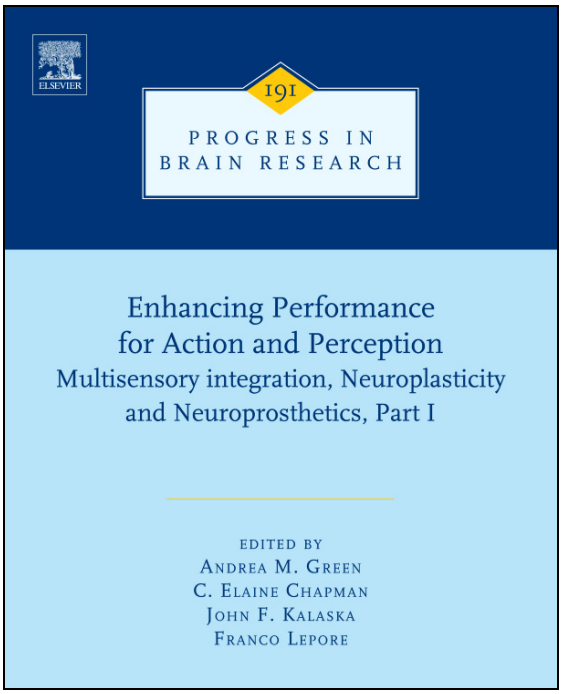

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CHAPTER 16

Adaptive crossmodal plasticity in deaf auditory cortex: areal and laminar contributions to supranormal vision in the deaf

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Abstract: This chapter is a summary of three interdigitated investigations to identify the neural substrate underlying supranormal vision in the congenitally deaf. In the first study, we tested both congenitally deaf and hearing cats on a battery of visual psychophysical tasks to identify those visual functions that are enhanced in the congenitally deaf. From this investigation, we found that congenitally deaf, compared to hearing, cats have superior visual localization in the peripheral field and lower visual movement detection thresholds. In the second study, we examined the role of "deaf" auditory cortex in mediating the supranormal visual abilities by reversibly deactivating specific cortical loci with cooling. We identified that in deaf cats, reversible deactivation of a region of cortex typically identified as the posterior auditory field (PAF) in hearing cats selectively eliminated superior visual localization abilities. It was also found that deactivation of the dorsal zone (DZ) of "auditory" cortex eliminated the superior visual motion detection abilities of deaf cats. In the third study, graded cooling was applied to deaf PAF and deaf DZ to examine the laminar contributions to the superior visual abilities of the deaf. Graded cooling of deaf PAF revealed that deactivation of the superficial layers alone does not cause significant visual localization deficits. Profound deficits were identified only when cooling extended through all six layers of deaf PAF. In contrast, graded cooling of deaf DZ showed that deactivation of only the superficial layers was required to elicit increased visual motion detection

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thresholds. Collectively, these three studies show that the superficial layers of deaf DZ mediate the enhanced visual motion detection of the deaf, while the full thickness of deaf PAF must be deactivated in order to eliminate the superior visual localization abilities of the congenitally deaf. Taken together, this combination of experimental approaches has demonstrated a causal link between the crossmodal reorganization of auditory cortex and enhanced visual abilities of the deaf, as well as identified the cortical regions responsible for adaptive supranormal vision.

Keywords: reversible deactivation; posterior auditory field; dorsal zone; congenital deafness; cortical plasticity.

Introduction

A remarkable feature of the brain is its ability to respond to change. Among other functions, this neuroplastic process endows a complex nervous system with the facility to adapt itself to its environment but, at the same time, also makes it susceptible to impoverished sensory or developmental experiences. For example, the expansion of somatosensory maps following limb amputation often results in spurious perceptual events known as "phantom limb pain" (e.g., Ramachandran and Hirstein, 1998) or untreated amblyopia results in the profound loss of visual acuity (reviewed by Webber and Wood, 2005). Neither of these neuroplastic effects have adaptive significance. However, there is a clear adaptive benefit when the inputs from another, intact modality substitute for those that have been lost (Collignon et al., 2009; Merabet and Pascual-Leone, 2010). Adaptive crossmodal plasticity can not only provide a form of partial compensation by one modality for another (e.g., auditory spatial localization in the blind) but also enhance perceptual performance within the remaining sensory modalities (but see Brozinsky and Bavelier, 2004; Finney and Dobkins, 2001). Numerous reports document improvement over intact subjects in auditory and somatosensory tasks in blind individuals (D'Anguilli and Waraich, 2002; Grant et al., 2000; Lewald, 2007; Sathian, 2000, 2005; Weeks et al., 2000), as well as enhanced performance in visual and tactile behaviors in the deaf (Bavelier et al., 2000; Levanen and Hamdof, 2001).

Although research has endeavored to identify the brain structures responsible for the behavioral enhancements resulting from adaptive crossmodal plasticity, it has been noted by many of these same studies that the specific neurological substrate for the effect is largely unknown (Doucet et al., 2006; Lambertz et al., 2005; Lee et al., 2003). Furthermore, the scant but growing literature on this topic seems to be fractionated into sides: one which asserts that crossmodal plasticity results in the wholesale reorganization of all of the affected regions, while the other indicates that crossmodal plasticity occurs only at selective regions therein (see review of Bavelier and Neville, 2002). Given that compensatory crossmodal plasticity appears not to affect brainstem structures (Langers et al., 2005, but see Shore et al., 2009), the suggestion that this phenomenon requires the cerebral cortex is supported by numerous studies (Rauschecker, 1995, 2002). Many of these investigations indicate that entire cortical representations vacated by the damaged sensory modality are completely replaced by inputs from the remaining systems (Bavelier and Neville, 2002). For example, imaging studies of crossmodal plasticity in early-deaf individuals have reported visual activation of auditory cortex partially including its core, or primary levels (Finney et al., 2001; Lambertz et al., 2005), and Braille reading or tactile tasks activated visual cortices in blind subjects

(Levanen and Hamdof, 2001; Sathian, 2000, 2005). Accordingly, these observations logically led to the general assumption that all cortical areas possess the ability for crossmodal plasticity. Indeed, the potential for such wholesale reorganization is supported by results from studies using a series of neonatal lesions in experimental animals (Roe et al., 1990; Sur et al., 1990). However, support for such global effects is not universal, and several studies (Nishimura et al., 1999; Weeks et al., 2000) specifically noted that primary auditory cortex was not crossmodally reorganized in their early-deaf subjects. Also, these observations favoring selective reorganization have been corroborated more directly by electrophysiological recordings from primary auditory cortices of congenitally deaf cats, which found no evidence of crossmodal plasticity (Kral et al., 2003). Therefore, while a clear and increasing effort has been directed toward investigating the neural bases for adaptive crossmodal plasticity, knowledge of the underlying brain circuitry remains virtually unexplored.

A modest number of studies have been directed toward revealing behavioral/perceptual effects of crossmodal plasticity. The most notable of these efforts is the work of Rauschecker and colleagues, who used visual deprivation to examine the effect of crossmodal compensatory plasticity in cortex. These now classic studies revealed that, in cats visually deprived from birth, the extent of the auditory field of the anterior ectosylvian sulcus (FAES) was greatly expanded (Rauschecker and Korte, 1993), its constituent neurons were more sharply spatially tuned (Korte and Rauschecker, 1993), and the behavioral localization of auditory stimuli was enhanced (Rauschecker and Kniepert, 1994). However, this ground-breaking work has not been furthered since the original series of reports and few, if any, other investigators have incorporated this model of crossmodal plasticity in their studies. In contrast, several labs have produced a highly engineered model of crossmodal plasticity through a strategic series of neonatal lesions in hamsters (Metin and Frost, 1989) and in ferrets (Pallas et al., 1999; Roe et al., 1990; Sur et al., 1990). However, such a model is as contrived as it is ingenious and, as such, it bears little semblance to naturally occurring neurological phenomena, such as blindness or deafness. Most profound examples of crossmodal plasticity result from loss of function in the peripheral sensory receptors or nerves, whereas central lesions that result in sensory loss generally are not available for reorganization because much of the affected area is essentially dead. However, a major effort has been directed toward understanding other forms of crossmodal effects, including plasticity (but not adaptive plasticity) involved in the visual calibration of auditory brainstem responses in barn owls (Gutfreund et al., 2002; Knudsen and Knudsen, 1989) and ferrets (King, 2002; King and Parsons, 1999). However, outside of these important efforts, the knowledge of cortical crossmodal reorganization is meager and a robust, repeatable, and more naturally occurring model of adaptive crossmodal plasticity has yet to be developed.

