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Distinct core thalamocortical pathways to central and dorsal primary auditory cortex

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ABSTRACT

The cat primary auditory cortex (AI) is usually assumed to form one continuous functional region. However, the dorsal and central parts of the AI iso-frequency domain contain neurons that have distinct response properties to acoustic stimuli. In this study, we asked whether neurons projecting to dorsal versus central regions of AI originate in different parts of the medial geniculate body (MGB). Spike rate responses to variations in the sound level and frequency of pure tones were used to measure characteristic frequency (CF) and frequency resolution. These were mapped with high spatial density in order to place retrograde tracers into matching frequency regions of the central narrow-band region (cNB) and dorsal AI. Labeled neurons projecting to these two parts of AI were concentrated in the middle and rostral thirds of the MGB, respectively. There was little evidence that differences in dorsal and central AI function could be due to convergent input from cells outside the ventral division of the MGB (MGBv). Instead, inputs arising from different locations along the caudal-to-rostral dimension of MGBv represent potential sources of response differences between central and dorsal sub-regions of AI.

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1. Introduction

Core auditory cortices are an essential first level of cortical processing of sound location, context and pattern and yet their functional organization has not been fully elucidated (Griffiths and Warren, 2004; King and Nelken, 2009; Rauschecker et al., 1997; Schreiner and Winer, 2007). All core auditory cortices receive thalamic input primarily from the ventral division of the medial geniculate body (MGBv) and have a topographic or cochleotopic organization of short latency characteristic frequency (CF) responses reflecting response topography of the sensory epithelium of the ear (Hackett, 2010). Though core regions share common features, such as a global cochleotopic organization and relatively short response latencies, they are also functionally specialized. Three core regions have been defined in several smaller mammals (i.e., primary (AI), anterior (AAF) and ventral (VAF) auditory fields (Hackett, 2010)) and in primate auditory cortex (AI, rostral (R) and rostral temporal (RT) fields (Hackett et al., 2001)). The cochleotopic gradient direction, and cortical area representing one octave can differ across neighboring core regions. For example, the direction, magnitude and frequency composition of cochleotopy, the spectral resolution and temporal response properties are different in AI versus AAF (Bizley et al., 2005; Imaizumi et al., 2004; Polley et al.,

Abbreviations: AI, primary auditory cortex; BB, broad band response area; bic, brachium of the inferior colliculus; CF, characteristic frequency at threshold; CTB, cholera toxin, subunit B; CTBG cholera toxin, subunit B conjugated to gold; cNB, central narrow bandwidth; D, dorsal nucleus of the MGB; DAB, diaminobenzidine; DD, deep dorsal nucleus of MGB; dNB1, first dorsal narrow bandwidth region; DS, dorsal superficial nucleus of the MGB; iMGBv, inferior part of the ventral division of the MGB; kHz, kilohertz; M, medial division of the MGB; MGB, medial geniculate body; MGBd, medial geniculate body, dorsal division; MGBv, ventral division and *pars lateralis* of the MGB; PAF, posterior auditory field; Ov, *pars ovoidalis* of the ventral division of the MGB; SG, medial geniculate body, suprageniculate nucleus; sMGBv, superior part of the ventral division of the MGB; V, ventral division and *pars lateralis* of the MGB; VL, medial geniculate body, ventral lateral nucleus; I–VI, auditory cortical layers; VAF, ventral auditory field.

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2007; Schreiner and Winer, 2007). On its ventral border, AI shares one continuous cochleotopy with VAF in cat and rat and its possible homologue, the posterior suprasylvian field (PSF), in ferret (Bizley et al., 2005; Kalatsky et al., 2005; Reale and Imig, 1980). Neighboring ventral core regions in small mammals have distinct and complementary response latencies, spectral resolutions, sound level tuning, and sensitivities to sound position cues without pronounced differences in cochleotopy (Bizley et al., 2005; Higgins et al., submitted for publication; Polley et al., 2007; Storace et al., 2010b). Primate core regions also have distinct and complementary sound sensitivities with or without marked differences in cochleotopy (Bendor and Wang, 2008; Recanzone et al., 2000).

Functional specializations can exist within sub-regions of a single core area. In the cat, AI is defined by a single cochleotopic organization, and yet sound frequency, level and binaural sensitivities vary systematically along its dorso-ventral or "iso-frequency" axis (Ehret and Schreiner, 1997; Mendelson et al., 1993; Middlebrooks and Zook, 1983; Nakamoto et al., 2004; Phillips et al., 1994; Read et al., 2001; Schreiner and Mendelson, 1990; Semple and Kitzes, 1993a). Dense multi-unit mapping studies find AI is divided into central and dorsal parts that can be further subdivided into smaller regions with distinct spectral bandwidths and corresponding spectral resolutions including: the central narrow (cNB) and broad (cBB) bandwidth regions and dorsal narrow (dNB) and broad (dBB) bandwidth regions (Schreiner et al., 2000). The cNB region has the highest spectral resolution (Q factor) measured with sound level at 40 decibels above threshold (Q_{40}). A small dNB region has higher spectral resolution than adjacent cBB and dBB regions but lower median spectral resolution than the cNB region (Imaizumi and Schreiner, 2007; Read et al., 2001; Schreiner et al., 2000). The cNB region covers a larger dorso-ventral cortical area than the frequency-matched dNB region creating a magnified representation of narrow bandwidths in central AI, as quantified with two-dimensional autocorrelations and linear cortical magnification factors (Imaizumi and Schreiner, 2007; Read et al., 2001). The dNB region has higher spatial variation or "scatter" of CF and a lower median tuning resolution (i.e., lower Q_{40}) than the cNB region (Ehret and Schreiner, 1997; Schreiner et al., 2000). Each narrow and broad bandwidth region is associated with a corresponding local maxima or minima in the topographic Q_{40} map of AI, quantified with two-dimensional autocorrelation (Read et al., 2001). This spatial organization allows for multiple representations of high and low spectral resolution in central and dorsal AI (Imaizumi and Schreiner, 2007) without marked differences in cochleotopy.

