Morphology of Heschl's gyrus reflects enhanced activation in the auditory cortex of musicians

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Using magnetoencephalography (MEG), we compared the processing of sinusoidal tones in the auditory cortex of 12 non-musicians, 12 professional musicians and 13 amateur musicians. We found neurophysiological and anatomical differences between groups. In professional musicians as compared to non-musicians, the activity evoked in primary auditory cortex 19–30 ms after stimulus onset was 102% larger, and the gray matter volume of the anteromedial portion of Heschl's gyrus was 130% larger. Both quantities were highly correlated with musical aptitude, as measured by psychometric evaluation. These results indicate that both the morphology and neurophysiology of Heschl's gyrus have an essential impact on musical aptitude.

Most current knowledge on cerebral processing of music comes from studies of normal listeners[1–7]. Positron emission tomography (PET)[8,9], magnetic resonance tomography (MRI)[10–12], electroencephalography (EEG)[13–16] and magnetoencephalography (MEG)[17–19] have all been used to identify differences between musicians and non-musicians. EEG and MEG studies typically report the late auditory evoked response (the evoked neuronal activity that peaks about 100 ms after the onset of a sound). Intracranial EEG[20], scalp EEG[21] and MEG[22,23] studies have shown that the earliest evoked activity of the auditory cortex occurs around 15–30 ms after stimulus onset with a negative–positive complex (N19-P30) in the auditory evoked potential. This complex reflects the postsynaptic neuronal activities of the initial thalamocortical input to the auditory cortex, corresponds to the N19m-P30m component of the auditory evoked magnetic field and originates from the medial half of the first transverse temporal gyrus of Heschl[20–23].

Cytoarchitectonic[24–26], myeloarchitectonic[26,27] and histochemical[27–29] studies show that the granular core field in humans, often referred to as the primary auditory cortex (PAC), is largely confined to the medial two-thirds of Heschl's gyrus (HG), namely the anteromedial portion of Heschl's gyrus (amHG)[27–29]. Considerable individual differences have been reported, however, in the size and location of PAC along HG and relative to the location of sulcal boundaries[27–31]. Volumetric MRI studies, therefore, can only provide gross anatomical landmarks for HG using the first transverse sulcus (FTS) as the anterior boundary and Heschl's sulcus (HS) or sulcus intermedius (SI) as posterior boundaries[32–34].

Plasticity in the frequency representation of the primary core field indicates that it is involved in the fine discrimination of pitch and tonal pattern[35,36]. We therefore reasoned that the greater tonal musical aptitude[37] of musicians might have an anatomical correlate in the auditory cortex. We found a substantial difference in the magnetic field component (N19m-P30m) of the PAC evoked by sinusoidal tones in musicians as compared to non-musicians. These neurophysiological differences corresponded with anatomical differences in HG morphology and with differences in musical aptitude.

RESULTS
Auditory evoked responses
After grouping our 37 subjects *a priori* into non-musicians, amateur musicians and professional musicians according to musical ability, we recorded each subject continuously over both hemispheres with a whole-head MEG system while sinusoidal tones with carrier frequencies of 100, 220, 500, 1,100, 2,500 and 5,600 Hz were presented. Tones were 100% amplitude-modulated to record the fast, steady-state response of the auditory cortex[23]. From the averaged steady-state responses, the primary N19m-P30m responses were computed off-line by deconvolution[23]. The source activity of the auditory cortex was calculated using equivalent dipoles[21,38,39] in the medial portion of the left and right HG (**Fig. 1** and Methods).

The primary N19m-P30m source activity of the auditory cortex evoked by tones with a carrier frequency of 500 Hz was markedly different between subject groups (**Fig. 2**). Signal amplitudes were about twice as large in professional musicians as in non-musicians. Similar response differences were seen at the other five frequencies, but the responses were largest at 500 Hz in all groups. The primary N19m-P30m source activity averaged over all frequencies and both hemispheres was 102 ± 16% larger in professional musicians than it was in non-musicians ($F_{1,22}$ = 58.7, $P < 0.0001$). The increase was highly significant at each
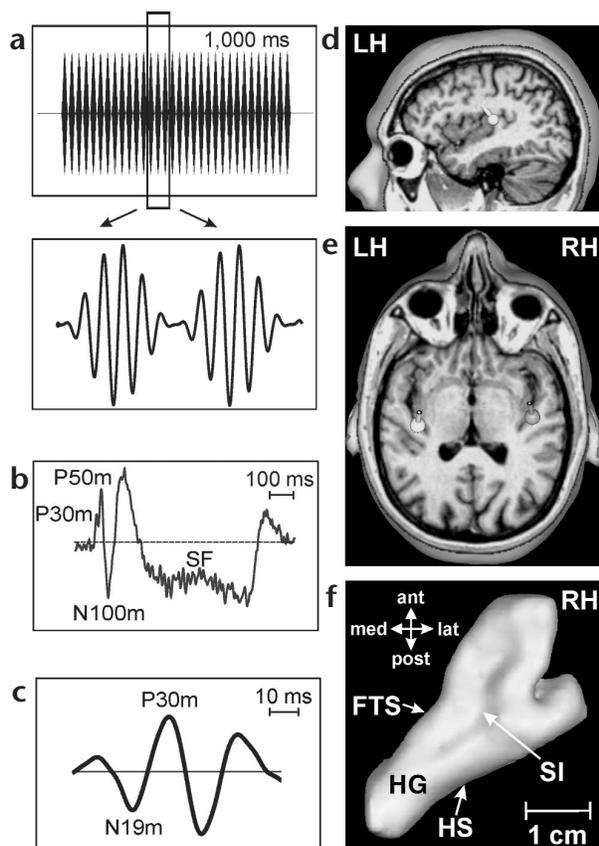
Fig. 1. The auditory stimulus, evoked magnetic fields and cortical anatomy. (**a**) Stimulus waveform. A modulation frequency of 26–37 Hz was superimposed on sinusoidal tones with carrier frequencies of 100–5,600 Hz to measure the responses to tone onset and to each modulation cycle. (**b**) Typical averaged response at an MEG sensor over the right auditory cortex shows middle latency onset components P30m and P50m, long latency components N100m and the sustained field (SF). The responses to the modulation cycles appear superimposed on the SF. (**c**) Typical early N19m-P30m response of the PAC after deconvolution of the modulated signals. (**d**, **e**) Source model with one equivalent dipole in each hemisphere depicted in sagittal and transversal T1-weighted MRI images. The transversal section is parallel to the supratemporal plane. The source activity is modeled with dipoles drawn in the left and right hemispheres. (**f**) Three-dimensional (3D) gray matter surface reconstruction of the right HG. The FTS defines the anterior boundary and the most posterior HS defines the posterior boundary. The first transverse HG is sometimes divided by the SI, a shallow sulcus which does not extend over its full length.