Congenitally deaf cat: a model for adaptive crossmodal plasticity

Like the visual system, auditory development passes through a sensitive period in which circuits and connections are established and then refined by experience (Knudsen, 2004; Kral et al., 2000). During this period, the functional maturation of auditory processing and perception is critically dependent on adequate auditory experience. Cats appear to progress through a critical phase at 2–3 months old, and complete their auditory maturation by 6 months (Kral et al., 2005). A similar, but more prolonged sensitive period seems to apply to humans (up to ~13 years; Doucet et al., 2006), as evidenced by congenitally deaf subjects who receive cochlear implants in early childhood and develop complete language competence. In contrast, those who do not receive such treatment

until later in life generally do not develop sophisticated language skills. The specific defects in the auditory system that underlie such persistent deficits remain to be identified. Some practitioners using imaging or EEG techniques have asserted that such deficits are the result of crossmodal plasticity that subsumes the nonfunctional parts of the auditory system into other sensory modes (Doucet et al., 2006; Finney et al., 2001; Lee et al., 2001). In contrast, studies done in congenitally deaf animals using single cell recording techniques have failed to show any crossmodal activation of primary auditory cortex (Kral et al., 2003) and that auditory nerve stimulation maintained access to primary auditory cortex even in congenitally deaf adults (Kral et al., 2002, 2005). Field A1 is functionally well characterized in congenitally deaf cats, with extensive deficits in spatiotemporal activity profiles as well as feature representation (Kral et al., 2009, Tillein et al., 2010) and corticocortical connectivity (reviewed in Kral and Eggermont, 2007). Chronic electrostimulation with a cochlear implant is known to show a sensitive period in cortical plasticity (reviewed in Kral et al., 2006). Thus, this model has been successful in demonstrating neurophysiological substrates of functional deficits after cochlear implantation. Ironically, despite the intense scrutiny that AI has received in these studies, with perhaps the exception of Sadato et al. (1996) in the visual cortex, virtually none of the crossmodally reorganized non-primary areas have been specifically identified. Although non-primary areas are "expected" to be reorganized, it is unclear whether these are similarly affected (and to the same degree). Therefore, the crucial debate in this regard is not only *if* deafness induces crossmodal plasticity, but *where* such plasticity occurs.

To that end, we initiated a series of experiments to examine adaptive crossmodal plasticity in the congenitally deaf cat. The cat is an appealing model system to use for these types of investigations on cerebral networks in auditory cortex. It is a simplified and tractable version of the more complex networks present in monkeys and humans. Cats are ideal because (1) they can quickly be trained to perform complex auditory tasks; (2) unlike the monkey, the majority of the auditory areas are easily approachable because they are exposed on the surfaces of gyri, rather than being buried in the depths of a sulcus; (3) each area is small enough so that it may be cooled by a single cryoloop (Lomber et al., 1999); and (4) they develop to maturity relatively quickly (over the course of months rather than years). Adult congenitally deaf cats show a Scheibe type of dysplasia in the organ of Corti with no hair cells present, although the spiral ganglion and cochlear bony structure are preserved (Heid et al., 1998). Preservation of the spiral ganglion cells is a major advantage when compared to pharmacologically deafened animals. The central auditory system of the congenitally deaf cat nonetheless shows expected deprivation-induced changes (Heid et al., 1998; Kral et al., 2006) although the central visual system appears normal in structure and function (Guillery et al., 1981; Levick et al., 1980). In the present study, deafness was confirmed by a standard screening method using auditory brainstem responses. In the first study, mature congenitally deaf cats and age-matched hearing cats were trained on a battery of seven visual psychophysical tests to identify those visual functions that are enhanced in the congenitally deaf. In the second study, we examined the role of "deaf" auditory cortex in mediating the superior visual abilities by reversibly deactivating specific cortical loci with cooling. This investigation revealed whether individual areas or collections of areas in deaf auditory cortex were the neural substrates for the superior visual functions. In the third study, graded cooling was applied to the areas identified in the second study to examine the laminar contributions to the superior visual abilities of the deaf. Overall, this combination of experimental approaches has demonstrated a causal link between the crossmodal reorganization of auditory cortex and enhanced

visual abilities of the deaf as well as identified the cortical regions responsible for supranormal vision.

Study 1: supranormal visual abilities of congenitally deaf cats

In the first study, the performance of adult hearing ($n=3$) and congenitally deaf cats ($n=3$) was compared on a battery of seven visual psychophysical tasks. For specific details on the tasks, see Lomber et al. (2010). The cats' ability to detect and localize flashed visual stimuli was assessed in a visual orienting arena (Fig. 1a) as we have done previously (Lomber and Payne, 2001; Malhotra et al., 2004). The six other tasks were conducted in a two-alternative forced-choice apparatus (Fig. 1b). To determine psychophysical thresholds, a standard staircase procedure was used, with three consecutive correct responses resulting in a decrease in the difference between the two stimuli, while each incorrect response resulted in an increase in the difference between the two comparison stimuli. Statistical significance was assessed using an analysis of variance and follow-up *t*-tests ($p<0.01$).

In the first task, we tested visual localization by placing the animals in an arena and examining their ability to accurately localize, by orienting and approaching, the illumination of red light-emitting diodes (LEDs) that were placed at 15° intervals across 180° of azimuth (Fig. 1a). In hearing controls, performance was excellent throughout the central 90° of the visual field (45° to the left and right), but accurate localization declined across the most peripheral targets tested (60–90°; Fig. 2a). In contrast, visual localization performance of deaf cats was maintained at higher levels throughout the most peripheral visual field (Fig. 2a). Performance of the deaf cats was significantly better for the 60°, 75°, and 90° positions ($p<0.01$), while there was no significant difference across the central 90° of the visual field (Fig. 2b). This result was consistent for both

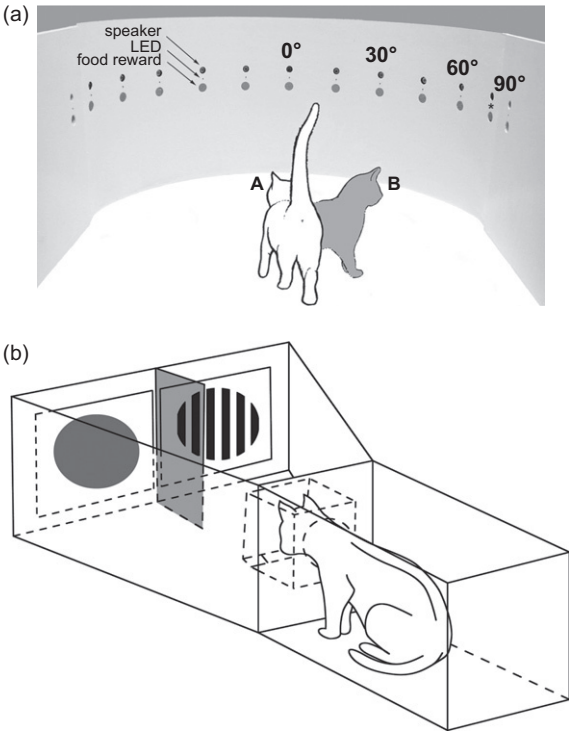

Fig. 1. (a) Orienting arena used for visual localization task. A loudspeaker (top circle) and a light-emitting diode (LED, black dot) were located above a food reward locus (lower circle) at each of 13 regularly spaced (15°) intervals (for sake of clarity, only 30° intervals are labeled). (A) The animal was first required to fixate on the central (0°) LED. (B) It then had to orient to, and approach, a secondary acoustic (100 ms broad-band noise) or visual (illumination of an LED) stimulus to receive a food reward. Adapted from Lomber et al. (2007). (b) Two-alternative forced-choice (2AFC) apparatus used for visual discrimination training and testing. The testing apparatus was a $52\times29\times41$ cm Plexiglas box with a 14 cm diameter opening at one end. This opening lead to a smaller Plexiglas enclosure into which the animal placed its head. This chamber contained two hinged transparent response keys which the cat could depress with its nose to register a response. The stimuli could be viewed through the response keys. The monitors were located 28 cm from the cat's eyes (thus 1 cm on the screen was 2 visual degrees). Beneath the response keys was the food reward terminal that dispensed a puree of beef liver and ground pork when the animal made a correct response.

