Attentional Modulation of Auditory Signal-in-Noise Processing

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Table of Contents

1 Zusammenfassung . . . . . 8

2 Introduction . . . . . 10
   2.1 The human auditory pathway . . . . . 11
      2.1.1 From cochlea to cortex . . . . . 11
      2.1.2 Auditory cortex . . . . . 13
   2.2 Frequency selectivity . . . . . 14
   2.3 Auditory masking . . . . . 17
   2.4 Auditory attention . . . . . 23
   2.5 Functional lateralization of auditory processing . . . . . 26
   2.6 Magnetoencephalography . . . . . 29
      2.6.1 Auditory evoked responses . . . . . 30
   2.7 Goals . . . . . 32

3 Attentional sharpening of frequency tuning (Experiment 1) . . . . . 33
   3.1 Introduction . . . . . 33
   3.2 Materials and methods . . . . . 36
      3.2.1 Subjects . . . . . 36
      3.2.2 MEG measurement . . . . . 36
         3.2.2.1 Experimental design and stimuli . . . . . 36
         3.2.2.2 Data acquisition and data analysis . . . . . 40
      3.2.3 Behavior measurement . . . . . 42
   3.3 Results . . . . . 43
      3.3.1 MEG measurement . . . . . 43
      3.3.2 Behavior measurement . . . . . 50
   3.4 Discussion . . . . . 52

4 Frequency-specific attentional modulation of frequency tuning
   (Experiment 2) . . . . . 57
   4.1 Introduction . . . . . 57
   4.2 Materials and methods . . . . . 60
      4.2.1 Subjects . . . . . 60
4.2.2 Stimuli and experimental design . . . . . . 60
4.2.3 Data acquisition and data analysis . . . . . 63
4.3 Results . . . . . 65
    4.3.1 N1m source strength and N1m latency . . . . . . 66
    4.3.2 Behavioral results . . . . . 70
4.4 Discussion . . . . . 71
4.5 Conclusion . . . . . 75

5 Interhemispheric support during demanding auditory signal-in-noise processing (Experiment 3) . . . . . . 76
5.1 Introduction . . . . . 76
    5.2 Materials and methods . . . . . 78
        5.2.1 Subjects . . . . . 78
        5.2.2 Auditory and visual stimuli . . . . . 78
        5.2.3 Manipulation of attention . . . . . 82
        5.2.4 Design . . . . . 84
        5.2.5 Procedure, data acquisition, and data analysis . . . . . . 84
5.3 Results . . . . . 85
    5.4 Discussion . . . . . 92

6 General discussion and outlook . . . . . . 98
    6.1 Attentional sharpening . . . . . 98
    6.2 Functional lateralization . . . . . 101
    6.3 Conclusion . . . . . 104

7 References . . . . . 106

8 Summary . . . . . 120
List of Figures:

Figure 2.1: The human auditory pathway . . . . . . 12
Figure 2.2: Frequency selectivity . . . . . . 15
Figure 2.3: Lateral inhibition . . . . . . 17
Figure 2.4: Classical simultaneous masking . . . . . . 19
Figure 2.5: The notched-noise method . . . . . . 20
Figure 2.6: The generation of MEG signals . . . . . . 30

Figure 3.1: Model . . . . . . 35
Figure 3.2: Experimental design . . . . . . 38
Figure 3.3: Representative single subject result . . . . . . 44
Figure 3.4: Estimated source locations of the N1m . . . . . . 45
Figure 3.5: Grand-averaged source strength waveforms . . . . . . 47
Figure 3.6: Normalized N1m source strength and N1m latency . . . . . . 49
Figure 3.7: Behavior measurement: error rate and reaction time . . . . . . 51

Figure 4.1: Model . . . . . . 59
Figure 4.2: Experimental procedure . . . . . . 61
Figure 4.3: Representative subject result . . . . . . 66
Figure 4.4: Grand-averaged source strength waveforms . . . . . . 67
Figure 4.5: N1m source strength . . . . . . 69
Figure 4.6: N1m latency . . . . . . 70
Figure 4.7: Error rates and reaction times . . . . . . 71

Figure 5.1: Amplitude spectra . . . . . . 80
Figure 5.2: Concept and timing of the auditory stimulation . . . . . . 81
Figure 5.3: Concept of the visual stimulation . . . . . . 82
Figure 5.4: Representative subject result . . . . . . 87
Figure 5.5: Grand-averaged source strength waveforms . . . . . . 88
Figure 5.6: N1m source strength . . . . . . 90
List of Tables:

Table 1: Overview regarding experimental conditions. . . . . . 83
Table 2: Overview regarding calculated planned contrasts on N1m source strength and N1m latency. . . . . . 89
List of Abbreviations:

A1: Primary auditory cortex
BEN: Band-eliminated noise
EEG: Electroencephalography
fMRI: Functional magnetic resonance imaging
MEG: Magnetoencephalography
MMN: Mismatch negativity
PET: Positron emission tomography
1 Zusammenfassung


Auf der Grundlage der bislang veröffentlichten Literatur wurden folgende Hypothesen formuliert und überprüft: (i) Auditorische Aufmerksamkeit verstärkt nicht nur aufgabenrelevante neuronale Aktivität,

Die folgenden Hauptergebnisse wurden beobachtet: (i) Experiment 1 zeigte, dass auditorische Aufmerksamkeit aufgabenrelevante neuronale Aktivität nicht nur verstärkt, sondern auch die Frequenzselektivität beteiligter Neuronenpopulationen schärft. (ii) Experiment 2 demonstrierte, dass diese Effekte von Aufmerksamkeit frequenzspezifisch sind. (iii) Experiment 3 zeigte, dass signalbezogene neuronale Aktivität in der rechten Hemisphäre relativ zur linken Hemisphäre erhöht ist, wenn das Signal-Rausch-Verhältnis schlecht ist und die Aufgabe gleichzeitig die Wichtigkeit präziser Signalverarbeitung indiziert. (iv) Alle drei Experimente zeigten eine insgesamt relativ erhöhte neuronale Aktivität in der linken Hemisphere während der Verarbeitung von akustischen Signalen in Rauschen im Vergleich zur rechten Hemisphere.

Diese Ergebnisse legen unter Berücksichtigung des aktuellen Forschungsstandes folgende Schlußfolgerungen nahe: (i) Es erscheint wahrscheinlich, dass der schärfende Effekt von Aufmerksamkeit eine aktive Unterdrückung nichtrelevanter neuronaler Aktivität widerspiegelt, welche über efferente, inhibitorische Verbindungen vermittelt wird. (ii) Die Ergebnisse reflektieren vermutlich eine grundlegende funktionelle Dominanz der linken Hemisphäre für die Verarbeitung von akustischen Signalen in Rauschen. (iii) Diese generelle funktionelle Dominanz der linken Hemisphäre für die Verarbeitung von akustischen Signalen in Rauschen kann unter ganz bestimmten Bedingungen durch Aufmerksamkeitsprozesse moduliert werden.

In ihrer Gesamtheit leisten die im Rahmen dieser Arbeit erhobenen Befunde einen signifikanten Beitrag zum besseren Verständnis der auditorischen Signalverarbeitung in natürlicher Umgebung.
2 Introduction

During daily life, our senses are commonly confronted with many events concomitantly. We do not only need to integrate stimuli simultaneously impinging on distinct sensory modalities, but also concurrent inputs within modalities. For instance, it is a matter of everyday experience that a certain sound is obscured during the presence of other sounds [Moore 2003]. However, we know from day-to-day experience that in a given situation usually not all events are analogically important to us. Depending on internal or external factors, certain events may be task-relevant, while others are irrelevant. The need to set processing priorities virtually poses the challenge to reliably extract relevant ‘signal’ from interfering, irrelevant ‘noise’ 1.

In certain situations or at certain instances, it is impossible or inappropriate to ease signal-in-noise processing by improving the signal-to-noise ratio (which could basically be achieved by either a relative increase in signal level or a relative reduction in noise level). However, we can voluntarily improve the processing of a signal interfered by noise by focusing attention on it. For example, picture yourself at a noisy party in a crowded room, brimming with multiple conversations. Not far away from the place where you are standing, your boss is talking at an important customer. Even though you know very well that you are not supposed to participate in this conversation, it would be quite interesting for you to know what your boss is saying in order to get an informational advantage. What could you do to better process the signal, without becoming conspicuous? One possibility would be to move closer; i.e., you could try to increase the signal level. However, you may not want to risk this, because your boss is a grim person. So alternatively, you could climb on a table, address the crowd, and ask everybody to lower their voices; i.e., you could try to reduce the noise level. In this particular situation (with your grim boss being around), you may decide this not to be an

1 Unless otherwise stated, ‘signal’ refers to a task-relevant auditory stimulus (equals not necessarily ‘target’), while ‘noise’ refers to task-irrelevant auditory background.
appropriate option. Finally and simply, you could stay where you are and voluntarily and covertly focus attention on the voice of your boss [cf. Cherry 1953].

This example, illustrating the influence of voluntary attention on auditory signal-in-noise processing, highlights a 'cognitively complex' [cf. Zatorre et al. 2002] auditory signal, namely speech. However, the effect of attention is by no means limited to cognitive stimuli like speech or music. On the contrary, it is evident that attention alters processing on the very basic 'acoustic feature level' [e.g., Hillyard et al. 1973; Picton and Hillyard 1974]. Nevertheless, the underlying neural mechanisms that enable the apparent amelioration of signal-in-noise processing by attention have remained elusive.

The present thesis reports three experiments that investigated the modulation of signal-in-noise processing by attention on the acoustic feature level in the auditory sensory modality of awake, behaving humans by means of magnetoencephalography (MEG). The following paragraphs provide a selective and functional (and inevitably fragmentary) introduction to certain concepts supportive for the understanding of the logic and the results of the experiments carried out, and finally lead to the experimental hypotheses that have been scrutinized in this project.

2.1 The human auditory pathway
2.1.1 From cochlea to cortex
The human auditory system, as other sensory systems, is subdivided into the peripheral and the central part. The peripheral auditory system consists of outer ear (pinna and ear canal), middle ear (tympanic membrane, ossicles, middle-ear muscles, Eustachian tube, and middle-ear cavities), and cochlea (organ of Corti, basilar membrane). The central auditory system is subclassified into the ascending and the descending part. The ascending auditory system is partitioned into the classical and the non-classical ascending pathways. The classical ascending auditory pathway consists of auditory nerve, cochlear nucleus, superior olivary complex, lateral lemniscus
and its nuclei, inferior colliculus, medial geniculate body, and auditory cerebral cortex (Figure 2.1). The non-classical ascending auditory pathways branch off the classical pathways at several levels. They project to cortical areas (e.g., secondary auditory cortex, anterior auditory field) other than the primary auditory cortex (A1), and therefore bypass the processing that occurs there. Descending auditory pathways travel reciprocally to the ascending pathways from the auditory cortex as far as to the cochlea. The most peripheral part of the descending pathways, the olivocochlear bundle, projects from the superior olivary complex to the outer hair cells of the cochlea (cf. Møller [2006] for an extensive overview regarding the anatomy of the auditory system).

Figure 2.1. The human auditory pathway. Overview regarding the most important relays and connections of the human classical ascending auditory pathways. Solid arrows indicate intrahemispheric connections, dotted arrows indicate interhemispheric connections.
2.1.2 Auditory cortex

Traditionally, the auditory cortex has been defined anatomically as the cortex which receives input from the medial geniculate, and physiologically as the cortex containing neurons responsive to acoustic stimulation [Zatorre 2007]. Compared to the visual cortex, the functional architecture of the human auditory cortex is still poorly understood [Eggermont and Ponton 2002]. The auditory cortex is a complex structure consisting of several different regions located deep inside the superior portion of the temporal lobe [Møller 2006]. Anatomical and electrophysiological studies suggest that the auditory cortex, like the visual cortex, is characterized by combined parallel and hierarchical organization [e.g., Belin et al. 2000].

In certain primate species, the core auditory cortex (A1) shows tonotopic frequency gradients, and contains neurons with narrow frequency tuning curves (details in 2.1.2). The core is surrounded by a belt of secondary fields and a more lateral parabelt of tertiary fields. Adjacent core areas influence each other strongly, and core areas are possibly responsible for activating neighboring belt areas. Moreover, core areas project via the corpus callosum to the core areas of the contralateral cerebral hemisphere; the densest axon terminations appear to be in tonotopically matched locations of the same areas, and in adjacent ipsilateral belt areas. The belt is an obligatory, second processing stage that is not bypassed and also shows tonotopic gradients. Belt areas are widely interconnected with each other, and they principally distribute to the parabelt areas.

Electric depth intra-cranial recordings in human epileptic patients identified the posteromedial part of Heschl’s gyrus as primary [Liégeois-Chauvel et al. 1991] and the lateral part as secondary auditory area [Liégeois-Chauvel et al. 1994]. However, the exact anatomical locations of the different components of the human auditory cortex vary considerably between individuals [Møller 2006]. Various depth intra-cranial [e.g., Howard et al. 1996], MEG [e.g., Pantev et al. 1988; Pantev et al. 1995; Lütkenhöner and Steinsträter 1998], as well as functional magnetic resonance imaging (fMRI)
recordings [e.g., Bilecen et al. 1998; Yang et al. 2000] demonstrated the tonotopic organization of the human auditory cortex. Basically, the human supratemporal auditory cortex is optimally located for neuromagnetic recordings [Hari 1990].

2.2 Frequency selectivity
‘Frequency selectivity’ is the most prominent property of the auditory nervous system; it is traceable at all anatomical levels. Frequency selectivity is also characterized as frequency resolution, frequency analysis, and frequency tuning [Moore 2003]. Humans are tremendously sensitive to frequency change; for example, even modestly trained individuals can detect the difference between a 1000 Hz and a 1003 Hz tone (i.e., a difference of 0.3 %) [Møller 2006].

Two alternative mechanisms have been postulated to explain the neurophysiological basis of frequency coding, and it still is an open issue whether these mechanisms are complementary (as appears likely) or redundant (e.g., Wever 1949). The ‘Place Principle’ claims that frequency discrimination is based on frequency being coded by the specific location in the cochlea, and subsequently throughout the auditory nervous system. In contrast, the ‘Temporal Principle’ states that frequency discrimination is based on coding of the sound waveform in the discharge patterns of auditory neurons (‘phase locking’). The frequency selectivity of the basilar membrane is assumed to be the source of the frequency tuning of auditory nerve fibers and cells in the classical ascending auditory pathways. Cochlear frequency selectivity is modified considerably at higher processing levels [Møller 2006].

The response threshold of a single auditory nerve fiber is lowest at one specific frequency, known as that fiber’s ‘characteristic frequency’. The response amplitude (or the ‘neural activity’) of a neuronal population is largest at the characteristic frequency. The plot of the response threshold of a single neuron (as well as the plot of the activity of a neuronal population) as a
function of the frequency of a test tone is known as ‘frequency tuning curve’ (Figure 2.2).

![Diagram showing frequency selectivity in the auditory system. The response threshold of a single neuron (blue) as well as the amplitude of the activity of the neuronal population (red) are at minimum respectively maximum at the neuron’s/ neuronal population’s characteristic frequency (black dotted line).]

**Figure 2.2. Frequency selectivity.** Schematic illustration of the principle of frequency selectivity in the auditory system. The response threshold of a single neuron (blue) as well as the amplitude of the activity of the neuronal population (red) are minimum respectively maximum at the neuron’s/ neuronal population’s characteristic frequency (black dotted line).

Due to the non-linearity of cochlear functioning, tuning curves widen with increasing sound intensity [e.g., Eggermont et al. 1983; Eggermont 1993]. Tuning curve shapes differ depending on frequency and auditory system level. Nerve fibers tuned to high frequencies show asymmetric tuning curves, with very steep high frequency skirts and rather shallow low frequency skirts. Nerve fibers tuned to low frequencies have much more symmetrical tuning curves [e.g., Kiang et al. 1965]. The tuning curve shapes of more centrally located auditory cells vary more; the diversity is largest in the auditory cortex. The shape diversity of the frequency tuning curves of cells from different nuclei can be explained by different degrees of convergence of nerve fibers onto a single nerve cell, and the interplay between inhibitory and excitatory influences on a neuron. This interplay may
sharpen the tuning by mechanisms known as 'lateral inhibition' [e.g., Møller et al. 1992; Sachs and Kiang 1968].

The auditory nerve fibers, the neurons of the auditory nuclei, and the neurons of the auditory cerebral cortex are anatomically arranged according to their characteristic frequencies. This systematic arrangement is known as ‘tonotopic organization’. Tonotopic maps depend on the frequency-based separation of sounds in the cochlea, but they are altered by the processing occurring in the nuclei of the ascending auditory pathways and the auditory cortex. Moreover, tonotopic maps are not static, but can be altered by expression of ‘neural plasticity’, particularly in auditory cortex [Møller 2006; Recanzone et al. 1993]. Neural plasticity is likely to underlie phenomena like auditory sensory memory, pre-attentive detection of sound novelty, the influence of visual processing on auditory perception, perceptual learning, and crucially, improved auditory processing during auditory focused attention [Jääskeläinen et al. 2007].