average signal that was $115 \pm 18\%$ larger over all frequencies in the right hemisphere ($F_{1,22} = 73.4$, $P < 0.0001$) and $87 \pm 17\%$ larger in the left hemisphere ($F_{1,22} = 43.6$, $P < 0.0001$). Non-musicians, by contrast, did not have significantly larger dipole amplitudes in the right than in the left hemisphere ($5 \pm 9\%$, $F_{1,11} = 3.6$, n.s). In amateur musicians, dipole amplitudes were $19 \pm 14\%$ larger in the right than they were in the left hemisphere ($F_{1,12} = 17.8$, $P < 0.01$). This was significant at three frequencies (100 Hz, 500 Hz and 1,100 Hz, $P < 0.05$).

There was a pronounced difference between the early and late auditory cortical responses. Whereas the early N19m-P30m complex was much larger in musicians, the late N100m component, which was evoked by the onset of the sinusoidal tones, showed similar amplitudes in all three groups over all frequencies (**Fig. 3b**). For all groups, the N100m was largest around 1,000 Hz.

Morphology of Heschl's gyrus
The large neurophysiological difference between musicians and non-musicians at the level of the PAC coincided with a large

frequency and ranged from 78% (1,100 Hz, $P < 0.0001$) to 144% (5,600 Hz, $P < 0.0001$).

We next averaged the peak-to-peak N19m-P30m dipole amplitudes for each group (**Fig. 3a**). Amateur musicians showed an intermediate average increase of $37 \pm 11\%$ over non-musicians ($F_{1,23} = 7.8$, $P < 0.05$). The difference between amateur musicians and non-musicians was significant only in the low frequency range (<1,000 Hz, $P < 0.05$). There was a frequency × group interaction ($F_{10,165} = 2.9$, $P < 0.01$) that ranged from 77% (100 Hz, $P < 0.01$) to 14% (2,500 Hz, nonsignificant (n.s.)).

In professional musicians, dipole amplitudes were significantly larger in the right than in the left hemisphere at all frequencies. On average, the N19m-P30m signal was $21 \pm 9\%$ larger in the right hemisphere ($F_{1,11} = 47.3$, $P < 0.0001$). Compared to non-musicians, professional musicians had an
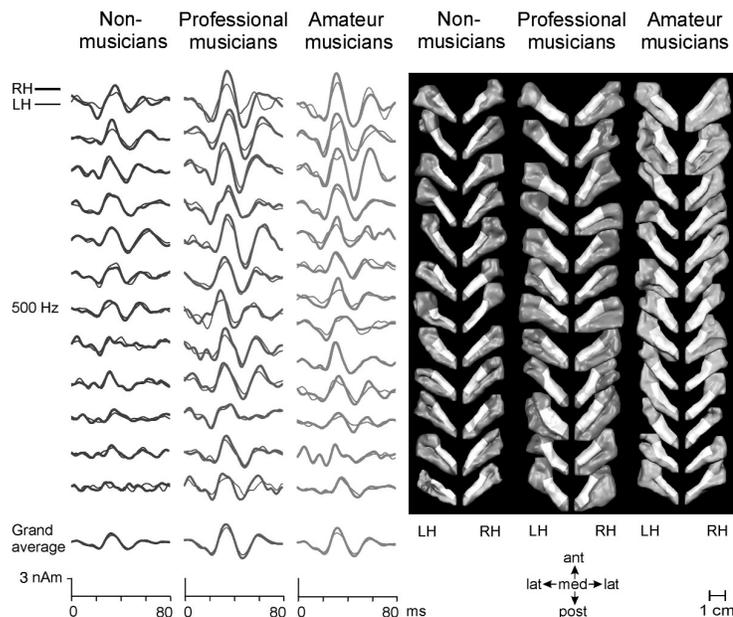
Fig. 2. Auditory evoked N19m-P30m signals and 3D gray matter surface reconstructions of HG for all subjects aligned in the same order. Both the neurophysiological and the anatomical data show a large increase in professional musicians and a smaller increase in amateur musicians. Left, dipole strength of the primary cortical response at 500 Hz. Source activities of the right (thick lines) and left (thin lines) hemispheres are superimposed. Right, highlighted areas show the amHG for each subject, aligned in the same order as the primary evoked responses.

