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The cat's meow: A high-field fMRI assessment of cortical activity in response to vocalizations and complex auditory stimuli

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ABSTRACT

Sensory systems are typically constructed in a hierarchical fashion such that lower level subcortical and cortical areas process basic stimulus features, while higher level areas reassemble these features into object-level representations. A number of anatomical pathway tracing studies have suggested that the auditory cortical hierarchy of the cat extends from a core region, consisting of the primary auditory cortex (A1) and the anterior auditory field (AAF), to higher level, auditory fields that are located ventrally. Unfortunately, limitations on electrophysiological examination of these higher level fields have resulted in an incomplete understanding of the functional organization of the auditory cortex. Thus, the current study uses functional MRI in conjunction with a variety of simple and complex auditory stimuli to provide the first comprehensive examination of function across the entire cortical hierarchy. Auditory cortex function is shown to be largely lateralized to the left hemisphere, and is concentrated bilaterally in fields surrounding the posterior ectosylvian sulcus. The use of narrowband noise stimuli enables the visualization of tonotopic gradients in the posterior auditory field (PAF) and ventral posterior auditory field (VPAF) that have previously been unverifiable using fMRI and pure tones. Furthermore, auditory fields that are inaccessible to more invasive techniques, such as the insular (IN) and temporal (T) cortices, are shown to be selectively responsive to vocalizations. Collectively, these data provide a much needed functional correlate for anatomical examinations of the hierarchy of cortical structures within the cat auditory cortex.

Introduction

Sensory systems are typically arranged in a processing hierarchy that begins with the coding of basic stimulus features at the sensory epithelium and leads to full-scale object representation in secondary and associative cortical areas. At each level of this ascending pathway, more complex features are represented. For example, in the visual system, neurons in primary visual cortex (V1) are most responsive to simple stimuli like spots or bars of light (Drager, 1975; Hubel and Wiesel, 1959, 1968; Singer et al., 1975). Ascending from V1, more complex stimuli are required for best activation eventually leading to two parallel streams processing spatial location ("where") dorsally or identification ("what") ventrally (Haxby et al., 1991; Ungerleider and Mishkin, 1982). These streams are comprised of individual areas specialized for specific stimuli such as visually-guided reaching (Karnath and Perenin, 2005; Singhal et al., 2013) in the dorsal stream or faces (Collins and Olson, 2014; Kanwisher et al., 1997; Liu et al., 2010) in the ventral stream. Auditory cortex is not understood in the same level of detail as the visual cortex. However, Chevillet et al. (2011) demonstrated that the core, belt, and parabelt regions within human auditory cortex can be delineated using pure tones, band-passed noise bursts, or vocalizations, respectively. Thus, an understanding of the way in which hierarchies of cortical fields are arranged has significant consequences for our interpretation of how stimuli in the world around us are encoded and reconstructed in the brain.

Rouiller et al. (1991) first proposed a hierarchical organization within auditory cortex of the cat that was based on anatomical connections (Figs. 1A,B). This study focused on the second auditory cortex (A2) and the four areas of the auditory cortex known to be organized by

Abbreviations: A1, primary auditory cortex; A2, second auditory cortex; AAF, anterior auditory field; *aes*, anterior ectosylvian sulcus; BBN, broadband noise; dPE, dorsal posterior ectosylvian; DZ, dorsal zone; FAES, auditory field of the anterior ectosylvian sulcus; FM, frequency modulated; fMRI, functional magnetic resonance imaging; IN, insular cortex; iPE, intermediate posterior ectosylvian; NBN, narrow band noise; PAF, posterior auditory field; *pes*, posterior ectosylvian sulcas; PSC, percent signal change; *ss*, suprasylvian sulcus; T, temporal cortex; V1, primary visual cortex; VAF, ventral auditory field; VPAF, ventral posterior auditory field; vPE, ventral posterior ectosylvian.

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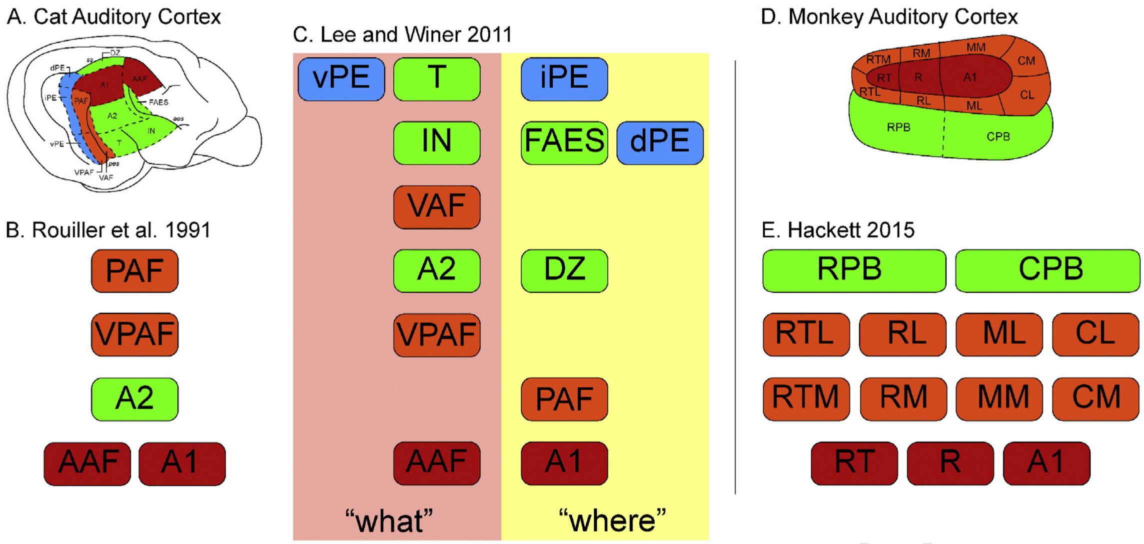