In animals, frequency selectivity can be determined by different methods (e.g., single cell recordings). When different measures of neural activity are used, the frequency tuning of auditory nerve fibers appears differently from threshold tuning curves [Møller 2006]. However, in humans frequency selectivity is usually demonstrated and measured by studying auditory masking [Moore 2003].

The neural response elicited by a tone at a fiber's characteristic frequency can be inhibited by another tone being in a certain range of frequency and intensity. Thus, inhibitory frequency response areas surround the response areas of each auditory nerve fiber [e.g., Sachs and Kiang 1968] (Figure 2.3).
2.3 Auditory masking

Since auditory masking can reflect the limits of frequency selectivity, it has widely been used for its quantification. Masking has been defined as the process/ the amount by which the threshold of audibility for a sound (the signal) is raised by the presence of another sound, the masker (or noise) [Moore 2003]. Depending on the temporal relationship between masker and test signal, three different types of masking can be differentiated: (i) during ‘forward masking’, the masker appears prior to the test signal. (ii) During ‘backward masking’, the test signal appears prior to the masker. (iii) During ‘simultaneous masking’, test signal and masker are overlaid. Maskers that have typically been used are noises (e.g., broadband noise, narrowband noise, lowpass or highpass noise), pure tones, and complex tones; test signals are usually simple tones or speech signals [Zwicker and Fastl 2007].

In a classical simultaneous auditory masking experiment, Fletcher [1940] measured the threshold of a sinusoidal signal as a function of the
bandwidth of a bandpass noise masker. The masker was strictly centered on the signal frequency, and the noise power density was held constant. Hence, total noise power increased with increasing bandwidth. The results showed that the threshold of the signal initially increased with noise bandwidth becoming wider, but then reached a peak at a particular bandwidth and flattened off. Further increments beyond that bandwidth did no longer change the signal threshold significantly.

Based on these results, Fletcher concluded that the cochlea behaves like a bank of bandpass filters with overlapping passbands (‘auditory filters’). Each basilar membrane location responds to a limited frequency range, so that each membrane locus corresponds to an auditory filter with a certain center frequency. In Fletcher’s experiment obviously only those masker components passing through the auditory filter corresponding to the signal frequency could have effectively masked the signal. However, once the masker bandwidth exceeded the bandwidth of the auditory filter, further increments in masker bandwidth could not augment the amount of noise passing through the filter. Thus, apparently there is a ‘critical bandwidth’, which reflects the width of the auditory filter (Figure 2.4). However, the critical bandwidth indicates only the ‘effective bandwidth’ of the filter, but not its shape [Sams and Salmelin 1994].
Nevertheless, auditory masking can indeed be used to derive the shape of the auditory filter. One procedure, which results in a so-called ‘psychophysical tuning curve’, is comparable to the determination of a neural tuning curve in animals. Neural tuning curves are obtained by determining the level of a tone signal necessary to produce a fixed output from a single neuron as a function of signal frequency. In order to obtain a psychophysical tuning curve, the signal is fixed at a rather low level (close to threshold); simultaneously, a narrowband noise is presented as masker. The center frequency of the masker is varied systematically, and the masker level needed to just mask the signal is determined. The resulting function indicates the masker level required to produce a fixed output from the auditory filter corresponding to the signal frequency as a function of frequency.
Another convenient procedure that can be used to derive the shape of the auditory filter is the so-called ‘notched-noise method’ [Patterson 1976]. This method is beneficial, since it prevents ‘off-frequency listening’ [Patterson and Nimmo-Smith 1980], and therefore assures that the listener factually uses the auditory filter corresponding to the signal frequency (Figure 2.5).

![Figure 2.5. The notched-noise method.](image)

Figure 2.5. The notched-noise method. Schematic illustration of the notched-noise method [Patterson 1976]. The gray rectangles indicate a band-eliminated noise (BEN), which is used as simultaneous masker. The green line sets limits to the auditory filter corresponding to the signal frequency. Dark gray areas denote noise energy passing through the auditory filter, light gray areas denote noise energy not passing through the filter.

In this procedure, a so-called ‘band-eliminated noise’ (BEN) is used as masker. A BEN is a broadband noise from which a frequency band of a certain width has been removed, leaving a ‘spectral notch’ of corresponding width. Assuming that the auditory filter is symmetric, the notch is usually centered at the signal frequency. In order to derive the filter shape, the notchwidth is varied systematically, while signal power and level as well as BEN level are held constant. As the notchwidth increases, less noise energy
passes through the auditory filter corresponding to the signal frequency, and the detection threshold drops. In contrast, as notchwidth decreases, more noise energy passes through the filter, and the signal threshold rises. The resulting function thus relates signal threshold to noise notchwidth. The shape of the auditory filter corresponding to the signal frequency for a given frequency deviation of the notchedge from the signal frequency can be derived from that function. Filter shapes determined with this method are characterized by rounded tops and quite steep skirts. The passband area of these filters can be well approximated by means of a Gaussian function.

Notably, the notched noise method (as well as other masking methods) is by no means limited to the behavioral level. Sams and Salmelin [1994] used this procedure to derive auditory filter shapes directly and noninvasively from an auditory cortex neuronal population in awake, behaving humans by means of MEG. The authors measured the effect of BEN masker notchwidth on the N1m response amplitude evoked by tonal signals. During the measurements, attention was distracted from the sound stimuli by means of a reading task. The BEN maskers affected the N1m amplitude evoked by the signals in a systematic way: the wider the notch, the larger was the amplitude (and the shorter the latency). Noteworthy, N1m source locations and orientations did not depend on BEN notchwidth in a systematic way, but concentrated in an area of less than 1 cm² on the supratemporal plane. The masking effect was frequency-specific, and the filter shape, which was modeled from the empirical data, revealed sharp frequency tuning and resembled filter shapes obtained in psychoacoustical experiments utilizing similar procedures. The authors emphasized that it is difficult to conclude exactly which auditory cortex areas had contributed to the measured response, given that the N1m is likely to be generated by simultaneously active core as well as secondary auditory cortex areas [Näätänen and Picton 1987]. Since, however, neither N1m source location nor orientation were influenced by BEN notchwidth, the maskers possibly affected various auditory areas in a similar manner.
Remarkably, the authors stressed that in their study filter shapes had beneficially been estimated during passive listening. Hence, the observed filter shapes probably reflect pure neuronal filtering of the sound signals, unaffected by criteria adopted by the subjects in a decision process. However, on the other hand, it would be very interesting to investigate whether, and if so how, auditory focused attention would alter the filter shape relative to passive listening. The results may yield new insight into the mechanisms by means of which attention improves auditory signal-in-noise processing. Unfortunately, the authors did not include an experimental condition during which attention was focused on the sound signals. Therefore, the study does not contribute to answering this question.

On the behavioral level, however, it has been shown repeatedly that focused attention can ameliorate auditory signal-in-noise processing, possibly via altering frequency selectivity. Schlauch and Hafter [1991] and Hafter et al. [1993] demonstrated that minimum uncertainty regarding the signal frequency (inviting the listener to direct the attention focus to the optimal auditory filter) improved signal-in-noise processing performance compared to maximum as well as relative/ partial uncertainty (forcing the listener to distribute attentional resources to several auditory filters simultaneously). Moreover, maximum as well as relative/ partial uncertainty regarding the signal frequency seemed to result in widened auditory filter bandwidths regarding the signal frequency. These results lend support for the view that auditory filters (as measured in auditory masking) are labile in ways that allow them to be affected by attentional factors. Moreover, Dai et al. [1991] demonstrated that the shape of the so-called ‘attention band’, which describes a region of enhanced sensitivity for frequencies surrounding an attended signal, resembles that of the auditory filter corresponding to the attended signal in the frequency range from 500 to 4000 Hz. Further, focused attention effectively modulated auditory signal-in-noise processing.

Unfortunately, on the behavioral level it is impossible to measure proband responses under a condition during which attention is totally
distracted from the signal; as long as a behavioral response to the signal is required, attention necessarily is (at least to a certain degree) allocated to the signal; what can be varied is merely the relative amount of attention focused on the signal. On the neuronal level, in contrast, it is possible to compare conditions with versus without auditory focused attention. Moreover, it is an empirical question (that has not yet been answered) whether attentional effects as described above could also be measured directly from neuronal populations in the behaving human auditory system. Beyond doubt, it would be important to measure such and similar effects on neuronal activity directly, since neural as compared to behavioral correlates may enable more sophisticated conclusions regarding the underlying neural mechanisms.

2.4 Auditory attention

Various manifestations of top-down control of sensory processing have been subsumed under the heading 'attention'. Attention is a term which is 'known' by everyone, but whose scientific description encompasses a diversity of operational definitions [Hafter et al. 2007], indicating that attention is a phenomenon which is not easily tangible. A recent operational definition states that auditory attention allows the fast and concise focusing of the 'acoustic searchlight' on sounds of interest in the acoustic environment. Auditory attention is flexible and dynamic, modulates many levels of auditory processing (ranging from association cortex to cochlea), and may rely on adaptive mechanisms that rapidly reshape receptive fields along with task demands and behavioral context [Fritz et al. 2007].

Attention can be top-down (i.e., voluntary or task-dependent) or bottom-up (i.e., 'pop-out' based on sound salience). Top-down attention can be characterized as selection process that delegates cortical processing resources towards the most relevant sensory information, in order to abide goal-directed behavior in presence of multiple competing distractions; further on, attention comprises several distinct behavioral and neural processes operating at multiple levels [Fritz et al. 2007].
At the behavioral level, attention enables enhanced information processing and improved behavioral sensitivity, as reflected in shortened response latencies and more accurate responses [Fritz et al. 2007]. Furthermore, for half a century it has been known that neural responses in auditory cortex can be strongly modulated by attention [e.g., Hubel et al. 1959], and several components of the event-related potential respectively field have been specifically linked to auditory attention [Hafter et al. 2007]. Numerous event-related potential [e.g., Hillyard et al. 1973; Woldorff and Hillyard 1991] and event-related field studies [e.g., Woldorff et al. 1993; Okamoto et al. 2007c] in humans have meanwhile shown that the cortically generated N1(m) waveform (latency ~ 100 ms) is sensitive to attention; moreover, effects of attention in auditory cortex can manifest as early as 20 – 50 ms after stimulus onset [Woldorff and Hillyard 1991; Woldorff et al. 1993].

Despite multitudinous studies addressing this issue, the uncovering of the neural basis of selective attention remains a fundamental challenge [Kauramäki et al. 2007]. Two alternative neural effects have been postulated to form the basis of selective attention: (i) multiplicative positive gain increase of sensory neurons (i.e., ‘amplification’) [e.g., Hillyard et al. 1973; Petkov et al. 2004; Rinne et al. 2005] versus (ii) feature selectivity enhancement of sensory neurons (i.e., ‘sharpening’) [e.g., Spitzer et al. 1988; Fritz et al. 2003; Ahveninen et al. 2006]. Presumably, amplification and sharpening mechanisms are complementary. In addition, it has been argued that selective attention may activate neural populations other than the sensory populations processing the stimuli [Näätänen 1992; Petkov et al. 2004].

Amplification of neural activity by attention has already been demonstrated by different methods in both the human visual and auditory systems. Sharpening effects of attention, however, have not yet been shown in the human auditory modality.

Unfortunately, a commonly accepted, quantifiable measure of attention has not yet been established. However, the magnitude of attentional modulation of neural activity is very likely to be correlated with task difficulty.
[Spitzer et al. 1988; Boudreau et al. 2006], and the presence or absence of attention is usually inferred from a combination of task design, subject behavioral performance, and the subsequent neural effects [Fritz et al. 2007].

Top-down auditory attention can improve the extraction of salient signals from a complex acoustic noise background by selectively focusing on a limited range of factually present (or even merely expected or recalled) feature dimensions of an acoustic signal [Hafer et al. 2007; Zatorre 2007]. Therefore, voluntary auditory attention is virtually the clue to pinpointing acoustic signal over noise, and to switching the attentional gaze to different acoustic features of interest within the acoustic scene.

In a recent study, Fritz et al. [2003] demonstrated by means of A1 unit recordings in ferrets, which were engaged in an auditory signal detection task, that task performance can rapidly and adaptively reshape cortical receptive field properties according to specific task demands and salient sensory cues in a frequency-specific manner. Attending to a specific signal frequency during the detection task reliably induced swiftly onsetting, long-lasting (i.e., several hours), and localized facilitative changes regarding spectral-temporal receptive field shape. The authors argued that such modulatory changes could enhance overall cortical responsiveness to the attended signal, and thereby increase the likelihood of signal receiving. In a follow-up study [Fritz et al. 2005b] the ferrets were initially trained on generalized, frequency-independent tasks (single-tone detection versus two-tone discrimination). While recording from identical A1 units or multi-units, spectral-temporal receptive fields were measured during resting (i.e., no task) versus successively performed frequency discrimination or single-tone detection tasks. Both tasks enhanced spectral-temporal receptive fields at the target signal frequency. Notably, in the frequency discrimination task, spectral-temporal receptive field depression was found for the non-target frequency. For both tasks, spectral-temporal receptive field changes were rapid and frequency-specific. During successive tasks, neurons responded differentially to identical tones, depending on whether the tone was target or non-target.
Presumably, the observed task-dependent differences in receptive-field plasticity reflect differences in meaning attributed to identical tones with respect to the context of presentation.

Taken together, these findings demonstrate that selective spectral attention can rapidly reshape neuronal receptive fields in primary auditory cortex in order to enhance responsiveness at the target signal frequency and depress responsiveness at adjacent frequencies. Crucially, similar spectral receptive-field effects were found during detection of a tonal signal in the midst of a noisy background [Fritz et al. 2007].

2.5 Functional lateralization of auditory processing

The possibly most well-known functional hemispheric asymmetry regarding auditory processing is the left-hemispheric dominance for speech processing, which originally had been observed in neurologic patients [Broca 1861; Wernicke 1874]. Meanwhile, also neuroimaging [e.g., Belin et al. 2000] and electrophysiological [Eulitz et al. 1995; Szymanski et al. 2001] studies have provided evidence for this functional lateralization. On the other hand, there are studies indicating a laterally reversed, right-hemispheric dominance for music processing [cf. Zatorre et al. 2002].

However, this functional lateralization may not be limited to speech and music sounds. Functional auditory cortex asymmetries have been observed on the acoustic feature level as well. Zatorre and Belin [2001] (utilizing ‘positron emission tomography’ (PET)), and Jamison et al. [2006] (utilizing fMRI) demonstrated that temporal variation is dominantly processed in the left auditory cortex, whereas spectral variation is dominantly processed in the right. Very recently, Okamoto et al. (submitted for publication) could confirm these findings by means of MEG.

Certainly, there is a link between ‘cognitive’ speech versus music processing on the one hand, and ‘basic’ temporal versus spectral acoustic feature processing on the other. Speech is highly dependent on rapidly changing broadband sounds, while music patterns are slower, even though
small and concise frequency changes are important [Zatorre et al. 2002]. Following Tallal et al. [1993] and Poeppel [2003], the functional hemispheric asymmetries regarding speech versus music processing may arise consequent on ‘asymmetric sampling in time’ properties of the two auditory cortices: the left auditory cortex is assumed to employ rather short temporal integration windows (~20 – 40 ms), whereas the right auditory cortex utilizes rather long (~150 – 250 ms) windows.

It is important to consider that auditory processing asymmetries are not necessarily driven by the stimulus-class (e.g., speech versus music or temporal versus spectral) per se. For instance, Brechmann and Scheich [2005] demonstrated with fMRI that top-down, task-related influences appear to select the specific auditory cortex area as well as the hemisphere specifically involved in processing stimuli that contain both spectral and temporal information, indicating that directing the attentional focus on different features of the same acoustic stimuli leads to differential hemispheric activation of auditory cortex.

Furthermore, functional auditory asymmetries seem to be related to the signal-to-noise ratio of sound inputs (i.e., noise level and/or signal quality). Utilizing a simultaneous auditory masking paradigm, Okamoto et al. [2007b] presented a comb-filtered noise as masker, while pass- and stop-band stimuli served as test signals. Masker and test signals were complex stimuli delivered either to the identical (ipsi-lateral or ‘peripheral masking’) or to different ears (contra-lateral or ‘central masking’), while the test subjects watched a silent movie of their choice (i.e., attention was distracted from the auditory stimuli). The results showed that neural activity (N1m source strength) evoked by the signal was less reduced in the left compared to the right hemisphere during masking, indicating a left-hemispheric dominance for auditory processing in noisy environments. Results were interpreted as reflection of a basic functional hemispheric specialization contributing to the processing of complex auditory stimuli like speech signals in noisy environments.
Shtyrov et al. [1998] argued that masking of speech signals by noise might change the leftward hemispheric speech processing lateralization. Using a passive oddball paradigm, standard and deviant syllable signals were presented in three different noise conditions (no noise, low noise, and medium noise), and the magnetic mismatch negativity (MMNm) was recorded. In the no noise condition, MMNm peak amplitude and dipole moment were larger in the left compared to the right hemisphere. In the noise conditions, however, MMNm peak amplitude and dipole moment decreased in the left, but increased in the right hemisphere relative to the no noise condition. These results could be confirmed in a follow-up study [Shtyrov et al. 1999]. Here, employing a very similar setup and experimental conditions, it was found that both P1m and P2m responses were depressed in the noise conditions compared to silence in the left hemisphere, while the P2m even increased in the right hemisphere during noise presence. Moreover, P1m, N1m, and P2m source locations differed only in the right hemisphere in noisy conditions relative to the silent condition. Activity increments and source location differences in the right hemisphere were interpreted in terms of recruitment of additional right-hemispheric resources during speech-signal-in-noise processing.

