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Somatosensory and Visual Crossmodal Plasticity in the Anterior Auditory Field of Early-Deaf Cats

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Abstract

It is well known that the postnatal loss of sensory input in one modality can result in crossmodal reorganization of the deprived cortical areas, but deafness fails to induce crossmodal effects in cat primary auditory cortex (A1). Because the core auditory regions (A1, and anterior auditory field AAF) are arranged as separate, parallel processors, it cannot be assumed that early-deafness affects one in the same manner as the other. The present experiments were conducted to determine if crossmodal effects occur in the anterior auditory field (AAF). Using mature cats ($n=3$), ototoxically deafened postnatally, single-unit recordings were made in the gyrus and sulcal portions of the AAF. In contrast to the auditory responsivity found in the hearing controls, none of the neurons in early-deafened AAF were activated by auditory stimulation. Instead, the majority (78%) were activated by somatosensory cues, while fewer were driven by visual stimulation (44%; values include unisensory and bimodal neurons). Somatosensory responses could be activated from all locations on the body surface but most often occurred on the head, were often bilateral (e.g., occupied portions of both sides of the body), and were primarily excited by low-threshold hair receptors. Visual receptive fields were large, collectively represented the contralateral visual field, and exhibited conventional response properties such as movement direction and velocity preferences. These results indicate that, following postnatal deafness, both somatosensory and visual modalities participate in crossmodal re-innervation of the AAF, consistent with the growing literature that documents deafness-induced crossmodal plasticity outside A1.

1.0 Introduction

Numerous studies have detailed the effect of peripheral deafness on brainstem nuclei as well as on the medial geniculate thalamus (Kitzes and Semple, 1985; Moore, 1994; Moore et al., 1994; Kral et al., 2000; Shepherd and Hardie, 2001). Thus, it should be expected that cochlear damage would have widespread effects on their ultimate projection targets in auditory cortex (e.g., see Kral et al., 2000; 2005; Kral, 2007; Tillien et al., 2010). However, although numerous auditory cortical fields have been identified, as well as their hierarchical relationship proposed (Roullier et al., 1991), the sensory nature of few cortices outside primary auditory cortex (A1) have been evaluated following deafness. Because it is well known that cortical areas deprived of their normal sensory inputs in early developmental stages can be reorganized by the remaining senses through the process of crossmodal

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plasticity, this phenomenon has been used as a measure of the sensory character of cortex in the deaf (or blind). However, amongst such studies, there seems to be little consensus on the crossmodal status of deafened A1. Some imaging studies of early-deaf humans have reported crossmodal innervation of A1 (Auer et al., 2007), limited crossmodal effects (Finney et al., 2001), or no A1 involvement at all (Hickok et al., 1997; Weeks et al., 1998; Kral et al., 2003). Little investigative attention has been directed toward deaf non-primary areas, although area A2, and others, have been reported to show visual activation in early-deaf humans (Weeks et al., 1998). Recently, the cat posterior auditory field (PAF), dorsal zone of auditory cortex (DZ), and auditory field of the anterior ectosylvian sulcus (FAES), have all been shown to crossmodally reorganize to perform visual behavioral tasks (Lomber et al., 2010; Meredith et al., 2011). Thus, there is a growing literature that establishes crossmodal effects in non-primary auditory cortices. However, in many species, the core auditory cortices are shared by A1 and area R (in primates), or anterior auditory field (AAF in carnivores) and virtually nothing is known about the influence of early-deafness on this important component of auditory core cortex, the AAF.

In the cat, the AAF is located largely on the anterior ectosylvian gyrus, although its tonotopy extends into at least the external half of the adjoining bank of the suprasylvian sulcus (Imig and Reale, 1980; Clemo et al., 2007). In the AAF, lower frequency tones are represented anteriorly with higher frequency bands posterior; their point of reversal represents the transition into the A1 representation (Merzenich et al., 1975; Knight, 1977; Reale & Imig, 1980). Some response properties of AAF and A1 neurons are similar, although AAF neurons are more broadly tuned and have shorter latencies than A1 neurons (Reale and Imig, 1980; Imaizumi et al., 2004; Carrasco and Lomber, 2009). Also, the thalamic inputs to AAF are largely independent of the thalamic inputs to A1, as few double labeled cells are identified in the auditory thalamus following frequency-matched retrograde tracer injections (Lee and Winer, 2008). Last, AAF and A1 are not functionally yoked, since deactivation of A1 has little to no influence on auditory processing in AAF (Carrasco and Lomber, 2009). Thus, because these structures are arranged as largely separate parallel processors of auditory information (Lee et al., 2004), it cannot be assumed that deafness affects one in the same manner as the other. Therefore, the goal of the present study was to examine the area corresponding to the auditory AAF of early-deafened cats for the presence of crossmodal reorganization. Because there was no *a priori* expectation for either visual or somatosensory reorganization in this region, both sensory modalities were evaluated. A preliminary abstract of this work has been presented (Meredith and Lomber, 2009).

