

Human Tonotopic Maps and their Rapid Task-Related Changes Studied by Magnetic Source Imaging

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ABSTRACT: A brief review of previous studies is presented on tonotopic organization of primary auditory cortex (A1) in humans. Based on the place theory for pitch perception, in which place information from the cochlea is used to derive pitch, a well-organized layout of tonotopic map is likely in human A1. The conventional view of tonotopy in human A1 is a layout in which the medial-to-lateral portion of Heschl's gyrus represents high-to-low frequency tones. However, we have shown that the equivalent current dipole (ECD) in auditory evoked magnetic fields in the rising phase of N100m response dynamically moves along the long axis of Heschl's gyrus. Based on analyses of the current sources for high-pitched and low-pitched tones in the right and left hemispheres, we propose an alternative tonotopic map in human A1. In the right A1, isofrequency bands for each tone frequency are parallel to the first transverse sulcus; on the other hand, the layout for tonotopy in the left A1 seems poorly organized. The validity of single dipole modelling in the calculation of a moving source and the discrepancy as to tonotopic maps in the results between auditory evoked fields or intracerebral recordings and neuroimaging studies also are discussed. The difference in the layout of isofrequency bands between the right and left auditory cortices may reflect distinct functional roles in auditory information processing such as pitch versus phonetic analysis.

RÉSUMÉ: Cartes tonotopiques humaines et changements liés aux tâches rapides étudiés par imagerie par résonance magnétique fonctionnelle.

Nous présentons une brève revue des études antérieures sur l'organisation tonotopique du cortex auditif primaire (A1) chez l'humain. Sur la base de la théorie du lieu de perception de la hauteur tonale, selon laquelle l'information sur le lieu provenant de la cochlée est utilisée pour inférer la hauteur tonale, il est probable qu'il existe un schéma bien organisé de carte tonotopique dans le A1 humain. La conception conventionnelle de la tonotopie dans le A1 humain est un schéma dans lequel la portion médiale à latérale du gyrus de Heschl représente les tonalités des fréquences de hautes à basses. Cependant, nous avons démontré que le dipôle de courant équivalent dans les champs magnétiques évoqués auditifs dans la phase ascendante de la réponse des ondes N100m se déplace dynamiquement le long du grand axe du gyrus de Heschl. Selon les analyses des sources de courant des hautes tonalités et des basses tonalités dans l'hémisphère droit et dans l'hémisphère gauche, nous proposons une carte tonotopique alternative du A1 humain. Dans le A1 droit, les bandes d'isofréquence pour chaque fréquence tonale sont parallèles au premier sillon transverse; d'autre part, le schéma tonotopique dans l'A1 gauche semble peu organisé. Nous discutons également de la validité de la modélisation au moyen d'un seul dipôle pour le calcul d'une source en mouvement et de la discordance entre les cartes tonotopiques quant aux résultats des champs évoqués auditifs ou des enregistrements cérébraux et des études de neuroimagerie. La différence entre le schéma des bandes d'isofréquence des cortex auditifs droit et gauche pourrait refléter des rôles fonctionnels distincts dans le traitement de l'information auditive comme la hauteur tonale par opposition à l'analyse phonétique.

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Topographical representations of external stimuli in the human sensory cortex are essential to discriminate and store the features of the stimuli. For auditory sensation processing, a fundamental attribute is to extract a pitch from complex harmonic sounds such as music and human speech. Since it is generally agreed that pitch is basically a correlate of the periodicity of a sound waveform, it can be derived by pattern recognition of the auditory nerve. However, there has been a debate as to whether timing or place information from the cochlea is used to derive pitch: i.e., the temporal theory versus the place theory. The former theory hypothesizes that temporal modulations of the neural activation patterns play an important role in pitch perception. On the other hand, the place theory predicts that topographic organization of the tone frequency or tonotopic representation throughout the auditory system

including the primary auditory cortex (A1) is essential for pitch perception. Although the temporal coding mechanism has been considered more important,¹⁻⁴ recent psychoacoustic work on pitch perception provides definitive evidence in favor of the place theory.^{5,6} Accordingly, investigating tonotopic representational maps of A1 is crucial for better understanding of the auditory processing mechanism. In this review, we will give an

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overview of human tonotopy obtained from previous neuroradiological and electrophysiological studies then introduce recent results on tonotopic maps and their task-related changes in human AI based on our data from magnetoencephalography (MEG).

