SPRINGER HANDBOOK OF AUDITORY RESEARCH
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David Poeppel
Tobias Overath
Arthur N. Popper
Richard R. Fay
Editors

The Human Auditory Cortex

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Springer Handbook of Auditory Research

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The Human Auditory Cortex

Springer

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The editors dedicate this book to Sheila E. Blumstein, the Albert D. Mead Professor of Cognitive, Linguistic and Psychological Sciences at Brown University. Sheila has made a number of key contributions to our understanding of speech recognition, word recognition, and aphasia. No colleague has been as effective in using (and bridging) auditory psychophysics, psycholinguistics, data from aphasic patient populations, and functional brain imaging. Her research has motivated many of our experiments and theories, and her scientific citizenship makes her a model for many of us in the field.

Series Preface

The Springer Handbook of Auditory Research presents a series of comprehensive and synthetic reviews of the fundamental topics in modern auditory research. The volumes are aimed at all individuals with interests in hearing research including advanced graduate students, post-doctoral researchers, and clinical investigators. The volumes are intended to introduce new investigators to important aspects of hearing science and to help established investigators to better understand the fundamental theories and data in fields of hearing that they may not normally follow closely.

Each volume presents a particular topic comprehensively, and each serves as a synthetic overview and guide to the literature. As such, the chapters present neither exhaustive data reviews nor original research that has not yet appeared in peer-reviewed journals. The volumes focus on topics that have developed a solid data and conceptual foundation rather than on those for which a literature is only beginning to develop. New research areas will be covered on a timely basis in the series as they begin to mature.

Each volume in the series consists of a few substantial chapters on a particular topic. In some cases, the topics will be ones of traditional interest for which there is a substantial body of data and theory, such as auditory neuroanatomy (Vol. 1) and neurophysiology (Vol. 2). Other volumes in the series deal with topics that have begun to mature more recently, such as development, plasticity, and computational models of neural processing. In many cases, the series editors are joined by a co-editor having special expertise in the topic of the volume.

Woods Hole, MA, USA Richard R. Fay
College Park, MD, USA Arthur N. Popper

Volume Preface

This volume brings the Springer Handbook of Auditory Research series to its first detailed examination of auditory cortex, with a strong emphasis on auditory processing in humans. Chapters are grouped into two sections or themes (methods and content areas), although, as seen in reading the chapters, many actually present material that covers the two general themes of the volume. Chapters 2 to 6 in Section I explain the main techniques currently available to study the human brain, with a specific focus on their use in investigating auditory processing. Chapters 7 to 13 in Section II cover different aspects of auditory perception and cognition.

In Chapter 2, Clarke and Morosan describe the anatomy of the human auditory cortex and introduce the nomenclature of the different subareas in the human auditory cortex, in a historical context. In Chapter 3, Howard, Nourski, and Brugge introduce a type of data that are extremely rare: intracranial recordings from patients undergoing neurosurgical procedures or presurgical evaluation.

Chapters 4 through 6 provide descriptions of the most typical methodologies available to study human auditory perception and cognition. Electroencephalography (EEG) is the topic of Chapter 4 by Alain and Winkler. The other noninvasive electrophysiological technique that is increasingly widespread is magnetoencephalography (MEG), outlined in Chapter 5 by Nagarajan, Gabriel, and Herman. In Chapter 6, Talavage, Johnsrude, and Gonzalez turn to functional magnetic resonance imaging (fMRI), an approach that provides excellent spatial resolution.

In Chapter 7, Hall and Barker discuss the neural processing of basic perceptual attributes and familiarize the reader with elementary problems such as the encoding of pure tones, pitch, and loudness. Following this, the concept of auditory objects or auditory streams is considered in Chapter 8 by Griffiths, Micheyl, and Overath.

One of the major naturalistic tasks for the auditory system, speech perception, is the topic of Chapter 9 by Giraud and Poeppel. The other auditory domain receiving a great deal of attention and generating a fascinating body of data concerns the cortical foundations of processing music, as discussed in Chapter 10 by Zatorre and Zarate. This is followed by a consideration of the multisensory role of the human auditory cortex by van Wassenhove and Schroeder in Chapter 11. In Chapter

12, Hickok and Saberi discuss the variety of function of the planum temporale, an area of the human cortex considered integral to processing many aspects of complex sounds.

The volume concludes with a consideration by Cariani and Micheyl in Chapter 13 of what is known with respect to computational models that link the data from the multiple methodologies in human and animal models in an explicit way.

A number of recent volumes in the Springer Handbook of Auditory Research series complement, and are complemented by, this volume on *Human Auditory Cortex*. Computation in the auditory system is considered at length in *Computational Models of the Auditory System* (Vol. 35, edited by Meddis, Lopez-Pevada, Fay, and Popper, 2010), whereas perception of music is the topic of *Music Perception* (Vol. 36, edited by Riess-Jones, Fay, and Popper, 2010). Human perception and sound analysis are considered most recently in *Loudness* (Vol. 37, edited by Florentine, Popper, and Fay, 2011), *Auditory Perception of Sound Sources* (Vol. 29, edited by Yost, Popper, and Fay, 2008), and *Pitch: Neural Coding and Perception* (Vol. 21, edited by Plack, Oxenham, Fay, and Popper, 2005).

