the former account rather than the latter.

The first piece of evidence in favor of the 'functional remapping account' is supported by the reported case study of an expert blind Braille reader who developed Braille alexia following an ischemic stroke that damaged her occipital cortex bilaterally (Hamilton et al., 2000). Studies using Transcranial Magnetic Stimulation (TMS) further corroborated this possibility by showing that a transient disruption in the activity of occipital regions impairs the behavioral performance in non-visual tasks in early-blind participants, thus strongly supporting the notion of a causal role for the occipital cortex in mediating non-visual processing in early-blind individuals relative to sighted controls (e.g., Cohen et al., 1997; Amedi et al., 2004; Collignon et al., 2007, 2009b; Ricciardi et al., 2011). It has to be acknowledged, however, that there is evidence suggesting that TMS stimulation not only leads

to direct effects at the site of stimulation but also affects functionally connected areas that are distant from the stimulation site (Paus et al., 1997; Paus and Wolforth, 1998). In other words, it may be that the drop in behavioral performance that has been repeatedly reported in early-blind participants as a consequence of TMS pulses to the occipital cortex (e.g., Amedi et al., 2004; Collignon et al., 2007; Ricciardi et al., 2011) may be driven by the concomitant disruption of other regions, even distant from the site of stimulation but anyway involved in the same, broader functional network (see also Collignon et al., 2007 for further discussion of this topic). The fact that sighted participants did not show a similar drop in performance in any of the aforementioned TMS studies suggests that major functional reorganization involving the visually deprived occipital cortex has taken place in early-blind adults, and that this reorganization contributes to behavior.

Given that early-blind adults have been shown to outperform sighted controls in many behavioral tasks involving the remaining and intact sensory modalities (e.g., Lessard et al., 1998; Gougoux et al., 2004; Voss et al., 2004; Collignon et al., 2006; Collignon and De Volder, 2009; Wong et al., 2011; Lewald, 2013; see for reviews Pavani and Röder, 2012), a legitimate question was whether this crossmodal recruitment played a role in these enhanced behaviors. A series of studies documented a correlation between the strength of the occipital crossmodal recruitment and the level of behavioral enhancement in the remaining senses in early-blind adults (e.g., Amedi et al., 2003; Gougoux et al., 2005; Raz et al., 2005). In addition, in the early-blind population a link between structural reorganizations in the deprived sensory cortex and improved behavioral performance has been recently demonstrated (Voss and Zatorre, 2012b; Voss et al., 2014). For instance, Voss et al. (2014) showed a positive correlation between behavioral performance in a series of auditory and tactile tasks, and both the myelination content and the concentration of gray matter measured in the occipital cortices of early-blind adults (Voss et al., 2014).

More recently, the notion of a crossmodal functional remapping has been further strengthened by demonstrating that such remapping does not occur randomly, but typically maintains the same functional preference reported for those same cortical regions in the control population (functionally selective crossmodal plasticity; see Dormal and Collignon, 2011). For example, despite a reorientation in modality tuning, the visually deprived occipital cortex of early-blind individuals seems to maintain a division of computational labor somewhat similar to the one characterizing the sighted brain (Amedi et al., 2005; Collignon et al., 2009a; Dormal and Collignon, 2011; Reich et al., 2012; Ricciardi et al., 2013). Functionally selective crossmodal recruitment has been demonstrated for several cognitive functions, such as the ability to recognize the shape of an object involving the recruitment of the lateral occipital cortex (LOC/LOtv; audition: Amedi et al., 2007; touch: Pietrini et al., 2004; Amedi et al., 2010); the ability to categorize nonliving stimuli such as tools or houses involving the recruitment of the ventral/medial fusiform gyrus (audition: He et al., 2013; touch: Pietrini et al., 2004); the ability to localize the position of stimuli in space involving the recruitment of the right dorsal extrastriate visual cortex (Collignon et al., 2007, 2011b; Renier et al., 2010; see Fig. 2); the ability to perceive motion involving the recruitment of the visual motion area (hMT+/V5; audition: Poirier et al., 2006; Bedny et al., 2010; Wolbers et al., 2010; touch: Ricciardi et al., 2007); the ability to recognize letters and to read words involving the recruitment of the visual word form area (VWFA; audition: Striem-Amit et al., 2012; touch: Büchel et al., 1998; Reich et al., 2011); and the ability to recognize body-shapes involving the recruitment of the extrastriate body area (EBA; audition: Striem-Amit and Amedi, 2014).

To summarize, the evidence supporting the notion that crossmodal plasticity as a consequence of early-blindness is functionally relevant and adaptive for behavior mainly arises from three pieces of converging evidence: (1) crossmodal plasticity is causally related to behavior, as TMS on occipital regions disrupts non-visual functions (e.g., Collignon et al., 2007) and early-blind adults with occipital damage experienced impaired non-visual perception (Hamilton et al., 2000); (2) crossmodal plasticity putatively supports enhanced behavior, as a correlation was reported between crossmodal plasticity and enhanced non-visual performance both at a functional (e.g., Gougoux et al., 2005) and at a structural level (e.g., Voss et al., 2014); (3) crossmodal plasticity is functionally organized, as the recruitment of occipital regions nicely mirrors what we know of the functional organization of the visual system in the sighted population (e.g., Bedny et al., 2010; Reich et al., 2011; Collignon et al., 2011b). Combined, this robust body of evidence enhances the notion that crossmodal plasticity is a *functional* phenomenon and not a mere epiphenomenon.

Cross-modal plasticity in the blind: brain mechanisms involved. A fundamental question directly arising from these results concerns the mechanisms mediating the extensive cross-modal recruitment. Arising evidence suggests that in blind humans, cross-modal plasticity stems from the strengthening of pre-existing bottom-up sensory connections between the auditory thalamus, or primary auditory cortex, to primary visual cortex (V1) (e.g., Collignon et al., 2013; Voss, 2013, but see also Bedny et al., 2011). In cases of early-blindness, the strengthening of these connections between early sensory structures is hypothesized to take place during early infancy, when the brain is particularly plastic (e.g., Collignon et al., 2009a, 2013; Voss, 2013). While animal studies have repeatedly reported that under normal developmental conditions many of the synapses connecting early visual and auditory regions are pruned away due to redundancy or inactivity, evidence arising from studies carried out with kittens that were visually deprived at birth reported instead a preservation of these extrinsic connections to the occipital cortex (Berman, 1991; Yaka et al., 1999). In blind humans, the evidence available suggests that crossmodal plasticity in this population may be mainly mediated by cortico-cortical rather than subcortical con-

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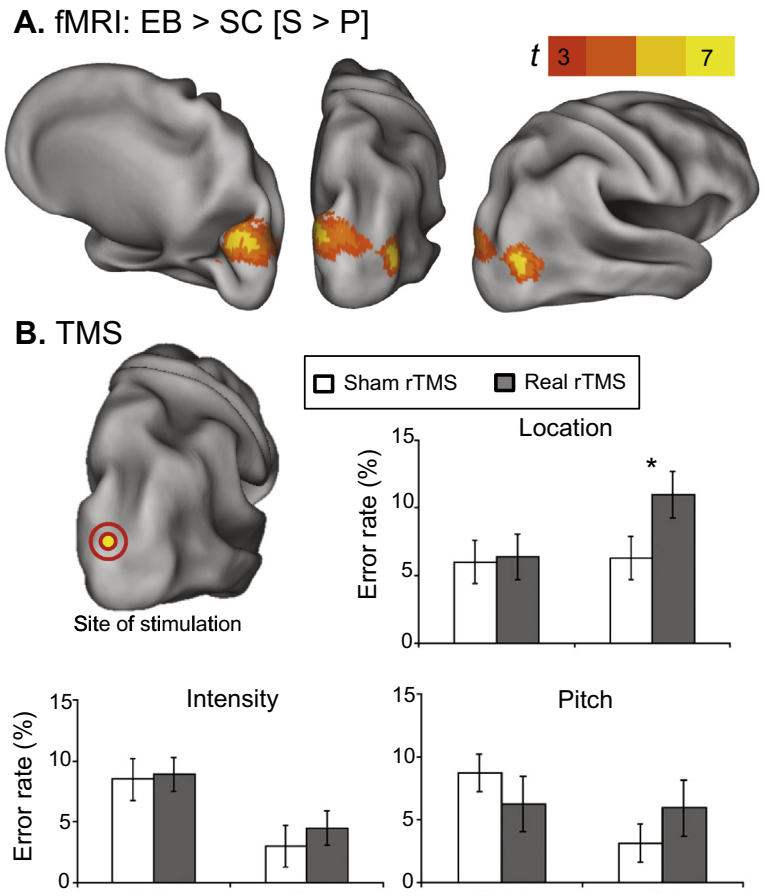

Fig. 2. Functionally selective crossmodal recruitment in early-blind adults: right dorsal extrastriate visual cortex. (A) Activations obtained when contrasting early-blind adults (EB) versus sighted controls (SC) when both groups of participants were processing spatial-related auditory information (S) versus pitch-related auditory information (P). Data from Collignon et al. (2011b). Figure modified with permission. (B) Effects of repetitive TMS (rTMS) delivered on the right dorsal extrastriate visual cortex of early-blind adults. rTMS interfered only with the sound-localization task. rTMS did not affect pitch and intensity discriminations. Data from Collignon et al. (2007). Figure modified with permission.

nections between auditory and visual structures (see also Collignon et al., 2013; Voss, 2013). For instance, neuroanatomical investigations reported a severe atrophy of the subcortical projections toward the occipital cortex in early-blind individuals (Noppeney et al., 2005; Shimony et al., 2006; Pan et al., 2007; Park et al., 2007; Ptito et al., 2008; see also Section 'The importance of early intervention' for further discussion on these results). Consequently, subcortical connections seem to be unlikely candidates for relaying auditory information to visually deafferented cortical areas (see also Voss, 2013).