In order to investigate the perception of speech signals corrupted by realistic, non-ideal environments, Liikkanen et al. [2007] utilized ‘uniform scalar quantization’ to degrade the quality of fully controlled, synthetic, but natural-sounding vowel signals in five different degrees in a controllable and replicable manner. Auditory evoked magnetic fields were recorded under instructions to ignore the auditory stimuli and watch a silent movie. The results demonstrated that the N1m amplitude increased in the right hemisphere with increasingly degraded signals, while the left-hemispheric N1m amplitude as well as the N1m latencies in both hemispheres remained unchanged. The results may reflect the particular involvement of the right auditory cortex in degraded speech processing as well as its potential compensator role for poor signal quality as indicated by its increased activity.
2.6 Magnetoencephalography

Electrical activity in the living body is generated by ion movements across cellular membranes. Ions are electrically charged particles, and movements of these particles (which are quasi 'natural electric currents') account for magnetic fields measurable outside the body. These fields are referred to as ‘biomagnetic fields’ [Williamson and Kaufman 1981].

In order to localize the sources of the biomagnetic fields inside the body, it is necessary to make assumptions regarding the source structure. The simplest physiologically sound and most commonly used model describes a biomagnetic source as a ‘current dipole’ [Nowak 2007], which is used as an equivalent source (i.e., as a source that best explains the measured field pattern) for the unidirectional primary current that may extend over relatively wide areas (e.g., of cortex). For many practical purposes, the spherical head model provides accurate enough source estimates, particularly when responses from parietal and temporal brain areas are of interest [Hämäläinen and Sarvas 1989]. However, when the sources are located deep in the brain or in frontal cortex areas, it is recommended to use more sophisticated, realistic head model approaches [Hämäläinen and Hari 2002; Wolters et al. 2006].

Biomagnetic fields, particularly neuromagnetic fields, are extremely weak, as for instance compared to the magnetic field of the Earth or the fields produced by urban sources. Most biomagnetic measurement systems utilize ‘gradiometers’ in order to reduce ambient magnetic noise. Gradiometers (as opposed to ‘magnetometers’) measure the magnetic field difference between pick-up coils. Gradiometers are extremely sensitive to sources close to the coils, and rather insensitive to uniform background fields [Nowak 2007].

MEG is completely noninvasive and at present (together with electroencephalography (EEG)) the only brain imaging tool that provides submillisecond temporal accuracy. MEG (as well as EEG) directly ‘sees’ neuronal activity through the skull (i.e., MEG does not measure indirect metabolic effects as do fMRI or PET), and (as opposed to scalp EEG) does
not spatially smear the signals coming from the brain [Hämäläinen and Hari 2002].

MEG is particularly suited to investigate neuronal activity originating from cortical sulci (strictly speaking from the walls of the sulci), since it is under realistic conditions selectively sensitive to tangentially oriented sources. The primary currents that give rise to measurable MEG signals are postsynaptic currents in pyramidal cells (Figure 2.6).

![Figure 2.6. The generation of MEG signals. Schematic illustration of a population of nearly tangentially (with regard to the skull surface) oriented, simultaneously active cortical pyramidal cells giving rise to an electric current and the associated biomagnetic field that would be measurable outside the head.](image)

2.6.1 Auditory evoked responses
Auditory evoked magnetic responses are commonly categorized into early (up to 10 ms, generated in subcortical structures), middle (10 – 70 ms, generated in subcortical/ cortical structures: N19m, P30m, P50m/ P1m), and long (70 – 250 ms, generated in cortical structures: N1m, P2m, sustained negativity/field, off-response) latency components. Auditory magnetic responses are evocable by any ‘abrupt’ sound onset or sound change; in experiments, usually clicks, tones, tone bursts, noises, or complex sounds such as speech signals are used. Both monaural and binaural auditory stimuli evoke bilateral
auditory cortex responses [Knösche et al. 2007]; in case of monaural sounds the response is larger in the contralateral hemisphere. Transient evoked responses (i.e., P1m, N1m, P2m, and off-response) [e.g., Pantev, Eulitz et al. 1996a] can be differentiated from sustained [e.g., Pantev et al. 1994] and steady-state responses [e.g., Pantev, Roberts, et al. 1996b; Draganova et al. 2008].

The most prominent and reliable auditory evoked magnetic response is the N1m. At the same time, the N1m is the best-investigated component of the auditory evoked field, providing the investigator with lots of a-priori information that can be used to analyze this component adequately. The generators of the N1m are located on the upper surface of the bilateral posterior temporal lobe [Knösche et al. 2007]. More specifically, a high-precision neuromagnetic study [Lütkenhöner and Steinsträter 1998] demonstrated that peak N1m arises from the planum temporale. Given the evident anterior-posterior polarity reversal at N1m latency [Elberling et al. 1980; Hari et al. 1980], it has been argued that its source may be modeled as a vertically oriented dipole at the level of the supratemporal plane [Näätänen and Picton 1987]. The N1m is an ‘onset response’, reflecting cortical activity related to any relatively abrupt change in the auditory environment [Hari et al. 1987], i.e., the N1m is evoked by the onset of a change in physical sound characteristics from an immediately stable level [Näätänen and Picton 1987]. During N1m analysis, as dependent variables N1m amplitude, latency, source location, and source orientation can be measured and modeled. The N1m is largely determined by both physical stimulus features and the general state of the listener. Important physical features to be considered in this regard are particularly sound intensity and tonal frequency; crucial subject factors are temporal and event uncertainty, degree of non-specific arousal, the attentional state, and task performance. Specifically, N1m amplitude enlargement and latency reduction have been shown to be generally associated with increasing sound intensity, decreasing tonal frequency,
relative temporal and event uncertainty, increasing arousal, focused attention, and task performance.

2.7 Goals
Based on the concepts and findings introduced in the preceding paragraphs, this project pursued three major goals. The first goal was to demonstrate the sharpening effect of auditory attention on population-level neural frequency tuning in the human auditory system. The second goal was to prove the frequency-specificity of this hypothesized attentional sharpening effect. The third goal was to demonstrate the functional dominance of the left hemisphere during auditory signal-in-noise processing, and to more thoroughly investigate attentional effects on functional hemispheric asymmetries during auditory signal-in-noise processing.

The paradigms utilized in the three experiments were variants of the notched-noise method [Patterson 1976; Sams and Salmelin 1994]. In order to measure attention effects on neuronal activity directly and non-invasively in the cerebral cortices of behaving humans, MEG was employed.
3 Attentional sharpening of frequency tuning (Experiment 1)

3.1 Introduction
The capability of the brain to process task-relevant sound signals even in noisy environments is important in daily human life. In most day-to-day situations, we are exposed to many different sounds simultaneously. Nevertheless, we can selectively improve the encoding of task-relevant sound signals by voluntarily focusing attention on them. Auditory focused attention might tune sound processing by both reinforcement of neural responses corresponding to task-relevant stimuli ('gain') and depression of task-irrelevant neural activity ('sharpening'). Despite extensive research, the tuning effects of attention in human auditory cortex remain to be exactly determined [Alain and Arnott 2000].

A recent fMRI study [Murray and Wojciulik 2004] showed that visually focused attention not only increased hemodynamic activation (i.e., gain), but also enhanced the selectivity of the neural population representing the attended visual object (i.e., sharpening). In a manner comparable to the visual system, auditory focused attention might also both cause an overall increase in auditory neural activity and improve the resolution of the tonotopic map, contributing to finer neural population-level encoding of attended sound signals (Figure 3.1 A).

The gain functions of attention in the human auditory system have been investigated using fMRI [Grady et al. 1997; Benedict et al. 1998] as well as other neuroimaging techniques. Pioneering EEG [Hillyard et al. 1973; Picton and Hillyard 1974] and MEG [Woldorff et al. 1993] works observed that auditory focused attention increased the auditory N1(m) response, which is known to originate from lateral aspects of Heschl's gyrus and the posterior temporal plane [Pantev et al. 1995; Eggermont and Ponton 2002]. A sharpening effect of attention, however, has not yet been shown in this area.

The effect of the efferent (top-down) neural system on frequency tuning has yet only been studied at single-neuron level. Polley et al. [2006]
investigated whether bottom-up sensory inputs or top-down task-dependent processes controlled cortical reorganization in adult rats. Between two groups of rats, the authors used identical auditory stimuli, but different attention tasks. The results showed that only top-down processes played an important role in the reorganization of primary and secondary auditory cortices. Attention focused on frequency cues might not only intensify bottom-up, but also top-down neural processes, and may expand the representation of the target frequency range within the cortical tonotopic map.

Based on the aforementioned results, the major goal of the present study was to investigate gain as well as sharpening effects of top-down auditory focused attention on population-level frequency tuning in human auditory cortex by means of MEG. We posit that attention might not only strengthen excitatory neural connections, but also inhibitory networks (Figure 3.1 A); this mechanism would contribute to finer frequency tuning and better auditory performance.
**Figure 3.1. Model.** Top-down attentional modulation of population-level frequency tuning. **A:** The figure illustrates how different effects of attention (gain vs. sharpening vs. combination of gain + sharpening) would modulate population-level neural activity corresponding to the 1000 Hz test stimulus (TS). Gain is reflected by increasing TS-related neural activity amplitude, sharpening is reflected by narrowing TS-related neural activity in the frequency axis. **B1, B2, B3, B4:** The figures illustrate the relationship of neural activity elicited by BEN respectively TS as predicted by the different attention effect models. Light gray areas represent neural activity exclusively elicited by BEN, dark gray areas represent neural activity exclusively elicited by TS. Black areas indicate overlap: neural activity in these areas would be evocable by both BEN and TS, but factually had already been evoked by BEN when TS was presented, due to stimulus timing. Dark gray areas represent N1m source strength as measured in this experiment, reflecting TS onset. **B1** displays neural activity evoked during
passive listening, i.e., without auditory focused attention (dull frequency tuning and weak neural activity as indicated by rather wide TS frequency ranges and shallow BEN notch slopes, and rather small TS and BEN amplitudes). B2 illustrates the gain model (i.e., dull TS frequency tuning and large neural activity as indicated by rather wide TS frequency ranges and shallow BEN notch slopes, and rather large TS and BEN amplitudes). B3 illustrates the sharpening model (i.e., sharp TS frequency tuning and weak neural activity as indicated by rather narrow TS frequency ranges and steep BEN notch slopes, and rather small TS and BEN amplitudes). B4 displays the combined gain + sharpening model (i.e., sharp TS frequency tuning and large neural activity as indicated by rather narrow TS frequency ranges and steep BEN notch slopes, and rather large TS and BEN amplitudes). Left diagrams denote a BEN containing a broad notch, right diagrams denote a BEN containing a narrow notch. Notably, the neural activity in both gain and combined models is enhanced due to the gain effect of attention. In addition, size ratios of dark gray areas between wide BEN and narrow BEN conditions differ between models: for B3 and B4, ratios are much closer to 1 compared to B1 and B2, reflecting the sharpening effect of attention on population-level frequency tuning.

3.2 Materials and Methods
3.2.1 Subjects
13 healthy subjects between 22 and 28 years of age (7 females, mean age 24.2 years) without history of psychiatric or neurologic disorders participated in the study. All subjects were right-handed (assessed with the 'Edinburgh Handedness Inventory' [Oldfield 1971]), and their hearing thresholds were within clinical norms in the frequency range from 125 to 8000 Hz as tested by means of clinical tone audiometry. Participants gave written informed consent for participation in the study in accordance with procedures approved by the Ethics Board of the Medical Faculty, University of Muenster.

3.2.2 MEG measurement
3.2.2.1 Experimental design and stimuli
In order to evaluate both gain and sharpening effects of auditory focused attention, we presented a test stimulus (TS) either in isolation or simultaneously each with four different BENs queued in a random sequence. The TS was a 40 Hz amplitude-modulated tone (modulation depth 100 %, 12.5 ms rise and fall times) with a carrier frequency of 1000 Hz, and a duration of 0.7 s. The sound onset asynchrony (SOA) between two
subsequent TSs was fixed to 3.0 s. In 10 % of the trials, the TS deviated in temporal structure from the standard TS. In these deviant trials, the TS contained a silent period of 50 ms duration (‘temporal gap’, 12.5 ms fall and rise times) starting randomly at either 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, or 600 ms after TS onset. The deviant TSs served to motivate auditory focused attention in a certain experimental condition. Auditory fields evoked by deviant TSs could not be analyzed appropriately, due to insufficient signal-to-noise ratio (resulting from the low number of trials) and contamination by motor artifacts (resulting from the button presses), and were therefore excluded.

BENs were prepared as follows: frequency bands with widths of either 20 Hz (BEN20), 40 Hz (BEN40), 80 Hz (BEN80), or 160 Hz (BEN160) centered on 1000 Hz (TS frequency) (Figure 2.2 B) were eliminated from 8000 Hz (upper frequency limit of the sound delivery system) low-pass filtered white noise. All BENs (duration 3.0 s with 12.5 ms rise and fall times) were presented starting 2.0 s prior to TS onset and ceasing 0.3 s after TS termination (Fig. 3.2 A). All sound stimuli were prepared as soundfiles and presented using ‘Presentation’ (Neurobehavioral Systems, Inc.). Between subsequent BENs were silent intervals of 40 ms duration due to time delays produced by the sound presentation system. 18000 Hz frequency tags (which are not perceivable) were attached to the heads of the TSs in order to obtain precise sound stimulation timing. SRM-212 electrostatic earphones (Stax, Ltd.) were used as transducers. Sounds were delivered through 60 cm silicon tubes (inner diameter of 5 mm) terminating at silicon earpieces fitting to the subjects’ ears. The hearing threshold for the standard TS was determined for each subject and each ear individually at the beginning of each MEG session. The TSs were presented binaurally at intensity of 35 dB SL; corresponding SPL levels varied between 41 and 51 dB (mean 47.7 dB ± S.D. 3.7 dB). The power of the BENs, which were also presented binaurally, was 15 dB larger than TS power. In each session, 180 trials of the standard TS for each BEN condition were presented in randomized order.
In order to investigate effects of attention, we contrasted two different attention conditions within subjects and between sessions: ‘active listening’ versus ‘distracted listening’. During active listening, subjects focused attention on the auditory stimuli and were required to press a response button as quickly as possible with their left or right index finger (randomized between subjects) for each deviant TS detection. During distracted listening, no task was required; subjects watched a silent movie of their choice. The
movie served to distract attention from the auditory stimuli, and to keep subjects in a stable alert state. Notably, we decided not to present the silent movie during active listening, because it might have distracted attention from the auditory stimuli despite clear instructions to focus attention on the stimuli, which in turn might have resulted in less contrast in the evoked responses between the two different attention conditions [Suzuki et al. 2005]. The sound stimulation was identical between the two conditions, which were performed as different sessions on different days. Session order was balanced across subjects.

The neuronal activity evoked by BEN respectively TS can be divided into three categories: (i) activity evoked exclusively by the BEN (Figure 3.1 B, light gray areas), (ii) activity evoked exclusively by the TS (Figure 3.1 B, dark gray areas), or (iii) activity evocable by both BEN and TS (Figure 3.1 B, black areas). The activity of auditory neurons, which could be activated by both BEN and TS, should decrease with BEN becoming wider and/or with frequency tuning becoming sharper. Thus, the diminution of overlapping areas (Figure 3.1 B, black areas) and the enlargement of areas activated solely by the TS (Figure 3.1 B, dark gray areas) would reflect improved population-level frequency tuning.

In this study, neurons corresponding to areas of overlap (Figure 3.1 B, black areas) could theoretically be activated by both BEN and TS, but in fact had already been activated by the BEN when TS was presented (Figure 3.2 A). Thus, the N1m response measured in this study reflects the activity of the neural group activated solely by the TS onset (Figure 3.1 B, dark gray areas). If attention would cause gain only, the ratios of TS-related neural activity evoked in case of each BEN condition (Figure 3.1 B, dark gray areas) as compared to the no-BEN condition (Figure 3.1 B, dark gray + black areas) would not differ between active and distracted listening conditions. In contrast, if attention would sharpen the population-level frequency tuning, the ratios would become larger in the active compared to the distracted listening condition. Thus, the overlay of BEN and TS stimuli allows to measure
population-level frequency tuning of alert human auditory cortex by means of MEG.