2.0 Materials and Methods

Six adult cats (3 early-deaf, 3 hearing) were examined in this study. All procedures were performed in compliance with the Guide for Care and Use of Laboratory Animals (NIH publication 86-23) and the National Research Council's *Guidelines for the Care and Use of Mammals in Neuroscience and Behavioral Research* (2003) and approved by the Institutional Animal Care and Use Committee at Virginia Commonwealth University.

2.1 Auditory lesions

Three normally pigmented neonatal cats from two litters were given bilateral ototoxic cochlear lesions near the time of auditory onset (7-8 days post-natal; Shipley et al., 1980). Each animal received a systemic injection of ethacrynate sodium (25 mg/kg, i.v.) followed by kanamycin (200 mg/kg, s.c.), according to the protocol of (Xu et al., 1993). Following recovery, each kitten was returned to its mother. After weaning (approximately 40 days) each animal had its auditory brainstem response tested (ABR; Nicolet Spirit 2000 Evoked Potential System, Nicolet Biomedical Inc., Madison WI; stimulus: 15-95 dB, 0.1 ms squarewave click, rarefaction; 1/sec with 2-5k repetitions through calibrated minispeaker;

leads: vertex-to-ipsilateral mastoid using subcutaneous needle electrodes) to assess hearing function. At that time, all animals displayed a ~45 dB hearing deficit and required a second treatment (all by 50 DPN; prior to onset of auditory critical period Kral et al., 2005), after which their ABRs showed hearing deficits >95dB.

2.2 Electrophysiological recording

The cats matured for at least 10 months (298, 373 and 592 DPN; note that 180 DPN represents auditory maturity, Kral *et al.*, 2005) prior to final ABR testing, implantation and recording. Three adult cats with normal hearing experience were used as controls. Preparation for recording involved the aseptic implantation of a recording well/head holding device that permitted restraint/support without wounds or pressure points. For implantation, each mature animal was anesthetized (sodium pentobarbital, 40 mg/kg, i.p.) and its head was secured in a stereotaxic frame. A craniotomy was performed to expose the auditory cortices and a re-sealable stainless steel recording well was placed over the opening, banked with gel foam and anchored with stainless steel screws and dental acrylic. The scalp was sutured closed around the implant and routine postoperative care was provided. Approximately 5-7 days elapsed before the initial recording experiment.

Each recording experiment was initiated by anesthetizing the animal (ketamine 35 mg/kg; acepromazine 0.4mg/kg, i.m.) and securing the implant to a supporting bar. The animal was intubated and ventilated; expired CO₂ was monitored and maintained at ~4.5%. Fluids (lactated Ringer's solution), supplemental anesthetics (0.5mg ketamine/kg/hr; 0.05mg acepromazine/kg/hr) and a muscle relaxant (pancuronium bromide, 1mg/hr; to prevent ocular drift or involuntary movements during somatosensory testing) were continuously administered through a saphenous vein cannula. This regimen was effective in that spontaneous movements (including ocular drift) were suppressed for at least 30 minutes following cessation of drug infusion at the end of each recording session. Contact lenses were applied to prevent corneal desiccation; an opaque lens was inserted into the ipsilateral eye to avoid potential conflicts from ocular misalignment. The recording well was opened and the electrode (glass-insulated tungsten, <1M Ω), supported by a modified electrode carrier, was manually lowered to the cortical surface and advanced a hydraulic microdrive. Neuronal activity was amplified, displayed on an oscilloscope, and played on an audiometer. Neuronal waveforms of at least 3:1 signal/noise ratio were sought and isolated for study. Neurons were initially identified by their spontaneous activity and by their responses to auditory stimuli (hisses, claps, whistles, pops, etc.), somatosensory (puffs of air through a pipette, brush strokes and taps, manual pressure and joint movement) and visual search stimuli (flashed or moving spots or bars of light from a hand held ophthalmoscope projected onto the translucent 90 cm diameter hemisphere). The retina was activated and visual receptive fields were mapped by projecting a slit or spot of light onto the hemisphere; the projected stimulus was moved in all directions until a responsive area was delimited. For large receptive fields, the initial plotted borders were rechecked for consistency. Sensitivity to visual stimulus movement direction was assessed by moving the spot of light in up, down, nasal, temporal or diagonally-oriented directions and counting the evoked responses. Responses that showed 2:1 differential for movements in opposing directions were defined as direction selective (after Stein et al., 1993). Visual movement velocity preferences were examined by determining responses to slowly (~5-10 deg/sec), intermediate (~40-50 deg/sec), or fast (>100deg/sec) moving spots of light projected into the receptive field (see also Stein et al., 1993). Somatosensory receptive fields were mapped using minimal stimulus force from a soft brush or calibrated fiberglass filament to avoid the effects of transmission. It is acknowledged that repeatable, electronically generated stimuli are advantageous for the quantification of the evoked responses and their statistical comparison such that subtle and subthreshold sensory effects are revealed (Allman et al.,

2009a, b), but such tests are not efficient mapping/searching paradigms for evaluating a large area of cortex in an unexamined/novel preparation. Furthermore, given that 94% of the neurons were successfully categorized (see Results), it seems unlikely that such quantitative paradigms would have substantially affected the present outcome.