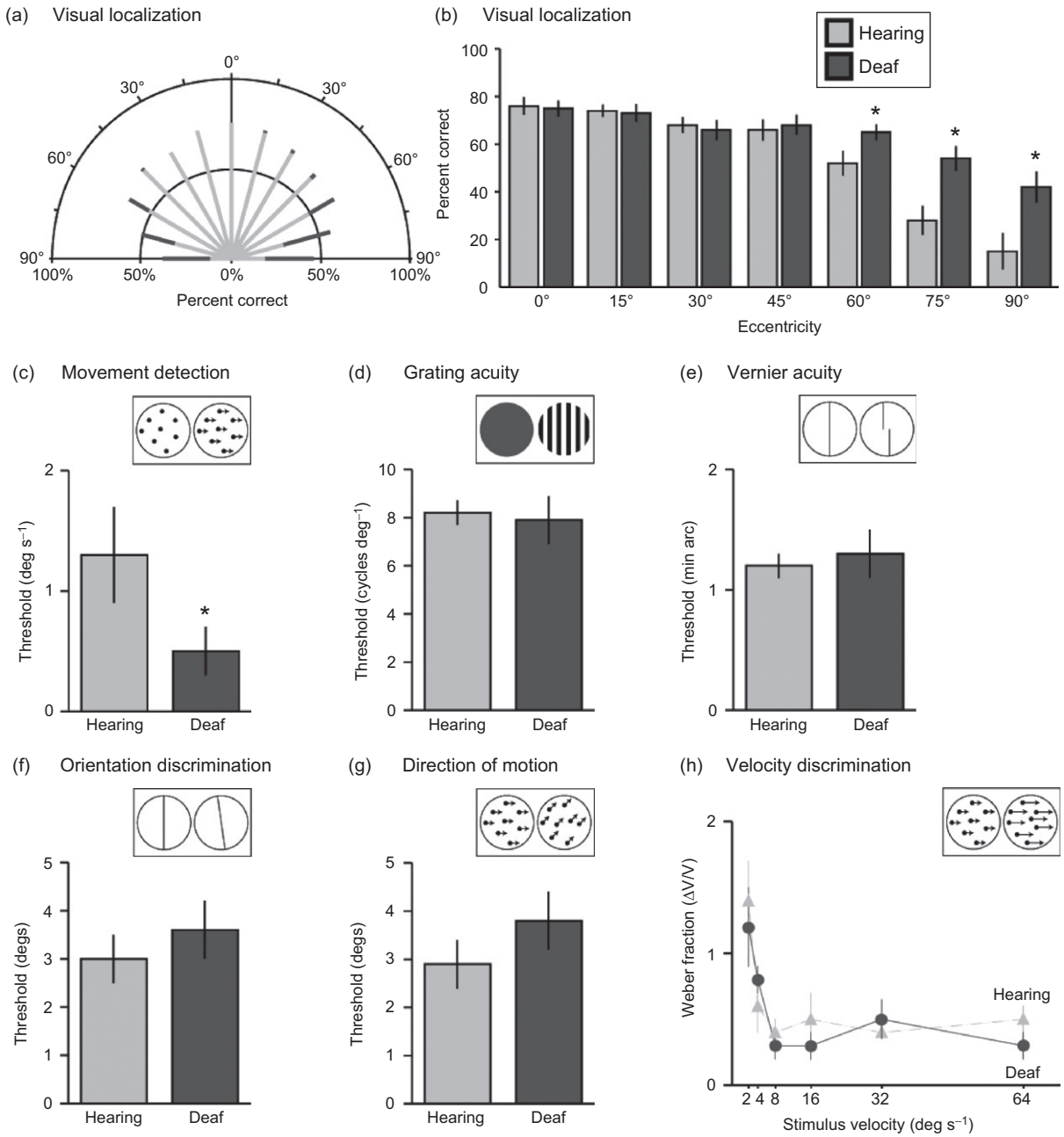

Fig. 2. Performance of hearing and deaf cats on the battery of seven visual psychophysical tasks. (a) Polar plot of the visual localization responses of hearing cats (light gray bars) and the superior performance of deaf cats (dark gray bars). The two concentric semicircles represent 50% and 100% correct response levels and the length of each colored line corresponds to the percentage of correct responses at each location tested. For both the hearing and deaf cats, data represent mean performance for 200 stimulus presentations at each peripheral target location and 400 stimulus presentations for the central target. (b) Histograms of combined data from left and right hemifields showing mean ± s.e. performance for the hearing (light gray) and deaf (dark gray) cats at each of the tested positions in the visual localization task. For both hearing and deaf cats, data represent mean performance for 400 stimulus presentations at each peripheral target location and 800 stimulus presentations for the central target (0°). (c–g) Mean threshold ± s.e. for the hearing and deaf cats on the movement detection (c), grating acuity (d), Vernier acuity (e), orientation (f), and direction of motion (g), discriminations. (h) Performance of the hearing and deaf cats on the velocity discrimination task. Data are presented as Weber fractions for six different stimulus velocities. Asterisks indicate significant differences ($p < 0.01$) between the hearing and deaf conditions. Sample stimuli are shown for each task. Figure adapted from Lomber et al. (2010).

binocular and monocular testing. Overall, the superior visual localization abilities of deaf cats correspond well with findings from prelingually deaf human subjects (Bavelier et al., 2006).

Six additional visual tests were all conducted in a two-alternative forced-choice apparatus using standard staircase procedures to determine psychophysical thresholds (Fig. 1b). In hearing cats, movement detection thresholds agreed with earlier reports (Pasternak and Merigan, 1980) and were identified to be $1.3 \pm 0.4^{\circ}\,s^{-1}$ (Fig. 2c). In contrast, movement detection thresholds for the deaf cats were significantly lower ($0.5 \pm 0.2^{\circ}\,s^{-1}$; Fig. 2c). For the remaining five tests of visual function (grating acuity, Vernier acuity, orientation discrimination, direction of motion discrimination, and velocity discrimination), performance of the deaf cats was not significantly different from hearing controls (Fig. 2d–h). Overall, in the first study, we found that congenitally deaf, compared to hearing, cats have supranormal visual abilities, specifically, superior visual localization in the peripheral field and lower visual movement detection thresholds.

Study 2: contributions of "deaf" auditory cortex to supranormal visual localization and detection

In the second study, portions of auditory cortex (Fig. 3a) were collectively and individually deactivated to determine if specific cortical areas mediated the enhanced visual functions. In both the deaf and hearing cats, individual cooling loops (Lomber et al., 1999) were bilaterally placed over the posterior auditory field (PAF), the dorsal zone of auditory cortex (area DZ), and primary auditory field (A1) because of their involvement in auditory localization in hearing cats (Malhotra and Lomber, 2007; Malhotra et al., 2008; Fig. 3b). An additional control cooling loop was placed over the anterior auditory field (AAF) because of its involvement in pattern, but not spatial, processing (Lomber and Malhotra, 2008).

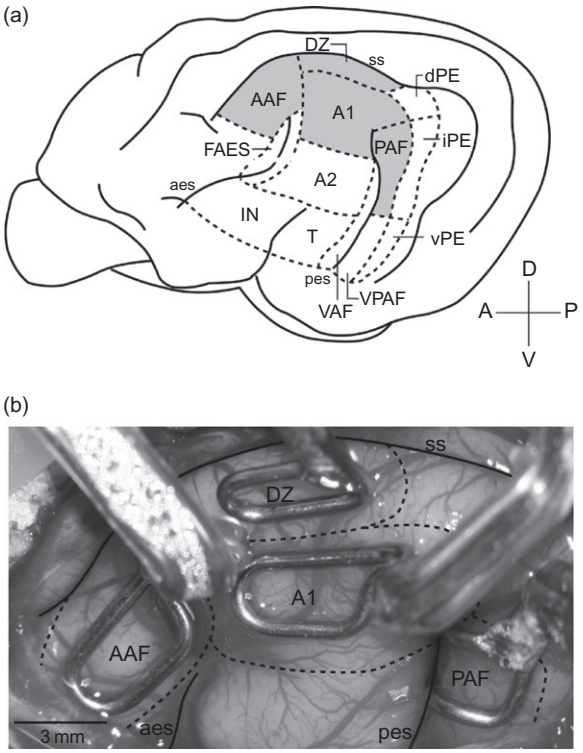

Fig. 3. Cortical areas examined in deaf auditory cortex. (a) Illustration of the left hemisphere of the cat cerebrum (adapted from Reinoso-Suárez, 1961) showing all auditory areas (lateral view) compiled from Reale and Imig (1980), de Ribaupierre (1997), and Tian and Rauschecker (1998). For abbreviations, see List. Areas examined are highlighted in gray. The areal borders shown in this figure are based on a compilation of electrophysiological mapping and cytoarchitectonic studies. (b) Cooling loops in contact with areas AAF, DZ, A1, and PAF of the left hemisphere of a congenitally deaf cat at the time of implantation. Left is anterior. The areal borders presented in this figure are based on the postmortem analysis of SMI-32 processed tissue from the brain shown in this photo. For abbreviations, see List. Figure adapted from Lomber et al. (2010).

