"Crossmodal plasticity in sensory loss"

Frasnelli, Johannes ; Collignon, Olivier ; Voss, Patrice ; Lepore, Franco

ABSTRACT

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

CITE THIS VERSION

Frasnelli, Johannes ; Collignon, Olivier ; Voss, Patrice ; Lepore, Franco. *Crossmodal plasticity in sensory loss.* In: *Progress in Brain Research*, Vol. 191, p. 233-249 (2011) http://hdl.handle.net/2078.1/189307 -- DOI : 10.1016/B978-0-444-53752-2.00002-3

A. M. Green, C. E. Chapman, J. F. Kalaska and F. Lepore (Eds.)
Progress in Brain Research, Vol. 191
ISSN: 0079-6123

CHAPTER 15

Crossmodal plasticity in sensory loss

Johannes Frasnelli[†,*], Olivier Collignon[†,§], Patrice Voss[‡] and Franco Lepore[†]

[†] *Département de Psychologie, Centre de Recherche en Neuropsychologie et Cognition, Université de Montréal, Montréal, Québec, Canada*
[‡] *International Laboratory for Brain, Music and Sound Research, Université de Montréal, Montréal, Québec, Canada*
[§] *Centre de Recherche CHU Sainte-Justine, Université de Montréal, Montréal, Québec, Canada*

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

Keywords: blindness; deafness; anosmia; crossmodal plasticity.

Introduction

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

*Corresponding author.
Tel.: +1-514-343-6111x0705; Fax: +1-514-343-5787
E-mail: frasnelli@yahoo.com

DOI: 10.1016/B978-0-444-53752-2.00002-3

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

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

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

Blindness

Behavioral reorganization in blindness

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

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

In recent experiments, we investigated the ability of blind participants to sharply focus their attention and quickly react to auditory or tactile spatial targets (Collignon and De Volder, 2009; Collignon et al., 2006). These studies demonstrated that blind subjects reacted faster than sighted controls to non visual spatial targets in selective and divided attention tasks further extending the

view that blind individuals are able to compensate their lack of vision by developing capacities in their remaining senses that exceed those of sighted individuals.

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

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

impaired their ability to integrate audio-tactile information across postural changes (Collignon et al., 2009a). Altogether, these results thus demonstrate that the default remapping of touch/proprioception into external coordinates is acquired during early development as a consequence of visual input.

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

Brain reorganization in blindness

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

It is, however, possible that these results simply reflect an association between stimulus presentation and cortical activation, without there being any functional involvement of occipital areas in nonvisual processing. Transcranial magnetic stimulation (TMS), which induces a focal and transient disruption of the proper functioning of a targeted area, has been used to demonstrate the necessity of the OC of the blind for Braille reading (Cohen et al., 1997; Kupers et al., 2007) and verbal (Amedi et al., 2004) processing. We also demonstrated that TMS applied over the right dorsal extrastriate cortex interfered with the use of a prosthesis substituting vision by audition and with the localization of sounds in blind subjects (Collignon et al., 2007). By contrast, TMS targeting the same cortical area had no effect on any auditory performance in sighted subjects and did not interfere with pitch and intensity discriminations in the blind. The demonstration that transient perturbation of OC with TMS selectively

disrupted specific auditory processing in the blind compared to sighted subjects illustrates that this "visual" area is functionally linked to the neural network that underlies this auditory ability. We thus concluded that early visual deprivation leads to functional cerebral reorganization such that the right dorsal visual stream is recruited for the spatial processing of sounds, a result which is in clear agreement with previous neuroimaging studies on nonvisual space processing in this population (Arno et al., 2001; Poirier et al., 2006; Ricciardi et al., 2007; Vanlierde et al., 2003; Weeks et al., 2000). In a recent fMRI study we compared brain activity of congenitally blind and sighted participants processing either the spatial or the pitch properties of sounds carrying information in both domains (the same sounds were used in both tasks), using an adaptive procedure specifically designed to adjust for performance level. In addition to showing a substantial recruitment of the occipital cortex for sound processing in the blind, we also demonstrated that auditory-spatial processing mainly recruited regions of the dorsal occipital stream. Moreover, functional connectivity analyses revealed that these reorganized occipital regions are part of an extensive brain network including regions known to underlie audio-visual spatial abilities in sighted subjects (Collignon et al., 2011). It is worth noting that dorsal occipital regions have previously been shown to be involved in visuospatial processing in sighted subjects (Haxby et al., 1991). The similarity in the activation foci between visuospatial processing in the sighted and auditory spatial processing in the blind suggests that these areas may retain their functional and neuronal coding ability, which would enable them to process input from a different sensory modality. These results suggest that spatial processing in the blind maps onto specialized subregions of the OC known to be involved in the spatial processing of visual input in sighted people (Haxby et al., 1991). Interestingly, a recent study reported activation of a subregion of the lateral-occipital complex normally responsive to visual and tactile object-related processing when blind subjects extracted shape information from visual-to-auditory sensory substitution soundscapes (Amedi et al., 2007; see also Pietrini et al., 2004 for ventral activations in tactile shape recognition in the blind). In a similar manner, mental imagery of object shape recruited more ventral occipital areas (De Volder et al., 2001), whereas mental imagery of object position recruited more dorsal occipital regions (Vanlierde et al., 2003) in the blind. It thus appears that a functional dissociation between a ventral "what?" stream for the processing of object shape and a dorsal "where?" stream for the processing of space may also exist for nonvisual stimuli processed in the OC of blind subjects (Collignon et al., 2009c; Dormal and Collignon, 2011).