Differences in frequency tuning for central versus dorsal AI could, in principle, stem from differences in feed-forward projections from the thalamus (de la Rocha et al., 2008; Liu et al., 2007; Miller et al., 2001; Series et al., 2004; Wu et al., 2008). The present study investigates MGBv and non-MGBv pathway connections as possible sources of response property differences between cNB and dorsal AI. Response differences could arise from MGBv connections, as frequency response resolution and frequency laminar organization have been shown to vary along the caudal-to-rostral dimension of MGBv in several mammals (Calford, 1983; Cant and Benson, 2007; Rodrigues-Dagaeff et al., 1989; Rouiller et al., 1989; Storace et al., 2010a, b). Alternatively, response differences in dorsal AI could be due to connections with non-MGBv nuclei that are characteristic of the neighboring dorsal zone (DZ) belt region in the cat (He and Hashikawa, 1998; Lee and Winer, 2008). Here we present evidence that response differences across central and dorsal AI predominately stem from differences in MGBv source location.

2. Methods

2.1. Surgery and recording

Cats were housed and handled according to approved guidelines by the Institutional Animal Care and Use Committee (University of California at San Francisco). Data examined here were obtained from four adult cats purchased from an approved vendor.

Previously, we described the corticocortical and thalamocortical connections to the cNB region for five animals (Read et al., 2008, 2001). The aim of the present study was to characterize thalamocortical connections to dorsal AI in three of these previously described cases (Read et al., 2008, 2001). We also review the areal patterns of cNB-projecting neurons for a fourth cat, case 591, that has been quantified previously (Read et al., 2008). Single- and multi-unit responses to a five-octave range of pure tone stimuli were recorded in layers IIIb and IV of AI in ketamine-anesthetized adult cats. Transient (100 ms duration, 3 ms rise time) pure tones were presented with identical sound pressure level and frequency to both ears and varied pseudo-randomly over a 70 dB and five-octave range, respectively. Single and multi-unit spike rate responses within the 100 ms tone presentation window were averaged across repeat sound conditions to generate a tone frequency response area (FRA). Parameters measured from the FRA include the sound frequency eliciting a response at the lowest threshold of all tested frequencies (i.e., CF), linear bandwidth, and tuning resolution (i.e., Q factor). Linear bandwidth was estimated as the difference between upper and lower frequency limits of the FRA at 40 dB above threshold and its inverse normalized to CF was computed as a metric of tuning resolution ($Q_{40} = \mathrm{CF}/\mathrm{bandwidth}$). Maps of CF and Q_{40} measured at each recording position were plotted, tessellated and spatially smoothed. The location and size of cNB and dNB and surrounding regions for three hemispheres of AI described here have been reported previously (Read et al., 2008, 2001). The Q_{40} map obtained in the fourth hemisphere for injection of cNB region is not illustrated.

2.2. Tracers and histology

Surgical and histological methods have been described in detail previously (Read et al., 2008, 2001). Retrograde tracers were wheat-germ agglutinin apo-horseradish peroxidase conjugated to colloidal gold (WAHG) (Basbaum and Menetrey, 1987), cholera toxin B subunit (CTB, List Biological Laboratories, Campbell, CA), and cholera toxin B subunit conjugated to gold particles (CTBG, List Biological Laboratories, Campbell, CA) (Luppi, Fort et al., 1990). Single WAHG or CTB injections were made in physiologically mapped cNB and dorsal AI in the right cerebral hemispheres of three cats. cNB and dorsal AI injections were made into regions with matched CF ($\pm$0.5 octaves) and matched Q_{40} ($>$1). In a fourth cat (case 591), CTB and CTBG were deposited into 4 and 12 kHz iso-frequency contours within the confines of cNB in a single hemisphere. Post-tracer survival in all cases was 3.5 ($\pm$1) days.

Following transcardial saline and formalin perfusion, brains were removed and the cortex was flattened and separated from thalamus. Fixed tissue was cut into 40 μm coronal sections. An adjacent series of sections was Nissl-stained with cresyl violet and examined microscopically to determine medial, ventral, dorsal and supragenicular (SG) divisions of the MGB thalamic nuclei corresponding to prior cytoarchitectonic studies (Morest, 1964). Anatomic features used to delineate borders included fiber bundles, laminar pattern, somatic cell size, and orientation. Nuclear borders corresponded well with similar studies (Middlebrooks and Zook, 1983; Winer, 1985) and standard references (Berman, 1982). Histological processing methods are detailed elsewhere (Read et al.,