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Chapter 1
Introduction: Why Human Auditory Cortex?

David Poeppel and Tobias Overath

This volume concentrates on current approaches to understanding the human auditory cortex.

Why auditory? The reasons why one would, could, and should study auditory processing ought to require little comment or motivation. That being said—and given the critical importance of hearing and speech for human communication and welfare—one might wonder why hearing research, in general, has remained the less popular stepchild and ugly duckling in the context of sensory neuroscience, in particular vision. (This question is discussed in more detail later.).

Why human? Our knowledge of nonhuman hearing is increasingly well developed, and there now exist excellent recent overviews of auditory processing at various levels of analysis, ranging from anatomy to neurophysiology to computational modeling of subtle hearing phenomena (e.g., Oertel et al., 2002; Manley et al., 2008; Meddis et al., 2010; Moore 2010; Winer & Schreiner 2010; Schnupp et al., 2011). The very existence of the extensive and thorough *Springer Handbook of Auditory Research* is a testament to the fact that this research arena is perceived as a growth area at the cutting edge of the behavioral and brain sciences. Yet, for human auditory processing, although our behavioral/psychophysical approaches are sophisticated, our *knowledge of the neural basis is still quite rudimentary*. A detailed focus on the human auditory system seems timely and necessary.

Why cortex? It goes without saying that the contributions of subcortical structures to virtually all aspects of human auditory perception are immense. The afferent auditory pathway is highly complex and richly structured; it is sometimes argued, for example, that the inferior colliculus constitutes a better comparison to primary visual cortex than primary auditory cortex itself (King & Nelken, 2009). Moreover,

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even higher-order tasks, including speech perception, are modulated by subcortical circuitry. Nevertheless, it is *cortical structures that lie at the basis of auditory perception and cognition*. To restrict the scope of coverage, and fully acknowledging the importance of other cerebral regions, the human auditory cortex is the target of this inquiry.

The study of the visual system—across species, levels of visual processing, and approaches—continues to be a dominant focus in the neurosciences. The amount of resources dedicated to vision is easy to understand: humans are highly visual creatures (if the criterion is the proportion of cerebral real estate allocated to visual processing in one form or another); animal models of human vision are remarkably successful, allowing for detailed mechanistic characterizations of various aspects of visual perception across species, including humans; and the experimental "management" of visual materials has made the research tractable for a long time, ranging from the simple holding up of an image to tachistoscopic presentation to sophisticated computer graphics.

Recently, more researchers are turning their attention to auditory processing. By analogy to vision, three trends are worth mentioning. First, investigators now acknowledge that humans are also highly auditory creatures, if the criteria are (1) the amount of cerebral territory implicated in hearing as well as (2) what humans are willing to pay for to be entertained, for example, iTunes®; second, animal models are highlighting important similarities but also showing some key differences between the human auditory system and well-studied nonhuman preparations, notably with respect to complex sound processing, speech, and music; and finally, new technologies have made manipulating auditory materials much easier—and many auditory studies doable to begin with. (Recall that crafting and editing digital audio files with such speed and ease is a rather recent development, in terms of the history of the work.) Moreover, and crucially, the development of new noninvasive recording and imaging techniques to study the human brain has opened up entirely new possibilities for investigating human hearing; the impact of these techniques on research in (human) auditory processing cannot be overstated. One key aspect of this volume is to highlight the existing techniques and illustrate how they are used to study various aspects of human auditory perception.

The book's chapters are roughly organized in two sections, *methodologies* and *content areas*. The chapters in the first section explain the techniques currently available to study the human brain, with a specific focus—and numerous examples—on auditory processing. The coverage is necessarily selective; for example, the volume does not cover recent experimental work using transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS), and near-infrared spectroscopy (NIRS). The chapters were designed to cover the areas of experimental inquiry in which a fairly extensive and robust body of results exists on human auditory cortical structure and function. It stands to reason that newer recording techniques will make major discoveries, but it seems prudent to restrict the focus on methodologies with a significant track record.

In the second group of chapters, different aspects of auditory perception and cognition are discussed, that is, the focus of each chapter lies on a specific content area (e.g., auditory objects, speech, music) or an aspect of auditory processing that cuts across domains (e.g., multisensory perception, perception–action interaction, etc.).

