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Auditory Cortex Projections Target the Peripheral Field Representation of Primary Visual Cortex

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Auditory Cortex Projections Target the Peripheral Field Representation of Primary Visual Cortex

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Abstract

The purpose of the present study was to identify projections from auditory to visual cortex and their organization. Retrograde tracer wheat germ agglutinin conjugated to horseradish peroxidase was used to identify the sources of auditory cortical projections to primary visual cortex (areas 17&18) in adult cats. Two groups of animals were studied. In the first group, large deposits were centered on the lower visual field representation of the vertical meridian located along the area 17&18 border. Following tissue processing, characteristic patterns of cell body labeling were identified in extrastriate visual cortex and the visual thalamus. In auditory cortex, of the four tonotopically-organized regions, neuronal labeling was identified in the supragranular layers of the posterior auditory field (PAF). Little to no labeling was evident in the primary auditory cortex (AI), the anterior auditory field (AAF), the ventral posterior auditory field (VPAF) or in the remaining six non-tonotopicaly organized regions of auditory cortex. In the second group, small deposits were made into the central or peripheral visual field representations of primary visual cortex. Labeled cells were identified in PAF following deposits into regions of primary visual cortex representing peripheral, but not central, visual field representations. Furthermore, a coarse topography was identified in PAF, with neurons projecting to the upper field representation being located in the gyral portion of PAF and neurons projecting to the lower field representation located in the sulcal portion of PAF. Therefore, direct projections can be identified from PAF to primary visual cortex.

Keywords: Area 17, Area 18, Auditory Cortex, Posterior Auditory Field, WGA-HRP, Multisensory, Cat

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I, Amee Hall, am submitting this thesis as partial fulfillment of the Master of Science Degree in Neuroscience. In all aspects of this work I played a principal role including, but not limited to, design, surgical procedures, data collection, data analysis, production of figures, and development of the manuscript for publication. Dr. Stephen G. Lomber was my primary supervisor and provided critical advice and assistance with all aspects of this work. He also provided neural tissue from previous studies which were included in this work to supplement results seen during the completion of this project.

This work is dedicated to my parents, Cory and Peggy Hall, for their eternal support in all aspects of my education and life. Also, it is dedicated to my brother and his wife, Ben and Melanie Hall, who have always been shining examples of love and understanding.

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List of Abbreviations

A - Anterior

AAF - Anterior Auditory Field

aes - anterior ectosylvian sulcus

AES - Anterior Ectosylvian Sulcus

AI - Primary Auditory Cortex

AII - Second Auditory Cortex

AL - Anterior Lateral auditory belt

ALLS - anterolateral lateral suprasylvian

AMLS - Anteromedial Lateral Suprasylvian

AUD - Nine auditory areas, except PAF, examined

cal - calcarine sulcus

CC - Corpus Callosum

C_{cx} - C-complex

CL - Caudal Lateral auditory belt

CM - Caudomedial auditory belt

CP - Caudal auditory Parabelt

D - Dorsal

DAB - Diamino Benzadine

DLS – dorsal lateral suprasylvian

dLGN - dorsal Lateral Geniculate Nucleus

DZ - Dorsal Zone

fAES - Anterior field of the Ectosylvian Sulcus

IN - Insular region

lf - lateral fissure

LGN - lateral geniculate nucleus

LPl - Lateral division of the Lateral-Posterior nucleus

MIN - Medial Interlaminar Nucleus

ML - Middle Lateral auditory belt

P - Posterior

PAF - Posterior Auditory Field

PBS - Phosphate Buffered Saline

PE - Posterior Ectosylvian

pes - posterior ectosylvian sulcus

PLLS - Posterolateral Lateral Suprasylvian

PMLS - Posteromedial Lateral Suprasylvian

R - Rostral area

RM - Rostromedial auditory belt

RP - Rostral auditory Parabelt

RT - Rostrotemporal area

RTL - Lateral Rostrotemporal auditory belt

RTM - Medial Rostrotemporal auditory belt

spl - splenial sulcus

ss - suprasylvian sulcus

STP - superior temporal polysensory area

sts - superior temporal sulcus

T - Temporal region

TMB - Tetramethylbenzidine

V - Ventral

V1 - Primary Visual Cortex

VAF - Ventral Auditory Field

VIP - ventral intraparietal area

VLS - ventral lateral suprasylvian

VPAF - Ventral Posterior Auditory Field

WGA-HRP - Wheat Germ Agglutinin conjugated to Horseradish peroxidase

List of Symbols

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CHAPTER 1 – Introduction and Literature Review

1.1 – Integration of the Senses

Sensory systems do not work in isolation. Different sensory inputs must influence each other and be integrated to more completely represent an individuals environment (Bulkin and Groh, 2006). Usually these interactions work to improve the quality of our perception. This can be demonstrated during scenarios where increased background noise makes it hard to understand normal levels of speech. The ability to see the speaker and watch their lip movements will, however, greatly increase correct perceptions. In fact, it has been found that primary and association auditory cortices are activated by silent lip reading (Calvert et al. 1997). With evidences such as this it is difficult to imagine the drawbacks associated with sensory integration.

Integration of sensory information becomes most apparent when there is a disparity between the provided information to each of the senses. This has been demonstrated by phenomenon such as the McGurk effect (McGurk and MacDonald, 1976). During these studies subjects watched a video with a person mouthing a syllable (e.g. "da"). Simultaneously an auditory cue was given that did not match the one being seen (e.g. "ga"). The auditory and visual cues melded together and resulted in the perception of a third, unused, syllable (e.g. "ba"). The McGurk effect demonstrates the minds attempt to interpret all stimuli being presented to it. Under normal circumstances these two stimuli match and the integration of the two goes unnoticed. However, when there is a disparity, such as that presented during the McGurk studies, subjects are unable to de-integrate the two and an incorrect perception occurs. Other phenomena can

demonstrate the integration of visual and vestibular cues and between auditory and vestibular systems (Stein and Meredith, 1993).

Advances in science and technology are introducing situations that we do not encounter naturally. These circumstances have pushed the limits of sensory integration and identified conditions where it is actually detrimental. One of these is the "oculogravic" illusion (Graybiel 1952) experienced by pilots who must perform high acceleration take-offs. During take off the nose of the aircraft rises and the gravitational force exerted on the vestibular system indicates a circular acceleration. This causes a visual perception of the nose rising too fast and, if left to the reflexes of the pilot, immediate corrective action would be taken possibly resulting in a crash. Thus, the pilot must learn to rely on his instruments to give him true information on the elevation of the nose.

Integration of sensory information has long been proposed to take place only after extensive processing within cortices devoted to a single modality (Ghazanfar and Schroeder 2006). After such processing, it is proposed that integration would occur in association cortices outside of sensory specific cortex (Bavelier and Neville 2002) in areas such as the superior temporal polysensory area (STP; Bruce et al. 1981; Hikosaka et al. 1988; Nosselt et al. 2007) and ventral intraparietal area (VIP; Avillac et al. 2007, Schlack et al. 2005, Schroeder and Foxe 2002) of the monkey, and the anterior ectosylvian sulcus (AES; Dehner et al. 2004) in the cat. However, more recent studies have suggested that multisensory integration may occur at early stages of visual processing in the cerebral cortex (Schroeder et al. 2003; Schroeder and Foxe 2005; Ghazanfar and Schroeder 2006).

1.2 – Audiovisual Integration in the Monkey

In order to address theories of multisensory integration at early stages of visual processing recent studies have begun to consider the possibility of non-visual cortical projections to V1. Little information is available on non-visual cortical projections to primary visual cortex because the vast majority of studies examining primary visual cortex (V1) connectivity have focused exclusively on inputs from other *visual* cortical structures (eg. Maunsell and van Essen 1983; Rockland and Van Hoesen 1994; Rockland et al. 1994a,b). Recent studies have focused on the audiovisual cortical projection to V1 and have described direct projections from both core (primary auditory cortex) and belt areas of auditory cortex (Clavagnier et al. 2004; Falchier et al. 2002; Rockland and Ojima 2003). These projections were described to specifically target the peripheral visual field representations in primary visual cortex (Clavagnier et al. 2004; Falchier et al. 2002; Rockland and Ojima 2003). The presence of direct projections from auditory cortex to the peripheral representation of primary visual cortex is of interest because the integration of acoustic and visual signals at an early level of processing could serve to enhance perceptual capabilities that could lead to improved detection in the visual periphery.

1.3 – Visual Inputs to Primary Visual Cortex of the Cat

1.3.1 – Areas 17 and 18 as Primary Visual Cortex

Area 17 of the cat cerebral cortex has historically been identified as primary visual cortex. However, more recent work has concluded that area 18 is not as dissimilar to area 17 as origionaly proposed. The two areas are architectonically distinct and contain separate representations of the visual field (for review see Payne and Peters 2003). Save

for those two exceptions, areas 17 and 18 are very similar and thus have collectively been identified as primary visual cortex (Payne and Peters 2003). One of the biggest similarities is the projection from the lateral geniculate nucleus (LGN) of the thalamus. This has been demonstrated by; antidromic stimulation of cells in areas 17 and 18 which activate similar neurons in the LGN (Stone and Dreher 1973), retrograde tracer injections into areas 17 and 18 result in double labeled cells in the LGN (Geisert 1980), and labeling of cells projecting from the LGN reveal axon collaterals which inervate both area 17 and 18 (Freund et al. 1985).

Hubel and Wiesel classified cells in areas 17 and 18 (Hubel and Wiesel 1959, 1962, 1965) according to their simple or complex receptive fields. They considered areas that contained simple receptive fields the initial point of visual processing (Hubel and Wiesel 1962). A simple receptive field is defined as having a distinct "on" and "off" region. Both areas 17 and 18 contain cells with simple receptive fields. Thus, by this definition, both areas 17 and 18 can be combined and collectively called primary visual cortex.

1.3.2 – Thalamic Inputs to V1

The lateral geniculate nucleus (LGN) of the thalamus serves as the major relay center for visual inputs from the retina to primary visual cortex. The optic tract enters the LGN on its ventral surface. A retinal map is maintained in this projection resulting in a retinotopic map within the LGN (Sanderson 1971), with vertical elevations represented along the anterior-posterior axis. Along this axis the lower visual field is represented most anterior, and the upper visual field represented posterior. Organization along the

azimuth is also maintained with the medial aspect of the LGN receiving inputs representing the center of the visual field and the lateral aspect representing the most lateral extent of the visual field. The retinotopic organization within the LGN results in projection columns of cells spanning all layers representing the same point of the visual field (Bishop et al. 1962; Sanderson 1971). Leaving the LGN dorsally, fibers from projection columns converge and form small bundles. These bundles then fan out, becoming the optic radiation, and systematically terminate in multiple cortical areas, with the largest projection being to V1. The retinotopic map is preserved in the projection to V1 with axons originating in anterior (lower visual field) or posterior (upper visual field) LGN terminating more rostral or caudal in V1, respectively.

The laminar configuration of the LGN provides an additional level of organization. Magnocellular layers A and A1, along with the parvocellular layers of the C-complex (C_{cx}) are the two major divisions of the LGN. Outputs from the magnocellular layers project exclusively to V1 (LeVay and Gilbert 1976) and projections from the parvocellular layers innervate primary visual cortex as well as other extrastriate visual cortical areas (Raczkowski and Rosenquist 1980).

1.3.3 – Visual Cortical Inputs to V1

The diverse connections of the visual cortex enable detailed processing of visual inputs. Beyond V1 there are eleven other generally recognized visual areas; Area 19, anteromedial lateral suprasylvian (AMLS), anterolateral lateral suprasylvian (ALLS), posteromedial lateral suprasylvian (PMLS), posterolateral lateral suprasylvian (PLLS), ventral lateral suprasylvian (VLS), dorsal lateral suprasylvian (DLS), and Areas 20a, 20b,

21a, and 21b. Of these eleven areas V1 projects to all but two areas, namely 20b and DLS (Symonds and Rosenquist 1984a). These findings did not seem unlikely since Hubel and Wiesel (1962, 1965) had proposed the hierarchical theory of the visual corticies. According to this theory, V1 serves as a primary cortical receiver of visual information, after which, the information would be processed further by progressively higher cortical areas. Interestingly, it has been found that all corticocortical connections are reciprocal. Thus, all areas receiving inputs from V1 also project back to V1 (Symonds and Rosenquist 1984a).

Current theories of cortical hierarchy have been inspired by feed forward and feedback pathways suggested by the patterns of connections between areas. Feed forward connections were found to originate from superficial layers and terminate in layer 4 of the target area (Rockland and Pandya 1979). Feedback connections were found to originate from deep and superficial layers while terminating outside of layer 4 (Rockland and Pandya 1979). Defined this way, different cortical structures can now be on the same hierarchical level which offers an explanation for the reciprocal connections that were observed by Symonds and Rosenquist (1984a).