3.2.2.2 Data acquisition and data analysis
Auditory evoked fields were measured with a helmet-shaped 275 channel whole-head neuro-gradiometer (OMEGA, CTF Systems Inc.) in a silent, magnetically shielded room. Participants were comfortably seated upright. Head position was fixed with cotton pads, and subjects were instructed not to move. Alertness and compliance were monitored via video camera. The measured auditory evoked fields were digitally sampled at a rate of 600 Hz. Epochs of data elicited by the standard TS, including a 300 ms pre TS onset interval and a 400 ms post TS onset interval, were averaged selectively for each BEN condition after rejection of artifact epochs containing field changes larger than 3 picotesla. The source locations and orientations of the evoked fields were determined in a head-based Cartesian coordinate system with the origin at the midpoint of the medio-lateral axis (y-axis) joining the center points of the entrances to the ear canals (positive toward the left ear). The posterior-anterior axis (x-axis) ran between nasion and origin, the inferior-superior axis (z-axis) ran through the origin perpendicularly to the x-y-plane.

The N1m response is known to be generated in a relatively focused cortical area (posterior temporal plane and lateral aspects of Heschl’s gyrus) [Pantev et al. 1995; Eggermont and Ponton 2002]. Therefore, we estimated N1m source locations and orientations by means of two single equivalent current dipoles (one for each hemisphere) based on the no-BEN condition using a spherical head model. We assumed identical locations and orientations for the different BEN conditions, since a previous MEG study [Sams and Salmelin 1994] showed that simultaneously presented BENs did not influence the calculated location and orientation of the N1m component elicited by the test tone. For analysis of the N1m component, the averaged magnetic field signals were 30 Hz low-pass filtered initially, followed by a baseline correction relative to the 300 ms pre-stimulus interval. The cortical
sources were approximated individually for each subject. Initially, the time point of maximum global field power, measured as root-mean square across all sensors around 100 ms after stimulus onset, was identified. Afterwards, the 10 ms time window prior to the peak was used for spatio-temporal source estimation. The estimated source for each hemisphere of each subject was fixed in its location and orientation, and the source strengths were calculated for all time points and each BEN condition (BEN160, BEN80, BEN40, and BEN20). The maximum N1m source strengths were calculated in time windows between 75 and 175 ms (no-BEN condition), 125 and 225 ms (BEN 160 condition), and 150 and 250 ms (BEN80, BEN40, and BEN20 conditions), respectively. The estimated N1m locations with respect to each axis were evaluated by repeated-measures ANOVAs using two factors (attention: active, distracted; hemisphere: left, right).

The 40 Hz amplitude-modulated tone used as TS in this study is known to generate the so-called auditory ‘steady state response’ [Makela and Hari 1987; Pantev et al. 1996b; Engelien et al. 2000; Ross et al. 2000]. However, it was not possible to clearly extract this response for the BEN20, BEN40, BEN80, and BEN160 conditions due to insufficient signal-to-noise ratio, and thus it was impossible to perform a steady-state response analysis.

For the evaluation of the sharpening effect of attention on the population-level frequency tuning, the maximum source strength of the N1m elicited by the TS for each BEN condition in each hemisphere was normalized with respect to the maximum N1m source strength in the no-BEN condition for each subject and each hemisphere individually. Normalization was applied in order to reduce the impact of both the typically observed inter-individual and inter-session variability in N1m source strength. The normalization procedure was not applied to N1m latency, given that the variability among subjects was negligible compared to source strength. The normalized source strengths and the latencies were then evaluated by repeated-measures ANOVAs using three factors (BEN type: BEN160, BEN80, BEN40, and BEN20; hemisphere: left, right; attention: active,
Post-hoc comparisons were performed using Bonferroni-Dunn’s multiple-comparisons correction (significance threshold: \( p < 0.0083 \)). In addition, non-normalized maximum N1m source strength was similarly analyzed, since the hypothesized gain effect of attention would get lost in normalized data.

### 3.2.3 Behavior measurement

In order to evaluate the deviant TS detection performance of the subjects, we conducted additional behavior measurements in a third session. These measurements took place in the MEG chamber, and therefore stimulation devices, stimuli, and experimental parameters were identical to the active listening MEG session, with the exception of likelihood of stimulus appearance: in the behavior test, both standard and deviants appeared with a likelihood of 50%. Stimulus order was pseudo-randomized; each deviant stimulus was presented eight times in each BEN condition, resulting in 96 standard and 96 deviant trials per BEN condition. Participants were instructed to press the response button with their right index finger as quickly as possible when detecting a deviant stimulus. Both response velocity (reaction time) and response accuracy (error rate: misses + false alarms) were recorded. Data were analyzed with repeated-measures ANOVAs (BEN type: BEN160, BEN80, BEN40, and BEN20), and post-hoc comparisons were performed using Bonferroni-Dunn’s multiple-comparisons correction (significance threshold: \( p < 0.0083 \)).

Theoretically, the possibility that participants changed the amount of allocated attention based on BEN condition cannot be ruled out. Subjects might have paid more attention to narrower compared to wider BENs. Such strategic behavior might have been reflected by larger attention effects for narrower compared to wider BENs. To rule out this possibility, just after the termination of the behavioral measurement we investigated whether the subjects were able to categorize the BENs with respect to task difficulty by asking them whether they had noticed that different BENs had been
presented. Ten participants had not noticed, but three subjects commented that BENs and task difficulties had differed. For these three participants, we extended the behavior measurement in order to evaluate whether they could link BEN type with task difficulty. Participants were asked to rank the BENs via button press (button 1 (easy) to button 4 (difficult)). Each BEN was presented 15 times for 3.0 s in randomized order.

3.3 Results
3.3.1 MEG measurement
Clearly identifiable auditory evoked fields were obtained from all subjects in all conditions. After artifact rejection, a number of 156 to 180 (mean 170) trials remained in each condition to be used for signal averaging. Waveforms, contour maps, and estimated source locations of the N1m evoked by no-BEN during active listening overlaid on the structural magnetic resonance image of one representative subject are displayed in Figure 3.3. Clear dipolar patterns over right and left hemispheres were observed. The goodness-of-fit of the underlying dipolar model for dipole estimation was in the range from 91.8 to 98.2 % (mean 95.8 % ± S.D. 1.78 %), confirming the adequacy of the chosen equivalent current dipole approach. Figure 3.4 displays the group-averaged dipole locations of the N1m for the active and distracted listening conditions with the 95 % confidence limits of the relative differences around the distracted listening condition.
Figure 3.3. Representative single subject result. A: Auditory evoked magnetic fields obtained in the no-BEN condition. 30 Hz low-pass filtered MEG waveforms are displayed in a flattened sensor position projection. B: Iso-contour maps of the magnetic fields corresponding to the maximum N1m response, showing dipolar patterns above both hemispheres at a latency of 0.1067 s. Red areas represent inward flux of magnetic fields to the brain, blue areas represent outward flux from the brain. C: Calculated dipole locations and orientations overlaid on the individual structural magnetic resonance image.
The repeated-measures ANOVAs applied to the dipole source locations of the N1m responses resulted in significant main effects for hemisphere in the posterior-anterior dimension (x-axis; $F_{(1, 12)} = 5.8, p < 0.05$), the medio-lateral dimension (y-axis; $F_{(1, 12)} = 6.3, p < 0.05$), and the inferior-superior dimension (z-axis; $F_{(1, 12)} = 20.5, p < 0.001$). There was no significant interaction or main effect of attention. Hence, the estimated source locations of the neural activities measured slightly differed between hemispheres, irrespective of whether the subjects had focused their attention on the stimuli or not. This asymmetric N1m location between hemispheres most likely reflects anatomical hemispheric differences [Rademacher et al. 2001]. At first
glance, the lack of a significant source location difference between active and
distracted conditions seems to be inconsistent with previous fMRI results
revealing significantly larger cortical activation during auditory focused
attention [Grady et al. 1997; Benedict et al. 1998], until it is considered that
the dipole fit approach only allows the estimation of the center of gravity of the
neural responses, and not the extent of activated areas. Thus, this extent may
have differed between the two sessions, even though the centers of gravity
were not significantly different.

The grand-averaged N1m cortical source waveforms across all
subjects (time range –300 to +400 ms) are displayed in Figure 3.5. This
figure demonstrates a clear N1m response peaking at around 100 ms after
TS onset for the no-BEN condition. The N1m responses in the BEN
conditions are delayed and show smaller peaks compared to the no-BEN
condition.
The averaged normalized N1m source strengths and the N1m latencies for the left and right hemispheres and each BEN condition with the 95% confidence limit error-bars are presented in Figure 3.6. The repeated-measures ANOVA applied to normalized N1m source strength resulted in significant main effects of BEN type ($F_{(3, 36)} = 22.8$, $p < 0.0001$), hemisphere ($F_{(1, 12)} = 7.4$, $p = 0.019$), and attention ($F_{(1, 12)} = 19.4$, $p < 0.001$), as well as a significant interaction BEN type $\times$ attention ($F_{(3, 36)} = 5.3$, $p = 0.014$). Post-hoc comparisons showed significant differences between BEN160 and BEN80 ($p < 0.0003$), BEN160 and BEN40 ($p < 0.0001$), BEN160 and BEN20 ($p < 0.0001$), and BEN80 and BEN20 ($p < 0.003$).

Moreover, since there was no significant interaction of hemisphere with any factor, we collapsed data across hemispheres and calculated
planned comparisons (paired two-tailed t-tests, Bonferroni-Dunn corrected significance threshold: $p < 0.0127$) between active and distracted attention states on normalized N1m source strength within each BEN condition, in order to directly compare the active and distracted conditions. The results showed significant differences between BEN160_active and BEN160_distracted ($p < 0.008$), BEN80_active and BEN80_distracted ($p < 0.0003$), BEN40_active and BEN40_distracted ($p < 0.0001$), as well as between BEN20_active and BEN20_distracted ($p < 0.0001$). Furthermore, we compared estimated linear slopes of change for the active and distracted conditions by means of paired t-test. The results show that the slope in the distracted listening condition was significantly steeper than the slope in the active listening condition ($t_{(12)} = 2.84$, $p = 0.015$).
Figure 3.6. Normalized N1m source strength and N1m latency. The graphs display the group means (N = 13) of the normalized N1m source strength (top) and N1m latency (bottom) for each BEN condition, with error-bars denoting the 95% confidence limits for the group means. Filled circles denote the responses during the active listening condition; open circles denote the responses during the distracted listening condition.

Hence, statistical analyses of normalized N1m source strength indicated that attention as well as BEN type and hemisphere significantly influenced the strength of the neural activities measured. Crucially, effects of attention and BEN type were not independent from each other, but interacted: the effect of auditory focused attention increases with narrowing BEN.

The repeated-measures ANOVA applied to N1m latency revealed significant main effects of attention ($F_{(1, 12)} = 8.1, p = 0.016$) and BEN type ($F_{(3, 36)} = 63.7, p < 0.0001$), but there was no significant interaction between factors. Significant differences between BEN160 and all other BEN types ($p <$
as well as between BEN80 and BEN20 \( (p < 0.0001) \) were found using post-hoc comparisons. Hence, both attention and BEN type influenced the timing of the neural activities measured, while the timing did not differ between hemispheres. The repeated-measures ANOVA applied to non-normalized N1m source strength resulted in significant main effects for attention \( (F_{(1, 12)} = 61.2, \ p < 0.0001) \) and BEN type \( (F_{(3, 36)} = 23.0, \ p < 0.0001) \). Thus, N1m source strength was significantly larger during active as compared to distracted listening. Attention as well as BEN type influenced the strength of the neural activities measured. This gain effect caused by auditory focused attention did not differ between hemispheres.

### 3.3.2 Behavior measurement

Error rates (false alarms + misses) became larger and reaction times became longer with narrowing BENs, as shown in Figure 3.7. The repeated-measures ANOVA applied to error rate showed a significant main effect of BEN type \( (F_{(3, 36)} = 103.1, \ p < 0.0001) \), and post-hoc comparisons revealed significant differences between all BEN types \( (p < 0.0005) \). Also, the repeated-measures ANOVA applied to reaction time showed a significant main effect of BEN type \( (F_{(3, 36)} = 46.5, \ p < 0.0001) \), and again post-hoc comparisons revealed significant differences between all BEN types \( (p < 0.001) \) except for BEN40 vs. BEN80 \( (p = 0.024) \).

The results of the BEN ranking test showed that those subjects who had noticed differences between BENs were unable to rank them reliably (mean \((1 = \text{easy to} 4 = \text{difficult}) \pm \text{S.D.: } \text{BEN20} = 2.62 \pm 0.41, \text{BEN40} = 2.64 \pm 0.60, \text{BEN80} = 2.69 \pm 0.15, \text{BEN160} = 2.76 \pm 0.65\)). Hence, participants were not able to identify the different BENs.

Moreover, in order to confirm relationships between behavioral and electrophysiological responses, we performed additional correlation analyses. For the MEG variables (normalized N1m source strength active and N1m latency active) we obtained the means per BEN condition (BEN160, BEN80, BEN40, and BEN20) across hemispheres and subjects; for the
behavior variables (reaction time and error rate), we obtained the means per BEN condition across subjects. Product-moment correlations (df = 2, critical value = 0.95) revealed significant relationships between normalized N1m source strength active and reaction time ($r = -0.961, p = 0.039$), N1m latency active and reaction time ($r = 0.969, p = 0.031$), as well as a correlation trend between N1m latency active and error rate ($r = 0.913, p = 0.087$).

**Figure 3.7.** Behavior measurement: error rate and reaction time. The diagrams display error rate (top) and reaction time (bottom) as a function of BEN type, with error-bars denoting the 95% confidence limits of the group (N = 13) means.
3.4 Discussion

The present study experimentally confirmed the hypothesis that auditory magnetic fields evoked by the TS depended on the type of simultaneously presented BEN as well as the subjects’ state of attention. The results showed that N1m source strength was significantly larger during active compared to distracted listening, particularly when BENs with narrow stopbands were presented at the same time. Identical auditory stimuli were used during active and distracted listening conditions; the attention state of the subjects, however, differed. Therefore, afferent auditory inputs alone cannot explain the significant differences observed. Our results strongly suggest that top-down auditory focused attention impacted the generators of the N1m, possibly via efferent neural connections.

In this study, we have investigated neural population-level frequency tuning by means of MEG. Each BEN activated a neuronal population which overlapped the population representing the TS. The degree of overlap, however, differed between BENs (Figure 3.1 B, black areas). In case of narrow BENs, less neurons were newly activated by the delayed TS onset (Figure 3.1 B, dark gray areas) as compared to wide BENs. N1m source strength elicited by TS onset represents the number of newly activated neurons, which in turn reflects population-level frequency tuning, as has been shown by Sams and Salmelin [1994]. Using a distracted listening condition, we replicated their results, demonstrating that wider BENs permitted larger TS-related N1m amplitudes. Most importantly, in addition we were able to demonstrate that the effect of BEN type significantly differed as a function of attention.

Pioneering EEG studies [Hillyard et al. 1973; Picton and Hillyard 1974] showed significantly increased N1 response amplitudes during auditory focused attention. The authors suggested that attention could modulate neural activity already at an early stage of auditory analysis. In contrast, Näätänen et al. [1978] and Näätänen [1982] argued that the overlapping ‘processing negativity’, a component of endogenous origin characterized by a
source differing from the N1 source [Woods and Clayworth 1987], had caused the N1 amplitude enlargement. In the present experiment, however, in line with Fujiwara et al. [1998], N1m location differences between active and distracted conditions were not observed. Therefore, it is likely to assume that the N1m enlargement observed here was caused by the modulation of neural activity affecting transmission, analysis, and representation of the stimulus information in the auditory pathway [Hansen 1990].

Normalized N1m source strength was significantly different between the active and distracted listening conditions, including a significant interaction between attention and BEN type: the difference became systematically larger with decreasing notchwidth (Figure 3.6). These results imply that top-down auditory focused attention did not only amplify neural activities, but also sharpened the frequency tuning in auditory cortex.

A series of psychoacoustical studies [Schlauch and Hafter 1991; Hafter et al. 1993; Hubner and Hafter 1995] supports this hypothesis. These studies demonstrated that reducing frequency uncertainty by means of presenting frequency cues lead to sharpened frequency tuning as well as improved tone detection performance. In the present study, however, we did not present frequency cues, but instead used only one single TS, which was fixed in frequency across all conditions. Hence, frequency uncertainty was minimum here as well, while frequency selectivity at the TS frequency was supposedly maximum. Therefore, the present results possibly reflect modulation of neurophysiological filtering in the area of the TS frequency by auditory focused attention.