Once a neuron was isolated, its response type (auditory, somatosensory, visual, multisensory, and unresponsive) was determined and a spreadsheet was maintained that correlated sensory properties with its depth, penetration location and number. To avoid resampling the same neuron within a given penetration, a minimum 100 μ m interval was required between sequential recording sites. Several recording penetrations were performed in a single experiment and successful recording penetrations were marked, at their conclusion, with a small electrolytic lesion.

2.3 Histological procedures

After a series of experiments (usually 4-6), the animal was overdosed with sodium pentobarbital (50mg/kg, i.p.) and perfused with physiological saline followed by formalin. The cerebral cortex was stereotactically blocked, removed and cryoprotected. Frozen sections (50 μ m) were cut in the coronal plane through the recording sites, processed using standard histological procedures and counterstained. A projecting microscope was used to trace sections and to reconstruct recording penetrations. Gyrus/sulcal patterns, cytoarchitectonic characteristics, and observed physiological properties were used to demarcate the relevant functional cortical subdivisions. For this study, only those neurons which were histologically verified within the posterior segment of anterior ectosylvian gyrus, the most anterior segment of the middle ectosylvian gyrus (with underlying anterior ectosylvian sulcal cortex present), or the outer half of the bank of the posterior limb of the rostral suprasylvian sulcus were included (as consistent with the criteria of Reale and Imig, 1980). Laterally, the AAF was distinguished from the FAES at the lip of the anterior ectosylvian sulcus, which is consistent with the cytoarchitectonic descriptions provided by Mellott et al. (2010).

Results

In mature, postnatally-deafened cats (n=3) as well as hearing cats (n=3), recordings were made and histologically reconstructed from the gyrus and sulcal aspects of the AAF, depicted in Fig 1A-B. For post-natally deafened animals, AAF neurons were identified that responded to somatosensory ($47.6\% \pm 4$ s.d.; n=120/245), visual ($12\% \pm 10$ s.d.; n=39/245), or both visual and somatosensory ($35\% \pm 20$ s.d.; n=70/245) stimuli, as graphed in Fig. 1C. In stark contrast, the AAF of hearing cats when tested in the same manner with the same auditory, visual and somatosensory stimuli, exhibited overwhelming levels of purely auditory activation ($93\% \pm 5$ STD; n=328/351), as depicted in Fig. 1C. Neurons that were unresponsive to sensory stimulation represented >7% of either sample (deaf=16/245; hearing control=16/351), indicating that the crossmodal sensory reorganization of AAF following early-deafening was robust.

3.1 Somatosensory responses

The response characteristics of somatosensory-responsive neurons in early-deafened AAF are summarized in Fig. 2. Most (70%) somatosensory-responsive neurons were activated by low-threshold hair receptors, as evidenced by their reliable responses to gentle air puffs or soft brush taps. A few neurons required stronger force for activation, like those associated with skin (10%) or muscle receptors (11%). Somatosensory receptive fields were never observed to be so small as to represent only a single digit or vibrissa, but generally covered one or two body regions (e.g., head, forelimb, etc). If the receptive field included the

vibrissae, then displacement of a vibrissa was effective, but no attempt was made to differentiate responses that may have been evoked from sinus hairs versus that elicited by the surrounding facial hair. Somatosensory receptive fields were identified on all regions of the body (Fig. 2B), but those on the anterior regions (head, forelimb) occurred more frequently than posterior regions (trunk, hindlimb, tail). Curiously, the majority (57%) of somatosensory receptive fields had components that occurred on both sides of the body: they were bilateral. Although this phenomenon included some receptive fields that were close to the midline on both sides, such as the mouth, many also occurred on both forepaws without including the intervening body surface, as depicted in Fig. 3. Furthermore, bilateral somatosensory receptive fields were usually symmetrical, as if sensitivity to a body segment on the left was mirrored by the same body region on the right, as shown in most of the bilateral receptive field examples depicted in Fig. 3.