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

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

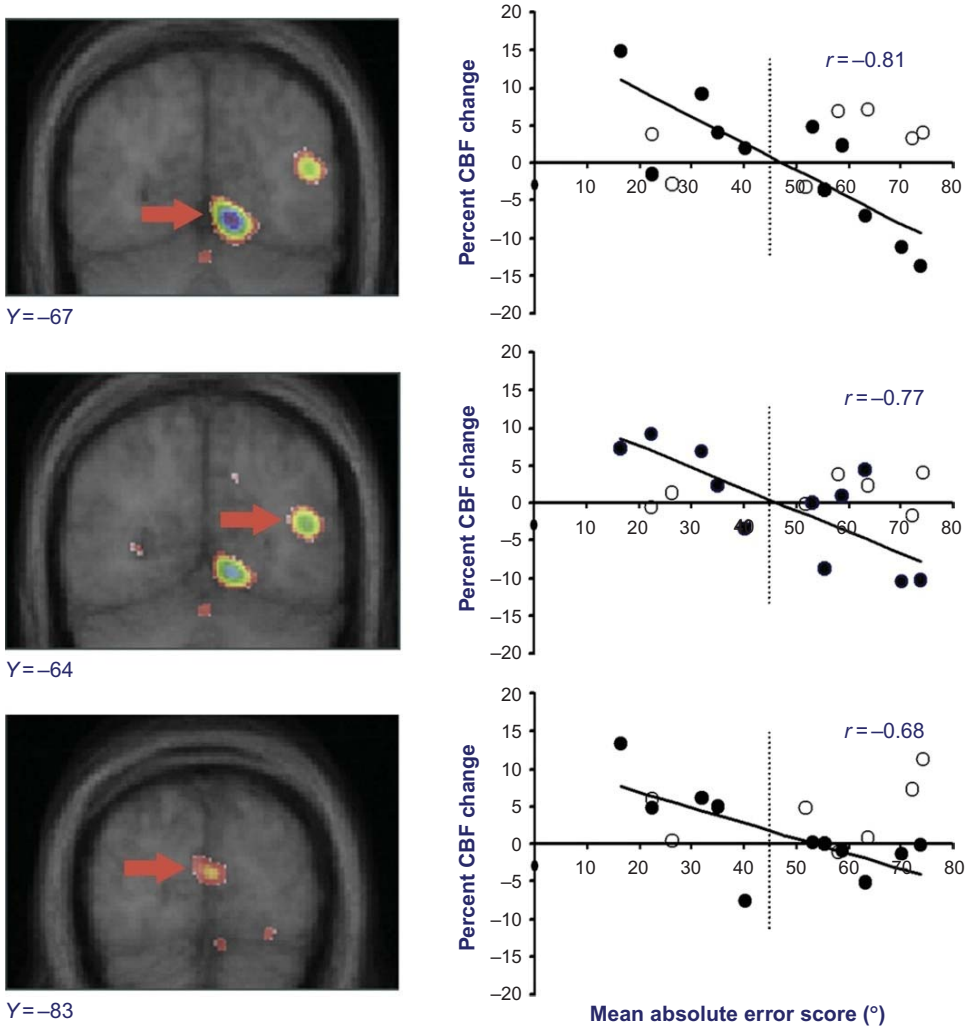

Fig. 1. Data of a correlational analysis between performance (mean absolute error) in a pointing task to monaurally presented sounds and cerebral blood flow (as measured by PET) in a group of blind subjects. The column of brain images illustrates regions in the ventral extrastriate (top), in the dorsal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

mechanisms, we used event-related TMS to disclose the time course of the spatial processing of sounds in the dorsolateral "where" stream of blind and sighted individuals (Collignon et al., 2008, 2009b). To address this issue, we induced a virtual lesion of either the right intraparietal sulcus (rIPS) or the right dorsal extrastriate occipital cortex (rOC) at different delays in blind and

sighted subjects performing a sound lateralization task. We observed that TMS applied over rIPS 100–150 ms after sound onset disrupted the spatial processing of sound in sighted subjects but surprisingly had no influence on the task performance in blind individuals at any timing. In contrast, TMS applied over rOC 50 ms after sound onset disrupted the spatial processing of sounds in blind and in sighted participants. These studies suggest an early contribution of rOC in the spatial processing of sound in blind but also, to some extent, in sighted participants and also point to a lesser involvement of rIPS in this ability in blind participants. Given the very short latency of the disruptive effect of TMS applied over rOC on auditory spatial processing and considering the absence of rIPS contribution to this function in the blind, we suggested that sounds may reach the OC in blind subjects either via subcortical connections (Piche et al., 2007) or direct "feedforward" afferent projections arising from the auditory cortex (Falchier et al., 2002). However, further studies are needed to better understand how these mechanisms combine together and the influence of age of onset of blindness on the installation of such mechanisms.

Deafness

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

Behavioral reorganization in deafness

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

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

et al., 2006). However, this hypothesis has been challenged by the results of a recent study showing faster reactivity to visual events in the deaf compared to hearing individuals, regardless of spatial location (both peripheral and central; Bottari et al., 2010). Moreover, while hearing subjects were substantially slower for peripheral targets (in relation to central ones), deaf subjects were equally efficient across all spatial locations, suggesting functional enhancements for the peripheral visual field that cannot be explained by different attentional gradients alone.

Brain reorganization in deafness

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

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

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

hand area, possibly related to more active use of the dominant hand in sign language.