Two recent studies used dynamic causal modeling (DCM) to investigate the effective connectivity between regions' underlying auditory activations in the V1 of early-blind individuals. The DCM approach is a powerful hypothesis-driven tool allowing us to infer the pattern of connections as well as the flow of information best explaining the functional magnetic resonance imaging (fMRI) activity observed (Friston et al., 2003). Klinge et al. (2010) first documented stronger cortico-cortical connections from the primary auditory cortex to the V1 in congenitally blind compared with sighted controls, whereas no significant differences were found concerning the thalamo-cortical connections (from medial geniculate nucleus to the V1) (Klinge et al., 2010). These results therefore suggest that plastic changes in cortico-cortical connectivity play a crucial role in relaying auditory information to the V1 of early-onset blind individuals. These results were further extended by Collignon et al. (2013) who demonstrated that auditory-driven activity in the V1 of the congenitally blind is better explained by direct connections with the primary auditory cortex (bottom-up) than by feedback inputs from parietal regions (feed-back) (Collignon et al., 2013).

Deafness

The evidence supporting the notion that crossmodal plasticity as a consequence of early-deafness is adaptive for behavioral outcomes is less straightforward compared to the literature on blindness (Pavani and Röder, 2012). As was similarly found in early-blind adults, several evidence documented enhanced behaviors in the remaining senses of early-deaf adults compared to hearing controls, particularly for visual behaviors (e.g., Proksch and Bavelier, 2002; Hauthal et al., 2013; Heimler and Pavani, 2014; Shiell et al., 2014; see for reviews Bavelier et al., 2006; Pavani and Röder, 2012).

In addition, in early bilateral deaf adults crossmodal recruitment of auditory regions has been reported for different visual inputs such as visual motion (Finney et al., 2001; Armstrong et al., 2002; Fine et al., 2005; Sadato et al., 2005; Vachon et al., 2013; Bottari et al., 2014), peripheral visual stimulations (Karns et al., 2012; Scott et al., 2014), non-sign-related hand-shapes (Cardin et al., 2013), as well as for the linguistic processing of sign language (e.g., Emmorey et al., 2003, 2007; Mayberry et al., 2011).

In contrast to the literature on blindness, evidence in favor of the causality of crossmodal recruitment in determining behavioral outcomes is scarcer. Nonetheless, initial evidence in this direction is starting to arise from the literature on early-deafness (e.g., Marshall et al., 2004; Bolognini et al., 2012). To the best of our knowledge there is only one study showing a correlation between crossmodal activations and behavioral outcomes in early-deaf adults (Karns et al., 2012). In particular, Karns et al. (2012) tested early-deaf and hearing participants in a double-flash somatosensory illusion while registering fMRI activity. In this illusion, a single flash of light paired with two or more task-irrelevant somatosensory stimuli is wrongly perceived as multiple flashes (Violentyev et al., 2005). Besides reporting a recruitment of primary and secondary auditory regions when processing visual stimuli, the study failed to report any correlation between the observed crossmodal recruitment and the performance to the task participants had undertaken (Karns et al., 2012). Yet, when taking into consideration the crossmodal recruitment elicited by the somatosensory modality, results revealed a positive correlation between the strength of the auditory recruitment and the strength of the somatosensory double-flash illusion in deaf participants (Karns et al., 2012), thus providing first evidence suggesting the correlation between crossmodal recruitment and behavior also in deaf adults.

Findings documenting a functional-selective recruitment of auditory regions in cases of early-deafness are also scarcer when compared to literature on blindness. In early-deaf adults, functionally selective crossmodal plasticity has been reported for the processing of sign language, which has been shown to recruit the temporo-frontal network typically associated with spoken language processing (e.g., MacSweeney et al., 2002; Emmorey et al., 2007; Mayberry et al., 2011; see MacSweeney et al., 2008 for a review; see Fig. 3A). In particular, several studies documented that in deaf native signers the left superior temporal gyrus and sulcus together with the inferior temporal gyrus were activated during comprehension tasks, analogously to the activations elicited by spoken-language comprehension tasks (e.g., Neville et al., 1998; Petitto et al., 2000; MacSweeney et al., 2002; Sakai et al., 2005; see Fig. 3A). Although less relevant in this context given the emphasis on auditory crossmodal recruitment, similar activations between sign and spoken languages emerged for both covert and overt production tasks, where deaf native signers activated the left inferior frontal gyrus, comparably to hearing speakers (e.g., McGuire et al., 1997; Petitto et al., 2000; Corina et al., 2003; Emmorey et al., 2003; San José-Robertson et al., 2004). Furthermore, lesion studies reported severe language-processing impairment (i.e., aphasia) as a consequence of selective damage to left fronto-temporal areas, which crucially were not present in case of damage to homologous cortical regions in the right hemisphere (e.g., Hickok et al., 1996; Marshall et al., 2004; Atkinson et al., 2005). These

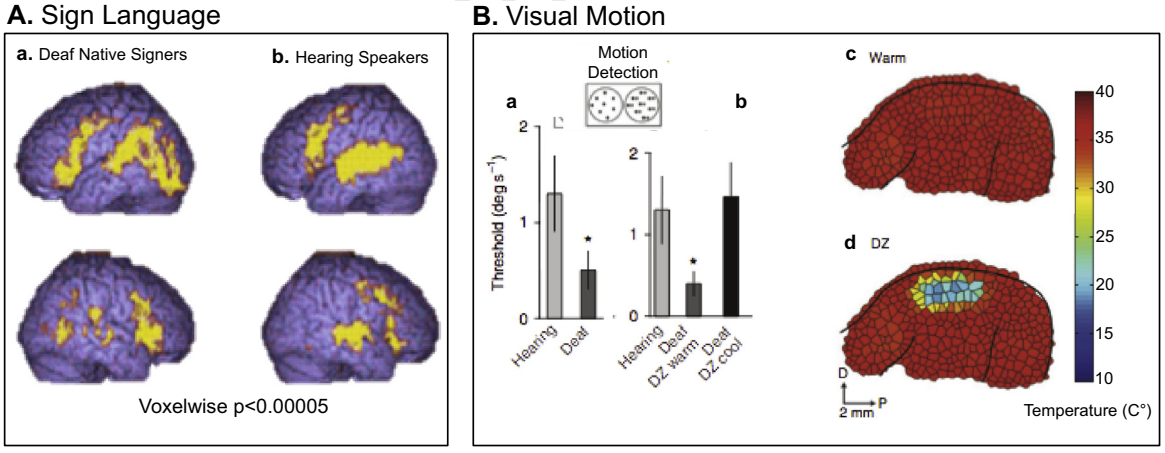

Fig. 3. Evidence of functionally selective crossmodal recruitment as a consequence of deafness. (A) Activations elicited in a sentence comprehension task in deaf native signers when processing sign-language (a) or in hearing speakers when processing audio-visually presented spoken sentences (b). Data from MacSweeney et al. (2002). Figure adapted from MacSweeney et al. (2008) with permission. (B) Evidence for functionally selective recruitment elicited by visual motion in deaf cats. (a) Deaf cats showed lower thresholds for visual motion detection compared to hearing cats. (b) Comparable thresholds for visual motion detection were observed in deaf and hearing cats following the temporary deactivation of DZ in deaf cats (DZ is the cortical area selectively responsive for auditory-motion in hearing cats). Deactivation was caused by selective cooling of the cortical area of interest. (c, d) Both images depict a dorsolateral view of the dorsal auditory cortex (sulci are indicated by thick black lines). They both represent thermal cortical maps constructed by generating Voronoi tessellations from 335 temperature recording sites (color-coded scale is represented on the right). (c) Cortical temperatures before cooling. (d) Thermal profile during selective cooling of DZ to 3 °C. Figure adapted from Lomber et al. (2010) with permission.