Reversible cooling deactivation

The cooling method to reversibly deactivate neural tissue is an exciting, potent, and appropriate technique for examining cerebral contributions to behavior and has a number of highly beneficial

and practical features (Lomber, 1999). (1) Limited regions of the cerebral cortex can be selectively and reversibly deactivated in a controlled and reproducible way. Baseline and experimental measures can be made within minutes of each other (Lomber et al., 1996). (2) Repeated coolings over months or years produce stable, reversible deficits, with little evidence of attenuation or neural compensations (Lomber et al., 1994, 1999). (3) Repeated cooling induces neither local nor distant degenerations that might compromise conclusions (Yang et al., 2006). (4) Compared to traditional ablation studies, fewer animals are needed because within-animal-comparisons and double dissociations are possible, permitting large volumes of high-quality data to be acquired from each animal (Lomber and Malhotra, 2008; Lomber et al., 1996). (5) Finally, as the major effect of cooling is to block synaptic transmission, activity in fibers of passage is not compromised (Bénita and Condé, 1972; Jasper et al., 1970). Overall, the technique induces localized hypothermia in a restricted region of the brain. The locus of the deactivation is kept small by the constant perfusion of warm blood into, and around, the cooled region. The cooling disrupts calcium channel function in the presynaptic terminal and disrupts normal neurotransmitter release (reviewed by Brooks, 1983).

We have verified that the surgical procedure to implant cryoloops, their presence in contact with the cerebrum, and their operation disrupts neither the normal structural nor functional integrity of cortex (Lomber et al., 1999; Yang et al., 2006). In every instance, cell and myelin stains are rich, and the cyto- and myelo-architecture of the region are characteristic of the region investigated, with no signs of pathology, as might be revealed by a marked pale staining of neurons or gliosis or light staining of cytochrome oxidase (Lomber and Payne, 1996). However, the lack of damage to the cortex means that it is not possible to use traditional histological techniques to determine the region that was deactivated. In the second study, cortical temperatures surrounding the cooling loops were measured using multiple microthermocouples (150 μm in diameter; Omega Engineering, Stamford, CT) to determine the region of deactivation (Carrasco and Lomber, 2009). Across the cortical surface, 300–400 thermal measurements were taken from positions 500 μm below the pial surface. From these measurements, thermal cortical maps from cooling each individual cryoloop were constructed (Fig. 4). Depth of the cooling deactivation was also measured at four different coronal levels to provide an assessment of cooling spread in the Z-dimension. This information is provided in the third study.

Cortical loci investigated

We used reversible cooling deactivation (Lomber et al., 1999) to examine the contributions of PAF, DZ, A1, and AAF to determine if specific cortical areas mediated the enhanced visual functions. The extent of the cooling deactivations (Fig. 4) was determined from direct cortical temperature recordings that were matched with adjacent sections processed for SMI-32 that permitted the delineation of the different areas of auditory cortex (Mellott et al., 2010) as we have done previously (Lomber and Malhotra, 2008). The positions of these four loci, as well as how they relate to the cortical maps of other investigators, are described below.

Cooling loops were placed on PAF (Phillips and Orman, 1984; Reale and Imig, 1980), located caudal and ventral to A1. Loops were ~6 mm long and extended from the anterior one-third of the dorsal-posterior ectosylvian gyrus to the fundus of the posterior ectosylvian sulcus (pes). A heat shielding compound was applied to the anterior side of the PAF loops to keep the cooling deactivations localized to the posterior bank of the pes. All deactivations extended down the posterior bank of the pes to the fundus and did not include the anterior bank. Therefore, the deactivated region included all of area PAF or area P (Fig. 4a; Imig et al., 1982; Phillips and Orman, 1984). For all DZ cooling loops, the dorsal

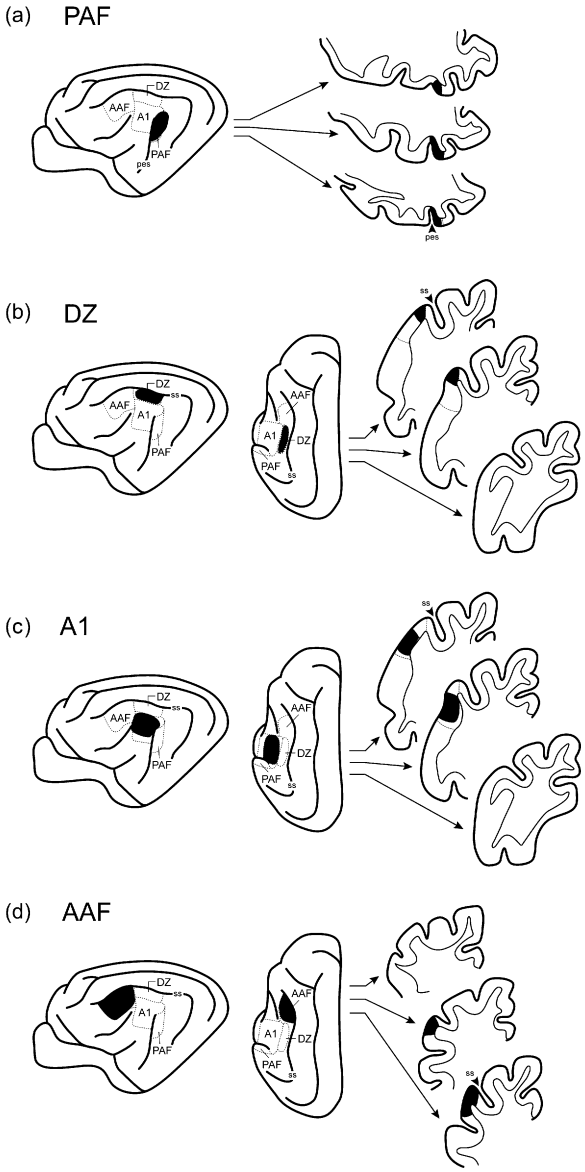

Fig. 4. Representative cooling deactivation reconstructions for the four cortical loci examined in the left hemisphere of a deaf cat. Black regions indicate deactivation extent as plotted from direct temperature measurements. The areal borders were determined by using SMI-32 staining criteria as we have done previously (Lomber and Malhotra, 2008). (a) Deactivation reconstruction showing a lateral (left is anterior) view of the left hemisphere with three horizontal sections in the vicinity of the cooling locus. (b–d) Reconstructions showing a lateral (left is anterior) and dorsal (top is anterior) view of the left hemisphere with three coronal sections in the vicinity of the deactivation locus. For abbreviations, see List.

edge of the middle ectosylvian gyrus along the lip of the middle suprasylvian sulcus (mss) was deactivated (Fig. 4b). The region of deactivation included the dorsal-most portion of the lateral bank of the mss. However, the cooling did not appear to directly affect either the anterolateral (ALLS) or posterolateral (PLLS) lateral suprasylvian visual areas (Palmer et al., 1978). For each loop, the deactivated region included the totality of the regions previously described as the DZ (Middlebrooks and Zook, 1983) and the suprasylvian fringe (Beneyto et al., 1998; Niimi and Matsuoka, 1979; Paula-Barbosa et al., 1975; Rose, 1949; Woolsey, 1960). For all A1 cryoloops, the central region of the middle ectosylvian gyrus between the dorsal tips of the anterior and pes was deactivated (Fig. 4c). The deactivations were from stereotaxic coronal levels A1–A12. The deactivated region did not include the dorsal-most aspect of the middle ectosylvian gyrus, along the lateral lip of the mss (Fig. 4c). For each loop, the deactivated region included the ventral 2/3's of the classically defined area A1 (Reale and Imig, 1980). The AAF (Knight, 1977; Phillips and Irvine, 1982; Reale and Imig, 1980) cryoloops were ~7 mm long and were located on the crown of the anterior suprasylvian gyrus between A10 and A17. All deactivations included the dorsal half of the lateral bank of the anterior suprasylvian sulcus and the dorsal half of the medial bank of the AES. Therefore, the deactivations included all of area AAF or area A (Fig. 4d), as defined by Knight (1977) and Reale and Imig (1980).

