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Quellenaktivität und tonotope Organisation des auditorischen Cortex bei Musikern und Nichtmusikern

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Source activity and tonotopic organization of the auditory cortex in musicians and non-musicians

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Quellenaktivität und tonotope Organisation des auditorischen Cortex bei Musikern und Nichtmusikern. In einer magnetoenzephalographischen (MEG) Studie wurde die Verarbeitung von Sinustönen im auditorischen Kortex von neun professionellen Musikern, neun Amateurmusikern und neun Nichtmusikern untersucht. Die Tonfrequenzen lagen im Bereich von 100 bis 5600 Hz. Die evozierte Quellenaktivität des primären auditorischen Kortex (19 bis 30 ms nach Tonbeginn) war bei Musikern durchschnittlich 87% stärker als bei Nichtmusikern. Die Erhöhung der späten sekundären Komponente (100 ms nach Tonbeginn) war beträchtlich kleiner (30%) und lag an der Signifikanzgrenze. Die Dipolstärke der primären Quellenaktivität korrelierte signifikant mit der musikalischen Begabung, gemessen mit dem Advanced Measure of Music Audiation (AMMA) Test ($r = 0.51$, $p < 0.01$). Eine Korrelation zum Anfangsalter des Musikunterrichtes wurde nicht gefunden. Diese Ergebnisse können als neurophysiologische Unterstützung der Hypothese angesehen werden, nach der die musikalische Begabung vorwiegend genetisch veranlagt ist (Gordon, 1987). Die frühe Quellenaktivität des primären auditorischen Cortex zeigte eine streng logarithmisch tonotope Anordnung (zu tiefen Frequenzen hin oberflächennaher, 2.3 mm/Oktave), die späte Quellenaktivität nach 100 ms im Planum temporale eine spiegelbildliche tonotope Abbildung (zu hohen Frequenzen hin oberflächennaher, 1.45 mm/Oktave). Eine Korrelation zur musikalischen Begabung wurde nicht gefunden.

Source activity and tonotopic organization of the auditory cortex in musicians and non-musicians. In a magnetoencephalographic (MEG) study we have compared the processing of sinusoidal tones in the auditory cortex of nine professional musicians, nine amateur musicians and nine non-musicians. The frequency of the tones ranged from 100 to 5600 Hz. On average, the evoked source activity of the primary auditory cortex occurring at 19–30 ms was 87% larger for musicians than for non-musicians. The increase of the late secondary component at 100 ms was considerably smaller (30%) and at the limit of significance. The magnitude of the primary source activity correlated significantly with music aptitude, measured by the standardized Advanced Measure of Music Audiation (AMMA) test ($r = 0.51$; $p < 0.01$). A correlation with starting age of musical education was not found. These results may be interpreted as neurophysiological support for the hypothesis of a predominant genetic predisposition of music aptitude proposed by Gordon (1987). The early source activity of the primary auditory cortex revealed a strong logarithmic tonotopic organization (the lower frequencies more superficial, 2.3 mm/octave), the late activity at 100 ms a mirror-imaged tonotopic map (the higher frequencies more superficial, 1.45 mm/octave) in the planum temporale. A correlation with the music aptitude was not found.

Contents

Chapter 1

Introduction

1.1 Perception of musical pitch

Though pitch is an essential feature in communication in general and particularly in music, the concept of pitch is less distinct as it might seem at first sight. Arnold Schönberg did not separate clearly the concept of pitch from the concept of timbre (Schönberg, 1921):

"*Ich kann den Unterschied zwischen Klangfarbe und Klanghöhe, wie er gewöhnlich ausgedrückt wird, nicht so unbedingt zugeben. Ich finde, der Ton macht sich bemerkbar durch die Klangfarbe, deren eine Dimension die Klanghöhe ist. Die Klangfarbe ist also das große Gebiet, ein Bezirk davon die Klanghöhe. Die Klanghöhe ist nichts anderes als Klangfarbe, gemessen in einer Richtung*".

Perceptual differences of musical pitch have been reported from both musicians and scientists. Between 1840 and 1850 an interesting discussion took place in the *Annalen of Physik und Chemie* between Ohm and Seebeck about the pitch of a complex tone. Such a tone is composed of several sinusoidal tones, the lowest in frequency being the fundamental, and the others (harmonics) having frequencies that are multiples of the frequency of the fundamental. Seebeck (1841) presented observations on sounds made with a mechanical siren. These sounds were periodic, containing controllably suppressed odd harmonics. Seebeck described how the pitch he associated with the sound as a whole always seemed to follow the fundamental, even if this fundamental component was very weak. He concluded that the fundamental frequency is not the only determinant of pitch, but that the upper harmonics contribute to the subjective pitch sensation. Ohm (1843), on the other hand, argued that our ears perform a real-time frequency analysis similar to the mathematical formulation of Fourier, where the frequency of the lowest spectral component determinates the pitch of the complex, and the other frequencies determinate the sound´s timbre. The strong fundamental pitch sensation in the absence of acoustic power reported by Seebeck therefore had to be based on an illusion. Twenty years later Helmholtz (1863) chose the side of Ohm in this debate and thereby settled the issue for almost a century to follow.

Schouten (1938) revived the Ohm-Seebeck debate by demonstrating that Seebeck´s conclusion was basically correct. With his optical equipment he could generate periodic complex tones devoid of any acoustical power at the fundamental frequency. Schouten was able to show that the pitch sensation associated with the *missing fundamental* (see Fig.1.1c), as it later became known, could not be explained as a nonlinear difference tone generated at the auditory periphery, as first Helmholtz (1863) and later Fletcher (1924) had argued. According to Schouten, the pitch sensation is caused by neural detection of periodic fluctuations in the envelope pattern of clusters of harmonics that the ear fails to resolve. If spectral resolution is insufficient, two or more summed harmonics will appear at the output of the cochlear filter. The periodicity of the envelope of such a summed signal is the same as the periodicity of the fundamental, even if the fundamental is physically absent. It can be picked through phase locking by fibers of the auditory nerve and transmitted to central parts of the brain. Since insufficient cochlear resolution is an essential element of Schouten´s pitch theory, this theory became known as the *residue theory of pitch* (Schouten, 1940).

Soon it became clear, however, that Schouten´s residue theory also failed to provide an adequate explanation of new experimental findings. Ritsma (1962) found a clear upper limit to the harmonic order beyond which no tonal residue, that is pitch, would be heard. He also reported that the existence region for the tonal residue would extend to combinations of harmonics that the cochlea should be able to resolve, which was in contradiction with th essence of the residue theory. Some years later Ritsma (1967) and Plomp (1967) found that the best harmonics to convey a pitch sensation of missing fundamental were of the order of 3, 4, and 5. In this so-called dominance region, harmonic frequencies differ by 25% or more and should be well resolved in the periphery of the auditory system. Certain experimental results of Houtma and Goldstein (1972) forced one to conclude that the pitch of complex tones would be mediated primarily by a central mechanism that would operate on neural signals from those stimulus harmonics spectrally resolved in the cochea.

However, the current knowledge of pitch perception, based on pattern recognition (Terhardt´s virtual pitch theory, 1972; Goldstein´s theory of a central processor, 1973; Wightman, 1973), periodicity coding (Schouten,

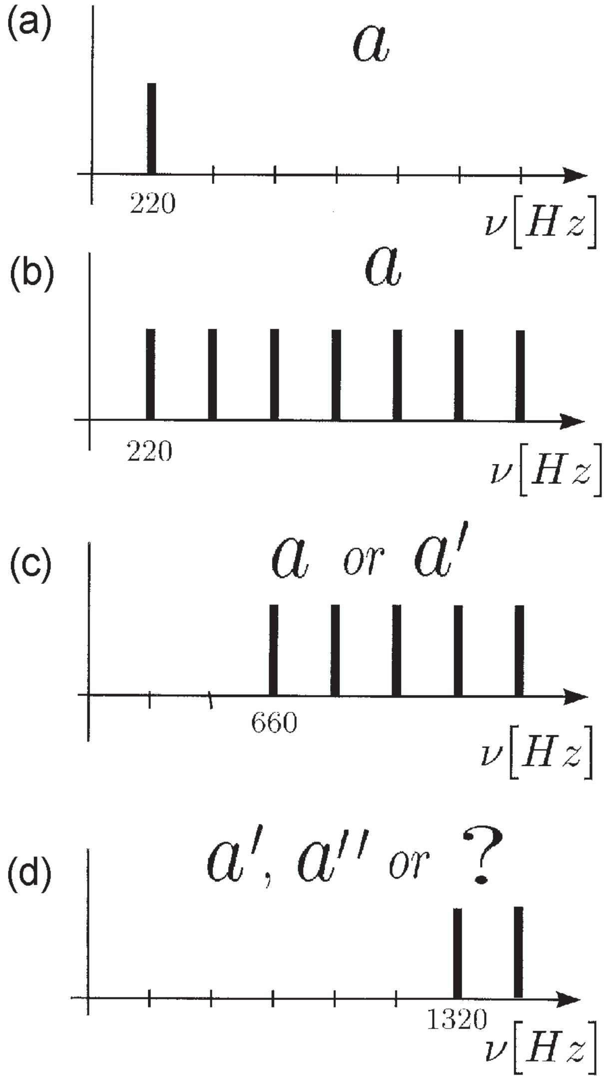


Figure 1.1: *Fourier spectrum of a sinusoidal (a) and three different complex tones. A sinusoidal tone (a) is perceived with a definite pitch uniquely related to the frequency (here* $A3 = a$, *220 Hz).A tone with the spectral representation (b) is also perceived with a definite pitch related to the frequency of the lowest partial* $A3 = a$. *The tone (c) is perceived by most peaple as an* $A3 = a$, *by some as an* $A4 = a'$, *440 Hz. In the case (d) most people do not ascribe adefinite pitch to this tone, some people perceive it as an* $A4 = a'$ *or* $A5 = a''$, *880 Hz.*

1940; Langner, 1992) or autocorrelation mechanisms (Licklider, 1951; Patterson, 1995) could only partially explain manifold ambiguities in pitch perception. Smoorenburg (1970) suggested, that analytic and holistic cues contributed to explain the subjective differences in pitch perception.

However, none of the theories was able to explain sufficiantly what conditions decide whether analytic or holistic pitch cues are used. In a recent psychoacoustic study on pitch perception (Schneider, 1996), in collaboration with H.G. Dosch and H.J. Specht from the University Heidelberg, this striking phenomenon was predominantlz described as a perceptual difference between professional musicians and non-musicians: if a complex tone composed of a small number of higher adjacent harmonics without fundamental was presented by earphones to different subjects, the musicians perceived rather the spectral pitch whereas the non-mucians predominantly perceived the fundamental pitch. The perceived pitch differed up to three octaves.

Therefore, the desire arose to expand the hitherto psychoacoustic research onto the neuronal level. In a collaboration with the Section of Biomagnetism, Department of Neurology, University Hospital of Heidelberg, headed by M. Scherg, a magnetoencephalographic (MEG) study was started in 1997 to investigate this phenomenon of strong perceptual differences in musicians and non-musicians. The aim was, in particular, to compare the psychoacoustical and neurophysiological findings with the same sample of musicians, amateur musicians and non-musicians. At a first result, we demonstrate that the music aptitude correlates strongly with the neuronal activity at the earliest stage of processing in the primary auditory cortex. Secondly, a clear concept of tonotopic organization of the human cortex could be opposed to the contradictory results found in the literature.

1.2 The auditory cortex

Fig.1.2 shows the human brain viewed from the left side. In our studies we are usually concerned with the uppermost layer of the brain, the cerebral cortex, which is a 2–4 mm thick sheet of gray tissue.

The cortex has a total surface area of about 2500 cm^2, folded in a complicated way, so that it fits into the cranial cavity formed by the skull. The brain consists of two hemispheres, separated by the longitudinal fissure (see Fig.1.2). The left and the right halves, in turn, are divided into lobes by two deep grooves. The Rolandic fissure runs down the side of both hemispheres, while the Sylvian fissure is mostly horizontal. There are four lobes in both halves of the cortex: frontal, parietal, temporal and occipital. The primary auditory cortex (AI) is in the temporal lobe buried within the Sylvian fis-

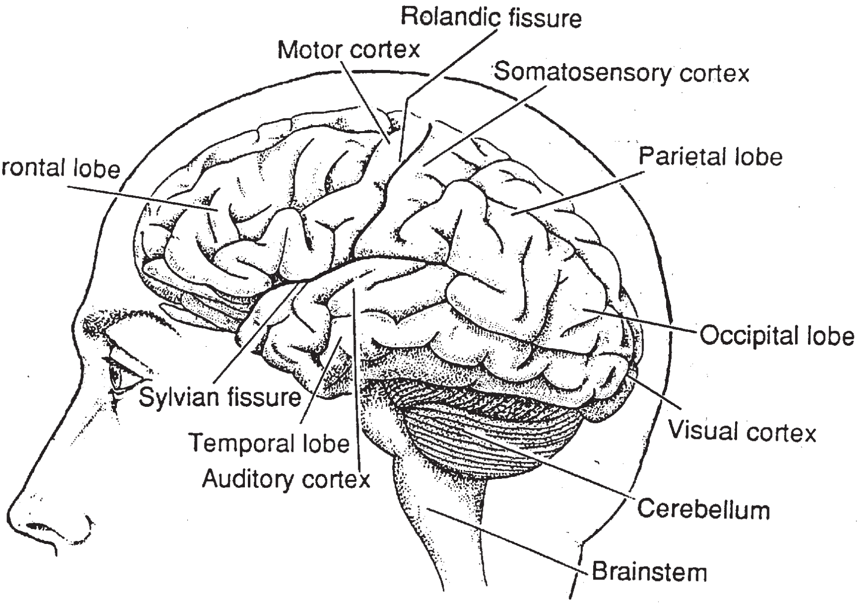


Figure 1.2: *The human brain viewed from the left side.*

sure. An individual MRI scan of the human brain can be seen in Figure 1.3. Arrows point at Heschl´s gyrus (HG). The primary auditory cortex (AI) is located in the medial aspect of HG (Braak,1978; Rademacher et al., 1993).

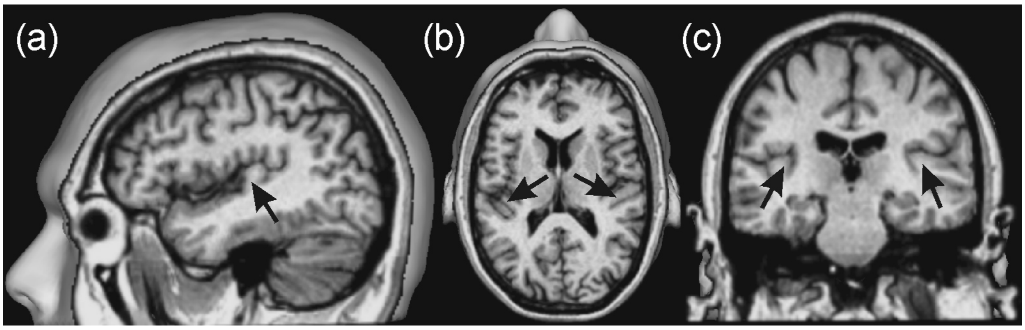


Figure 1.3: *Sagittal (a), transversal (b), and coronal (c) view of the human auditory cortex, situated in the superior temporale plane. Arrows point at Heschl´s gyrus (HG). The primary auditory cortex (AI) is located in the medial aspect of HG (Braak,1978; Rademacher et al., 1993).*

The geniculate axons coming from the medial geniculate nucleus of the thalamus terminate in the primary auditory cortex. A “blueprint” of the auditory pathways is depicted in Fig.1.4.

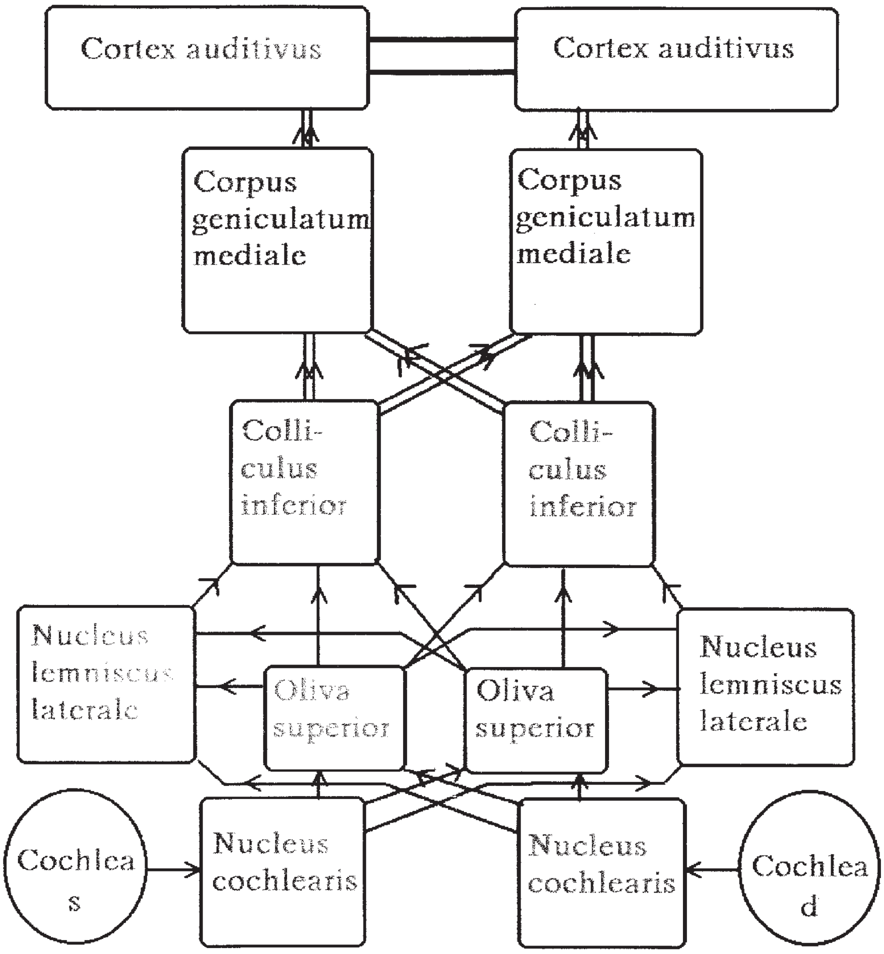


Figure 1.4: *Schematic map of the auditory pathways. The central auditory pathways extend from the cochlear nucleus to the primary auditory cortex.*

Very rouhgly speaking the cochlea operates as a short-term Fourier analyzer separating complex acoustic signals into their frequency components. More precisely is the concept of wavelet-analysis (Kaiser et al., Patterson et al., 1995). Such filtering mechanisms are used to transform an incoming wideband signal into a set of parralel narrowband channels to match the channel capacity to the neural system. The peripheral processes in the right (d) and left (s) cochlea are transferred via the eighth nerve to the nuclear cochlearis. The central auditory pathways extend from the cochlear nucleus to the primary auditory cortex and include the processing at the brainstem level up to the inferior colliculus and the thalamic processing at the level of the corpus geniculatum mediale, which project directly into the primary auditory cortex. Every major nucleus between the cochlea and the cortex has been found to be cochleotopically organized (see Merzenich et al., 1977).

1.3 EEG and MEG

Electroencephalography (EEG), the measurement of electric potential differences on the scalp, is a widely applied method of long clinical standing. The measurement of magnetic fields is closely related to EEG. In both methods, the measured signals are generated by the same synchronized neuronal activity in the brain. When information is processed in the human brain, small currents in the nAm-range flow in the neural system and produce both a weak magnetic field in the femtoTesla-range, provided that thousands of nearby neurons act in concert, and a potential difference on the scalp, which both can be measured noninvasively:

1. using a set of scalp electrodes, placed on the scull; this method of recording is called electroencephalpography (EEG). If acoustic stimuli are presented, the EEG records the auditory evoked potentials (AEP) on the scalp.

2. using a SQUID magnetometer, placed outside the skull. This method of recording is called magnetoencephalography (MEG). If acoustic stimuli are presented, the MEG records the auditory evoked fields (AEFs) outside the scalp.

The superconducting quantum interference device or SQUID is a sensitive detector of magnetic flux, introduced in the late 1960s by James Zimmerman (Zimmerman et al., 1970).

The time resolution of EEG and MEG is in the millisecond range, orders of magnitude better than in imaging methods. Thus with EEG and MEG it is possible to follow the rapid changes in cortical activity that reflect ongoing signal processing in the brain; the electrical events of single neurons typically last from one to several tens of milliseconds. A very important advantage of EEG and MEG is that they are completely noninvasive. One only measures brain activity as a result of sensory stimuli such as sounds.

Fig.1.5 shows schematically the progression of the auditory evoked potentials (AEPs) over time.

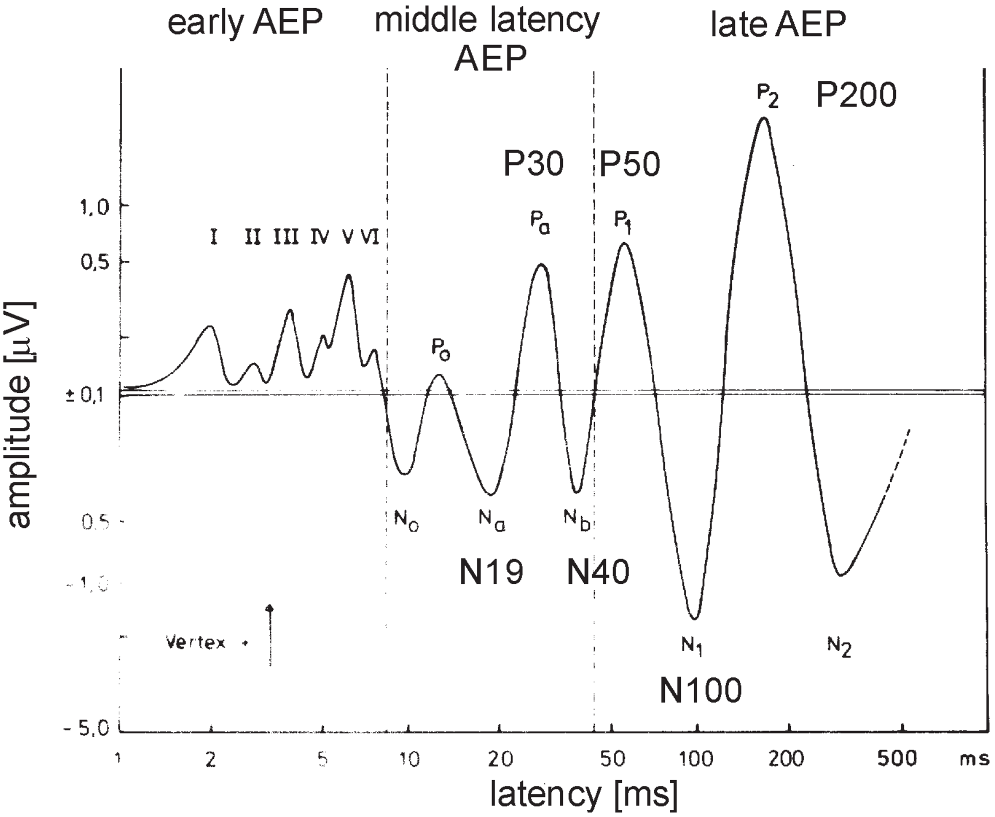


Figure 1.5: *Auditory evoked potentials (AEP) on a logarithmic time scale (adapted from Picton et al., 1974).*

According to the latency (time from stimulus onset to peak), the AEPs are subdivided in three groups: early AEPs (1–10 ms) including the brainstem AEPs, middle latency AEPs (10–50 ms) and late AEPs (50–250 ms). The middle latency AEPs consist of about three small deflections (N19, P30, N40) at about 19 ms, 30 ms and 40 ms after the stimulus onset. The late AEFs include the P50 peak, a prominent peak (N100) at 100 ms and another peak at about 200 ms (P200). P indicates that the corresponding deflection in electric potential (EEG) measurement is positive at the top of the head; N, that it is negative; and m refers to magnetic.

A typical AEF response, evoked by an amplitude modulated sinusoidal tone burst of 1 second length in our magnetoencephalographic study is shown in Fig.1.6.