Fig. 1. Hierarchy of auditory cortex. A) Lateral view of the cat cortical surface with the thirteen acoustically responsive areas outlined as defined by electrophysiological and anatomical investigations. Core (red), tonotopic non-core (orange), non-tonotopic (green) and multisensory (blue) areas are also indicated. B) Hierarchy of cat auditory cortex as originally proposed by Rouiller et al. (1991) including only 5 of the 13 cortical areas. C) More recent hierarchy of cat auditory cortex as proposed by Lee and Winer (2011) included all 13 areas. D) Auditory cortex of the old world monkey with core (red), tonotopically organized belt (orange), and non-tonotopic para-belt (green) areas indicated. E) Most recent hierarchy within old world monkey auditory cortex as proposed by Hackett (2015).

frequency (i.e. those with tonotopic organization); primary auditory cortex (A1), the anterior auditory field (AAF), the posterior auditory field (PAF), and the ventral posterior auditory field (VPAF). Based on anatomical connectivity, Rouiller et al. placed A1 and AAF at the base of the hierarchy, with A2, VPAF, and PAF at increasingly higher levels. More recent anatomical investigations have confirmed the separation between low-level (A1 and AAF) and higher-level (A2, VPAF, PAF) cortical areas (Fig. 1C; see Lee and Winer, 2011 for review). In addition, anatomical evidence suggests that there are parallel processing streams in the auditory cortex (Lee et al., 2004; Lee and Winer, 2011) that may be analogous to the separate ventral and dorsal streams of visual cortex (Ungerleider and Mishkin, 1982; Lomber et al., 1996). While these studies have been critical to establishing a proposed hierarchy within the auditory cortex of the cat, complementary functional data are necessary to provide a complete understanding of perception within the auditory system.

Electrophysiological (Harrington et al., 2008; Carrasco et al., 2013; Carrasco and Lomber, 2009a, 2011) and functional imaging (Hall and Lomber, 2015) studies have confirmed that A1 and AAF are at similar, low level of cortical processing (Fig. 1). Collectively, these fields appear to be analogous to the auditory core of old world monkeys (Figs. 1D,E; Carrasco et al., 2013, 2015; Hackett, 2011, 2015; Hall and Lomber, 2015; Ma et al., 2013; Petkov et al., 2006; Schönwiesner et al., 2014), which also consists of multiple areas. Beyond core areas, it has been proposed that information flow within auditory cortex of the cat proceeds postero-ventrally (Carrasco and Lomber, 2011; Hackett, 2011). Latencies within individual areas are increasingly longer moving ventrally with AAF and A1 having similar, shorter latencies and A2 and PAF having longer latencies (Harrington et al., 2008; Carrasco and Lomber, 2011). Also, there is some anatomical (Andersen et al., 2004) electrophysiological evidence (Carrasco and Lomber, 2009a, 2009b) to support parallel processing streams within auditory cortex of the cat while behavioral studies have identified areas that are selective for localization but not for discrimination, and vice versa (Lomber and Malhotra, 2008; Malhotra et al., 2004; Malhotra and Lomber, 2007). Indeed, functional evidence for dual-stream processing in auditory cortex has also been observed in humans (DeWitt and Rauschecker, 2012, 2013; Rauschecker, 1997), and monkeys (Rauschecker, 1997; Rauschecker and Tian, 2004; Rauschecker et al., 1995, 1997). However, functional investigations of cortical processing in the cat have provided only a limited glimpse of the hierarchy of cortical processing due to three major limitations: 1) electrophysiological studies often focus on only one or two cortical areas per animal, 2) the position of the external auditory meatus typically limits investigations to the more dorsal fields of auditory cortex, and 3) these studies have traditionally relied on simple acoustic stimuli which may not be well-suited to evoking activity in higher-level cortical areas.

While electrophysiological methods may be limited to dorsal auditory cortex, functional magnetic resonance imaging (fMRI), which has been used extensively with human and non-human primate subjects, provides the ability to observe activity throughout cortex. Recently, fMRI has also been used to image sound processing in the auditory cortex of the cat. Differential patterns of activity have been observed in response to broadband noise and tonal stimuli (Hall et al., 2014). Moreover, responses to pure tones of different frequencies have been employed to illustrate the capacity of fMRI to represent tonotopic gradients in A1, AAF, PAF, and VPAF in accordance with those measured electrophysiologically (Hall and Lomber, 2015). Finally, fMRI has also been shown to be capable of measuring higher-level feature extraction in the cat (Butler et al., 2015). Thus, fMRI is well suited to investigate the function of ventral auditory cortex in the cat, including the ventral auditory field (VAF), insular cortex (IN) and temporal cortex (T). In addition, the present investigation employs a variety of more complex stimuli including conspecific vocalizations, narrow band noise (NBN), frequency modulated (FM) sweeps, harmonics, and broadband noise (BBN) that are better suited to elicit activity from higher-level auditory cortical areas. We hypothesize that these complex stimuli will most effectively activate areas outside of core auditory cortex. Also, static stimuli will be presented with no location information, such that the functional stream dedicated to discrimination or identification, will be preferentially activated.

Methods

Ten adult (>6 month) domestic shorthair cats were selected for this project. All animals were housed as a clowder and obtained from a commercial breeding facility (Liberty Labs, Waverly, NY). The University of Western Ontario's Animal Use Subcommittee approved all procedures. All procedures were also in accordance with the National Research Council's *Guidelines for the Care and Use of Mammals in Neuroscience*

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