The coverage of the book is as follows. In Chapter 2, Clarke and Morosan describe the neurobiological infrastructure that lies at the very foundation of the entire research area: the anatomy of the human auditory cortex. The data have derived mainly from cytoarchitectonic analyses of postmortem brains, but now also incorporate recent insights from other anatomic approaches. The chapter also introduces, in a historical context, the nomenclature of the different subareas in human auditory cortex. The quip that “anatomy is destiny” is attributed to Sigmund Freud—and, to our knowledge, he was not referring to the structure and function of the auditory system. It is clear, however, that human auditory research needs to be much more granular about the computational contribution each putative cortical region makes. The success and destiny of the research program is indeed predicated on whether it is possible to forge detailed linking hypotheses between anatomic structures and computational subroutines.

In Chapter 3, Howard, Nourski, and Brugge introduce a type of data that most researchers rarely have access to: intracranial recordings from patients undergoing neurosurgical procedures or presurgical evaluation. Although such direct invasive neurophysiological recordings are much harder to come by—and are associated with the typical limitations of the clinical situation—these new data sets are gaining currency and provide a window onto auditory function that allows us to make important connections between noninvasive imaging and the neurophysiological data obtained in animal studies. The chapter introduces the nuts and bolts of how auditory research is done in this context.

Chapters 4, 5, and 6 provide descriptions of the most typical methodologies currently in use to study human auditory perception and cognition. Electroencephalography (EEG), the topic of Chapter 4 by Alain and Winkler, has been available for cognitive neuroscience research since the 1930s. Although its popularity has waxed and waned over the years, it is fair to say that EEG data are now richly appreciated in auditory research and have provided the most data (and perhaps insight) about auditory function, in particular with respect to the temporal properties of perception. The other noninvasive electrophysiological technique that is currently growing in use is magnetoencephalography (MEG), a cousin of EEG. The technique is outlined by Nagarajan, Gabriel, and Herman in Chapter 5, where a number of examples illustrate how MEG can be used to investigate aspects of auditory processing that can be more challenging than with other electrophysiological approaches. The balance between temporal and spatial resolution afforded by MEG makes the technique well suited to investigate research questions in which localization of function plays a role that cannot be addressed effectively with, say, EEG.

In Chapter 6, Talavage, Gonzalez, and Johnsrude turn to the hemodynamic recording approaches, principally functional magnetic resonance imaging (fMRI). The fantastic spatial resolving power of this imaging technique is now well known. Because of some of the quirks of this technique—it is quite loud to be inside the scanner as a participant, and the response that is quantified develops over several seconds (hemodynamics are slow relative to electricity)—the utility of fMRI in auditory research was initially somewhat limited. However, technical innovations in the last few years have rendered this tool an excellent window through which to view human auditory cortex as it processes signals ranging from single tones to extended narratives. The chapter provides a thorough description of the underlying neurophysiology, design, and analysis of fMRI data.

Chapters 7 to 13 form the second part of the book, now with less explicit emphasis on the particular methods, but rather a concentration on specific perceptual and conceptual challenges that the human auditory system faces. In Chapter 7, Hall and Barker discuss the basic acoustic constituents that comprise the auditory environment. The chapter familiarizes the reader with elementary problems such as the encoding of pure tones, the representation of sounds with larger bandwidths and more complex spectral structure, the analysis of pitch, and the effect of loudness. The perceptual attributes described and discussed in this chapter form the basis of representations of an intermediate complexity, lying between encoding at the auditory periphery, on the one hand, and the perceptual interpretation as high-level objects, including speech or music, on the other. The level of representation that is the centerpiece of this chapter might be considered the "perceptual primitives" of auditory cognition; these are the attributes that humans can independently assign to an auditory stimulus, regardless of its category membership. For example, whether humans are characterizing an environmental stimulus, a musical motif, or a spoken word, we can talk about the pitch, the spatial position, or the loudness of the signal.

The concept of what auditory objects or auditory streams actually are—already raised in the description of EEG (Chapter 4)—is tackled more directly in Chapter 8 by Griffiths, Micheyl, and Overath. The question of what constitutes an auditory object has proven to be remarkably controversial. In part, this difficulty may stem because this concept derives by and large from vision research and may not have a one-to-one transfer function to audition (e.g., the temporal dimension is arguably more important in audition). To generalize the notion of object, other dynamic features of an object must now come to fore, enriching the discussion of what is considered to be an elementary representation in a sense that satisfies both visual and auditory theories. The chapter describes the empirical research that has contributed to clarifying the problems, notably work on streaming, grouping, and sequencing. Both hemodynamic and electrophysiological studies are described that aim to elucidate this complex notion.

One of the major naturalistic tasks for the auditory system, speech perception, is the theme of Chapter 9, by Giraud and Poeppel. There, a decidedly neurophysiological perspective is provided, focusing especially on the perceptual analysis of connected speech—and not on how individual vowels, syllables, or words are analyzed. Whereas there exists a fairly large literature on the neurobiological activity associated with perceiving individual speech sounds, a growing body of empirical work is focusing on connected speech. That issue is taken up here, outlining in particular the potential role of neuronal oscillations in analyzing speech. The brain basis of speech is, unsurprisingly, a central focus of much research in human hearing.