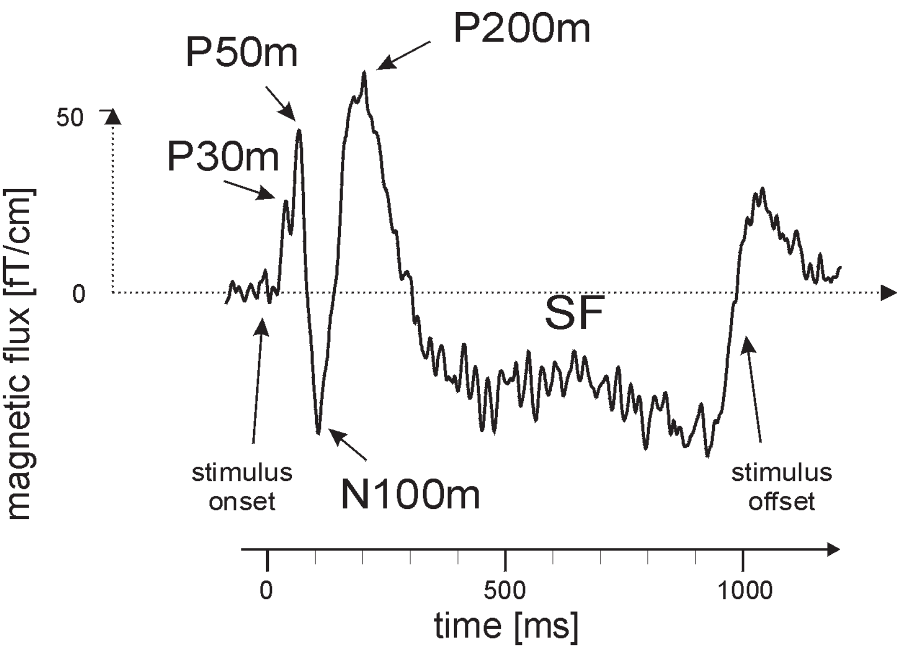


Figure 1.6: *Typical auditory evoked field (AEF) as a function of time, measured with MEG close to the subject´s auditory cortex. The signal was evoked by a 1000 ms amplitude modulated tone. The signal consists of the following components: two small deflections (P30m and P50m) at about 30 ms and 50 ms after the stimulus onset, the prominent N100m peak, the P200m peak a and the sustained field (SF) lasting throughout the duration of the stimulus. The early evoked fields of the brainstem seen with EEG in Fig. 1.5 can not be seen in MEG recordings because of their radial orientation.*

Intracranial studies by Liégeois-Chauvel et al. (1991, 1994) and Celesia (1976), patient studies (Scherg and van Cramon, 1986) and recent MEG-studies (Hashimoto et al., 1995; Gutschalk et al., 1999) have shown that the earliest evoked cortical activity occurs at 15–30 ms after stimulus onset in the medial portion of Heschl´s gyrus (see Fig.1.2). This area represents the primary auditory cortex (AI), as reported by cytoarchitectonic studies (Braak, 1978; Rademacher, 1993).

Generators of the P50m component are supposed to be situated more laterally on the Heschl´s gyrus (Scherg and Picton, 1991; Liégeois-Chauvel et al., 1994). The N100m peak originates predominantly from the planum temporale posterior to the Heschl´s gyrus (Liégeois-Chauvel et al., 1994) as can be seen in Fig.1.3b whereas the sustained field (SF) originates predominantly in or near the core areas on the Heschl´s gyrus (Gutschalk et al., 2000).

In interpreting EEG and MEG data, one is dealing with the electromagnetic inverse problem, i.e., with the deduction of the source currents responsible for the externally measured field. Hermann von Helmholtz showed in 1853 that this problem has no unique solution. One must therefore use source models, such as current dipoles, or special estimation techniques to interpret the data. (see Hämäläinen et al., 1993). In the following investigation, the sources are modeled with one macroscopic equivalent dipole in each hemisphere providing an inverse solution, which models reliably the measured surface waveforms (Scherg, 1986, 1990, 1991, 1993, 1996).

Many important imaging methods of the human brain are available today. Anatomical structures can be investigated precisely by means of computer-assisted x-ray tomography (CAT) and by magnetic resonance imaging (MRI) and functional magnetic resonance imaging (fMRI). Both these techniques provide high-quality but static pictures of living tissues. The MRI technique provides an ideal medium for linking the functional MEG information to anatomical data. In our investigation, magnetic resonance images were coregistered with the MEG data.

Functional information about the brain can be obtained also with single-photon-emission computed tomography (SPECT) and with positron-emission tomography (PET) used for example by Zatorre et al (1991, 1994, 1998) to investigate the processing of pitch and melodies in the human auditory cortex. All these methods permit studies of the brain without opening the skull, but the subject is exposed to x rays, to radioactive tracers, or to time-varying and strong static magnetic fields.

Chapter 2

Motivation of this investigation

2.1 Music aptitude and dipole amplitude

In 1863 Hermann von Helmholtz noted:

"*Doch hat ein musikalisch geübter Beobachter darin einen wesentlichen Vorzug vor einem ungeübten, daß er sich leicht vorstellt, wie die Töne klingen müssen, welche er sucht, während der Ungeübte sich diese Töne immer wieder angeben muß, um ihren Klang frisch in Erinnerung zu haben*".

More than a century later, Edwin Gordon coined the term "audiate" in order to define what Helmholtz called the power of figuring sound: "*to audiate is to hear and comprehend music for which the sound is not physically present*" (Gordon, 1987, 1998). Introducing the Advanced Measure of Music Audiation (AMMA) test, Gordon demonstrated that audiation is the basis of music aptitude (Gordon, 1989).

It is unclear whether differences of music aptitude are paralleled by quantifiable differences in the sensory processing of the auditory system. The current knowledge about neuronal processing of music is mostly obtained from investigations on normal listeners independent of their music aptitude (cf. Zatorre, 2000). Nevertheless, some studies have been devoted to find differences between musicians and non-musicians.

In the 1970s and 1980s a considerable number of dichotic listening studies were performed to observe the dominance of the right or left ear, implicating the dominance of the opposite hemisphere. Some of these investigations, carried out in musicians as compared to non-musicians, are summarized in the following: Bever (1980) has claimed strong support for his contention that musicians process music preferentially with the left hemisphere whereas non-musicians are more likely to do so with the right hemisphere (Bever and Chiarello, 1974; Johnson, 1977; Messerli et al., 1995). Using popular melodies such as “Frère Jacques”, Messerli et al. (1995) suggested that the lateralization effects depend not only of the level of competence of the subjects, as hypothesized by Bever and Chiarello (1974), but also on the musical features of the stimuli. Zatorre (1979) found that music perception generally implies a left ear - right hemisphere superiority for both musicians and non-musicians in agreement with Kimura (1964), Mazzuchi et al. (1981) and Corballis (1983). In contrast, the perception of rhythm was found to elicit a right ear - left hemisphere dominance (Gordon, 1978; Prior et al., 1988).

EEG studies on music processing tend to support the advantage of the left hemisphere in musicians (Davidson and Schwartz, 1977; Hirshkowitz et al., 1978) or the right sided lateralization in non-musicians (Altenmüller, 1986) and thus corroborate Bever´s position.

Using positron emission tomography (Zatorre et al., 1994, 1998) as well as behavioral lesion techniques (Zatorre, 1984, 1988, 1989), Zatorre demonstrated in contrast to the findings of Bever and Chiarello (1974), that right-hemisphere mechanisms are predominant for tonal processing in both non-musicians and professional musicians. Whereas the right primary auditory area appeared to be crucial for fine-grained representation of pitch perception (Zatorre, 1988; Zatorre et al., 1991), the melody perception was found to require higher-order cortical areas and interaction with the right frontal cortex (Zatorre et al., 1985). Thus, Zatorre claimed a strong support to his early findings in the dichotic listening study (Zatorre, 1979).

In vivo magnetic resonance morphometry showed that outstanding musical ability is associated with increased leftward asymmetry of cortex subserving music related functions (Schlaug et al., 1995). Furthermore, the corpus callosum was found to be increased in musicians, especially if they began their training before the age of seven (Schlaug et al., 1995a).

Investigations on evoked otoacoustic emission (EOAE) demonstrated larger efferent influences in both ears in musicians which are supposed to reflect an enhanced activity of the cortical auditory structures rather than differences in cerebral hemispheric asymmetry (Micheyl et al., 1997; Perrot et al., 1999).

Pantev et al. (1998) have compared the magnitude of the auditory N100m field evoked by piano and pure sinusoidal tones. They observed that piano tones evoked a N100m that was on average 25% larger in musicians than in non-musicians. The enhancement was absent if the stimulus was a sinusoidal tone.

We have studied the early (N19m-P30m) and the late (N100m) magnetic field components of the auditory cortex evoked by sinusoidal tones in musicians and non-musicians to answer the following questions (see chapter four):

1. Is there already a difference in the neuronal signals at the level of the

primary auditory cortex?

2. Does it depend on the frequency?

3. Does it depend on the hemisphere?

2.2 Multiple tonotopic fields

Tonotopy is a general principle of functional organization of the mammalian auditory pathway. It reflects a topographical arrangement of frequency specific neurons. Romani et al. (1982) was the first, who demonstrated in humans with only one SQUID sensor that the tonotopic (cochleotopic) organization of the cochlea (von Bekesy, 1960) in a logarithmic mapping is maintained at the level of the auditory cortex. In the subsequent 15 years, many investigations using PET (Lauter et al., 1985), SPECT (Ottaviani, 1997), fMRI (Wessinger et al. 1997; Strainer et al., 1997, Lantos et al., 1997), microelectrodes (Howard et al., 1996) or neuromagnetic methods (Elberling et al, 1982; Pantev et al., 1988, 1989, 1995, 1996; Bertrand et al., 1991; Yamamoto et al., 1992; Tiitinen et al., 1993; Cansino et al., 1994; Lütkenhöner & Steinsträter, 1998) corroborated that at least parts of the human auditory cortex must be tonotopically organized.

A further question was if the tonotopic organization of the auditory cortex would be restricted to one principal area or rather be extended to several different areas of the cortical surface. Microelectrode studies in the auditory cortex of macaque monkeys revealed two or three cochleotopic (tonotopic) organized core fields, among which the primary auditory cortex (AI) is the largest, most caudally located field (Merzenich and Brugge, 1973; Morel et al., 1993; Rauschecker et al., 1995). Auditory information is then distributed from the core areas to a surrounding belt of up to five to seven areas that show a broader tuning of the frequencies implying a less precise cochleotopic organization. The areas are generally more responsive to complex stimuli than tones (Kaas et al., 1999, see Fig.2.1). Furthermore, adjacent areas were expected to show mirror-image tonotopic maps (Morel et al., 1993; Kaas et al., 1999).

The tonotopic organization of the core areas and most belt areas have been shown by Morel et al. (1992) and Merzenich and Brugge (1973), depicted with an arrow from the higher towards the lower frequencies in Fig. 2.1a. The tonotopy of CL has been shown by Rauschecker et al., 1995.

These findings raise the question if multiple frequency representations could be observed also in the human auditory cortex. Pantev et al. (1995)

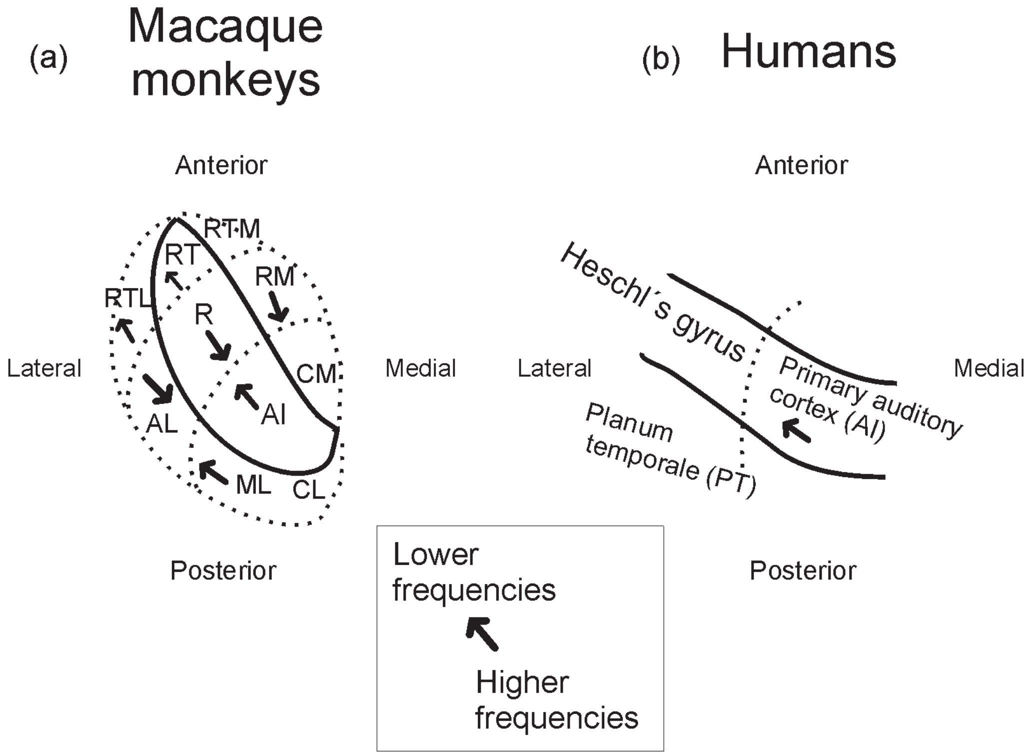


Figure 2.1: *The left panel (a) shows the top view on the left supratemporal plane in macaque monkeys, schematically adapted from Kaas et al. (1999) and Gutschalk (1999a). In the center can be seen the core field, composed of three cochleotopic fields: the primary auditory cortex (AI), the rostral field (R) and the rostrotemporal field (RT). The three core fields project to a narrow surrounding belt area comprising approximately seven fields, at least four of which exhibit cochleotopic organization. The arrows show the tonotopic gradient from higher towards lower frequencies. Adjacent areas like AI and R show mirror-image tonotopic maps. RTL: lateral rostrotemporal field; AL: anterolateral field; ML: middle lateral field; CL: caudolateral field; CM: caudomedial field, RM: rostromedial field; RTM: medial rostrotemporal field (cf. Kaas et al., 1999). The right panel (b) shows a schematic top view of the human left auditory cortex, in particular Heschl´s gyrus, whose medial aspect includes the primary auditory cortex AI (Braak, 1978; Rademacher et al., 1993).*

used inverse modeling of both magnetic and electric scalp recordings to provide evidence for two tonotopic areas within the human auditory cortex showing a mirrored tonotopic organization. The first tonotopic map, derived from a middle latency P30m-P50m pattern, located in the primary auditory cortex (AI) and showed a logarithmic tonotopic organization with the lower frequencies more medial (2.2 mm/octave). The N100 map was found posterior to the Heschl´s gyrus in the planum temporale showing a mirrored tonotopic organization with the lower frequencies more lateral.

The localization of the generators of the middle latency and the N100m response reported by Pantev et al. (1995) is consistent with the literature (Liégeois-Chauvel, 1991; Liégeois-Chauvel, 1994, Lütkenhöner and Steinsträter, 1998). However, two puzzling facts remain unanswered:

- The tonotopic gradient found by Pantev at al. (1995) for the primary auditory cortex had the opposite direction as found in investigations on the tonotopic organization of the primary auditory cortex, using PET (Lauter et al., 1985), SPECT (Ottaviani et al., 1997), microelectrodes (Howard et al., 1996) and fMRI (Wessinger et al. 1997; Strainer et al., 1997, Lantos et al., 1997). These investigations consistently report a tonotopic gradient in the primary auditory cortex (AI) with the lower frequencies more lateral, seen also in animal studies (see Fig.2.1a).
- The auditory N100m response exhibits a perplexing view of its tonotopic progression: at least four different statements about its tonotopicity can be found in the literature as summarized in chapter 5.1.4. This could be due to the fact, that multiple areas are involved in the generation of the N100m response (Näätänen et al., 1987; Scherg et al., 1989; Liégeois-Chauvel, 1994; Lütkenhöner and Steinsträter, 1998; Gutschalk et al., 1998).

We have studied the tonotopicity of the early (N19m-P30m) and the late (N100m) magnetic field components of the auditory cortex in musicians and non-musicians to answer the following questions (see Chapter five):

1. Is the mirror-imaged tonotopic organization of the primary and secondary auditory areas reported by Pantev et al. (1995) reproducible in our investigation?
2. Is there a difference in the tonotopic organization of the auditory cortex in musicians as compared to non-musicians?
3. Does it depend on the hemisphere?

Chapter 3

Methods

3.1 Subjects

27 normal hearing right-handed adults (18 male, 9 female, mean age 33 years), subdivided in nine professional musicians, nine amateur musicians, and nine non-musicians, were recruted for this investigation. Each subject had to carry out the following test program:

- a MEG session with 2400 successively played modulated tones (duration about 90 min)
- a MEG session with 6000 successively played short pure tones (duration about 70 min, 19 of 27 subjects)
- a MRT session to obtain the individual T1-weighted structural 3D-MRI (duration about 30 min, 23 subjects)
- the AMMA test (duration about 20 min).

It should be noted that most of the test subjects were interested in music and listened regularly mostly to classical music.

3.2 Selection criteria

The definition of a "musician" varies widely in the literature. For example, in one investigation four years of music lessons already qualified a musician (Bever and Chiarello, 1974). Here, two selection criteria were used to classify the subjects:

- Professional musicians, which had undergone a professional education and played an instrument regularly. Our sample of musicians comprised professors of music, conductors, piano tuners and church musicians.
- Amateur musicians, which were playing an instrument regularly.
- Non-musicians, which had not played an instrument for at least the last five years.

The AMMA test by Gordon (see chapter 3.3) provided the possibility to objectify and validate the music aptitude. Therefore a second selection criteria based on music aptitude could be defined to separate musicians from non-musicians.

3.3 AMMA test

3.3.1 Contents of the test

The Advanced Measure of Music Audiation (AMMA), introduced by Gordon (1989), was standardized with a sample of more than 5,000 students in the U.S. and is today widely used by conservatories. The test includes 30 questions, each containing a pair of short melodies, separated by four seconds. The melodies of about eight seconds are presented and repeated in a form slightly modified either tonally or rhythmically. In some cases, the repeated melody is unchanged.

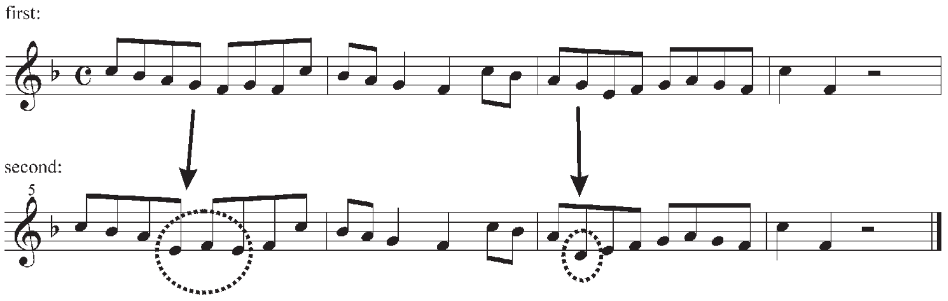
The subjects had to decide whether:

1. the two melodies are the same
2. the second melody is different, caused by at least one tonal change (see Fig.3.1a)
3. the second melody is different, caused by at least one rhythm change (see Fig.3.1b)

However, there was never both a tonal change and a rhythm change.

Three test scores are evaluated based on the difference between correct and false answers:

- a tonal score
- a rhythm score


(a) AMMA test, example 12
(tonal change)

Edwin E. Gordon (1989)


(b) AMMA test, example 15
(rhythm change)

Edwin E. Gordon (1989)

Figure 3.1: *Example of a test question with tonal change (a) and a test question with rhythm change (b).*
The test questions are clustered neither in terms of difficulty nor in terms of tonality, keyality, meter, or tempo. They were composed specifically for the test, performed by a professional musician on a Yamaha DX-7 synthesizer. Comprising easy and difficult tasks, the AMMA test was qualified for both musicians and non-musicians.

- a total score (the total of the Tonal score and the Rhythm score)

All three scores are derived from the same thirty test questions.

Three types of scores are provided with the Advanced Measures of Music Audiation test:

- raw scores
- adjusted raw scores
- percentile norm ranks

The raw score was a simple count of the questions answered correctly on a test. A disadvantage of the raw score is that it is difficult to interpret, because it has no standard meaning: the meaning of the raw score changes with the length and difficulty of the given test question. As a result, the raw scores are transformed into standard scores to compare students´ standings in a test and to compare a student´s relative standing in different tests. Thus, raw scores are generally transformed into percentile norm ranks, the most widely used type of standard score. In our study, the percentile norm ranks for High School students, given by Gordon (1989), were used as score for all subjects. 28 of 30 correctly answered questions resulted in a percentil norm rank of 100%, whereas one third of randomly reached correct answers (10 of 30) corresponded to a percentile norm rank of only 1%. The percentile norm rank of our non-musicans ranged between 19% and 50%, the percentile norm rank of our amateur musicians between 39% and 93% and professional musicians between 56% and 98%. Most of our subjects agreed that the AMMA test was difficult.

3.3.2 Music aptitude

Essentially, the AMMA test is a music aptitude test. Music aptitude is a measure of the student´s potential to achieve in music. Gordon found, that research in psychoacoustics, socio-musicology, and cognitive psychology contributed little to identifying the source of music aptitude. He refers to indirect findings of neurophysiologists in regard to auditory asymmetry and lateral dominance in the cerebral cortex (cf. the dichotic listening studies mentioned in chapter 2.1), coupled with the direct findings of music psychologists (Révész, 1953; Gabriel, 1981), which produce a more comprehensive explanation of the source of music aptitude. There are two important stages which describe the evaluation of musical aptitude:

- The developmental music aptitude stage (from birth to age nine)

- The stabilized music aptitude stage (from age nine on)

Therefore, music aptitude is a product of nature and nurture: both contribute in unknown proportions to music aptitude. From birth to age nine, one is in the developmental music aptitude stage. From age nine on, one is in the stabilized music aptitude stage: the level of music aptitude one has at age nine remains ostensibly the same throughout life (Gordon, 1987).

3.3.3 Music achievement

Music achievement is a measure of what the student has learned. In contrast to music aptitude, it can be expected to develop in music achievement throughout life, but never to a level higher than that of the music aptitude. According to this definition, the AMMA test is not a music achievement test.

Both music aptitude and music achievement are according to Gordon largely based on audiation.

3.3.4 Music audiation

Audiation is the ability to hear and comprehend music for which the sound is not physically present. Therefore, it is different from aural imagery, memorization or imitation, which is all possible without audiating. Gordon describes six stages of audiation, which are hierarchical and cumulative:

1. Short series of pitches and durations were retained as immediate impressions just a moment after perception.

2. The retained short series of pitches and durations of stage 1) were silently imitated.

3. The tonality and the meter of the silently imitated music of stage 2) is established.

4. New tonal patterns and rhythmic patterns were audiated in relation to tonality and meter, that are retained in audiation.

5. Tonal patterns and rhythmic patterns were recalled, that were audiated and organized in other pieces of music perhaps hours, days, or years ago.

6. Tonal patterns and rhythmic patterns were predicted, that will be heard next in music.

3.3.5 Tonal test and rhythm test

Here we show the relation between the tonal AMMA test and the rhythm AMMA test. As can be seen from Fig.3.2, the tonal score correlates strongly with the rhythm score ($r = 0.86$; $p < 0.0001$). Here, the scores of our 27 subjects (a) were shown together with those of a larger sample of 53 subjects (b) including the subjects of (a) and a group of music students. The musicians were subdivided in musicians having absolute pitch (AP) and having relative pitch (RP) to control if AP musicians score higher in the AMMA test as suggested from our sample in Fig.3.2a. As can seen from Fig.3.2b there was no significant difference between AP- and RP musicians.

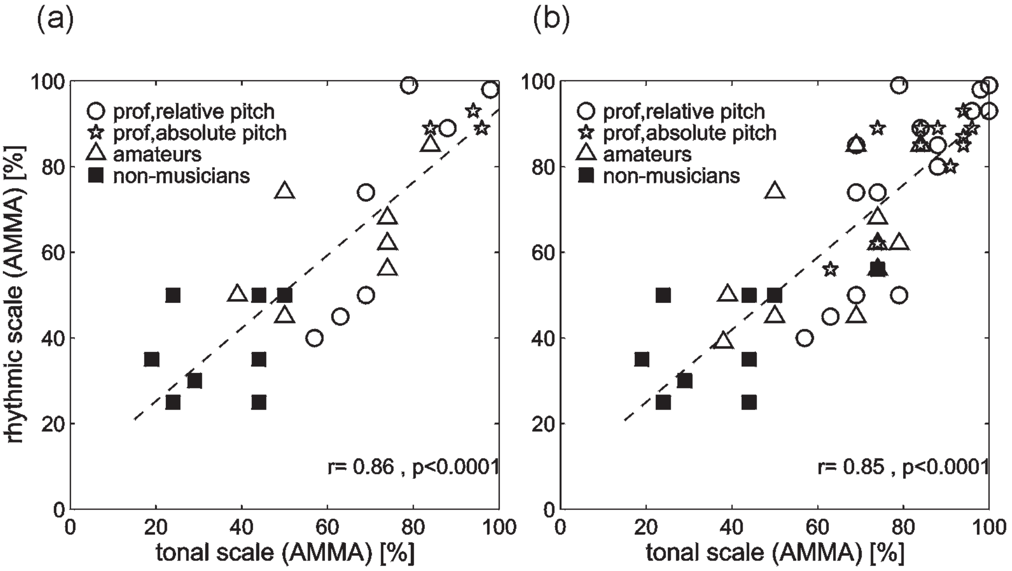


Figure 3.2: *(a) shows the strong correlation of the tonal AMMA test with the rhythm AMMA test for our 27 subjects (*$r = 0.86$; $p < 0.0001$*). As can be seen, the AMMA test corroborated our categorization in professionals, amateurs, and non-musicians. The AMMA test was performed additionally with a group of students of the conservatory in Mannheim, to test a possible influence of absolute pitch (AP). (b) shows the results for the total sample of 53 subjects including the 27 subjects of (a). The left panel suggests that musicians having absolute pitch (AP) score extremely high in both the tonal and the rhythm test. The larger sample in (b) shows that the highest scores are reached by musicians having relative pitch (RP) and the averaged scores are not significantly higher for AP musicians than for RP musicians.*

As can be seen from Fig.3.2, the AMMA test corroborated our categorization in professional musicians and non-musicians. To our knowledge this was the first time that a standardized test has been used in neurophysiological research in order to quantify the music aptitude of the subjects.