1.4 – Audiovisual Integration in the Cat

Similar to the monkey, nearly all previous studies in the cat have focused on inputs to primary visual cortex from other visual cortical structures (eg. Bullier et al. 1984; Symonds and Rosenquest 1984a). Cat primary visual cortex consists of both areas 17 and 18 (Tretter et al. 1975). The only studies to consider non-visual cortical projections to primary visual cortex have concentrated on exuberant projections that occur during

development. Indeed, during development there are robust projections from primary auditory cortex that terminate in primary visual cortex (Clarke and Innocenti 1990; Dehay et al. 1988; Innocenti et al. 1988). However, most of these projections are lost by the time the animal reaches adolescence (Clarke and Innocenti 1990; Dehay et al. 1988; Innocenti et al. 1988).

1.5 – Present Investigation and Hypothesis

Previous studies of audiovisual pathways in the monkey (Clavagnier et al. 2004; Falchier et al. 2002; Rockland and Ojima 2003) have shown a direct projection from the auditory cortex to V1. In the cat, previous work has concentrated on the presence of dense transient connections between auditory and visual cortex during development (Clarke and Innocenti 1990; Dehay et al. 1988; Innocenti et al. 1988). The purpose of this study was to examine projections from auditory cortex to primary visual cortex of the cat. We specifically sought to test the hypothesis that, similar to the monkey, there would be direct projections from primary and non-primary auditory cortex to primary visual cortex of the cat. (Fig. 1).

Two groups of cats were examined. In the first group we made large retrograde tracer deposits (spanning both central and peripheral retinotopic representations) in areas 17 and 18. The results from these deposits show that nearly all labeled neurons in auditory cortex were contained in the posterior auditory field (PAF). Therefore, in the second group of cats we made small deposits at locations in the central, paracentral, or peripheral visual field to determine if this projection targeted specific representations in primary visual cortex. Indeed, in this group of animals we found that PAF projections to

primary visual cortex specifically target neurons that represent sites in the visual periphery. Finally, we further defined a loose topography in the projections emitting from PAF. Therefore, we refuted the first part of our hypothesis because we failed to observe any projections from primary auditory cortex to primary visual cortex. However, we confirmed the second part of our hypothesis by demonstrating projections from PAF to primary visual cortex. Overall, the present results in the cat are quite similar to those previously identified in the monkey (Falchier et al. 2002; Rockland and Ojima 2003).

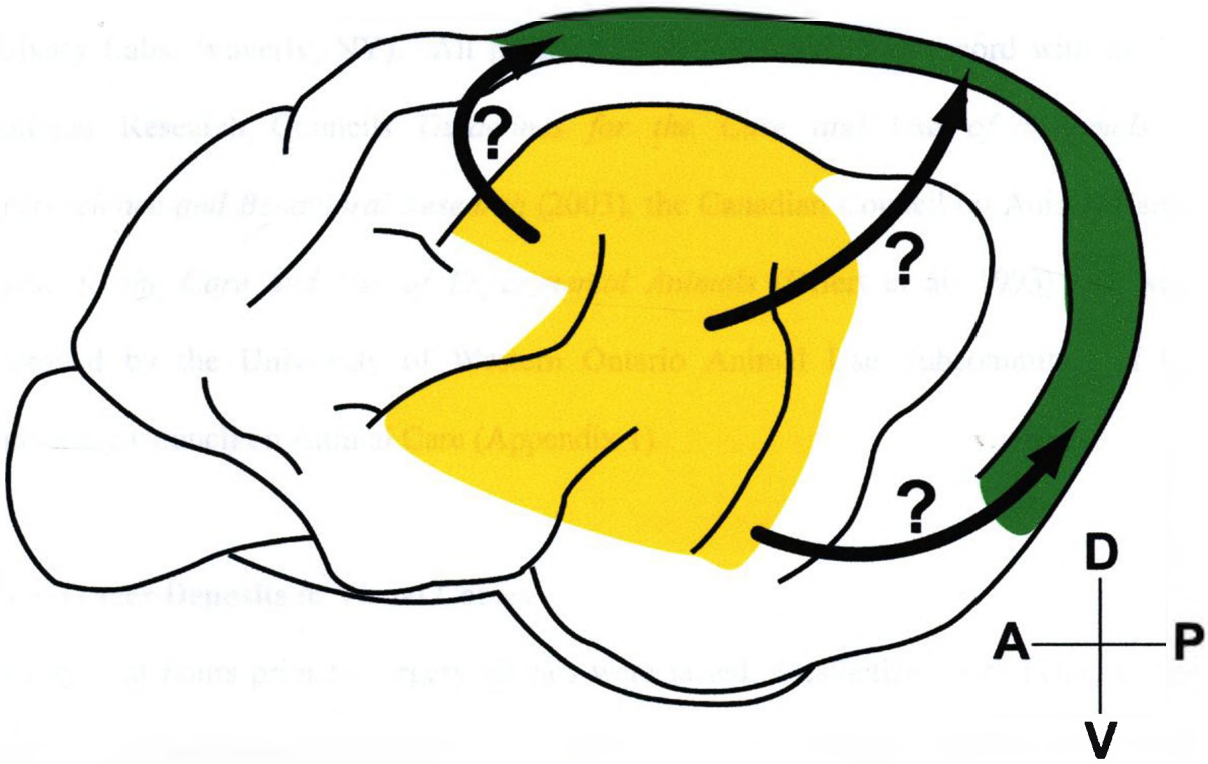


Fig. 1. Lateral view of the left hemisphere of the cat cerebrum. The yellow region highlights auditory cortex and the green region highlights primary visual cortex (areas 17 and 18). The purpose of the present study was to identify the origins of auditory projections to primary visual cortex (arrows with question marks). (A – anterior, D – dorsal, P – posterior, V – ventral).

CHAPTER 2 – Materials and Methods

Auditory cortex projections to primary visual cortex were examined in 14 mature (>6M) cats (Table 1). Cats were acquired from a commercial laboratory animal breeding facility (Liberty Labs, Waverly, NY). All procedures were conducted in accord with the US National Research Councils *Guidelines for the Care and Use of Mammals in Neuroscience and Behavioral Research* (2003), the Canadian Council on Animal Care's *Guide to the Care and Use of Experimental Animals* (Olfert et al. 1993) and were approved by the University of Western Ontario Animal Use Subcommittee of the University Council on Animal Care (Appendix 1).

2.1 – Tracer Deposits in Visual Cortex

Twenty-four hours prior to surgery all cats were fasted, anesthetized with ketamine (20 mg/kg im) to facilitate cannulation of the cephalic vein with an indwelling feline catheter, and an anti-inflammatory medication (dexamethasone, 1.0 mg/kg iv) was administered. On the day of surgery, the animals were anesthetized using sodium pentobarbital (25 mg/kg iv, or to effect). A second dose of dexamethasone was given and atropine (0.03 mg/kg sc) was administered to reduce respiratory and alimentary secretions. In cases where tracer deposits were made into the medial wall of area 17, mannitol (1 gm/kg iv) was infused to make cortex more malleable for lateral displacement. Additional sodium pentobarbital was administered, as needed, to maintain anesthesia throughout the procedure. Heart rate, respiration and temperature were continuously monitored. Body temperature was maintained through the use of a water-filled heating pad.

The animals were placed in a stereotaxic apparatus and prepared for surgery using antiseptic procedures. A midline incision was made along the scalp and the left temporalis muscle was detached and reflected laterally. A craniotomy was made over the marginal gyrus and the underlying dura was incised and reflected to expose the left cerebrum. Wheat germ agglutinin conjugated to horseradish peroxidase (5% WGA-HRP) was then pressure injected (Nanoliter 2000; World Precision Instruments, Sarasota, FL) at specific retinotopic locations (Table 1). For each penetration, two tracer deposits of WGA-HRP (0.1 μl each) were made at ~500 μm and 1200 μm below the pial surface. All deposits were confined to primary visual cortex (areas 17 and 18; Tretter et al. 1975).

Two groups of cats were examined. In the first group (n=2), a deposit consisting of seven tracks was made along the dorsal surface of the marginal gyrus that targeted a large area centered on the border between areas 17 and 18 (Payne 1990). These large deposits were directed at the lower vertical meridian visual field representation between areas 17 and 18 as described by Tusa et al. (1978, 1979). For the second group (n=12) each cat received smaller deposits, consisting of two tracks, with deposits targeting central (<2°, n=2), para-central (2°-10°, n=2), upper peripheral (>10°, n=2), horizontal peripheral (>10°, n=2), or lower peripheral (>10°, n=4) visual field representations.

Following completion of each deposit, the dura was replaced or artificial dura (Gelfilm®; Upjohn Co., Kalamazoo, MI) was placed over the cerebrum. The bone piece was replaced and secured with dental acrylic. An additional administration of dexamethasone and fluids (2.5% dextrose and half-strength lactated ringer solution, 20 ml/kg sc) was provided. In all cases recovery was uneventful.

Table 1. Retinotopic centers and AP levels of each WGA-HRP deposit into primary visual cortex for each of the 14 cases examined. Cell counts reflect numbers in every fifth serial section.

Case #	Areas Targeted	Retinotopic Center of Deposit (Azimuth, Elevation)	Tracer Deposits (AP Levels)	Number of Labeled Cells in PAF	Number of Labeled Cells in LPl
B1	Area 17/18	Vertical Meridian	P5, P2.5, AP0, A2.5, A5.0, A7.5, A10.0	172	232
B2	Area 17/18	Vertical Meridian	P5, P2.5, AP0, A2.5, A5.0, A7.5, A10.0	129	151
C1	Area 17/18	0,-1	P3, P4	3	143
C2	Area 17	2, 2	P4,P5	7	120
PC1	Area 17	5,-1	P3, P2	5	89
PC2	Area 17	10,-5	P1, AP0	12	103
U1	Area 17	0,20	P7,P8	85	98
U2	Area 17/18	0,25	P8,P9	72	116
L1	Area 17	5,-35	A13.5, A14.5	69	106
L2	Area 17	5,-35	A13, A14	79	98
L3	Area 17/18	0,-40	A13,A15	116	140
L4	Area 17/18	0,-50	A13,A15	134	151
H1	Area 17	50,-5	P1,A1	135	148
H2	Area 17	30,10	P3,P5	162	181

2.2 – Perfusion and Tissue Fixation

Forty-eight hours following the tracer deposits each cat was deeply anesthetized with sodium pentobarbital (40 mg/kg, iv). An anti-coagulant (heparin (10,000U) iv) and a vasodilator (1% sodium nitrite (1ml iv)) were administered. The cat was then perfused, through the ascending aorta, with 0.1M phosphate buffered saline (PBS) for 5 minutes. Next, the arterial system was infused with aldehyde fixatives (1.5% gluteraldehyde/ 1% paraformaldehyde in 0.1M PBS) for 20 minutes. Finally, 10% sucrose in 0.1M PBS was perfused for 5minutes to help cryoprotect the tissue. All solutions were buffered at pH 7.4 and infused at a rate of 100ml/min. The net effect of the procedures was to exsanguinate the cat, a method which complies with the recommendations of the American Veterinary Medical Association Panel on Euthanasia (Beaver et al. 2001), and to fix tissue for the identification of tracers. The head was then placed in a stereotaxic apparatus, the brain was exposed, blocked at Horsley-Clarke coronal level A22, and removed from the cranium. Each brain was photographed to provide a permanent record and, for cryoprotection, placed in 30% sucrose in 0.1M PBS until it sunk.

Brains were frozen and coronal sections (50μm thick) were cut and collected serially for the entire hemisphere and thalamus. The first series of sections, at 250 μm intervals, was exposed to tetramethylbenzidine (TMB) and hydrogen peroxide according to the protocol of Olucha et al. (1985) to reveal the presence of WGA-HRP. Series 2 was treated with diamino benzadine (DAB) and hydrogen peroxide (Gonatas et al. 1979; Mesulam 1982) to reveal the presence of WGA-HRP. Series 3 was stained with cresyl violet to reveal the presence of Nissl bodies. Series 4 was processed histochemically to demonstrate the presence of cytochrome oxidase using procedures described in previous

studies (Payne and Lomber 1996). Selected sections from series 5 were processed for the presence of tracer, as needed, using any of the previously described methods. All histochemicaly reacted sections were then mounted onto gelatinized glass slides, dehydrated, and coverslipped.