The other domain that is receiving a great deal of attention and generating a fascinating body of data concerns the cortical foundations of processing music, discussed by Zatorre and Zarate in Chapter 10. Three aspects of music processing receive special attention. First, the concept of pitch and its foundational role for melody and melodic processing is discussed from several vantage points. Second, some of the major anatomic issues are revisited, including the interesting hemispheric asymmetries associated with processing auditory signals as well as the controversial contribution of dorsal stream structures to auditory processing. Third, the fascinating issues surrounding cortical plasticity after training and cortical deficits after lesion/genetic anomaly are laid out. Music processing is a domain that, in an important sense, illustrates how different methodologies and different concepts (object, stream, action–perception loop, etc.) come together to highlight the neurobiological foundations of complex auditory processing.

Although this volume is about the human auditory cortex, it now goes without saying that there is a fundamental role for the other senses in auditory processing. The multisensory role of the human auditory cortex is the theme of Chapter 11. There, the neurophysiological foundations, to date largely based on results from animal studies, are outlined by van Wassenhove and Schroeder. Nevertheless, a growing literature in human cognitive neuroscience shows convincingly the direct and seemingly causal interactions in multisensory contexts. Several compelling psychophysical phenomena are explained, including ventriloquism and the famous audiovisual speech McGurk illusion. It is becoming increasingly clear that the notion of purely unisensory areas is highly problematic, if not entirely incorrect. The temporally (and anatomically) very early effects of multisensory influence and integration highlight the fact that it is very fruitful to incorporate the rich and highly modulatory multisensory inputs and their effects into any model.

In Chapter 12, an almost mythical area in human auditory neuroscience, the planum temporale, is discussed by Hickok and Saberi. When one talks about the neural basis of speech and language processing, there are two brain areas that invariably lie at the center of the discussion: Broca's region in the frontal lobe and planum temporale in the superior temporal lobe. These brain areas have been argued to be strongly lateralized in the human brain, and have been shown to correlate in important ways with properties of speech perception and production as well as language comprehension and production. Three aspects of planum temporale function are discussed in this chapter: its role in the analysis of spatial features of sounds and localization, its role for the analysis of objects, and its role in auditory motor mapping.

The volume concludes with Chapter 13, wherein Cariani and Micheyl summarize where we stand with respect to computational models that link the data from the multiple methodologies in human and animal models in an explicit way. Although our understanding of neural coding is incomplete and woefully inadequate, enough is known to begin to explore how the neural code forms the basis for auditory perception and cognition. This chapter serves to remind us, from many different angles, what some of the computational requirements and coding strictures are. To develop a theoretically well motivated, computationally explicit, and neurobiologically realistic model, linking hypotheses that are sensitive to the toolbox of computational neuroscience will be essential.

This volume constitutes a fair representation of what is currently known about human auditory cortex. If the topic is revisited in 10 years, where should the field be?

Given the fantastic rate of progress—in terms of computational sophistication, experimental subtlety, and methodological innovations with ever better resolution—here are some decadal desiderata. First, the anatomical characterization of human auditory cortex needs to be at least as granular as the specifications now available for, say, macaque visual cortex. Not just areal delineation, cytoarchitecture, and receptor distributions, of course, but circuit-level considerations are also necessary. Achieving this for the human brain in general, and for auditory cortex in particular, is a tremendous challenge.

Second, it would be invaluable to have an inventory of the elementary operations (or computations) that are executed by cell groups in a given anatomic circuit or region. In some sense, this amounts to identifying the "atoms of hearing." Ultimately, the goal will be to develop linking hypotheses between the anatomic circuitry and the computational primitives (or atoms). It is likely that such a mapping between anatomy and computational functions will be many to many; the structure of cortex is such that a subgroup of elements can execute different formal operations.

Third, it would constitute a great success to have a model of how the primitive operations—that are anatomically grounded—conspire to create the elementary perceptual attributes, as these are unlikely to be neurobiological primitives. For example, there are many ways to create the elementary perceptual experience of pitch, or of loudness, from which it follows that the underlying operations that form the basis for that experience are even more elementary. Some of the considerations outlined in the concluding chapter point toward general issues to think about in formulating such theories.

Fourth, none of this can be achieved without concomitant progress in advancing the resolution power of the available methodologies. It goes without saying that the loudness of the fMRI environment is extremely detrimental to auditory neuroscience. Presumably, were the scanner to produce visual noise, MRI technicians and researchers would have scrambled and found a way to reduce this by now (some 20 years after the conception of BOLD imaging); but because the scanner "only" produces acoustic noise, a significant reduction of the acoustic noise of fMRI (mainly due to hardware and acquisition techniques) remains the holy grail for auditory neuroscience.

Further, the simultaneous combination of techniques (e.g., EEG and fMRI) would provide an important step forward in elucidating the relationships between various aspects of the neural signature(s) in auditory cortex.