3.4 Stimulation

3.4.1 Amplitude modulation

In order to isolate the middle latency N19m-P30m responses, the tones were 100% amplitude modulated at low frequencies ranging from 26 to 37 Hz (see Fig.3.3). This technique provided the possibility to average over the onset of each envelope cycle of the modulation. The tones had a duration of 1.0 s including approximately 30 modulation cycles generated with the Praat program (Boersma and Weenink, 1992). thus stimuli were computede by applying the mathematical function

$$y(t) = (1 - \cos(2\pi t f_m))(\sin(2\pi t f_c))$$

(f_m= modulation frequency, f_c= carrier frequency)

Several different modulation frequencies f_m were used to obtain an unequivocal solution for the calculated underlying middle latency responses. Seven different values for the f_m in the 25.6 to 37.0 Hz range corresponding to the modulation periods of 27, 29, 31, 33, 35, 37 and 39 ms were used.

In one session, we measured 6 blocks with carrier frequencies of 100, 220, 500, 1100, 2500 and 5600 Hz. These carrier frequencies were chosen to be equidistant on a logarithmic frequency scale corresponding to the musical interval of a major ninth (see Fig.3.4). Perceptually, the modulated tones sounded similar to the pure tones with an added small roughness.

3.4.2 Rising and falling slope

The rising slope of the modulation was long enough to avoid the generation of an additional click which would disturb the perception. Generally, both a smooth rising slope and a smooth falling slope of at least 15 ms are required to provide an undisturbed perception of the applied stimuli. In the literature on auditory processing of pure tones, this condition is fulfilled to some extend in several investigations, using a ramp in the 10 to 15 ms range: 10 ms (Bertrand et al., 1991; Tiitinen et al., 1993; Langner et al., 1997; Lütkenhöner and Steinsträter, 1998) and 12 ms (Cansino et al., 1994) to 15 ms (Pantev et al., 1988), generating only a weak additional click perception. But a 3 ms ramp (Pantev et al., 1995; Verkindt et al., 1995) implicates a

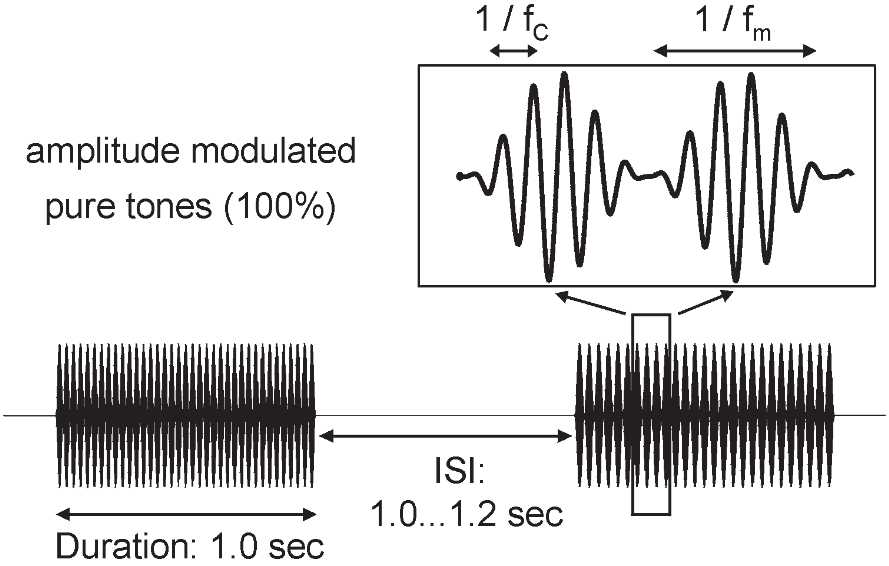


Figure 3.3: *Experimental setup: 100% amplitude modulation with a set of seven slightly different values (26 to 37 Hz range) of a sinusoidal modulation frequency (f_m) within each block was used to provide the possibility to average over the onset of each modulation cycle. The carrier frequency (f_c) was a sinusoidal tone varying only between the blocks (100 to 5600 Hz range).*

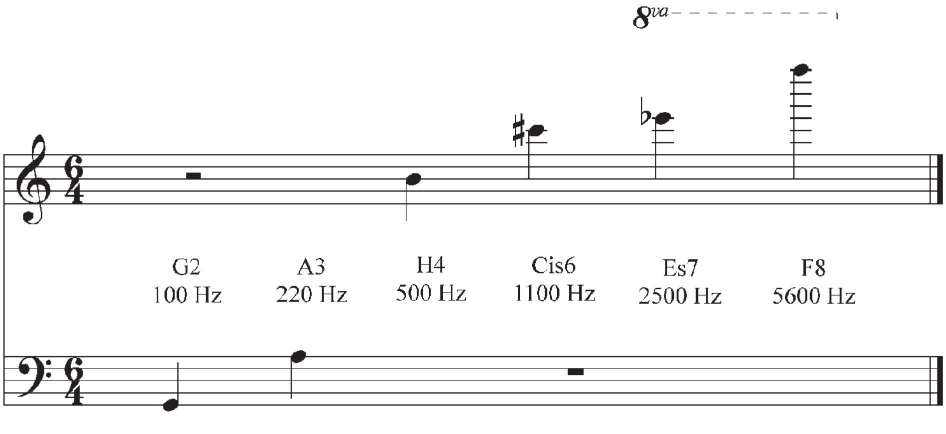


Figure 3.4: *Musical notation (midi standard notation) of the pitch of the amplitude modulated tones, which was determined by the carrier frequency.*

rather strong additional unwanted click perception. In our investigation, the duration of the ramp was defined by the half cycle of a modulation period, therefore ranging from 13.5 to 19.5 ms. Using only an integer number of modulation cycles in one tone, also a click free ending of the tones was obtained. Therefore the total duration of the tones was only roughly the target duration of 1000 ms (999, 1015, 992, 990, 1015, 999, 1014 ms with increasing modulation period from 27 to 39 ms) corresponding to a total number of 37, 35, 32, 30, 29, 27 and 26 modulation cycles respectively.

3.4.3 Design of the tone sequences

One block was composed of a sequence of about 400 tones with constant f_c but varying f_m. Both the interstimulus interval (1.0–1.2 s) and the tone sequence of different f_m-values were pseudo-randomized. To minimize stimulus artifacts, the tone polarity was reversed from one tone to the next. In one session, we measured 6 blocks with carrier frequencies of 100, 220, 500, 1100, 2500 and 5600 Hz. The total session time was 84 minutes.

3.4.4 Unmodulated tones

Unmodulated sinusoidal tones were used in an additional experiment to check a possible influence of the modulation on the response. The unmodulated tones were presented within the same paradigm as the modulated tones (frequency range from 100 to 5600 Hz) apart from a change in duration and ISI of the stimuli: to obtain a large number of averages the duration of the tones was reduced to 150 ms including 20 ms rising and falling slope and the interstimulus interval was reduced to the pseudo-randomized 400–600 ms range (see Fig.3.5). Though the reduction of ISI affects the absolute magnitude of the responses, no effect is expected on the inter-individual differences in magnitude. Here, one block was composed of 1000 tones with constant frequency. Here, the total session time was 66 minutes.

3.5 Apparatus

MEG recordings were performed with the Neuromag-122 channel whole head MEG system (Ahonen, 1993; Hämäläinen, 1993; see Fig.3.6). 122 planar gradiometers were fixed at 61 sensor positions in a helmet-shaped arrangement, the dewar. At each sensor position, two sensors with orthogonal orientations measure the planar gradients of the magnetic flux emerging from the head.

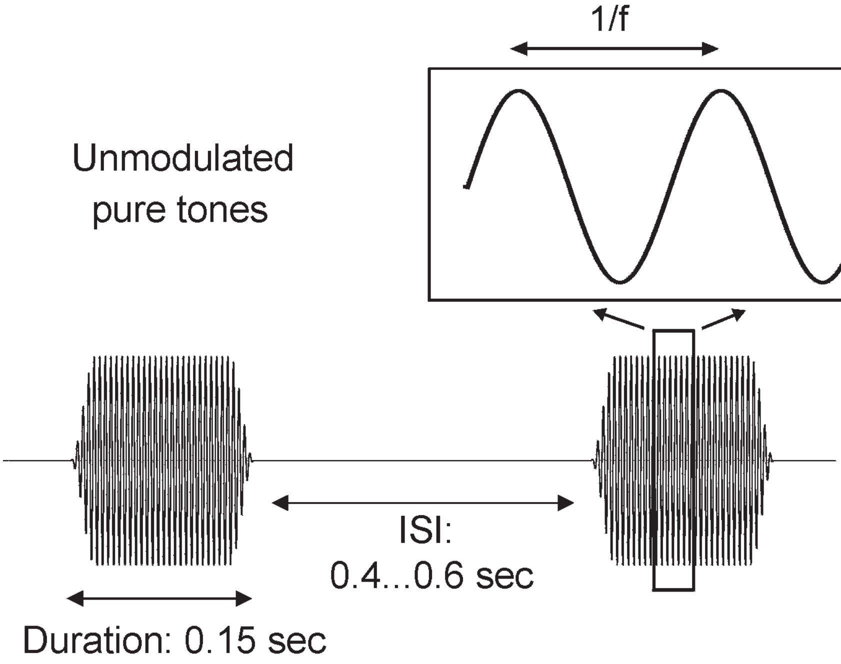


Figure 3.5: *Experimental setup for the unmodulated pure tones to check a possible influence of the modulation on the response.*

3.6 Procedures

3.6.1 Preparation of an MEG recording session

Subjects were instructed to disrobe all garments containing metallic pieces in any form, also to take off glasses, tuning forks (important for musicians), moneybags, wedding rings or keys. If necessary, some simple cotton clothes were available.

In a preparation room, three pairs of electrodes were attached to head and body providing the possibility to record eye movements, eye blinks and heartbeats during the measurement. Furthermore, to enable the coregistration with the individual MRI, recorded in a separate session, the location of four head position indicator coils together with a set of 35 surface points including the nasion and the two pre-auricular points were digitized (Druen, 2000).

Then the subjects were led to the magnetically shielded room, where the MEG measure took place (Fig.3.6). They were requested to sit relaxed for the following 90 minutes. Foam ear pieces were connected via 90 cm plastic tubes (diameter 3 mm) to small shielded transducers fixed on the back of the

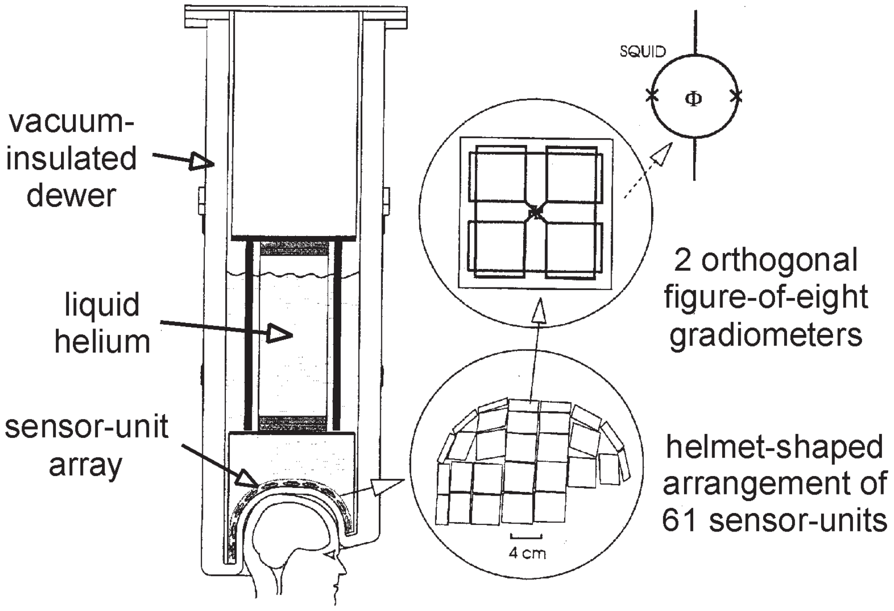


Figure 3.6: *The Neuromag-122 channel whole head MEG system. At each of 61 sensor positions in the head-shaped arrangement of this system, two figure-of-eight gradiometers with orthogonal orientations measure the planar gradients of the magnetic flux emerging from the head.*

chair receiving the stimuli.

3.6.2 Loudness matching

To account for the filter characteristics of the plastic tubes (about 20 dB attenuation at 5000 Hz) and also for slight differences in loudness due to the depth of the foam piece in the left versus right ear canal, the subjects were requested to match the loudness of all frequencies to an equal subjective loudness perception before the measurement. Generally, stimuli were presented binaurally at a level of approximately 50 dB nHL.

3.6.3 MEG-recording

The head position in the dewar of the Neuromag–122 channel MEG system was determined at the beginning of each of the six blocks. The subjects were instructed to listen passively to the sounds while watching a silent video of their own choice.

The auditory evoked fields were recorded from both hemispheres continuously with a bandpass filter of 0.01–250 Hz and a sample rate of 1000 Hz.

3.6.4 Data preprocessing

3.6.4.1 Averaging over the modulated tones

Prior to averaging, the data were inspected to exclude external artifacts. On average, about 2–5 noisy (bad) channels were excluded from further analysis. Trials exceeding a gradient of 600 $\frac{fT}{cm*sec}$and epochs with eyeblinks were rejected using a semi-automatic artifact rejection tool (BESA event-related fields ERF Modul). Altogether, about 5–10% of the sweeps were rejected. A baseline amplitude, calculated over the 100-ms interval before the onset of the tones was subtracted from the data.

For each carrier frequency and each of the 122 channels about 400 artifact-free responses were averaged off-line using the BESA ERF module. The resulting 122 channel waveforms are depicted in Fig.3.7, showing also the relative positions of the sensors in the dewar (in this case, no bad channels were excluded).

3.6.4.2 Averaging over each modulation cycle

Responses were averaged again over all cycles for each modulation frequency and combined in a linear deconvolution technique (Gutschalk et al., 1999) to

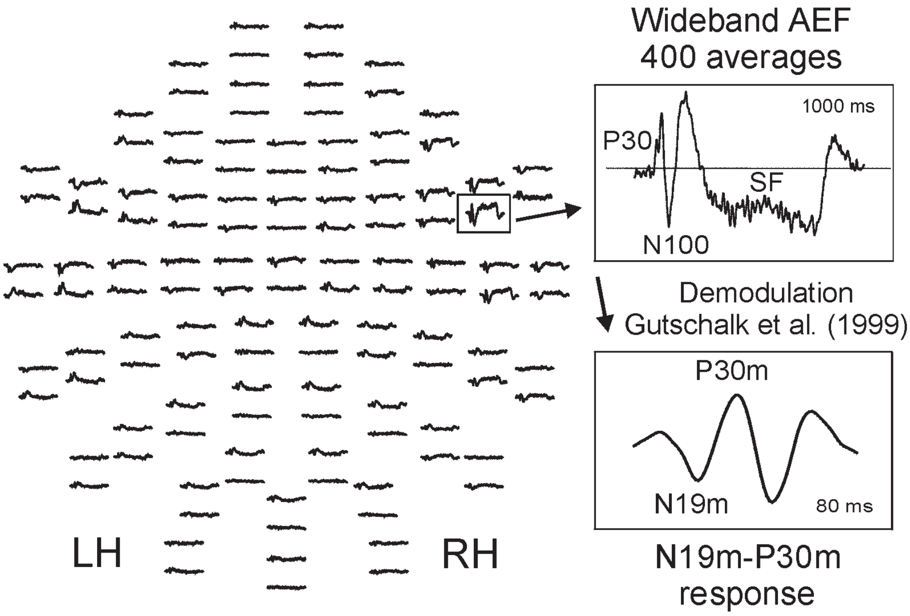


Figure 3.7: *Wideband auditory evoked fields (AEF), measured with the Neuromag-122 channel whole head MEG system. For each channel an average over 400 responses over an epoch of 100 ms pre- and 1200 ms post-stimulus onset is displayed. Responses to the single modulation cycles can be seen overlapped on the sustained field and were analyzed using a demodulation technique introduced by Gutschalk et al. (1999).*

obtain the primary N19m-P30m component corresponding to an average of 12000 responses at each carrier frequency.

3.6.4.3 Filtering

To accentuate the reflected response, the averaged data were filtered prior to source analysis. This procedure allowed for a better separation of the involved superimposed activities. The N100m response was generally filtered with a bandpass-filter (zero-phase shift Butterworth filter) from 3 Hz (6 dB/oct.) to 30 Hz (12 dB/oct.). The primary N19m-P30m responses were bandpass-filtered (zero-phase shift Butterworth filter) from 20 Hz (6 dB/oct.) to 120 Hz (12 dB/oct.).

3.7 The inverse problem

A sensory stimulus initially activates a small portion of the cortex. This process is associated with a primary current source related to the movement of ions due to their chemical concentration gradients. In addition, passive ohmic currents are set up in the surrounding medium. This so-called volume current completes the loop of ionic flow so that there is no builtup of charge. The magnetic field is generated by both the primary and the volume currents. If the primary source and the surrounding conductivity distribution are known, the resulting electric potential (EEG) and magnetic field (MEG) can be calculated from the Maxwell´s equations (forward problem). It follows from the linearity of Maxwell´s equations that once the solution for the elementary current dipole is possessed, the fields of more complex sources can be obtained readily by superposition.

In certain finite conductor geometries the volume current causes an equal but opposite field to that generated by the primary current. The net external field is then zero. For example, only currents that have a component tangential to the surface of a spherically symmetric conductor produce a magnetic field outside; radial sources are thus externally silent. Therefore, MEG measures mainly activity from the fissures of the cortex, which often simplified the interpretation of the data. Fortunately, all primary sensory areas of the brain including the auditory cortex are located within fissures.

In interpreting MEG and EEG data, one is dealing with the electromagnetic inverse problem, i.e., with the deduction of the source currents responsible for the externally measured field. Hermann von Helmholtz showed in 1853 that this problem has no unique solution. One must, therefore, use source models, such as current dipoles, or special estimation techniques to interpret the data.

In particular, Helmholtz showed that a current distribution inside a conductor G cannot be retrieved uniquely from the knowledge of the electromagnetic field outside. There are primary current distributions that are either magnetically silent ($\boldsymbol{B} = 0$ outside G), electrically silent ($\boldsymbol{E} = 0$ outside G), or both. A simple example of a magnetically silent source that produces an electric field is a radial dipole in a spherical symmetric conductor (a). An example of the opposite case is a current loop, which is electrically silent but which produces a magnetic field (b). In both cases, the potential V due to the primary current $\boldsymbol{J}_p$ vanishes: in case (a) the primary current$\mid \boldsymbol{J}_p \mid$ is constant over a closed surface S inside a homogenous subregion of the conductor G and $\boldsymbol{J}_p$ is normal to S. Therefore, the potential $V_0(r)$ due to J_p in a infinite homogeneous medium with unit conductivity will vanish, since

$$V_0(r) = \frac{J_p}{4\pi}\int_S \boldsymbol{n}(r')\boldsymbol{\nabla}'\frac{1}{R}dS' = \frac{J_p}{4\pi}\int_G \boldsymbol{\nabla}'\boldsymbol{\nabla}'\frac{1}{R}dv' = 0$$

Now, there is evidence that also the magnetic field $B(r)$ outside the head will vanish:

$$\boldsymbol{B(r)} = \frac{\mu_0}{4\pi}J_p\int_S \boldsymbol{n}(r') \times \boldsymbol{\nabla}'\frac{1}{R}dS' = \frac{\mu_0}{4\pi}J_p\int_G \boldsymbol{\nabla}' \times \boldsymbol{\nabla}'\frac{1}{R}dv' = 0$$

Thus this source produces no elecromagnetic field outside the conductor.

In case (b) of a current loop, J_p is solenoidal ($\boldsymbol{\nabla J}_p = 0$) and therefore $V_0 = 0$.

Because of the nonuniqueness, we must confine ourselves to finding a solution among a limited class of source configurations (see Hämäläinen et al., 1993).

In the present investigation, the sources are modeled with one equivalent dipole in each hemisphere providing an inverse solution, which robust estimates the scalp waveforms (Scherg, 1986, 1990, 1991, 1993, 1996).

3.8 Source reconstruction

3.8.1 Source model

The BESA (Brain Electromagnetic Source Analysis) software (MEGIS Software GmbH) was used to model the source activity with one equivalent dipole in each hemisphere (Scherg et al., 1990). Using spatio-temporal source analysis (Scherg, 1984; Scherg and von Cramon, 1986), the source waveforms were calculated. The source waveforms provide an image of brain function in terms of the magnitude and timing of the source currents (Scherg and Ebersole, 1993). Essentially, two different components of the auditory evoked fields were analyzed independently:

1. The main source activity of the N19m-P30m response, modeled with one equivalent dipole in each hemisphere located in the medial portion of the Heschl´s gyrus (see Fig.3.8).
2. The main source activity of the N100m response, modeled with one equivalent dipole in each hemisphere located in the lateral part of the planum temporale directly posterior to the Heschl´s gyrus.

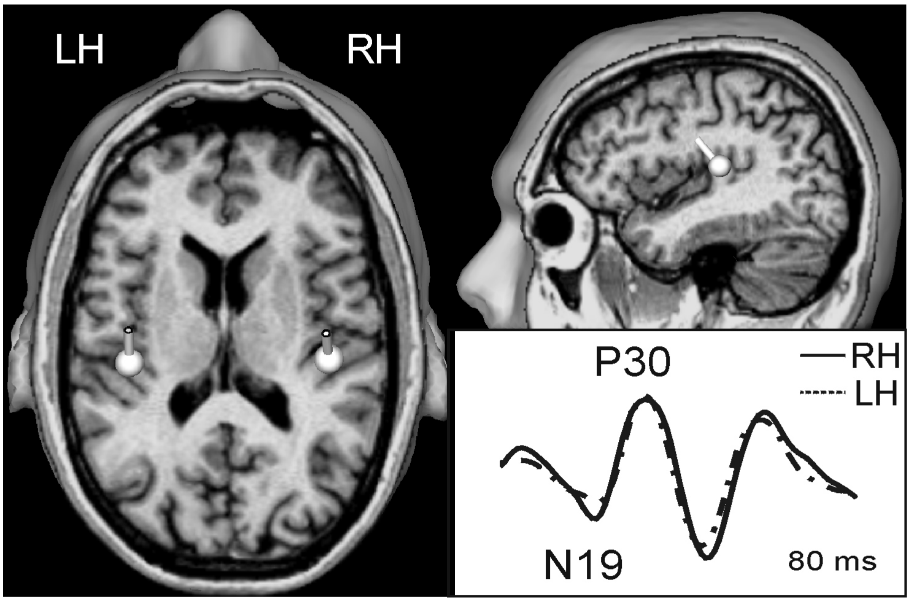


Figure 3.8: *Source model: the source activity of the N19m-P30m response was modeled with one equivalent dipole in the right and the left primary auditory cortex, respectively. For robust estimation of the dipole moment, the sources were seeded systematically into the medial portion of Heschl´s gyrus and the orientation fitted to the N19m-P30m peak-to-peak interval. The morphology of the resulting middle latency source waveforms are similar in both hemispheres.*

3.8.2 Strategies

Two strategies were employed to establish the source model: the fitting technique and the seeding technique.

- Fitting technique: using spatio-temporal source analysis (Scherg and von Cramon, 1986), the locations, orientations and the temporal activity patterns of the equivalent dipole sources were estimated underlying the auditory evoked MEG responses.
- Seeding technique: the BrainVoyager program (Brain Innovation, Dr. R. Goebel) was used for coregistration between the MEG data and structural magnetic resonance image data (MRI). For robust estimation of the dipole magnitude, the equivalent dipole sources were seeded systematically to the known generation sites from individual 3D-MRI datasets.

3.8.3 Coordinate systems

In the following three different types of coordinate systems were used to analyze the data:

1. System coordinate system of the 3D MRI
2. Head coordinate system of the MEG head model
3. Coordinate systems based on the individual anatomy of the auditory cortex

3.8.3.1 System coordinate system of the 3D-MRI

In this system, x, y and z-axis define

- the xy-plane as the axial or transversal plane,
- the yz-plane as the sagittal plane
- the xz-plane as the coronal plane

The abbreviations x_s, y_s and z_s are used in the following to indicate the system coords.