Fig. 3. Frequency dependence of the primary N19m-P30m and the late N100m dipole moments. Solid lines depict the data for the right hemisphere with standard error bars. Dashed lines depict the corresponding mean group data for the left hemisphere with slightly smaller early dipole moments. (**a**) The professional musicians (circles) showed much larger early response signals over all frequencies than non-musicians (squares); the amateur musicians (triangles) had larger signals only at frequencies below 1,000 Hz. (**b**) N100m dipole moments were similar in all groups.
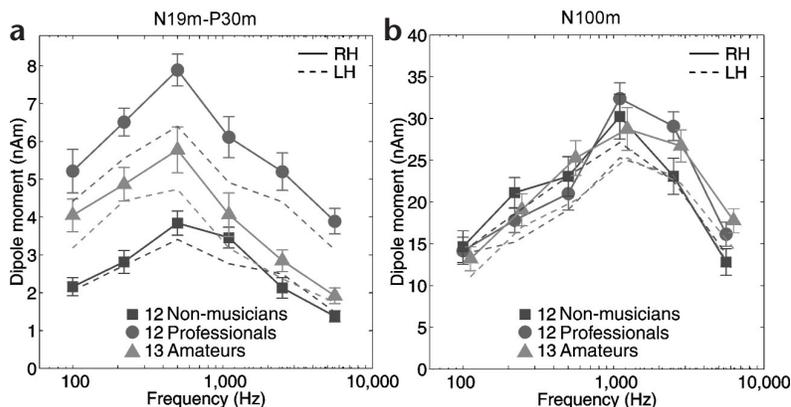
morphological difference. From the three-dimensional (3D) gray matter surface reconstructions of the right and left HG (**Fig. 2**, right), we estimated the volumes of the gray and white matter of HG and its macroanatomical subdivisions (**Fig. 1f**). The whole HG was defined as extending to the lateral border of the temporal plane, with the FTS as the anterior boundary and the most posterior HS as the posterior boundary. The anterior portion of Heschl's gyrus (aHG) was defined by the SI, if present, or otherwise by the most anterior HS as posterior boundary[33], and the amHG was defined as the medial two-thirds of aHG.

The MRI-based volumetry of these structures showed much larger gray matter volumes in musicians than in non-musicians, particularly in amHG (**Table 1**). Averaged over both hemispheres, the amHG gray matter volume was $130 \pm 23\%$ larger in professional musicians ($F_{1,22} = 71.2$, $P < 0.0001$). The mean differences by hemisphere were $122 \pm 15\%$ in the right and $136 \pm 19\%$ in the left ($F_{1,22} = 2.0$, n.s.). The difference was considerably less, but still significant, when the gray matter volumes of the whole HG or aHG were considered (aHG, $67 \pm 19\%$, $F_{1,22} = 18.1$, $P < 0.001$; HG, $37 \pm 15\%$, $F_{1,22} = 8.3$, $P < 0.01$). White matter volumes were not significantly different between professional musicians and non-musicians, apart from a slightly larger amHG volume in professionals ($30 \pm 16\%$, $F_{1,22} = 4.5$, $P < 0.05$). Gray matter had a considerably larger influence than did white matter on this

difference (tissue × group interaction, $F_{1,22} = 77.1$, $P < 0.0001$). Compared with non-musicians, amateur musicians showed significantly more gray matter volume in only the anterior portions of HG (amHG, $60 \pm 21\%$, $F_{1,23} = 11.4$, $P < 0.01$; aHG, $61 \pm 22\%$, $F_{1,23} = 10.7$, $P < 0.01$). White matter volumes were not significantly different between amateurs and non-musicians.

For all three groups, there was a strong correlation ($r = 0.87$, $P < 0.0001$) between the neurophysiological (individual peak-to-peak N19m-P30m dipole amplitudes averaged over all frequencies and both hemispheres) and the anatomical (mean gray matter volume of amHG) parameters (**Fig. 4a**). This functional–anatomical correlation was also significant within each group: non-musicians ($r = 0.68$, $P < 0.01$), amateurs ($r = 0.67$, $P < 0.01$) and professionals ($r = 0.58$, $P < 0.05$). Combining the professional and amateur musicians into one group supported the strong correspondence between the primary auditory source activity and the gray matter volume of amHG ($r = 0.78$, $P < 0.0001$). The correlation over all groups was much weaker ($r = 0.32$ instead of 0.87, $P < 0.05$) when the whole HG was used as the anatomical reference.

The gray matter volume of amHG separated professional musicians (range 536–983 mm³) from non-musicians (172–450 mm³),

Table 1. Volumetry of Heschl's gyrus.