Finally, successful explanations of how the human auditory cortex provides the basis for the representation and processing of ecologically natural signals such as speech, music, or natural sounds need to be directly grounded in the anatomic and computational infrastructure (bottom-up constraints) while permitting the seamless integration with high-level representations, and the entire predictive machinery that is the memory system (top-down constraints). In summary, the systematic linking of a computational inventory with the right level of anatomic circuitry constitutes a goal that is ambitious but would yield great scientific payoff and have compelling clinical implications.

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Part I
The Methods

Chapter 2
Architecture, Connectivity, and Transmitter Receptors of Human Auditory Cortex

Stephanie Clarke and Patricia Morosan

Abbreviations

A1	primary auditory area
AChE	acetylcholine esterase
CB	calbindin
CO	cytochrome oxidase
CR	calretinin
HG	Heschl's gyrus
PAC	primary auditory cortex
PP	planum polare
PT	planum temporale
PV	parvalbumin
STG	superior temporal gyrus
STS	superior temporal sulcus

2.1 Introduction

Human auditory cortex, located on the supratemporal plane, comprises in the vicinity of primary auditory cortex (PAC) several nonprimary auditory areas. Architectonic studies that benefited from methodological advances, such as observer-independent

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analysis and functionally related stains, have identified specific areas whose involvement in speech analysis, sound recognition, and auditory spatial processing has been established in activation studies. Postmortem and in vivo tracing studies have revealed a complex pattern of intra- and interareal connections that partially resemble those described in nonhuman primates but that also display specifically human attributes. Current evidence reveals a model of parallel and hierarchical organization of the early-stage auditory areas with an early separation of specific processing streams.

2.2 Historic Concepts and Maps of Human Auditory Cortex

At the beginning of 20th century, Paul Flechsig identified the superior temporal gyrus (STG) as the cortical site of the human auditory system. By using a myelogenetic approach, Flechsig (1908) succeeded in tracking the auditory pathway from the thalamus to the upper bank of the STG. He also observed that a distinct region on the first transverse temporal gyrus, or Heschl's gyrus (HG), receives denser thalamic inputs from the medial geniculate body than the surrounding cortex. This region, initially called the "auditory sphere," is the PAC.

Flechsig's reports on local differences in anatomical connectivity shifted the focus of auditory research away from brain macroanatomy to the finer, microscopic details of cortical organization. The necessary methodological framework for a well-founded histological examination of brain tissue was then provided by Nissl (1894) and Weigert (1882), who introduced useful stains for demonstrating cell bodies and myelinated fiber tracts, respectively. The stained cells and fiber tracts appeared black against a very light background, and this high contrast encouraged many researchers to study the cellular (cyto-) and fiber (myelo-) architecture of human cerebral cortex.

Campbell (1905) was among the first to study the cyto- and myeloarchitecture of human auditory cortex. He identified an "audito-sensory" area on the upper bank of the STG that possessed architectonic features entirely different from those of any other part of the temporal lobe. According to Campbell (1905), the "audito-sensory" area was coextensive with Flechsig's "auditory sphere" and thus represented the architectonic correlate of the human PAC. Campbell also identified a second, nonprimary auditory or "audito-psychic" area, which mainly covered dorsocaudal and lateral portions of the superior temporal gyrus (Fig. 2.1A).

The most influential architectonic parcellation of human auditory cortex, however, was published few years later by Brodmann (1909). Brodmann, a co-worker of Cecile and Oskar Vogt at the Kaiser Wilhelm Institute in Berlin, confirmed the existence of an architectonically distinct PAC (area 41 according to Brodmann), but refined the concept of nonprimary auditory cortex by segregating it into two major areas, areas 42 and 22 (Fig. 2.1B). In addition, Brodmann identified a new area, area 52, at the medio-anterior border of area 41. Brodmann's research was based on the assumption that each architectonically distinct cortical area also differs in functionality. Although microstructure–function relationships in the human brain could not be rigorously tested at that time, old (Vogt & Vogt, 1919) and more recent (Luppino et al., 1991; Matelli et al., 1991) studies in nonhuman primates