In somatotopically organized cortical areas (such as S1 to SV), recording penetrations that parallel its columnar organization typically reveal receptive fields that are centered on a particular body location; recording penetrations that course obliquely across columns typically encounter a smooth progression of receptive field locations (e.g., see Kaas et al. 1979). Furthermore, when the progression of receptive field locations exhibit a reversal in their spatial arrangement, it is widely accepted that a border between adjoining representational areas has been crossed, such as along the digit representations of the cat SII and SIV (Burton and Kopf, 1984). In the present study, most recording penetrations tracked obliquely across the gyral or sulcal aspects of the AAF. In these recordings, the progression of somatosensory receptive field locations seemed disjointed even among closely adjoining neurons. An example is depicted in Fig. 3A where the recording track passed obliquely across the gyral aspect of the AAF. The receptive fields encountered during that penetration are depicted in sequence, and it is easily apparent that receptive field positions shift abruptly from head (in the superficial layers) to body (and whole body), then hindlimb and back to head before transitioning to forelimb (bilateral; in the deepest layers) across the cortical distance of only a few millimeters. Furthermore, although some bilateral receptive fields could be grouped with other similarly bilateral fields, but even in these neighboring neurons the receptive field locations shifted dramatically (bilateral head at 625 μ m, to bilateral whole body just 125 μ m deeper, to bilateral hindlimb/tail at the next neuron at 1250 μ m). Receptive field organization did not appear to be that much better for neurons with purely contralateral receptive fields where, for example, neurons just 250 μ m apart (at 2375 and 2625) exhibited vastly different receptive field locations. These same effects are illustrated for a different recording penetration depicted in Fig. 3B. Here again, in the span of less than 5mm, receptive field positions changed from forelimb to head to whole body, then to head, whole body again, posterior body and finally forelimb. However, in this penetration in which more somatosensory receptive fields were encountered (than in 3A), there appears to be a clustering phenomenon where similar receptive field locations are represented in neighboring groups of neurons that was interrupted by an abrupt change. For both depicted penetrations (Figs 3A and B), it also needs pointed out that visual responses were interspersed are recording sites along each of these penetrations (not illustrated). Collectively, these observations are not consistent with the presence of a single or well-ordered somatotopy within the reorganized AAF region.

3.2 Visual responses

Intermingled amongst neurons with somatosensory inputs, neurons responsive to visual stimulation were encountered in both sulcal and gyral aspects of AAF. Fig. 4A, which overlays plots of all mapped visual receptive fields, shows that they covered the full extent of contralateral visual space (except the superior and inferior extremes) as well as extended ~20 degrees into the ipsilateral field. Of the mapped visual receptive fields, 58% (n=31/53)

included the representation of the central visual field (i.e., area centralis). Visual receptive fields were generally large in size, averaged 46 degrees in diameter (± 16 deg s.d.; average of longest azimuth and elevation diameters), and were not observed smaller than 20 degrees in diameter (see Fig. 4B). Most visually-responsive neurons showed distinct response properties characteristic of visual cortical neurons in hearing animals, such as direction selectivity (90% of sample) and preference for fast movement velocity (e.g., >100 deg/sec; 79% of sample).

In visuotopically organized cortical areas (such as V1, etc.), recording penetrations that parallel its columnar arrangement exhibit receptive field progressions that are centered on a particular location in visual space; recording penetrations that course obliquely across columns typically encounter a smooth progression of receptive field locations (e.g., see Hubel and Wiesel, 1965). In addition, reversals in receptive field order/location define borders between adjoining representations, such as between visual areas 17 and 18, or 18 and 19 (Tusa et al., 1979; Orban et al., 1980). In the present study, examples of recording penetrations through early-deafened AAF are illustrated in Fig. 5, where both near-vertical and obliquely-oriented penetrations are depicted. In Fig. 5A, where the recording track was approximately parallel to the cortical columns of the region, corresponding visual receptive fields shifted from far-peripheral to central locations with depth of recording. In Fig. 5B, the penetration coursed obliquely across the cortical columns, and the corresponding visual receptive fields shifted from central to far peripheral with the depth of recording. However, in another oblique recording track (Fig. 5C), visual receptive fields shifted from central to peripheral and then abruptly back to central locations. In this and other examples, reversals in visual receptive field location occurred over relatively short cortical distances in the reorganized AAF that is inconsistent with the presence of a single, well-ordered retinotopic representation.

3.3 Bimodal neurons

Bimodal, visual-somatosensory properties were identified in 70/245 AAF neurons and, as plotted in Fig. 1, were identified throughout the anterior-posterior extent of the AAF. Bimodal neurons generally did not appear to exhibit somatosensory or visual response features that distinguished them from their unimodal counterparts. The multisensory integrative capacity of the bimodal neurons was not examined in these experiments.

4.0 Discussion

These results demonstrate, at the neuronal level, that the effects of crossmodal plasticity are manifest in the cortical area of early-deafened cats corresponding to the AAF. In contrast to the almost exclusive auditory responsiveness of the hearing AAF, crossmodal plasticity in the early-deafened AAF was evidenced by visual as well as somatosensory activation. In fact, somatosensory responses predominated. The somatosensory properties identified in AAF of early-deafened cats resembled several features of crossmodal somatosensory properties in late-deafened ferret auditory cortex (Allman et al., 2009a). In both animal models, crossmodal somatosensory responses were most frequently activated by low-threshold hair receptors, exhibited large receptive fields that could include more than one body region, tended to represent the anterior aspects of the body (e.g., head, forelimb), often the receptive fields occupied bilateral aspects of the body surface, and the receptive field arrangement was not consistent with the presence of a single, well-ordered somatotopy. Thus, although a great deal has been revealed concerning the role of the visual modality in crossmodal plasticity following early deafness (Bavelier and Neville, 2002), the somatosensory system also is a significant and consistent contributor to the effect (see also Levanen and Hamdorf, 2001; Auer et al., 2007; Merabet and Pascual-Leone, 2010).