An overview of tonotopic maps of human auditory cortex

Romani et al⁷ first studied steady-state auditory evoked magnetic fields (AEFs) in two subjects and found that the evoked field source systematically increased in depth beneath the scalp with increasing frequency of the tone. In magnetic source imaging, a single dipole modeling estimates that the equivalent current dipole (ECD) is located in the “center of gravity” of the summed intracellular currents through the apical dendrites of pyramidal cells in the activated cortical area.⁸ Their results suggested that a high frequency tone is represented in the medial portion of Heschl’s gyrus, though brain MRI examination was unavailable at that time. Also, they showed that the tonotopic progression can be described as a logarithmic mapping, which is in line with the feature of mammalian AI tonotopic map; i.e., the characteristic frequency (CF) in AI tonotopic map is progressively displaced as a function of the logarithm of the CF. Since Romani’s work, human tonotopic maps have been studied primarily with neuroradiological imaging methods that demonstrate metabolic or hemodynamic changes in the auditory cortex after tone stimulation. Using positron emission tomography, Lauter et al⁹ showed a posterior-medial to anterior-lateral mapping of high-to-low frequencies within the human AI as a result of intersubject averaging. In studies of functional magnetic resonance imaging (fMRI), the loud tone stimuli mixed with significant background noise arising from the MRI scanner may cause activation of rather wide areas in the superior temporal plane, which might reflect effects of subject’s attention to the target tone. Nevertheless, Wessinger et al¹⁰ demonstrated that activation for high-frequency tones is located more posterior and medially in Heschl’s gyrus than that for low-frequency tones. On the other hand, Bilecen et al¹¹ showed that the activated areas for the high frequency tone were found more frontally and medially than those for the low frequency tone.

In addition, tonotopic maps also have been examined in terms of the locations of N100m dipole sources for high-pitched and low-pitched tones in the human auditory cortex. Here, a “dipole source” or “current dipole” stands for the source-sink combination in the neural networks. For example, an excitatory synapse of the pyramidal cell in the superficial layer of the cortex causes current to flow across the local membrane of the soma or the basal apical dendrite in the deeper layer, through the extracellular fluid, across the synaptic membrane at the dendrite, and back to the soma through the intracellular fluid. So, the current source in the deeper layer and its sink in the superficial layer of the cortex encounter the extracellular electric field comprising negativity on the cortical surface and positivity on the white matter side. Therefore, the N100 response culminating at around 100 ms after the sound onset, distributed over the scalp, reflects the negativity of the surface of the auditory cortex; in general, EEG reflects the extracellular potential produced by a current dipole that is oriented perpendicular to the cortical surface. On the other hand, MEG detects the magnetic field generated by the simultaneous intracellular current of the apical

dendrite as a result of synaptic potential. Thus, N100m response in AEFs represents the tangential component of the multiple N100 sources in EEG recordings.¹² The N100m dipole for a high frequency tone reportedly is located more medially¹³⁻¹⁷ or more posteriorly^{15,18,19} than that for a low frequency tone. Taken together with the results obtained from the neuroradiological studies, tonotopic maps in human AI have been regarded as having the following layout: the medial-to-lateral portion of Heschl’s gyrus represents high-to-low frequency tones. Some studies analyzing N100m dipole at the peak latency of the N100m response found no such tonotopic maps.²⁰⁻²² These authors claimed that N100m arises from the secondary auditory cortex and not from AI. We will discuss this in a later section.

Liégeois-Chauvel et al^{23,24} argue that the human AI is limited to the dorso-postero-medial part of Heschl’s gyrus where the earliest intracerebral AEP responses such as N/P16 or N/P30 are encountered. However, it is still debated as to the extent of the primary auditory cortex in the Heschl’s gyrus in neuroanatomical studies.²⁵⁻²⁷ Using a computer-based, quantitative grey level index measures, Morosan et al²⁸ found that the human AI cortex corresponds to area Te1 occupying roughly the medial two-thirds of Heschl’s gyrus; area Te1 is divided into sub portions of Te1.1, Te1.0 and Te1.2 toward the lateral direction where area Te1.1 presumably corresponds to the generator source for N/P16 or N/P30 of the study by Liégeois-Chauvel et al.^{23,24} Cytoarchitectonic organization of the auditory region in humans has been characterized by “koniocortex” similar to that in the rhesus monkey. The general features of the “konio” fields are the followings; the cell packing density is the highest in layers II-IV; layer V shows a clear broad stripe because of its relative hypocellularity and parvocellularity; and layer V appears as a rather dense parvocellular narrow stripe (Galaburda and Sanides²⁵). The auditory koniocortex defined by Galaburda and Sanides²⁵ includes areas Te1.1, Te1.0 and Te1.2, surrounded by less granular auditory parakoniocortex. On the other hand, based on the staining pattern of cytochrome oxidase, acetylcholinesterase and NADPH-diaphorase activity, Rivier and Clarke²⁷ divided the Heschl’s gyrus into AI and other subportion areas (auditory association areas); however, the area of AI ranges from 2.7 to 3.1 square cm (i.e., roughly 1 x 2.7~3.1 cm, in width x length) so that AI defined by Rivier and Clarke²⁷ must include areas of Te1.1 and Te1.0 identified by Morosan et al.²⁸ Further, to compare cytoarchitectonic feature of AI with macroscopic findings such as sulcal landmarks, Rademacher et al²⁹ have found no reliable macroanatomic sign to differentiate the boundary between AI and other areas or the border of subdivisions of AI. Moreover, they noticed a significant inter-subject or inter-hemispheric variety in 3-D topography or size of cytoarchitectonically defined human AI cortex.^{26,29} In this context, one should consider human AI cortex as extended to the lateral portion of the Heschl’s gyrus and not restricted to the dorso-postero-medial part.