3.8.3.2 Head coordinate system

The individual head coordinate system was determined with three 3D digitized points on the individual head surface: the nasion and the two preauricular points (Drüen, 2000). Relative to the system coord system, the y-axis of the head coordinate system is tilted slightly upwards.

The abbreviations x_{HC}, y_{HC} and z_{HC} are used in the following to indicate the head coordinate system.

x_{HC}-axis and x_s-axis were both also called mediolateral x-axis.

In all subjects, the center of the spherical head model was defined to be positioned 15 mm anterior and 5 mm superior to the posterior commissure.

3.8.3.3 Coordinate systems based on the anatomy

For each subject we define two separate coordinate systems for each hemisphere based on the individual anatomy of the auditory cortex seen in the individual structural MRI (Fig.3.9).

The first system was determined by an x_{HG}-axis along the (first) Heschl´s gyrus called HG-system in the following. The origin of the x_{HG}-axis was situated in the center of the Hschl´s gyrus 4 mm lateral to the most medial point, referred to as x_0 (see Fig.3.9a, marked as no.1 in the HG). The second system will be determined by an x_{PT}-axis in the planum temporale posterior to the Heschl´s gyrus as depicted in Fig.3.9a, denoted as PT-system in the following. The origin of the x_{PT}-axis was situated 14 mm lateral to the most medial point x_0.

For frequency-dependent analysis, a row of 30 adjacent dipoles were seeded in 1 mm steps on each x_{HG}-axis and each x_{PT}-axis (see Fig.3.9a) for each subject. These rows of 30 adjacent dipoles were mainly used in chapter five to calculate the tonotopic gradients.

3.8.4 Test of the source model

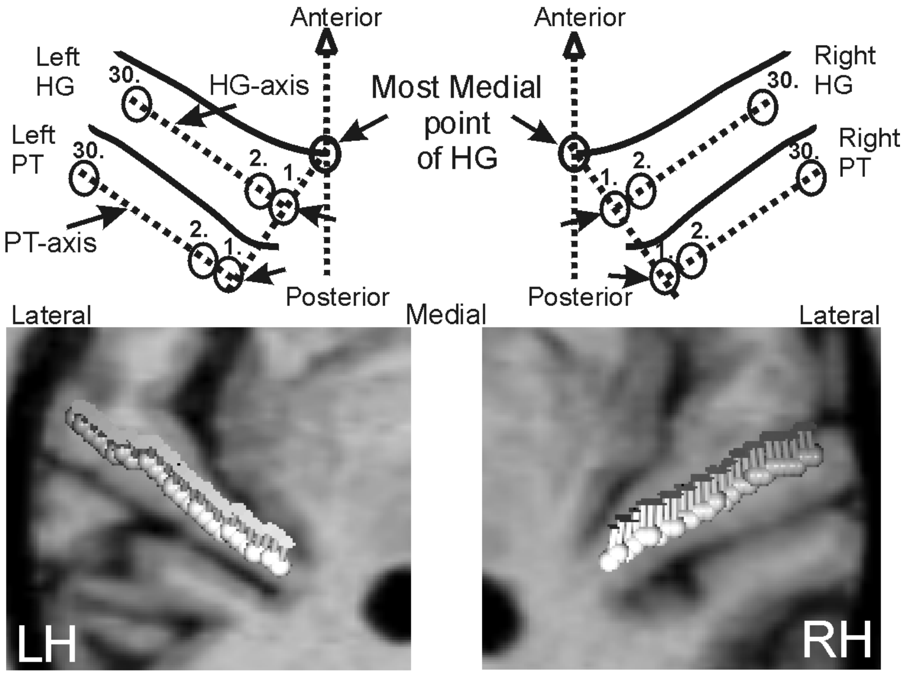
The source model of one equivalent dipole in each hemisphere was chosen to analyze the auditory evoked N19m-P30m and the N100m response. Here, we asked, whether the dipoles would fit in the auditory cortex.

Using spatio temporal source analysis, the dipoles were consistently fitted to the N19m-P30m peak-to-peak interval of the N19m-P30m response and to the N100m peak, respectively (see Fig. 3.10).

Here we point out why the fit intervals were strongly related to the progression of the individual source waveforms:

- The individually defined fit intervals are important because the latency in both the N19m-P30m and the N100m response are strongly frequency-dependent. (see chapter five, Fig.5.4)
- The fit of the dipole orientation is important because the orientation of both the N19m-P30m and the N100m response is also frequency-dependent (see chapter five, Fig.5.5.)

(a) Top view



(b) Lateral view

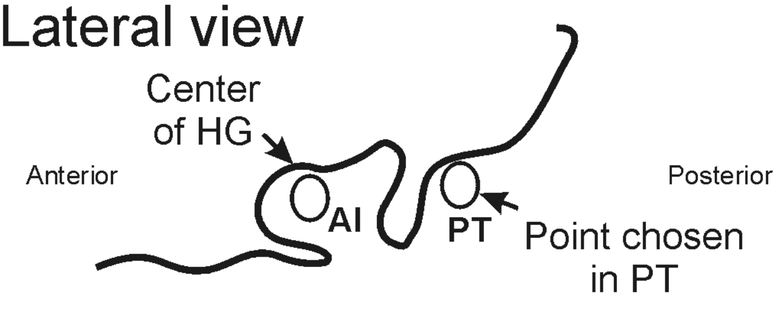


Figure 3.9: *For frequency-dependent analysis, a row of 30 adjacent dipoles were seeded in 1 mm steps on each* x_{HG}*-axis and each* x_{PT}*-axis (a) for each subject. The y- and z-value-range of both the HG-axis and the PT-axis is shown in (b).*

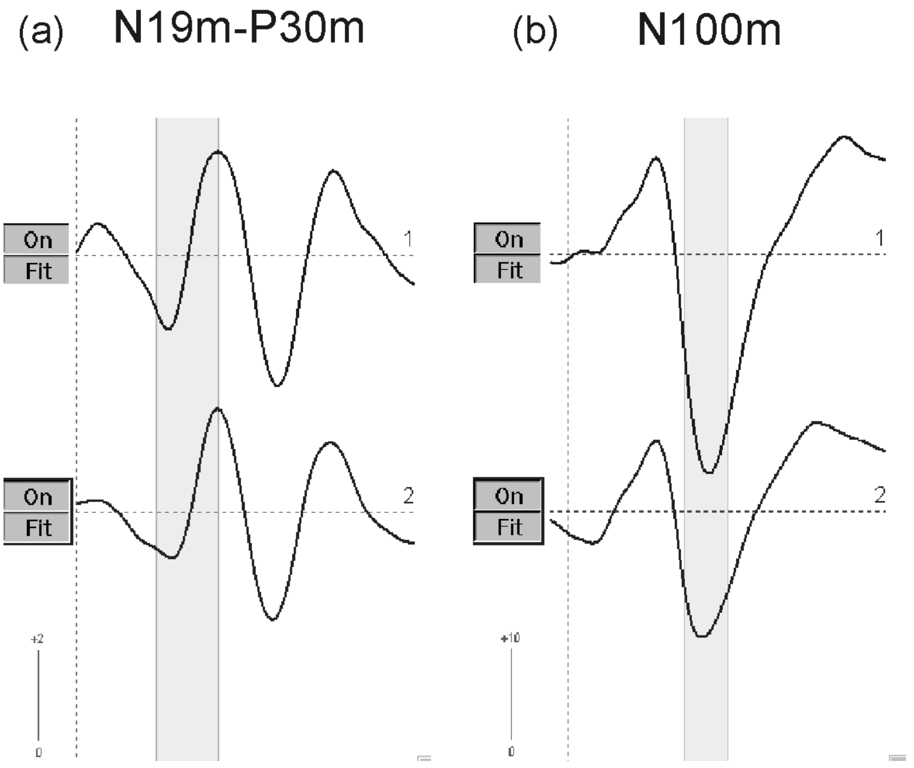


Figure 3.10: *The left panel shows the N19m-P30m peak-to-peak fit interval. The right panel depicts the N100m peak fit interval used to fit the data.*

The distance to the x_{HG}-axis and the distance to the x_{PT}-axis were calculated to express the goodness of the location. For the N19m-P30m response, the averaged relative y-distance was 2 mm posterior to Heschl´s gyrus and the averaged relative z-distance was 6 mm superior to Heschl´s gyrus (see Fig.3.11).

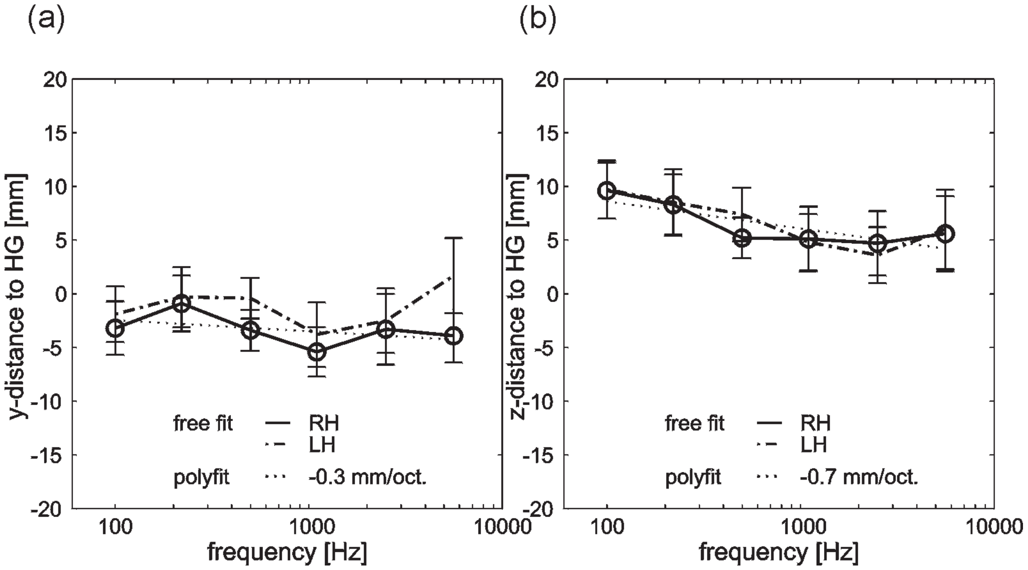


Figure 3.11: *Fitting technique: The N19m-P30m source, fitted without constraint to the N19m-P30m peak-to-peak interval, was located on average over all frequencies and 23 subjects 2 mm posterior and 6 mm superior to the Heschl´s gyrus. Error bars indicate the standard error.*

The free fitted N19m-P30m location showed no effects on the frequency relative to the Heschls´s gyrus axis (y-distance to HG: $F(5, 110) = 1.4$, n.s.; z-distance to HG: $F(5, 110) = 2.2$, n.s.). Effects on the hemisphere were not found in the direction of the z-axis and at the edge of significance in the direction of the y-axis (y-distance to HG: $F(1, 22) = 4.1$, $p = 0.05$; z-distance to HG: $F(1, 22) = 0.05$, n.s.).

For N100m, the averaged relative y-distance was 4 mm anterior to PT and the averaged relative z-distance was 2 mm inferior to the PT (see Fig.3.12).

The free fitted N100m location showed effects on the frequency relative to the planum temporale axis at the edge of significance (y-distance to PT: $F(5, 110) = 3.0$, $p < 0.05$; z-distance to PT: $F(5, 110) = 1.3$, n.s.). A slight hemisphere effect was found for the relative z-distance to the planum temporale axis (y-distance to PT: $F(1, 22) = 0.3$, n.s.; z-distance to PT: $F(1, 22) = 6.8$, $p < 0.05$).

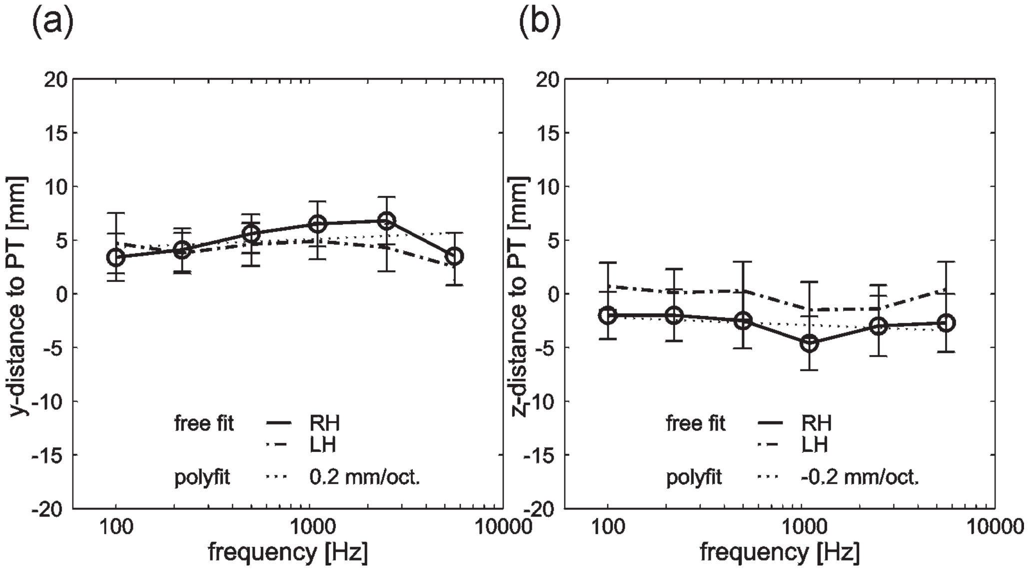


Figure 3.12: *Fitting technique: The N100m source, fitted without constraint to the N100m peak interval, was located on average over all frequencies and 23 subjects 4 mm anterior and 2 mm inferior to the upper border of the planum temporale.*

3.8.5 Calculation of the dipole magnitude

3.8.5.1 Definition of the generation sites

In each hemisphere, two locations with fixed position relative to the individual auditory cortex will be determined in the following. They were expected to be a reliable approximation for the generation sites of the N19m-P30m response and the N100m response, respectively (see Fig.3.13). The N19m-P30m responses were expected to be generated on average in the center of the primary auditory cortex and the N100m response 12 mm more laterally, calculated in chapter five from Fig.5.2, where the frequency dependent depth values x_D could be averaged over all subjects and all frequencies. In particular the following five steps were performed to determine the two centered locations in AI and PT:

1. The most medial point (x_0) of the Heschl´s gyrus on the mediolateral axis was found by scrolling through the sagittal yz-plane of the individual 3D-MRI along the mediolateral x_S of the system coordinate system (Brain Voyager program, Brain Innovation, Dr. R. Goebel). Scrolling was continued until the beginning of structural change in the sylvian fissure was detected (see Fig.3.13a).

2. The "equivalent" depth $x_{D(AI)}$ value which should be in the center of the primary auditory cortex was determined by scrolling $\mid x_{D(AI)} - x_0 \mid = 13$ mm more laterally through the sagittal plane, beginning with the x_0 plane (see Fig.3.13a). This difference value of $\mid x_{D(AI)} - x_0 \mid = 13$ mm can be calculated in chapter five (see Fig.5.2) as an grand average of all individual $\mid x_{D(AI)} - x_0 \mid_i$ values and over all frequencies; GA=Grand average):
$$\mid x_{D(AI)} - x_0 \mid_{GA} = \sum_{i=1}^{n} \frac{\mid x_{D(AI)} - x_0 \mid_i}{n}$$
This AI-centered depth value of $\mid x_{D(AI)} - x_0 \mid_{GA} = 13$ mm was ordered to be strictely the same in all subjects.

3. In the same manner, the relative distance of $\mid x_{D(PT)} - x_0 \mid_{GA} = 25$ mm along the mediolateral x-axis was calculated for the N100m response.

4. The resulting relative depth values at $\mid x_{D(AI)} - x_0 \mid_{GA} = 13$ mm and $\mid x_{D(AI)} - x_0 \mid_{GA} = 25$ mm lateral to x_0 were calculated in each subject by scrolling through the sagittal plane.

5. In the $yz \mid_{x=13mm}$ plane (the $yz \mid_{x=25mm}$ plane, resp.) the dipoles were seeded to the (y,z)-points depicted in Fig.3.12b in the sagittal $x_{D(AI)}$ plane ($x_{D(PT)}$ plane, resp.).

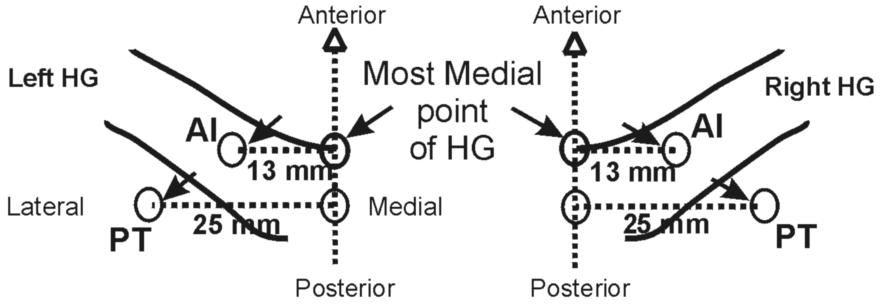
This procedure to define the averaged generation sites could be applied in 23 of 27 subjects, for which an MRT dataset was available. In the remaining four cases, we could use the strong correlation between the head radius defined in the BESA head model and the 23 seeded $x_D\,'$ values in the head coordinate system to estimate the four remaining $x_D\,'$ values with an exactness of 1–2 mm (see Fig.3.14).

In this case, the transformation $(x_D)'_{HC} = (x_D)_{HC} + (x_D)_{cot}$ must be used to adjust a possible slight right-left asymmetry in the head coordinates caused by a not vanishing x_{HC} value of the center of the head coordinate system, protocoled in the head center file.

3.8.5.2 Seeding technique

In a first run, the dipole amplitudes were calculated in each condition exactly at the two locations defined above. In each hemisphere one equivalent dipole was seeded from the 3D-MRI at these averaged generation sites. The location was kept constant in all conditions, but each time the dipole orientation was fitted to the N19m-P30m peak-to-peak interval (and to the N100m peak, respectively, see Fig.3.10). The results will be shown in chapter four.

(a) Top view



(b) Lateral view

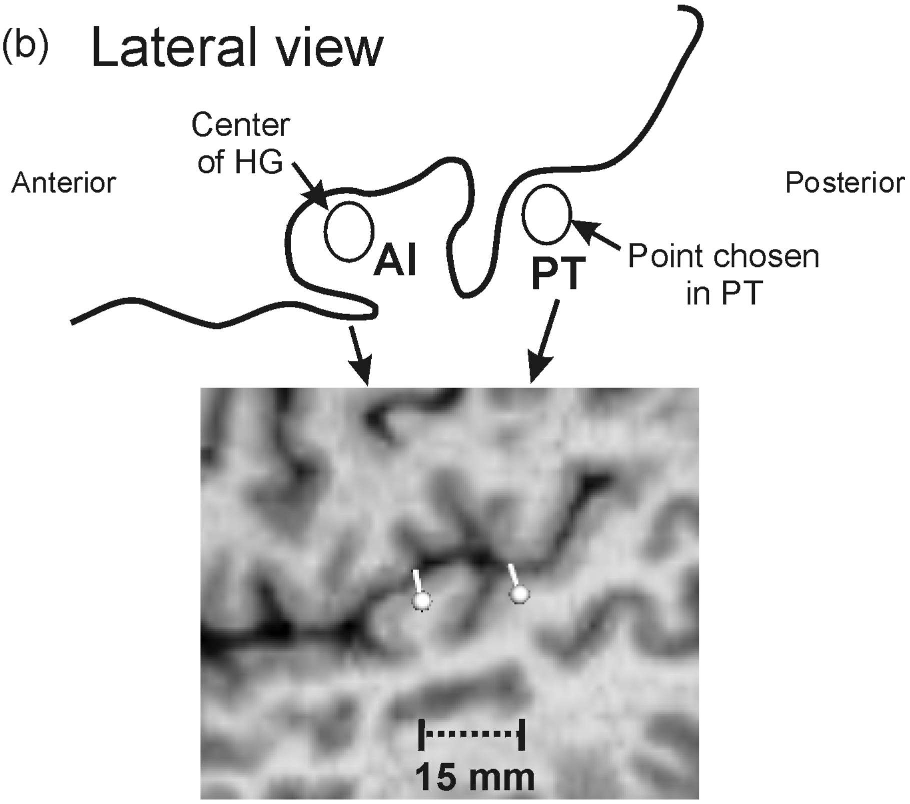


Figure 3.13: *Schematic top view (a) and lateral view (b) of the left and right auditory cortex showing the fixed position of the seeded dipoles.*

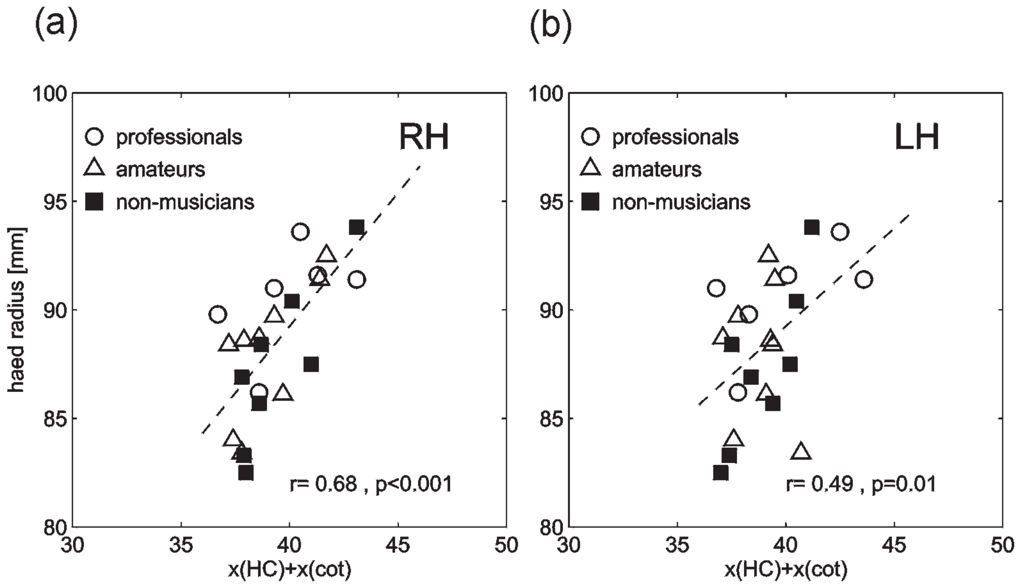


Figure 3.14: *Correlation between the averaged generation site in the AI and the head radius defined in the BESA program. The correlation was stronger in the right hemisphere (*$r = 0.68$*,* $p < 0.001$*), but still pronounced in the left hemisphere (*$r = 0.49$*,* $p = 0.01$*).*

3.8.5.3 Combined fitting and seeding technique

A slightly modified procedure was applied additionally to determine the dipole amplitudes from a combined fitting and seeding technique. This procedure consisted of three steps:

1. The two equivalent dipole sources were fitted without constraints only in the most stable 500 Hz condition to the N19m-P30m peak-to-peak interval and the N100m peak, respectively.

2. The seeding technique of Method 1 was applied only on the (mediolateral) x-axis because dipole amplitude is most sensitive to depth. Therefore, the fitted x_{HC} value in the head coordinate system was replaced with the strictly fixed x_{HG} values of the seeded dipole in method 1, transformed to head coordinates.

3. The resulting dipole location was kept constant for all conditions, but each time the dipole orientation was fitted individually to the N19m-P30m peak-to-peak interval and to the N100m peak, respectively, similar to method 1.

The relative y- and z-distance between the fitted location in the 500 Hz condition and the expected generation site was generally less than 5 mm (see Fig.3.11 and Fig.3.12). However, if averaged over all subjects, the methods 1 and 2 produced no significant difference in calculating the dipole amplitude. But in few subjects there exist still a not negligible difference which may be caused by a systematic error, in particular a systematic z-shift in the location. This z-shift is also visible if averaged over all subjects (see Fig. 3.11b). However, The yz-fit used in method 2 could take into account this z-shift. Therefore, the reported results in chapter four refer to the method 2.

3.9 Error sources

Analysis of variance was performed with SAS (Version 8.0), using the general linear model (ANOVA for repeated measurements). In the figures, the error bars generally indicate the standard error (for example see Fig.3.11 and 3.12).

Possible systematic errors at different levels of the measurement and evaluation of the data are strongly kept to a minimum as demonstrated in the following:

- The restriction of one dipole in each hemisphere to model the source activity is not supposed to cause a significant systematic error. Principal component analysis (PCA) revealed that for each response generally a smaller second source activity may be involved (Gutschalk et al., 1998, 1999, 2000), but in a first approximation, already our model of one dipole in each hemisphere can account for more than 95% of the variance if fitted to the peak interval.