In the early-deafened AAF, crossmodal visual responses were observed in the minority of neurons examined. Visually-responsive neurons exhibited receptive field boundaries as well as specific response properties, such as velocity and direction tuning. Given that the majority of receptive fields were quite large and contained the representation of the area centralis, these visual receptive fields revealed numerous similarities to those described for the ectosylvian visual area (Olson and Graybiel, 1980; Scannell et al., 1996), a higher-order visual cortex. Similarly, the surgical re-routing of visual inputs to auditory structures revealed A1 neurons that exhibited large receptive fields as well as showed movement, velocity and orientation preferences (Sur et al., 1988; Roe et al., 1992). Thus, as in other examples of visual crossmodal plasticity, the observed visual responses in deafened AAF appeared to be far from aberrant or abnormal.

It is also important to recognize that only a small number of neurons were unresponsive to sensory stimuli, and these were in proportion with unresponsive neurons in the AAF of the control, hearing animals. Therefore, the crossmodal reinnervation of the early-deafened AAF is quite robust with no apparent loss of overall sensory activation.

4.1 AAF and A1 Comparison

The present study, to our knowledge, is the first investigation of crossmodal plasticity in the AAF following early-deafness. In contrast, the other core auditory area A1 has been the focus of most examinations so far, although their results appear contradictory. In congenitally deaf cats, visual inputs were not observed in A1 (Kral et al., 2003). Similarly, some human studies of the effects of early deafness have likewise failed to identify visual effects in A1 (Weeks *et al.*, 1998) although another fMRI study observed that visual stimulation reported “several voxels... within area 41 (primary auditory cortex; Finney et al., 2001).” Thus, the consensus of this corpus of work suggests that visual crossmodal plasticity in both congenitally deaf and early-deafened A1 was sparse at best. The study by Auer et al. (2007) provided fMRI observations of somatosensory activation of A1 in early-deaf individuals. However, given that somatosensory information normally has access to a variety of auditory cortical areas in hearing individuals (e.g., Foxe et al., 2000), it seems curious that the Auer et al. (2007) study indicated only the involvement of A1. In contrast, the crossmodal reorganization of the AAF in the present study is unambiguous, where >90% of neurons in AAF revealed robust crossmodal responses. These vastly different crossmodal effects ultimately provide further support for the notion that A1 and AAF represent largely separate parallel processors in the auditory system (Lee et al., 2004).

4.2 Single-unit studies of crossmodal plasticity

Most studies of crossmodal plasticity, especially those induced by deafness, have employed imaging or macroscopic recording techniques to evaluate the presence of stimulus-driven neural activity. Such techniques provide an important window into human brain function (and dysfunction), but are renowned for their coarse spatial/temporal resolution. Therefore, virtually nothing is known about the structure of crossmodal reorganization at the neuronal and receptive field levels. Alternatively, surprisingly few studies have examined crossmodal cortical plasticity using high spatial resolution techniques such as single-neuron recording. Although single-unit recordings were used to examine the clever preparations generated by the Frost (Frost and Metin, 1985) and Sur (Sur et al., 1988) groups, their crossmodal effects were surgically engineered and have not been correlated with naturally-occurring sensory disorders. On the other hand, the classic studies of Rauschecker and Korte (1993) showed that neurons in the ectosylvian visual area (AEV) of visually deprived cats not only exhibited auditory responsivity, but those neuronal responses also revealed enhanced auditory localization sensitivity consistent with a compensatory behavioral role (Korte and Rauschecker, 1993; Rauschecker and Knierp, 1994; see also King and Parsons, 1999).

Another single-unit study that evaluated the primary visual cortex of neonatally blind (enucleated) rats demonstrated that approximately a third of neurons showed crossmodal auditory activation with higher frequency and intensity thresholds (than hearing A1), but were not tonotopically arranged (Piche *et al.*, 2007). In visually-deprived cats, only subthreshold auditory activation was observed in a few (14%) V1 neurons (Sanchez-Vives *et al.*, 2006). In primary auditory cortex (A1), neurons of congenitally deaf mice respond to visual and to somatosensory stimulation (Hunt *et al.*, 2006), although A1 in these species normally appears to receive a large number of non-auditory inputs (Budinger *et al.*, 2006). This is also in contrast to neurons in A1 of congenitally deaf cats (Kral *et al.*, 2003), which exhibited no evidence of crossmodal plasticity. At the single-unit level, deafness has also been shown to have effects on the functional properties of auditory cortical neurons in the form of neurotransmitter and biophysical changes that alter their temporal processing functions (Xu *et al.*, 2007; Sarro *et al.*, 2008).