TMB is a very sensitive WGA-HRP reaction which degrades rapidly over time (Olucha et al. 1985). Therefore, TMB processed tissue was used to reconstruct all injection sites and for cell counts in auditory cortex. Although DAB is not as sensitive a reaction as TMB (Olucha et al. 1985) it is much longer lasting. Thus, tissue was exposed to DAB to enable future analysis of tissue.

2.3 – Data Collection and Analysis

Injection sites were manually plotted on standardized coronal sections adopted from Reinoso-Suarez (1961). The retinotopic extent of the uptake zones was determined by comparison with retinotopic maps of areas 17&18 (Tusa et al. 1978, 1979). The laminar extent of each uptake zone was determined by comparison with adjacent sections that were stained for Nissl bodies.

The areas of auditory cortex (Fig. 3) and their lamination were identified using cyto- and myeloarchitectonic features in Nissl (Rose 1949) and myelin (Gallyas, 1979) stains, and cytochrome oxidase histochemistry (Payne and Lomber 1996). As done previously (Lomber et al. 1995) the borders in the extrageniculate visual thalamus were identified using myeloarchitectonic methods. We used the nomenclature of Graybiel and Berson (Berson and Graybiel 1978, 1983; Graybiel 1972) to identify the subdivisions of the extrageniculate visual thalamus.

Within the auditory cortex, cell bodies found to contain WGA-HRP were plotted on a standardized flattened rendering adopted from Imig and Reale (1980) and Reale and Imig (1980) containing boundaries for AAF, AI, AII, DZ, PAF, VPAF, and VAF. Three other auditory areas of interest; AES (Clarey and Irvine 1986; Meredith and Clemo 1989), IN (Clasca et al. 1997, 2000), and T (Clasca et al. 1997, 2000), were also examined for labeled cells. Laminar distributions of labeled cells were delineated through comparison to surrounding tissue which was stained for Nissl bodies.

Identification and quantification of labeled cells (Fig. 2) followed several criteria. For a cell to be considered "labeled", and not an artifact of the reaction process, a nucleus had to be present. Also, the entirety of the soma membrane had to be present. Portions of a cell or remnants of a membrane were not counted. When labeled cells were found on the border of two auditory areas, or in a transitional zone between two areas, the total number of cells in question was evenly distributed to each of the two areas. To more accurately represent the number of labeled cells, numerous focal levels were taken through the z-plane to ensure the full thickness of the section was examined.

For quantitative comparisons, labeled cells in the lateral division of the lateral-posterior (LPl) nucleus were counted on every fifth section in a manner similar to that in auditory cortex. The number of labeled neurons in auditory cortex were standardized against LPl because it has strong and consistent projections to areas 17&18 (Berson and Graybiel 1978; Symonds et al. 1981; Updyke 1983), it contains a well-defined map of the lower visual field, including the vertical meridian (Hutchins and Updyke 1989; Raczkowski and Rosenquest 1981), and its borders can be easily distinguished in cytochrome oxidase stained sections (Payne and Lomber 1996).

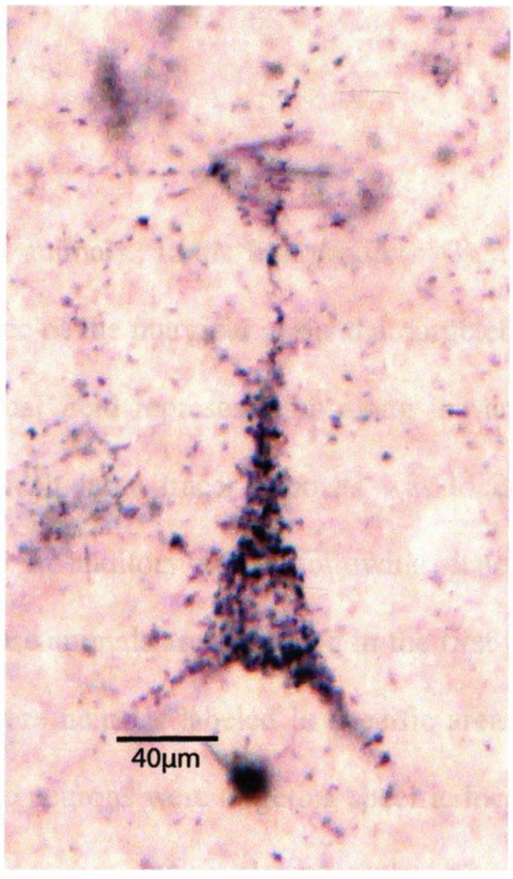


Fig. 2. An example of a labeled pyramidal cell in a TMB processed section. The top is toward the pial surface. The cell was visualized in case PC2.

CHAPTER 3 – Results

3.1 – Overview

We examined two groups of animals. In the first group (n=2), a large tracer deposit was made along the dorsal surface of the marginal gyrus that targeted an area centered on the lower vertical meridian visual field representation along the area 17/18 border (Payne 1990). The rationale for such large tracer deposits was to determine if any labeled neurons could be identified in auditory cortex following deposits into primary visual cortex. The results from these animals are presented in the first part of the results. Once we determined that there were neurons labeled in specific areas of auditory cortex, we next sought to examine if the neurons were targeting specific locations in V1. Therefore, the second group (n=12) of cats received smaller tracer deposits with subgroups targeting central (<2°, n=2), para-central (2°-10°, n=2), upper peripheral (>10°, n=2), horizontal peripheral (>10°, n=2), or lower peripheral (>10°, n=4) visual field representations. In the final portion of the results we present an analysis of the topography of labeled neurons in auditory cortex as a function of where they project in primary visual cortex.

3.2 – Large Deposits

3.2.1 – Injection Sites

In two cases (B1 and B2) seven neighboring penetrations were made along the crown of the marginal gyrus. These deposits resulted in an uptake zone stretching along the dorsal surface of the marginal gyrus (Fig. 3A) from Horsely-Clarke coronal level A11 to P6. In both cases the center of deposit and the uptake zone were confined to primary visual

cortex (areas 17 & 18). The deposit sites were similar in both cases. The spread of the deposits extended through all six cortical layers (Fig. 3B). When the uptake zone was compared to previously described retinotopic maps (Tusa et al. 1978, 1979) the deposit site was identified to include a strip of the visual field, along the vertical meridian, extending from an elevation of ~+2° to ~-40° (Fig. 3C). Therefore, the large deposits included both central and peripheral visual field representations.

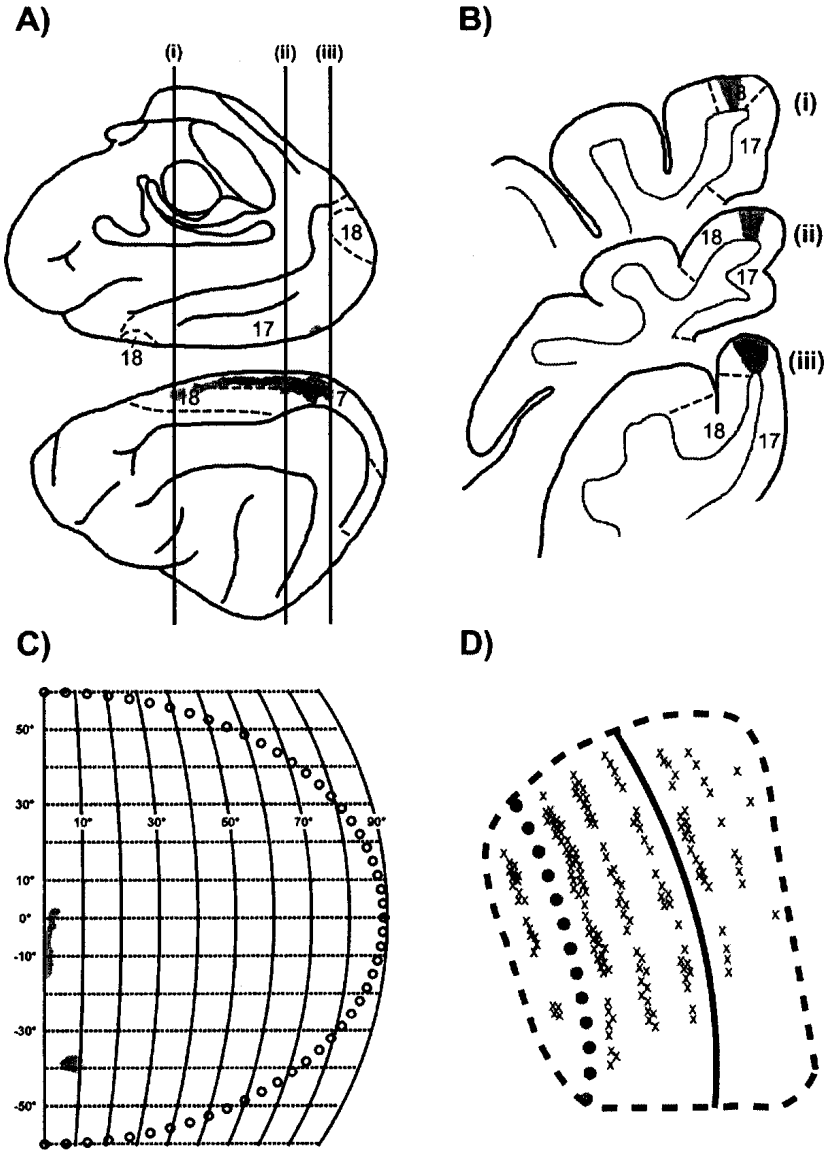
3.2.2 – Cell Labeling

Ten auditory areas (Fig. 4) were examined for the presence of labeled cells; primary auditory field (AI), second auditory field (AII), anterior auditory field (AAF), anterior field of the ectosylvian sulcus (fAES), dorsal zone (DZ), insular region (IN), posterior auditory field (PAF), temporal region (T), ventral auditory field (VAF), and the ventral posterior auditory field (VPAF). No area, with the exception of PAF, contained greater than 10% of the total number of labeled cells within auditory cortex (Fig. 5). The largest percentage of labeled cells was found within PAF (79.1%±5.9; mean±s.e.m.). The majority of these cells were in the supragranular layers. The area with second highest percentage of labeled cells was DZ which contained 7.6±2.8% of the labeled cells. Many of the auditory areas contained less than 1% of the labeled neurons (AAF, FAES, IN, and VAF; Fig. 5).

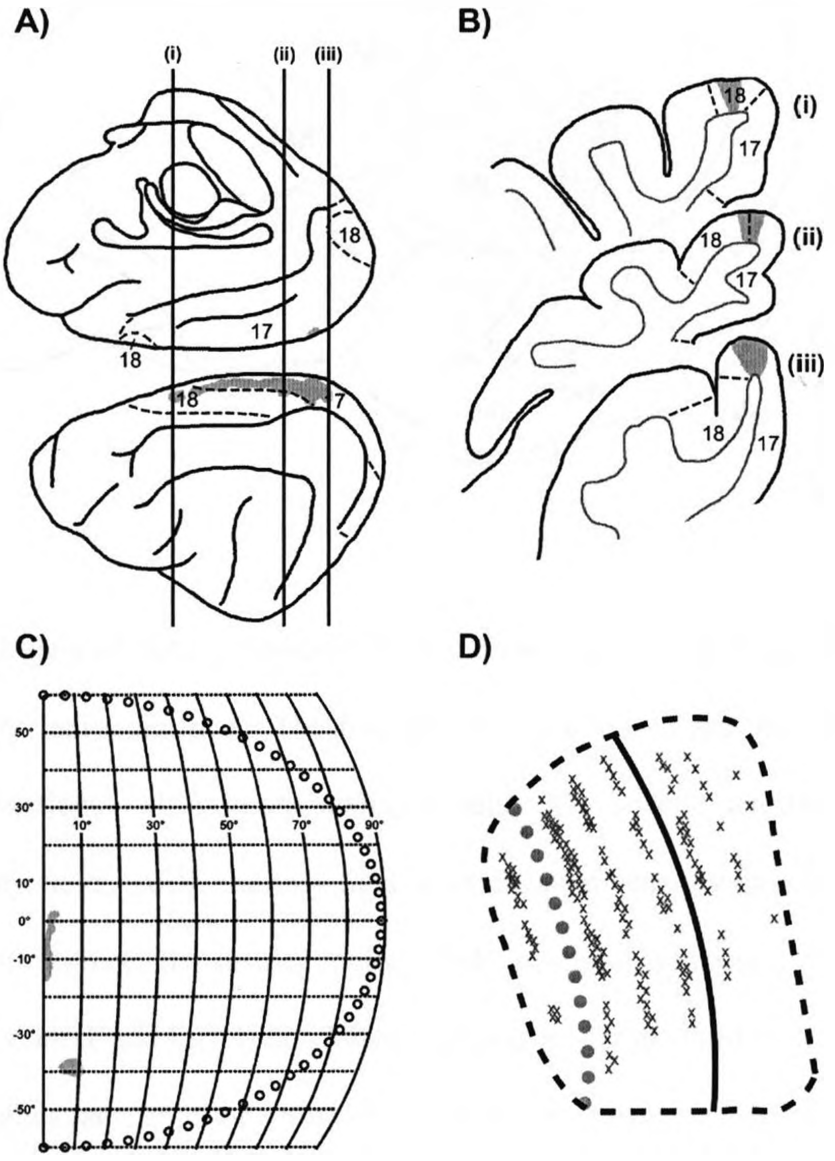
Fig. 3. Large tracer deposits along the area 17/18 border corresponding to the representation of the vertical meridian in the lower visual field. A) Dorsolateral (lower) and medial (upper) views of the left hemisphere. Left is anterior. Numbered vertical lines show positions of coronal sections in B. Dashed lines designate the boundaries of areas 17 and 18. The shaded area specifies the tracer uptake field. B) Anterior (i), middle (ii), and posterior (iii) coronal sections with tracer uptake field shaded in grey. Thin dark grey lines represent the white-grey matter interface. Solid wide lines indicate the pial surface. Left is lateral. C) Extent of contralateral (right) visual field indicated by open circles. The retinotopic location of tracer uptake field (grey shading), as determined by comparison with existing maps (Tusa et al. 1978, 1979). D) Flattened rendering of the posterior auditory field (PAF). Solid wide black line identifies the posterior lip of the posterior ectosylvian sulcus and the dotted line denotes the fundus. Grey Xs indicate individual labeled cells observed within TMB processed sections. Top is dorsal and left is anterior. Data from case B1.