- The fit interval was strongly related to the progression of the individual source waveform (see Fig.3.10). If more than one source would contribute to the response, this strong relation of the fit intervall to the source waveform would ensure to measure always the same superposition of different sources. Therefore a possible systematic error due to the variability of the sources was not supposed.

- The great number of 27 subjects which participated in our investigation provided not only a small standard error but also the possibility to minimize systematic subjective influences (apart from the slight z-shift reportet in chapter 3.8.4).

- The magnitude and timing of the N19m-P30m source waveforms demonstrated the strong replicability in seven repeated measurements with the same subject (see Fig.4.13).
- The N19m-P30m source waveforms were calculated from an average of 12000 responses at each carrier frequency (see chapter 3.6.4).
- The MEG data were accurately coregistered with the individual 3D MRI scan using a set of 35 3D-digitized head surface points (Druen, 2000).

Already the clear form of the source waveforms (see Fig. 4.1 and Fig. 4.2) of most subjects demonstrate the small influence of systematic errors in our investigation.

Chapter 4

Enhanced activation in musicians

Pantev et al. (1998) found that piano tones evoked a N100m component that was 25% larger in musicians as compared to non-musicians if evoked by piano tones and that this enhancement was not significant if the stimulus was a sinusoidal tone (see chapter 2.1).

From an investigation on the magnetic fields evoked by sinusoidal tones we report in the following, that

1. the tone-evoked source activity of the primary auditory cortex occurring at 19-30 ms was 87% larger for musicians than for non-musicians.
2. the increase of the late secondary component at 100 ms was considerably smaller (30%) and at the limit of significance.
3. the magnitude of the primary source activity correlated significantly ($r = 0.51$; $p < 0.01$) with the musical aptitude, measured by the standardized Advanced Measure of Music Audiation test (AMMA).
4. a correlation with starting age of musical education was not found.
5. the magnitude of the primary component was 15% larger in the right hemisphere.

4.1 Individual source waveforms

The individual middle latency source waveforms for the 500 Hz tone are displayed in Fig 4.1 for each tested subject and each hemisphere. Those for the other five frequencies look very similar. Already from this figure a clear distinction between the signal amplitudes of musicians and non-musicians became apparent.

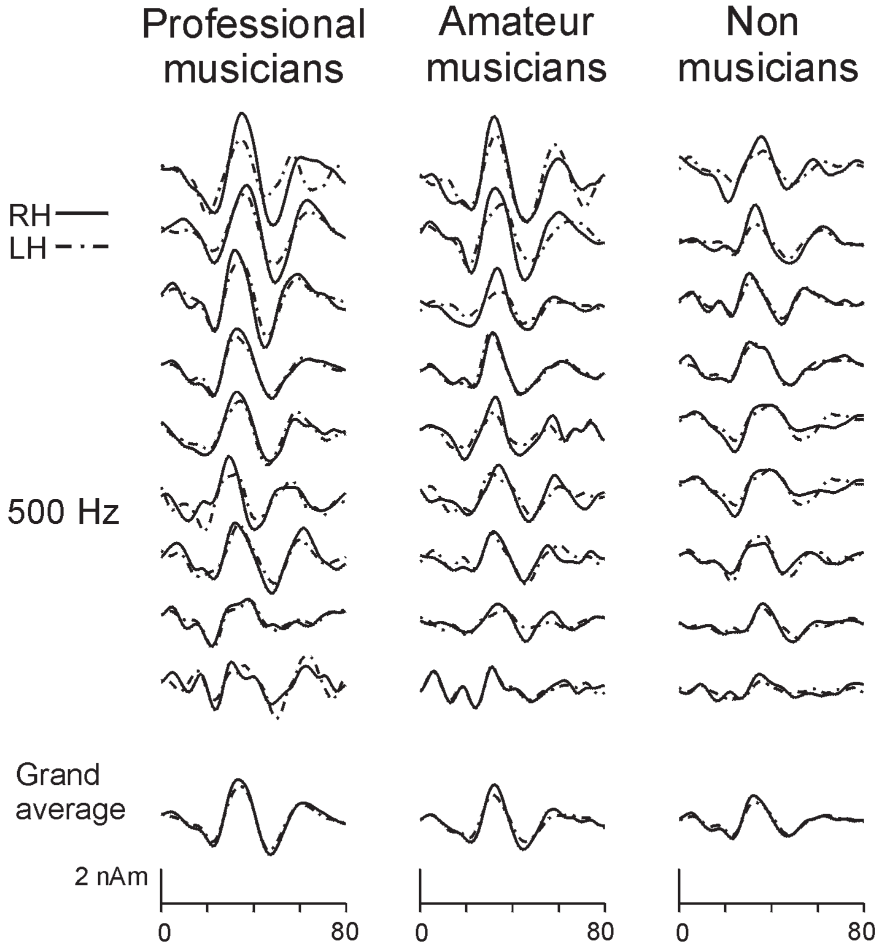


Figure 4.1: *Individual N19m-P30m source waveforms (0-80 ms, onset at 1/2 ramp of the amplitude modulated tones, 20-120 Hz zero-phase bandpass filter) are shown for nine professionals, nine amateur musicians and for nine non-musicians. The systematic increase in dipole moment amplitude can be seen in both hemispheres from the non-musicians to the professional musicians. This is also evident from the grand averages at the bottom.*

Similarly, the individual late latency source waveforms around the N100m peak for the tone with 1100 Hz are displayed in Fig.4.2 for each test subject and each hemisphere. Here, a large variance of the N100m dipole amplitude is visible in each group.

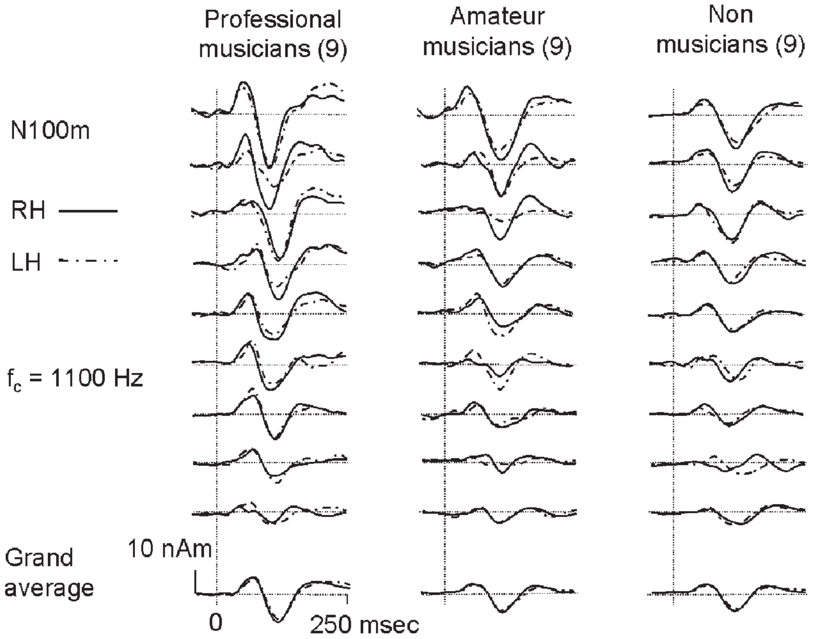


Figure 4.2: *Individual N100m source waveforms (30 ms pre- and 250 ms post-stimulus interval, 3-30 Hz zero-phase bandpass filter) are shown for the same groups. The large variance of the N100m dipole amplitude can be seen in each group.*

4.2 Dipole magnitude

The individual N19m-P30m peak-to-peak dipole amplitudes of nine professional musicians, nine amateur musicians and nine non-musicians are displayed in Fig.4.3, averaged over both hemispheres. The large difference in dipole magnitude between the professionals and the non-musicians is already visible from this figure.

The individual N100m baseline-to-peak dipole amplitudes are shown in Fig.4.4, averaged over both hemispheres. Here, a large variance in each group makes it rather difficult to analyze the data.

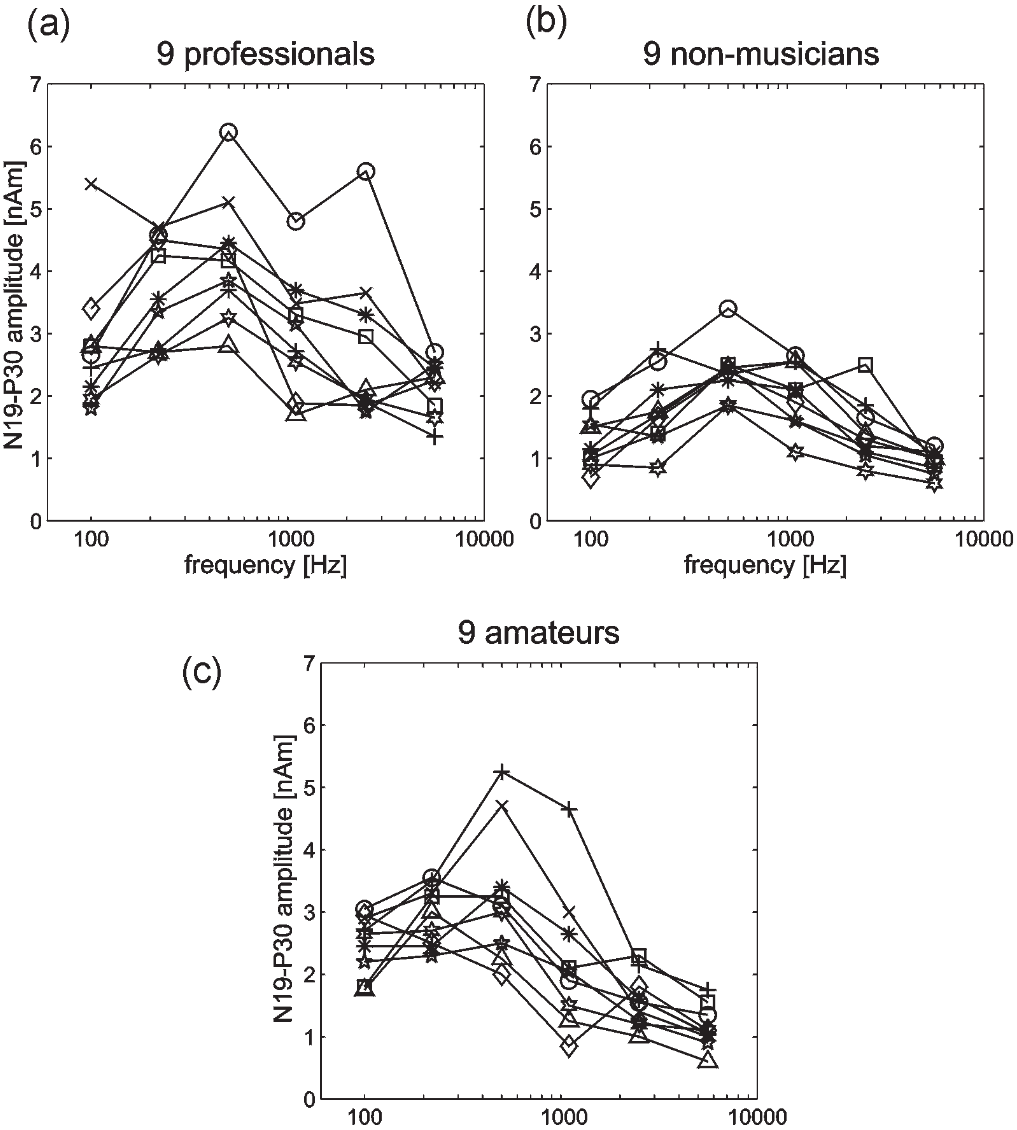


Figure 4.3: *Individual N19m-P30m peak-to-peak dipole amplitude, shown separately for professionals (a), amateurs (b) and non-musicians (c) and averaged over both hemispheres.*

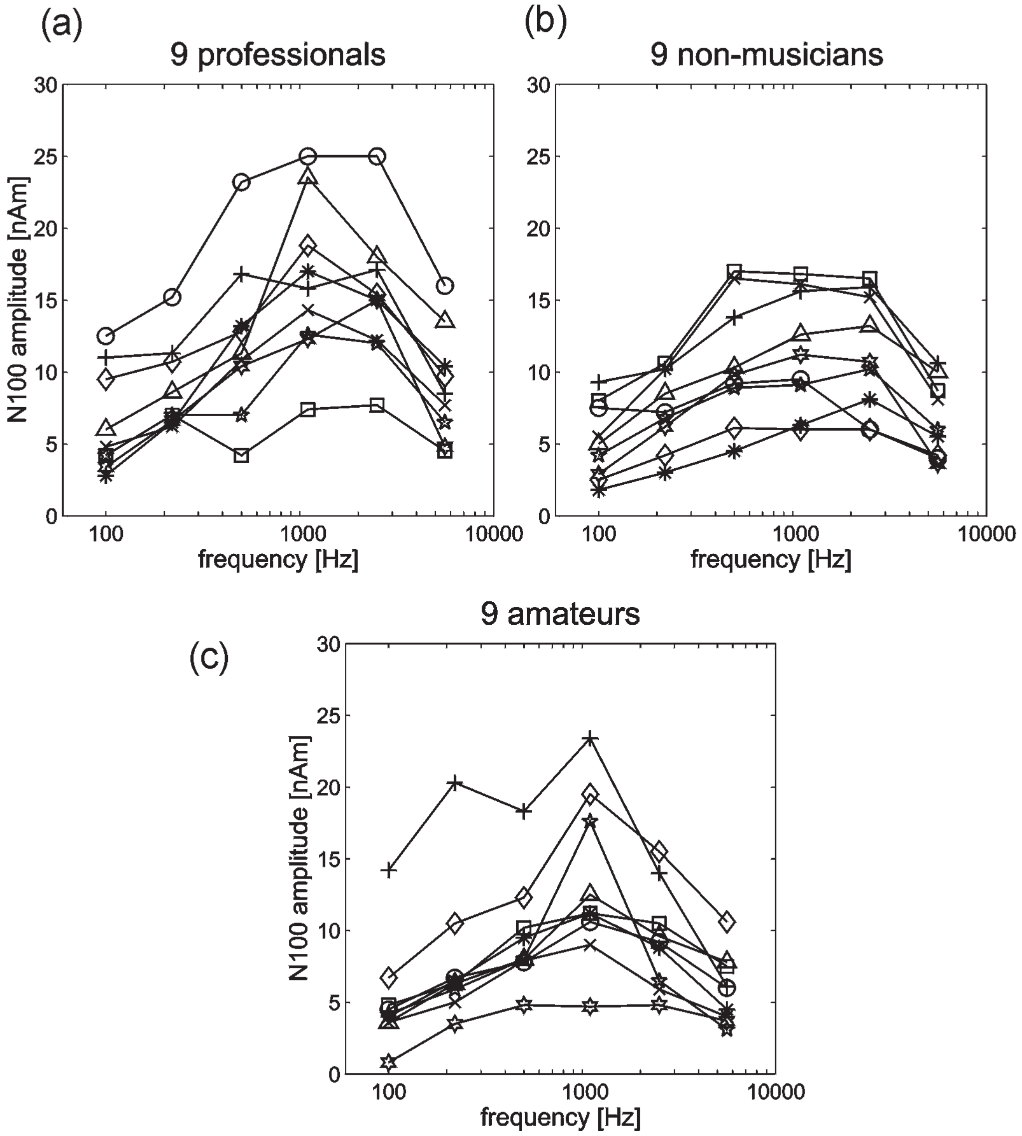


Figure 4.4: *Individual N100m dipole amplitude, shown separately for professionals (a), amateurs (b) and non-musicians (c) and averaged over both hemispheres.*

Fig.4.5 depicts the dependence of dipole magnitude on frequency beginning from the earliest up to the latest cortical responses in four steps: the N19m-P30m magnitude (Fig.4.5a), the P50m response (Fig.4.5b), the N100m response (Fig.4.5c) and finally the sustained field (SF, Fig.4.5d). The N19m-p30m dipole amplitude was calculated at a fixed point 13 mm lateral to the most medial point of the Heschl´s gyrus (x_0) as described in chapter 3.8.5, the P50m and SF response 19 mm lateral and finally the N100m response 25 mm lateral to x_0.

In Fig.4.5a, a large parallel displacement of about 1.5 nAm between the musicians and the non-musicians is clearly visible. The primary N19m-P30m source activity averaged over all frequencies and both hemispheres was found to be 87% larger for the professional musicians as compared to non-musicians. The increase was highly significant for all frequencies (group: $F(1,16) = 28.4$, $p < 0.001$) and slightly larger (13%) in the right hemisphere (hemi: $F(1,16) = 8.8$, $p < 0.01$)). Overall, source activity was largest around 500 Hz. In contrast to the strong enhancement of the signal of musicians at the primary level at all frequencies the situation was more subtle for the N100m component. As visible from Fig.4.5b, there was a significant frequency-group interaction (Freq*group: $F(5,80) = 3.1$, $p = 0.01$). Paire-wise test showed that a significant increase of the signals in musicians has been observed only for the tone with 1100 Hz (pairwise univariate post-hoc-test $F(1,16) = 5.8$, $p < 0.05$). If averaged over all frequencies and both hemispheres, the increase was 30 % but not statistically significant (group: $F(1,16) = 2.3$, n.s.).

In Fig.4.5b a new important result can be seen: the P50m response showed an undiminished strong increase of 88% in musicians as compared to non-musicians ($F(1,16) = 33.4$, $p < 0.0001$), which was indeed approximately the same as found for the N19m-P30m magnitude (see Fig.4.5a). In contrast, the sustained field (SF, see Fig.4.5d) revealed only a 10% increase in musicians as compared to non-musicians (group: $F(1,16) = 0.6$, n.s.). The magnitude of the sustained field seemed rather evaluated for the amateurs, but this effect was not significant (group amateurs versus rest: 30% increase in the amateurs, $F(1,25) = 3.0$, n.s.).

The ANOVA for repeated measurements, calculated over all three groups, revealed always a strong group effect for the N19m-P30m response (Fig.4.5a, $F(2,24) = 15.2$, $p < 0.0001$). The group effect was stronger for the P50m response (Fig.4.5b, $F(2,24) = 22.6$, $p < 0.0001$) but not significant for the N100m response (Fig.4.5c): $F(2,24)$, n.s.). However, in the latter case, the frequency-group interaction (Freq*group, $F(5,80) = 2.6$, $p < 0.01$) was significant. Musicians and non-musicians differed significantly at 2 frequencies, i.e. for the 1100 Hz tone (pairwise univariate post-hoc-test ($F(1,25) = 3.4$, $p < 0.05$) and the 5600 Hz tone (pairwise univariate post-hoc-test $F(1,25) =$

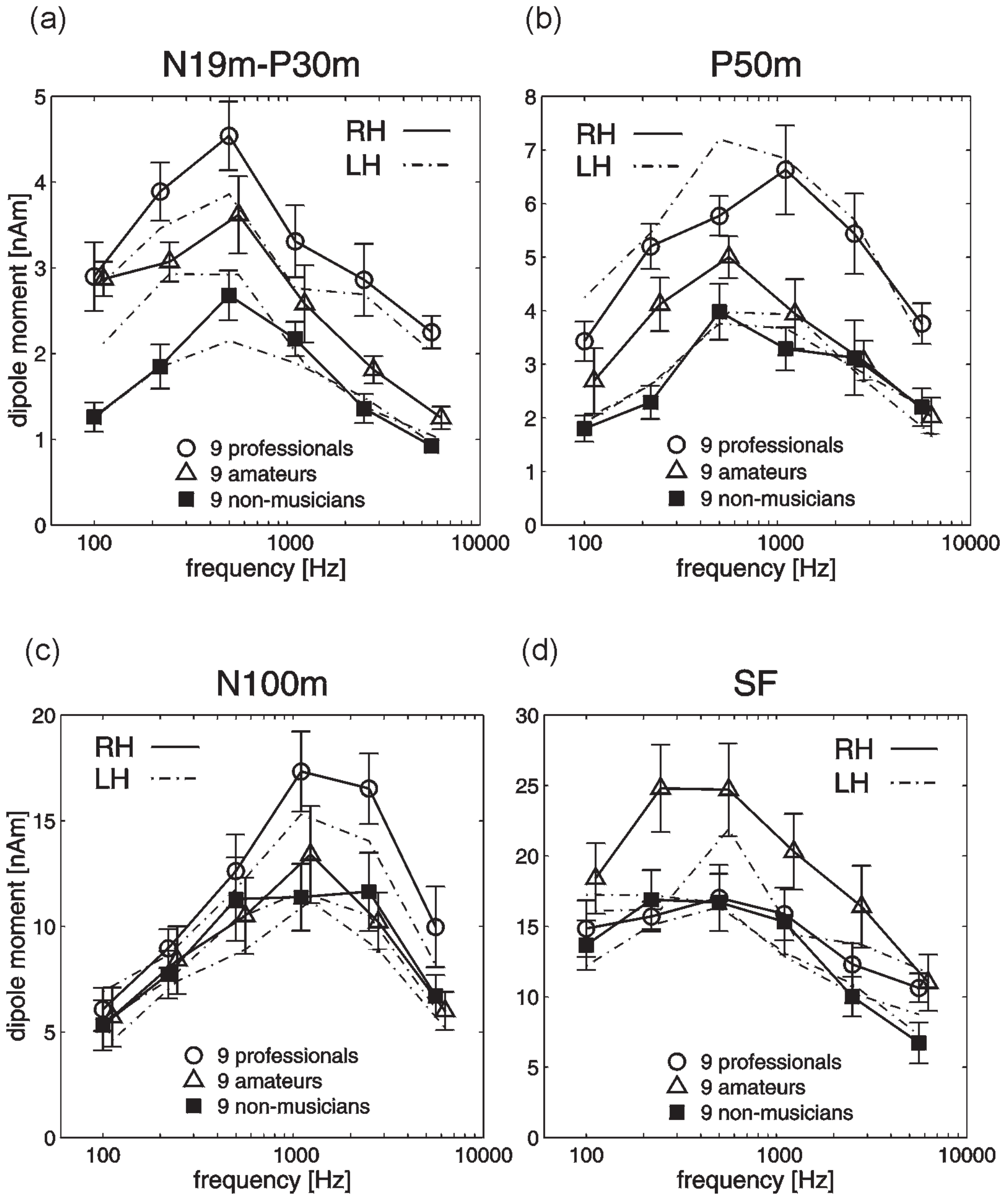


Figure 4.5: *Progression from the middle latency responses over the P50m response and the N100m response up to the sustained field (SF) is opposed, including the averaged dipole amplitude for nine amateur musicians.*

4.0, $p = 0.05$).

Fig.4.6 points out the main result of 87% enhanced activation of the primary auditory cortex in musicians opposed to the weak effect on the N100m component. The frequency dependence of the peak-to-peak dipole amplitude for the N19m-P30m and the baseline-to-peak dipole amplitude for the N100m response of musicians and non-musicians and for both hemispheres are separately displayed for musicians and for non-musicians.

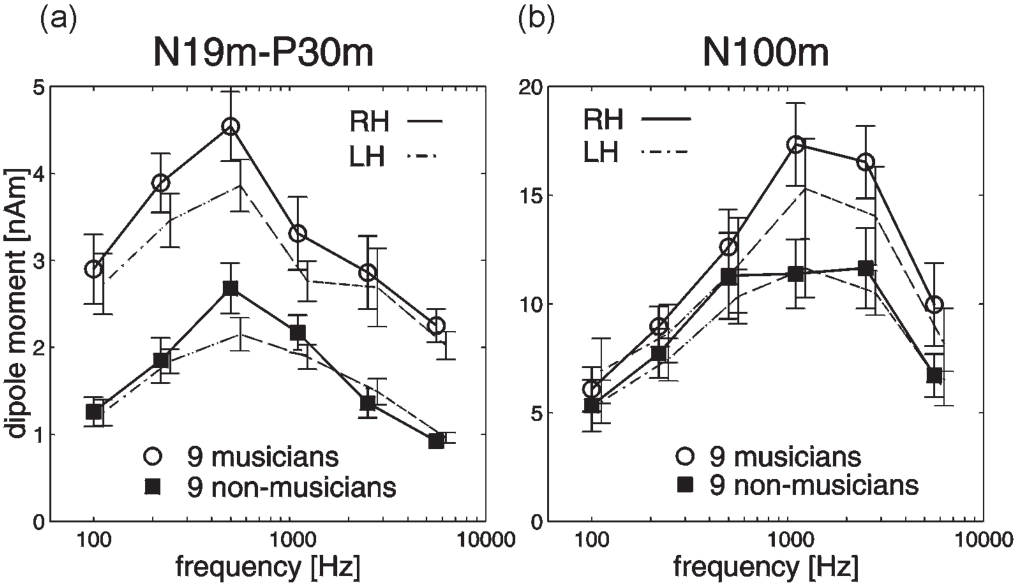


Figure 4.6: *The peak-to-peak dipole amplitude of the N19m-P30m (a) and baseline-to-peak dipole amplitude of the N100m response (b) are shown on a logarithmical frequenca scale, comparing the grand average of 9 professional musicians with the grand average of 9 non-musicians. The primary N19-P30 component was 87% larger for the musicians, whereas the 30 % increase for the N100m component was not significant.*

4.3 Correlation with the AMMA test

4.3.1 Dipole amplitude and music aptitude

Fig.4.7 depicts the dependence of dipole magnitude on tonal music aptitude beginning with the earliest up to the latest cortical responses in the same four steps used in the previous chapter.