4.3 Crossmodal Spatiotopy?

In hearing cats, the AAF spans stereotaxic levels A10 to A15 as well as extends across the anterior ectosylvian gyrus for several millimeters into the adjoining suprasylvian and anterior ectosylvian sulci. Therefore, the AAF encompasses an area of 36-40 mm², across in which there is represented a single cochleotopic progression (Knight, 1977; Reale and Imig, 1980; Phillips and Irvine, 1982) that is reported to be disrupted in deaf animals (Dinse *et al.*, 1997; 2003; Raggio and Schreiner, 1999; Fallon *et al.*, 2009). Within this same area in early-deafened cats, there was an intermingled representation of somatosensory and visual inputs, each of which was characterized by multiple discontinuities in spatial receptive field locations as well as receptive field reversals. These data clearly indicate that the singular tonotopic organization of the hearing AAF has not been replaced by a similar spatiotopic representation in the substitute modalities. Furthermore, the tonotopic representation in AAF consists of isofrequency bands that extend across its medio-lateral axis largely parallel to the coronal plane. In other words, AAF recording penetrations in the coronal plane sample neurons whose auditory preferences are nested closely around a particular sound frequency/cochlear location. In stark contrast, the AAF of early-deafened cats exhibits multiple receptive field locations, discontinuities and reversals within the same coronal plane. Therefore, the present observations are not consistent with the replacement of the spatiotopic relationship seen between the cochlea and the cortex in hearing animals with a similar relationship between the body surface or retina in the crossmodally reorganized AAF. That said, spatial receptive fields in the deafened AAF are not random, either. The present study observed instances of receptive field progressions over relatively short distances (<2mm) as well as occasional clustering of receptive fields with related spatial properties. These observations were obtained from recording penetrations in the coronal plane across the medio-lateral axis of the AAF where, especially for the somatosensory modality, neurons with similar receptive fields sometimes appeared to cluster and then change in a stepwise fashion. These features have an uncanny resemblance to the cortical arrangement of binaural properties described by Middlebrooks and Pettigrew (1981). Therefore, although completely speculative at this time, it is tempting to suggest that the organization of crossmodal replacements in deafened cortex may be influenced by the faint remnants of auditory organization for which early development has provided a scaffold. Comparisons of crossmodal reorganization in the early-deaf with that of the congenitally-deaf should be able to address this possibility.

4.4 Age at Deafness Onset and Crossmodal Plasticity

In the present investigation the subjects were rendered moderately deaf (45 dB hearing deficit) by the systemic application of ototoxic drugs at 7-8 days postnatal. A second application of the same drugs between days 40 and 50 resulted a profound deafness (>95 dB

hearing deficit) as assessed with an ABR. Therefore, the animals experienced an approximately six week period of moderate hearing loss which may have influenced the results of the study. However, both the results of the study and the work of others on both auditory and visual systems suggests otherwise.

In the visual system, it is well established that the ocular dominance critical period can be influenced by visual experience (see review of Wandell and Smirnakis, 2009). For example, the critical period can be prolonged by dark rearing (Cynader and Mitchell, 1980; Cynader et al., 1980; Mower et al., 1985; Timney et al., 1980; Mower, 1991) or even reactivated by housing adult animals in a completely dark environment (He et al., 2006, 2007). However, as little as six hours of visual experience during an early period of light deprivation can prevent the elongation of the critical period (Mower et al., 1983). Similar results have been identified in the auditory system (Kral and Eggermont, 2007) where the maturation of cortical properties is delayed during both congenital auditory deprivation (Kral et al., 2005) and during exposure of normal hearing animals to continuous masking noise (Chang and Merzenich, 2003). However, in congenital deprivation after a given age (~ 2 months in the cat) maturation proceeds, albeit in an altered developmental sequence compared to hearing controls (Kral et al., 2005). In the context of the present experiment, the cited within-modality studies could suggest that the short period of impaired acoustic exposure could have limited the amount of crossmodal plasticity in AAF. However, considering the number of neurons displaying cross-modal plasticity (~95%) it is difficult to imagine that *more* plasticity could have been possible if profound deafness had been congenital or been initiated before the onset of any level of hearing. Nevertheless, the converse may be true, and *less* crossmodal plasticity might be evident if there is no hearing impairment until day 50, but crossmodal plasticity in auditory cortex following adult-onset deafness does not support this suggestion (Allman et al., 2009a). To directly answer this question, it would be worthwhile examining the crossmodal plasticity of animals rendered profoundly deaf at 50 days that experienced no period of acoustic impairment prior to the onset of deafness.