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latter studies unequivocally demonstrated the causality of the left fronto-temporal recruitment for sign language processing.

Apart from language, only a few studies have documented functionally selective crossmodal recruitment in deaf adults. For instance, seminal studies have proposed that crossmodal recruitment was elicited in the early-deafened auditory cortex by attended peripheral visual motion (Finney et al., 2001, 2003; Fine et al., 2005). These studies localized the crossmodal recruitment within a right temporal area including primary and secondary auditory cortices (Finney et al., 2001; Fine et al., 2005). Given that in hearing individuals the right auditory cortex, and in particular the planum temporale, shows a specialization for auditory motion processing (e.g., Baumgart et al., 1999; Ducommun et al., 2004), these authors ultimately suggest that this crossmodal recruitment may be functionally selective in nature, as the reported right selectivity of temporal activations may reflect the predisposition of the right auditory cortex to process motion stimuli (Fine et al., 2005). All the aforementioned studies were designed to test and manipulate the effect of attention on motion processing (see also Finney et al., 2001) and they therefore lack a relevant control condition to directly support the claim for the functional specialization of the crossmodal recruitment (e.g., a condition in which the exact same stimulus, yet static for instance, was presented to the participants). Furthermore, other studies testing peripheral visual motion in the early-deaf population failed to report activity in right auditory cortices (Bavelier et al., 2000, 2001; Vachon et al., 2013). Therefore, the question of whether visual motion recruits the deprived auditory cortex of early-deaf adults in a functional specific fashion remains open. Importantly, a study by Lomber et al. (2010) carried out with congenitally deaf cats demonstrated that the temporary deactivation of a region known to mediate auditory motion processing in the hearing cats eliminated the behavioral advantage for peripheral visual motion perception reported in the same deaf animals before the deactivation (see Fig. 3B). This research demonstrated that the enhanced visual behavior for visual motion is causally mediated by a functional selective recruitment of the deafferented auditory cortices (Lomber et al., 2010).

Early-deaf and hearing participants were recently tested in a visual Mismatch Negativity (vMMN) task (Bottari et al., 2014). vMMN is a well-known electrophysiological marker of sensory expectancies, thought to reflect the automatic detection of visual changes occurring in the environment (see Kimura et al., 2011). Change-detection is a skill that has been primarily ascribed to the auditory system, as Mismatch Negativity has been primarily investigated in the auditory modality, and considered specific to audition (see Näätänen et al., 1978, 2001). However, more recently its visual counterpart has been discovered (Pazo-Alvarez et al., 2003). Testing whether early-deaf adults were able to develop this type of skill even without auditory experience and whether such type of computation would recruit the deafferented auditory cortex, represents relevant questions to address to shed further light on the properties of deafness-related crossmodal plasticity. To this aim, Bottari et al. (2014) applied source-estimate localization analyses to investigate the origin of vMMN-related activity in deaf adults compared to hearing controls. Results revealed that only early-deaf adults recruited their auditory cortices for the automatic detection of visual changes and, moreover, that this recruitment emerged within the typical vMMN time-window (i.e., 150–400 ms; e.g. Kimura et al., 2011). In early-deaf participants this recruitment of temporal regions was paired with a reduction of response within visual cortices, suggesting a shift from visual to auditory cortices as part of the computational process (Bottari et al., 2014; see Fig. 4A, B). Taken together, these results suggest the maintenance of automatic change-detection functionality within the deafferented auditory cortex of early-deaf adults (Bottari et al., 2014). To what extent this crossmodal recruitment influences behavior is still unknown.

Overall, with the exception of findings coming from sign language processing in deaf humans (e.g., Emmorey et al., 2003; Marshall et al., 2004) or from studies with deaf animals (e.g., Lomber et al., 2010; Meredith et al., 2011), the notion that crossmodal plasticity in cases of deafness is ultimately adaptive for behavior and functionally selective, relies on less empirical evidence when compared to the field of blindness. Future studies should further assess the principles driving crossmodal plasticity in cases of early-deafness. Such an approach will ultimately help to address the crucial issue regarding the extent to which the principles guiding crossmodal reorganizations in blindness overlap with those guiding crossmodal reorganizations in cases of deafness, therefore putatively providing a unified vision of how the brain copes with the loss of one sense.

Possible reasons behind the disparity between the results documenting adaptive crossmodal plasticity as a consequence of blindness and deafness. A direct comparison between the strength of the evidence documenting adaptive crossmodal plasticity in blindness and deafness clearly highlights that results coming from the former population are much more prevalent. This discrepancy may be explained by several possible reasons. The first explanation, which is also the most simplistic one, is that studies addressing deafness-related plasticity are less abundant than those focusing on blindness-related plasticity. This is probably due to the difficulties in communication that often characterize the interactions between deaf and hearing communities. These difficulties primarily concern linguistic issues since deaf people communicate mainly through sign language and often do not totally master spoken and written languages, whereas hearing people only very rarely know sign languages. This in turn may create additional boundaries when aiming at starting research collaborations between deaf associations and university institutions, thus limiting the access to this population.

A second and not mutually exclusive explanation concerns the possibility that deaf adults have been compared with hearing controls using a non-optimal set of tasks. Indeed, studies on deaf cognition have mainly

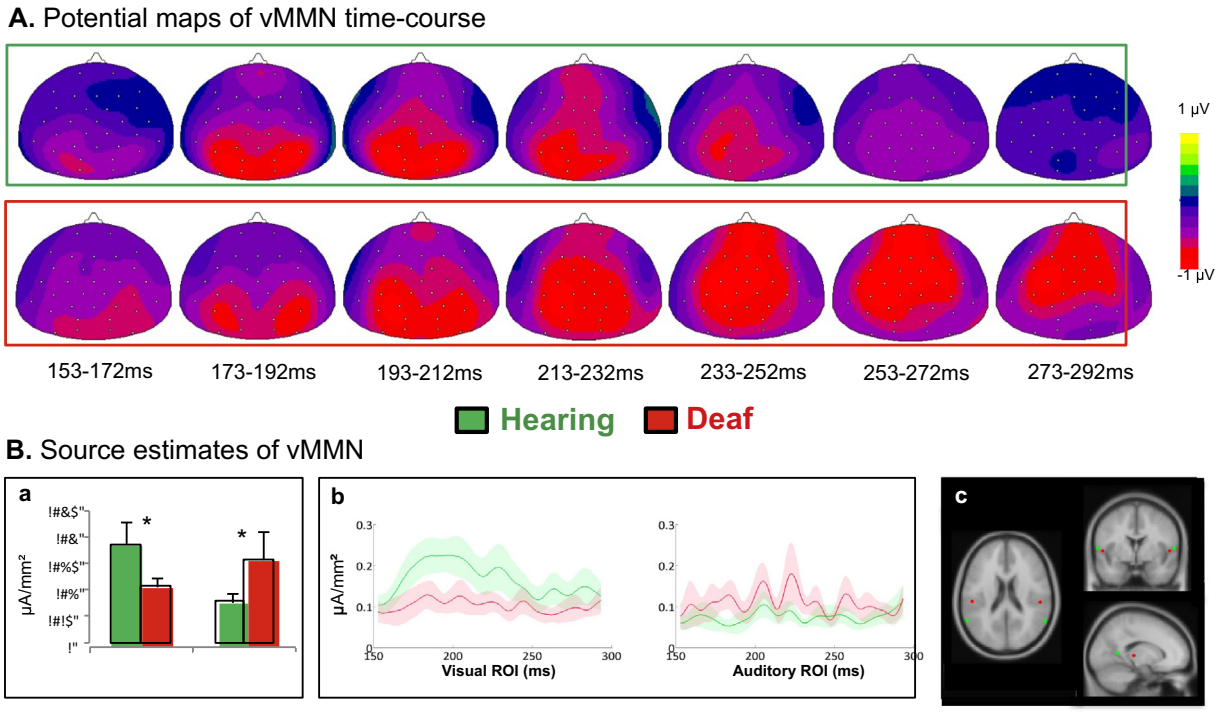

Fig. 4. (A) Potential maps of vMMN time-course (seven adjacent 20-ms time windows) in hearing (green box) and deaf participants (red box). (B) Source estimates of vMMN. (a, b) Source estimates of vMMN obtained with sLORETA (Pascual-Marqui, 2002). For these analyses two regions of interest (ROIs) were selected: a visual ROI, which comprised Brodmann areas 18 and 19 (i.e., extrastriate visual areas); an auditory ROI, which comprised Brodmann areas 41 and 42 (i.e., primary and secondary auditory cortex, respectively). (a) Source estimates averaged over the whole 140-ms vMMN time-course (153–292 ms), separately for each group of participants and for each ROI. Early-deaf adults (red bars) showed overall reduced activation in the visual ROI but enhanced activation in the auditory ROI compared to hearing controls (green bars). (b) Time-course of the source estimates within visual and auditory ROIs for the whole vMMN 140-ms time window reported separately for hearing (green lines) and for deaf participants (red lines). (c) Dipole modeling results calculated on a 20-ms window around the grand average vMMN peak of each group (hearing: 193 ms; deaf: 252 ms). Reported in the figure are vMMN dipoles for each group (hearing: green; deaf: red) projected on an average MNI brain. Dipole coordinates indicated a more anterior and ventral solution for the vMMN in deaf participants compared to hearing controls, compatible with auditory cortices, within the superior and middle temporal gyri. Figure adapted with permission from Bottari et al. (2014).