Some arguments about tonotopic maps of the primary auditory cortex

Looking at the results of animal experiments, cortical representation of tone is fundamentally distributed along the primary auditory cortex.³⁰ Although the area of the AI cortex initially activated after CF stimulation is as small as 1 mm in

diameter and the latency variation of the initial response is minimal, neurons with short and long latency responses are found along each isofrequency band,³¹ suggesting that there is serial intracortical activation along the isofrequency band in the AI. In the rat and cat, the isofrequency band for each tone frequency (CF) extends in a dorsoventral orientation, which is closely correlated with the direction of the horizontal collaterals of the pyramidal neurons that are initially activated after receiving impulses from the thalamocortical fibers.³²⁻³⁴ In optical recordings from the slices of rat auditory cortex, Kubota et al³⁴ have shown a spread of excitation in the supragranular (II/III) layer following antidromic electrical stimulation to the border between the white matter and layer VI. Another route for intracortical propagation of activation in the auditory cortex is the horizontal fibers of the pyramids in layer V/VI.³³ Intracortical propagation of excitation conveyed by the horizontal collaterals of pyramidal neurons has been found in the visual,^{35,36} somatosensory³⁷ and motor cortices³⁸ as well as in the auditory cortex.

It is probable that a horizontal spread of cortical activation as a result of intracortical propagation of excitation can be detected with the magnetoencephalography (MEG) recording method, since the MEG has an advantage of a high spatial resolution on a mm scale and a high temporal resolution on a ms scale, though the current source in MEG is estimated to be located in the “center of gravity” of the activated area.⁸ For example, when an activated area expands concentrically along its time course, we will find a transient increase in the power of the ECD (dipole strength) but no or little change in location of the ECD. On the other hand, when an activated area expands or moves in a certain direction along the time course, we will find a transient or dynamic change in location of the ECD instead of an increase in the power of the ECD.

There has been a long-standing argument as to the validity of the single dipole modeling to disclose a moving current source, in the case of simultaneous activation of two different areas. For example, when two fixed sources that are a little apart from each other become simultaneously active in phase, the single dipole search gives a false solution where a single fixed source is located in the intermediate position between the two fixed sources; in this case, the goodness-of-fit (GOF) value will be low because the observed magnetic fields that are generated by the two fixed sources are different from the fields theoretically produced by the “estimated single source”. On the other hand, when the two fixed sources become sequentially active in the different phase, the single-dipole modeling may give another false solution where it seems as if a single source moves between the locations of the two active fixed sources, from the location of the initially active source to that of the secondly active source.³⁹ In this situation, the GOF values in the single dipole modeling will be high enough in the earliest and latest periods of dipole source moving since the weaker current source out of the two fixed sources does not contribute to the magnetic fields; but they will be low in the intermediate period where two fixed sources become equally active to contribute to the generation of the magnetic fields. In other words, in the case of such a spurious source movement caused by attempting to fit a magnetic field resulted from a single source to that from two sources, the chances to estimate this movement with high GOF values seem

to be slim in temporal and spatial domains.³⁹ Therefore, the continuity of high GOF value of the estimated ECDs during the analysis period is essential to avoid the inaccurate source modeling described above. The analyses of somatosensory evoked fields with the GOF values > 90-95 % have disclosed that N20m in the primary somatosensory cortex dynamically moves in a mediolateral direction.⁴⁰⁻⁴² In the previous reports on AEFs, we showed that the movement of the N100m ECD lasts for 30 ms with the GOF value of $\geq 90\%$ or $\geq 85\%$, which can be reasonably explained by a single dipole model and not by a multi-dipole model.^{43,44} In general, the multi-dipole search would give a false source configuration with a high GOF value unless one recognizes the exact number and locations of the current sources.⁴⁵