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

Anosmia, ageusia, loss of trigeminal chemosensation

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

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

Behavioral reorganization in chemosensory loss

Olfactory dysfunctions can be categorized into quantitative dysfunctions (reduced sense of smell—hyposmia; loss of sense of smell—anosmia) and qualitative dysfunctions (altered perception of existing odors—parosmia; perception of inexistent odors—phantosmia; Leopold, 2002). These are relatively common conditions as up to 5% and 15% of the population are thought to exhibit anosmia and hyposmia, respectively (Bramerson et al., 2004; Landis and Hummel, 2006; Landis et al., 2004). Next to the physiological age related decline of olfactory function, the major etiologies of olfactory dysfunction are sinunasal diseases (polyps,

chronic rhino-sinusitis), viral infections (persisting dysfunction after upper respiratory tract infection), traumatic brain injury, neurodegenerative diseases (Parkinson's and Alzheimer's disease, etc.), and others. Up to 1% of the anosmic individuals exhibit congenital anosmia (Kallmann's syndrome, isolated congenital anosmia; Temmel et al., 2002).

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

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

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

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

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

There is indeed also evidence from imaging studies for such a flavor sense. The chemical senses share important central processing areas. For example, it has been shown that the orbitofrontal cortex (OFC) and its different subdivisions are activated by olfactory (e.g., Gottfried and Zald,

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

Brain reorganization in chemosensory loss

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

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

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

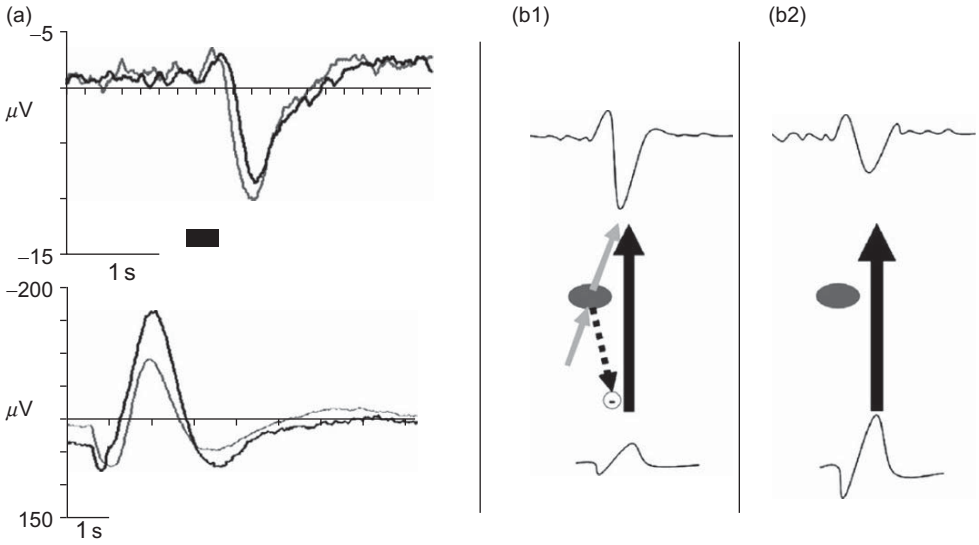

Fig. 2. Effects of loss of olfactory function on the trigeminal chemosensory system. (A) Grand means of trigeminal event-related potentials (central measure; top) and negative mucosal potential (NMP; peripheral measure; bottom) following stimuli of 60% (v/v) CO_2 in subjects with acquired anosmia (black)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

Conclusion

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

References

Alary, F., Duquette, M., Goldstein, R., Elaine Chapman, C., Voss, P., La Buissonniere-Ariza, V., et al. (2009). Tactile acuity in the blind: A closer look reveals superiority over the sighted in some but not all cutaneous tasks. *Neuropsychologia*, *47*, 2037–2043.

Alary, F., Goldstein, R., Duquette, M., Chapman, C. E., Voss, P., & Lepore, F. (2008). Tactile acuity in the blind: A psychophysical study using a two-dimensional angle discrimination task. *Experimental Brain Research*, *187*, 587–594.

Albrecht, J., Kopietz, R., Frasnelli, J., Wiesmann, M., Hummel, T., & Lundstrom, J. N. (2010). The neuronal correlates of intranasal trigeminal function—An ALE meta-analysis of human functional brain imaging data. *Brain Research Reviews*, *62*, 183–196.

Alimohammadi, H., & Silver, W. L. (2000). Evidence for nicotinic acetylcholine receptors on nasal trigeminal nerve endings of the rat. *Chemical Senses*, *25*, 61–66.

Amedi, A., Floel, A., Knecht, S., Zohary, E., & Cohen, L. G. (2004). Transcranial magnetic stimulation of the occipital pole interferes with verbal processing in blind subjects. *Nature Neuroscience*, *7*, 1266–1270.

Amedi, A., Raz, N., Pianka, P., Malach, R., & Zohary, E. (2003). Early 'visual' cortex activation correlates with superior verbal memory performance in the blind. *Nature Neuroscience*, *6*, 758–766.

Amedi, A., Stern, W. M., Camprodon, J. A., Bermpohl, F., Merabet, L., Rotman, S., et al. (2007). Shape conveyed by visual-to-auditory sensory substitution activates the lateral occipital complex. *Nature Neuroscience*, *10*, 687–689.

Arno, P., De Volder, A. G., Vanlierde, A., Wanet-Defalque, M. C., Streel, E., Robert, A., et al. (2001). Occipital activation by pattern recognition in the early blind using auditory substitution for vision. *Neuroimage*, *13*, 632–645.

Auvray, M., & Spence, C. (2008). The multisensory perception of flavor. *Consciousness and Cognition*, *17*, 1016–1031.