4.5 Adaptive plasticity?

Crossmodal plasticity has come to be regarded as synonymous with ‘adaptive’ or ‘compensatory’ plasticity, whereby the replacement of lost inputs by functioning sensory modalities generates enhanced, supranormal performance in those modalities. Indeed, early blindness has been demonstrated to improve auditory localization processing and behavior (Rauschecker and Knierpert, 1993; Korte and Rauschecker, 1993) as has early-deafness enhanced processing and detection of peripheral visual stimuli (Bavelier et al., 2000; Bavelier and Neville, 2002; Merabet and Pascual-Leone, 2010; Lomber et al., 2010). Although there is a wealth of literature detailing the organization and connectional precision underlying, for example, auditory or visual localization in normal systems, little is known about the circuitry and its properties that subserve their crossmodal enhancements in the deaf or blind (but see Lomber et al., 2010). On the other hand, it is unknown if early-deafened AAF participates in functional crossmodal augmentation, and recent experiments indicate that AAF is not involved in a variety of visual tasks in congenitally deaf cats (Lomber et al., 2010). Given the present results in AAF of early-deaf cats, it seems possible that crossmodal activity in AAF is either too disorganized to effectively initiate a behavioral task or percept, or it may be involved in somatosensory-related tasks that are yet to be evaluated.

4.6 Mechanisms Underlying Crossmodal Plasticity

Most evaluations of cortical crossmodal reorganization suggest that the effects are due to plasticity in the cortex itself (Rauschecker, 1995; Bavelier and Neville, 2002). Current thought regarding the possible mechanisms underlying such plasticity include the in-growth

and stabilization of new axons from novel sources, or the unmasking of latent inputs already resident in the region. With regard to the first scenario, the AAF borders on several somatosensory areas (areas SII, SIV, and SV as well as multisensory area FRS, Clemons et al., 2007), each of which could act as a source of ingrowth of novel somatosensory axons by simply extending across their borders to invade the 'vacated' AAF territory. This scenario, however, would produce a serious mismatch between the new corticocortical connections and the extant thalamocortical and callosal connections, unless the latter are somehow induced to change as well. Furthermore, ingrowth from neighboring regions could not completely account for the majority of somatosensory neurons that showed bilateral receptive fields, which would seem to require substantial callosal involvement. How such massive postnatal callosal/thalamocortical re-targeting might be effected is not known. Alternatively, there have been no demonstrations, to our knowledge, of subthreshold somatosensory or visual effects in the cat AAF (or in the primate homologue, area R, which seems to be spared from the crossmodal effects seen in A1 and area CM; Foxe et al., 2000; Kayser et al., 2008). Consequently, there is presently little evidence to suggest that the observed crossmodal plasticity resulted from the unmasking of normally silent inputs to the region. It should be pointed out that such a scenario would mean that a large number of silent bilateral inputs would normally be present in AAF, whereas bilateral receptive fields are an infrequent occurrence in most somatosensory cortices. Therefore, within the current rubric, there does not appear to be a satisfactory candidate for the mechanism of cortical crossmodal plasticity in the early-deafened AAF.

An alternative mechanism for the somatosensory component of deafness-induced cortical crossmodal reorganization has recently been proposed (Allman et al., 2009a) which posits that the primary location where plasticity occurs is actually in the brainstem. It has been demonstrated that, following hearing loss, neurons in the dorsal cochlear nucleus become more susceptible to somatosensory activation (Shore et al., 2008). Under these conditions, because the primary auditory nucleus is changed to encode somatosensory information, projections from that area into the ascending auditory pathway and its targets should carry somatosensory signals as well. Thus, plasticity at brainstem levels could result in functional reorganization in auditory cortex without fundamental connectional changes in thalamocortical or corticocortical circuitry. Additional support for this hypothesis includes the identification of crossmodal (somatosensory) inputs to the cochlear nucleus (Shore et al., 2000; Kanold and Young, 2001) and inferior colliculus (Aitken et al., 1981) of hearing animals. In addition, adult-deafened animals show somatosensory reorganization of the auditory cortices without reorganization of the relevant cortico-cortical or thalamo-cortical connections (Allman et al., 2009a). Further investigations are currently under way to examine this possibility in early-deafened animals.

5.0 Summary and Conclusions

When compared with hearing animals, early-deafened cats demonstrate a crossmodal reorganization of the AAF. This reorganization was robust and occurred predominantly in the form of somatosensory responses, although visual inputs were also observed. Single-unit analysis indicated that the response and receptive field properties were vigorous and consistent with those of higher-level sensory cortical areas of hearing animals, except that most somatosensory receptive fields occupied bilateral positions on the body surface and neither somatosensory nor visual representation exhibited a single, well-ordered spatiotopic organization. These observations not only underscore the well-known distinctions between the core auditory cortical areas AAF and A1, they also contribute to a rapidly growing literature demonstrating the crossmodal susceptibility of deafened auditory cortices outside A1.

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Figure 1.