With PAF containing the largest number of labeled cells, it became our region of interest. Labeled cells within PAF were plotted onto standardized flattened renderings (Fig. 6B) adopted from Imig and Reale (1980) and Reale and Imig (1980). The result, depicted in Fig. 3D, shows a large number of labeled cells spread throughout PAF with the highest concentration on the posterior bank of the posterior ectosylvian sulcus (the sulcal portion of PAF). The apparent bands of cells are an artifact of the series sampling where each coronal section of a specific series is 250 μm apart.

Lower Vertical Meridian



Lower Vertical Meridian



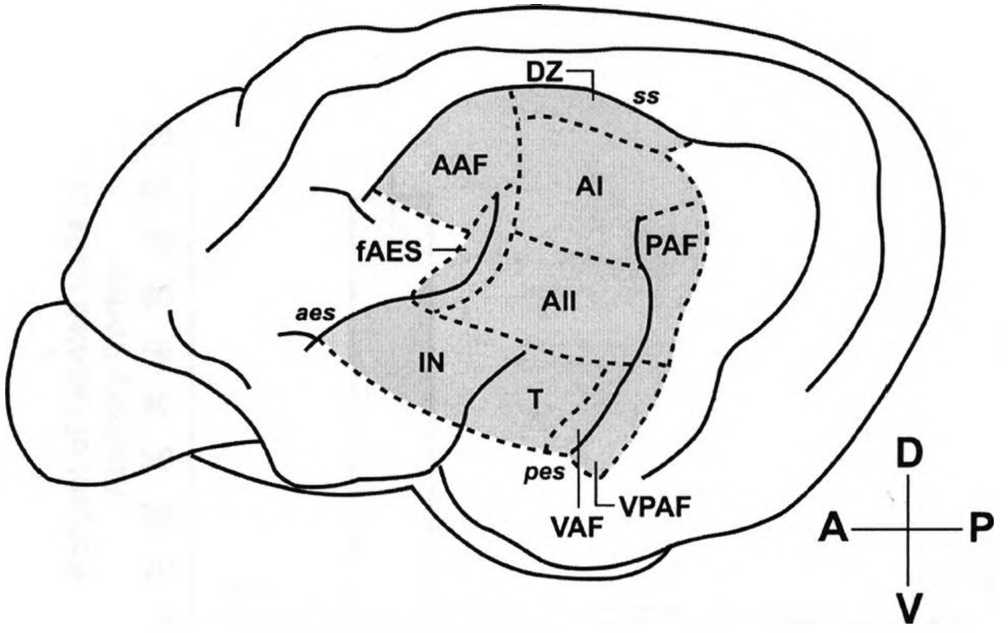


Fig. 4. Lateral view of the left hemisphere of the cat cerebrum showing the locations of the ten auditory loci examined. The boundaries of each area are indicated by dashed lines. Abbreviations: AI, primary auditory field; AII, second auditory field; AAF, anterior auditory field; fAES, auditory field of the anterior ectosylvian sulcus; DZ, dorsal zone of auditory cortex; IN, insular region; PAF, posterior auditory field; T, temporal region; VAF, ventral auditory field; VPAF, ventral posterior auditory field. Sulci are indicated by italics: aes, anterior ectosylvian sulcus; pes, posterior ectosylvian sulcus; ss, suprasylvian sulcus. For other conventions, see Fig. 1.

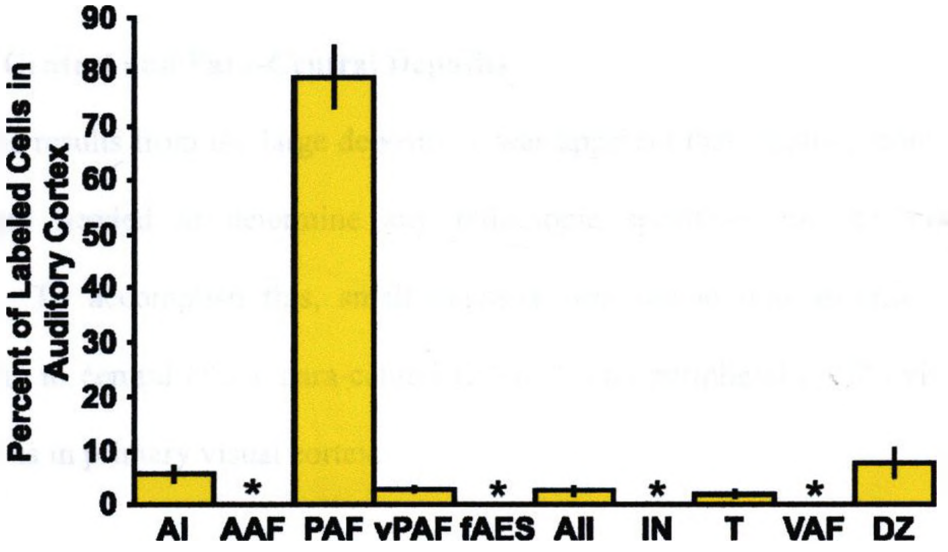


Fig. 5. Histogram showing the percentage of labeled cells in each of the auditory areas, as a function of all labeled neurons in auditory cortex following WGA-HRP deposits along the vertical meridian representation in primary visual cortex. For each area, mean and standard error are provided. Asterisks indicate areas that had less than one percent of labeled cells. Data from cases B1 and B2.

Extrastriate visual areas were also found to have patterns and densities of labeled cells that were characteristic of projections previously identified within extrastriate visual cortex (Symonds and Rosenquist 1984a,b). Characteristic patterns of labeling were also identified within the thalamus (Symonds et al. 1981).

3.3 – Small Central and Para-Central Deposits

In light of the results from the large deposits, it was apparent that smaller, more specific, deposits were needed to determine any retinotopic specificity to the audiovisual projections. To accomplish this, small deposits were made into specific locations corresponding to central (<2°), para-central (2°-10°), and peripheral (>10°) visual field representations in primary visual cortex.

3.3.1 – Injection Sites

The four cases that received small deposits targeted at the central (n=2) or para-central (n=2) visual field representations resulted in small uptake fields confined to the marginal gyrus (Figs. 7A and 8A, respectively). In both central cases (C1 and C2, Table 1) the injection site was concentrated on the border between areas 17 and 18 at Horsely-Clarke coronal level P3. Both central cases had similar deposit sites (Fig. 7A). The two para-central cases (PC1 and PC2, Table 1) were centered on the marginal gyrus at Horsely-Clarke coronal level AP0, just ventral of the suprasplenial sulcus. These tracer deposits were confined to area 17. Both para-central cases had similar deposit sites (Fig. 8A). The spread of both central and para-central deposits extended across all cortical layers (Figs. 7B, 8B). When the uptake zone was compared to previously described retinotopic

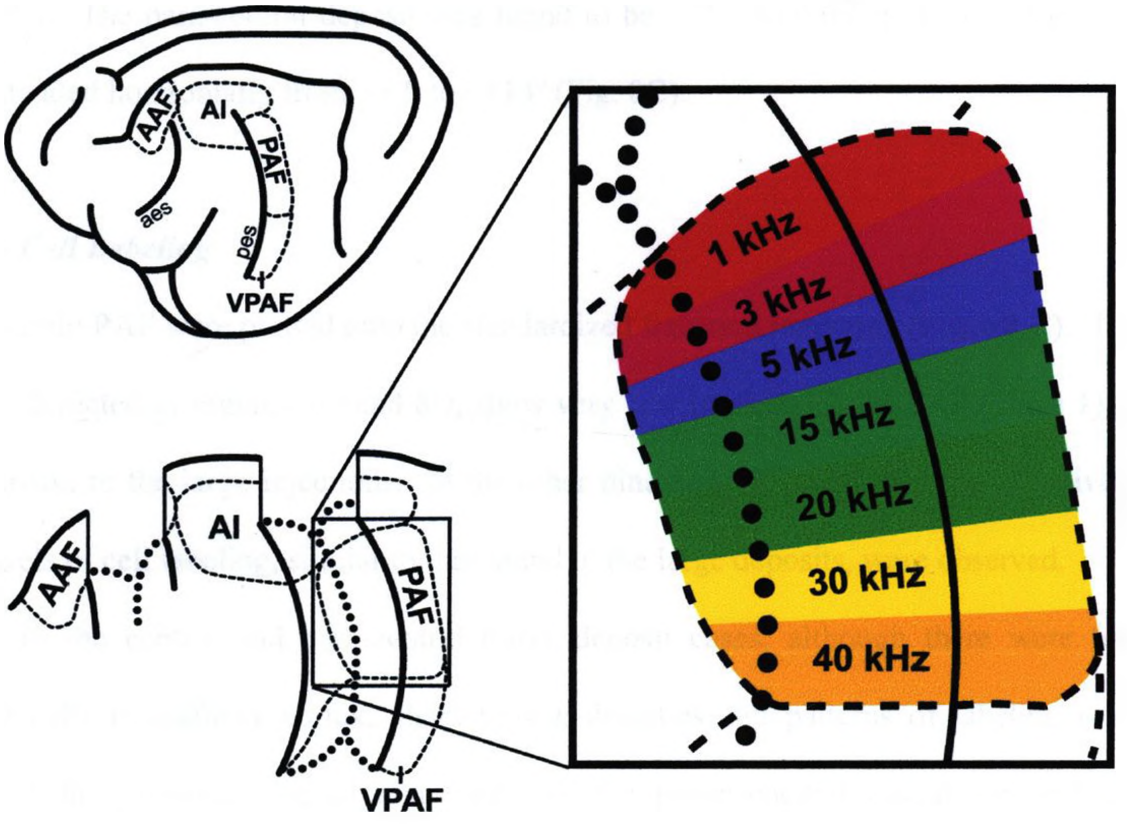


Fig. 6. Lateral view of the cat cerebrum (A) with the four tonotopic areas outlined. For abbreviations, see Fig. 4. B) An expanded, flattened rendering of the four areas. The wide black lines indicate the apertures of the sulci and the dotted lines indicate the sulcal fundi. Thin solid lines indicate discontinuities on gyral surfaces resulting from flattening. C) An enlargement of PAF showing the orientation of frequency bands adapted from Imig and Reale (1980) and Reale and Imig (1980).

maps (Tusa et al. 1978, 1979) the central deposit was identified to correspond to a small region of the visual field from an elevation of ~+2° to ~-2° and extending horizontally ~2° (Fig. 7C). The para-central deposit was found to be ~2° below the horizontal meridian and extended horizontally from ~+7° to ~+14° (Fig. 8C).

3.3.2 – Cell Labeling

Cells within PAF were plotted onto the standardized flattened rendering (Fig. 6B,C). The results, depicted in Figures 7D and 8D, show very few labeled cells in PAF (Table 1) in comparison to the large injections. In the other nine areas of auditory cortex relatively low levels of cell labeling, similar to that found in the large deposits, were observed.