Axelrod, S. (Ed.), (1959). *Effect of early blindness: Performance of blind and sighted children on tactile and auditory tasks*. (Research Series No. 7) New York: American Foundation for the Blind.

Bavelier, D., Brozinsky, C., Tomann, A., Mitchell, T., Neville, H., & Liu, G. (2001). Impact of early deafness and early exposure to sign language on the cerebral organization for motion processing. *The Journal of Neuroscience*, *21*, 8931–8942.

Bavelier, D., Dye, M. W. G., & Hauser, P. C. (2006). Do deaf individuals see better? *Trends in Cognitive Sciences*, *10*, 512–518.

Bavelier, D., & Neville, H. J. (2002). Cross-modal plasticity: Where and how? *Nature Reviews. Neuroscience*, *3*, 443–452.

Bavelier, D., Tomann, A., Hutton, C., Mitchell, T., Corina, D., Liu, G., et al. (2000). Visual attention to the periphery is enhanced in congenitally deaf individuals. *The Journal of Neuroscience*, *20*, RC93.

Bengtsson, S., Berglund, H., Gulyas, B., Cohen, E., & Savic, I. (2001). Brain activation during odor perception in males and females. *Neuroreport*, *12*, 2027–2033.

Bosworth, R. G., & Dobkins, K. R. (1999). Left-hemisphere dominance for motion processing in deaf signers. *Psychological Science*, *10*, 256–262.

Bottari, D., Nava, E., Ley, P., & Pavani, F. (2010). Enhanced reactivity to visual stimuli in deaf individuals. *Restorative Neurology and Neuroscience*, *28*, 167–179.

Boyle, J. A., Frasnelli, J., Gerber, J., Heinke, M., & Hummel, T. (2007). Cross-modal integration of intranasal stimuli: A functional magnetic resonance imaging study. *Neuroscience*, *149*, 223–231.

Boyle, J. A., Heinke, M., Gerber, J., Frasnelli, J., & Hummel, T. (2007). Cerebral activation to intranasal chemosensory trigeminal stimulation. *Chemical Senses*, *32*, 343–353.

Bramerson, A., Johansson, L., Ek, L., Nordin, S., & Bende, M. (2004). Prevalence of olfactory dysfunction: The skovde population-based study. *The Laryngoscope*, *114*, 733–737.

Bross, M. (1979). Residual sensory capacities of the deaf—Signal-detection analysis of a visual-discrimination task. *Perceptual and Motor Skills*, *48*, 187–194.

Brozinsky, C. J., & Bavelier, D. (2004). Motion velocity thresholds in deaf signers: Changes in lateralization but not in overall sensitivity. *Cognitive Brain Research*, *21*, 1–10.

Buchel, C., Price, C., Frackowiak, R. S. J., & Friston, K. (1998). Different activation patterns in the visual cortex of late and congenitally blind subjects. *Brain*, *121*, 409–419.

Buck, L., & Axel, R. (1991). A novel multigene family may encode odorant receptors: A molecular basis for odor recognition. *Cell*, *65*, 175–187.

Burdach, K. J., Kroeze, J. H., & Koster, E. P. (1984). Nasal, retronasal, and gustatory perception: An experimental comparison. *Perception & Psychophysics*, *36*, 205–208.

Burton, H., Sinclair, R. J., & McLaren, D. G. (2004). Cortical activity to vibrotactile stimulation: An fMRI study in blind and sighted individuals. *Human Brain Mapping*, *23*, 210–228.

Cerf-Ducastel, B., & Murphy, C. (2003). FMRI brain activation in response to odors is reduced in primary olfactory areas of elderly subjects. *Brain Research*, *986*, 39–53.

Cerf-Ducastel, B., Van de Moortele, P. F., MacLeod, P., Le Bihan, D., & Faurion, A. (2001). Interaction of gustatory and lingual somatosensory perceptions at the cortical level in the human: A functional magnetic resonance imaging study. *Chemical Senses*, *26*, 371–383.

Chaudhari, N., Landin, M. A., & Roper, S. D. (2000). A metabotropic glutamate receptor variant functions as a taste receptor. *Nature Neuroscience*, *3*, 113–119.

Cohen, L. G., Celnik, P., PascualLeone, A., Corwell, B., Faiz, L., Dambrosia, J., et al. (1997). Functional relevance of cross-modal plasticity in blind humans. *Nature*, *389*, 180–183.

Collignon, O., Charbonneau, G., Lassonde, M., & Lepore, F. (2009). Early visual deprivation alters multisensory processing in peripersonal space. *Neuropsychologia*, *47*, 3236–3243.

Collignon, O., Davare, M., De Volder, A. G., Poirier, C., Olivier, E., & Veraart, C. (2008). Time-course of posterior parietal and occipital cortex contribution to sound localization. *Journal of Cognitive Neuroscience*, *20*, 1454–1463.

Collignon, O., Davare, M., Olivier, E., & De Volder, A. G. (2009). Reorganisation of the right occipito-parietal stream for auditory spatial processing in early blind humans. A transcranial magnetic stimulation study. *Brain Topography*, *21*, 232–240.

Collignon, O., & De Volder, A. G. (2009). Further evidence that congenitally blind participants react faster to auditory and tactile spatial targets. *Canadian Journal of Experimental Psychology*, *63*, 287–293.

Collignon, O., Lassonde, M., Lepore, F., Bastien, D., & Veraart, C. (2007). Functional cerebral reorganization for auditory spatial processing and auditory substitution of vision in early blind subjects. *Cerebral Cortex*, *17*, 457–465.