Inhibitory neural interactions might play an essential role for the observed sharpening effect. Previous studies have shown that the classical lateral inhibition concept [von Békésy 1967; Suga 1995; Pantev et al. 2004; Okamoto et al. 2005; Okamoto et al. 2007c] can account for the sharpening of frequency tuning in the central auditory system. Afferent neural signals consist not only of excitatory, but also broadly tuned inhibitory inputs, which suppress surrounding neural activity, resulting in improved spectral contrast.
On the other hand, a co-tuned excitatory and inhibitory neural model based on recent single neuron studies [Wehr and Zador 2003] can also explain the sharpening effect. This study demonstrated that frequency tuning curves of excitatory and inhibitory inputs are similar. However, inhibitory inputs follow excitatory inputs with a few milliseconds delay. Co-tuned neural activity can improve temporal coding by shortening the duration of excitatory neural activity, and also induce finer frequency tuning by suppressing excitatory activity [Tan et al. 2004]. Thus, enhancement of co-tuned neural activity by auditory focused attention could also improve frequency tuning.

In the present study, the inhibitory system, intensified by top-down auditory focused attention, might have sharpened the population-level frequency tuning via efferent auditory pathways. As a consequence, neurons corresponding to the edge frequencies of the BENs might have been less activated by the initial part of the BENs during active listening, due to steeper frequency tuning characteristics (black areas in Figure 3.1 B). Hence, relatively more neurons could be activated by the delayed TS onset, due to relatively small overlap with neurons already activated by the initial part of the BENs, resulting in an increased N1m source strength during active compared to distracted listening, particularly in case of narrow BENs. To summarize, inhibitory neural activity in auditory cortex, intensified by top-down auditory focused attention, might explain the sharpening effect observed here in response to attended stimuli.

Single cell recording studies revealed that frequency tuning can be modulated by learning-induced plasticity in inferior colliculus [Gao and Suga 1998], medial geniculate body [Edeline and Weinberger 1992; Lennartz and Weinberger 1992], primary auditory cortex [Weinberger et al. 1984; Ohl and Scheich 1996; Fritz et al. 2005b], and secondary auditory cortical fields [Diamond and Weinberger 1984]. Suga et al. [2002] showed that electrical stimulation in auditory cortex could cause expanded or compressed reorganization in this area and also subcortical auditory nuclei via efferent inputs: the tuning curves of neurons either shifted toward the parameter-
values of behaviorally important sounds (expanded reorganization, gain) or away from those values (compressed reorganization, sharpening). Attention might also modulate receptive fields of the cortex and subcortical auditory nuclei via the efferent auditory pathways. However, the comparison between plasticity of frequency tuning observed in single cell responses and attentional modulation of population-level frequency tuning of human auditory cortical responses might be inappropriate [Ohl and Scheich 2005].

Woldorff et al. [1993] observed significant attentional gain effects on both P1m and N1m responses, but the effect was larger in case of N1m. An fMRI study showed that the mesial part of the human auditory cortex is a stimulus-driven area that was always activated by a sound stimulus regardless of the subjects’ state of attention, whereas the activation of the lateral auditory cortex depended on the state of attention regardless of sound properties [Petkov et al. 2004]. Even though the lowest level of the auditory system on which sharpening occurs remains to be determined, these results indicated that the modulation of population-level neural activity by attention might take place mainly on cortical levels. Thus, it is reasonable to assume that in the present study attention mainly modulated the inhibitory neural conductance of the lateral auditory cortex.

Furthermore, we observed significant hemispheric differences in normalized N1m source strength, which was larger in the left hemisphere during both active and distracted listening conditions. Hence, this laterality effect cannot be explained by the mere presence of the task during active listening. Previous studies have shown that the left hemisphere may be dominant for processing requiring fine temporal resolution [Zatorre and Belin 2001], and temporal coherence seems to be crucial for the segregation of target sounds (i.e., signals) from non-target sounds (i.e., noise) [Barbour and Wang 2002]. Other authors [Tallal 1993; Poeppel 2003; Boemio et al. 2005] have suggested the ‘asymmetric sampling in time’ hypothesis. This concept suggests that the left auditory cortex dominantly exploits short temporal integration windows (20 - 40 ms), whereas the right auditory cortex exploits
longer ones (150 - 250 ms). In the present study, information from short temporal integration windows would be important for the quick detection of the TS onset masked by the BENs. Thus, the left hemispheric dominance observed here may imply that the left hemisphere plays a superior role in monitoring and analyzing auditory signals in noisy environments.

One can hypothesize that subjects may allocate more or less attention to solving a task depending on its difficulty. In this study, subjects were unable to strategically adjust the amount of allocated attention before TS onset, based on BEN type. Moreover, transient and sustained auditory evoked fields elicited by the onset and initial part of the different BENs did not differ systematically, but were generally larger in case of auditory focused attention. Sustained auditory evoked fields elicited by the BENs overlapped with neural activities elicited by TS onset. However, by means of applying baseline correction, we eliminated the sustained neural activities elicited by the BENs (Figure 3.1 B, black and light gray areas), and we were able to isolate neural responses elicited exclusively by the TS (Figure 3.1 B, dark gray areas).

In conclusion, this study has shown for the first time that top-down auditory focused attention cannot only amplify neural activity (gain effect), but also sharpen population-level frequency tuning in human auditory cortex, possibly via the inhibitory system. Auditory cortex neurons seem to be influenced by both bottom-up physical sound features and top-down attention processes. Effects of bottom-up and top-down processes on excitatory and inhibitory neural networks within human auditory cortex result in enhanced and sharpened population-level neural responses, which are reflected by the N1m response during auditory focused attention.
4 Frequency-specific attentional modulation of frequency tuning (Experiment 2)

4.1 Introduction
Humans can effortlessly process task-relevant sound signals despite the usual presence of concurrent noises, which are often task-irrelevant. Auditory focused attention eases this perception process. Recent MEG [Okamoto et al. 2007c] and EEG [Kauramäki et al. 2007; Bidet-Caulet et al. 2007] studies revealed that auditory focused attention not only amplifies task-relevant (‘gain’), but crucially also suppresses task-irrelevant neural activity (‘sharpening’) in human auditory cortex. Despite extensive research regarding attentional gain effects during auditory processing [Hillyard et al. 1973; Picton and Hillyard 1974; Näätänen and Picton 1987; Woldorff et al. 1993; Grady et al. 1997; Ross et al. 2004], the neurophysiological sharpening effects of attention in human auditory cortex remain elusive.

Each auditory neuron is characterized by a specific tuning curve exhibiting minimum threshold at a characteristic frequency [Calford et al. 1983; Robles and Ruggero 2001]. The neurons of the auditory pathway are systematically distributed according to their characteristic frequencies, and this ‘tonotopic’ alignment is still preserved in the auditory cortex [Reale and Imig 1980; Romani et al. 1982; Pantev et al. 1995]. Although auditory focused attention can amplify and sharpen neural activity in human auditory cortex, it is still unsettled whether these attentional effects depend on the specific location of neurons within the tonotopic maps. Psychoacoustical studies indicated that frequency-specific auditory attention sharpens the tuning for an attended relative to an unattended frequency (Figure 4.1 A), as was reflected in a detection advantage for the former compared to the latter [Hafter et al. 1993; Hübner and Hafter 1995]. Neurophysiological studies have uncovered possible underlying neural mechanisms. On the one hand, an fMRI study [Petkov et al. 2004] showed that auditory focused attention enhanced hemodynamic activation mainly in the lateral compared to the mesial auditory
cortex. This result indicates that attentional modulation mainly takes place on higher levels. On the other hand, single-neuron studies revealed that the cochlea not only passively translates vibration of air into neural activity, but also receives efferent neural inputs via the olivocochlear pathway, which actively modulates the displacement of the basilar membrane via the outer hair cells [Ruggero and Rich 1991; Robles and Ruggero 2001]. This ‘efferent system’ may contribute to the localized tuning refinement driven by frequency-specific auditory attention. Previous studies [Scharf et al. 1997; Khalfa et al. 2001; Perrot et al. 2006] supported this hypothesis by demonstrating the existence of human auditory efferent systems ranging from auditory cortex as far as to the cochlea. Therefore, attentional neural activity modulation might affect both central and peripheral auditory systems.

Based on these results and considerations, the goal of the present study was to investigate by means of MEG in awake, behaving humans whether population-level frequency tuning can be modulated by attention in a frequency-specific manner. Previous studies [Sams and Salmelin 1994; Okamoto et al. 2007c; Kauramäki et al. 2007] demonstrated the possibility to measure population-level frequency tuning by overlaying a pure tone with broadband noises containing spectral notches of different widths centered at the frequency of the tone (Figure 4.1 B). We hypothesized population-level frequency tuning to be sharper in a condition that invited subjects to focus attentional resources on one specific auditory filter (by presenting solely tones of identical frequency) relative to a condition forcing subjects to distribute attentional resources to several different auditory filters at the same time (by randomly presenting tones of several different frequencies).
Figure 4.1. **Model.** Schematic models of population-level frequency tuning sharpness with respect to the frequency-specific attention (test stimulus (TS) with fixed frequency; left column) and the frequency-nonspecific attention condition (random TS frequency; right column). The arrows indicate the attended frequencies. Attentional 'gain' size is represented as neural activity amplitude; degree of attentional 'sharpening' corresponds to the width of the frequency band that effectively evokes neural activity. A: Neural activity corresponding to the TS frequency (thick line) and other frequencies (thin lines). In fixed TS conditions, the neural activity corresponding to the TS frequency is larger and frequency tuning is sharper compared to other frequencies, due to frequency-specific attentional 'gain' and 'sharpening' effects. In contrast, in random TS conditions, attentional effects are widely distributed among frequencies, resulting in identical gain size and frequency tuning sharpness for TS and non-TS frequencies. B: Neural activity elicited by TS and band-eliminated noises (BENs). Left and right columns represent the frequency-specific attention (fixed TS) and frequency-nonspecific attention (random TS) conditions. The top, middle, and bottom rows represent wide (1 critical band (CB)),
middle (1/2 CB), and narrow (1/4 CB) BEN conditions. The three differently colored areas represent three distinct neural groups: (i) neurons merely activated by BEN (light gray areas), (ii) neurons merely activated by TS (dark gray areas), and (iii) neurons evocable by both BEN and TS (black areas). The dark gray areas correspond to N1m source strength elicited by TS-onset, since the neural activity represented by the light gray and black areas has been masked by the simultaneously presented (and earlier starting) BEN. Notably, the neural activity surrounding the TS frequency in the fixed TS conditions is larger and sharper due to the frequency-specific attentional ‘gain’ and ‘sharpening’ effects, as shown in Figure 1A.

4.2 Materials and methods
4.2.1 Subjects
14 healthy subjects (7 females) between 23 and 30 years of age (mean 26.4 years) participated in the present study. All subjects were right-handed (assessed with the ‘Edinburgh Handedness Inventory’ [Oldfield 1971]), and their hearing thresholds were within normal hearing level as tested by means of clinical pure-tone audiometry. Subjects gave written informed consent for their participation in the study in accordance with procedures approved by the Ethics Commission of the Medical Faculty, University of Muenster.

4.2.2 Stimuli and experimental design
We presented pure tones as test stimuli (TS) simultaneously with BENs (Figures 4.1 B and 4.2). The TS had a duration of 0.6 s (10 ms rise and fall times), and a frequency of either 250, 350, 450, 570, 700, 840, 1000, 1170, 1370, 1600, 1850, 2150, 2500, 2900, 3400, or 4000 Hz (one critical band (CB) steps [Zwicker and Fastl 2007]). In 50 % of the trials, the TS contained a silent gap of 10 ms duration (with 10 ms rise and fall times) starting at latency 285 ms (deviant test stimulus, cf. Figure 4.2). The TSs with temporal gaps were targets for behavioral responses during the MEG measurement (reaction times and error rates) and ensured the subjects’ compliance regarding the focus of attention. The sound onset asynchrony between two subsequent TSs was fixed to 3.0 s.
Figure 4.2. Experimental procedure. Concept and time course of the auditory stimulation with respect to the fixed frequency and random frequency conditions. Passbands and stopbands of the band-eliminated noises (BENs) are represented by the light gray and white areas, respectively. The bandwidth of a BEN (white area) is either 1/4, 1/2, or 1 critical band (CB). Target and non-target test stimuli (TS) are represented as red lines with gap (target TS, requiring a button press) and black lines without gap (non-target TS), respectively. During the frequency-specific attention condition (fixed frequency: upper graph), TS has identical frequency (i.e., either 250, 350, 450, 570, 700, 840, 1000, 1170, 1370, 1600, 1850, 2150, 2500, 2900, 3400, or 4000 Hz), whereas during the frequency-nonspecific attention condition (random frequency: lower graph) TS has different frequencies (i.e., 250, 350, 450, 570, 700, 840, 1000, 1170, 1370, 1600, 1850, 2150, 2500, 2900, 3400, and 4000 Hz). The TS frequency differed between frequency-specific attention blocks. In total, identical bottom-up auditory inputs are provided during the frequency-specific and frequency-nonspecific attention conditions.
The simultaneously presented BENs were prepared as follows: From 8000 Hz low-pass filtered white noise (sampling rate: 48000 Hz), spectral frequency bands with widths of either 1/4 critical band (1/4 CB), 1/2 critical band (1/2 CB), or 1 critical band (1 CB) centered at the frequency of the simultaneously presented TS were eliminated (Figure 4.2). All BENs (duration 3.0 s; 10 ms rise and fall times) started 2.2 s prior to TS onset and ceased 0.2 s after TS termination. All sound stimuli were prepared as sound files and presented under control of ‘Presentation’ (Neurobehavioral Systems, Albany, CA). 18000 Hz frequency tags (not perceivable) were attached to the onset of each TS in order to obtain precise timing. SRM-212 electrostatic earphones (Stax, Saitama, Japan) transduced air-conducted sounds which were delivered through silicon tubes (length: 60 cm; inner diameter: 5 mm) and silicon earpieces fitting to each subject’s ears. The hearing threshold for the 1000 Hz TS was determined for each ear of each individual at the beginning of the MEG session. The 1000 Hz TS was presented binaurally at intensity of 35 dB above individual sensation level. The power of the other TSs, which were also presented binaurally, was adjusted to the power of the 1000 Hz TS. The power of the binaurally presented BENs was 15 dB larger than TS.

In order to investigate the effects of attentional frequency-specificity, we contrasted two different conditions within subjects: ‘frequency-specific attention (fixed frequency)’ and ‘frequency-nonspecific attention (random frequency)’. In the frequency-specific attention session, 30 TS with identical frequency (either solely 250, 350, 450, 570, 700, 840, 1000, 1170, 1370, 1600, 1850, 2150, 2500, 2900, 3400, or 4000 Hz) were successively (and pseudo-randomly) presented simultaneously with either the 1/4, 1/2, or the 1 CB BEN. In the frequency-nonspecific attention session, 30 TS with different frequencies were presented, pseudo-randomly chosen from the same frequencies as in the frequency-specific attention blocks (250, 350, 450, 570, 700, 840, 1000, 1170, 1370, 1600, 1850, 2150, 2500, 2900, 3400, or 4000 Hz). As in the frequency-specific attention condition, BENs with notches of either 1/4, 1/2, or 1 CB were presented simultaneously and pseudo-randomly.
(Figure 4.2). Crucially, the overall amount of bottom-up auditory input was identical between frequency-specific attention and frequency-nonspecific attention conditions, while the patterning of stimuli was different. During all conditions, subjects were instructed to focus their attention on the auditory stimuli, and to press a response button as quickly as possible with their left or right index finger (randomized between subjects) whenever a TS with gap was detected. Frequency-specific attention and frequency-nonspecific attention blocks alternated, and block order was counterbalanced between subjects. In total, 160 trials (10 trials for 16 frequencies) for each BEN condition in each attention condition were presented and subjected to data analysis.

4.2.3 Data acquisition and data analysis
Auditory evoked fields were measured with a helmet-shaped 275 channel whole head magneto-gradiometer (Omega; CTF Systems, Coquitlam, British Columbia, Canada) in a silent magnetically shielded room. During the measurement, participants were comfortably seated upright, instructed not to move, and to fixate their eyes on the cross in the center of the screen in order to avoid eye movements. Head position was fixed with cotton pads and monitored via video camera. Alertness and compliance were also monitored via button press detecting the deviant TS as described above. The measured magnetic fields were digitally sampled at a rate of 600 Hz. Epochs of data elicited by TS with and without temporal gap, including a 300 ms pre-TS-onset interval and a 300 ms post-TS-onset interval, were averaged selectively for each BEN and attentional condition (irrespective of frequency) after rejection of artifact epochs containing field changes larger than 3 pT. We excluded magnetic fields with latencies longer than 300 ms from the analysis, due to the overlap of motor responses and auditory evoked responses elicited by the temporal gap. The evoked field source locations and orientations were determined in a head-based Cartesian coordinate system, with the origin at the midpoint of the medio-lateral axis joining the center of the entrances of the
ear canals. The posterior-anterior axis and the inferior-superior axis ran through nasion and origin and the origin perpendicularly to the medio-lateral and posterior-anterior axis.