Visual localization in the peripheral field

For the visual localization task, the first step was to determine if auditory cortex could be mediating the enhanced visual performance of the deaf cats.

Therefore, we simultaneously deactivated all four areas (PAF, DZ, A1, and AAF) bilaterally, which resulted in a significant reduction in visual localization performance restricted to the most peripheral positions (60°, 75°, and 90° positions; Fig. 5a and b). Although the animals often failed to accurately or precisely localize the stimulus in the far periphery, they were not blind to the onset of the stimulus as the illumination of any LED always triggered a response. Therefore, the nature of the deficit was one of localization and not detection. Errors made during bilateral deactivation of all four areas were almost always undershoots of 30–60° (97.8% of all errors). Rarely (4.3% of all errors) were errors made to the incorrect hemifield. These results demonstrated that auditory cortex does have a role in mediating the enhanced visual localization performance of the congenitally deaf cats.

In order to ascertain if the enhanced localization skills could be further localized to specific cortical loci, each of the four auditory areas was individually bilaterally deactivated. In the deaf cats, bilateral deactivation of PAF significantly reduced localization performance to the most peripheral targets (60°, 75°, and 90° positions, $p < 0.01$) while leaving localization performance for the 0°, 15°, 30°, and 45° targets unchanged (Fig. 5c). The reduction in visual localization at the most peripheral locations resulted in performance that was not different from deactivating all four areas simultaneously (Fig. 5b). Moreover, the localization performance of the deaf cats during bilateral cooling of PAF was not different from hearing cats (Fig. 5g). Neither bilateral nor unilateral deactivation of DZ, A1, or AAF modified visual localization performance (Fig. 5d–f). Unilateral deactivation of PAF resulted in reduced visual localization to the same peripheral positions; however, the deficit was specific to the contralateral hemifield (Lomber et al., 2010). Consequently, the neural basis for the enhanced visual localization skills of the deaf cats can be ascribed to PAF. This is an intriguing finding because, in hearing cats, PAF is normally involved in the accurate localization of acoustic stimuli (Fig. 6; Lomber and Malhotra, 2008; Malhotra and Lomber, 2007). Bilateral deactivation of PAF in hearing cats results in profound *acoustic* localization deficits across the frontal field (Fig. 6). Therefore, the present results demonstrate that in deafness, PAF maintains a role in localization, albeit visual rather than acoustic. These results demonstrate that crossmodal plasticity can substitute one sensory modality for another while maintaining the functional repertoire of the reorganized region.

Visual motion detection

For the supranormal visual motion detection abilities identified in the congenitally deaf cats, a similar experimental approach was taken to ascertain if "deaf" auditory cortex played a role in the enhanced motion detection. To determine if auditory cortex could be mediating the enhanced motion detection performance of deaf cats, we simultaneously deactivated all four areas (PAF, DZ, A1, and AAF). Bilateral deactivation of all four areas significantly increased motion discrimination thresholds from 0.44 ± 0.19 to $1.39 \pm 0.35° s^{-1}$ (Fig. 7a). This finding established that auditory cortex does have a role in mediating the enhanced motion detection performance of the deaf cats.

Next, to determine if a specific auditory region could be mediating the enhanced visual motion detection skills of deaf cats, areas PAF, DZ, A1, and AAF were individually bilaterally cooled. Bilateral deactivation of DZ significantly increased the motion detection thresholds from 0.40 ± 0.15 to $1.46 \pm 0.4° s^{-1}$ (Fig. 9c). This increase resulted in performance that was not different from deactivating all four areas simultaneously (Fig. 7c). Moreover, the increase in threshold resulted in performance that was not different from performance of the hearing cats (Fig. 7f). There was no evidence of any functional lateralization, as unilateral deactivation of either left or right DZ did not alter performance (Lomber et al., 2010). Neither bilateral (Fig. 7b, d, and e) nor unilateral (Lomber et al.,

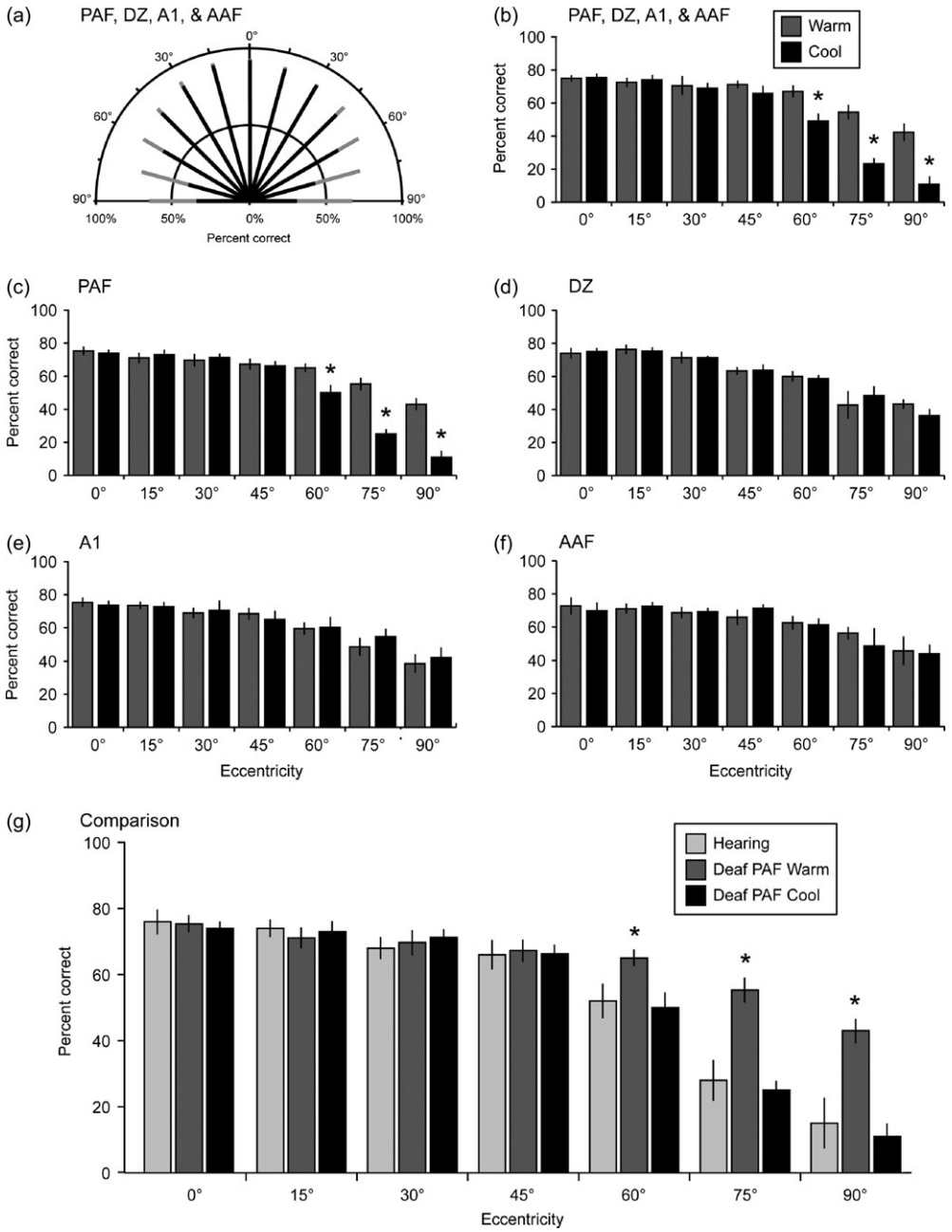

Fig. 5. Visual localization task data from deaf cats during bilateral reversible deactivation of PAF, DZ, A1, and AAF. (a) Polar plot of the visual localization responses of deaf cats while cortex was warm (dark gray) and active and during simultaneous cooling deactivation of PAF, DZ, A1, and AAF (black). (b–f) Histogram of combined data from the left and right hemifields showing mean ± s.e. performance for deaf cats while cortex was warm (dark gray) and active and while it was cooled (black) and deactivated. Asterisks indicate a significant difference ($p < 0.01$) between the warm and cool conditions. (b) Data from the simultaneous deactivation of PAF, DZ, A1, and AAF. (c–f) Data from individual area deactivations. (g) Visual localization data comparing performance at each position for hearing cats (light gray), deaf cats while PAF was warm (dark gray), and deaf cats while PAF was cooled (black). Asterisks indicate a significant difference ($p < 0.01$) from the hearing and deaf PAF cool conditions. Figure adapted from Lomber et al. (2010).