Collignon, O., Renier, L., Bruyer, R., Tranduy, D., & Veraart, C. (2006). Improved selective and divided spatial attention in early blind subjects. *Brain Research*, *1075*, 175–182.

Collignon, O., Vandewalle, G., Voss, P., Albouy, G., Charbonneau, G., Lassonde, M., & Lepore, F. (2011). Functional specialization for auditory-spatial processing in the occipital cortex of congenitally blind humans. *Proceedings of the National Academy of Sciences*, *108*, 4435–4440.

Collignon, O., Voss, P., Lassonde, M., & Lepore, F. (2009). Cross-modal plasticity for the spatial processing of sounds in visually deprived subjects. *Experimental Brain Research*, *192*, 343–358.

De Volder, A. G., Toyama, H., Kimura, Y., Kiyosawa, M., Nakano, H., Vanlierde, A., et al. (2001). Auditory triggered mental imagery of shape involves visual association areas in early blind humans. *Neuroimage*, *14*, 129–139.

Deems, D. A., Doty, R. L., Settle, R. G., Moore-Gillon, V., Shaman, P., Mester, A. F., et al. (1991). Smell and taste disorders, a study of 750 patients from the University of Pennsylvania Smell and Taste Center. *Archives of Otolaryngology—Head & Neck Surgery*, *117*, 519–528.

Diderot, D., 1749. Lettre sur les aveugles à l'usage de ceux qui voient (London).

Diekmann, H., Walger, M., & von Wedel, H. (1994). Sense of smell in deaf and blind patients. *HNO*, *42*, 264–269.

Dormal, G., & Collignon, O. (2011). Functional selectivity in sensory deprived cortices. *Journal of Neurophysiology*, doi:10.1152/jn.00109.2011.

Dye, M. W. G., Baril, D. E., & Bavelier, D. (2007). Which aspects of visual attention are changed by deafness? The case of the Attentional Network Test. *Neuropsychologia*, *45*, 1801–1811.

Eimer, M. (2004). Multisensory integration: How visual experience shapes spatial perception. *Current Biology*, *14*, R115–R117.

Emmorey, K., Allen, J. S., Bruss, J., Schenker, N., & Damasio, H. (2003). A morphornetric analysis of auditory brain regions in congenitally deaf adults. *Proceedings of the National Academy of Sciences of the United States of America*, *100*, 10049–10054.

Falchier, A., Clavagnier, S., Barone, P., & Kennedy, H. (2002). Anatomical evidence of multimodal integration in primate striate cortex. *The Journal of Neuroscience*, *22*, 5749–5759.

Fieger, A., Roder, B., Teder-Salejarvi, W., Hillyard, S. A., & Neville, H. J. (2006). Auditory spatial tuning in late-onset blindness in humans. *Journal of Cognitive Neuroscience*, *18*, 149–157.

Fine, I., Finney, E. M., Boynton, G. M., & Dobkins, K. R. (2005). Comparing the effects of auditory deprivation and sign language within the auditory and visual cortex. *Journal of Cognitive Neuroscience*, *17*, 1621–1637.

Finney, E. M., Clementz, B. A., Hickok, G., & Dobkins, D. R. (2003). Visual stimuli activate auditory cortex in deaf subjects: Evidence from MEG. *Neuroreport*, *14*, 1425–1427.

Finney, E. M., & Dobkins, K. R. (2001). Visual contrast sensitivity in deaf versus hearing populations: Exploring the perceptual consequences of auditory deprivation and experience with a visual language. *Cognitive Brain Research*, *11*, 171–183.

Frasnelli, J., Schuster, B., & Hummel, T. (2007a). Interactions between olfaction and the trigeminal system: What can be learned from olfactory loss. *Cerebral Cortex*, *17*, 2268–2275.

Frasnelli, J., Schuster, B., & Hummel, T. (2007b). Subjects with congenital anosmia have larger peripheral but similar central trigeminal responses. *Cerebral Cortex*, *17*, 370–377.

Frasnelli, J., Schuster, B., & Hummel, T. (2010). Olfactory dysfunction affects thresholds to trigeminal chemosensory sensations. *Neuroscience Letters*, *468*, 259–263.

Frasnelli, J., Schuster, B., Zahnert, T., & Hummel, T. (2006). Chemosensory specific reduction of trigeminal sensitivity in subjects with olfactory dysfunction. *Neuroscience*, *142*, 541–546.

Frasnelli, J., van Ruth, S., Kriukova, I., & Hummel, T. (2005). Intranasal concentrations of orally administered flavors. *Chemical Senses*, *30*, 575–582.

Gizewski, E. R., Gasser, T., de Greiff, A., Boehm, A., & Forsting, M. (2003). Cross-modal plasticity for sensory and motor activation patterns in blind subjects. *Neuroimage*, *19*, 968–975.

Goldreich, D., & Kanics, I. M. (2003). Tactile acuity is enhanced in blindness. *The Journal of Neuroscience*, *23*, 3439–3445.

Gottfried, J. A., & Zald, D. H. (2005). On the scent of human olfactory orbitofrontal cortex: Meta-analysis and comparison to non-human primates. *Brain Research Reviews*, *50*, 287–304.

Gougoux, F., Lepore, F., Lassonde, M., Voss, P., Zatorre, R. J., & Belin, P. (2004). Neuropsychology: Pitch discrimination in the early blind. *Nature*, *430*, 309.