In the central and para-central tracer deposit cases, although there were few labeled cells in auditory cortex, characteristic densities and patterns of labeling were observed in extrastriate visual areas such as the posteromedial lateral suprasylvian (PMLS; Fig. 9A), posterolateral lateral suprasylvian (PLLS), and anteromedial lateral suprasylvian (AMLS) cortices (Einstein 1996; Symonds and Rosenquist 1984a,b). Characteristic patterns of thalamic labeling were also identified following tracer deposits into the central and para-central representations of V1. Large numbers of labeled cells were observed in layers A, A1, and the C-complex (parvocellular and magnocellular portions of the C-layers) of the dorsal lateral geniculate nucleus (dLGN; Fig. 9B) of the thalamus, the lateral division of the lateral posterior (LPl) nucleus, and the pulvinar nucleus (Symonds et al. 1981). The presence of labeling in thalamic and extrastriate visual cortical areas confirmed the success of the deposits in labeling retrograde

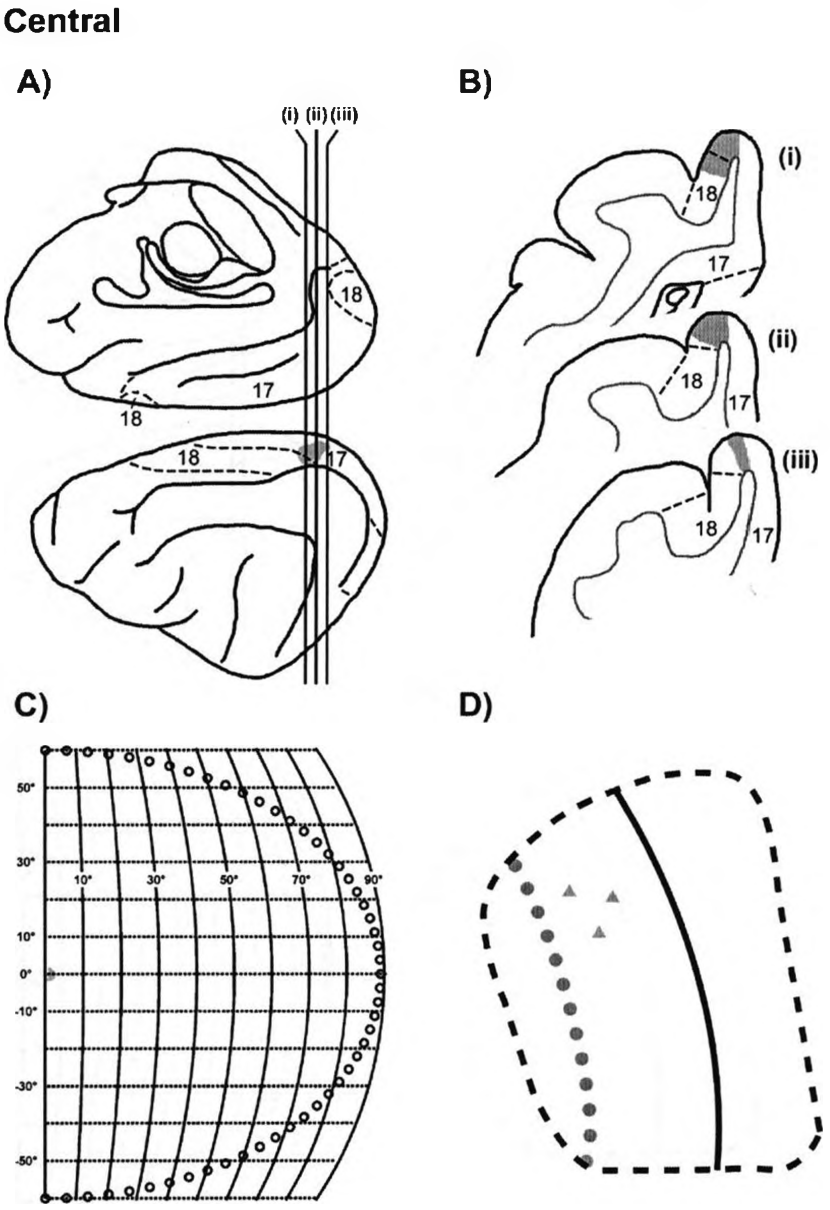


Fig. 7. An example of a tracer deposit in the central (<2°) visual field. For conventions see Fig 3. In D, grey triangles indicate individual labeled cells identified in PAF. Data from case C1. Note few labeled neurons.

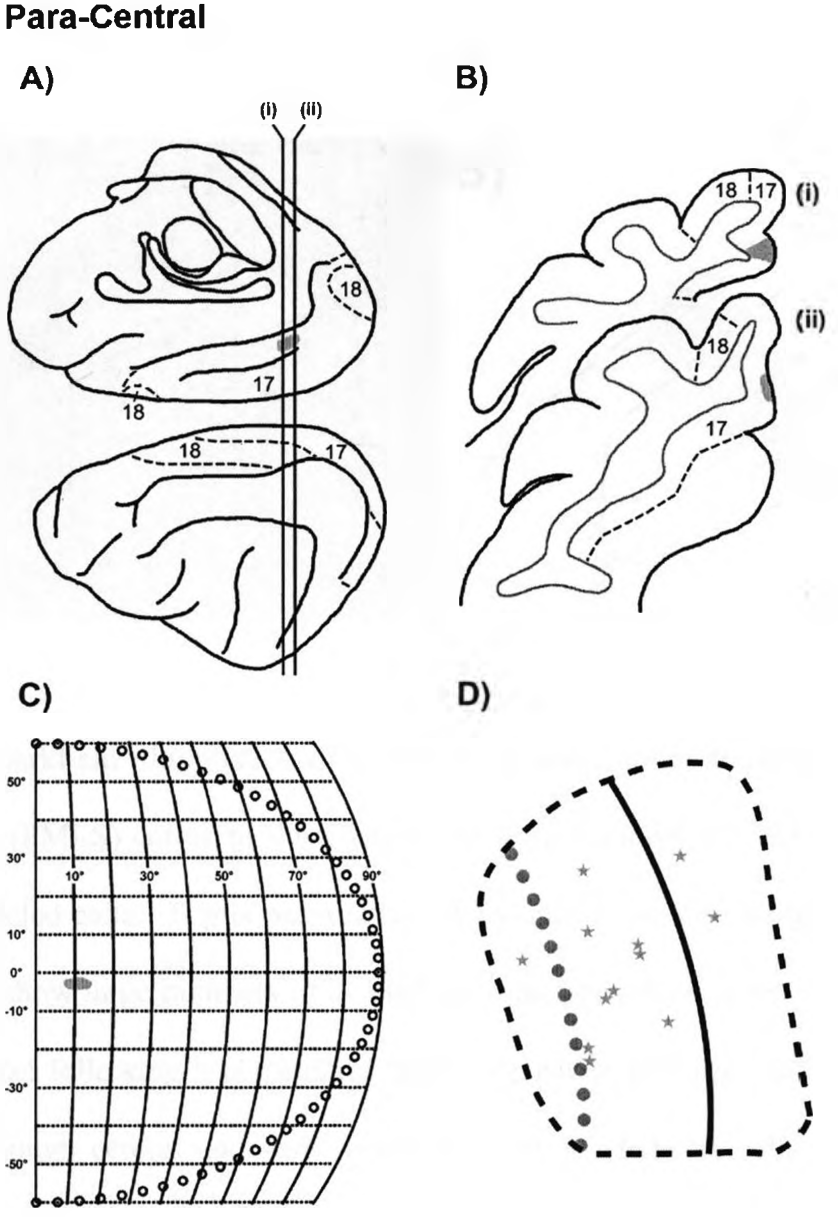


Fig. 8. An example of a tracer deposit in the paracentral (2°- 10°) visual field. For conventions see Fig 3. In D, grey stars indicate individual labeled cells identified in PAF. Data from case PC2. Note few labeled neurons.

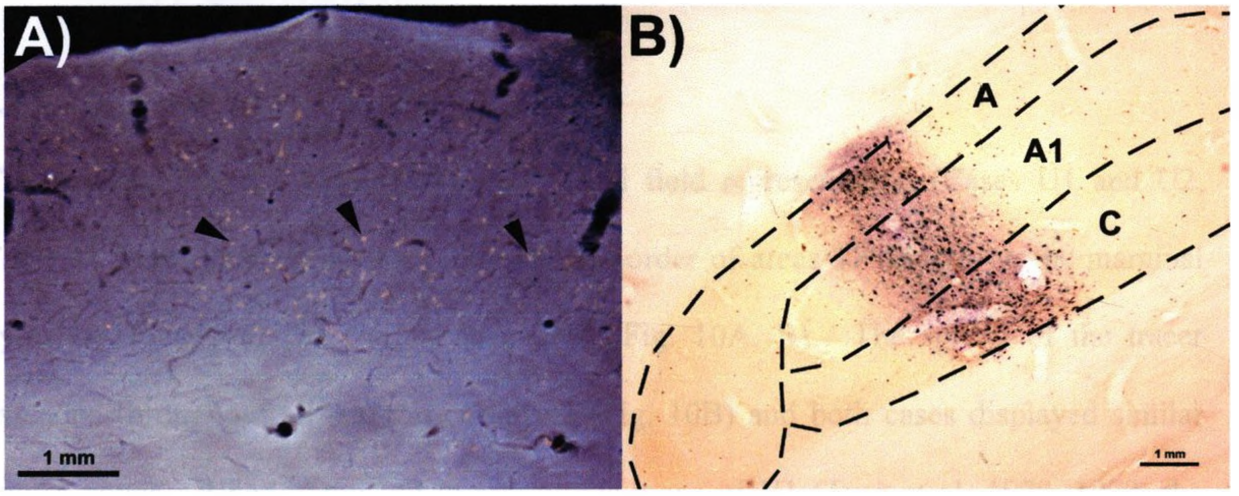


Fig. 9. A) Darkfield illumination of a coronal section through the posteromedial lateral suprasylvian (PMLS) cortex to show labeled neurons (case PC2). Black arrows indicate exemplar labeled cells. Top is pial surface. B) Coronal section through the left LGN of case PC2 to show large numbers of labeled neurons throughout layers A, A1, and the C-complex (Ccx) following a paracentral tracer deposit in primary visual cortex. Left is lateral. Although central and para-central deposits labeled few cells in PAF, they did label many neurons in extrastriate visual cortex (A) and thalamus (B).

pathways. The absence of labeled cells in PAF indicated a weak projection from PAF to the central and para-central visual field representations within V1.

3.4 – Small Peripheral Deposits

3.4.1 – Injection Sites

The deposits into the upper peripheral visual field representation (Cases U1 and U2, Table 1) were centered on the ventromedial border of areas 17 and 18 on the marginal gyrus at Horsely-Clarke coronal level P10 (Fig. 10A, B). The spread of the tracer extended throughout all six cortical layers (Fig. 10B) and both cases displayed similar uptake zones. When compared to retinotopic maps of V1 (Tusa et al. 1978, 1979) the deposit site was located on the vertical meridian and extend from an elevation of ~+20° to ~+30° (Fig. 10C).

In cases H1 and H2 (Table 1), deposits directed at the horizontal peripheral visual field representation were centered on the dorsal bank of the splenial sulcus at Horsely-Clarke coronal level AP0 (Fig. 11A,B). The spread of the label extended across all cortical layers (Fig. 11B) and both cases showed similar uptake zones. In retinotopic terms, the deposit site was identified to be at an elevation of ~-10° and extend horizontally from ~40° to ~85° (Fig. 11C).