For the analysis of the major component of the auditory evoked field, the N1m, the averaged magnetic field signals were 30 Hz low-pass filtered, followed by a baseline correction relative to the 300 ms pre-stimulus interval. Initially, the time point of maximum global field power, measured as root-mean square across all sensors around 150 ms after stimulus onset, was identified as N1m response. Afterwards, the 10 ms time window around the peak was used for dipole source estimation. The source locations and orientations were estimated by means of two single equivalent current dipoles (one for each hemisphere) based on the grand-averaged MEG waveforms for each subject. Finally, the estimated source for each hemisphere of each subject was fixed in its location and orientation, and source strengths were calculated for each BEN condition (BEN_1/4CB, BEN_1/2CB, and BEN_1CB) and each attention condition (frequency-specific attention and frequency-nonspecific attention).

In order to evaluate the gain and sharpening effects of attentional frequency-specificity, the maximum source strengths and latencies of the N1m responses elicited by the TS for each condition were analyzed separately via repeated-measures analyses of variance (ANOVA) using the factors BEN type (BEN_1/4CB, BEN_1/2CB, and BEN_1CB), hemisphere (left, right), and attention (frequency-specific, frequency-nonspecific). Post-hoc comparisons were performed using Bonferroni-Dunn's multiple-comparisons correction yielding a significance threshold of p < 0.0167. The behavioral data collected during MEG recording were analyzed similarly. Error rates (misses + false alarms) and reaction times were analyzed via repeated-measures ANOVAs using the factors BEN type (BEN_1/4CB, BEN_1/2CB, and BEN_1CB) and attention (frequency-specific, frequency-nonspecific). Post-hoc comparisons again entailed Bonferroni-Dunn’s multiple-comparisons corrections.
4.3 Results

Clearly identifiable averaged auditory evoked fields were obtained from all subjects. There were no systematic N1m source location or orientation differences between BEN conditions. Previous MEG studies [Sams and Salmelin 1994; Okamoto et al. 2007c] also demonstrated that simultaneously presented BENs did not systematically influence the calculated locations and orientations of the N1m sources. The goodness-of-fit of the underlying dipolar source model for the grand-averaged MEG waveforms was above 90 % for all subjects (mean ± SD: 95.3 ± 2.12 %). Waveforms, iso-contour field maps, and estimated source locations of the N1m overlaid on the structural magnetic resonance image of one representative subject are displayed in Figure 4.3. Clear dipolar patterns over the left and right hemispheres were observed, legitimating the use of the single dipole source estimation method. The dipolar sources were located on the superior temporal plane, which is assumed to be the generator site of the N1m response [Pantev et al. 1995; Eggermont and Ponton 2002].
Figure 4.3. Representative subject result. A: Averaged auditory evoked magnetic fields (30 Hz low-pass filtered) of one representative subject. The waveforms exhibit clear N1m responses peaking at the latency of 170 ms. B: Magnetic contour maps and estimated single dipoles at the latency of the maximum N1m response are illustrated together with skin and brain modeled from the individual magnetic resonance image. Red and blue contour lines represent outbound and inbound flow of magnetic fields from and to the brain. The contour maps show clear dipolar patterns above the left and right auditory cortices. The spheres and barrels in the brain indicate the locations and orientations of single dipoles in left (green) and right (red) hemispheres. The larger N1m source strength in the left hemisphere is represented by the larger dipole size.

4.3.1 N1m source strength and N1m latency
The grand-averaged N1m source waveforms across all subjects (time range from –100 to +300 ms) are displayed in Figure 4.4. The N1m responses in the frequency-nonspecific attention and the narrow BEN conditions are delayed
and reduced in peak amplitude as compared to the frequency-specific attention and the wide BEN conditions.

Figure 4.4. Grand-averaged source strength waveforms. Mean N1m source strengths (N=14) in left and right hemispheres, respectively. Solid lines represent the frequency-specific attention conditions (FIX), and dotted lines represent the frequency-nonspecific attention conditions (RD). Each color represents a band-eliminated noise (BEN) condition (blue: 1 critical band; green: 1/2 critical band; red: 1/4 critical band).

The mean N1m source strengths and latencies for left and right hemispheres in each condition with the 95% confidence limits are presented in Figures 4.5 and 4.6. The repeated-measures ANOVA evaluating N1m source strength and N1m latency resulted in significant main effects for hemisphere (source strength: $F_{(1, 13)} = 12.77, p < 0.004$; latency: $F_{(1, 13)} = 19.70, p < 0.0008$), attention (source strength: $F_{(1, 13)} = 9.73, p < 0.009$; latency: $F_{(1, 13)} = 58.82, p < 0.0001$), and BEN type (source strength: $F_{(2, 26)} = 30.39, p < 0.0001$; latency: $F_{(2, 26)} = 159.05, p < 0.0001$). Moreover, there
were significant interactions between hemisphere and BEN type (source strength: \(F_{(2, 26)} = 4.62, p < 0.02\)), and between attention and BEN type (source strength: \(F_{(2, 26)} = 12.13, p < 0.0003\); latency: \(F_{(2, 26)} = 24.40, p < 0.0001\)). The latter interactions show that whereas there was no attentional effect (a difference between the frequency-specific and frequency-nonspecific attention conditions) in the wide BEN condition, the narrow BENs show an enhanced N1m source strength for the frequency-specific as compared to the frequency-nonspecific condition. Post-hoc comparisons for N1m source strength and latency showed significant differences between BEN_1/4CB and BEN_1/2CB (source strength: \(p < 0.004\); latency: \(p < 0.0001\)), BEN_1/2CB and BEN_1CB (source strength: \(p < 0.0001\); latency \(p < 0.0001\)), and BEN_1/4CB and BEN_1CB (source strength: \(p < 0.0001\); latency \(p < 0.0001\)).
Figure 4.5. **N1m source strength.** Group means (N=14) of the N1m source strengths in the left and in the right hemispheres for each experimental condition, including error-bars denoting the 95% confidence limits of the differences to the mean N1m source strength across all conditions within hemisphere within subject. Filled circles denote the N1m source strengths elicited by the test stimulus (TS) during the frequency-specific attention conditions (fixed TS), and open circles denote the N1m source strengths during the frequency-nonspecific attention conditions (random TS).
4.3.2 Behavioral results

The mean error rates and reaction times with 95 % confidence limits are shown in Figure 4.7. The repeated-measures ANOVA revealed significant main effects of attention (error rate: $F_{(1, 13)} = 9.94, p < 0.008$; reaction time: $F_{(1, 13)} = 18.31, p < 0.001$) and BEN-type (error rate: $F_{(2, 26)} = 233.3, p < 0.0001$; reaction time: $F_{(2, 26)} = 17.60, p < 0.0001$). There was no significant interaction between factors (error rate: $F_{(2, 26)} = 0.61, p = 0.55$; reaction time: $F_{(2, 26)} = 0.52, p = 0.60$). Post-hoc comparisons revealed significant differences between BEN_1/4CB and BEN_1/2CB (error rate: $p < 0.0001$; reaction time: $p < 0.007$), BEN_1/2CB and BEN_1CB (error rate: $p < 0.0001$; reaction time: $p < 0.007$), and BEN_1/4CB and BEN_1CB (error rate: $p < 0.0001$; reaction time: $p < 0.0001$).
4.4 Discussion

Our present results confirmed the hypothesis that frequency-specific auditory attention (as compared to frequency-nonspecific attention) sharpens population-level frequency tuning in human auditory cortex in the tonotopic region of the attended frequency. N1m responses were significantly larger in the condition during which the test stimulus had a fixed frequency compared to the condition with random TS frequencies, particularly when BENs with narrow stop-bands were simultaneously presented. Because the total amount of stimulation received at each frequency was identical between the fixed and random conditions, it is the difference in patterning of the stimuli, one pattern allowing attentional resources to be directed to a specific frequency and the other pattern not, that must be responsible for the findings.
In order to investigate the mechanism underlying neural population-level frequency tuning we utilized overlays of TS and BEN and measured auditory evoked fields by means of MEG. Neural activity, which was evoked by TS–BEN overlays, could be schematically divided into three categories: (i) neural activity evoked solely by the TS (dark gray areas in Figure 4.1 B), (ii) neural activity triggered merely by the BEN (light gray areas), and (iii) neural activity elicitable by both the TS as well as the BEN (black areas). The N1m responses analyzed in this experiment represent neural groups solely activated by TS onset (dark gray area), since distinct neural groups (black and light gray areas) had already been activated and masked by preceding BENs when TS appeared. We found that the smaller notchwidth of BEN could cause smaller N1m source strength, as shown in Figure 4.5. The presentation of narrow BENs might result in comparably large overlap between neural populations representing BEN versus TS, and therefore comparably little neural activity was elicited by the late TS onset. Frequency-specific attention may cause sharper and larger neural activity at the attended frequency, and broader and smaller neural responses at the unattended frequencies, compared to frequency-nonspecific attention (as schematized in Figure 4.1 A). That would result in little neural activity overlap (black area in Figure 4.1 B) and large neural activity elicited by the TS onset (dark gray area), especially in case of narrow BEN conditions. We confirmed this hypothesis by demonstrating large N1m source strength differences between the frequency-specific and frequency-nonspecific attention conditions in case of narrow BEN conditions, and similar N1m responses between these two attention conditions in case of wide BENs (Figure 4.5).

Our findings are not easily explained by invoking attentional gain alone [e.g., Hillyard et al. 1973]. It is possible that attentional gain may have been higher for the fixed compared to the random condition, because subjects could allocate their attention to a specific frequency in the fixed condition, but had to divide it across frequencies in the random condition. However, the differential dependence of N1m enhancement on BEN type, with N1m
enhancement declining with the bandwidth of the notch more in the random relative to the fixed condition, implies that the sharpness of tuning was an important additional factor.

Inhibitory neural interactions in the auditory system are known to contribute to sharpening frequency tuning [von Békésy 1967; Pantev et al. 2004; Okamoto et al. 2005; Okamoto et al. 2007a, c]. Recent animal studies recording single neural activity demonstrated that afferent auditory neurons project broadly tuned inhibitory in addition to focally tuned excitatory inputs, resulting in relatively stronger inhibition of the auditory neurons corresponding to frequencies that neighbor the test frequency [Wehr and Zador 2003; Higley and Contreras 2006; Wu et al. 2008]. This balanced (regarding excitatory and inhibitory inputs) neural activity contributes to sharpening the frequency tuning and to improving spectral contrasts. In the model of Figure 4.1, enhanced inhibitory effects on the task-irrelevant neural activity are depicted as reduced activity evoked by the BEN sound in the fixed compared to the random condition.

In the present design, subjects rapidly appreciated when a fixed-frequency block was presented, and could under these conditions focus their attention on a particular stimulus frequency for the duration of the block (30 trials). Similarly, in a random-frequency block, subjects understood that the focus of attention had to be divided across several stimulus frequencies. Because this task knowledge was evident, it is possible that frequency tuning was modulated by top-down attentional mechanisms between these two conditions [Sarter et al. 2001], enhancing excitatory neural pathways and sharpening by enhancing inhibitory neural circuits in the fixed- compared to the random-frequency condition. Alternatively, a dual tuning process may have been driven by cumulative bottom-up inputs within a block in the fixed- compared to the random-frequency condition. Either of these mechanisms (top-down or bottom-up) is compatible with evidence for a ‘winner take all’ strategy of auditory tuning reported by Schulze et al. [2002] and Kurt et al. [2008]. Their findings indicated that slightly higher neural activity elicited by
one specific sound (‘winner’) inhibited neural activity corresponding to other sounds (‘losers’). In the present study, top-down frequency-specific attention could have defined the neural activity corresponding to TS as ‘winner’ in advance of the TS onset, dynamically sharpening frequency tuning for the relevant sound in a fixed-frequency block. Alternatively, repetition of a specific frequency within the block might have achieved the same outcome by a bottom-up process.

The lowest system level, on which frequency-specific attentional sharpening occurs, remains to be determined. However, attentional modulation of neural activity might affect structures as peripheral as the movement of the basilar membrane in the cochlea. Previous studies in cat indicated that the efferent pathway reaches the cochlea via the olivocochlear bundle [Wiederhold and Kiang 1970; Liberman and Brown 1986], and attention could modulate cochlear functions in humans possibly via this bundle [Lukas 1980; Khalfa et al. 2001; Maison et al. 2001]. Thus, it is reasonable to assume that in the present study frequency-specific auditory attention modulated outer hair cell functioning corresponding to the attended frequency via top-down neural inputs prior to TS onset, possibly via the olivocochlear bundle. In case of frequency-nonspecific attention, the olivocochlear bundle may not effectively work before the actual TS onset, since the upcoming TS frequency was undetermined. However, the frequency tuning regarding the TS frequency in the cochlea may be sharpened after the detection of the TS frequency via the neural feedback loops between peripheral and central auditory systems. The delayed N1m responses in the present as well as corresponding delay in a previous psychoacoustical study [Scharf et al. 2007] during frequency-nonspecific attention might reflect the time course of the neural feedback loop in the human auditory pathway [Backus and Guinan 2006]. Alternatively, it is possible that tuning enhancement occurs via interactions among populations of neurons within central auditory structures. While the site of tuning enhancement is presently unknown, the outcome of tuning is expressed at the level of the auditory
cortex, where the generators of the N1m are found [Pantev et al. 1995; Eggermont and Ponton 2002].

In the present study, we observed larger N1m source strengths in the left compared to the right hemisphere. Noteworthy, it is known that the right hemisphere N1m response elicited by a pure tone in a silent environment has similar or even larger amplitudes [Kanno et al. 1996] and shorter latencies [Roberts et al. 2000] compared to the left hemisphere. Therefore, the results of the present study support the hypothesis that the left hemisphere plays a dominant role in monitoring and processing auditory signals in noisy environments [Okamoto et al. 2007b].

Previous studies [Butler 1968; Ulanovsky et al. 2003] demonstrated that the repetition of identical auditory stimuli reduces corresponding neural activity (‘habituation’). In the present study, TS were identical in the frequency-specific attention condition, which theoretically could have lead to larger habituation effects and smaller N1m responses compared to the frequency-nonspecific attention condition. However, in contrast the N1m responses were significantly larger in the frequency-specific attention condition. Hence, the top-down gain effects of frequency-specific auditory attention seem to have overcome the habituation effects.

4.5 Conclusion
Our findings suggest that auditory focused attention, whether achieved by top-down, bottom-up, or both processes, can improve population-level frequency tuning in humans in a frequency-specific manner. Interactions between excitatory and inhibitory neural networks, intensified by attention processes, sharpen population-level frequency tuning in a frequency-specific manner, leading to enhanced auditory performance.
5 Interhemispheric support during demanding auditory signal-in-noise processing (Experiment 3)

5.1 Introduction

Auditory signal-in-noise processing in humans has been investigated with ‘simultaneous masking’ paradigms, by overlaying signals (e.g. tone, speech sound) with maskers (e.g. white noise), at behavioral [Zwislocki et al. 1968; Zwicker and Fastl 2007] and electrophysiological levels [Hari and Makela 1988; Brancucci et al. 2004; Morita et al. 2006; Okamoto et al. 2007c]. Using MEG, Sams and Salmelin [1994] showed that the amplitude of the auditory N1m response (generated in non-primary auditory cortex [Pantev et al. 1995; Eggermont and Ponton 2002]) evoked by a tone was a function of the width of the frequency band that had been eliminated from simultaneously presented noise maskers overlapping the tone spectrum. Thus, auditory processing is systematically influenced by the signal-to-noise ratio of bottom-up neural inputs. However, top-down processes also modulate auditory signal-in-noise processing. We have shown recently [Okamoto et al. 2007c] that auditory focused attention not only amplified the amplitude of the auditory N1m response evoked by a tone during simultaneous masking, but also sharpened the frequency tuning in the human auditory system, indicating that bottom-up neural inputs and top-down processes interact during auditory signal-in-noise processing.

Recent neuroscience research has revealed functional asymmetries of left and right auditory cortices during sound processing. On the one hand, studies indicated relatively increased activation in the left hemisphere during the processing of speech [Eulitz et al. 1995; Alho et al. 1998; Belin et al. 2000; Szymanski et al. 2001] as well as temporal acoustic features [Zatorre and Belin 2001; Jamison et al. 2006]. Noteworthy, the speech processing-related leftward lateralization of brain activation is in accordance with works demonstrating a behavioral right-ear advantage for speech stimuli [e.g., Hugdahl and Anderson 1984; Bryden 1988]. On the other hand, relatively
increased activation in the right hemisphere during the processing of music [cf. Zatorre et al. 2002] as well as spectral acoustic features [Zatorre and Belin 2001; Jamison et al. 2006] has been observed.