Gougoux, F., Zatorre, R. J., Lassonde, M., Voss, P., & Lepore, F. (2005). A functional neuroimaging study of sound localization: Visual cortex activity predicts performance in early-blind individuals. *PLoS Biology*, *3*, 324–333.

Gudziol, H., Rahneberg, K., & Burkert, S. (2007). Anosmiker schmecken schlechter als Gesunde. *Laryngo-rhino-otologie*, *86*, 640–643.

Gudziol, H., Schubert, M., & Hummel, T. (2001). Decreased trigeminal sensitivity in anosmia. *ORL; Journal of Otorhinolaryngology and its Related Specialties*, *63*, 72–75.

Haxby, J. V., Grady, C. L., Horwitz, B., Ungerleider, L. G., Mishkin, M., Carson, R. E., et al. (1991). Dissociation of object and spatial visual processing pathways in human extrastriate cortex. *Proceedings of the National Academy of Sciences of the United States of America*, *88*, 1621–1625.

Hotting, K., & Roder, B. (2009). Auditory and auditory-tactile processing in congenitally blind humans. *Hearing Research*, *258*, 165–174.

Hummel, T., Barz, S., Lotsch, J., Roscher, S., Kettenmann, B., & Kobal, G. (1996). Loss of olfactory function leads to a decrease of trigeminal sensitivity. *Chemical Senses*, *21*, 75–79.

Hummel, C., Frasnelli, J., Gerber, J., & Hummel, T. (2007). Cerebral processing of gustatory stimuli in patients with taste loss. *Behavioural Brain Research*, *185*, 59–64.

Hummel, T., Futschik, T., Frasnelli, J., & Huttenbrink, K. B. (2003). Effects of olfactory function, age, and gender on trigeminally mediated sensations: A study based on the lateralization of chemosensory stimuli. *Toxicology Letters*, *140–141*, 273–280.

Husner, A., Frasnelli, J., Welge-Lussen, A., Reiss, G., Zahnert, T., & Hummel, T. (2006). Loss of trigeminal sensitivity reduces olfactory function. *The Laryngoscope*, *116*, 1520–1522.

Iannilli, E., Del Gratta, C., Gerber, J. C., Romani, G. L., & Hummel, T. (2008). Trigeminal activation using chemical, electrical, and mechanical stimuli. *Pain*, *139*, 376–388.

Iannilli, E., Gerber, J., Frasnelli, J., & Hummel, T. (2007). Intranasal trigeminal function in subjects with and without an intact sense of smell. *Brain Research*, *1139*, 235–244.

James, W. (1890). *Principles of psychology* (Vol. 1). New York: Henry Holt and Company.

Kim, D. J., Park, S. Y., Kim, J., Lee, D. H., & Park, H. J. (2009). Alterations of white matter diffusion anisotropy in early deafness. *Neuroreport*, *20*, 1032–1036.

Kitazawa, S. (2002). Where conscious sensation takes place. *Consciousness and Cognition*, *11*, 475–477.

Kobal, G., Van Toller, S., & Hummel, T. (1989). Is there directional smelling? *Experientia*, *45*, 130–132.

Kujala, T., Alho, K., Huotilainen, M., Ilmoniemi, R. J., Lehtokoski, A., Leinonen, A., et al. (1997). Electrophysiological evidence for cross-modal plasticity in humans with early- and late-onset blindness. *Psychophysiology*, *34*, 213–216.

Kupers, R., Beaulieu-Lefebvre, M., Schneider, F. C., Kassuba, T., Paulson, O. B., Siebner, H. R., & Ptito, M. (2011). Neural correlates of olfactory processing in congenital blindness. *Neuropsychologia*, doi:10.1016/j.neuropsychologia.2011.03.033.

Kupers, R., Pappens, M., de Noordhout, A. M., Schoenen, J., Ptito, M., & Fumal, A. (2007). rTMS of the occipital cortex abolishes Braille reading and repetition priming in blind subjects. *Neurology*, *68*, 691–693.

Landis, B. N., & Hummel, T. (2006). New evidence for high occurrence of olfactory dysfunctions within the population. *The American Journal of Medicine*, *119*, 91–92.

Landis, B. N., Konnerth, C. G., & Hummel, T. (2004). A study on the frequency of olfactory dysfunction. *The Laryngoscope*, *114*, 1764–1769.

Landis, B. N., Scheibe, M., Weber, C., Berger, R., Bramerson, A., Bende, M., et al. (2010). Chemosensory interaction: Acquired olfactory impairment is associated with decreased taste function. *Journal of Neurology*, *257*, 1303–1308.

Laska, M., Distel, H., & Hudson, R. (1997). Trigeminal perception of odorant quality in congenitally anosmic subjects. *Chemical Senses*, *22*, 447–456.

Leopold, D. (2002). Distortion of olfactory perception: Diagnosis and treatment. *Chemical Senses*, *27*, 611–615.

Lessard, N., Pare, M., Lepore, F., & Lassonde, W. (1998). Early-blind human subjects localize sound sources better than sighted subjects. *Nature*, *395*, 278–280.

Lewald, J. (2002). Vertical sound localization in blind humans. *Neuropsychologia*, *40*, 1868–1872.

Lindemann, B. (1996). Taste reception. *Physiological Reviews*, *76*, 719–766.

Lindemann, B. (2000). A taste for umami. *Nature Neuroscience*, *3*, 99–100.

Loke, W. H., & Song, S. R. (1991). Central and peripheral visual processing in hearing and nonhearing individuals. *Bulletin of the Psychonomic Society*, *29*, 437–440.

Meier, R. P. (1991). Language-acquisition by deaf-children. *American Scientist*, *79*, 60–70.