In the four remaining cases (L1-4, Table 1), deposits directed at the lower peripheral visual field representation were centered on the marginal gyrus at the border between areas 17 and 18 at Horsely-Clarke coronal level A14 (Fig. 12A, B). The spread

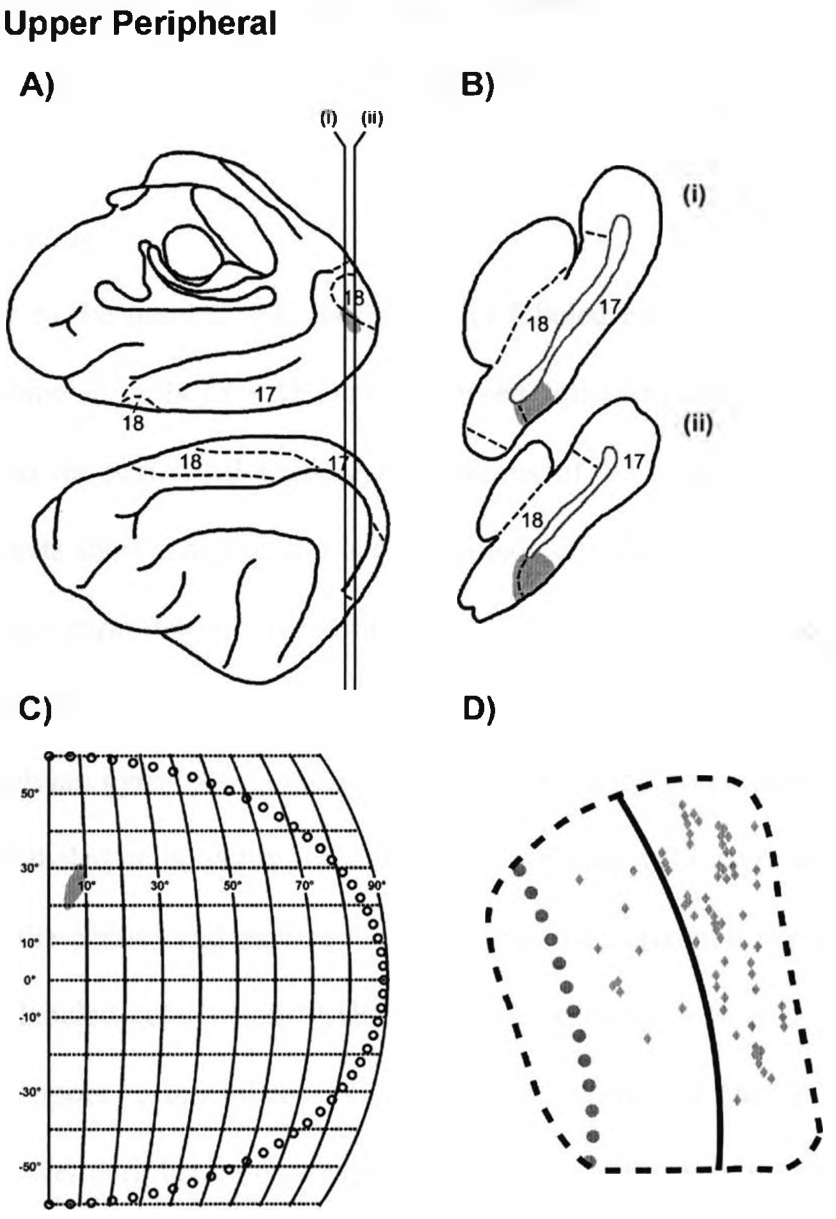


Fig. 10. An example of a tracer deposit in the peripheral (>10°) upper visual field. For conventions see Fig 3. In D, grey diamonds indicate individual labeled cells identified in PAF. Data from case U2. Note labeled neurons in the gyral portion of PAF.

of the deposits extended throughout all six cortical layers (Fig 12B) and all four cases there was little variation in the uptake zones. Retinotopically, the deposit sites were found to extend from an elevation of ~-30° to ~-55° (Fig. 12C).

3.4.2 – Cell Labeling

Overall, similar to the number and distribution of labeled cells in the large deposits, an abundance of labeled cells in PAF were observed following deposits into the upper, horizontal, or lower peripheral field representations of V1. The results of the upper peripheral deposits show a higher number of labeled cells (Table 1) in comparison to the central and para-central deposits (compare Fig. 10D to Figs. 7D,8D). The labeled cells are distributed throughout PAF with a higher concentration located in anterior third of the posterior ectosylvian gyrus (the gyral portion of PAF). In the horizontal peripheral cases the number of labeled cells within PAF, depicted in Figure 11D, were also much higher (Table 1) than the central and para-central cases. In the horizontal peripheral cases the distribution of labeled cells within PAF appears to be more even (Fig. 11D) than that identified in the upper peripheral cases (Fig. 10D). The third and final group of deposits, made into the lower peripheral visual representation of V1 also resulted in a much higher number of labeled cells (Table 1; Fig. 12D). The labeled cells are distributed throughout PAF with a higher concentration located in the posterior bank of the posterior ectosylvian sulcus (the sulcal portion of PAF). Therefore, these results demonstrate that the audiovisual projection from PAF specifically targets the peripheral visual field representation in V1.

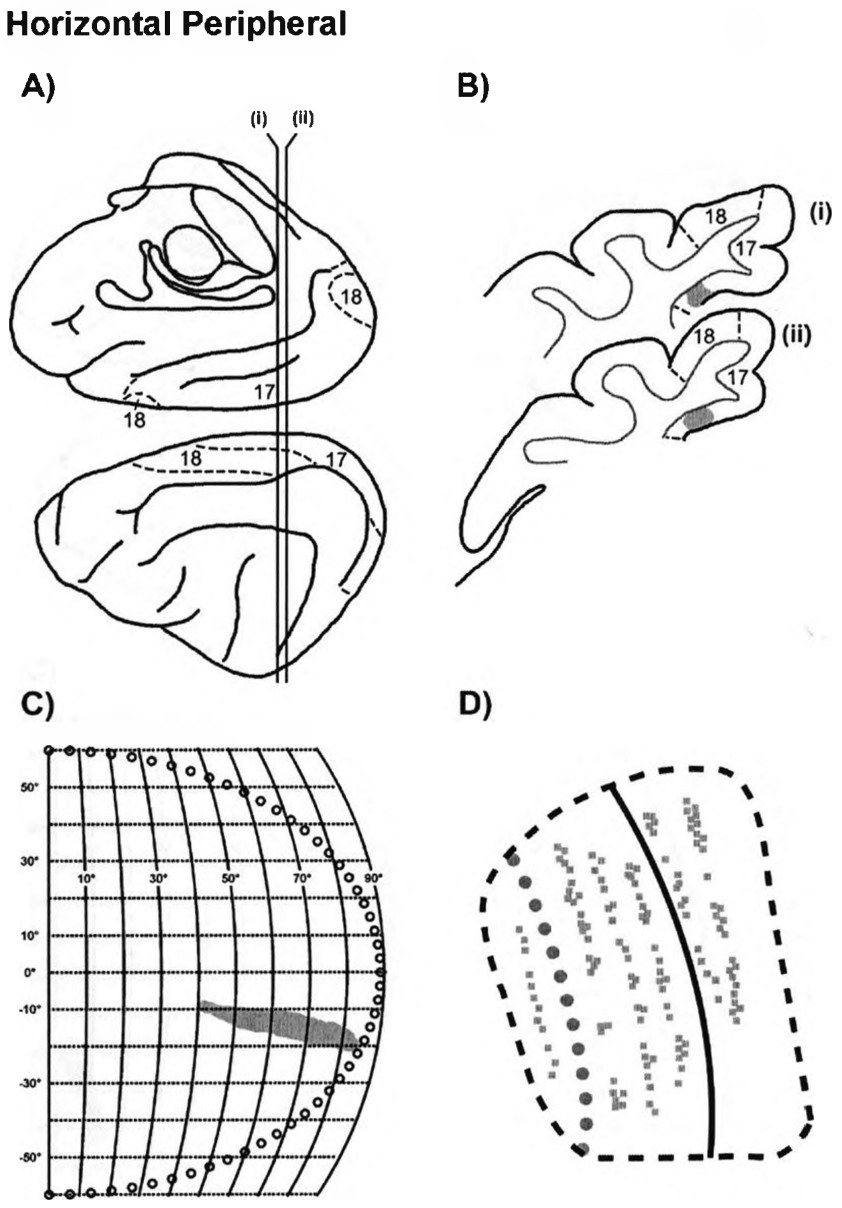


Fig. 11. An example of a tracer deposit in the peripheral (>10°) visual field just below the horizontal meridian. For conventions see Fig 3. In D, grey squares indicate individual labeled cells identified in PAF. Data from case H1. Note labeled cells throughout PAF.

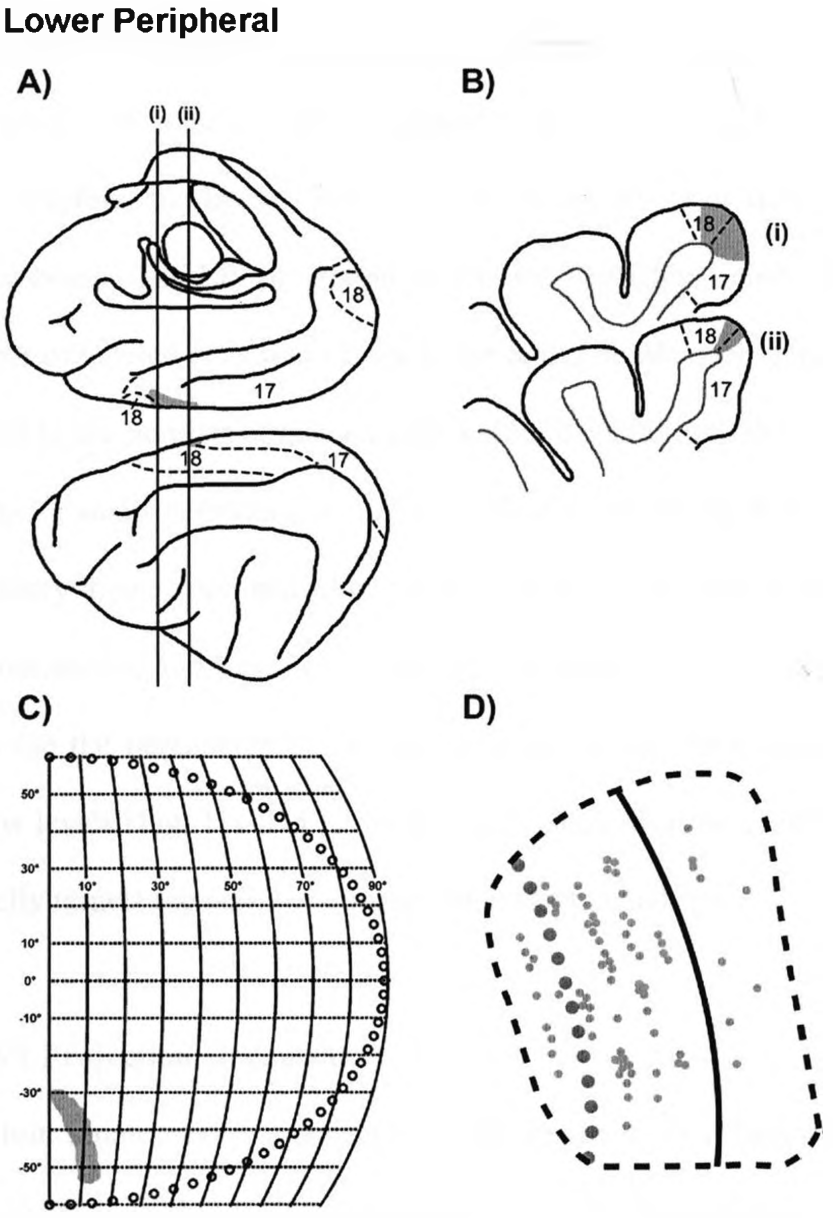


Fig. 12. An example of a tracer deposit in the peripheral (>10°) lower visual field. For conventions see Fig 3. In D, grey circles indicate individual labeled cells in PAF. Data from case L2. Note labeled cells in the sulcal portion of PAF.

3.5 – Small Deposits Comparison

To enable comparison of the percentages of labeled cells between individual cases, the numbers of labeled cells were normalized against a structure that had consistent labeling in all cases. Therefore, the lateral division of the lateral posterior (LPl) nucleus of the thalamus was chosen. The LPl projection to V1 was consistent across all cats and the resulting number of labeled cells was similar to the larger numbers observed in PAF.

When compared to the number of labeled cells within the LPl, both the central and para-central cases had a small percentage (<10%) of labeled cells within PAF and within the other nine auditory areas examined (AUD; Fig. 13A,B). The three types of peripheral cases (upper, horizontal, and lower), had a large percentage (all >70%) of labeled cells within PAF while the percentage of labeled cells within the other nine auditory areas remained at low levels (Fig. 13C,D,F). These results show that the projection from PAF to V1 specifically targets the peripheral representation of visual space.