tried to answer the intuitive question of whether or not deaf adults see better than hearing controls (e.g., Bavelier et al., 2006). On one side, this approach led to compare deaf and hearing participants in spatial tasks (e.g., Proksch and Bavelier, 2002; Chen et al., 2006; Bottari et al., 2011a; Hauthal et al., 2013; Heimler and Pavani, 2014; see Pavani and Bottari, 2012 for a review), namely, the set of abilities for which vision conveys the most reliable information (e.g., Charbonneau et al., 2013). Most notably for this context, however, seminal studies have proposed that predisposition to better convey a certain set of information reflects also the preferential computational properties of specific sensory cortices, rather than strictly the properties of specific sensory modalities (e.g., Pascual-Leone and Hamilton, 2001). Within this framework, it is relevant to highlight that audition has been shown to better convey temporal (e.g., Shams et al., 2000) rather than spatial information. Therefore, by applying this notion to crossmodal plasticity effects in cases of deafness, the interesting hypothesis emerges that the reason for the lack of convincing evidence in favor of the occurrence of adaptive crossmodal recruitment in early-deaf adults may depend on the fact that spatial, rather than temporal abilities have been primarily investigated. There is a growing body of evidence suggesting that several of the documented visuo-spatial behavioral advantages in the deaf population may rely on intramodal plasticity, namely, on plastic changes occurring within the visual system rather than involving the auditory cortex. For instance, an increased electrophysiological activity of primary and secondary visual cortices, but no changes in the auditory cortex, has been shown to underlie the faster detection of abrupt onsets of visual stimuli, which is one of the most robust visual enhancements reported in the deaf population (Bottari et al., 2011b). Furthermore, Codina et al., 2011 showed a correlation in deaf adults between the ability to better detect peripheral moving stimuli in a kinetic perimetry task and the dimensions of the neural rim areas of the optic nerve. This latter result indicates that enhanced peripheral visual motion processing in early-deaf adults may also be at least partially mediated by intramodal visual changes occurring at the periphery of the nervous system. Future studies could focus on temporal rather than spatial abilities, ultimately questioning whether crossmodal plasticity emerges more consistently when testing the core functionality of the deprived auditory cortices (see Bottari et al., 2014 for initial results in this direction).

On the other side, because of the primary focus on answering the intuitive question of whether or not deaf adults see better than hearing controls (e.g., Bavelier et al., 2006), reorganization occurring in the other spared

sensory modalities, such as touch, remained largely unexplored. Interestingly though, the very few neuroimaging studies investigating tactile processing in early-deaf and hearing participants consistently reported primary auditory cortex recruitment in the deaf population (Levänen et al., 1998; Auer et al., 2007; Karns et al., 2012). Furthermore, as reported in the previous paragraph, results coming from the study by Karns et al. (2012) provide initial evidence suggesting that somatosensory crossmodal recruitment of the primary auditory cortex correlates with behavioral performance in the deaf population. Whether this crossmodal recruitment follows the functional organization of the hearing auditory cortices (i.e., functional-selective recruitment) is currently unknown. One possibility is that this consistent tactile crossmodal recruitment may be due to the greater functional similarities between somatosensory and auditory modalities compared to the functional similarities between audition and vision. In fact, both audition and touch have enhanced temporal precision compared to vision (e.g., Shams et al., 2000; Violentyev et al., 2005). The functional similarity between audition and touch may be especially strong for vibrotactile stimulations, which share several physical properties with auditory inputs. For instance, in both types of stimulation, information is conveyed through mechanical pressure generating oscillatory patterns, ultimately constructing frequency percepts (e.g., for a review see Soto-Faraco and Deco, 2009). Moreover, within a certain frequency range, the very same oscillatory pattern can be perceived simultaneously by the peripheral receptors of both sensory modalities (i.e., the basilar membrane of the cochlea and the skin, respectively; e.g., Von Békésy, 1959; Gescheider, 1970; Soto-Faraco and Deco, 2009), despite consistent differences between the two senses for what concerns the final *qualia* of the two stimulations (i.e., touch vs. sound). Finally, enhanced crossmodal plasticity for touch in deaf adults may partially be due to the mere structural proximity between the auditory and tactile systems. There is some evidence documenting audio-tactile integration and even tactile processing by itself occurring in the primary auditory cortex in hearing monkeys (e.g., Kayser et al., 2005; Schürmann et al., 2006; Lakatos et al., 2007).

Is crossmodal plasticity necessarily adaptive for the preserved senses?

The brief overview presented above suggests that crossmodal reorganization in sensory-deprived individuals mediates at least some enhanced behaviors in the remaining senses (see also Pavani and Röder, 2012). These findings promoted the widespread notion that crossmodal plasticity in cases of sensory loss is *adaptive* or *compensatory* for behavior. However, aside from enhanced behaviors, there is a growing body of evidence reporting behavioral impairments in both populations in some specific tasks. In particular, blind individuals have been shown to be impaired compared to sighted controls in specific spatial tasks such as auditory localization in the vertical plane (Lewald, 2002; Zwiers et al., 2001). It has also been repeatedly reported that early-blind individuals do not automatically activate an allocentric representation of external space (i.e., object-centered representations), rather they perform spatial tasks based on an egocentric, anatomical representation of space (i.e., body-centered representations; see for reviews Cattaneo et al., 2008; Röder et al., 2008; Crollen and Collignon, 2012). This qualitative difference between blind and sighted individuals in the automatic remapping of sensory inputs into a different spatial reference frame produces performance advantages in blind adults compared to sighted controls in those tasks in which adopting by default an anatomically anchored reference system facilitates performance (e.g., Röder et al., 2004; Collignon et al., 2009c; Crollen et al., 2011). However, in tasks in which adopting an automatic external remapping reference frame is facilitatory to perform well in the task, blind individuals typically perform worse than sighted controls (e.g., Collignon et al., 2009c; Ruggiero et al., 2009; Pasqualotto et al., 2013).

Similarly, deaf adults compared to hearing controls have been shown to be impaired in some specific temporal tasks such as the discrimination of durations (Kowalska and Szelag, 2006; Bolognini et al., 2012). In addition, higher thresholds in a simultaneity judgment task carried out both in the visual and in the tactile modality have been reported in deaf adults compared to hearing controls (Heming and Brown, 2005). Seminal studies have documented that the ability to create and manipulate spatial maps of space (needed to perform the aforementioned spatial tasks; e.g., Knudsen and Knudsen, 1985; King and Carlile, 1993), or having a fine-grained temporal precision (needed to perform duration discrimination or simultaneity judgments; e.g., Blair, 1957; Withrow, 1968) may not properly develop as a consequence of visual or auditory deprivation, respectively. In other words, an intact visual or auditory system may be necessary to efficiently develop these specific abilities, giving rise to the important concept that those abilities are primarily calibrated by the missing sensory modality (vision and audition, respectively; e.g., Poizner and Tallal, 1987; Lewald, 2002; Collignon et al., 2009a; Gori et al., 2013). For the context of the current review, the relevant issue raised by these studies is whether crossmodal reorganization also mediates *maladaptive* behavioral outcomes. Unfortunately, studies addressing the plastic modifications mediating these impaired behaviors are currently missing. However, evidence coming from the deaf literature hints at the intriguing perspective that this may indeed be the case. A recent TMS study demonstrated that the tactile auditory recruitment reported in a duration discrimination task was somewhat maladaptive for the behavior of early-deaf adults (Bolognini et al., 2012). The authors tested spatial (localization) and temporal (durations) discrimination abilities in early-deaf adults and hearing controls within the somatosensory modality. Behavioral results showed comparable tactile spatial discrimination abilities in the two groups, but impaired tactile duration discrimination abilities in deaf adults compared to hearing controls. By delivering TMS on the superior temporal sulcus (STS), Bolognini et al. (2012) further showed that the later STS was involved in the temporal task after

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stimulus presentation, the better participants were able to discriminate between durations. In other words, the authors showed that the impairment reported in the deaf group depended on deaf participants recruiting STS earlier in time after stimulus presentation compared to hearing controls (Bolognini et al., 2012). One might speculate that the recruitment of the primary auditory cortex by tactile stimulation in the deaf population (Levänen et al., 1998; Auer et al., 2007; Karns et al., 2012) might lead somatosensory processing to reach higher order auditory areas, as STS, earlier than when these same areas are reached by somatosensory processing of hearing controls (Bolognini et al., 2012), ultimately triggering impairments in performance. Such findings challenge the view of crossmodal plasticity as intrinsically beneficial for behavior. Future studies should address this crucial issue more systematically in order to shed further light on the properties of crossmodal recruitment in cases of sensory deprivation.