Dynamic movement of N100m dipole reflects activation of the isofrequency band

Using a single dipole search, we have found that N100m dipole dynamically moves in the anterolateral direction.^{43,44,46} We also speculated that dynamic anterolateral movement of N100m dipole results from sequential activation of the isofrequency band which presumably extends along the long axis of Heschl's gyrus.⁴⁶ However, based on the results of AEF and intracerebral potentials obtained from the same patients, the N100m response, comprising an ascending and descending phase, is presumably generated from different portions of the primary auditory cortex or the adjacent areas.⁴⁷ In the intracerebral recordings from the white matter of Heschl's gyrus, P50 and P75 potentials generated from the intermediate and lateral portion of the Heschl's gyrus, respectively, may contribute to a rising phase of the scalp-recorded N100 and magnetically-recorded N100m.^{24,47} Therefore, one may argue that single ECD estimation for the magnetic fields caused by the two sequentially active fixed sources of P50 and P75 could spuriously result in a moving source.

However, it is not clarified as yet whether or not P50 and P75 claim to be generated from the intermediate and lateral portion of the Heschl's gyrus are in fact fixed sources, since no recordings along the long axis of the whole Heschl's gyrus have been made. On the contrary, Liégeois-Chauvel et al²⁴ showed that the peak latency is prolonged according to change of the recording site from medial to lateral portion, suggesting that the activated area dynamically moves toward the lateral direction. Similarly, P50 or P75 recorded from the intracerebral electrodes in the Heschl's gyrus or the adjacent areas show that their peak latencies alter in proportion to changes of the recording sites.^{24,47} Together with the findings obtained from animal experiments showing successive activation of the adjacent columns in the AI cortex, we suggest that, in the rising phase of N100m response, a dynamic antero-lateral movement of the N100m ECD along the long axis of the Heschl's gyrus reflects successive intracortical activation of the human AI cortex, representing the isofrequency band of the stimulated tone.

A representative illustration of the dynamic movement of N100m ECD in the rising phase of N100m response in pure tone evoked AEFs is presented in Figure 1. Figure 1A shows the superimposed waveforms of the AEFs recorded from the right hemisphere to left ear 400 Hz tone stimulation and Figure 1B illustrates sequential changes of the isocontour map of the

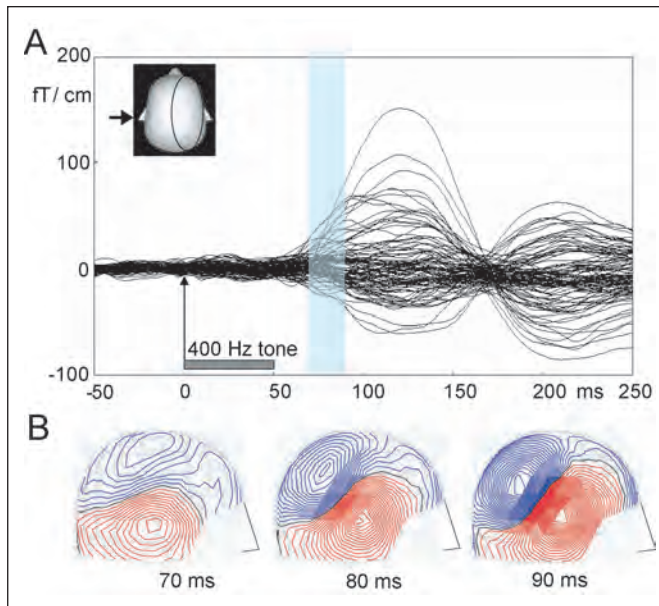


Figure 1: A: The auditory evoked magnetic signals recorded from the right hemisphere following left ear 400 Hz tone stimulation (80 dB SPL, interstimulus interval of 1 sec) in a 25-year-old man. The traces illustrate the superimposed field derivatives along the longitude (positive signal counterclockwise) and along the latitude (positive signal from vertex to decreasing latitude). B: Magnetic fields at 70, 80, and 90 ms (right lateral view) are represented as isocontour map by 20 fT step. Note that the distance between the maximum of flux-out (red contours) and that of flux-in (blue contours) is shortening from 70 to 90 ms, suggesting that the equivalent current source decreases in depth beneath the scalp.

magnetic fields from 70 to 90 ms poststimulus. Notably, the distance between the maximum of flux-out and that of flux-in sequentially shortens over 20 ms, suggesting that the dipole is approaching toward the surface of cerebral convexity beneath the scalp. As shown in Figure 2B, the N100m dipole for 400 Hz tone, superimposed on to the subject's MRI, dynamically moves along the medio-lateral direction. In this subject, the N100m dipole for 4000 Hz tone also dynamically moves in the same direction (Figure 2A). All the current dipoles for 400 Hz and 4000 Hz tones are located on the supratemporal plane of the right hemisphere (Figures 2A and 2B); the dipoles for a high frequency tone are mapped anteriorly and travel over a shorter distance (Figure 2C). When Heschl's gyrus mostly extends in the lateral direction as in the case of this subject, it is probable that the isofrequency bands for 400 Hz and 4000 Hz tones are roughly parallel to the anterior border of the Heschl's gyrus, the first transverse temporal sulcus.