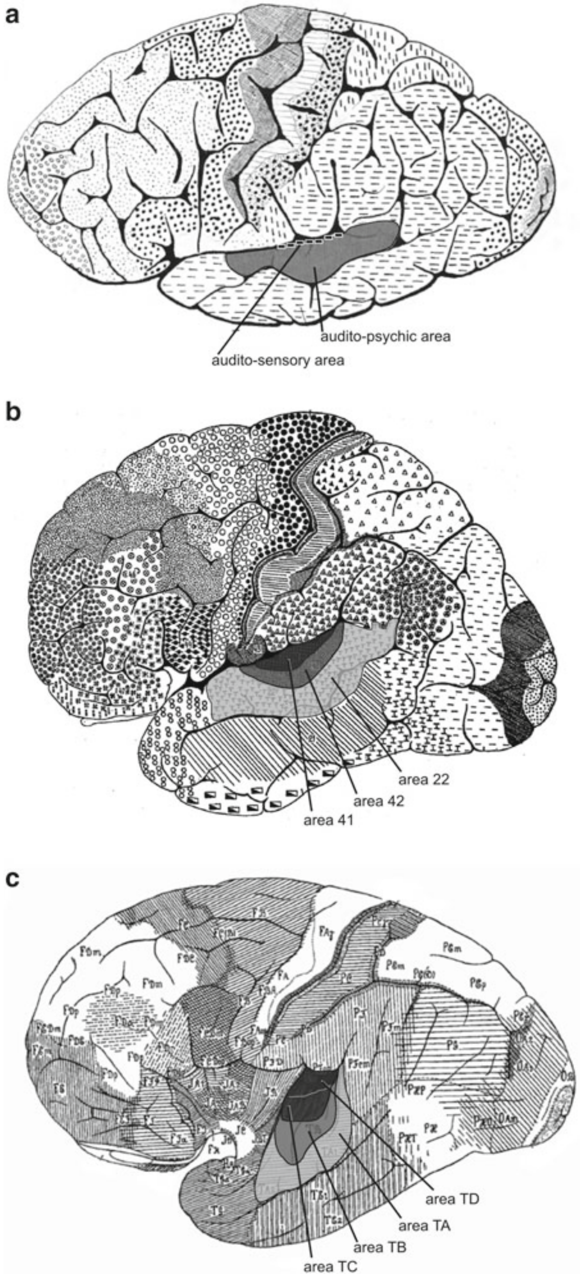

Fig. 2.1 Historic architectonic maps of human auditory cortex. Lateral view. (**a**) Myelo- and cytoarchitectonic map of Campbell (1905). (**b**) Cytoarchitectonic map of Brodmann (1909). (**c**) Cytoarchitectonic mapof von Economo and Koskinas (1925)

have demonstrated by means of combined electrophysiological–neuroanatomical studies that Brodmann's basic idea was true. Brodmann, however, did not argue for an extreme localization concept, that is, he did not try to relate complex function to one distinct architectonic area.

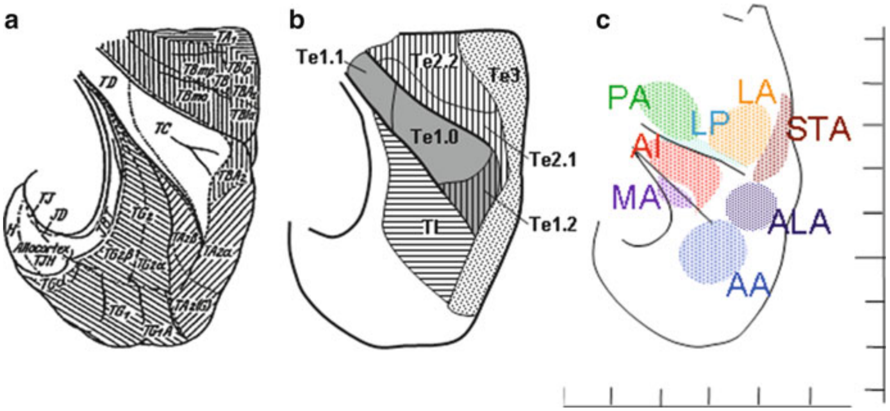

Fig. 2.2 Topography or primary and nonprimary auditory areas. (**a**) Classic cytoarchitectonic map of von Economo and Horn (1930). (**b**) Combined cyto- and receptor architectonic map (adapted from Morosan et al., 2001, 2005a). Areal borders were confirmed by using an algorithm-based, observer-independent method for detecting changes in cortical architecture. 3D stereotaxic probabilistic maps of the cortical areas and useful tools for anatomical localization of functional imaging data are available at http://www.fz-juelich.de/inm/index.php?index=397. (**c**) The primary (AI) and seven nonprimary auditory areas as identified histologically by Rivier and Clarke (1997) and Wallace et al. (2002), positioned within the Talairach coordinate system. All representations are upper views of the supratemporal plane with the temporal pole pointing down

A detailed and comprehensive description of the cytoarchitecture of human auditory cortex was published by von Economo and Koskinas (1925). The authors described meticulously, and partly quantitatively, the cytoarchitectonic properties of primary and nonprimary auditory areas, including information on topography, laminar dimensions, cell types, sizes, and densities. PAC (area TC according to von Economo and Koskinas [1925]) occupies central and anterior portions of HG, whereas the posterior portion of the gyrus contains area TD, a presumably additional primary auditory area (Fig. 2.1C). Areas TC and TD are bordered caudally by the nonprimary auditory area TB, which, in turn is bordered by area TA. The combined areas TC and TD correspond to Brodmann's area 41, whereas areas TB and TA resemble Brodmann's areas 42 and 22, respectively. More detailed topographic comparisons, however, reveal discrepancies between the two maps. In contrast to Brodmann's area 22, for instance, the nonprimary auditory area TA does not extend onto the middle temporal gyrus.