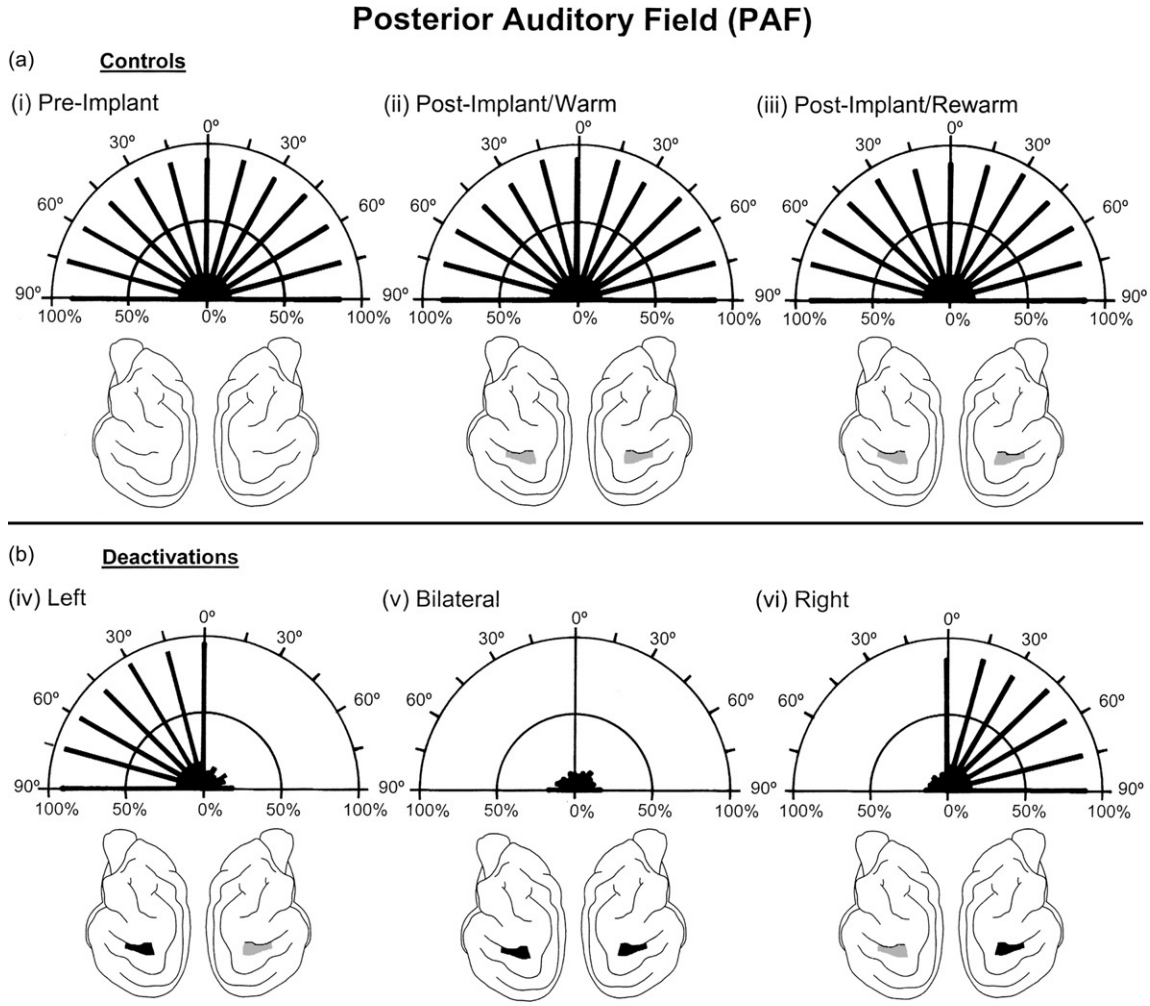

Fig. 6. Orienting responses to an acoustic stimulus during deactivation of PAF. Lateral view icons of the cat brain indicate the presence and position of a cryoloop (gray shading), and its operational status (black indicates loop was on and cortex was deactivated). For conventions, see Fig. 2. (a) Control data collected: (i) prior to PAF cryoloop implantation, (ii) after PAF cryoloop implantation and prior to cooling in each testing session, and (iii) shortly after termination of cooling. (b). Deactivation data collected: (iv) during cooling of left PAF, (v) during bilateral cooling of PAF, and (vi) during cooling of right PAF. Note that unilateral deactivation of PAF caused sound localization deficits in the contralateral field with no impairments in the ipsilateral hemifield. Bilateral deactivation of PAF resulted in bilateral sound localization deficits. Data summarized from seven animals. Figure adapted from Malhotra and Lomber (2007).

2010) deactivation of PAF, A1, or AAF resulted in any change in motion detection thresholds. These results demonstrate that DZ cortex mediates the superior visual motion detection thresholds of deaf cats. DZ has neuronal properties that are distinct from A1 (He et al., 1997; Stecker et al., 2005) and is involved in sound source localization (Malhotra et al., 2008) and duration coding (Stecker et al., 2005). Here, we show DZs involvement in visual motion detection in deaf cats. A role for DZ in

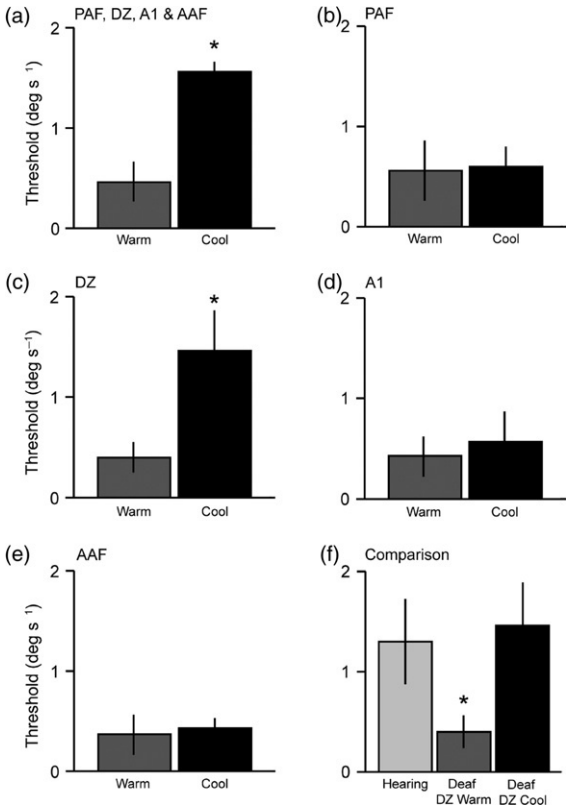

Fig. 7. Motion detection thresholds for the deaf cats before and after cooling deactivation and during bilateral reversible deactivation. (a–e) Histograms showing mean ± s.e. motion detection thresholds for deaf cats while cortex was warm (dark gray) and active and while it was cooled (black) and deactivated. Asterisks indicate a significant difference ($p < 0.01$) between the warm and cool conditions. (a) Motion detection thresholds from deaf cats during bilateral reversible deactivation of PAF, DZ, A1, and AAF. (b–e) Data from individual area deactivations. (f) Motion detection thresholds to compare performance of hearing cats (light gray), deaf cats while DZ was warm (dark gray), and deaf cats while DZ was cooled (black). Asterisks indicate a significant difference ($p < 0.01$) from the hearing and deaf DZ cool conditions. Figure adapted from Lomber et al. (2010).

acoustic motion processing has yet to be investigated. Overall, in the second study, we were able to ascribe superior visual localization functions to PAF (Fig. 5g) and the superior motion detection abilities to DZ (Fig. 7f) in the same animals.

Deactivation of auditory cortex in hearing cats does not alter visual function

As we have demonstrated that "deaf" auditory cortex is the neural substrate for the enhanced visual abilities of the deaf, it was essential to also demonstrate that the auditory cortex of hearing cats does not contribute to visual function. Therefore, for the group of hearing cats, we both simultaneously and individually deactivated the four auditory areas on each of the seven visual tasks. Overall, neither simultaneous nor individual deactivation of the four auditory regions altered the ability of the hearing cats to perform any of the seven visual tasks (Lomber et al., 2010). These results demonstrate that in the presence of functional hearing, the auditory cortex does not contribute to any of the visual tasks examined. Therefore, deficits in visual function identified during bilateral deactivation of PAF or DZ in the deaf cats must be caused by underlying crossmodal adaptive plasticity in each area.