Area	Side	Gray matter volume (mm³)			White matter volume (mm³)		
		Non-musicians	Professional musicians	Amateur musicians	Non-musicians	Professional musicians	Amateur musicians
HG	L	$2,083 \pm 212$	$2,607 \pm 215$	$2,694 \pm 411$	929 ± 72	861 ± 128	883 ± 116
	R	$1,868 \pm 110$	$2,814 \pm 197$**	$2,256 \pm 256$	946 ± 90	$1,172 \pm 165$	$1,018 \pm 188$
	(L+R)/2	$1,976 \pm 153$	$2,710 \pm 201$**	$2,475 \pm 308$	937 ± 52	$1,018 \pm 132$	951 ± 144
	δ_{HG}	-0.11 ± 0.06	0.08 ± 0.04	-0.18 ± 0.10	0.02 ± 0.09	0.31 ± 0.12*	0.22 ± 0.10
aHG	L	925 ± 107	$1,513 \pm 115$**	$1,435 \pm 181$*	434 ± 44	516 ± 56	504 ± 82
	R	824 ± 57	$1,406 \pm 142$**	$1,379 \pm 170$**	353 ± 46	484 ± 65	453 ± 50
	(L+R)/2	873 ± 77	$1,461 \pm 112$***	$1,407 \pm 138$**	394 ± 39	505 ± 48	502 ± 59
	δ_{aHG}	-0.11 ± 0.07	-0.07 ± 0.09	-0.04 ± 0.11	-0.21 ± 0.13	-0.06 ± 0.15	-0.11 ± 0.18
amHG	L	328 ± 58	776 ± 68***	523 ± 57*	176 ± 18	220 ± 27	246 ± 35
	R	296 ± 31	659 ± 39***	448 ± 47*	160 ± 22	227 ± 27	208 ± 26
	(L+R)/2	311 ± 27	716 ± 39***	494 ± 46**	172 ± 15	223 ± 18*	227 ± 28
	δ_{amHG}	-0.10 ± 0.12	-0.16 ± 0.10	-0.15 ± 0.11	-0.09 ± 0.13	0.03 ± 0.18	-0.16 ± 0.15

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ (ANOVA, professionals/amateurs versus non-musicians). Values given as mean ± s.e.m. δ, hemispheric asymmetry (Methods).
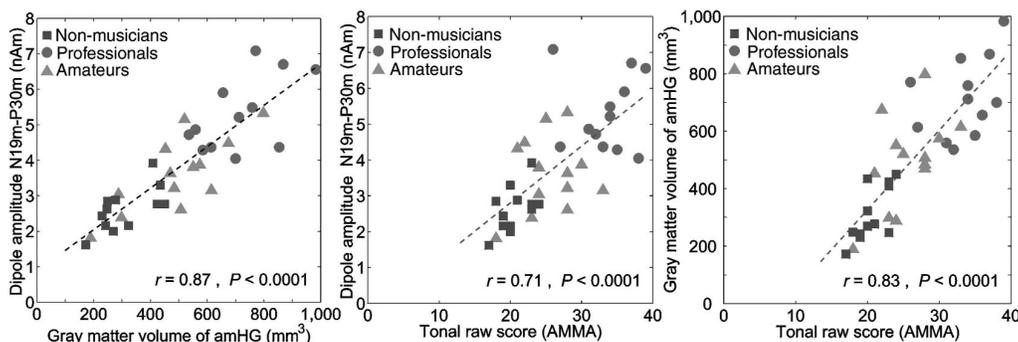
Fig. 4. Correlations between early neurophysiological source activity, amHG gray matter volume and musical aptitude. (**a**) The N19m-P30m dipole moment was strongly correlated with the mean gray matter volume of amHG. Values were averaged over the right and left hemispheres. (**b, c**) The tonal raw score of musical aptitude (AMMA test) was highly correlated with both the N19m-P30m dipole moment (**b**) and the gray matter volume of amHG (**c**).

and amateur musicians showed an intermediate gray matter volume (189–798 mm³). The total volume of HG, including white and gray matter, showed a larger variance and could not separate the groups (non-musicians, 1,955–4,694 mm³; professionals, 2,629–6,297 mm³; amateurs, 2,151–7,603 mm³). The asymmetry measures (Methods) showed only one significant effect: the total volume of HG was 14% larger in the right hemisphere of professional musicians (right, 3,986 ± 305 mm³; left, 3,468 ± 263 mm³; δ_{HG} = 0.14 ± 0.04; $F_{1,11}$ = 11.7, P < 0.01).

Correlation with musical aptitude
For all three groups, there was a high correlation between the N19m-P30m signal amplitude and musical aptitude as measured by the AMMA tonal test (**Fig. 4b**). Both the primary source activity and the tonal score of musical aptitude completely separated the professional musicians from the non-musicians. The amateur musicians showed an intermediate range of musical aptitude and dipole amplitudes that overlapped with the two other groups. Within groups, the correlation was significant for non-musicians (r = 0.55, P < 0.05), but not for amateurs (r = 0.19, n.s.) or professionals (r = 0.05, n.s.). In general, professional musicians had high AMMA scores, high signal amplitudes and large gray matter volumes of amHG. When analysis was restricted to amateur and professional musicians, the correlation was significant (r = 0.52, P < 0.01).

Similarly, the gray matter volume of amHG was highly correlated with musical aptitude (**Fig. 4c**). Within groups, the correlation was significant for non-musicians (r = 0.71, P < 0.001) and amateurs (r = 0.56, P < 0.05), but not for professionals (r = 0.40, n.s.). When all amateurs and professionals were combined, however, the correlation was highly significant (r = 0.70, P < 0.0001). This correlation was smaller when considering the gray matter volume of aHG in its full lateral extent (r = 0.44, P < 0.01) and was nonsignificant when the whole gray matter volume of HG was calculated (r = 0.26, n.s.). No correlation was found between musical aptitude and white matter volumes of HG.

Under the assumption that anatomical size determined the signal strength, a partial correlation was calculated to eliminate the influence of amHG gray matter volume of on the correlation between N19m-P30m amplitude and AMMA score. This partial correlation was only r = –0.04 (n.s.), indicating that anatomical size was the key parameter.

Influence of external variables
We found no influence of the covariates sex, age or head size on either the early dipole amplitudes or on the gray matter volume of amHG. To exclude influences of attention during MEG recording and of the frequency modulation in the stimulus, we carried out two additional control sessions in a subgroup of 24 stochastically selected subjects. While watching a video, subjects detected deviant tones of a different frequency (1,100 Hz instead of the standard 500 Hz) and indicated them by button press in the attention experiment. We found no significant effect of attention on the primary N19m-P30m component. Within noise limits, the N19m-P30m signals for the onset of pure sinusoidal tones agreed with the signals deconvoluted from the modulated tones[23,40].