Murphy, C., & Cain, W. S. (1986). Odor identification: The blind are better. *Physiology & Behavior*, *37*, 177–180.

Nava, E., Bottari, D., Zampini, M., & Pavani, F. (2008). Visual temporal order judgment in profoundly deaf individuals. *Experimental Brain Research*, *190*, 179–188.

Neville, H. J., & Lawson, D. (1987). Attention to central and peripheral visual space in a movement detection task: An event-related potential and behavioral study. II. Congenitally deaf adults. *Brain Research*, *405*, 268–283.

Neville, H. J., Schmidt, A., & Kutas, M. (1983). Altered visual evoked-potentials in congenitally deaf adults. *Brain Research*, *266*, 127–132.

Nishimura, H., Hashikawa, K., Doi, K., Iwaki, T., Watanabe, Y., Kusuoka, H., et al. (1999). Sign language 'heard' in the auditory cortex. *Nature*, *397*, 116.

Pallas, S. L., Roe, A. W., & Sur, M. (1990). Visual projections induced into the auditory pathway of ferrets. 1. Novel inputs to primary auditory-cortex (Ai) from the Lp pulvinar complex and the topography of the MGN-AI projection. *The Journal of Comparative Neurology*, *298*, 50–68.

Pascual-Leone, A., Amedi, A., Fregni, F., & Merabet, L. B. (2005). The plastic human brain cortex. *Annual Review of Neuroscience*, *28*, 377–401.

Penhune, V. B., Cismaru, R., Dorsaint-Pierre, R., Petitto, L. A., & Zatorre, R. J. (2003). The morphometry of auditory cortex in the congenitally deaf measured using MRI. *Neuroimage*, *20*, 1215–1225.

Petitto, L. A., Zatorre, R. J., Gauna, K., Nikelski, E. J., Dostie, D., & Evans, A. C. (2000). Speech-like cerebral activity in profoundly deaf people processing signed languages: Implications for the neural basis of human language. *Proceedings of the National Academy of Sciences of the United States of America*, *97*, 13961–13966.

Piche, M., Chabot, N., Bronchti, G., Miceli, D., Lepore, F., & Guillemot, J. P. (2007). Auditory responses in the visual cortex of neonatally enucleated rats. *Neuroscience*, *145*, 1144–1156.

Pietrini, P., Furey, M. L., Ricciardi, E., Gobbini, M. I., Wu, W. H. C., Cohen, L., et al. (2004). Beyond sensory images: Object-based representation in the human ventral pathway. *Proceedings of the National Academy of Sciences of the United States of America*, *101*, 5658–5663.

Poirier, C., Collignon, O., Scheiber, C., Renier, L., Vanlierde, A., Tranduy, D., et al. (2006). Auditory motion perception activates visual motion areas in early blind subjects. *Neuroimage*, *31*, 279–285.

Poizner, H., & Tallal, P. (1987). Temporal processing in deaf signers. *Brain and Language*, *30*, 52–62.

Proksch, J., & Bavelier, D. (2002). Changes in the spatial distribution of visual attention after early deafness. *Journal of Cognitive Neuroscience*, *14*, 687–701.

Ricciardi, E., Vanello, N., Sani, L., Gentili, C., Scilingo, E. P., Landini, L., et al. (2007). The effect of visual experience on the development of functional architecture in hMT. *Cerebral Cortex*, *17*, 2933–2939.

Rice, C. E., & Feinstein, S. H. (1965). Sonar system of the blind: Size discrimination. *Science*, *148*, 1107–1108.

Rice, C. E., Feinstein, S. H., & Schusterman, R. J. (1965). Echo-detection ability of the blind: Size and distance factors. *Journal of Experimental Psychology*, *70*, 246–255.

Rockland, K. S., & Ojima, H. (2003). Multisensory convergence in calcarine visual areas in macaque monkey. *International Journal of Psychophysiology*, *50*, 19–26.

Roder, B., Focker, J., Hotting, K., & Spence, C. (2008). Spatial coordinate systems for tactile spatial attention depend on developmental vision: Evidence from event-related potentials in sighted and congenitally blind adult humans. *The European Journal of Neuroscience*, *28*, 475–483.

Roder, B., Rosler, F., & Spence, C. (2004). Early vision impairs tactile perception in the blind. *Current Biology*, *14*, 121–124.

Roder, B., Teder-Salejarvi, W., Sterr, A., Rosler, F., Hillyard, S. A., & Neville, H. J. (1999). Improved auditory spatial tuning in blind humans. *Nature*, *400*, 162–166.

Roe, A. W., Pallas, S. L., Kwon, Y. H., & Sur, M. (1992). Visual projections routed to the auditory pathway in ferrets: Receptive fields of visual neurons in primary auditory cortex. *The Journal of Neuroscience*, *12*, 3651–3664.

Rosenbluth, R., Grossman, E. S., & Kaitz, M. (2000). Performance of early-blind and sighted children on olfactory tasks. *Perception*, *29*, 101–110.

Sadato, N., Yamada, H., Okada, T., Yoshida, M., Hasegawa, T., Matsuki, K., et al. (2004). Age-dependent plasticity in the superior temporal sulcus in deaf humans: A functional MRI study. *BMC Neuroscience*, *5*, 56.

Savic, I., & Gulyas, B. (2000). PET shows that odors are processed both ipsilaterally and contralaterally to the stimulated nostril. *Neuroreport*, *11*, 2861–2866.