CROSS-MODAL PLASTICITY IN CASES OF SENSORY RESTORATION

Contrary to the studies of crossmodal plasticity in cases of sensory loss, studies addressing the issue of the effects of cross-modal plasticity in cases of sensory restoration mainly originate from literature on auditory rather than on visual recovery. Therefore, we will first describe findings obtained as a result of auditory restoration, and then move to the initial findings obtained as a result of sight restoration.

Deafness

Auditory restoration through cochlear implantation is a well-established procedure to recover at least partially from deafness. CIs are devices that aim at replacing normal cochlear function by converting auditory signals into electric impulses directly delivered to the acoustic nerve (see Mens, 2007 for more detailed information). Given the fast development of biotechnology, CIs are increasingly becoming more efficient due to remarkable improvements in the quality of these systems, which are stabilizing as common clinical practices. It follows that the number of deaf people undergoing this intervention is continuously increasing. The U.S. Food and Drug Administration (FDA) declared at the end of 2010 that approximately 219,000 people had received a CI worldwide, whereas by the end of 2012 the number had risen to approximately 324,000 (www.nidcd.nih.gov). The degree of auditory recovery after cochlear implantations is still variable and quite unpredictable (e.g., Sharma et al., 2014). However, thanks to prolific research in this field, several principles that help to predict the outcomes of CIs have started to emerge, and, importantly, these principles have now started to guide clinical practices outside laboratory settings. A careful evaluation of these principles is crucial since they shape the guidelines used to develop rehabilitation programs.

Predictors of CI outcome. Age at implantation. A robust body of evidence indicates that the age at which a deaf person undergoes a cochlear implantation has a huge impact on the consequent auditory recovery (Kral et al., 2002, 2005; Sharma et al., 2005, 2007, 2014). Specifically, several studies have consistently demonstrated that in cases of early bilateral deafness, cochlear implantation must take place before the age of 3.5 years to have the greatest chance to develop a typically functional auditory system, and no later than the age of 7 years, after which very poor restoration outcomes have been reported (Sharma et al., 2002, 2005, 2007, 2014; Sharma and Dorman, 2006; Geers, 2006; Dunn et al., 2013). These two distinct cut-offs for achieving proper auditory development after cochlear implantation (i.e., 3.5 years; 7 years of age) strongly support the notion, mainly demonstrated through animal studies, of the existence of two intertwined types of developmental periods, namely *critical* and *sensitive* periods respectively. The term *critical period* refers to the optimal temporal window during which the development of a particular sensory system should be pursued (Knudsen, 2004). Once the critical periods are closed, there would be no possibility of restoring that particular sensory modality to a level comparable to the control population (Hubel and Wiesel, 1970; Cynader and Chernenko, 1976; Cynader and Mitchell, 1977; Knudsen, 1988, 2004; Daw, 2009a,b; Barkat et al., 2011). In fact, the lack of the *natural* sensory input of a specific sensory cortex during its corresponding critical period may prevent, or at least strongly limit, the wiring of the connections necessary for the efficient functioning of that specific sensory modality (Kral and Sharma, 2012; Kral, 2013). In other words, during these atypical critical periods, connections that may be essential for the adequate processing of the absent sensory modality may either not develop or may be pruned away due to prolonged inactivity (Kral, 2013). After the closure of critical periods, connections stabilize and the plasticity of sensory systems decreases with age (e.g., Zhang et al., 2002; Chang and Merzenich, 2003), making it increasingly difficult to modify the system (e.g., Graham et al., 2009; Illg et al., 2013). This particular period, during which plasticity is still present but slowly decaying, is generally referred to as *sensitive* period of development (e.g., Voss, 2013). It follows that sensory recovery has a much higher chance of being successful if a deprived sensory cortex is re-afferented when its corresponding *critical* period is still open, thus maximally increasing the chances for the connections necessary for the optimal functioning of that sensory modality to normally develop (i.e., cochlear implantations undertaken before the age of 3.5; e.g., Sharma and Dorman, 2006; Sharma et al., 2014). However, before the closure of the more prolonged *sensitive* period, an optimal auditory recovery may still be possible, albeit the outcome of this recovery is much more variable and much less predictable (i.e., cochlear implantations carried-out between 3.5 years and 7 years of age; e.g., Sharma and Dorman, 2006; Sharma et al., 2014).

Crossmodal plasticity. One crucial and still open question regarding the prediction of CI outcomes concerns the effects of crossmodal plasticity on auditory recovery. If the deprived auditory regions have

reorganized to functionally process an ectopic modality (e.g., vision or touch), how will this reorganization process interact, coexist or interfere with the newly reacquired auditory input? This issue is of fundamental relevance because many interventions for auditory restoration are still carried out during adulthood or after the closure of critical and sensitive periods. Furthermore, even if cochlear implantations are undertaken within the critical/sensitive periods, crossmodal plasticity may still take place (e.g., Sharma et al., 2014).

Overall, data collected both on humans and on animals support the idea that crossmodal plasticity interferes with the resettlement of the regained sensory inputs (e.g., Kral and Sharma, 2012; Sharma et al., 2014). It has been consistently demonstrated that the success of CIs, typically quantified in terms of spoken language recovery, is inversely correlated with the amount of visual activity recorded in the auditory cortex of CI recipients before the intervention (e.g., Lee et al., 2001, 2005, 2007; Giraud and Lee, 2007) as well as with the amount of crossmodal activity still recorded following the intervention (e.g., Doucet et al., 2006; Buckley and Tobey, 2011; Rouger et al., 2012; Sandmann et al., 2012; Sharma et al., 2014). It is important to highlight that the majority of the latter set of studies we have mentioned were carried out with deaf individuals who acquired deafness late in life (i.e., during adulthood, or after they had acquired language; e.g., Doucet et al., 2006; Rouger et al., 2012; Sandmann et al., 2012).

Merging these results in a unified framework with those obtained with early-deaf implanted children (e.g., Buckley and Tobey, 2011; Sharma et al., 2014) has to be done with caution, as several studies conducted in the blind population consistently showed that the mechanisms of crossmodal plasticity differ between early- and late-deprived individuals (e.g., Voss et al., 2008; Bedny et al., 2010; Collignon et al., 2013). These latter results revealed that the properties of crossmodal recruitment are highly influenced by the age at which deprivation occurred (e.g., Collignon et al., 2013). Besides the fact that the mechanisms mediating crossmodal plasticity may differ between early- and late-deaf individuals, results obtained with both deaf populations are consistently documenting a negative impact of crossmodal plasticity on auditory recovery. However, in the following paragraphs we will focus on evidence documenting the properties of auditory recovery in early-deaf individuals only, in line with the topic of the present review.

Buckley and Tobey (2011) recorded electrophysiological responses of early-deaf CI recipients elicited by visual motion and correlated the amplitudes of the evoked potentials with sentence and word perception scores collected in the same patients. Source-localization analyses revealed right temporal activation linked to the perception of visual motion in the group of CI recipients. The authors observed a negative correlation between the strength of crossmodal recruitment and scores to linguistic tests, thus ultimately suggesting that crossmodal takeover interferes with proper language recovery (Buckley and Tobey, 2011; see also Sharma et al., 2014; and see Sandmann et al., 2012 for converging results with late-deaf CI patients). These results are in line with seminal findings obtained with Positron Emission Tomography (PET) in early-deaf children before they underwent a CI intervention (e.g., Lee et al., 2001, 2005, 2007; Oh et al., 2003; Giraud and Lee, 2007). Crucially, after the intervention, the authors performed a series of linguistic tests on the same participants and correlated the results with the spontaneous metabolic activity recorded prior to implantation. Results showed that the less spontaneous glucose metabolic activity present in the auditory cortex before CI intervention, the better the linguistic performance of CI recipients following the intervention (e.g., Lee et al., 2001, 2005, 2007). These studies show that the level of spontaneous metabolic activity in CI candidates increased together with age at implantation (i.e., with the duration of deafness; e.g., Lee et al., 2005, 2007). The increased glucose metabolic activity has been interpreted as evidence suggesting crossmodal takeover of the auditory cortex by the spared sensory modality, thus ultimately preventing a proper auditory recovery through cochlear implantation (e.g., Giraud and Lee, 2007). These findings promoted the assumption that crossmodal plasticity may be one of the main sources of the high variability observed in CI outcomes (e.g., Buckley and Tobey, 2011; Sandmann et al., 2012; Sharma et al., 2014). Furthermore, these results strongly supported the notion that crossmodal plasticity is ultimately and unavoidably *maladaptive* for optimal auditory recovery and that its presence should be considered as a negative predictor of successful auditory restoration through cochlear implantation (see for reviews Kral, 2013; Sharma et al., 2014).