DISCUSSION
Here we found a large difference in the early neurophysiological activity of the auditory cortex in musicians versus non-musicians, using simple tonal stimuli. In addition, we found strong correlations of this activity with the gray matter volume of amHG and with musical aptitude. Using partial correlations, we showed that the gray matter volume of amHG was the key parameter influencing the early evoked response of the auditory cortex. The larger gray matter volume in professional musicians was most pronounced for amHG (130% greater than in non-musicians) and dropped to 37% more volume than in non-musicians when the whole HG was used for anatomical reference. Together with evidence from previous EEG[20] and MEG[21–23] studies that localized the origin of the primary auditory-evoked N19-P30 source activity to amHG, our findings provide evidence for the augmentation of PAC gray matter in musicians.

This functional–anatomical interpretation is consistent with the microanatomical[24–29] finding that amHG comprises most of the primary granular core field. However, the macroanatomically defined amHG is only an approximate measure of the location and extent of PAC, because there is considerable individual variability[27–31]. Non-primary cortical fields are most likely to be found near the lateral and posterior edges of amHG[2,27–29]. Thus, the larger volume of gray matter in musicians may comprise PAC as well as surrounding belt areas. The strong functional–anatomical correspondence at the level of amHG is probably related to the stimulation with sinusoidal tones. Whereas functional MRI[41,42] and PET[43] studies have shown

that simple tonal stimuli primarily activate the auditory core regions, the fine time resolution of MEG and EEG allowed us to distinguish the initial primary source activity evoked by pure tones, and to compare the data with human intracranial recordings[20].

Our anatomical data extend earlier findings of enlarged Heschl's gyri in musicians. Morphometric post-mortem case studies[44] have reported an abnormally large anterior 'Heschl convolution' in two eminent musicians. Furthermore, a histological study[45] has reported larger volumes of cytoplasm in nerve cells in layers 3–6 of Heschl's first transverse convolution in two professional musicians as compared to non-musicians. This is in accordance with our finding that thicker amHG gray matter, not white matter, was the main factor contributing to the morphological volume difference between musicians and non-musicians.

At the neurophysiological level, we found a striking difference between the early and late evoked responses of the auditory cortex. The finding that the late N100m component was not enhanced in musicians is in agreement with a previous MEG study that reports an increase of 25% in the amplitude of N100m with piano tones, but not with sinusoidal tones[17]. It has been suggested that structural differences in the white matter of the planum temporale of musicians[10] (which has been identified as the predominant generating substrate of N100m[20]) underlies this effect. In combination, these and our findings indicate that the early and late auditory evoked responses reflect different stages and areas of functional processing in the human auditory cortex. Thus, the increase in the activity and structure of particular regions of the auditory cortex in musicians seems to be related to the processing of specific stimulus properties and may therefore reflect multiple structural and neurophysiological specializations in the auditory cortex of musicians.

The increase in the early dipole source activity was larger in the right hemisphere of professional musicians, whereas the gray matter volumes of amHG did not show significant hemispheric differences. This result should be interpreted with caution because MEG is largely insensitive to radial current flow. Hence, MEG cannot measure the full size of the net dipole source vector, and the hemispheric differences could be due, in part, to different effective orientations in the groups of professionals and non-musicians. Despite this uncertainty about the full dipole moment, the correlation between the primary source activity and the gray matter volume of amHG was highly significant for all anatomical measures, irrespective of whether the right hemisphere alone, the left hemisphere alone, or both together were considered.

What are the causes for the striking increases in the gray matter volume of the anteromedial portion of HG and the early neurophysiological activities of the auditory cortex in musicians? No influence of attention was found. The role of musical practice[40,49], however, remains unclear. In the group of musicians, there was a ceiling effect in the correlation between AMMA score and dipole amplitude (**Fig. 4b**). Therefore, only the amateur musicians are an appropriate sample for studying the influence of musical practice on the dipole amplitude. The number of amateur musicians in this study was too small, however, to obtain significant results regarding the effects of starting age and intensity of musical practice in childhood.

Functional long-term and short-term plasticity might influence the amplitude of the late auditory evoked N100m response[17,46], as well as the frequency representation and temporal information processing in the PAC[35,36] of non-human primates. On the other hand, developmental stability around

age seven has been demonstrated for the human HG and planum temporale in morphometric[34,47] and myeologenetic[48] studies. This maturation age is consistent with that observed for the psychometric variable of our study, musical aptitude. The level of musical aptitude reached by the age of nine remains the same throughout life[37]. In conclusion, our results indicate that the morphology and neurophysiology of HG have an essential impact on musical aptitude. The question remains, however, whether early exposure to music[49] or a genetic predisposition[50] leads to the functional and anatomical differences between musicians and non-musicians.

METHODS

Subjects. Thirty-seven right-handed adults with normal hearing were divided into three groups: 12 non-musicians (age range 26–43 years; 6 men, 6 women), 12 professional musicians (age 29–55; 6 men, 6 women) and 13 amateur musicians (age 24–62; 7 men, 6 women). As there is no standard definition of 'musician'[8–19], we classified the three subject groups as follows: non-musicians had never played an instrument beyond standard school education, professional musicians had undergone a professional music education ending with a diploma and were actively performing at the time of examination, and amateur musicians had received special instruction in one or more musical instruments. This classification was validated by the advanced measure of music audiation (AMMA) tonal test[37] (see below).