A few years later, von Economo and Horn (1930) published a much more complex cytoarchitectonic map of human auditory cortex, thus proposing that the structure of human auditory cortex is much more heterogeneous than initially believed (Fig. 2.2A). More significant, however, the analysis of a large number of brains (14 hemispheres) revealed striking intersubject and interhemispheric variations in the architecture and topography of auditory areas. These findings were confirmed by Sarkissov and colleagues (1955), who again used the terminology of Brodmann (1909).

One of the most important myeloarchitectonic maps of human auditory cortex was published by Hopf (1954). Hopf's map shows auditory cortex segregated into five major auditory areas: the highly myelinated PAC (or area ttr.1) and four nonprimary auditory areas (areas ttr.2, tpart, tsep, and tpari). Further, slight differences in myeloarchitecture enabled the segregation of each of those areas into a varying number of subareas. Area ttr1, for instance, was subdivided into four subareas along the anterior–posterior and themedial–lateral trajectories of Heschl's gyrus.

In the 1950s, the classic, purely subjective architectonic mapping strategies of human cerebral cortex begun to be subjected to careful and critical scrutiny (Bailey & von Bonin, 1951). Although the segregation of human auditory cortex into a primary and a nonprimary auditory region was still accepted, it has been argued that all other cortical subdivisions were not based on anatomical criteria that were objectively demonstrable. Indeed, the fundamental problem with classic architectonics was that many different criteria were used for parcellation, often introducing a major element of subjectivity in determining the areal borders, and thus the configuration of brain maps produced by different cartographers. It is, for example, generally accepted that the human PAC is confined to HG, but the exact position of the areal borders as well as the number and topographies of putative subdivisions remain a matter of debate (Campbell, 1905; Brodmann, 1909; von Economo & Koskinas, 1925; Beck, 1930; von Economo & Horn, 1930; Hopf, 1954, 1968; Sarkissov et al., 1955; Braak, 1978; Galaburda & Sanides, 1980; Ong & Garey, 1990; Rademacher et al., 1993; Rivier & Clarke, 1997; Clarke & Rivier, 1998; Hackett et al., 2001; Morosan et al., 2001; Wallace et al., 2002; Sweet et al., 2005; Fullerton & Pandya, 2007).

Several decades ago, however, Hopf (1968) introduced new quantitative techniques to describe the architecture of cortical areas and paved the way for modern, more objective and less observer-dependent architectonic mapping strategies of human auditory cortex (Schleicher et al., 1999, 2005). In addition, new mapping techniques have been developed that reflect functionally highly relevant information based on, for example, immunohistochemistry of transmitters and cytoskeletal elements and receptor autoradiography (Zilles et al., 2002b).

2.3 Primary Auditory Area

2.3.1 *Relationship Between Heschl's Gyrus and Primary Auditory Cortex*

HG as the cortical site of human PAC is an important, functionally relevant macroanatomical landmark of auditory cortex. PAC, however, is not coextensive with HG (von Economo & Horn, 1930; Rademacher et al., 1993, 2001; Morosan et al., 2001). Portions of PAC may surpass the framing sulci of HG and reach anteriorly the planum polare (PP) or posteriorly the planum temporale (PT). Equally possible, nonprimary auditory areas can partly extend on HG. In addition, the incidental occurrence of the intermediate sulcus complicates the cortical surface pattern of HG and its relationship to the architectonically defined PAC. This sulcus may mark the posterior border of PAC, but here again the overlap is far from perfect. Another critical region is the lateral border. The medio-to-lateral extent of PAC varies considerably between subjects, and the lateral flattening of HG or other canonical boundaries (Rademacher et al., 1993) are rather vague anatomic guides to the lateral end point of architectonically defined PAC.

Given that HG is a clearly visible anatomic structure at the spatial resolution of modern in vivo magnetic resonance (MR) imaging, it regularly serves as a structural marker for the localization of activation clusters obtained by functional neuroimaging. The discrepancies between HG and the architectonic borders of PAC, however, reveal that additional architectonic information is clearly needed for the definition of state-of-the-art structure–function relationships.

Moreover, it has been shown that the absolute size of PAC is grossly overestimated by any approach that interprets HG as the structural equivalent of PAC (Rademacher et al., 2001). This needs to be kept in mind when inferences about the size of PAC are made on the basis of in vivo HG volumetry (Penhune et al., 1996) or when gyral variations are taken as MR visible indicators of individual variations in physiology and behavior (Leonard et al., 1993; Rojas et al., 1997; Schneider et al., 2002; Warrier et al., 2009).