However, functional asymmetries may not only depend on the cognitive quality (speech versus music) or the composition of the sound signal on the acoustic feature level (temporal versus spectral), but also on the presence or absence of ‘noise’ as well as the attentional state of the listener. Regarding the role of noise, Shtyrov et al. [1998] observed significant increments (relative to a silent control condition) of both MMN and P2m amplitude [Shtyrov et al. 1999] in the right hemisphere during processing of consonant-vowel syllables masked by white noise. Results were interpreted as reflecting an increased right-hemisphere role in speech sound processing under noisy conditions, involving recruitment of additional right auditory cortex resources. Other studies observed relatively larger N1m amplitudes in the left auditory cortex compared to the right during processing of tonal signals masked by noises, during non-attentive listening as well as auditory focused attention [Okamoto et al. 2007b, c]. Results indicated left hemispheric dominance for auditory processing in noisy environments. Regarding the role of attention, it has for instance been demonstrated that directing attention to the right ear during the dichotic presentation of speech sounds increased the right-ear advantage, whereas directing attention to the left ear reduced the right-ear advantage [Hugdahl and Andersson 1986; Asbjørnsen and Hugdahl 1995]. Moreover, utilizing fMRI it was found that focusing of attention on vowel sounds and spoken words (as compared to passive listening and attended pseudo-words) increased temporal lobe activation with a leftward asymmetry [Hugdahl et al. 2003]. Going one step further, Tallus et al. [2007] demonstrated that top-down attention as well as bottom-up sound intensity interactively influenced response laterality for speech sounds on the behavioral level.

However, at this point it appears unsettled whether, and if so how, hemispheric asymmetries during auditory non-speech signal processing could
be interactively influenced by both the signal-to-noise ratio and the attentional state of the listener at the same time. Here, investigating this issue by means of MEG, a tonal signal was delivered monaurally and simultaneously with binaural BENs containing either ‘wide’ or ‘narrow’ stopbands, thereby varying signal-to-noise ratio (or task difficulty, respectively). Furthermore, listeners were supposed to direct their attention either to the signal or away from the signal, thereby altering the attentional state (or the importance of correct signal processing, respectively). Based on aforementioned findings, results were expected to bear evidence for the (i) global left hemisphere dominance in noisy environments, and potentially (ii) increased right auditory cortex activity under demanding and relevant conditions.

5.2 Materials and Methods

5.2.1 Subjects
22 right-handed (assessed via the ‘Edinburgh Handedness Inventory’ [Oldfield 1971]) subjects (12 males; mean age 25.48 years (SD 1.73)) participated in the study. All participants had normal hearing in the frequency range from 250 to 8000 Hz, as tested by clinical audiometry. After having been informed about the nature of the study, subjects gave written consent. The study protocol has been approved by the Ethics Committee of the University Hospital Muenster, and the study was performed in accordance with the Declaration of Helsinki.

5.2.2 Auditory and visual stimuli
Five different auditory stimuli were used in order to evoke auditory magnetic fields. Four of these stimuli were spectrally complex overlays of BEN and tonal test stimulus (TS); the fifth stimulus was TS in isolation (No-BEN). BENs served as simultaneous maskers, TS was the test signal. TS was presented randomly monaurally to either the left or the right ear only. In contrast, BENs were presented strictly binaurally. During data analyses, No-BEN was used for source localization estimation purposes only, and thus not included in
statistical analyses, since its frequency spectrum differs qualitatively from BEN-TS overlays. BENs were prepared by digitally eliminating (Gaussian filter) frequency bands of different widths (either 330 Hz (BEN330), 160 Hz (BEN160), 80 Hz (BEN80), or 40 Hz (BEN40), respectively) from 8000 Hz low-pass filtered white noise (sampling rate 48000 Hz). Resulting notches were spectrally located symmetrically around 1000 Hz (cf. Figure 5.1). BEN330 and BEN160 can be considered as rather ‘wide’ (i.e., outreaching the critical bandwidth of the auditory filter centered on 1000 Hz), while BEN80 and BEN40 are rather ‘narrow’ (i.e., within the critical bandwidth of the auditory filter). TS was a 40 Hz amplitude-modulated pure tone (modulation depth 100%), with a carrier frequency of 1000 Hz. BENs had a duration of 3.0 s, TS had a duration of 700 ms. The SOA between subsequent TSs was fixed to 3.0 s; TS-onset was 2.0 s delayed with respect to BEN-onset (cf. Figure 5.2).
Figure 5.1. Amplitude spectra. Amplitude spectra of the different band-eliminated noises (BENs) in the frequency range from 500 Hz to 2000 Hz. BENs contain spectral notches of either 40 Hz (BEN 40), 80 Hz (BEN 80), 160 Hz (BEN 160), or 330 Hz (BEN 330). Notches are spectrally centered at 1000 Hz.

In addition to the auditory standard TS introduced above, so-called ‘auditory target TSs’, which had to be detected by the subjects, were used in order to effectively implement selective attention to the left or the right ear, respectively. Auditory target TSs contained one of six different temporal gaps of 50 ms duration, which were variable in their positions (beginning at either 100 ms, 200 ms, 300 ms, 350 ms, 450 ms, or 550 ms after TS onset, respectively) (cf. Figure 5.2).
Visual stimuli were random configurations of one up to nine ‘X’-s, which could appear simultaneously in nine predefined locations on the screen. One specific ‘X’ served as fixation cross and was permanently visible in the center of the screen. The visual stimuli were solely used to distract attention from the auditory modality in a certain experimental condition (cf. Figure 5.3). Visually evoked responses were not of interest and thus not analyzed.

In order to effectively implement selective attention to the screen, so-called ‘visual target configurations’, which had to be detected by the subjects, were used in addition to the standard configurations. Visual target
configurations contained exactly one small square constituted of four ‘X’s appearing in one of the four corners of the screen (cf. Figure 5.3).

![Figure 5.3. Concept of the visual stimulation. Stimuli are random configurations of one to nine ‘X’s appearing simultaneously in predefined locations on the screen. Visual target configurations (e.g., G, H, and I) contain exactly one small square constituted of four ‘X’s appearing in one of the four corners of the screen (as indicated by the white dotted lines). Non-target configurations (e.g., A to F) did either not contain a small square (e.g., D, E, and F) or more than one small square (e.g., A, B, and C).]

5.2.3 Manipulation of attention
Before each experimental block, subjects were instructed to focus their attention either on their left ear, right ear, or the screen only, and to ignore the other channels. Throughout the whole experiment, irrespective of the location of the attention focus, auditory and visual stimuli were presented simultaneously, but were uncorrelated.
The following three attention conditions were of interest. (i) Relevant auditory attention (REL_AUD): the auditory TS appeared in the attended ear. (ii) Irrelevant auditory attention (IRR_AUD): the auditory TS appeared in the non-attended ear. (iii) Irrelevant visual attention (i.e. distraction of attention from the auditory modality) (IRR_VIS): the auditory TS appeared in the left or the right ear (Table 1). The IRR_VIS condition served as baseline condition. Even though the state of attention differed between REL_AUD, IRR_AUD, and IRR_VIS, the auditory and visual bottom-up inputs were identical between these conditions.

In addition to the mere instruction to focus attention on a certain channel and ignore other channels, auditory and visual target detection tasks were applied in order to effectively implement selective attention. Subjects were instructed to press a response button as quickly as possible with their right index finger when detecting targets (10 % probability) while ignoring standard stimuli (90 % probability). In case of auditory focused attention (i.e. left ear or right ear attention), ‘auditory target TSs’ had to be detected in the attended ear; in case of attention focused on the screen, specific ‘visual target configurations’ had to be detected.

Table 1. Overview regarding experimental conditions. In the relevant auditory attention condition, the spatial locations of attention focus and signal are identical (either left or right ear). In the irrelevant auditory attention condition, attention is focused on either the left or the right ear, and the signal appears in the non-attended ear. In the irrelevant visual attention condition, attention is focused on the screen; the signal appears either in the left or the right ear. Band-eliminated noises (BENs) are presented strictly binaurally.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Attention Focus / Auditory Signal</th>
<th>BEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relevant Auditory Attention</td>
<td>Left Ear / Left Ear <strong>AND</strong> Right Ear / Right Ear</td>
<td>Both Ears</td>
</tr>
<tr>
<td>Irrelevant Auditory Attention</td>
<td>Left Ear / Right Ear <strong>AND</strong> Right Ear / Left Ear</td>
<td>Both Ears</td>
</tr>
<tr>
<td>Irrelevant Visual Attention</td>
<td>Screen / Left Ear <strong>AND</strong> Screen / Right Ear</td>
<td>Both Ears</td>
</tr>
</tbody>
</table>
5.2.4 Design
As dependent variable, N1m source strength was measured, whereat *BEN type* ((wide (BEN330, BEN160), narrow (BEN80, BEN40)), *attention* (REL_AUD, IRR_AUD, IRR_VIS), and *hemisphere* (left, right) served as factors. For each subject, two MEG recording sessions on different days were performed. In each session, 1200 auditory TSs were presented in total. *BEN type* was delivered randomly within subject and session. Attention was manipulated in blocks within subject and session (9 blocks per session; 3 blocks per attention condition per session). The block order was pseudo-randomized and counterbalanced between subjects. One block lasted approximately 6 minutes, and the total duration of one session was approximately 1 hour.

5.2.5 Procedure, data acquisition, and data analysis
In the beginning of each MEG recording session, the hearing threshold for TS was determined for each subject and each ear individually. TS had loudness of 35 dB above individual threshold, while the power of BENs was 15 dB larger than TS power. BENs were always presented binaurally, TS was presented monaurally, randomly either to the left or the right ear (Table 1). Auditory evoked fields were recorded with a helmet-shaped 275-channel whole head neuro-gradiometer (OMEGA, CTF Systems Inc.) in a silent magnetically shielded room. Participants were comfortably seated upright. Head position was fixed with cotton pads, and subjects were instructed not to move. Head position and compliance were monitored continuously by video camera during the MEG recordings. Auditory evoked fields were digitally sampled at a 600 Hz rate and 150 Hz low-pass filtered during acquisition. Artifact epochs containing field changes larger than 3 picotesla were rejected. Data epochs elicited by standard TS, including a 100 ms pre-TS-onset baseline interval and a 500 ms post-TS-onset interval, were averaged selectively for each session, *BEN type*, and attentional condition. Source locations and orientations were determined in a head-based Cartesian
coordinate system, with the origin at the midpoint of the medio-lateral axis (y-axis) joining the center points of the entrances to the ear canals (positive towards the left ear). The posterior-anterior axis (x-axis) ran between nasion and origin, the inferior-superior axis (z-axis) ran through the origin perpendicularly to the x-y-plane.

The auditory evoked N1m response is generated in a relatively restricted cortical area (posterior temporal plane and lateral aspects of Heschl’s gyrus [Pantev et al. 1995; Eggermont and Ponton 2002]). Therefore, N1m source locations and orientations were estimated for each subject and session individually, by means of single equivalent current dipoles (one per hemisphere) based on the grand-averaged No-BEN condition, using a spherical head model. A previous MEG study [Sams and Salmelin 1994] had shown that estimated location and orientation of the N1m component elicited by a tonal stimulus are unaffected by simultaneously presented BENs. The averaged evoked magnetic fields were 30 Hz low-pass filtered, followed by a baseline correction relative to the 100 ms pre-stimulus interval. The time point of maximum global field power, measured as root-mean square across all sensors around 100 ms after stimulus onset, was identified. Afterwards, the 10 ms time window prior to the peak was used for fixed source estimation. The goodness-of-fit of the underlying dipolar source model was above 90 % for all included subjects and sessions (mean 96.33 % (SD 1.74)), legitimating the utilization of the single dipole source model. The estimated source for each hemisphere of each subject and each session was fixed in location and orientation, and source strength was calculated for all time points for each BEN type (BEN330, BEN160, BEN80, and BEN40) and for each attentional state (REL_AUD, IRR_AUD, and IRR_VIS), respectively.

5.3 Results
Clearly identifiable auditory evoked fields were observed from 17 out of the 22 subjects measured. For 5 subjects, it was difficult to estimate reliable dipolar sources (goodness-of-fit ≥ 90 %). Therefore, data from these subjects
were not included into further analyses. As in our previous study [Okamoto et al. 2007c], the subjects in the present study could not identify the different BENs.

Contour maps and estimated source locations of the N1m including confidence limits [Fuchs et al. 2004], overlaid onto the MRI of one representative subject for the grand-averaged No-BEN-condition, are displayed in Figure 5.4. Clear dipolar patterns over both hemispheres were observed. The grand-averaged N1m cortical source waveforms across 17 subjects (time range –100 to +300 ms) are displayed in Figure 5.5, demonstrating the clear N1m response peaking at around 100 ms after TS onset for the BEN330 condition. N1m responses for narrower BEN-TS combinations are to a certain degree delayed and smaller in amplitude.

Paired t-tests applied to the dipole source locations of the N1m response revealed significant hemispheric differences in posterior-anterior (x-axis: $t_{(33)} = -3.588, p = 0.001$) and inferior-superior (z-axis: $t_{(33)} = 4.174, p < 0.0001$) dimensions. Hence, estimated locations of the measured neural activities slightly differed between hemispheres. These differences most likely reflect anatomical differences between hemispheres [Morosan et al. 2001; Rademacher et al. 2001].
Figure 5.4. **Representative subject result.** Contour maps (A, B) and dipole source locations, strengths, and orientations (C, D) for the grand-averaged No-BEN-condition of one session of one representative subject based on the boundary element head model created on basis of the structural individual magnetic resonance image. Blue lines indicate inward flow of magnetic fields, red lines denote outward flow (A, B). Green/ red dipoles indicate left-/ right-hemispheric sources. Ellipsoids indicate the 95% confidence volume limits of the estimated dipolar sources (C, D).
Figure 5.5. Grand-averaged source strength waveforms. Source waveforms grand-averaged across all included subjects. The graphs show clear N1m responses for all conditions. The left panel (A, C) displays left-hemispheric responses; the right panel (B, D) displays right-hemispheric responses. The top row (A, B) shows the relevant auditory attention condition, and the bottom row (C, D) shows the irrelevant auditory attention condition.

Planned contrasts were calculated. Notably, the contrasts 
\([\text{REL\_AUD}\text{Left, Wide} - \text{IRR\_AUD}\text{Left, Wide}] - [\text{REL\_AUD}\text{Left, Narrow} - \text{IRR\_AUD}\text{Left, Narrow}]\) (7) in Table 2) and 
\([\text{REL\_AUD}\text{Right, Wide} - \text{IRR\_AUD}\text{Right, Wide}] - [\text{REL\_AUD}\text{Right, Narrow} - \text{IRR\_AUD}\text{Right, Narrow}]\) (13) in Table 2) were calculated to test the interactions between attention (REL\_AUD vs. IRR\_AUD) and BEN type (Wide vs. Narrow) for the left and right hemispheres separately. All performed contrasts including corresponding F- and p-values are shown in Table 2.
Table 2. Overview regarding calculated planned contrasts on N1m source strength and N1m latency. F- and p-values (* = p < .05) are provided. Left / Right = left / right hemispheres, REL_AUD / IRR_AUD / IRR_VIS = relevant auditory attention / irrelevant auditory attention / irrelevant visual attention conditions, WIDE, WIDE/ NARROW, NARROW = wide/ narrow BENs.

<table>
<thead>
<tr>
<th>Contrast</th>
<th>Source Strength</th>
<th>Latency</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) [ Left - Right]</td>
<td>25.3</td>
<td>.001 *</td>
</tr>
<tr>
<td>(2) [ REL_AUD_Left - IRR_AUD_Left]</td>
<td>0.5</td>
<td>.48</td>
</tr>
<tr>
<td>(3) [ REL_AUD_Left - IRR_VIS_Left]</td>
<td>5.9</td>
<td>.027 *</td>
</tr>
<tr>
<td>(4) [ IRR_AUD_Left - IRR_VIS_Left]</td>
<td>4.6</td>
<td>.048 *</td>
</tr>
<tr>
<td>(5) [ (REL_AUD_Left - IRR_AUD_Left) - IRR_VIS_Left]</td>
<td>5.6</td>
<td>.031*</td>
</tr>
<tr>
<td>(6) [ WIDE_Left - NARROW_Left]</td>
<td>40.3</td>
<td>.001 *</td>
</tr>
<tr>
<td>(7) [ (REL_AUD_Left, Wide - IRR_AUD_Left, Wide) - (REL_AUD_Left, Narrow - IRR_AUD_Left, Narrow)]</td>
<td>0.8</td>
<td>.39</td>
</tr>
<tr>
<td>(8) [ REL_AUD_Right - IRR_AUD_Right]</td>
<td>9.2</td>
<td>.008 *</td>
</tr>
<tr>
<td>(9) [ REL_AUD_Right - IRR_VIS_Right]</td>
<td>12.3</td>
<td>.003 *</td>
</tr>
<tr>
<td>(10) [ IRR_AUD_Right - IRR_VIS_Right]</td>
<td>2.5</td>
<td>.137</td>
</tr>
<tr>
<td>(11) [ (REL_AUD_Right - IRR_AUD_Right) - IRR_VIS_Right]</td>
<td>6.9</td>
<td>.018 *</td>
</tr>
<tr>
<td>(12) [ WIDE_Right - NARROW_Right]</td>
<td>24.7</td>
<td>.001 *</td>
</tr>
<tr>
<td>(13) [ (REL_AUD_Right, Wide - IRR_AUD_Right, Wide) - (REL_AUD_Right, Narrow - IRR_AUD_Right, Narrow)]</td>
<td>6.8</td>
<td>.019 *</td>
</tr>
</tbody>
</table>

Overall, N1m source strength was significantly larger in the left compared to the right auditory cortex (Table 2, contrast (1)). In both hemispheres, N1m source strength was significantly larger in case of auditory focused (REL_AUD, IRR_AUD) compared to visually focused attention (IRR_VIS) (Table 2, contrasts (5), (11)). Moreover, N1m source strength was significantly larger for wide (160 Hz, 330 Hz) than for narrow (40 Hz, 80 Hz) BENs in both hemispheres (Table 2, contrasts (6), (12)). In the left hemisphere, there was neither a significant N1m source strength difference between REL_AUD and IRR_AUD (Table 2, contrast (2)), nor a significant interaction between attention (REL_AUD vs. IRR_AUD) and BEN type (wide vs. narrow) (Table 2, contrast (7)). In contrast, the main effect (Table 2, contrast (8)) and the interaction were both present for the right hemisphere,
where N1m source strength was significantly larger during REL_AUD than IRR_AUD, but only for narrow BENs (Table 2, contrast (13)) (cf. Figure 5.6).