3.6 – PAF to V1 Projection Organization

PAF is one of four tonotopically organized auditory areas (Fig. 6A; Imig and Reale 1980; Reale and Imig 1980). Within PAF there are bands of cells which respond best to similar frequencies and are organized so that cells responding to lower frequencies are more dorsal while cells responding to higher frequencies are more ventral (Fig. 6C). As V1 has a retinotopic organization (Tusa et al. 1978, 1979), the sites it receives projections from (afferents) and the sites it sends projections to (efferents), also tend to have some form of retinotopic organization (Grant and Shipp 1991; Hutchins and Updyke 1989; Palmer et al. 1978; Sanderson 1971; Tusa and Palmer 1980; Updyke 1986). Therefore, a

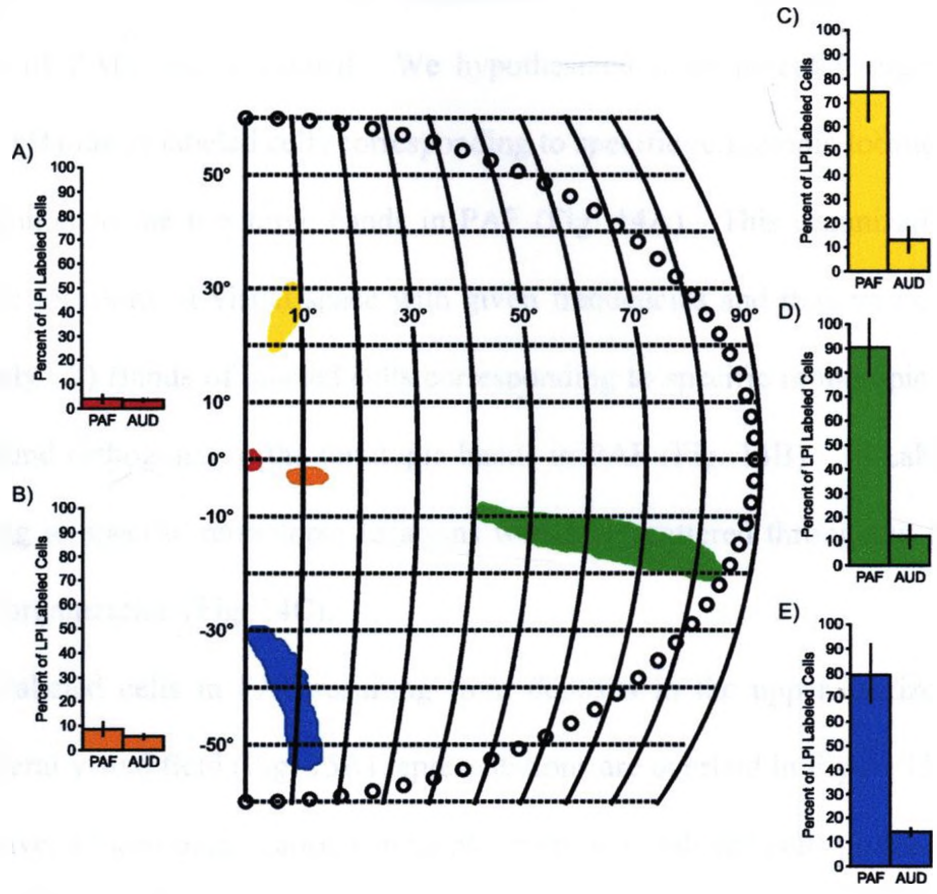


Fig. 13. A contralateral (right) visual map showing tracer deposits in the central (red; <2°), para-central (orange; 2°-10°) and peripheral (>10°) upper (yellow), horizontal (green) and lower (blue) visual field representations. Histograms show the percentages of labeled cells as a function of the number of labeled cells in the lateral division of the lateral posterior (LPl) nucleus of the thalamus. Percentage of labeled cells in PAF and all other auditory cortices (AUD) are shown for central (A), para-central (B) and upper peripheral (C), horizontal peripheral (D) and lower peripheral (E) deposits. Histograms show mean percentage and standard errors for all cases. Note the large percentage of labeled cells in PAF following tracer deposits in the peripheral representation of area 17.

possible retinotopic organization of the projection to V1, with respect to the tonotopic organization of PAF, was examined. We hypothesized three potential organizational scenarios; 1) Bands of labeled cells corresponding to specific retinotopic locations would be found parallel to the tonotopic bands in PAF (Fig. 14A). This organization would align specific locations of visual space with given frequencies and thus was considered the least likely. 2) Bands of labeled cells corresponding to specific retinotopic locations would be found orthogonal to the tonotopic bands in PAF (Fig. 14B). 3) Labeled cells corresponding to specific retinotopic locations would be scattered throughout PAF with no apparent organization (Fig. 14C).

The labeled cells in PAF resulting from deposits in the upper, horizontal, and lower peripheral visual field (Fig. 15A) representations are overlaid in Figure 15B. From this perspective, a loose organization can be observed, with labeled cells projecting to the lower visual field representation (blue) concentrated in the posterior ectosylvian (PE) sulcus, and those cells projecting to the upper visual field representation (yellow) concentrated on the PE gyrus. To quantitatively confirm this observation, labeled cells from each of the peripheral conditions were classified as residing on the PE gyrus or in the PE sulcus and calculated as a percentage of all labeled cells within PAF (Fig. 15C). From this analysis we identified that, within PAF, the majority of cells projecting to the upper peripheral visual field representation in V1 are located on the PE gyrus (84.3±1.9%), while the majority of cells projecting to the lower peripheral representation are located on the posterior bank of the PE sulcus (76.9±4.7%). Therefore, the projection from PAF to V1 has a loose topographic organization roughly corresponding to the second hypothesized organizational scenario (Fig. 14B).

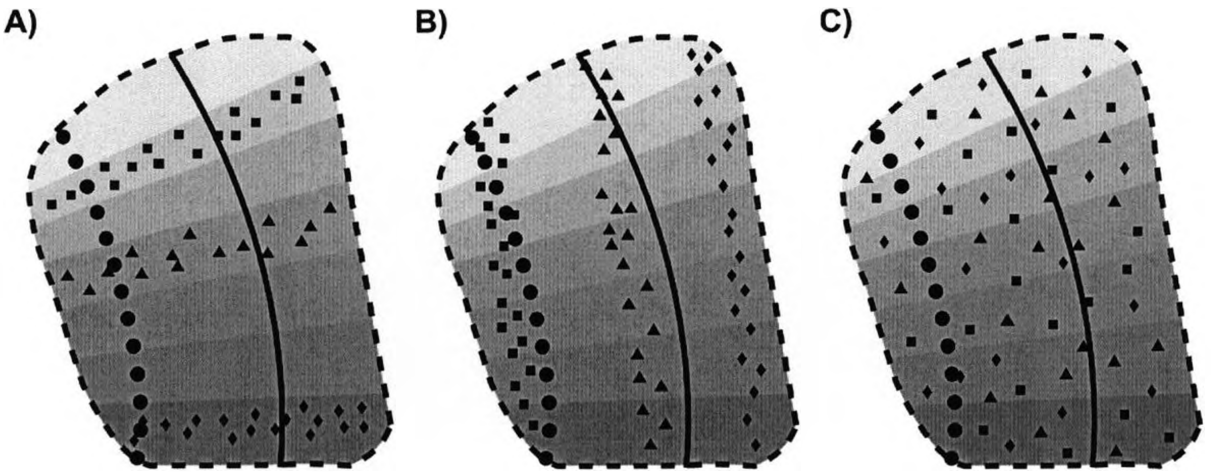
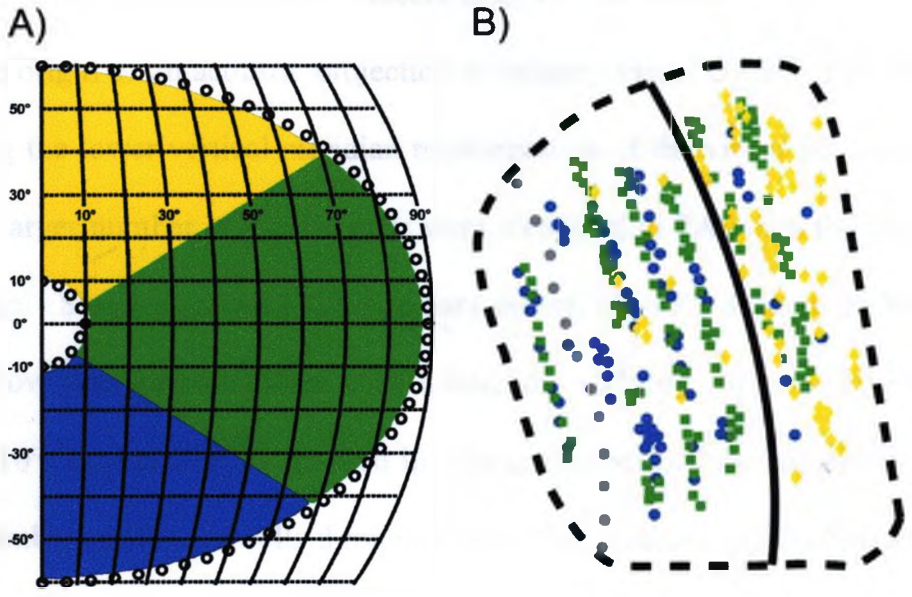
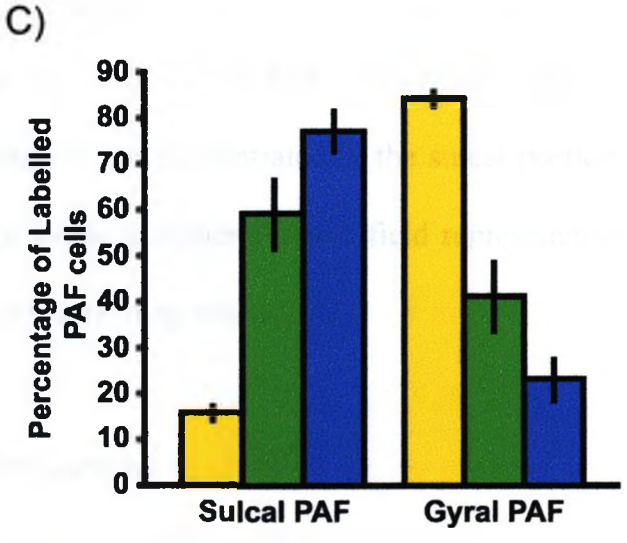


Fig. 14. Three organizational scenarios within PAF were hypothesized following tracer injections into areas 17 & 18. Each symbol corresponds to a hypothetical injection at a different retinotopic location in the visual field. A) Bands of labeled cells parallel to the frequency bands. B) Bands of labeled cells orthogonal to the frequency bands. C) Scattered cells throughout PAF.

Fig. 15. Organization of labeled cells identified in PAF as a function of the retinotopic location of the tracer deposit. A) Contralateral (right) visual field with peripheral segments dissociated. Yellow, green and blue sections representing upper, horizontal and lower visual fields, respectively. B) Overlay of the labeled PAF cells identified in three exemplar cases. Diamonds, squares and circles correspond to upper, horizontal and lower peripheral deposits, respectively. C) Percentage of labeled cells in the sulcal and gyral portions of PAF with relation to the retinotopic position of the tracer deposit. Color coding corresponds to those found in A. Histogram shows mean percentage and standard errors for all cases. Cells projecting to the upper peripheral visual field representation tended to be located in the gyral portion of the PAF while cells projecting to the lower peripheral field representation tended to be located in the sulcal portion of PAF.


A)
B)
50°
30°
10°
0°
-10°
-30°
-50°
10°
30°
50°
70°
90°


C)
Percentage of Labelled PAF cells
90
80
70
60
50
40
30
20
10
0
Sulcal PAF
Gyral PAF

CHAPTER 4 – Discussion

4.1 – Summary

In this study we deposited retrograde tracers into V1 and examined auditory cortex to determine the origin of an acoustic projection to primary visual cortex. Following large deposits along the lower vertical meridian representation of the visual field within V1, a substantially larger number of labeled cells were identified in PAF than the remainder of auditory cortex. Smaller central (<2°) and para-central (2°-10°) deposits in V1 resulted in relatively low numbers of labeled cells throughout auditory cortex. However, small peripheral (>10°) deposits in V1 resulted in a large number of labeled cells within PAF with small numbers of labeled cells throughout the other auditory areas. Further analysis of the pattern of labeled cells in PAF revealed a loose retinotopic organization in the PAF to V1 projection. Cells projecting to the upper peripheral visual field representation are concentrated on the gyral portion of PAF and cells projecting to the lower peripheral visual field representation are concentrated in the sulcal portion of PAF. Therefore, the projection from PAF to the peripheral visual field representation of V1 is robust and is organized in a coarse spatial map within PAF.

4.2 – Audiovisual Projections

In examining cortical connections, most studies focus on projections within a particular modality. Therefore, most reports of projections to primary visual cortex exclusively describe cortical projections from other visual areas. Indeed, such is the case in the cat, with nearly all previous studies focusing on inputs to primary visual cortex from other

visual cortical structures (eg. Bullier et al. 1984; Symonds and Rosenquest 1984a). The only studies to examine non-visual cortical projections to primary visual cortex have concentrated on the development of these projections. Overall, these studies have reported dense exuberant projections from auditory cortex to primary visual cortex during postnatal development (Clarke and Innocenti 1986; Dehay et al. 1988; Innocenti and Clarke 1984). However, over time, these projections are lost and only a meager number remain by the time the animal reaches adolescence (Clarke and Innocenti 1986; Innocenti et al. 1988). The results from these investigations beg the question as to why the PAF to V1 projection was not readily identified in these earlier studies? It is likely that the answer to this question lies in the specificity of the projection. The present study identified audiovisual projections to the peripheral representation in primary visual cortex. The exposed, and most accessible portion of primary visual cortex is the central visual field representation lying along the crown of the marginal gyrus (Tusa et al. 1978, 1979). Therefore, it is likely that the retrograde tracer deposits made in these earlier studies were not large enough to include the peripheral field representations in primary visual cortex, thus not labeling this projection.