A stochastically chosen subgroup of 24 subjects, divided into 8 non-musicians (age 26–43, 4 men, 4 women), 7 professional musicians (age 29–51, 3 men, 4 women) and 9 amateur musicians (age 24–62, 5 men, 4 women) participated in additional experiments. Averaged over the groups, there were no significant differences in age, sex or head size. All participants gave their informed consent to the study. Experimental procedures were approved by the local ethics committee.

AMMA test. This test, which has been standardized with more than 5,000 students, presents 30 pairs of short melodies. The repeated melody has a small change in pitch (10 pairs) or rhythm (10 pairs) or is unchanged (10 pairs). Subjects detected the modification in a three-way forced choice task. As our study used tonal stimuli, only tonal raw test scores were calculated. The tonal raw score was calculated as 20 plus the number of correct responses, minus the number of false alarms. Non-musicians scored less than 25 on a scale of 0–40 (range 17–24), professional musicians had a raw score of at least 26 (range 26–39) and amateur musicians scored in an intermediate range (18–33).

Stimuli. 100% amplitude-modulated pure tones with a duration of 1 s including approximately 30 modulation cycles (**Fig. 1a**) were presented binaurally at a level of 50 dB SL (sensation level). The tones were delivered in blocks with one fixed carrier frequency through shielded transducers connected to the subject through 90 cm plastic tubes and foam earpieces. In one session, six blocks with carrier frequencies of 100, 220, 500, 1,100, 2,500 and 5,600 Hz were presented. These carrier frequencies were chosen to be equidistant on a logarithmic frequency scale corresponding to the musical interval of a major ninth. Within each block, 430 tones were presented at seven different modulation frequencies in the range of 26–37 Hz in pseudorandom order, with an interstimulus interval ranging from 1.0 to 1.2 s. To minimize stimulus artifacts, tone polarity was reversed from one tone to the next. The modulated tones sounded similar to pure tones with an additional small roughness.

In the additional tonal experiment, unmodulated tones were presented with the same frequencies ranging from 100 to 5,600 Hz. To obtain about 2,000 averages per frequency, the duration of the tones was reduced to 150 ms including a 20 ms rise and fall time. Interstimulus interval was reduced to the pseudo-randomized 400–600 ms range.

In the main and additional tonal experiments, subjects listened passively to the sounds while watching a silent video of their own choice. In the additional attention experiment, modulated tones of 500 Hz (standards) and 1,100 Hz (deviants) were presented in an oddball task and subjects were asked to indicate the deviants by button press.

Procedures. MEG was recorded continuously over both hemispheres with a whole-head Neuromag-122 system (Neuromag, Helsinki, Finland) in a magnetically shielded room using a band-pass filter of 0.01–250 Hz and a sampling rate of 1,000 Hz. For coregistration with MRI, the locations of four indicator coils and 35 surface points, including the nasion and two pre-auricular points, were digitized. The head position in the Dewar was determined at the beginning of each recording block. For each carrier frequency, about 400 artifact-free responses were averaged off-line by excluding trials with eye-blinks or MEG gradients greater than 600 fT/cm. One of the resulting 122 averaged MEG waveforms over the right auditory cortex is depicted in **Fig. 1b**. About 2–5 noisy channels were excluded from further analysis. The amplitude of the N100m component was measured against the prestimulus baseline by subtracting the average signal over a 100 ms interval before tone onset. The fast primary N19m-P30m component was analyzed after applying a zero phase shift band-pass filter from 20 Hz (12 dB/octave) to 120 Hz (24 dB/octave).

Deconvolution technique. To obtain the primary N19m-P30m components from the steady-state responses, we applied a linear deconvolution technique[23] to the period modulation cycles. Responses were averaged over all cycles at each modulation frequency. The averaged cyclic responses (total ~12,000) were then combined to deconvolute the time course of the transient N19m-P30m response elicited by each modulation cycle (**Fig. 1c**). Intrinsically, this deconvolution technique[23] uses the varying phase lag and overlap of the underlying components at each modulation frequency for the reconstruction. The deconvoluted responses had a very large signal-to-noise ratio and were highly similar to the N19m-P30m response recorded with short transient stimuli. The advantage of the deconvolution technique was that it separated the primary N19m-P30m response (**Fig. 1c**) from later overlapping responses such as P50m-N100m (**Fig. 1b**), which originate outside the PAC. Decomposed and transient N19m-P30m responses had similar source localizations in the medial portion of the anterior HG[23].

Source analysis. The BESA software (MEGIS Software GmbH, Graefelfing, Germany) was used to model the source activity of the auditory cortex with one equivalent dipole in each hemisphere[38,39]. When the dipoles were fitted to the measured magnetic evoked fields in the 19–30 ms range, locations near the anteromedial portion of the HG were found with a mean deviation of 3 mm in the posterior direction and 5 mm in the superior direction. As dipole depth is the weakest parameter in MEG dipole fitting and has a strong inverse correlation with dipole amplitude, a fixed depth value was defined using the mean dipole depth over all frequencies and subjects[40]. This depth point was 10 mm from the medial boundary of the anterior HG for N19m-P30m, and 22 mm from the boundary for N100m. Thus, the dipole sources were seeded systematically[40] along the individual anterior HG at these distances, laterally from its medial boundary. Location parameters in the anterior–posterior and inferior–superior directions were retained from the fit procedure, and orientations were fitted individually to N19m-P30m and the peak of N100m. Using this two-dipole model, robust source waveforms were calculated for both components. These provided an image of brain function in terms of the magnitude and timing of the compound source currents in the region of HG.