Studies carried-out with animals strengthen this notion by unraveling further its plausible neurophysiological substrate. In particular, they suggest that if the *natural* sensory modality is missing during its corresponding critical/sensitive periods for cortical development, then crossmodal connections, for instance connecting the deprived sensory cortex to intact sensory cortices/subcortical structures, may be established or strengthened, whereas other necessary connections may not even develop (see Kral et al., 2005; Kral and Sharma, 2012; Kral, 2013). In particular, these works describe an intact auditory system as comprised of a dense network of bottom-up and top-down reciprocal connections, which guarantees an intense comparison of information (Kral and Sharma, 2012). Crossmodal takeover of auditory cortices by the intact sensory modalities is proposed to trigger a *functional decoupling* between the bottom-up and top-down connections reaching the auditory cortex (e.g., Kral et al., 2005; Kral, 2013), ultimately preventing the possibility for the top-down connections to properly develop and thus to the auditory system to fully function if re-afferented (e.g., Kral et al., 2006; Kral, 2007). In fact, Kral (2013) recently pointed out that with age, top-down connections become increasingly more relevant in sensory processing, ultimately allowing brain-networks to generalize their responses and to store relevant patterns of neural responses. The occurrence of functional decoupling may prevent the possibility of developing such generalizations.

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It has been further proposed that functional decoupling may contribute to the closure of auditory sensitive periods not only in animals, but also in humans (Kral, 2007; Kral and Sharma, 2012; Sharma et al., 2014). Thus, the occurrence of functional decoupling has been proposed as the mechanism preventing a complete neurophysiological recovery of the auditory system if CI interventions occur after the closure of cortical/sensitive periods (e.g., Kral, 2007). Consistently with studies on deaf humans, animal studies appear to suggest that if implantation occurs later in life, the development of atypical crossmodal connections would prevent the proper recovery of audition (e.g., Kral, 2007).

Is crossmodal plasticity necessarily maladaptive for CI outcome?. The role of functional-selective crossmodal plasticity. Animal models are very reliable for understanding the neurophysiological impact of hearing loss on the auditory cortex and on its complex functioning. However, what these models never took into account is that every cognitive function or 'functional unit' has its own critical/sensitive period of development, which is specific to each particular function (Knudsen, 2004; Lewis and Maurer, 2005). In other words, we argue that the development of a given cortical area depends on the fulfillment of both the critical period related to the maturation of the sensory pathways (in this case auditory connections) and the critical periods related to the development of the specific functions a particular cortical area is mostly dedicated to. The driving hypothesis underlying the framework of the current review is that these *parallel* critical periods relative to the development of specific functional networks may be independent from the critical periods for the proper physiological development of the auditory modality (see also Lyness et al., 2013). If this reasoning is valid, in cases of early-deafness the proper development of specific functional units may be triggered also by a different sensory modality than audition (e.g., vision or touch). To be effective, this atypical coupling between a specific function and an ectopic sensory modality should occur within the critical period of that particular function. Within this framework, the presence of functionally selective crossmodal recruitment of sensory-deafferented regions may be conceived as a landmark pinpointing the efficient development of a particular functional unit within its corresponding critical period, ultimately disclosing the remarkable possibility that certain aspects of cross-modal reorganization might instead turn out to be adaptive for CI outcomes.

In early-deaf adults, as already stated in the dedicated section above (see Section 'Deafness'), sign language processing is the only cognitive function for which a clear functionally selective recruitment of the deafferented auditory cortex has been reliably reported (e.g., Petitto et al., 2000; MacSweeney et al., 2002; Emmorey et al., 2007; Mayberry et al., 2011). In line with the notion that crossmodal recruitment is maladaptive for optimal sensory recovery, exposure to a sign language prior to cochlear implantation has been intensively discouraged by clinicians, as visual linguistic inputs are believed to prevent the proper processing of auditory linguistic inputs, after audition is restored (Nishimura et al., 1999; Lee et al., 2001; Giraud and Lee, 2007). The idea behind this clinical practice is that the use of visual language will facilitate the takeover of the auditory cortex by visual input, which has repetitively (see above) been correlated with reduced CI success (e.g., Lee et al., 2001, 2005; Giraud et al., 2007).

A recent retrospective study compared early-implanted deaf children coming from deaf families (and thus native signers) with early-implanted deaf children coming from hearing families (and thus with limited, if any, access to sign language) at various times following implantation (Hassanzadeh, 2012). Results showed that implanted deaf native signers outperformed implanted deaf non-signers on measures of speech perception, speech production and language development (Hassanzadeh, 2012; see also Lyness et al., 2013). These initial results suggest that early exposure to a sign language paired with early CI implantation may be beneficial for optimal spoken language development, rather than interfering with it. In fact, these findings support the notion that exposure to a sign language early in life allows the linguistic system of deaf children to develop within its critical period (Meadow-Orlans et al., 2004). Moreover, these initial results raise the promising possibility that the development of functional units within their corresponding critical periods elicited through a different sensory modality than their preferential one (vision instead of audition in the case of sign language), might facilitate sensory recovery, thus highlighting a form of crossmodal plasticity that may turn out to be adaptive for sensory restoration.

We therefore propose that when considering the development of the deprived auditory system, it would be important to consider the existence of at least partially independent critical/sensitive periods for (1) the development of connections subtending proper auditory processing and (2) the development of functionally specific cognitive units, which are prerogative of the auditory cortices (e.g., language; see also Lyness et al., 2013). This proposal suggests that early CI intervention is essential to allow the complete neurophysiological development of the auditory system (Kral et al., 2005; Sharma et al., 2005, 2014; Kral and Sharma, 2012). However, we suggest that in order to allow the typical development of specific cognitive functions within their corresponding critical periods, the presence of ectopic inputs coming from the remaining and intact sensory modalities may be beneficial for CI outcomes rather than interfering with it. Crucially, we propose that such crossmodal recruitments may drive the development of those functional units typically tuned toward the auditory modality. It is important to emphasize that we do not propose that crossmodal recruitment occurring in the deaf population will turn out to be necessarily beneficial for CI outcomes, as it is possible that not all aspects of crossmodal plasticity are functionally organized (see Section 'Possible reasons behind the disparity between the results documenting adaptive crossmodal plasticity as a consequence of blindness and deafness'). We therefore believe that further investigating the complex

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interplay between the adaptive versus maladaptive outcomes of crossmodal plasticity in cases of CI interventions represents a promising avenue of research.

Implications for rehabilitation procedures. We propose that the presence of functionally selective crossmodal plasticity may be exploited, after CI interventions, by rehabilitation programs aiming at maximizing auditory recovery. For instance, in rehabilitation programs for spoken language recovery following CI, the ectopic visual modality, which is crossmodally recruiting the linguistic system for sign language processing (i.e., left fronto-temporal cortex; e.g., Petitto et al., 2000; Emmorey et al., 2003), may be paired to the newly re-acquired auditory inputs in order to guide its recruitment of the targeted functional unit. In other words, appropriate audio–visual training may rely on functionally selective crossmodal plasticity mechanisms to eventually promote the transfer of auditory linguistic inputs toward its appropriate functional unit, eventually driving a switch of preferential sensory tuning from visual linguistic inputs to auditory ones.

Such an integrated audio–visual approach may be particularly beneficial for patients undergoing cochlear implantation later in life (i.e., when critical periods are closed but sensitive periods are still open; between 3.5 and 7 years of age), when CI outcomes may still be successful but are more variable than when the intervention is carried-out before the end of the critical period for auditory development (i.e., before 3.5 years of age; see Sharma et al., 2014). In these patients, crossmodal plasticity is expected to be more pervasive and therefore its exploitation for rehabilitation may be enhanced.

The proposition of specific audio–visual training contrasts with the common guidelines implemented in rehabilitation programs after cochlear implantation, which are often focused on training the auditory modality alone (Chan et al., 2000; Hogan et al., 2008; Yoshida et al., 2008; Ingvalson and Wong, 2013). However, there is already some promising evidence hinting at the beneficial effects of focused bimodal, multisensory trainings for optimal spoken language recovery. For instance, early exposure to visuo-auditory language training (i.e., speech-reading therapy; pairing sign language with spoken language during rehabilitation) has been shown to substantially improve CI outcomes (Bergeson et al., 2005; see also Strelnikov et al., 2011, 2013).

It is crucial to highlight that linguistic information is used here as a conceptual model having preliminary support from the literature, but such audio–visual training may, in theory, be applied to a variety of sensory/cognitive functions like object/voice recognition, auditory spatial perception, or auditory motion perception.