The peak-to-peak N19m-P30m dipole amplitude correlated strongly with the tonal aptitude as measured by the AMMA test. The correlation coeffi-

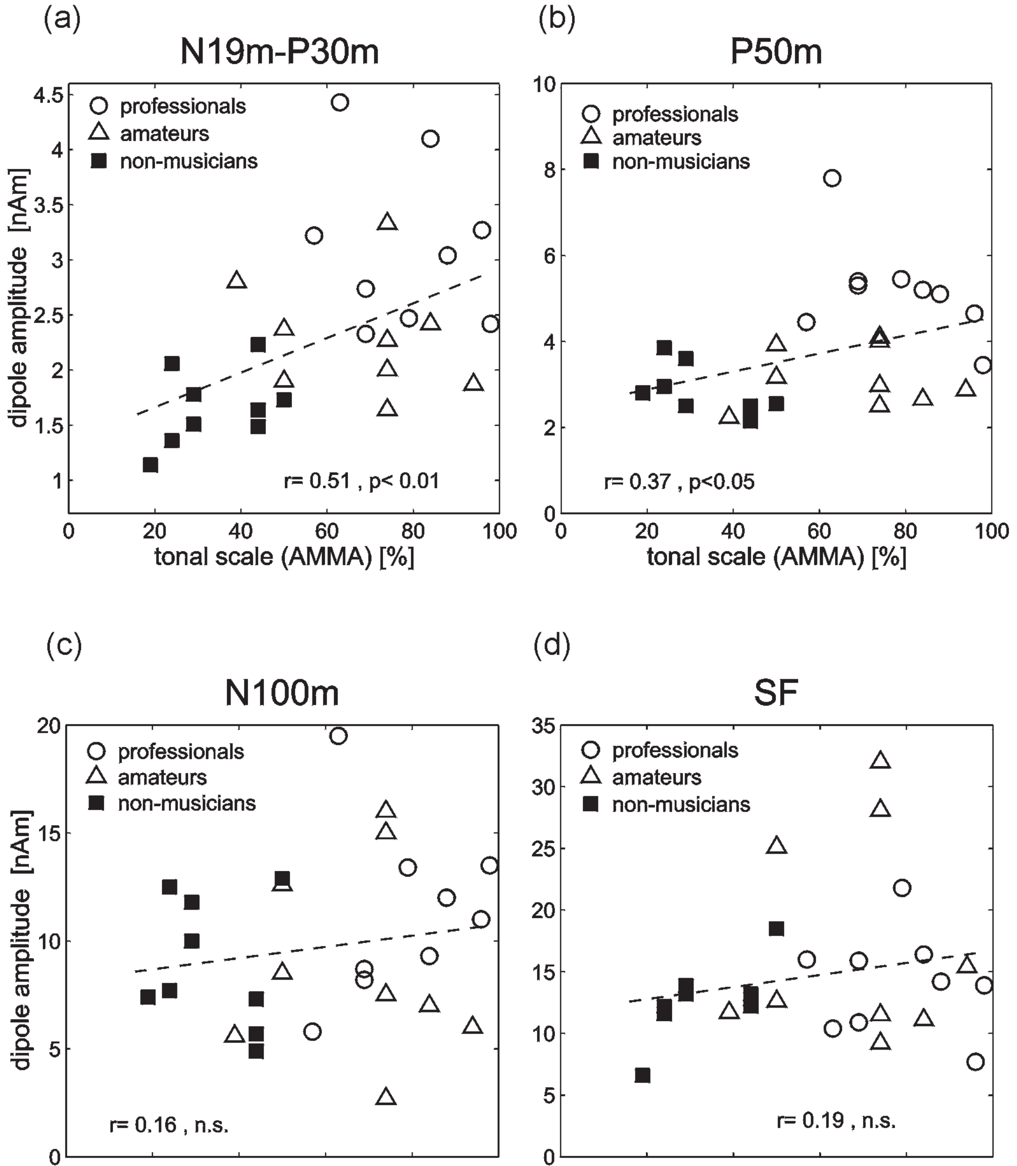


Figure 4.7: *The scatterplots shows the dipole amplitude averaged over all frequencies against the tonal scale of the AMMA test. The dipole amplitude of the N19m-P30m component is seen to correlate strongly with the music aptitude (a). Towards the later responses (b–d), the correlation decreased progressively.*

cient for the grand average was $r = 0.51$ ($p < 0.01$, see Fig.4.7a). The grand average of the P50m component was still significant ($r = 0.37$, $p < 0.05$), whereas there was no more significant correlation found for both the N100m component ($r = 0.16$, n.s.) and the sustained field ($r = 0.19$, n.s.).

The variance of the dipole amplitudes seen in these scatterplots was related to the variances shown in Fig.4.3.

4.4 Differences between the hemispheres

Since hemispheric differences are received some interest in the recent literature, we have also investigated whether the dipole amplitudes are larger in the right hemisphere as compared to the left hemisphere (Zatorre, 1991; Zatorre, 1994; Zatorre, 1998; Yvert, 1998, see Fig.4.8). The N19m-P30m peak-to-peak amplitude was 15% larger in the right hemisphere averaged over all frequencies (hemi: $F(1, 26) = 22.2$, $p < 0.0001$) and largest for the tone with 500 Hz (hemi*freq: $F(5, 130) = 2.6$, $p < 0.05$). The right hemispheric dominance was not significant for the N100m response ($F(1, 26) = 1.8$, n.s.).

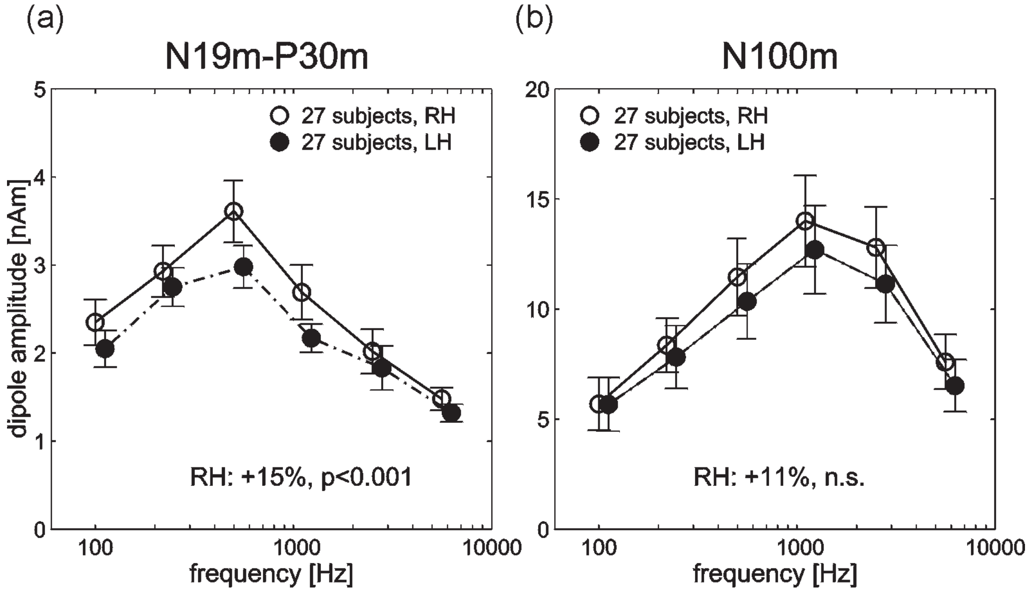


Figure 4.8: *Dominance of the right hemisphere: there is a strong effect for the N19m-P30m response but no significant effect for the N100m response. This can be seen from the standard error bars.*

Fig.4.8 shows the frequency dependence of the dipole amplitude, averaged over all groups (27 subjects). It is clearly visible, that the source activity was largest at 500 Hz (1100 Hz, respectively) and decreases towards the higher and lower frequencies. this average shows the consistency of the right hemispheric dominance over all frequencies for N19m-P30m.

4.5 Further investigations

In order to get information on possible reasons for this striking difference between neuronal signals of musicians and non-musicians, further investigations were performed on musical training and the potential effects of modulation and attention.

4.5.1 Musical training

21 of the 27 subjects including also some non-musicians underwent continuous musical education for at least five years. Between the age when musical education started and the size of both the N19m-P30m (see Fig 4.9) and the N100m dipole amplitude, no significant correlation was found ($r = -0.05$ resp. $r = -0.09$, n.s.). For pianists, however, Pantev et al. (1998) did observe such a correlation for the N100m component evoked by piano tones.

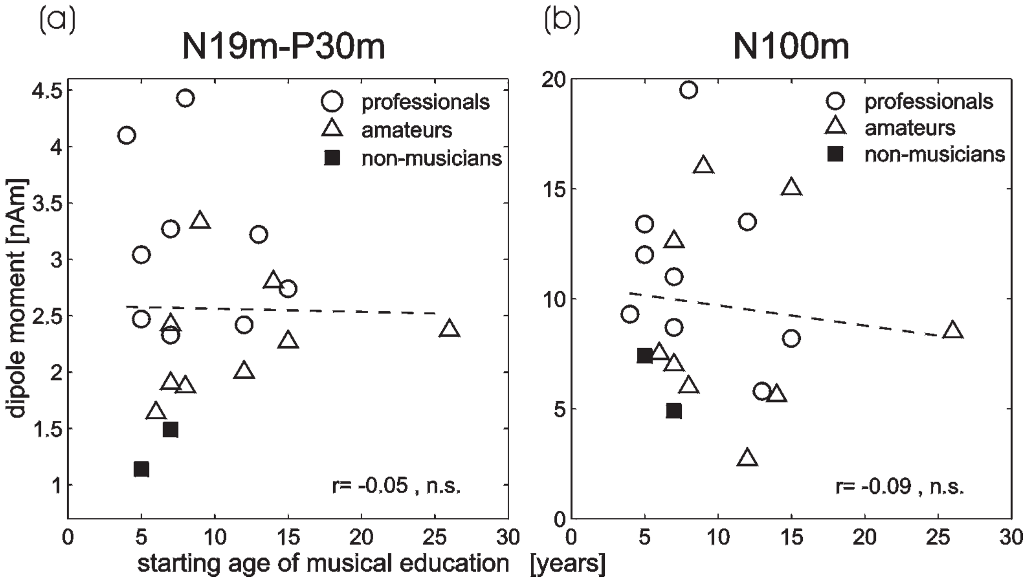


Figure 4.9: *21 of the 27 subjects including also some non-musicians underwent continuous musical education for at least 5 years. No correlation was found between the N19m-P30m dipole amplitude and the age, when musical education started ($r = -0.021$, n.s).*

4.5.2 Modulation

The stimuli were not static sinusoidal tones but modulated with a low frequency of about 30 Hz, and this could be musically more interesting than static tones. In order to check if the modulation of the pure tones had some influence on the difference between musicians and non-musicians, we repeated the investigation with unmodulated sinusoidal tones in a subgroup of 19 subjects. The temporal resolution in this case was much worse due to the reduced signal to noise ratio resulting from the lower number of averages, but it was still possible to isolate the peak-to-peak N19m-P30m dipole amplitude. The increase of the N19m-P30m component in musicians as compared to non-musicians was 79%, again the increase of the N100m response was again much weaker (on average 20%, n.s.) compared to the primary component. (see Fig.4.10). The tonal music aptitude correlated again with the N19m-P30m peak-to-peak dipole amplitude ($r = 0.49$, $p = 0.01$) but not with the N100m dipole amplitude ($r = 0.19$, n.s.), as can be seen in Fig.4.11.

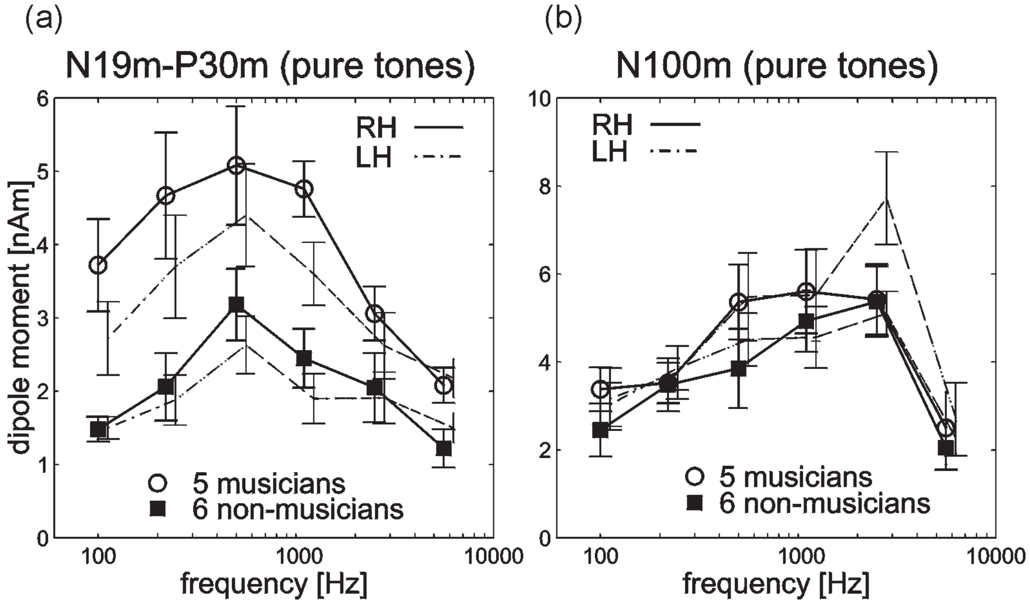


Figure 4.10: *Using pure tones, the results were similar to those of the condition with modulated tones. The increase of the N19m-P30m component for musicians as compared to non-musicians was 79% (a), the increase for the N100m was on average 20%, n.s. (b).*

Overall, the differences to the results of the modulated tones were marginal both for the early and late components.

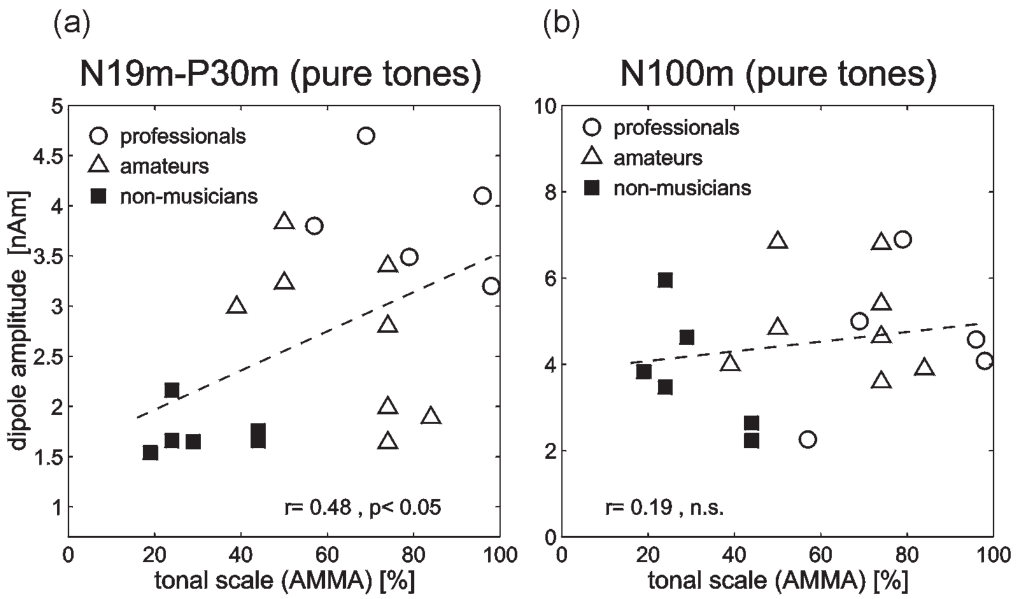


Figure 4.11: *Using pure tones, the tonal score of the AMMA test correlated again with the peak-to-peak dipole amplitude of the N19m-P30m (a) and not with the N100m amplitude (b).*

4.5.3 Attention

In the main study the evoked magnetic field was measured while the subjects were watching a silent movie. In a subgroup of seven subjects the measurements were repeated with attention directed towards the stimuli and without watching a video. In this case the amplitude of the N100m dipole moment was indeed increased considerably (on average by 65%, Fig.2.14) in agreement with studies on selective attention in the human auditory cortex (Woldorff and Hillyard, 1987), whereas there was no significant effect on the primary N19m-P30m component (see Fig.4.12).

4.5.4 Replicability

In one subject the measurement was repeated seven times within a half year to check for reliability. It could be expected, that the subjective constitution, the vigilance or other influences might change not only the N100m magnitude as seen in the case of varied attention (see the previous chapter), but also the primary component. The resulting seven different source waveforms, identically calculated in one fixed condition (the 500 Hz tone) are overplotted in Fig.4.13 for the right and the left hemisphere.

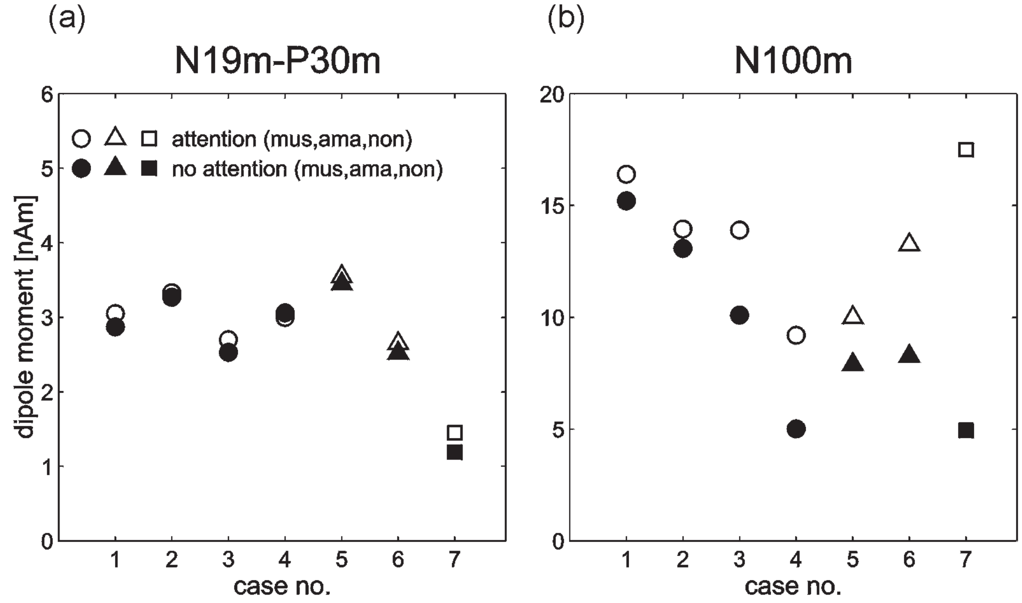


Figure 4.12: *In a subgroup of seven subjects the measurements were repeated with attention directed towards the stimuli. The conditions 'attention' (white symbols) and 'no attention' (black symbols) were opposed for the seven subjects. In contrast to the N100m magnitude, the primary N19m-P30m component could not be significantly increased by attention.*

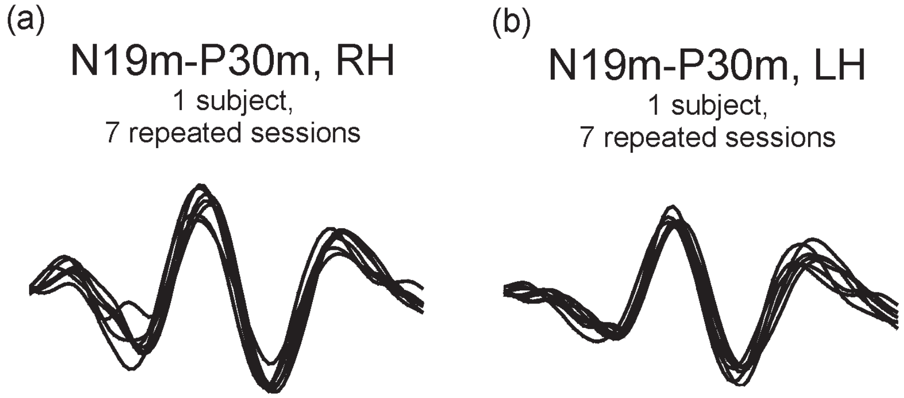


Figure 4.13: *Seven repeated measurement were carried out in one subject within a half year to check for reliability. The resulting seven different N19m-P30m source waveforms, calculated in the same way and in the same condition (500 Hz tone) at the same point in the Heschl´s gyrus (see chapter three, Fig.3.12a), were overplotted. (a) depicts the overplot of the source waveforms calculated in the right hemisphere and (b) the overplot of the source waveforms of the left hemisphere. As can be seen there was no significant difference although the test subject had unintentionally fallen asleep in one session.*

Both the magnitude and timing of the primary N19m-P30m response remained substantially unchanged for all seven measurements. This early component seems to occur automatically and reflects only the objective qualities of the signal, as for example its frequency, and was therefore highly reproducible.

4.6 Discussion

Coming back to the observation of Helmholtz that a "*musically trained observer has an essential advantage over one not so trained in his power to figuring to himself how tones ought to sound*", we see that indeed there is a striking difference between musicians and non-musicians not only on the level of apperception (cf. Helmholtz, 1863), but also at the sensory level.

N19m-P30m response

The strength of the primary signal completely separated the group of musicians from the non-musicians and correlates strongly with the tonal music aptitude as determined by the standardized AMMA test by Gordon. This difference raises an obvious question: are subjects with large primary signals musical because of the large signal or are the large signals an effect of musical training ?

The presented additional tests indicate that musical training is not a major factor responsible for the difference of neuronal activity at the primary level between musicians and non-musicians:

- The N19m-P30m dipole amplitudes of the sinusoidal tones did not correlate with the age when musical training started (Fig 4.9). The starting age of musical training does not allow direct conclusions on the intensity which is difficult to assess. But an early starting age does mostly imply an environmental background with strong exposure to music.

- We have observed no effect of attention on the primary N19m-P30m component. In particular, when non-musicians were asked to listen very attentively to the signals, the primary responses were not increased. This is in agreement with Woldorff and Hillyard (1987) who demonstrated in a study on selective attention that the N19m amplitude remained completely unchanged and the P30m amplitude was only slightly modified. However, Recanzone et al. (1993) reported, that attention can modify the tonotopic organization of the primary auditory area (suggesting plasticity).

- The effect is strong for sinusoidal tones although sinusoidal tones are not specific for music. They are likewise important as components of speech, and it is implausible that speech training could cause a difference between musicians and non-musicians since everyone is exposed to speech in earliest childhood.

The individual primary N19m-P30m responses showed a stable magnitude, if the stimulus was the same (see Fig. 4.13). Neither attention nor musical training had an effect on its magnitude. It reflects only the objective qualities of the signal, as for example its frequency, and is therefore highly reproducible if the signal is the same.

N100m response

In contrast, there exist reasons to assume that the secondary N100m component can be modified by musical training:

- Pantev et al. (1998) reported a significant correlation between the mean N100m dipole moment and the age where musical training started.
- We observed a clear effect of attention on the N100m dipole amplitude except for two musicians who were probably unable to attenuate their attention while watching a video. This is consistent with Woldorff and Hillyard (1987) who showed that the N100m dipole amplitude was considerably enlarged by selective attention.

Conclusions

However, Gordon pointed out that there is a difference between three stages of music aptitude: 1) the music aptitude stage at birth, 2) the developmental music aptitude stage from birth to age nine, and 3) the stabilized music aptitude stage (from about age nine on). Accordingly, we might conclude on the basis of our results what Gordon (1989) reportet from the music aptitude tests:

- *“From birth to age nine, one is in the developmental music aptitude stage, where the music aptitude can develop. The younger a child is, the more and the more quickly music aptitude will increase.*

- *From age nine on, one is in the stabilized music aptitude stage: The level of musical aptitude at the age of nine remains ostensibly the same throughout life. That should not be interpreted to mean that after age nine one cannot learn music. What it does mean is that one can be expected to reach in music achievement a level no higher than that at which the potential (music aptitude) to achieve has stabilized.*
- *However, the music aptitude will never reach a higher level than that with which one was born. There is reason to believe that, because of a lack of understanding of how to measure the music aptitude of a newborn child, the level of innate music aptitude the neonate possesses begins to decrease shortly after birth. Possibly as a result, it seems, that none of us has developed the music aptitude to its highest possible level".*

This suggests, that the development of music aptitude depends on both genetic and nongenetic influences, whereas nongenetic influenceshave been reported mostly from the earliest youth. Schlaug et al. (1995) supposed that prenatal factors are likely to play a role in the generation of morphologic differences and plasticity. It remains unclear whether the anatomy may also be susceptible to some postnatal plastic change. In a recent study on heredity of perfect pitch, Baharloo, S. (1998, 2000) found that both early musical training and genetic predisposition are needed for the development of perfect pitch implying a high degree of musical aptitude (see Fig.3.2).