Morphometry. To obtain morphological measures of the right and left HG, the surfaces of the gray and gray–white matter boundaries were rendered from the individual T1-weighted 3D-MRI images (Philips Edge System, Eindhoven, Netherlands; 1.5 T, 1 mm slices, **Fig. 1d–f**) using the segmentation tools of the BrainVoyager program (Brain Innovation B.V., Maastricht, Netherlands). The inclusion range of image gray values was calculated from the individual intensity histograms by identifying the peaks corresponding to gray and white matter and their half-amplitude side lobes. For gray matter surface segmentation, both the white and gray matter peaks were included with their side-lobes. For white matter segmentation, only the white matter peak was included up to the midpoint between the peaks of white and gray matter. These rendered surfaces were then used together with macroanatomically defined anterior, posterior, medial and inferior boundaries to calculate the white and gray matter volumes of HG, aHG and amHG. FTS defined the anterior boundary in

all cases (**Fig. 1f**). SI defined the posterior boundary of aHG in 35 of 74 hemispheres. The first, most anterior HS was used in 39 hemispheres. The medial boundary was drawn from the medial end of FTS to the medial end of the most posterior HS. The inferior boundary was derived by an intersecting surface running from the depth of FTS to the depth of HS. Hemispheric asymmetry was determined by the coefficient $\delta = (V_R - V_L)/(0.5 \times (V_R + V_L))$.

1. Zatorre, R. J. & Peretz, I. The biological foundations of music. *Ann. NY Acad. Sci.* **930**, (2001).
2. Zatorre, R. J. & Binder, J. R. in *Brain Mapping the Systems* (eds. Toga, A. W. & Mazziotta, J. G.) 365–402 (Academic, San Diego, California, 2000).
3. Liégeois-Chauvel, C., Peretz, I., Bahaï, M., Laguitton, V. & Chauvel, P. Contribution of different cortical areas in the temporal lobes to music processing. *Brain* **121**, 1853–1867 (1998).
4. Maess, B., Koelsch, S., Gunter, T. C. & Friederici, A. D. Musical syntax is processed in Broca's area: an MEG study. *Nat. Neurosci.* **4**, 540–545 (2001).
5. Blood, A. J., Zatorre, R. J., Bermudez, P. & Evans, A. C. Emotional responses to pleasant and unpleasant music correlate with activity in paralimbic brain regions. *Nat. Neurosci.* **2**, 382–387 (1999).
6. Schiavetto, A., Cortese, F. & Alain, C. Global and local processing of musical sequences: an event-related brain potential study. *Neuroreport* **10**, 2467–2472 (1999).
7. Patel, A. D. & Balaban, E. Human pitch perception is reflected in the timing of stimulus-related cortical activity. *Nat. Neurosci.* **4**, 839–844 (2001).
8. Zatorre, R. J., Evans, A. C. & Meyer, E. Neural mechanisms underlying melodic perception and memory for pitch. *J. Neurosci.* **14**, 1908–1919 (1994).
9. Zatorre, R. J., Perry, D. W., Beckett, C. A., Westbury, C. F. & Evans, A. C. Functional anatomy of musical processing in listeners with absolute pitch and relative pitch. *Proc. Natl. Acad. Sci. USA* **95**, 3172–3177 (1998).
10. Schlaug, G., Jäncke, L., Huang, Y. & Steinmetz, H. *In vivo* evidence of structural brain asymmetry in musicians. *Science* **267**, 699–701 (1995).
11. Schlaug, G., Jäncke, L., Huang, Y., Staiger, J. F. & Steinmetz, H. Increased corpus callosum size in musicians. *Neuropsychologia* **33**, 1047–1055 (1995).
12. Münte, T., Kohlmetz, C. & Altenmüller, E. Superior auditory spatial tuning in conductors. *Nature* **409**, 580 (2001).
13. Altenmüller, E. Electrophysiological correlates of music perception in the human brain. *Eur. Arch. Psychiatry Neurol. Sci.* **235**, 342–354 (1986).
14. Wayman, J. W., Frisina, R. D. & Walton, J. P. Effects of musical training and absolute pitch ability on event-related activity in response to sine tones. *J. Acoust. Soc. Am.* **91**, 3527–3531 (1992).
15. Crummer, G. C., Walton, J. P., Wayman, J. W., Hantz, E. C. & Frisina, R. D. Neural processing of musical timbre by musicians, nonmusicians, and musicians possessing absolute pitch. *J. Acoust. Soc. Am.* **95**, 2720–2727 (1994).
16. Koelsch, S., Schröger, E. & Tervaniemi, M. Superior pre-attentive auditory processing in musicians. *Neuroreport* **10**, 1309–1313 (1999).
17. Pantev, C. *et al.* Increased auditory cortical representation in musicians. *Nature* **392**, 811–813 (1998).
18. Elbert, T., Pantev, C., Wienbruch, C., Rockstroh, B. & Taub, E. Increased cortical representation of the left hand in string players. *Science* **270**, 305–307 (1995).
19. Hirata, Y., Kuriki, S. & Pantev, C. Musicians with absolute pitch show distinct neural activities in the auditory cortex. *Neuroreport* **10**, 999–1002 (1999).
20. Liégeois-Chauvel, C., Musolino, A., Badier, J. M., Marquis, P. & Chauvel, P. Evoked potentials recorded from the auditory cortex in man: evaluation and topography of the middle latency components. *Electroencephalogr. Clin. Neurophysiol.* **92**, 204–214 (1994).
21. Scherg, M. & von Cramon, D. Evoked dipole source potentials of the human auditory cortex. *Electroencephalogr. Clin. Neurophysiol.* **65**, 344–360 (1986).
22. Rupp, A. *et al.* Fast temporal interactions in human auditory cortex. *Neuroreport* **11**, 3731–3736 (2000).
23. Gutschalk, A. *et al.* Deconvolution of 40 Hz steady-state fields reveals two overlapping source activities of the human auditory cortex. *Clin. Neurophysiol.* **110**, 856–868 (1999).
24. Braak, H. The pigment architecture of the human temporal lobe. *Anat. Embryol.* **154**, 214–240 (1978).
25. Galaburda, A. & Sanides, F. Cytoarchitectonic organization of the human auditory cortex. *J. Comp. Neurol.* **190**, 597–610 (1980).
26. Rademacher, J., Caviness, V. S., Steinmetz, H. & Galaburda, A. M.