Study 3: laminar contributions to supranormal vision in the deaf

As we have demonstrated that individual areas of deaf auditory cortex contribute to supranormal visual localization in the periphery or visual motion detection, we next sought to determine if these functions could then be further localized in the laminar domain (Lomber and Payne, 2000; Lomber et al., 2007). Our approach was to apply lesser or greater levels of cooling to PAF or DZ to deactivate the cortical thickness in a graded, yet consistent, way, the more-superficial layers alone or in combination with the deep layers (Lomber and Payne, 2000; Lomber et al., 2007).

With PAF cryoloop temperatures between 10 and 38 °C, deaf cats are proficient at accurately reporting the location of a peripheral visual stimulus (Fig. 8a). Cooling to progressively lower temperatures (< 10 °C) first initiated and then maximized an impairment in peripheral visual

localization, which was reduced to performance levels of hearing animals, at a cryoloop temperature of 3±1 °C (Fig. 8a). Similarly, cooling of the DZ loop to progressively lower temperatures resulted in a rise in visual detection threshold (Fig. 8b). Visual motion detection threshold began to rise at cryoloop temperatures of 14 °C and continued to rise to performance levels no different from hearing animals, until a temperature of 8 °C were reached (Fig. 8b). However, the initiation temperature for the change in performance (14 °C) and the temperature producing a maximal deficit (8 °C) were both lower in all three deaf cats examined than the respective temperatures identified on the visual localization task for the same animals during PAF cooling.

The different temperatures for initiation and maximum deficit for the two cortical areas can potentially be explained by changes in the laminar extent of cooling to disrupt visual localization in PAF rather than visual motion detection in DZ. As 20 °C is the critical temperature below which neurons are silenced by blockade of synaptic transmission from afferent fibers (Bénita and Condé, 1972; Jasper et al., 1970; Lomber et al., 1999), we used arrays of microthermocouples to measure temperatures at more than 300 sites below each of the cryoloops (PAF and DZ) to ascertain the position of the 20 °C thermocline. The positions of the temperature measurements were reconstructed using microlesions and depth measurements to determine the temperature profiles in the deaf cats from which the recordings were made. For each of the cooling loop locations (PAF and DZ), data were collected from each of the three deaf cats. A compilation of data from multiple tracks with a DZ cryoloop sequentially cooled to two different temperatures (8 °C and 3 °C) is presented in Fig. 9. Cortex between the 20 °C thermocline and the cryoloop (gray field) has temperatures of <20 °C and is deactivated by the cooling, whereas locations more distal from the cryoloop than the 20 °C thermocline have temperatures >20 °C and remain active (Fig. 10). Similar laminar deactivations were also determined for PAF (Fig. 11) cooling loops.

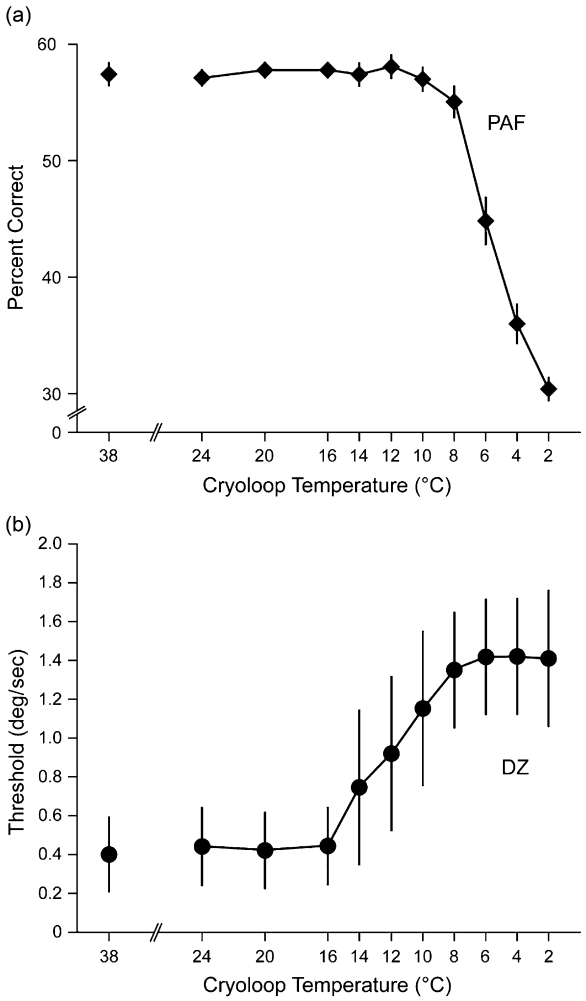

Fig. 8. Graphic representation of performance levels of deaf cats on the visual localization task (a) and the motion detection task (b) as a function of PAF or DZ cryoloop temperature, respectively. Each graph shows mean±s.e. performance for blocks of trials collected at different cryoloop temperatures. (a) Black diamonds and lines represent mean performance of deaf cats performing the visual orienting task (mean performance across the three peripheral-most positions (60°, 75°, and 90°)) during bilateral cooling of PAF. (b) Black circles and lines represent mean performance of deaf cats performing visual motion detection task during bilateral cooling of DZ. Note that for the motion detection task (b) that thresholds begin to increase at cryoloop temperatures below 16 °C and reaches a maximum deficit at 8 °C. In contrast, visual localization performance (a) begins to fall at cryoloop temperatures below 10 °C and reaches a maximum deficit at 2 °C.

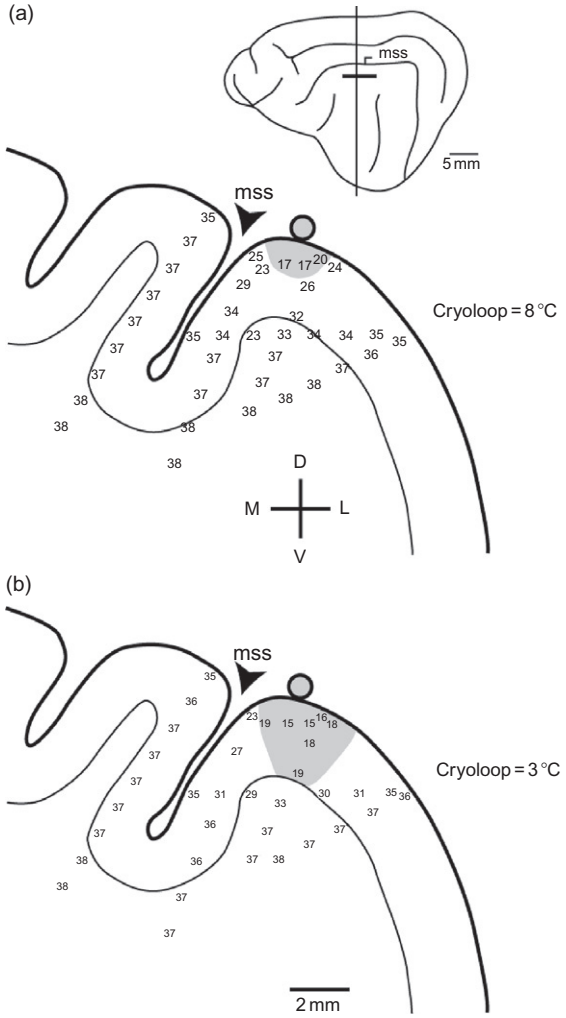

Fig. 9. Temperature measurements recorded from identical sites in, and around, the dorsal zone (DZ) of auditory cortex when the cooling loop (circle with gray fill) was cooled to 8 °C (a) and 3 °C (b). Vertical line on the lateral view of the left cerebrum shows the position of the coronal section shown in (a) and (b). Gray region indicates the depth of cortex that was at, or below, 20 °C as estimated from these measurements. For abbreviations, see List.