Location of cat anterior auditory field and its recorded sensory activity following early-deafness. (A) On the lateral view of the cat cortex, the hash-marks outline the auditory cortices. Labeled are the core areas of A1 (primary auditory cortex) and AAF (anterior auditory field). The vertical line indicates level from which the coronal section (right) was taken to show the gyral and sulcal extent of the AAF as well as the location of the surrounding auditory fields (FRS=field of rostral suprasylvian sulcus; FAES=field of anterior ectosylvian sulcus; PAF=posterior auditory field). (B) Coronal sections through AAF recording sites from 3 early-deaf cats show the location of recording penetrations (vertical lines) and the sensory activity identified therein (cross-mark = neuronal recording). Not every neuron is shown due to overlap. (C) Single-units recorded from hearing cats (grey bars; $n=3$; neurons =351) were dominated by auditory responsiveness, while those from early-deafened cats (black bars; $n=3$; neurons = 245) were dominated by somatosensory responses. Error bars indicate standard deviation. A=auditory, V=visual, S=somatosensory, VA=visual-auditory, VS=visual-somatosensory, AS=auditory somatosensory, VAS=trimodal, Un=unresponsive; scale bar = 1mm.

Figure 2.

Somatosensory response properties of neurons in early-deafened AAF. (A) Most (70%) neurons with somatosensory inputs were activated by low-threshold, hair receptors, with only a few responsive to higher threshold inputs from the skin or muscle (deep). (B) Somatosensory receptive fields were found on all parts of the body surface, but the representation of anterior body parts (head, forelimb) predominated. HD=head, FL=forelimb, TK=trunk, HL=hindlimb, WB=whole body. (C) The majority (57%) of somatosensory receptive fields demonstrated responses to stimulation of both the right and left sides of the body; the receptive fields were bilateral (Bilat) while the remainder was located on only the contralateral body surface (Contra). None were located exclusively on the ipsilateral (ipsi) surface.

Figure 3.

Somatosensory representation in early-deaf AAF. (A) The coronal section (left) shows the area corresponding to the AAF and a reconstructed recording penetration through it. Each circle represents a neuron that corresponds to a receptive field (numbers=depth in microns) plotted on the right. On each plot of a cat's body surface, the filled black areas represent the somatosensory receptive field of a recorded AAF neuron. In this penetration that obliquely traversed the columnar organization of the region, the location of the receptive fields did not shift systematically with changes in depth. Instead, the region seemed to represent clusters of neurons representing different body regions. Superficially, small receptive fields on the head or rostral body parts (e.g., neurons at 375-625 μ m), but at slightly deeper locations the receptive fields included large trunk/whole body regions (e.g. neurons at 750-2000 μ m), but became smaller again at the deepest levels (e.g., neurons >2375 μ m). In addition, transitions were abrupt, shifting from head to whole body in just 125 μ m (e.g., at 625-750 μ m) or from hindlimb to ear (e.g. at 2375-2625 μ m). Note also that neurons with bilateral receptive fields were not necessarily clustered together nor did all adjacent neurons represent similar bilateral regions of the body. Small arrowheads help to indicate locations of some small receptive fields. The same conventions are used in part (B). This recording penetration spanned nearly 5mm and encountered 24 neurons with somatosensory receptive fields. The locations of the receptive fields seem to cluster around a particular region or configuration before abruptly jumping to the next. Superficial neurons had receptive fields largely on head

and forelimb, which at 3000 μ m shifted to whole body until 4000 μ m, where they shifted back to head/forelimb representations.

Figure 4.

Visual representation in early-deafened AAF. (A) The visual field is shown with the receptive fields of all mapped AAF neurons plotted. This plot demonstrates that the entire contralateral visual hemifield (excepting extreme superior and inferior positions) is represented within the early-deafened AAF, as well as $\sim 20^\circ$ of ipsilateral space. (B) Most visual receptive fields tended to be large (mean = $45.6^\circ \pm 16.6$ s.d.). (C) Most (89%) neurons with visual inputs showed response preferences for the direction of stimulus movement (DS=direction selective; NDS= not direction selective). (D) Most (79%) visually-responsive neurons preferred fast moving stimuli (e.g., >100 deg/sec).

Figure 5.

Distribution of visual receptive fields in early-deafened AAF. (A) On the representation of the visual field, the numbered receptive fields (shaded grey) correlate with the sequence of visually-responsive neurons (grey dots) recorded in the penetration depicted on the coronal section through the AAF. Although this penetration was nearly orthogonal to the pial surface (~parallel to columnar arrangement), the location of visual receptive fields progressively shifted from temporal to nasal with depth of recording. (B) In a recording penetration just 0.5 mm lateral to that depicted in part 'A,' this recording penetration encountered neurons whose visual receptive fields progressively shifted in the nasal to temporal direction. (C) A third penetration yielded visually-responsive neurons whose receptive field locations shifted abruptly with depth (compare #5 and #6).