A morphological study of human AI in postmortem brains showed a wide variation in orientation of the Heschl's gyrus; while the Heschl's gyrus extends in the lateral direction in some cases, it extends in the anterior direction in others.²⁶ In line with the study above, there are subjects in which N100m dipole moves in an anterior direction. As shown in Figure 3B, the border between flux-out and flux-in is displaced toward the anterior direction in the rising phase of the N100m response

(between 56 ms and 70 ms post-stimulus). The estimated dipoles during this period dynamically moves anteriorly (Figure 3B, right panel) and all the dipoles are located on the supratemporal plane of the right hemisphere. The anterior movement of the N100m dipole suggests that Heschl's gyrus of the right hemisphere in this subject mostly extends in the anterior direction.

The N100m dipole movement for right and left hemispheres contralateral to the tone stimulation was determined for each subject in the rising phase of N100m response where a high GOF value of the N100m ECD continues for ≥ 10 ms. Based on the analysis of changes in the N100m dipole locations in each subject, we first obtained the mean location of the N100m ECDs at the peak latency for both hemispheres.⁴⁴ Then we calculated the normalized or relative movement of the N100m ECDs in right and left hemispheres as the sequential changes in 3-D locations from the mean locations of the ECDs at the N100m peak.⁴⁴ Normalized movements of N100m dipoles for 400 Hz and 4000 Hz on the horizontal (x-y) plane are presented in Figure 4. The movement plots represent the layout of the isofrequency bands for 400 Hz and 4000 Hz. Our data from intersubject averaging are in good agreement with the three-dimensional probability map of the primary auditory cortex, based on the

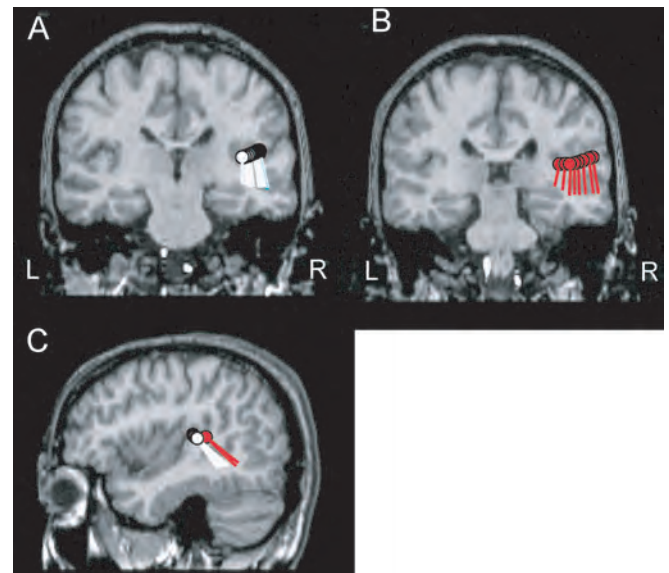


Figure 2: The locations of the current sources of N100m for left ear 4000 Hz tone (white circles and bars in A) and for left ear 400 Hz tone (red circles and bars in B) that are obtained from the same subject in Figure 1. Circles indicate the locations of the dipoles and, bars, the orientations of the current dipoles. In A, the estimated N100m current sources in the rising phase of the N100m response for 4000 Hz tone at 60–80 ms (by 2 ms step) overlaid onto the MRI. In B, the estimated N100m current sources for 400 Hz tone at 70–90 ms (by 2 ms step) overlaid onto the MRI. In C, the estimated N100m current sources for 400 Hz and 4000 Hz are superimposed onto the MRI. Dynamic mediolateral movement of the N100m current dipoles during 20 ms are clearly shown in A and B. Also note that the dipoles for the high-pitched tone are located more anteriorly.