Blindness

Evidence documenting visual recovery is more limited, in contrast with the literature on hearing loss and auditory restoration. The main reason for this disparity is the most pragmatic one, namely, that in contrast to auditory restoration no well-established approach for sight restoration has been achieved. This is mainly due to the retina having a much more complex organization than the cochlea, and the incoming information (i.e., light) exits this first structure of visual processing in the form of an electrical signal conveying much more composite information compared to cochlear output. Compared to CIs, which have achieved a relatively effective reconstruction of cochlear output, the prevailing and most promising attempts to reconstruct retinal output by directly stimulating the retina, namely retinal prosthesis, are still quite experimental and currently provide extremely low-resolution sight restoration (Luo and da Cruz, 2014). Furthermore, these approaches require at least partial retinal spare functioning, whereas complete blindness can cause total retinal destruction (Luo and da Cruz, 2014). Even in the case where this constraint is respected, complete blindness can result in damage to different types of retinal cells/retinal connections and different retinal implants rely on different retinal residual functioning (e.g., subretinal implants positioned in the outer surface of the retina or epiretinal implants positioned in the inner surface of the retina; see for instance Djilas et al., 2011; Zrenner et al., 2011; Humayun et al., 2012; Wang et al., 2012). This in turn creates an additional difficulty for the stabilization of a unified approach for visual restoration, as each developing technique is only suited to the recovery of specific types of blindness and not for others. However, given the fast advances in biotechnological methods, retinal prostheses (Luo and da Cruz, 2014) and other approaches such as gene therapy (Busskamp et al., 2010) and transplantation of photoreceptors (Yang et al., 2010) are rapidly improving and might become a successful option in coming years.

Initial evidence coming from sight restoration. Given the lack of a systematic approach for sight restoration, the available data documenting visual recovery is mainly found in the few reports describing the regaining of vision in early-blind individuals as a consequence of bilateral cataract removal (e.g., Ley et al., 2013; Röder et al., 2013; Grady et al., 2014; Kalia et al., 2014), corneal transplantation (e.g., Gregory and Wallace, 1963; Gregory, 1974), or as a result of experimental sight restoration procedures such as stem-cell transplants (e.g., Fine et al., 2003). Understanding in this field of research has been strongly influenced by two seminal cases reporting limited recovery of visual functions as a consequence of early-blindness. In both cases, interventions for sight restoration had been undertaken during adulthood (e.g., Von Senden, 1960; Gregory and Wallace, 1963; Fine et al., 2003). SB lost effective sight at 10 months of age and received a corneal transplantation after 50 years of blindness (Gregory and Wallace, 1963; Gregory, 1974). MM was blind since 3 years of age, and received a stem-cell transplant in his right eye at the age of 46 (Fine et al., 2003; Saenz et al., 2008; Levin et al., 2010). Interestingly, SB and MM presented consistent similarities in their visual abilities following sight restoration. Despite the patients never completely recovering basic visual functions such as visual acuity, they succeeded in recovering certain higher order functions such as color and simple shape recognition as well as

perception of visual motion (see also Dormal et al., 2012). However, both patients were never able to recover other higher order visual functions such as recognition of complex shapes, including faces and everyday life objects, or perception of depth cues and the detection of illusory contours.

These initial results strongly limited the hopes for efficient sight recovery for early-acquired blindness treated during adulthood. This notion has been further strengthened by reports documenting that MM, 7 years after the intervention, still had poor spatial resolution and limited visual abilities that prevented him from efficiently relying on vision in his everyday life (Saenz et al., 2008; Levin et al., 2010). These results have been generally interpreted as supporting evidence for pioneering animal studies suggesting the existence of critical periods for the development of visual functions, which if missed, unavoidably prevent the proper development of the visual system (e.g., Blakemore and Cooper, 1970; Hubel and Wiesel, 1970; Cynader and Chernenko, 1976; Cynader and Mitchell, 1977; see also Section 'Predictors of CI outcome'). Other subsequent works have further corroborated this notion. For instance, one recent study used electrophysiology (EEG) to test whether the selectivity of responses to faces compared to objects could be developed in a group of individuals who were born with a congenital cataract and underwent an intervention of bilateral cataract removal at different ages (range of ages at surgery: 2 months–14 years; Röder et al., 2013). Results reported the presence of the electrophysiological component typically selective for faces in all patients. However, differently from sighted controls, in the patients group this component was recorded also when viewing objects, and this was the case even in those individuals who underwent an intervention for sight restoration within the first few months of life (Röder et al., 2013). A recent fMRI study reached similar conclusions (Grady et al., 2014). Grady et al. (2014) tested the processing of faces in a group of visually restored adults who underwent interventions for bilateral cataract removal within the first year of life. The authors measured fMRI activity elicited by faces within an extended network including together with the core face regions (fusiform gyrus; occipital face area; STS), regions involved in processing the emotional valence of faces such as the insula, amygdala and striatum (Adolphs et al., 1994; Haber and Knutson, 2010), and regions more involved in theory of mind and self-reference such as the anterior temporal cortex, medial prefrontal cortex and posterior parietal cortex (e.g., Graham et al., 2003; Spreng and Grady, 2010). The authors showed that the cataract group recruited the exact same extended network to passively process faces and to judge different facial characteristics compared to controls, but the whole network (especially the extended part) was overall less active in the patient group when passively viewing face stimuli. In addition, differently from controls, the face-network was also responsive to objects (Grady et al., 2010).

In contrast with these studies, Pawan Sinha and colleagues documented good sight recovery in early-blind individuals regaining vision relatively late in life (e.g., Held et al., 2011; Kalia et al., 2014). These data challenge the predominant notion proposing that if critical periods are not met, a proper visual recovery can never be achieved (e.g., Dormal et al., 2012). For instance, Kalia et al. (2014) tested a group of early-blind individuals who underwent intervention for bilateral cataract removal only after the age of 8 years. The authors concentrated on assessing the recovery of contrast sensitivity, a basic visual function for which the closure of critical periods has been documented around 7 years of age in normally sighted children (e.g., Bradley and Freeman, 1982). Patients showed a recovery of contrast sensitivity, which was limited to low-spatial frequencies (Kalia et al., 2014). However, only five of the eleven patients that were tested exhibited a clear contrast sensitivity recovery (Kalia et al., 2014). Although potentially intriguing, these results must be considered with caution, as Kalia et al. (2014) reported that prior to intervention, their patients showed some residual visual abilities beyond light perception (Kalia et al., 2014). As is often the case with blind individuals, access to complete medical files may prove to be difficult and therefore it is challenging to reliably assert the etiology of blindness and the complete absence of functional vision since birth. Thus, these data cannot exclude that the absence of complete blindness early in life, or the residual vision before the intervention may have played a crucial role in appropriately tuning the visual system for the perception of low visual frequencies. One can imagine that such a functional tuning may stay silent for the period of deprivation, yet greatly facilitate functional recovery once vision is properly restored. If this is the case, the observed improvement in contrast sensitivity in these patients (Kalia et al., 2014) may be more optical rather than neural in origin.

The importance of early intervention. We have seen in the previous section that specific visual functions have their distinct critical period for development, during which the absence of visual inputs may potentially permanently impair their proper functioning (see Lewis and Maurer, 2005). These results have been interpreted as evidence in favor of proper visual functioning never being achieved if critical periods are over (e.g., Dormal et al., 2012).

In addition, the optic tracts and radiations show substantial atrophy in early-blind adults (Noppeney et al., 2005; Shimony et al., 2006; Pan et al., 2007; Park et al., 2007; Ptito et al., 2008; see Fig. 5), raising serious concerns regarding whether these altered visual tracks may be able to convey the reafferented visual signal delivered electrically via retinal prostheses (see Merabet et al., 2005).