Studies of projections from auditory cortex to primary visual cortex, in the mature cat, confirm the present observations. Deposits of anterograde tracers into areas AI and AII of cats older than 34 postnatal days results in few, if any, labeled axons in primary visual cortex (Innocenti et al., 1988). This finding supports the results of the present study which found that, regardless of the retinotopic position of the retrograde tracer deposit in primary visual cortex, few neurons were labeled in areas AI or AII. Therefore,

previous anterograde and retrograde studies of the audiovisual projection in cats support the present findings.

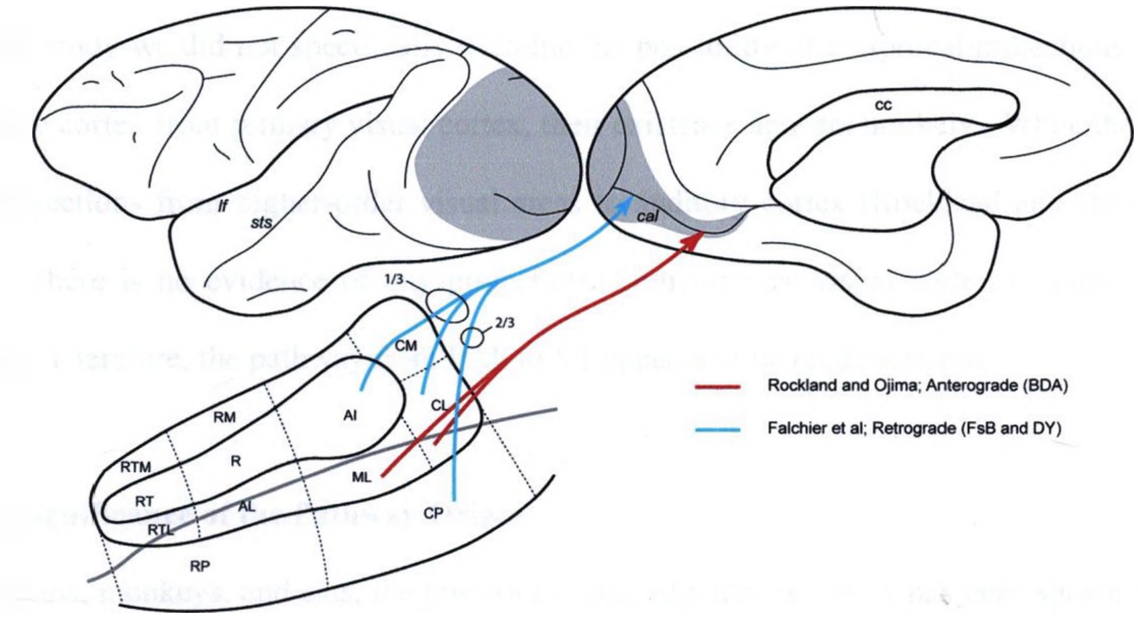
The present findings closely match similar observations made in the monkey. Several recent studies have examined audiovisual projections in the mature monkey. In these studies, projections from auditory association cortex within the caudal parabelt (CP) were identified terminating in the peripheral visual field representation of V1 (Fig. 16A; Clavagnier et al. 2004; Falchier et al. 2002; Rockland and Ojima 2003). Furthermore, in the monkey, meager auditory cortex projections to the central visual field representation of primary visual cortex were identified (Clavagnier et al. 2004; Falchier et al. 2002; Rockland and Ojima, 2003;). Therefore, in both cats and monkeys, projections from specific posterior regions of auditory cortex target the peripheral field representation in primary visual cortex (Fig.16).

4.3 – Is the Projection Reciprocal?

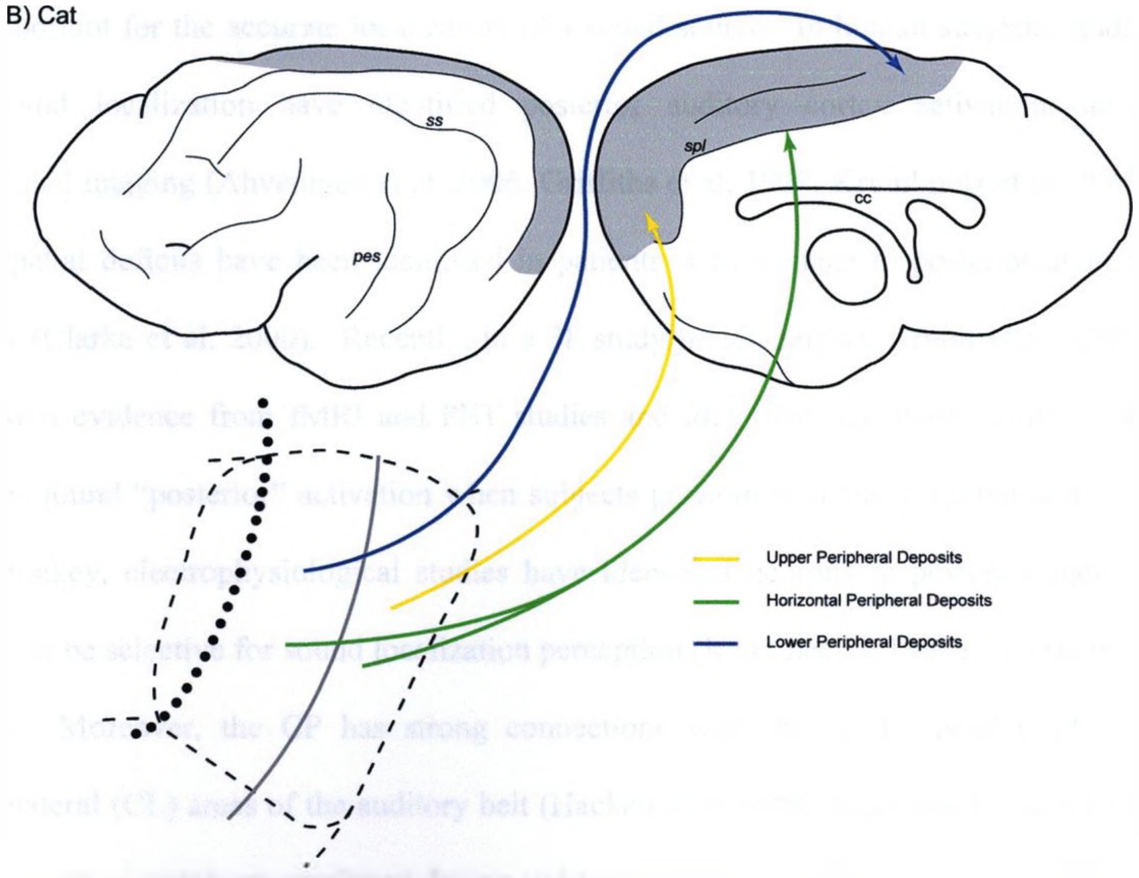
Within visual or auditory cortex, projections between areas are largely reciprocal (Felleman and Van Essen 1991; Lee and Winer 2008; Rockland and Pandya 1979) with only a small number being identified as unidirectional (Felleman and Van Essen 1991). Thus, it is conceivable that reciprocal projections, arising in primary visual cortex and projecting to posterior auditory cortex, may exist. However, earlier studies in the cat failed to identify a direct projection from primary visual cortex to PAF (Innocenti and Clarke 1984; Innocenti et al. 1988). Furthermore, Falchier et al. (2002) specifically

Fig. 16. Audiovisual pathways terminating in primary visual cortex of the monkey (A) and cat (B). Grey areas on the medial (right) and lateral (left) views indicate primary visual cortex (V1). Dashed lines indicated auditory area boundaries, dotted lines indicate the sulcal fundus, and thin grey lines indicate the lip of the sulcus. Abbreviations: AI, primary auditory cortex; AL, anterior lateral auditory belt; CC, corpus callosum; CL, caudal lateral auditory belt; CM, caudomedial auditory belt; CP, caudal auditory parabelt; ML, middle lateral auditory belt; R, rostral area; RM, rostromedial auditory belt; RP, rostral auditory parabelt; RT, rostrotemporal area; RTL, lateral rostrotemporal auditory belt; RTM, medial rostrotemporal auditory belt. Sulci are indicated by italics: aes, anterior ectosylvian sulcus; cal, calcarine sulcus; lf, lateral fissure; pes, posterior ectosylvian sulcus; spl, splenial sulcus; sts, superior temporal sulcus.

A) Monkey



B) Cat



tested for the possibility of reciprocal connections by placing retrograde tracers into auditory cortex of the monkey and failed to label any neurons in area 17. Although in the present study we did not specifically examine the possibility of reciprocal projections to auditory cortex from primary visual cortex, their existence appears unlikely. While there are projections from higher-order visual areas to auditory cortex (Rockland and Ojima 2003), there is no evidence of any projections from primary visual cortex to auditory cortex. Therefore, the pathway from PAF to V1 appears to be unidirectional.

4.4 – Significance of the Pathway Origin

In humans, monkeys, and cats, the posterior region of auditory cortex has been shown to be important for the accurate localization of a sound source. In human subjects, studies of sound localization have identified posterior auditory cortex activation during functional imaging (Ahveninen et al. 2006; Griffiths et al. 1998; Krumbholz et al. 2005), and spatial deficits have been identified in patients with damage to posterior auditory cortex (Clarke et al. 2000). Recently, in a 38 study meta-analysis, Arnott et al. (2004) reviewed evidence from fMRI and PET studies and identified that the majority of the studies found "posterior" activation when subjects performed acoustic spatial tasks. In the monkey, electrophysiological studies have identified neurons in posterior auditory cortex to be selective for sound localization perception (Rauschecker 1998a, b; Tian et al. 2001). Moreover, the CP has strong connections with the caudomedial (CM) and caudolateral (CL) areas of the auditory belt (Hackett et al. 1998; Kaas and Hackett 1998, 2000), both of which are employed during auditory localization (Recanzone 2000; Tian et al. 2001). The presence of these dense interconnections has led others to propose that the

CP is especially suited for spatial processing of auditory information (Clavagnier et al. 2004; Kaas and Hackett 2000). Finally, in the cat, both electrophysiological and behavioral studies have demonstrated the importance of posterior auditory cortex, specifically PAF, to sound localization function (Malhotra et al. 2004; Malhotra and Lomber 2007; Stecker et al. 2003). Therefore, in humans, monkeys, and cats, regions of posterior auditory cortex play a significant role in sound localization.

Of all the areas in auditory cortex that could give rise to a projection to primary visual cortex, it is intriguing that the projection originates from PAF. Reversible deactivation of PAF produces profound sound localization deficits (Malhotra et al. 2004; Malhotra and Lomber 2007) and of all the auditory areas that contribute to sound localization, it appears to make the largest contribution (Malhotra et al. 2008). Likewise, removal of primary visual cortex in the cat produces severe visual localization deficits (Shupert et al 1993). Overall, the audiovisual pathway described in this study provides a direct link between the region of auditory cortex most responsible for acoustic localization, and a region of visual cortex responsible for accurate visual localization. We propose that this pathway may be involved in either the enhancement or reduction of visual localization functions in the peripheral visual field in the presence of a novel acoustic stimulus.

4.5 – PAF to V1 Projection Contribution to Integration

The integration of sensory information has long been proposed to occur only after processing within cortices devoted to a single modality. After such processing, it is proposed that multisensory integration occurs in association cortices outside of sensory specific cortex (Bavelier and Neville 2002). However, more recent studies have

suggested that multisensory integration may occur at early stages of visual processing in the cerebrum (Ghazanfar and Schroeder 2006; Schroeder et al. 2003; Schroeder and Foxe 2005). For example, studies in human subjects have reported V1 activity in response to acoustic stimulation (Giard and Peronne 1999; Noesselt et al. 2007). In fact, Watkins et al. (2007) noted that not only was activity higher in V1 when an acoustic stimulus was present but that the area of heightened activity was located in the region of V1 corresponding to the perceived location of a stimulus. However, the origin of this input has remained elusive. In light of this, we would propose that when active, this pathway could show retinotopically specific activity in V1 similar that observed by Watkins et al. (2007) and may make significant contributions to multisensory integration at the earliest levels of visual cortical processing.

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