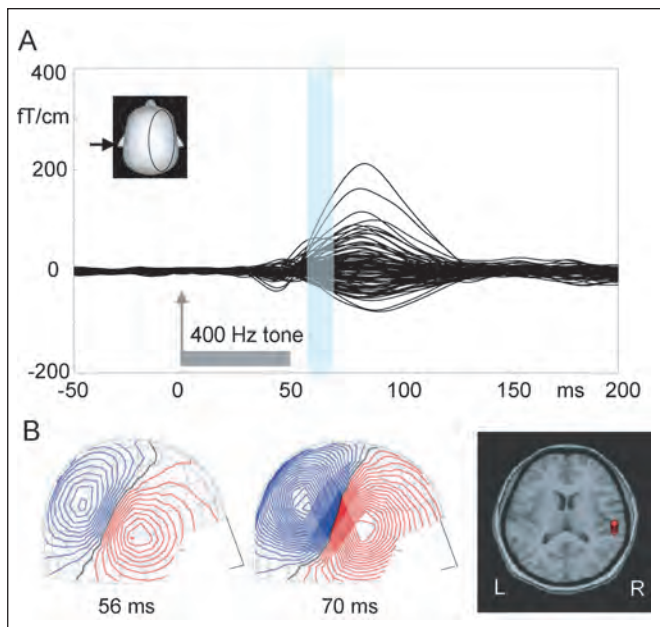


Figure 3: A: The auditory evoked magnetic signals recorded from the right hemisphere following left ear 400 Hz tone stimulation (80 dB SPL, interstimulus interval of 1 sec) in a 33-year-old woman. The traces illustrate the superimposed field derivatives along the longitude (positive signal counterclockwise) and along the latitude (positive signal from vertex to decreasing latitude). B: Magnetic fields at 56 and 70 ms (red contours for flux-out, blue contours for flux-in, 20 fT step) and the N100m dipoles from 56 to 70 ms (by 2 ms step) superimposed on to the subject's MRI. Note that the estimated dipoles (red circles) move in the anterior direction.

morphological analysis of AI across 27 postmortem brains.²⁹ Firstly, the bands for the left hemisphere are located posteriorly than those for the right hemisphere and, perhaps, the locations of ECDs in the rising phase of N100m response occupy the medial half of Heschl's gyrus in both hemispheres. Secondly, anterolateral extent of cytoarchitecturally defined AI in the right hemisphere is in line with the orientation of normalized movements of N100m ECDs for 400 Hz and 4000 Hz tones, suggesting that the isofrequency bands extend in an anterolateral direction along the long axis of Heschl's gyrus.

The well-organized, parallel arrangement of the isofrequency bands for high-pitched and low-pitched tones in the right AI is in line with the distinct functional role of the right hemisphere where the differences in pitch of the tones and music are analyzed.⁴⁸ These results support the place theory. In contrast, the isofrequency bands for 400 Hz and 4000 Hz tones in the left hemisphere are not parallel with each other, suggesting a less-organized layout. Perhaps, the left auditory cortex is specialized in phonetic analysis of the linguistic sounds that contain two or more formant frequencies as vowel or consonant sounds and thereby, each vowel or consonant bands or clusters may exist in the left AI, which will facilitate phonetic analysis of the linguistic sounds. Further studies will be needed to test this hypothesis for the functional mapping of the left AI.

Possible tonotopic map in human right auditory cortex revealed by the analysis of AEFs

Based on the analysis of AEFs, we have proposed a tonotopic map in the right auditory cortex where tone frequencies are represented along the axis perpendicular to the first transverse sulcus, as shown in Figure 5. The transverse temporal gyrus of Heschl in the postmortem brain has an area of approximately 10 mm width x 30 mm length. As mentioned above, the equivalent current dipole in the rising phase of the N100m response moves in an anterolateral direction along the long axis of Heschl's gyrus. Therefore, the axis of the frequency for 20 – 20,000 Hz tones that are audible for humans presumably occupies up to approximately 10 mm. Since each isofrequency band for the frequency representation is displaced as a function of the logarithm of the frequency,^{30,31} the isofrequency bands representing the tones of frequencies between 20 and 20,000 Hz with the difference of a factor of 10 in humans will be about 3 mm apart from each other. For example, the distance between the bands for 200 Hz tone and 2000 Hz tone (with the difference of a factor of 10) will be approximately 3 mm, which is in line with the results of the analysis of AEFs in right auditory cortex; the