2.3.2 Architectonic Features of Primary Auditory Cortex

Human PAC has been repeatedly mapped on the basis of cortical architecture since the beginning of the last century (Campbell, 1905; Brodmann, 1909; von Economo & Koskinas, 1925; Beck, 1930; von Economo & Horn, 1930; Sarkissov et al., 1955; Hopf, 1954, 1968; Braak, 1978; Galaburda & Sanides, 1980; Ong & Garey, 1990; Rademacher et al., 1993; Rivier & Clarke, 1997; Clarke & Rivier, 1998; Hackett et al., 2001; Morosan et al., 2001; Wallace et al., 2002; Sweet et al., 2005; Fullerton & Pandya, 2007). The *koniocortical* appearance, that is, the predominance of small granular cells in all cortical layers, easily segregates it from the neighboring nonprimary auditory areas in cytoarchitectonic specimens (Campbell, 1905; von Economo & Koskinas, 1925; Galaburda & Sanides, 1980; Rademacher et al., 1993; Hackett et al., 2001; Morosan et al., 2001; Sweet et al., 2005; Fullerton & Pandya, 2007). The staining of layers II–IV appears dense and almost uniform and a slightly lighter stripe is found in lower layer V (Fig. 2.3A). The inner granular layer (layer IV) is generally well developed, presumably reflecting the dense thalamic inputs from the medial geniculate body targeting this layer. Layer III is populated by small to medium-sized pyramidal cells; larger neurons are rare. In strictly orthogonally cut brain sections, the small pyramidal cells of layer III are arranged in short radial columns, which partially extend into the neighboring cortical layers. This feature is usually referred to as the “rain shower formation” because it is reminiscent of fine, droplike laces (von Economo & Koskinas, 1925).

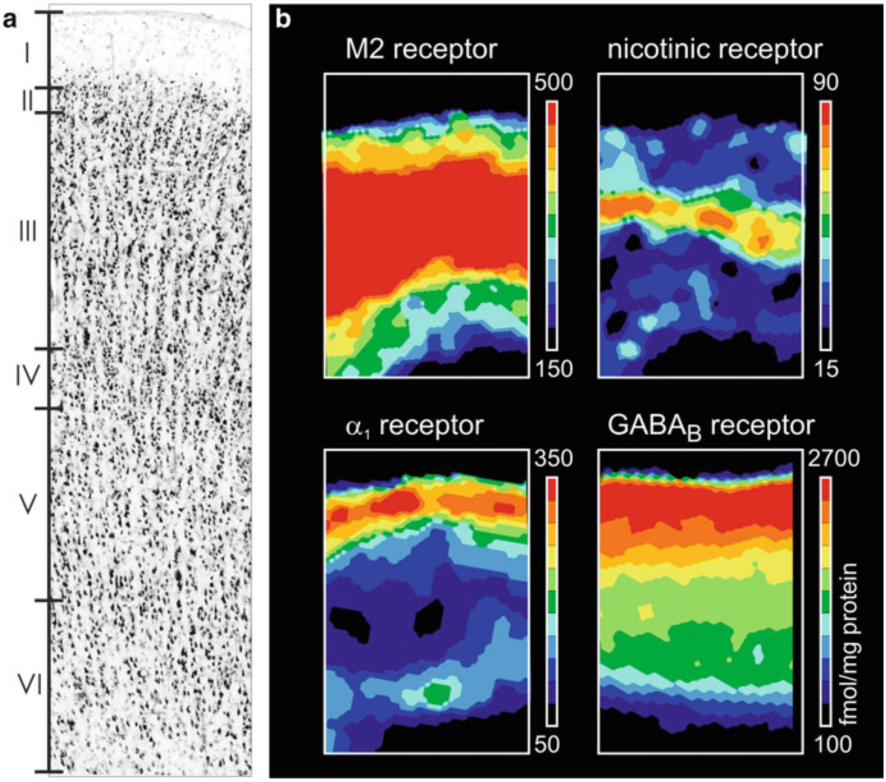

Fig. 2.3 Architecture of human primary auditory cortex (area Te1.0). (**a**) Cytoarchitecture. (**b**) Receptor architecture

In brain sections stained for myelin, primary auditory cortex attracts attention by its strong myelination in which radial fiber bundles can be followed from layer III to the white matter boundary (Campbell, 1905; Beck, 1930; Hopf, 1954; Hackett et al., 2001). The density of myelination is highest on the crown of HG (Hopf, 1954), and decreasing staining intensities have been observed from caudal to rostral portions of the gyrus (Hackett et al., 2001). The myeloarchitecture of PAC has been described as *astriate* (i.e., no horizontal stripes are visible in layers 4 or 5b due to almost uniformly dense fibrillarity from layer 4 through 6) (Hackett et al., 2001) to (*prope-*) *unistriate* (i.e., only layer 4 is visible due to relatively weaker myelination in layer 5a and uniformly dense staining of layers 5b and 6) (Hopf, 1954; Hackett et al., 2001). In this latter case, PAC is *internodensior* (i.e., layer 4 is less densely stained than layer 5b).

Chemoarchitectonically, PAC (area A1) is characterized by very high levels of acetylcholine esterase (AChE) and cytochrome oxidase (CO) activity (Hutsler & Gazzaniga, 1996; Rivier & Clarke, 1997; Clarke & Rivier, 1998; Hackett et al.,