Schwenn, O., Hundorf, I., Moll, B., Pitz, S., & Mann, W. J. (2002). Do blind persons have a better sense of smell than normal sighted people? *Klinische Monatsblätter für Augenheilkunde*, *219*, 649–654.

Shibata, D. K. (2007). Differences in brain structure in deaf persons on MR imaging studied with voxel-based morphometry. *American Journal of Neuroradiology*, *28*, 243–249.

Simon, H. J., Divenyi, P. L., & Lotze, A. (2002). Lateralization of narrow-band noise by blind and sighted listeners. *Perception*, *31*, 855–873.

Sladen, D. P., Tharpe, A. M., Daniel, A., & Grantham, D. W. (2005). Visual attention in deaf and normal hearing adults: Effects of stimulus compatibility. *Journal of Speech, Language, and Hearing Research*, *48*, 1529–1537.

Small, D. M., Gregory, M. D., Mak, Y. E., Gitelman, D., Mesulam, M. M., & Parrish, T. (2003). Dissociation of neural representation of intensity and affective valuation in human gustation. *Neuron*, *39*, 701–711.

Small, D. M., Jones-Gotman, M., Zatorre, R. J., Petrides, M., & Evans, A. C. (1997a). A role for the right anterior temporal lobe in taste quality recognition. *The Journal of Neuroscience*, *17*, 5136–5142.

Small, D. M., Jones-Gotman, M., Zatorre, R. J., Petrides, M., & Evans, A. C. (1997b). Flavor processing: More than the sum of its parts. *Neuroreport*, *8*, 3913–3917.

Small, D. M., Zald, D. H., Jones-Gotman, M., Zatorre, R. J., Pardo, J. V., Frey, S., et al. (1999). Human cortical gustatory areas: A review of functional neuroimaging data. *Neuroreport*, *10*, 7–14.

Smith, R. S., Doty, R. L., Burlingame, G. K., & McKeown, D. A. (1993). Smell and taste function in the visually impaired. *Perception & Psychophysics*, *54*, 649–655.

Stevens, C., & Neville, H. (2006). Neuroplasticity as a double-edged sword: Deaf enhancements and dyslexic deficits in motion processing. *Journal of Cognitive Neuroscience*, *18*, 701–714.

Stinton, N., Atif, M. A., Barkat, N., & Doty, R. L. (2010). Influence of smell loss on taste function. *Behavioral Neuroscience*, *124*, 256–264.

Temmel, A. F., Quint, C., Schickinger-Fischer, B., Klimek, L., Stoller, E., & Hummel, T. (2002). Characteristics of olfactory disorders in relation to major causes of olfactory loss. *Archives of Otolaryngology—Head & Neck Surgery*, *128*, 635–641.

Vachon, P., Voss, P., Lassonde, M., Leroux, J. M., Mensour, B., Beaudoin, G., et al. (2009). Global motion stimuli and form-from-motion stimuli: Common characteristics and differential activation patterns. *The International Journal of Neuroscience*, *119*, 1584–1601.

Vanlierde, A., De Volder, A. G., Wanet-Defalque, M. C., & Veraart, C. (2003). Occipito-parietal cortex activation during visuo-spatial imagery in early blind humans. *Neuroimage*, *19*, 698–709.

Veldhuizen, M. G., Bender, G., Constable, R. T., & Small, D. M. (2007). Trying to detect taste in a tasteless solution: Modulation of early gustatory cortex by attention to taste. *Chemical Senses*, *32*, 569–581.

Veraart, C., Devolder, A. G., Wanetdefalque, M. C., Bol, A., Michel, C., & Goffinet, A. M. (1990). Glucose-utilization in human visual-cortex is abnormally elevated in blindness of early onset but decreased in blindness of late onset. *Brain Research*, *510*, 115–121.

Voss, P., Lassonde, M., Gougoux, F., Fortin, M., Guillemot, J. P., & Lepore, F. (2004). Early- and late-onset blind individuals show supra-normal auditory abilities in far-space. *Current Biology*, *14*, 1734–1738.

Wakefield, C. E., Homewood, J., & Taylor, A. J. (2004). Cognitive compensations for blindness in children: An investigation using odour naming. *Perception*, *33*, 429–442.

Wan, C. Y., Wood, A. G., Reutens, D. C., & Wilson, S. J. (2010). Early but not late-blindness leads to enhanced auditory perception. *Neuropsychologia*, *48*, 344–348.

Wanet-Defalque, M. C., Veraart, C., De Volder, A., Metz, R., Michel, C., Dooms, G., et al. (1988). High metabolic activity in the visual cortex of early blind human subjects. *Brain Research*, *446*, 369–373.

Weeks, R., Horwitz, B., Aziz-Sultan, A., Tian, B., Wessinger, C. M., Cohen, L. G., et al. (2000). A positron emission tomographic study of auditory localization in the congenitally blind. *The Journal of Neuroscience*, *20*, 2664–2672.

Wong, M., Gnanakumaran, V., & Goldreich, D. (2011). Tactile Spatial Acuity Enhancement in Blindness: Evidence for Experience-Dependent MechanismsTactile Spatial Acuity Enhancement in Blindness: Evidence for Experience-Dependent Mechanisms. *The Journal of Neuroscience*, *31*, 7028–7037.

Zatorre, R. J., Jones-Gotman, M., Evans, A. C., & Meyer, E. (1992). Functional localization and lateralization of human olfactory cortex. *Nature*, *360*, 339–340.

Zwiers, M. P., Van Opstal, A. J., & Cruysberg, J. R. (2001). A spatial hearing deficit in early-blind humans. *The Journal of Neuroscience*, *21*, RC142, 1–5.