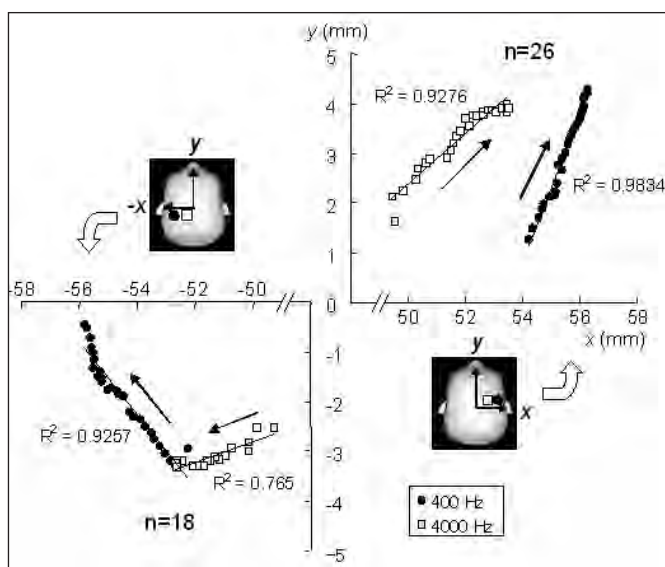


Figure 4: Isofrequency bands for 400 Hz (closed circles) and 4000 Hz (open squares) tones are represented as normalized movement of the N100m dipoles on the x-y plane in left and right hemispheres. The origin of the 3-D head coordinate system is determined as the midpoint of the pre-auricular points; the x-axis pointed to the right pre-auricular point, and the y-axis to the nasion. Arrows indicate the direction of N100m dipole movement from the starting time analyzed to the peak latency. R^2 indicates a correlation coefficient in linear regression analysis. In the right hemisphere, the isofrequency bands for two frequencies are in parallel arrangement; the mean difference between the two bands for 400 Hz and 4000 Hz tones is approximately 3 mm. (Reprinted with permission from Ozaki I, et al. Dynamic movement of N100m dipoles in evoked magnetic field reflects sequential activation of isofrequency bands in human auditory cortex. *Clin Neurophysiol* 2003; 114: 1681-1688.)

isofrequency band for 400 Hz tone and that for 4000 Hz tone is about 3 mm apart from each other (Figure 4, right panel).

N100m dipole for high frequency tone does not travel for a long distance compared to that for the low frequency tone. As shown in Figure 2, the bands for high-pitched tones are shorter than those for low-pitched tones. In general, AEFs and auditory evoked potentials have smaller amplitudes of N100m or N100 response when the stimulated tone frequency becomes higher. A schematic drawing in Figure 5 shows that the higher a tone frequency is, the shorter the length of the isofrequency band becomes. To obtain the tonotopic distance between the two tones of different pitches, one can estimate the distance or space between two vectors represented by N100m dipole movement for the tones of different pitches; when the frequency difference of the pitches reaches a factor of 10, the tonotopic distance will be approximately 3 mm. On the other hand, in many previous studies on AEFs to obtain tonotopic maps, locations of N100m dipoles for the tones of different pitches have been measured at the peak latency of N100m response. In our measurements, the distance between locations of the N100m dipoles for the tones of different pitches at the peak latency does not reflect "actual tonotopic distance" changing as a function of the logarithm of the frequency but the difference in the length of the isofrequency bands for the tones of different pitches. Furthermore, relative positions of the N100m dipoles for high and low pitched tones at the peak latency may be altered according to the difference in 3-D topography of the auditory cortex. Therefore, diverse and sometimes contradictory results on tonotopy may be obtained if the N100m dipole locations are estimated at the peak latency. Moreover, the generator sources for the N100m ECD at the peak latency may consist of the Heschl's gyri and the secondary auditory area such as planum temporale.⁴⁹ Our interpretation reasonably explains the discrepancy in tonotopic representation obtained from the AEF studies during the past two decades.

Our suggestion as to the tonotopic map of human AI shown in Figure 5 challenges the conventional view of tonotopy of human AI, i.e. the medial-to-lateral portion of Heschl's gyrus representing high-to-low frequency tones. Recently, using silent, event-related fMRI at 7 Tesla, Formisano et al⁵⁰ found mirror-symmetric tonotopic maps in the human AI. With high spatial resolution, they presented two mirror-symmetric gradients of best frequency (high-to-low, low-to-high) along the first transverse sulcus, the anterior border of Heschl's gyrus. They argue that two tonotopic maps in two adjacent subdivisions of AI share a low-frequency border, are mirror-symmetric, and are homologous to those in the macaque monkey. If this is the case, the length of the isofrequency band for low-pitched tone should be shorter than that for high-pitched tone; but, it is contrary to the findings obtained from AEF studies. Therefore, further studies will be needed to elucidate the tonotopy of human AI as to whether tonotopic maps differ between right and left hemispheres or whether tonotopic maps shows mirror-symmetric feature in subdivisions of human AI.

Task-dependent changes in tonotopic maps during auditory attention

Long-term plastic changes of human AI have been studied with AEFs in terms of enlargement of N100m response. Pantev et al⁵¹ presented piano tones or pure tones in normal subjects and