Our results have shown that the music aptitude correlates strongly with the neuronal activity at the earliest stage of processing in the primary auditory cortex. It may be interpreted as neurophysiological support for the hypothesis of a predominant genetic predisposition of musical aptitude proposed by Gordon (1987). It is unclear and an interesting topic of further studies, to which degree genetic and nongenetic influences contribute to the strong signal in the primary auditory cortex of musicians.

Chapter 5

Tonotopic organization

5.1 Introduction

Tonotopy is a general principle of functional organization of the auditory system. It arises in the cochlea and is maintained along the central auditory pathway, up to the primary auditory cortex (Merzenich et al., 1977). It reflects a topographical arrangement of frequency specific neurons.

Pantev et al. (1995) found evidence for two tonotopic areas within the human auditory cortex showing a mirrored tonotopic organization. The first tonotopic map, derived from a middle latency P30m-P50m pattern, located in the primary auditory cortex (AI) and showed a logarithmic tonotopic organization with the lower frequencies more medial (2.2 mm/octave). The N100 map was found posterior to the Heschl´s gyrus in the planum temporale showing a mirrored tonotopic organization with the lower frequencies more lateral (c.f. chapter 2.2).

From an investigation on the tonotopicity of the magnetic fields evoked by sinusoidal tones we foundthat

1. Similar to Pantev et al. (1995), a mirrored tonotopic organization of two tonotopic areas was observed in the human auditory cortex. However, our results indicate the opposite directions and are in agreement with Romani et al. (1982).

2. The early source activity of the primary auditory cortex revealed a strong logarithmic tonotopic organization (the lower frequencies more lateral, on average 2.3 mm/octave); the late source activity at 100 ms revealed a mirror-imaged tonotopic map (the lower frequencies more medial, on average 1.45 mm/octave), located in the planum temporale.

3. A significant correlation of tonotopicity with the music aptitude was not found.

5.1.1 Tonotopic organization in animals

In cats (Woolsey, 1971; Merzenich et al., 1975; Schreiner et al., 1991), squirrels (Merzenich et al., 1976) and monkeys (Merzenich and Brugge, 1973; Morel et al., 1993; Rauschecker et al., 1995) microelectrode recordings have been used to explore the tonotopic organization within the auditory cortex. Importantly, adjacent frequency maps in primary (AI) and secondary (R) auditory areas are organized in opposing directions, such that high-to-low frequencies are mapped posterior-anteriorly in AI and anterior-posteriorly in R (Morel et al., 1993). Much or all of the core area of the primate auditory cortex was considered to be the classical primary auditory field AI. However, recent studies in macaques have revealed that the core contains three cochleotopically organized fields (Kaas et al., 1999, see chapter two, Fig.2.1a). In AI, the largest, most caudal field of the core area, low-to-high frequencies are mapped anterior-laterally to posterior-medially, whereas the rostral core field (R) shows a posterior-to anterior representation of low-to-high frequencies according the results of Merzenich and Brugge (1973) and Morel et al. (1993). The rostrotemporal field (RT) was described as third field in the core area, the smallest, most rostral field showing that low-to-high frequencies are mapped again reversed to R. Kaas et al., 1999 reported that the three core fields project to a narrow surrounding belt area comprising approximately seven fields, at least four of which exhibit cochleotopic organization (see chapter two, Fig. 2.1a). In the auditory cortex of the rhesus monkey, Rauschecker et al. (1997) observed that spectral processing is carried out in parallel across subareas of the core and serially from the core to the belt.

5.1.2 Tonotopic organization in humans

Romani et al. (1982) performed neuromagnetic studies, using one SQUID sensor but multiple measurement sites, indicating the existence of an orderly projection of frequencies onto the human auditory cortex: auditory evoked steady-state fields evoked by amplitude modulated (32 Hz) sinusoidal tones with different carrier frequencies showed that the human auditory cortex was tonotopically organized with the lower frequencies more lateral. In two subjects, the progression was found to be a linear function of the logarithm of frequency with a relative distance of 3.5 mm /octave, corresponding a depth gradient of 2.3 mm/octave. The findings of Romani et al. (1982) are the first proof that the tonotopic organization of the cochlea (von Bekesy, 1960) is maintained at the level of auditory cortex in humans.

5.1.3 Tonotopic organization of AI

Lauter et al. (1985) used subtraction PET methods to examine the tonotopic organization of the human auditory cortex. With monaural stimulation of two pure-tone frequencies, 500 and 4000 Hz, Lauter et al. demonstrated a posterior-medial to anterior-lateral mapping of high-to-low frequencies within the human primary auditory cortex, consistent with the findings of Romani et al. (1982). These findings are also in agreement with Ottaviani et al. (1997) who used single photon emission computer tomography (SPECT) and several fMRI studies (Wessinger et al. 1997, Strainer et al. 1997, Lantos et al., 1997). However, Wessinger et al. (1997) showed a more orderly topographic organization in the left auditory cortex than in the right. Howard et al. (1996) demonstrated tonotopic organization in the human medial Heschl´s gyrus directly with single-unit recordings from a surgically implanted depth electrode with the lower frequencies more lateral.

5.1.4 Frequency dependence

Frequency-dependent information concerning middle latency responses is limited (Scherg and Volk, 1983; Scherg et al.,1989; Rupp et al., 2000).

The tonotopic progression of the N100m component is not described consistently in the literature. At least three different statements about the tonotopicity of the N100m component are published:

Anterior shift towards lower frequencies

Elberling et al. (1982) used the SQUID technique to investigate the tonotopic organization of the late auditory evoked source activity from the right hemisphere of the human brain. They observed for N100m an anterior shift in dipole location towards lower frequencies (3mm / octave).

Anterior shift towards higher frequencies

Bertrand et al (1988, 1991) analysed both sequential scalp potential and scalp current density maps and showed that the N100 maximum shifted in the anterior direction with higher stimulus frequencies. Consistent with these findings, Woods et al. (1991, 1993) and Näätänen et al. (1992) showed that the scalp maxima for higher tones were anterior compared to those for lower tones, thus implying a tonotopic organization of auditory cortex. Langner et al. (1997) reported an orthogonal arrangement of tonotopic and periodotopic gradients using pure versus complex tones, mainly observed in the sagittal plane perpendicular to the mediolateral axis. In the case of sinusoidal tones, the N100 component elicited in most subjects a shift from superior-posterior to inferior-anterior towards higher frequencies with an average gradient of 7.1 mm/octave.

Mapping on the mediolateral axis

Pantev et al. (1988) reported that the depth estimated for the generator site of the N100m component shows a logarithmic dependence on test frequency. Pantev found a logarithmic mapping with the lower frequencies more lateral, with a difference in depth of about 2.2 mm/octave (see his fig.6), in agreement with Romani et al. (1982a) despite the fact, that he used a different stimulus paradigm. In 1989, Pantev et al. replicated a depth gradient of about 2.4 mm/octave. Using neuromagnetic methods, Yamamoto et al. (1988, 1992) localized the N100m response in the primary auditory cortex, with source position calculated to shift medially as stimulus frequency increased. Tiitinen et al. (1993) corroborated the finding from Pantev et al. (1988) and Yamamoto et al. (1992) and suggested that the auditory N100m response is generated in tonotopically organized auditory cortex. Cansino et al. (1994) found that the magnetic source image for the N100m component exhibits a similar tonotopic mediolateral progression as reported by Romani et al. (1982), which lies about 1 cm more posterior to that of the steady-state response (Pelizzone et al., 1984). In a single case study, Lütkenhöner and Steinsträter (1998) demonstrate that the peak N100m arises from the planum temporale.

Roberts and Poeppel (1996) failed to resolve spatial tonotopy for the N100m component. Arlinger et al. (1982) and Tuomisto et al. (1983) revealed no significant shift in the location of the source of the N100 component when the stimulus frequency was changed.

5.1.5 Identification of multiple tonotopic fields

Pantev et al. (1995) used inverse modeling of both magnetic and electric scalp recordings to provide evidence for two tonotopic areas within the human auditory cortex showing mirrored tonotopic organization; one area, believed to be the source of N100 wave, exhibited higher frequencies at progressively deeper locations, while the second area, believed to be the source of the P30 wave, exhibited higher frequencies at progressively more superficial locations.

The P30 map was located in the primary auditory cortex anterior to the N100 mirror map.

5.1.6 Questions

The findings of Pantev et al (1995) show clearly the existence of at least two tonotopic fields in the human auditory cortex. The first tonotopic area was located in the primary auditory cortex in the medial aspect of Heschl´s gyrus (Braak, 1978; Rademacher, 1993). The second tonotopic area was found posterior to the Heschl´s gyrus in the planum temporale (Pantev et al. 1995). Intracranial studies by Liégeois-Chauvel (1991) showed that the middle latency responses originate in the primary auditory cortex, whereas the N100m wave was found to originate in the planum temporale posterior to the Heschl´s gyrus (Lütkenhöner and Steinsträter, 1998; Liégeois-Chauvel, 1994; Pantev et al., 1995). However, two puzzling facts remain unanswered:

1. The gradient of the tonotopic progression of the P30m component in the primary auditory cortex as reported by Pantev et al. (1995) had the reversed sign in further investigations on the tonotopic organization of especially the primary auditory cortex (Lauter et al., 1985; Howard et al., 1996; Wessinger et al., 1997; Strainer et al., 1997)
2. The N100m component exhibits a perplexing view of its tonotopic progression: we could summarize at least four different statements about its tonotopic organization.

Therefore, we investigated in a first step the tonotopic organization of our subjects independent of their music aptitude. In a second step we asked if the tonotopic organization is different for musicians as compared to non-musicians.

5.2 Tonotopic organization: Results

5.2.1 Evidence from the fitting technique

One equivalent dipole in each hemisphere was fitted without constraints to the N19m-P30m peak-to-peak interval of the N19m-P30m response and to the N100m peak, respectively. The solution, calculated with BESA in the head coordinate system, was transformed into the x_{HG}-coordinates of the individual HG-system for the N19m-P30m response (resp. PT-system for the N100m response). In Fig. 5.1 the x_{HG}-coordinate (resp. x_{PT}-coordinate) is depicted versus the frequency on a logarithmic scale, averaged over all 23 of our 27 subjects, from which a structural MRI could be obtained. For the N19m-P30m response the unconstrained fit revealed a strong tonotopic gradient along the x-axis of the HG-system (relative distance: -1.9 mm/octave) with the lower frequencies more lateral (freq: $F(5, 110) = 26.6$, $p < 0.0001$). For the N100m response a small not monoton tonotopic gradient was found (0.6 mm/octave, freq: $F(5, 110) = 6.0$, $p < 0.05$).

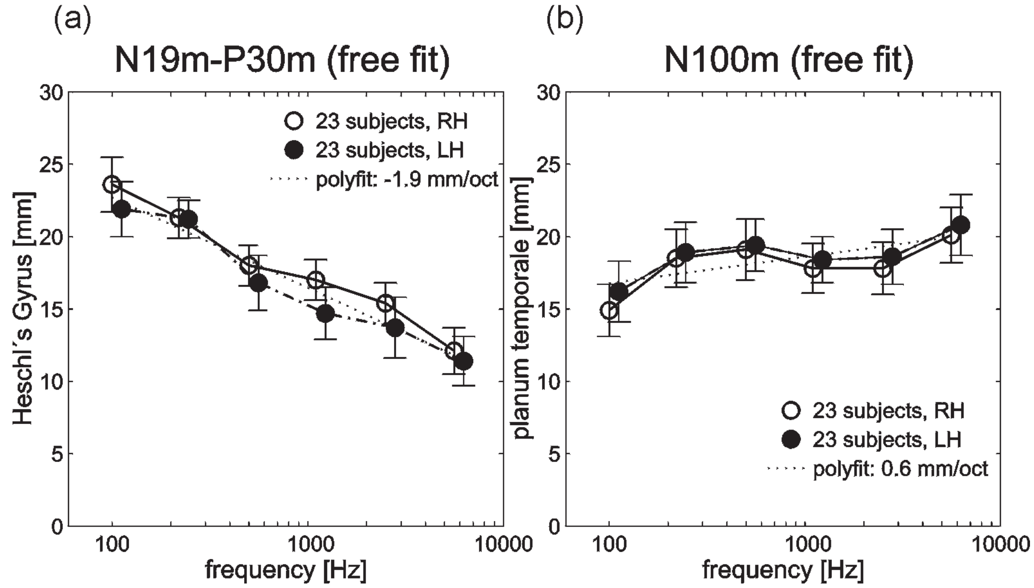


Figure 5.1: *Frequency dependent mapping in two different areas of the human auditory cortex, revealed with the fitting technique. A strong logarithmic tonotopic mapping of the N19m-P30m response, can be seen from the fitting technique (a). The tonotopic gradient was -1.9 mm/octave. Using the fitting technique, the progression of the N100m map remains rather unclear (b).*

A tonotopic gradient perpendicular to the individual HG-axis resp. PT-axis was not found (see Fig.3.10 and Fig.3.11). Therefore it was evident that the progression mapped only parallel to the Heschl´s gyrus.

5.2.2 Evidence from the seeding technique

For more robust estimation of the mediolateral dipole localization we used the set of 30 adjacent dipoles in each hemisphere described in chapter 3.6. In the opposite hemisphere two equivalent dipoles with orthogonal orientation, e.g. a regional source, was seeded to a fixed point in the center of the opposite Heschl´s gyrus resp. planum temporale (see chapter three, Fig.3.12). This was done to avoid influences due to the dipole source activity in the opposite hemisphere. Now only the orientation of the 30 adjacent dipoles was fitted to the N19m-P30m peak-to-peak interval (to the N100m peak, resp., see chapter three, Fig.3.9) with one diploe active at a time. The dipole solution with minimal residual variance could be extracted unequivocally for one of the 30 dipoles (the minimal residual variance plotted against the location of the 30 dipoles on the HG-axis can be described as a peak with one unequivocal maximum). This location on the individual Heschl´s gyrus was estimated to be the location of the source activity. For each condition this location was mapped against the logarithm of the frequency and averaged over the 23 subjects (see Fig.5.2).

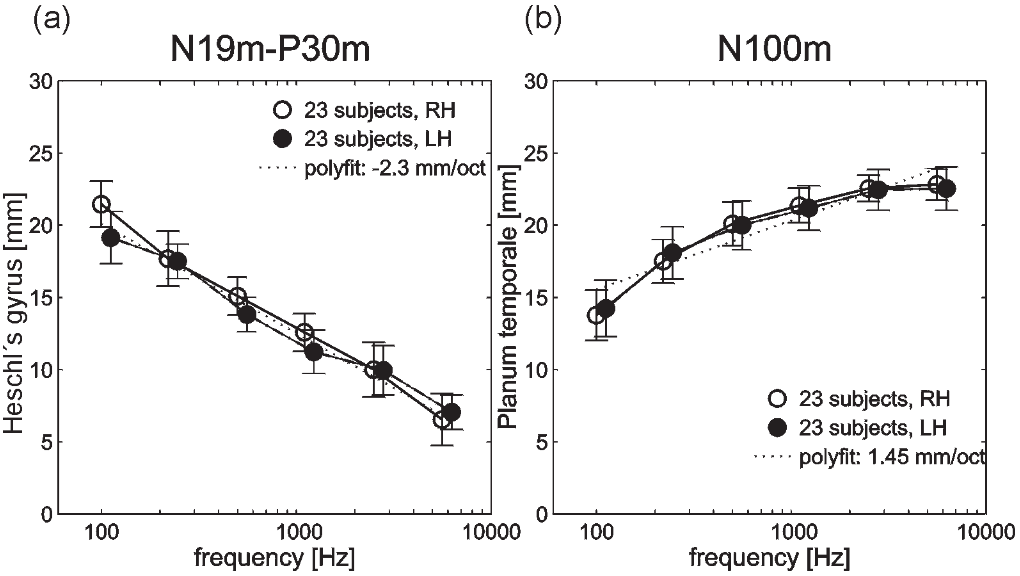


Figure 5.2: *The seeding technique revealed a frequency dependent mapping in two different areas of the human auditory cortex. (a) depicts the strong logarithmic tonotopic mapping of the N19m-P30m response along the medial portion of Heschl´s gyrus, (b) the nearly logarithmic mirror-imaged tonotopic mapping of the N100m response in the planum temporale.*

For the N19m-P30m response, the seeding technique revealed nearly the same tonotopic gradient (2.3 mm/octave; lower frequencies more lateral) as reported in the free fit case. As expected from the previous investigation on the dipole magnitude the seeding technique reduced the variance considerably and improved linearity on the logarithmic frequency scale. Therefore the frequency dependence (freq: $F(5, 110) = 64.3$, $p < 0.0001$) was even stronger as seen from the fitting technique.

For the N100m response, the seeding technique revealed a strong tonotopic gradient (1.45 mm/octave; freq: $F(5,110) = 52.9$, $p < 0.0001$), which had indeed the opposite direction with the lower frequencies more medial.

The tonotopic organization of the primary source activity was not investigated with unmodulated sinusoidal tones due to the large superposition of the P50m response.

5.2.3 Hemispheric asymmetries in tonotopy

The tonotopic organization showed no significant left-right asymmetry for both the early and the late source activity (see Fig.5.1; Fig.5.2).

5.2.4 Musicians versus non-musicians

As depicted in Fig.5.3., the tonotopic organization showed no significant differences in professional musicians, amateur musicians and non-musicians for both the N19m-P30m response (group: $F(2,20) = 1.1$, n.s.) and the N100m response (group: $F(2,20) = 0.9$, n.s.). We did not find a significant correlation between the music aptitude and any parameter of the tonotopic organization.

5.2.5 Latency and dipole orientation

To a certain extent the tonotopic mapping was reflected in the frequency dependence of the latency (e.g. time from stimulus onset to peak) of the P30m peak and N100m peak (see Fig.5.4). As can seen in Fig.5.4a, the P30m peak occured at 37 ms if the carrier frequency was 100 Hz, at 30 ms, if the carrier frequency was around 1000 Hz and at 27 ms if the carrier frequency was 5600 Hz. Here, a parallelism to the running time of the traveling wave in the cochlea is obvious, which averages about 10 ms from the helicotrema to the apex.

The N100m peak occured at 110 ms if the carrier frequency was 100 Hz, at 100 ms if the carrier frequency was around 1000 Hz, and at around 90 ms if the carrier frequency was 3000 Hz. Roberts and Poeppel (1996) reported a minimum N100 latency occurring at approximately 1000 Hz and a systematic latency increase towards the higher and the lower frequencies.

The frequency dependence of the latency showed a strong logarithmic slope for the N19m-P30m response, which may reflect the exponential increase of the traveling wave velocity in the cochlea.

The yz-orientation of the fitted dipoles again showed an almost logarithmic frequency-dependence (see Fig.5.5). In spite of a large inter-individual

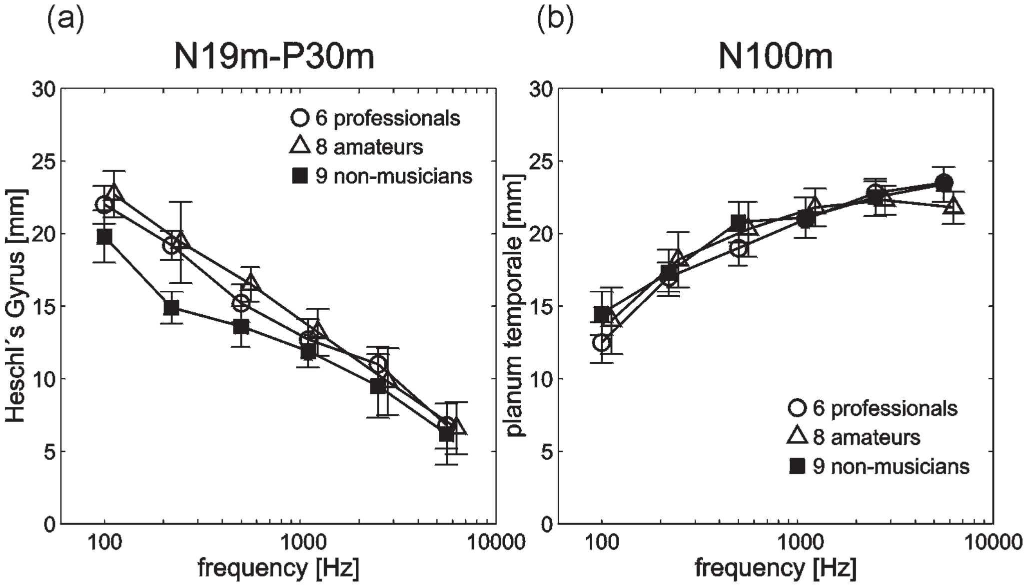


Figure 5.3: *Frequency dependent mapping in two different areas of the human auditory cortex, revealed with the seeding technique and subdivided into the groups of professional musicians, amateur musicians and non-musicians. The tonotopic organization was comparable in all groups.*

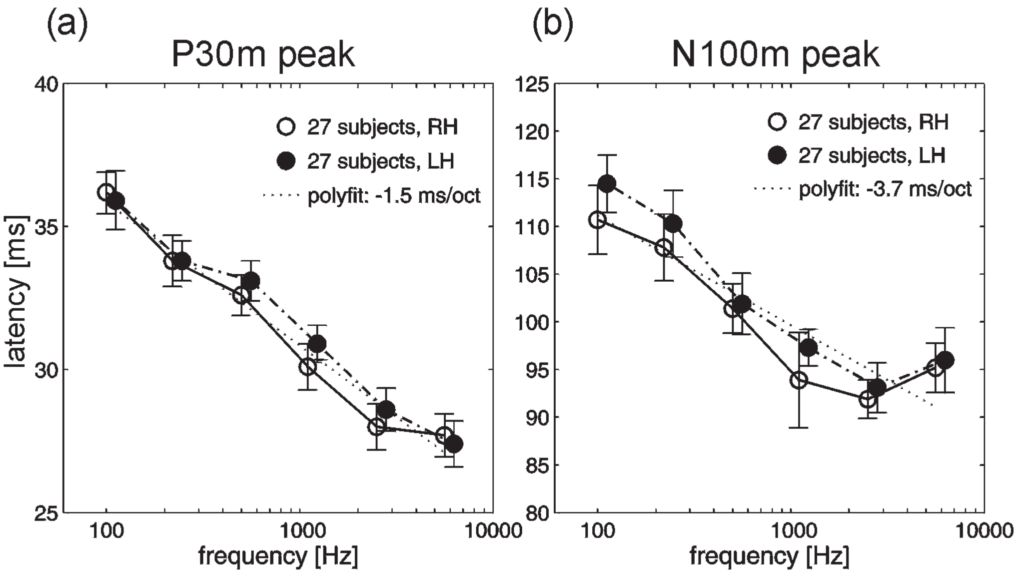


Figure 5.4: *The latency of the P30m and N100m peak was strongly frequency-dependent.*

variance, the yz-orientation of the fitted dipoles in the sagittal plane showed a decay of about 4°/octave towards the higher frequencies. Such a frequency-dependent orientation, reported also by Bertrand et al. (1991) and Rosburg et al (1999) in the left hemisphere, may be due to the location of the tonotopic maps on the folded surface of the supratemporal plane. The interhemispheric differences of the frequency dependence reported by Rosburg et al. (1999) could not be verified in our investigation (see Fig.5.5).

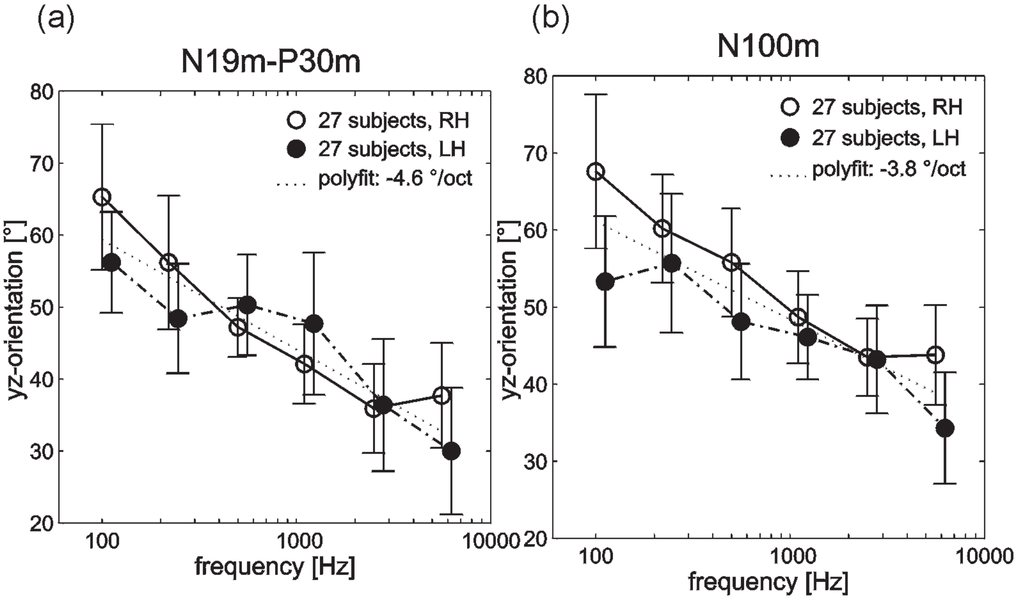


Figure 5.5: *The yz-orientation of the N19m-P30m and N100m component was also frequency-dependent.*

5.3 Discussion

Our results confirmed the existence of at least two tonotopic fields in the human auditory cortex as reported by Pantev et al. (1995). Furthermore in agreement with Pantev et al. (1995) were the following six findings:

1. The main tonotopic gradient for both tonotopic fields was found along the mediolateral axis;
2. The first tonotopic area was located in the medial portion of the Heschl´s gyrus, known as primary auditory cortex whereas the second tonotopic area was located posterior to the Heschl´s gyrus in the planum temporale;

3. The N19m-P30 map was located in the primary auditory cortex;
4. The N100m map was mirrored to the N19m-P30m map;
5. The tonotopic progression can be described as a logarithmic mapping;
6. The tonotopic field along the Heschl´s gyrus showed a constant progression of about 2.3 mm/octave

In contrast to Pantev et al. (1995), in our investigation the sign of the tonotopic gradient is found to be reversed for both the N19m-P30m map and the N100m map: the N19m-P30m map showed a tonotopic organization with the lower frequencies more lateral whereas the N100m map showed a tonotopic organization with the lower frequencies more medial.