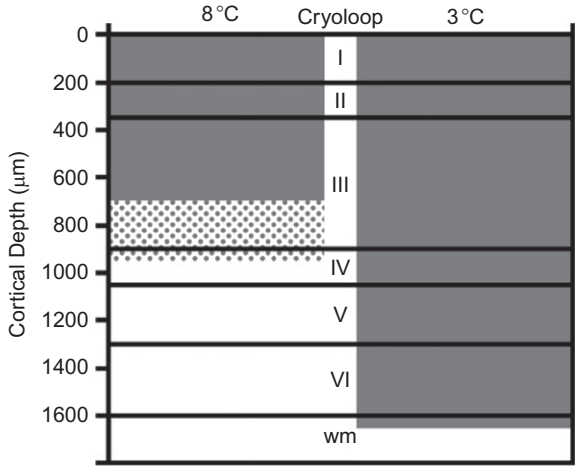

Fig. 10. Summary of deactivation depth when a cryoloop was cooled to 8 and 3 °C. Temperatures <20 °C, where synaptic transmission is eliminated, are indicated by the gray field. Temperature between 20 and 24 °C, where synaptic activity is impaired, is indicated by light stipple. Adapted from Lomber et al. (2007).

It is readily apparent from Figs. 9 and 11 that the effect of reducing cryoloop temperature from 8 to 3 °C pushed the 20 °C thermocline from the middle cortical layers to the gray/white matter interface. Therefore, when the cooling loop was at 8 °C, the resulting deactivation silenced the superficial layers (I–III) alone, and when the cooling loop was at 3 °C, the resulting deactivation silenced the superficial and deep layers together. However, instead of the change in cortical deactivation depth explaining the behavioral results observed, it is possible that the change in lateral expansion of the deactivation could underlie the behavioral results. There was a slight lateral expansion in the extent of layers I–III that was deactivated as the cryoloop temperature was lowered from 8 to 3 °C. For each of the two regions examined (PAF and DZ), in cross-sectional terms, estimates of lateral movement of the 20 °C thermocline on the cortical surface as cooling loop temperature was lowered from 8 to 3 °C show an increase in surface area of <25%, while the depth of cortex deactivated by lowering the temperature of the cryoloop in this way was increased by >140%. Thus, the major effect of the additional cooling was to push the 20 °C thermocline across the deep layers of cortex with minor lateral surface movement.

The most parsimonious interpretation of the differences in extents of deactivations is that

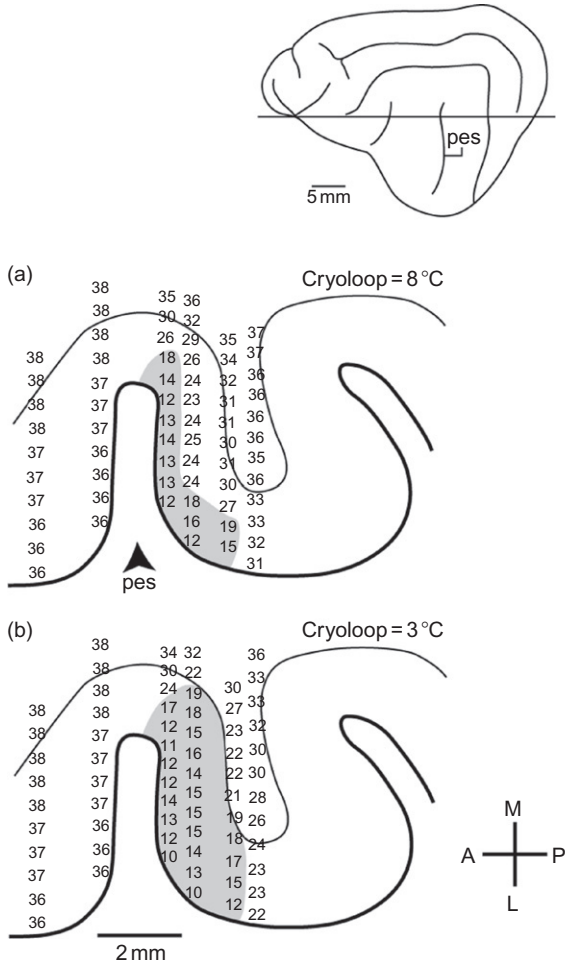

Fig. 11. Temperature measurements recorded from identical sites in the posterior ectosylvian suclus (pes) when a PAF cooling loop was cooled to 8 °C (a) and 3 °C (b). Horizontal line on the lateral view of the left cerebrum (top right) shows the position of the horizontal section shown in (a) and (b). Gray region indicates the depth of cortex that was at, or below, 20 °C as estimated from these measurements. Note that temperatures remain high in the anterior bank of the posterior ectosylvian sulcus due to the application of a heat shielding compound to the anterior surface of the cooling loop. For abbreviations, see List.

motion detection processing in deaf DZ is critically dependent upon the superficial cortical layers and that visual localization processing in deaf PAF is critically dependent upon the deep cortical layers. A critical component in acceptance of this interpretation is the recognition that deep layer neurons remain active when upper layer neurons are silenced. Control physiological measures made in other cats verify deep layer activity in the absence of upper layer activity, and confirm the results of others in the visual system of intact cats that deep layer neurons remain active in the absence of activity in the superficial layers (Ferster et al., 1996; Schwark et al., 1986; Weyand et al., 1986, 1991).

In the deaf cats, we observed deactivation of PAF eliminates supranormal visual localization abilities. We further observed that it is necessary to cool both the superficial and deep layers of PAF in order to completely eliminate the visual localization sensory enhancements. These results are interesting for two reasons. First, in hearing cats, PAF is normally involved in the accurate localization of *acoustic* stimuli (Fig. 6; Lomber and Malhotra, 2008; Malhotra and Lomber, 2007). This suggests that in deafness, PAF maintains a role in localization, albeit visual rather than acoustic. This is consistent with the hypothesis that the behavioral role of a crossmodally reorganized area is related to its role in hearing/sighted individuals (Lomber et al., 2010; Meredith et al., 2011). Second, in hearing cats, in order to eliminate accurate acoustic localization, it is only necessary to deactivate the superficial layers of PAF (Lomber et al., 2007). Therefore, only the superficial layers of PAF need to be deactivated to disrupt acoustic localization in hearing animals, while both the superficial and deep layers of PAF must be deactivated in order to disrupt the supranormal visual localization abilities of congenitally deaf cats. Taken together, it will be interesting to examine possible differences in the input and output circuitry of the superficial and deep layers of PAF in congenitally deaf cats compared to hearing animals. Identification of the circuitry underlying crossmodal plasticity is essential toward providing a substrate on which the phenomenon can be studied and manipulated to reveal the fundamental principles governing its organization, function, and potential for therapeutic intervention.

Significance

Collectively, these results provide new and comprehensive insight into the crossmodal effects induced by congenital deafness to a level that is essentially unobtainable through other methods. In addition, these observations form the basis for a robust and repeatable model of adaptive crossmodal plasticity that will be used to uncover the basic principles that characterize this phenomenon as well as better understand its relation to neuroplastic processes as a whole. By characterizing the regions of auditory cortex that are susceptible to crossmodal plasticity following deafness, we may be able to reveal the roles of intrinsic constraints and environmental input in determining cortical functional specificity. Such information will be critical for predicting and evaluating the success of sensory implants in humans (Kral and O'Donoghue, 2010; Rauschecker and Shannon, 2002; Zrenner, 2002). Specifically, crossmodal reorganization in deprived auditory cortex, like that identified in the present investigations, may hinder the ability of auditory cortex to process new auditory input provided by a cochlear implant (Bavelier and Neville, 2002; Kral and Eggermont, 2007). Studies suggest that deaf subjects, in whom crossmodal plasticity was the most extensive, were the least likely to benefit from cochlear prosthetics (Lee et al., 2001). Therefore, further investigations are necessary in order to more closely examine the link between crossmodal plasticity in deprived auditory cortex and the functional outcomes of cochlear prosthetics. Ultimately, future experiments could use this model of crossmodal plasticity to empirically assess potential windows for therapeutic interventions.

Acknowledgments

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Abbreviations

A	anterior
AAF	anterior auditory field
aes	anterior ectosylvian sulcus
AI or A1	primary auditory cortex
AII or A2	second auditory cortex
D	dorsal
dPE	dorsal-posterior ectosylvian area
DZ	dorsal zone of auditory cortex
FAES	auditory field of the anterior ectosylvian sulcus
IN	insular region
iPE	intermediate posterior ectosylvian area
L	lateral
M	medial
mss	middle suprasylvian sulcus
P	posterior
pes	posterior ectosylvian sulcus
PAF	posterior auditory field
ss	suprasylvian sulcus
T	temporal region
V	ventral
VAF	ventral auditory field
VPAF	ventral posterior auditory field
vPE	ventral posterior ectosylvian area

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