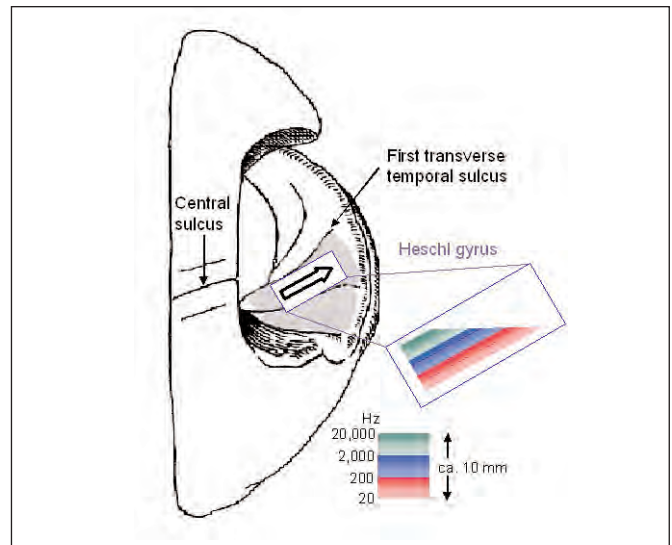


Figure 5: Schematic drawing of the tonotopic maps in the right hemisphere. The square outlined in blue represents the primary auditory cortex (AI) in Heschl's gyrus. A white arrow indicates unidirectional spread of cortical activation in the AI, presumably resulting in a dynamic movement of current dipole in the rising phase of N100m response. Unidirectional activation of AI will reflect sequential activation of the isofrequency band of the stimulated tones. Tonotopic map is represented as the layout of the isofrequency bands; in green for 2,000 to 20,000 Hz, blue for 200 to 2,000 Hz, and red for 20 to 200 Hz. The band for higher-pitched tones is located more anterior and medial and the length of isofrequency band for higher-pitched tones is shorter than that for low-pitched tones.

musicians and measured the N100m. They discovered augmentation of the N100m to piano tones in musicians. In animal experiments of AI plasticity, Recanzone et al⁵² found that, after training to discriminate differences in the frequency of sounds, the frequency map of the target sounds was enlarged in the isofrequency bands of the monkey AI. They also found that accuracy of the performance to respond to the frequency of the target sounds was correlated with the enlargement of the frequency representational map. These results suggest that receptive field plasticity of AI plays an important role in analyzing and storing information of sound features. The plastic change of AI also occurs from the perinatal period to adulthood (see review by Yan⁵³).

As to short-term change in human AI during auditory attention, many studies reported enhancement of the N100m response⁵⁴⁻⁵⁶ or N100 (N1) potential^{57,58} as well as P50m⁵⁶ or P50 potential.⁵⁸ In accordance with augmented short-latency response in AEFs or auditory evoked potentials during auditory attention tasks, functional brain mapping studies in humans have shown an increase of blood flow in several brain areas including AI and adjacent areas.^{59,60} These results suggest that the activated areas during auditory attention tasks can occupy a substantial portion of AI. It is likely therefore that AI is involved in an initial cognitive stage for identifying the differences in pitch of the

tones and that tonotopic maps for the tones with different pitches are modulated depending on the task performance. To test the above hypothesis, we presented sounds (400 Hz and 4000 Hz tones) at the right or left ear of normal subjects and measured N100m responses when subjects paid selective attention to differences in pitch or to laterality of the tones.⁴⁶ We found that locations of N100m dipoles for the tones with different pitches are segregated dynamically in the right hemisphere when subjects try to discriminate the differences in pitch of the tones and that they did not alter in the control condition where subjects are not requested to discriminate the differences in pitch of the tones.⁴⁶

In animal experiments, intermittent electrical stimulation of the nucleus basalis, paired with an auditory stimulus, rapidly enlarges the representational map for the tone of stimulated frequency in the auditory cortex.^{61,62} Acetylcholine release in sensory cortex enhances sensory responsiveness, which may contribute to improved behavioral performance in sensory-cognitive tasks.⁶³ In addition, recent animal studies revealed that active listening is accompanied by rapid task-related receptive field plasticity in the AI.^{64,65} The modulation of AI receptive fields in the waking animal is driven by selective attention to a salient acoustic feature necessary for task performance. This modulation occurs rapidly, within minutes of a change in task requirements or acoustics.⁶⁵ Rapid task-related changes are most likely the result of unmasking, disinhibition or potentiation of previously existing connections. On the basis of the above, we suggest that rapid task-dependent changes in AI, which are demonstrated by our MEG recordings, may reflect short-term receptive field plasticity of AI. Rapid task-dependent changes in the primary somatosensory cortex also have been reported in the studies on MEG.⁶⁶⁻⁶⁸ In general, MEG is insensitive to a radially-oriented current source; in other words, it is sensitive exclusively to activation of the fissural cortex, causing a tangentially-oriented current dipole. Nevertheless, since the MEG has an advantage of a high spatial resolution on a mm scale and a high temporal resolution on a ms scale, it will provide rapid as well as chronic changes in cortical representational maps as a result of cortical plasticity in various modalities. Furthermore, MEG studies in future will promise to elucidate mechanisms of attention and cognition of the human brain.

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