Topographical variation of the human primary cortices: implications for neuroimaging, brain mapping, and neurobiology. *Cereb. Cortex* **3**, 313–329 (1993).

27. Hackett, T. A., Preuss, T. M. & Kaas, J. H. Architectonic identification of the core region in auditory cortex of macaques, chimpanzees and humans. *J. Comp. Neurol.* **441**, 197–222 (2001).

28. Rivier, F. & Clarke, S. Cytochrome oxidase, acetylcholinesterase, and NADPH-diaphorase staining in human supratemporal and insular cortex: evidence for multiple auditory areas. *Neuroimage* **6**, 288–304 (1997).

29. Wallace, M. N., Johnston, P. W. & Palmer, A. R. Histochemical identification of cortical areas in the auditory region of the human brain. *Exp. Brain Res.* **143**, 499–508 (2002).

30. Rademacher, J. *et al.* Probabilistic mapping and volume measurement of human primary auditory cortex. *Neuroimage* **13**, 669–683 (2001).

31. Morosan, P. *et al.* Human primary auditory cortex: cytoarchitectonic subdivisions and mapping into a spatial reference system. *Neuroimage* **13**, 684–701 (2001).

32. Steinmetz, H. *et al.* Cerebral asymmetry: MR planimetry of the human planum temporale. *J. Comput. Assist. Tomogr.* **13**, 996–1005 (1989).

33. Penhune, V. B., Zatorre, R. J., MacDonald, J. D. & Evans, A. C. Interhemispheric anatomical differences in human primary auditory cortex: probabilistic mapping and volume measurement from magnetic resonance scans. *Cereb. Cortex* **6**, 661–672 (1996).

34. Leonard, C. M., Puranik, C., Kuldau, J. M. & Lombardino, L. J. Normal variation in the frequency and location of human auditory cortex. Heschl's gyrus: where is it? *Cereb. Cortex* **8**, 397–406 (1998).

35. Recanzone, G. H., Schreiner, C. E. & Merzenich, M. M. Plasticity in the frequency representation of primary auditory cortex following discrimination training in adult owl monkeys. *J. Neurosci.* **13**, 87–103 (1993).

36. Kilgard, P. M. & Merzenich, M. M. Plasticity of temporal information processing in the primary auditory cortex. *Nat. Neurosci.* **1**, 727–731 (1998).

37. Gordon, E. E. *Learning Sequences in Music* (GIA, Chicago, Illinois, 1997).

38. Scherg, M. in *Auditory Evoked Magnetic Fields and Electric Potentials* Vol. 6 (eds. Grandori, F., Hoke, M. & Romani, G. L.) 165–193 (Karger, Basel, Switzerland, 1990).

39. Scherg, M. & von Cramon, D. Two bilateral sources of the late AEP as identified by a spatio-temporal dipole model. *Electroencephalogr. Clin. Neurophysiol.* **62**, 32–44 (1985).

40. Schneider, P. *Source Activity and Tonotopic Organization of the Auditory Cortex in Musicians and Non-musicians.* Thesis, Univ. Heidelberg (2000).

41. Talavage, T. M. *et al.* Frequency-dependent responses exhibited by multiple regions in human auditory cortex. *Hear. Res.* **150**, 225–244 (2000).

42. Wessinger, C. M. *et al.* Hierarchical organization of the human auditory cortex revealed by functional magnetic resonance imaging. *J. Cogn. Neurosci.* **13**, 1–7 (2001).

43. Zatorre, R. & Belin, P. Spectral and temporal processing in human auditory cortex. *Cereb. Cortex* **11**, 946–953 (2001).

44. Meyer, A. in *Music and the Brain* (eds. Critchley, M. & Henson, R. A.) 255–281 (Heinemann, London, 1977).

45. Somogyi, J. Über das morphologische Korrolat der musikalischen Fähigkeiten. *Mschr. Psychat. Neurol.* **75**, 113–169 (1930).

46. Menning, H., Roberts, L. E. & Pantev, C. Plastic changes in the auditory cortex induced by intensive frequency discrimination training. *Neuroreport* **11**, 817–822 (2000).

47. Preis, S., Jäncke, L., Schmitz-Hillebrecht, J. & Steinmetz, H. Child age and planum temporale asymmetry. *Brain Cogn.* **40**, 441–452 (1999).

48. Yakovlev, P. I. & Lecours, A. R. in *Regional Development of the Brain in Early Life* (ed. Minkowski, A.) 3–70 (Blackwell, Oxford, 1967).

49. Monaghan, P., Metcalfe, N. B. & Ruxton, G. D. Does practice shape the brain? *Nature* **394**, 434 (1998).

50. Thompson, P. M. *et al.* Genetic influences on brain structure. *Nat. Neurosci.* **4**, 1253–1258 (2001).