The tonotopic gradient for the N100m response was 1.45 mm/octave and therefore considerable smaller as reported by Langner et al (1997), who found a relative distance of 5-7 mm/octave.

The noticeable difference to the direction of the tonotopic gradient requires a detailed discussion carried out in the following, at first for the N19m-P30m response and subsequently for the N100m response.

N19m-P30m response

Pantev et al. (1996) investigated the tonotopic organization of the 40 Hz auditory steady state field (SSF), elicited when tone pulses were presented at a repetition rate of 40 Hz. They found that the tonotopic organization of the SSF was reversed to the tonotopic organization of the P30m response reported in a previous investigation (Pantev et al., 1995). The tonotopic gradient reported by Romani et al. (1982) using amplitude modulated tones with a modulation frequency of 30 Hz was the same as Pantev´s 40 Hz SSF but opposite to his P30m response. Therefore, Pantev et al. (1996) concluded that the results of Romani et al. (1982) would call into question the view that auditory SSFs consist of summarized middle latency responses occurring at about 20–50 ms following transient stimulation.

However, the following two findings suggest that the tonotopic organization of the 40 Hz auditory SSF and the N19m-P30m response relates to the same neuronal substrate:

1. Several neuromagnetic studies clearly demonstrate, that the SSF results mainly from a superposition of middle latency responses (Galambos et al., 1981; Hari et al., 1989; Gutschalk et al., 1999).

2. SSF sources could not be spatially differentiated from P30m sources and therefore seem to be generated within the same tonotopic organized field in the primary auditory cortex (Pantev et al., 1993).

The investigation of both the tonotopic organization of the transient middle latency responses (Scherg et al., 1989), 30 Hz amplitude modulated tones (Romani et al., 1982) and 40 Hz SSFs (Pantev et al., 1996) as well as our results for the modulated tones corroborate the hypothesis that the tonotopic gradient for the middle latency responses, observed as transient or as steady-state responses, was always the same with the lower frequencies more lateral. The inconsistency of the reversed P30 map reported by Pantev et al. (1995) probably was due to an incomplete isolation of the P30m responses, superposed with the P50m response particularly at the higher frequencies (cf. Pantev 1995, Fig.5).

Moreover, there was evidence from further investigations using PET (Lauter et al., 1985), SPECT (Ottaviani et al., 1997), fMRI (Wessinger et al., 1997; Strainer et al., 1997; Lantos et al., 1997) and microelectrodes (Howard et al., 1996), that the mediolateral tonotopic organization with the lower frequencies more lateral appears to be a general feature of the primary auditory cortex.

N100m response

In analogy to the previous investigation, the situation was more subtle for the N100m component. The existing diversity of statements about the tonotopic progression of the auditory evoked N100(m) made it rather difficult to analyze the facts. However, there was converging evidence, that multiple areas are involved in the generation of the N100m as suggested by Scherg (1985), Näätänen et al., 1987, scherg et al., 1989, Liégeois-Chauvel (1994), Lütkenhöner and Steinsträter (1998) as well as Gutschalk et al. (1998). Nevertheless, the localization of the N100m peak was focused predominantly on an area lying about 10 mm posterior (Lütkenhöner and Steinsträter, 1998; Pelizzone et al.,1984, Cansino et al., 1994 and Pantev et al., 1995) and at least 10 mm laterally to the primary auditory cortex (Liégeois-Chauvel, 1994; Gutschalk et al., 1998). In this area the principal component of the N100m field seemed to originate. If we assume that different areas contribute to the N100m field, it would be possible that the cumulative observed superposed tonotopic gradient may be extinguished. Indeed, Roberts and Poeppel (1996), Arlinger et al. (1982) and Tuomisto et al. (1983) failed to observe a tonotopic organization of the N100m response. The remaining fact, that a tonotopic organization would exist not at all for the N100m component, is rather implausible, because there was converging evidence in the literature, that the N100m response shows a strong tonotopic organization (Elberling et al., 1982; Pantev et al., 1988; Bertrand et al., 1991; Tiitinen et al., 1993; Cansino et al., 1994; Pantev et al., 1995; Lütkenhöner and Steinsträter, 1998).

The tonotopic gradient reported for the N100m component in the literature depends on the location. For example, Yamamoto et al., (1992) observed the N100m response in the primary auditory cortex and found there a tonotopic progression with the lower frequencies more lateral, known for this area.

With this background we seem able to explain our results. In our investigation we used two different techniques to observe the N100m response:

- The dipole sources were fitted without constraint. In this case, the observed tonotopic gradient was 0.6 mm/octave. This could be explained by the hypothesis of the existence of multiple areas contributing to the N100m response: the observed ambiguous tonotopic gradient would correspond to a cumulative tonotopic gradient which may be superposed bydifferent single field gradients.
- The dipoles were seeded in the planum temporale. In this case, the N100m response revealed a strong tonotopic map of especially this area mirrored to the progression in the primary auditory cortex with a relative distance of 1.45 mm/octave.

This difference between the fitting and the seeding method suggests the existence of multiple generators of the N100m response in different areas.

Comparison to other results

The reversed sign for the tonotopic P30m-P50m map and the N100m map reported by Pantev et al. (1995) may suggest that the underlying observed areas may not be the same. Indeed, the mediolateral position of the P30m-P50m map and the N100m map observed by Pantev et al. (1995) were different to ours: Pantev´s P30m-P50m map was situated more laterally as his N100m map (see Pantev et al., 1995, Fig.5) but our N19m-P30m map was situated 12 mm more medial as the N100m map.

The hypothesis, that the underlying areas were different may explain the reversed sign of the tonotopic gradient: Pantev et al. (1995), observed the areas 2) and 4) and we observed the areas 1) and 3) as depicted in Fig.5.6b. The tonotopic gradients then were all together consistent with the gradients

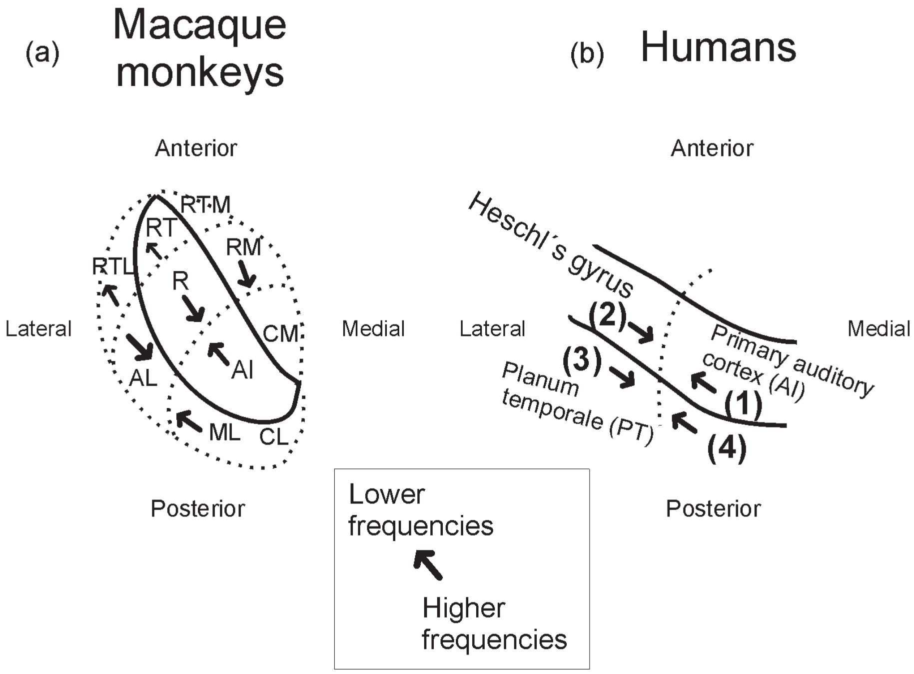


Figure 5.6: *(a) was adapted from Kaas et al. (1999) and Gutschalk et al. (1999), cf. Fig. 2.1. (b) includs the areas 1 to 4 in the human auditory cortex which have been described above. In our investigation were found the areas **1** and **3** , showing a reversed tonotopic gradient as in the areas **2** and **4** found by Pantev et al. (1995). The hypothesis, that the underlying areas were different, may explain the reversed sign of the tonotopic gradient.*

reported from animal studies (see Fig.5.6a). In this view we suggest that a separation of four different tonotopically organized areas in the human auditory cortex (marked as areas **1** to **4** in Fig.5.6b) could be possible in further studies.

Chapter 6

Summary and Outlook

In a magnetoencephalographic (MEG) study we have compared the processing of sinusoidal tones in the auditory cortex of nine professional musicians, nine amateur musicians and nine non-musicians. The frequency of the tones ranged from 100 to 5600 Hz. On average, the evoked source activity of the primary auditory cortex occurring at 19–30 ms was 87% larger for musicians as compared to non-musicians. The increase of the late secondary component at 100 ms was considerably smaller (30%) and at the limit of significance. The magnitude of the primary source activity correlated significantly ($r = 0.51$; $p < 0.01$) with musical aptitude, measured by the standardized Advanced Measure of Music Audiation test (AMMA). A correlation with starting age of musical education was not found. These results may be interpreted as neurophysiological support for the hypothesis of a predominant genetic predisposition of musical aptitude proposed by Gordon (1987). It is unclear and an interesting topic of further studies, to which degree genetic and environmental influences contribute to a strong signal in the primary auditory cortex.

The early source activity of the primary auditory cortex revealed a strong logarithmic tonotopic organization (the lower frequencies more superficial, on average 2.3 mm/octave). The late source activity at 100 ms revealed a mirror-imaged tonotopic map (the higher frequencies more superficial, on average 1.45 mm/octave), located in the planum temporale. A correlation with the musical aptitude was not found. The hypothesis, that multiple tonotopic fields are situated in the human auditory cortex and that the tonotopic organization would be mirrored in adjacent areas as known from animal studies, may explain that Pantev et al. (1995) reported a tonotopic gradient with reversed sign.

Our findings, with respect to both, the activation and tonotopic organization of the auditory cortex, supplement and extend the findings of Romani et al. (1982) and Pantev et al. (1995, 1998). However, our study was carried out with sinusoidal tones. It would be an interesting topic of further studies

1. to observe the subtle effects reported for the N100m component in a paradigm with experimental variation of selective attention;

2. to understand the large increase of 88% in musicians as compared to non-musicians found for the P50m component (cf. chapter 4.2); however it was difficult to isolate the P50m response from the P30m and the N100m response;

3. to analyze potential morphological differences of the Heschl´s gyri in musicians and non-musicians (cf. Appendix), mainly concerning a possible correlation of the fork bifurcation depth and the N19m-P30m dipole magnitude in the right hemisphere;

4. to investigate the processing of complex tones in musicians and non-musicians to define objective and subjective components of pitch perception independent of the restriction on sinusoidal tones. Pantev et al. (1989) found, that the tonotopic organization of the primary auditory cortex reflects the perceived pitch rather than the frequency of the stimulus. He showed that an incomplete complex tone with four adjacent harmonics of order 5 to 8 (as shown in Fig. 1.1c) and a sinusoidal at the missing findamental frequency of the complex tone would locate on the same place in the human auditory cortex. Contradictory findings were reported by Langner et al. (1997), who proposed an orthogonal mapping of frequency and periodicity in the human auditory cortex with a tonotopic gradient of 5-7 mm/octave, revealed by MEG. Therefore, it seems to be a challenge to clarify in detail the processing of incomplete and complete complex tones in musicians and non-musicians. A corresponding pilot study has already been started.

Appendix A

The individual structure of the auditory cortex is comparatively shown in a subgroup of 6 professional musicians, 6 amateur musicians and 6 non-musicians. For each subject, four different maps are joined together:

1. A sagittal view of the left sylvian fissure (left outside),
2. A top view on the left supratemporal plane (left center),
3. A top view on the right supratemporal plane (right center), and
4. A sagittal view of the right sylvian fissure (right outside).

The top view on the supratemporal plane shows always the Heschl´s gyrus in the full length. Therefore the view plane was tilted at around 25° downwards to the transversal plane of the head coordinate system into the direction of the individual Heschl´s gyri. This transformation was performed with the BrainVoyager program (Brain Innovation, Dr. R. Goebel). In some subjects a second Heschl´s gyrus exists posterior to the first (for example in P1, RH; P2, RH; P3, LH; P4, RH; A2, LH and RH). Moreover, in several subjects, the Heschl´s gyrus looks like a fork (P1, LH; P4, LH; P5, RH; A1, RH; A5, RH; N2, RH; N3, LH).

It would be an interesting topic of further studies to analyze the differences in detail, but here, a simple comparison of the MRI maps already shows two pronounced differences in musicians as compared to non-musicians:

- The point, were the Heschl´s gyri split up to a fork, is generally more medial in musicians, in particular in the right hemisphere.
- The medial portion of Heschl´s gyri is thicker in musicians.

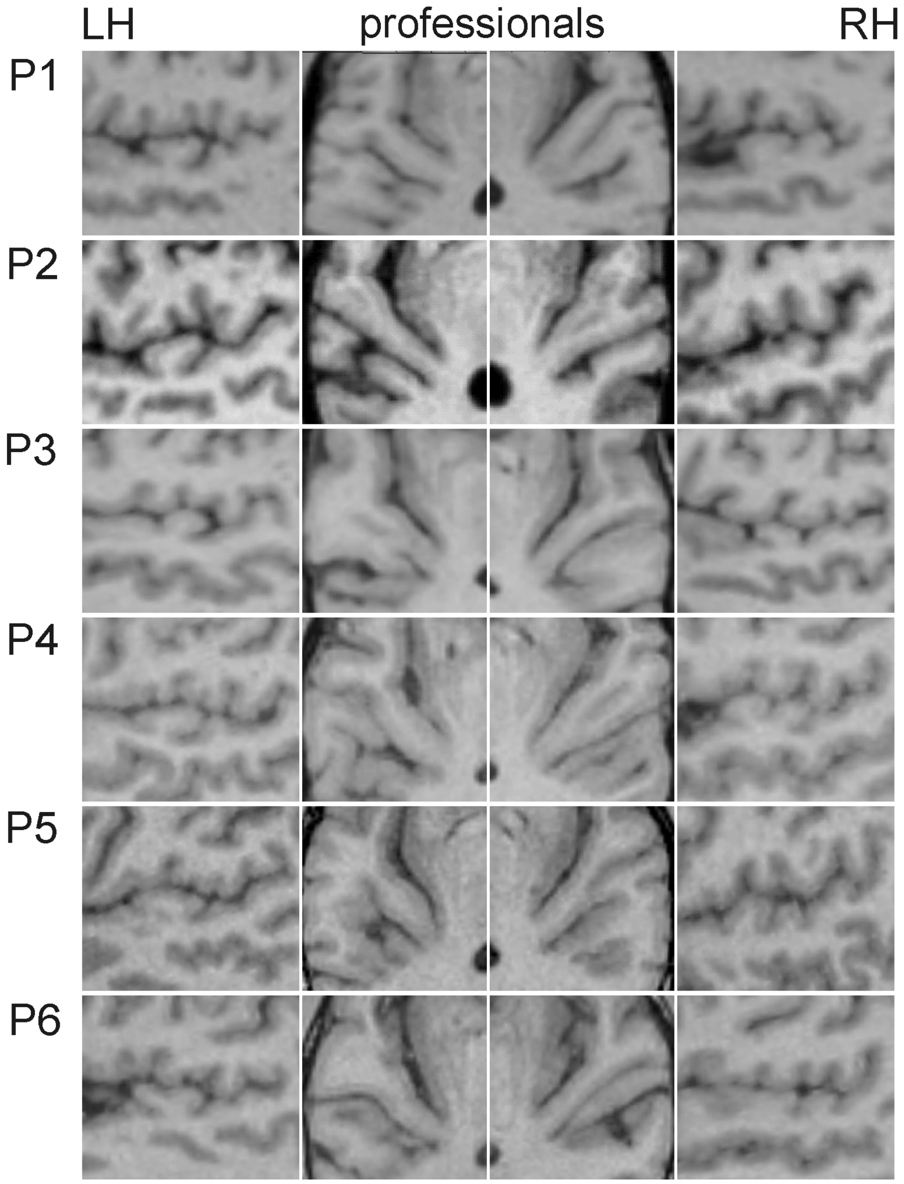


Figure 6.1: *MRI scans of the auditory cortex in 6 professional musicians.*

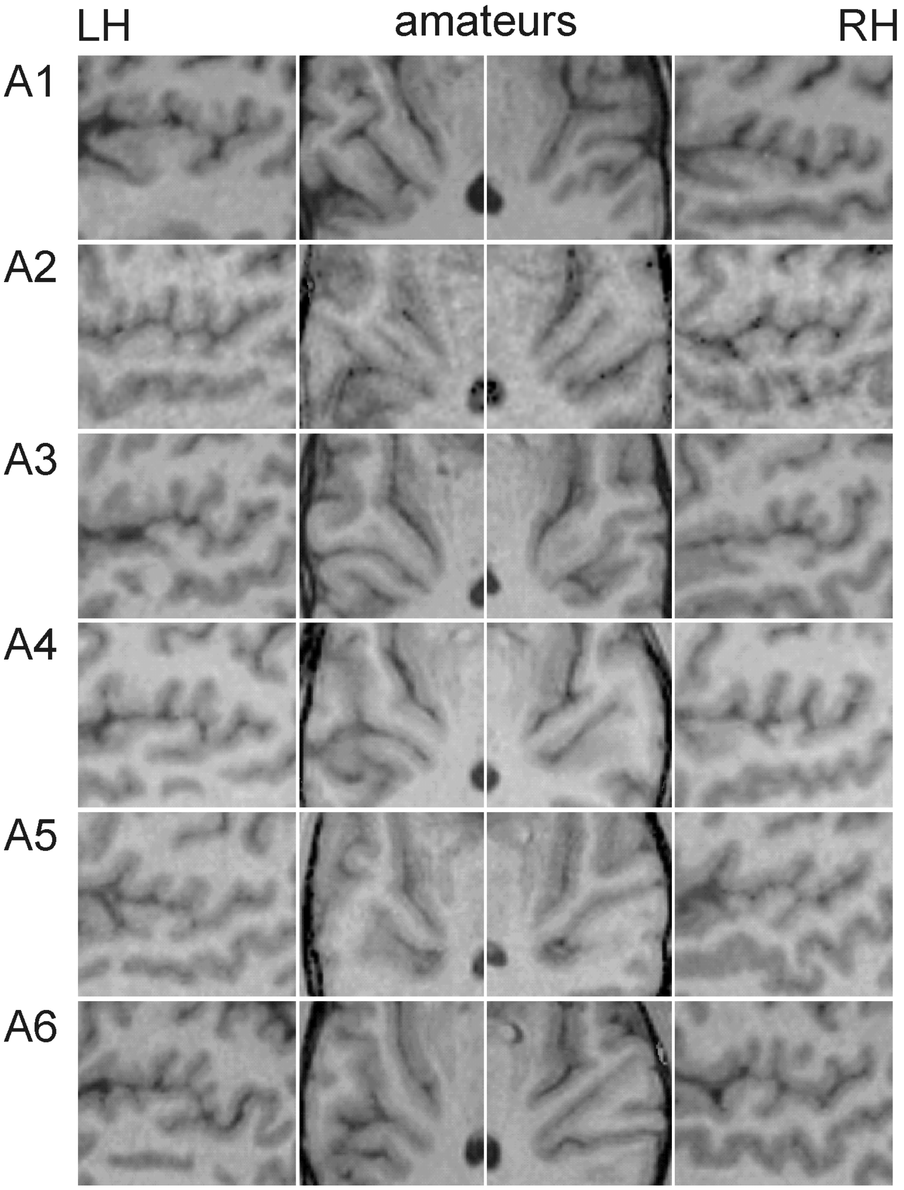


Figure 6.2: *MRI scans of the auditory cortex in 6 amateur musicians.*

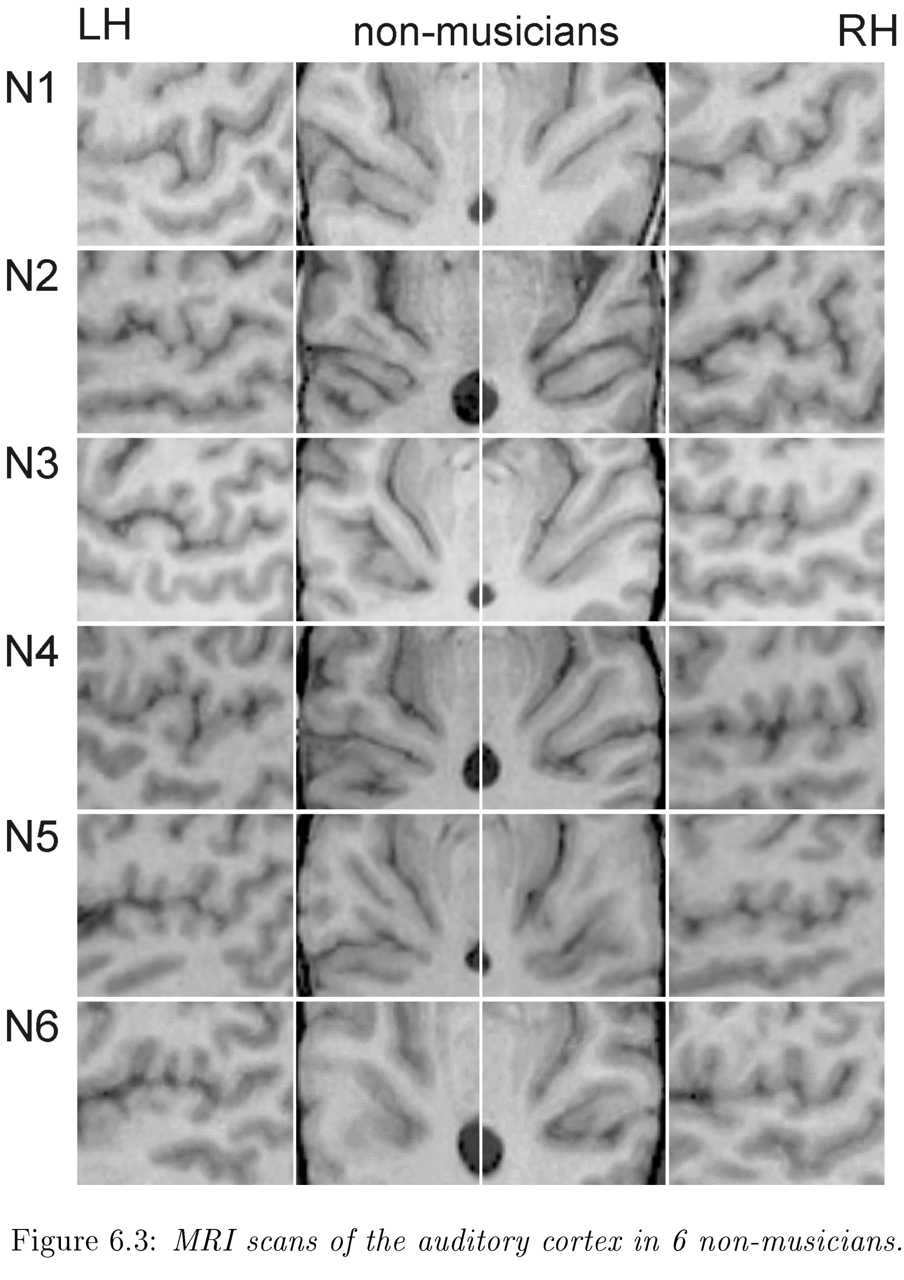


Figure 6.3: *MRI scans of the auditory cortex in 6 non-musicians.*

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