Both lines of evidence suggest that the sooner in life an individual undergoes an intervention for sight restoration, the higher the chances for achieving a satisfactory visual recovery. In fact, early sight restoration may permit visual functions to develop within their corresponding critical periods, and may at the same time prevent the documented deterioration of visual structures. However, there are data documenting that certain aspects of vision failed to properly develop even when the intervention for sight restoration had taken place before the end of the

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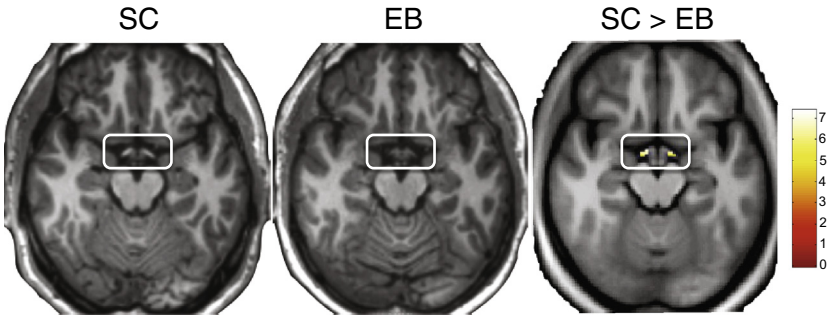

Fig. 5. Optic tract atrophy in the adult brain as a consequence of early-blindness. Left: Optic tract of one sighted control (SC). Central: Optic tract of one early-blind adult (EB). Both images are the result of MRI structural scan at 3 Tesla (TRIO TIM System-Siemens): voxel size = 1 × 1 × 1.2 mm^3; matrix size = 240 × 256; repetition time = 2.300 ms; echo-time = 2.91 ms. Right: Areas of atrophy in an early-blind group compared to a sighted control group as assessed by voxel-based morphometry (unpublished data). Structural scans are taken from Collignon et al. (2011b).

critical period identified in sighted children for the typical development of that particular function. This has been shown to be the case for several visual abilities such as holistic face processing (Le Grand et al., 2004) or contrast sensitivity for mid and high spatial frequencies (Maurer et al., 2006). These effects have been named 'sleeper effects': early, and relatively short visual deprivation may prevent the formation of the neural substrates of a specific visual function, even if the targeted function would emerge at a much later point in development (Maurer et al., 2007). One intriguing explanation for these effects may concern the learning state of the brain at the moment of the intervention. Kral (2013) pointed out that at the initial juvenile state of the brain, learning is dominated mainly by bottom-up mechanisms and high plasticity. In this state, the brain has a neuronal architecture that allows easy and fast incorporation of information into the neuronal networks based on bottom-up gathered information. However, with increasing age, top-down mechanisms come into play ultimately allowing brain-networks to generalize their responses (Kral, 2013). In this more experienced state, learning becomes more determined by stored patterns, and the influence of sensory input decreases (Kral, 2013). Perhaps 'sleeper effects' (Maurer et al., 2007) depend on the fact that when visual restoration occurs, the learning state of the brain has already partly abandoned its initial juvenile state during which learning is fast and mainly driven by bottom-up mechanisms. Consequently, it may be that certain specific bottom-up-driven learning, which nonetheless may be fundamental to acquire specific visual functions, could not properly take place, resulting in a 'sleeper effect' for a particular visual function.

One potentially impacting perspective, which could also overcome the occurrence of 'sleeping effects', relates to current progress in methods allowing the restoration of the juvenile brain's ability for plasticity by 're-opening' critical periods of development (see Kral, 2013). Recent work with animals supports this possibility by proposing that the release of some molecular 'breaks' of plasticity may trigger the reopening of critical periods, thus resetting juvenile brain plasticity and ultimately favoring visual recovery (Pizzorusso et al., 2002; Morishita and Hensch, 2008; Duffy and Mitchell, 2013; see Kral, 2013). The aforementioned studies focused on monocular deprivation rather than complete sensory deprivation. Therefore, future studies should determine whether the same approach might also be effective in resetting the brain to its initial juvenile state in cases of sensory deprivation.

Is crossmodal plasticity necessarily maladaptive for sight restoration?. Similarly to what was proposed for auditory restoration (e.g., Giraud and Lee, 2007), the extensive crossmodal reorganization documented in the deprived occipital cortex of blind individuals is classically considered to prevent proper visual recovery and potentially even interfere with it (e.g., Merabet et al., 2005; Collignon et al., 2011a). In this section, we would like to suggest that this may not be necessarily the case.

In parallel with what we proposed for auditory restoration (see Section 'Predictors of CI outcome'), we advocate the idea that the critical periods subtending the proper physiological development of the sensory wiring of the visual system may be partially independent from the critical periods relative to the proper development of specific functional processing networks. Within this framework, functional-selective crossmodal plasticity phenomena may be conceived as possible evidence in favor of the efficient development of a given functional unit within its corresponding critical periods, despite the different modality tuning of that particular unit compared to the control population (see also Maidenbaum et al., 2014). To develop a typically functional visual system, both types of critical periods must be fulfilled. We propose that functional-selective crossmodal plasticity, if paired with early interventions for sight restoration, may turn out to be beneficial, or *adaptive,* for sensory recovery. In other words, we propose that this type of crossmodal recruitment *adaptively* allows the development of specific cognitive functions to occur within their corresponding critical periods even in the absence of their typically preferred sensory modality.

Implications for rehabilitation programs. Similarly to what we have proposed for auditory recovery (see Section 'Predictors of CI outcome'), functional-selective crossmodal plasticity may turn out to be a favorable tool to exploit in rehabilitation programs after visual restoration. We propose that focused audio–visual or visuo-tactile trainings based on crossmodal functionally

selective recruitments may help the re-setting of visual functions. For example, it has been shown in early-blind adults that the recognition of tactile shapes (Amedi et al., 2010) activates the LOC/LOtv in a functionally selective crossmodal fashion. Within rehabilitation programs, pairing the visual presentation of objects with the concomitant presentation of the same objects through touch may facilitate the emergence of the ability to recognize objects through the visual modality. Likewise, the same logic can be applied to the visual recovery of the other functional units for which functionally selective crossmodal recruitments have been successfully demonstrated, like, for instance, the perception of visual motion (see Section 'Blindness'). Crucially and differently from deaf adults, for whom functionally selective crossmodal recruitment has been reliably demonstrated only for language processing (see Section 'Deafness'), in blind individuals, functional-selective crossmodal recruitment has been documented for a variety of functional units (see Section 'Blindness'). This offers the intriguing perspective of testing the potential adaptive role of functional-selective crossmodal plasticity for sight recovery in a variety of cognitive functions. Adopting such an approach would ultimately permit further investigation as to what extent critical periods related to the development of single functional units are indeed independent from critical periods related to the development of the physiological connections necessary for a fully functional visual system to normally evolve.

GENERAL CONCLUSIONS

The main aim of this review was to present and highlight the limits of strictly adopting the classical conceptualization of crossmodal plasticity as exerting a double-edged sword effect on behavior: necessarily adaptive for sensory deprivation and maladaptive for sensory recovery. In the present review we attempted to depict a more balanced framework of the impact of crossmodal plasticity, with some aspects of potential *maladaptive* outcomes in cases of sensory deprivation, as well as some aspects of potential *adaptive* outcomes in cases of sensory restoration (see Table 1). We provided some evidence suggesting that several abilities known to be mainly calibrated by the missing sensory modality (vision or audition) may never optimally develop in the remaining senses of early-blind or deaf individuals (e.g., Lewald, 2002; Bolognini et al., 2011). On the other side, we provided initial evidence suggesting that functionally selective crossmodal plasticity might be *adaptive* in cases of early sensory restoration, ultimately facilitating sensory recovery rather than interfering with it (Hassanzadeh, 2012; see also Lyness et al., 2013), especially if properly exploited with rehabilitation programs (e.g., Bergeson et al., 2005). Overall, the construction of this framework unifies the recent evidence and shapes modern theoretical conceptions that may foster further research aimed at developing a more complete conceptualization of the variegated effects that crossmodal plasticity exerts on behavior.

Table 1. A more balanced framework summarizing adaptive (green) and maladaptive effects (red) of crossmodal plasticity (CP) in cases of early sensory deprivation (upper row) and in cases of early sensory restoration (lower row)

Adaptive and Maladaptive Effects of Crossmodal Plasticity (CP) for Early Sensory Deprivation and Restoration

	Adaptive	Maladaptive
Sensory Deprivation	CP mediates enhanced behaviors in the remaining senses CP correlates with some enhanced behaviors CP is functionally selective	CP may potentially relate to impaired functions in the remaining senses
Sensory Restoration	Functionally selective CP may facilitate sensory rehabilitation by supporting the recovery of specific cognitive functions through preserved sensory inputs	CP interferes with optimal sensory recovery

Finally, it appears clear throughout the review that the complementary nature of the results arising from the literature investigating the impact of blindness or deafness on brain functions allows a more integrated framework to be built-up regarding the adaptive and maladaptive effects of crossmodal plasticity on the deprived/reafferented sensory cortices, ultimately going beyond the specific missing sensory modality (vision or audition). Even if the results coming from either of the two deprived populations are extremely useful to test complementary predictions in the other population, a more systematic testing of the predictions arising from one population on the other may unravel important differences in the principles underlying the reorganizations elicited by early-blindness and early-deafness. We therefore strongly advocate for this 'dual' approach, which holds the potential to significantly enrich our understanding of the functioning of the visual and auditory cortices as well as of the way sensory cortices react to the deprivation/restoration of their preferred sensory modality. A more systematic testing of the complex interplay between the adaptive and maladaptive nature of crossmodal plasticity may eventually pave the way for adapted guidelines for rehabilitation.

UNCITED REFERENCE

Capek et al. (2013). Q5

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