**Figure 5.6. N1m source strength.** Interaction plots illustrating N1m source strength grand-averaged across all included subjects with respect to relevant auditory attention and irrelevant auditory attention conditions. The left panel (A) displays left-hemispheric responses, the right panel (B) displays right-hemispheric responses. The circles (A, B) denote the relevant auditory attention condition, and the triangles (A, B) denote the irrelevant auditory attention condition. Error bars indicate the 95% confidence limits of the mean.

So far, both left- and right-ear stimulation and left- and right-ear attention had been pooled together in the analysis on attentional relevance effects, which were of particular interest in this study. However, recent studies [Bryden et al. 1988; Hugdahl et al. 2000; Saetrevik and Hugdahl 2007] indicated that stimulated ear and attended ear should be separated as factors influencing auditory processing. We thus evaluated whether N1m source
strength varied systematically as function of *stimulation side* (left, right) or *attention side* (left, right). Therefore, source waveforms were grand-averaged across BEN types (excluding No-BEN), hemispheres, and the 17 included subjects. Planned contrasts showed that N1m source strength did not differ between left- or right-ear attention ($F_{(1,33)} = 0.302, p = 0.586$). However, N1m source strength was significantly larger for right-ear than for left-ear stimulation ($F_{(1,33)} = 8.305, p = 0.007$).

Motivated by the latter results, we performed an additional behavioral test on 17 age-matched subjects in order to evaluate potential differences between stimulation sides. This test was conducted in the MEG room, and the auditory stimuli used were identical to those used during the MEG measurement. *BEN type* (BEN330, BEN160, BEN80, BEN40) and *stimulation side* (left, right) served as independent factors, while response accuracy (hit rate) and velocity (reaction time) served as dependent variables. As in the MEG measurement, BENs were presented binaurally, whereas TS was presented randomly to the left or the right ear. As opposed to the MEG measurement, TS was target (or non-target) in 50% of trials. Subjects were instructed to direct attention (block-wise) to their left or to their right ear only, and to press a response button as quickly as possible with their right index finger when detecting a target TS in the attended ear. The repeated-measures ANOVA calculated on hit rates revealed a significant main effect of *BEN type* ($F_{(3,48)} = 59.278, p < 0.001$). Crucially, there was no main effect of *stimulation side* ($F_{(1,16)} = 0.783, p = 0.389$) and no interaction between *BEN type* and *stimulation side* ($F_{(3,48)} = 0.087, p = 0.967$). A similar pattern was found for reaction times: while there was a significant main effect for *BEN type* ($F_{(3,48)} = 35.606, p < 0.001$), there was no main effect for ($F_{(1,16)} = 1.725, p = 0.208$) nor an interaction ($F_{(3,48)} = 0.907, p = 0.444$) with *stimulation side*.
5.4 Discussion
The present study yielded three major findings. (i) An overall hemispheric difference was observed, with N1m source strength significantly larger in the left than in the right hemisphere. (ii) Overall, N1m responses were larger for right-ear than for left-ear stimulation, even though the test stimulus was not a speech signal. (iii) Crucially, interactive effects were found for hemisphere, attentional relevance, and BEN type: whereas N1m source strength was similar for relevant auditory attention and irrelevant auditory attention conditions in the left hemisphere, an interaction between attentional relevance and BEN type was observed in the right hemisphere. Here, relative to the irrelevant auditory attention condition, N1m source strength was larger for narrow, but not for wide BENs in the relevant auditory attention condition.

The effects observed in the present study partly seem to result from the interactive interplay of bottom-up neural inputs and top-down processes. The characteristic bottom-up input in this experiment was the spectral overlap between masker and signal, which was operationalized as function of the eliminated bandwidth of the different BENs. In case of wide BENs, spectral overlap between BEN and TS was rather small, and therefore the signal (TS) was relatively easy to detect and to process by the auditory system. In contrast, in case of narrow BENs (stopband widths ½ or ¼ critical bandwidth, respectively), spectral overlap was quite large, and it appears very likely that part of the noise passed through the auditory filter centered on the signal (Patterson 1976), resulting in a reduced effective signal-to-noise ratio. Possibly, TS-related neural activity was attenuated by lateral inhibitory processes consequent on the noise (Okamoto et al. 2007a), and therefore TS was harder to process under these conditions.

The characteristic top-down manipulation concerned the locus of the attentional focus. In the irrelevant visual attention condition, attention resources were allocated to the visual modality. Hence, top-down processing regarding the auditory signal was weak. In the relevant auditory attention condition, attention resources were optimally allocated and focused with
respect to modality (auditory) and location (stimulated ear). Finally, in case of the irrelevant auditory attention condition, attention resources were also allocated to the auditory modality, but the focus was not on the stimulated ear (Table 1).

In the present experiment, N1m source strength was overall larger in the left compared to the right auditory cortex (hemispheric asymmetry effect; Figure 5.6 A vs. B). Moreover, N1m source strength was larger during auditory focused attention than during visually focused attention in both hemispheres (inter-modal attentional gain effect; Table 2). Additionally, in both hemispheres, wide BENs favored larger N1m source strengths than narrow BENs (spectral overlap-dependent masking effect; Figure 5.6 A, B). With regard to overall hemispheric differences, these results indicate basal left auditory cortex dominance during auditory signal-in-noise processing.

This is further substantiated by the observed right-ear advantage (reflected in the overall increased N1m source strength for right-ear as compared to left-ear stimulation), given that auditory projections are contralaterally dominant in the auditory cortex. Notably, this right-ear advantage could not be confirmed on the behavioral level. However, in the behavior test, stimulation side and attention side necessarily were perfectly confounded, and thus only responses to the attended ear could be analyzed. In the MEG measurement, in contrast, it was possible to decouple effects of attention side and stimulation side by means of selective signal averaging (irrelevant auditory attention condition). Thus, response levels are not fully comparable. Moreover, the mean overall hit rates (left ear: 86.7 %; right ear: 85.3 %) indicate that the stimuli might not have been hard enough to uncover differences at the behavioral level in the relevant auditory attention condition. However, stimuli were optimized for the MEG measurement (which was of primary interest for this study), and for the sake of comparability stimuli were held identical between MEG and behavioral tests.

Crucially, an interactive hemispheric difference was revealed in addition to the overall hemispheric asymmetry. While the left auditory cortex
showed no N1m source strength differences between relevant auditory attention and irrelevant auditory attention conditions, N1m source strengths in the right hemisphere differed significantly as a function of attentional relevance, but only for narrow and not for wide BENs. Thus, for the left hemisphere it did not seem to make a difference whether attention was focused on the correct or a wrong location, as long as attentional resources were allocated to the auditory modality (Figure 5.6 A). This indicates the ‘robustness’, in addition to the dominance, of the left auditory cortex during attentive auditory signal-in-noise processing. For the right hemisphere, in contrast, it did not seem to make a difference whether attention was distracted to the visual modality, or wrongly focused within the auditory modality. If, however, precise auditory signal-in-noise processing was clearly required (relevant auditory attention condition: attention optimally allocated and focused) and circumstances were demanding (narrow BENs: large spectral overlap between BEN and TS), neuronal activity in the right auditory cortex was significantly larger compared to situations where such precise auditory signal-in-noise processing was not required (irrelevant auditory attention and irrelevant visual attention conditions) (Figure 5.6 B).

The N1m source strength difference between the relevant auditory attention and irrelevant auditory attention conditions, which was observed in the right hemisphere for narrow BENs, could reflect either a decrement in the irrelevant auditory attention condition or an increment in the relevant auditory attention condition. However, since the irrelevant visual attention and irrelevant auditory attention conditions in the right hemisphere did not differ, increased neuronal activity in the relevant auditory attention condition seems more likely. This interpretation is supported by close inspection of the graphs in Figure 5.6, showing a monotonic decrease of the cortical N1m source strength with narrowing BENs, in all conditions except the relevant auditory attention condition in the right hemisphere for BEN40 compared to BEN80.

N1m source strength as measured by MEG depends on the number of activated neurons and on the degree of synchronicity of activity of the
involved neurons [Pantev et al. 1998]. Therefore, the increased neuronal activity observed in the right hemisphere for narrow BENs during the relevant auditory attention condition might reflect recruitment of additional neurons, improved phase-locking of involved neurons, or most likely, a combination of both.

The novel result pattern observed here may reflect an ‘interhemispheric support mechanism’. Basically, the left auditory cortex seems to be both dominant and robust during auditory signal-in-noise processing (as indicated by the overall larger neuronal activity and the similarity of the relevant auditory attention and irrelevant auditory attention conditions). If, however, accurate performance under demanding circumstances is requested, the right auditory cortex offers assistance (as indicated by increased neuronal activity in exactly such instances). Previous experimental findings have been interpreted in a similar vein. Relative to a complete silence condition, Shtyrov et al. [1998; 1999] observed increments in both MMNm- and P2m-amplitude in the right hemisphere during the processing of syllables simultaneously masked by white noise. These results point to an increased role of the right hemisphere during speech sound processing in noisy conditions, taken to be a reflection of the consumption of ‘supplemental’ right hemispheric resources. Furthermore, Liikkanen et al. [2007] observed a right-hemispheric augmentation in N1m source strength during the processing of vowels which were ‘degraded’ by means of uniform scalar quantization. Results were interpreted in terms of right-hemispheric compensation for poor speech signal quality.

The signal applied in the present study was not a speech sound. Instead, a simple 1000 Hz tone had to be detected and processed during the presence of interfering noise. Nevertheless, the present major finding is completely in line with the results obtained in previous experiments focusing on speech processing [Shtyrov et al. 1998; 1999; Liikkanen et al. 2007]. Hence, it appears highly probable that the right-hemispheric supplementation observed here is not unique for the processing of masked or degraded
speech, but rather reflects a basic brain mechanism that enables reliable auditory signal-in-noise processing. Thus, the present data probably uncovered a proficiency of the brain that is highly relevant in many day-to-day situations.

The amplitude-modulated tone, which was used as signal in this study, is known to generate the so-called auditory steady-state response [Rees et al. 1986; Hari et al. 1989; Pantev et al. 1993]. The auditory steady-state response, as opposed to the N1m, is known to be of primary auditory cortex origin [Pantev et al. 1996b; Draganova et al. 2008]. Therefore, the present study theoretically has the potential to assess whether the hypothesis of hemispheric specialization applies to primary as well as non-primary auditory cortex areas. However, similar to the study of Okamoto et al. [2007c], it proved to be impossible to extract auditory steady-state response source waveforms for the BEN conditions, due to insufficient signal-to-noise ratio. Thus, the conclusions drawn here are confined to non-primary auditory cortex areas.

Here, the signal (as opposed to the BENs) was presented monaurally, causing a larger response in the contralateral compared to the ipsilateral hemisphere. However, an equal number of trials with left- respectively right-ear stimulation contributed to each experimental condition (cf. Table 1), making sure that potential monaural stimulation-related hemispheric asymmetries were eliminated during selective signal averaging. Therefore, monaural signal presentation cannot account for the functional hemispheric asymmetries observed in this experiment. In addition, our interpretation of left hemispheric dominance in noisy environments is supported by a previous study employing a very similar paradigm, but binaural signals [Okamoto et al. 2007c].

In the present experiment, N1m latency was overall shorter in the right compared to the left hemisphere. Similar findings had already been observed in previous MEG studies investigating auditory responses evoked by tonal signals [e.g., Gabriel et al. 2004]. Moreover, N1m latencies were shorter in
case of auditory compared to visually focused attention; this has also been observed earlier [cf. Okamoto et al. 2007c]. Finally, N1m latencies were shorter for wide compared to narrow BEN conditions [cf. Sams and Salmelin 1994].

Previous fMRI studies [e.g., Petkov et al. 2004] had also suggested correlates of attention in lateral areas of auditory cortex involved in N1m generation. Due to the poor temporal resolution capabilities of fMRI, fine-scale timing of neural responses cannot be obtained with this method. On the contrary, MEG principally offers the possibility to unravel these attentional effects with high temporal precision, and may therefore be utilized to uncover potential early attention effects [cf. Woldorff et al. 1993]. However, the N1m response, contrariwise to other responses arising earlier (e.g. P1m) or later (e.g. P2m), is robust and stable. The present experiment is based on this N1m robustness and stability, and was explicitly designed for N1m evaluation. It was not intended to analyze other auditory evoked responses.

In conclusion, the present results provide evidence for increased neuronal activity in the right auditory cortex during auditory signal-in-noise processing, when signal-to-noise ratio is poor and adequate performance is explicitly relevant. The increased neuronal activity presumably reflects increased involvement of the right auditory cortex in the sense of additional consumption of right hemispheric resources in particularly demanding conditions. These findings could be interpreted as an indication of ‘right hemispheric support’ for the (basically dominant and robust) left auditory cortex during difficult and relevant auditory signal-in-noise processing.
6 General discussion and outlook

In summary, the present project yielded several innovative findings, providing deeper insight into the effects of attention on auditory signal-in-noise processing in the awake human brain. (i) Experiment 1 demonstrated that auditory focused attention sharpened population-level frequency tuning in the human auditory system. (ii) Experiment 2 showed that sharpening effects of attention were frequency-specific. (iii) Experiment 3 indicated that right auditory cortex activity was relatively increased during attentive compared to non-attentive auditory signal-in-noise processing under conditions characterized by poor signal-to-noise ratio. (iv) Experiments 1, 2, and 3 demonstrated that left auditory cortex activity was overall relatively increased during auditory signal-in-noise processing compared to right auditory cortex activity.

6.1 Attentional sharpening

The sharpening effect of attention on human auditory processing has been demonstrated here for the very first time. Hence, the confirmation of this effect would strongly fortify its validity. Fortunately, confirmation has meanwhile been accomplished by a different research group utilizing a different investigation tool (however, choosing a somewhat more general overall point of view): Kauramäki et al. [2007] employed a paradigm very similar to that of the present Experiment 1, and utilized EEG in order to reveal what they designated to be the neural basis of auditory selective attention. Using slightly different BENs (compared to the present Experiment 1) as simultaneous maskers and a 1000 Hz sinusoidal as test signal, as well as frequency deviant and duration deviant detection tasks as compared to an ‘ignore sounds’ condition, the authors came to the conclusion that “auditory selective attention in humans cannot be explained by a [simple] gain model, where only the neural activity level is increased, but [it appears] rather [likely] that selective attention additionally enhances auditory cortex frequency
selectivity” [Kauramäki et al. 2007, p. 7]. Despite the slightly different perspective, basically these findings replicate, complement, and validate the present results.

Even though the sharpening effect of auditory attention on frequency tuning is considered to be valid and reliable, the precise neural mechanisms that underlie this effect could not be observed directly here by means of MEG. N1m amplitude represents the synchronous, excitatory activity of a large number of similarly (and tangentially) oriented cortical pyramidal cells, reflecting number of active neurons as well as degree of synchronicity of active neurons within a certain time interval of interest relative to a stimulus. Unfortunately, MEG is neither capable of measuring single neuron activity (which would be necessary to precisely define neural mechanisms) nor population-level inhibitory activity.

Nevertheless, given that BENs had been used here as simultaneous maskers, it appears very likely that stimulation with those maskers may have concealed excitatory neural activity within the tonotopic area corresponding to the signal [cf. e.g., Norena et al. 2000]. The effectiveness of this masking on neuronal activity evoked by the signal would have depended on the width of the notch, with BENs containing narrower notches suppressing signal-related activity more strongly than BENs containing wider notches (consequently causing a signal-related N1m amplitude decrement with BEN notchwidth becoming narrower).

Moreover, it has been demonstrated repeatedly that lateral inhibitory processes contribute significantly to the sharpening of the frequency tuning of auditory neurons that is evident with increasing auditory system level [e.g., Katsuki 1958]. Here, it has been shown that auditory focused attention can also sharpen frequency tuning (whereupon top-down activity is likely to be transmitted via the well-pronounced efferent auditory system). Hence, it appears plausible to assume that attention would modulate auditory inhibitory systems, implying that attention could actively suppress task-irrelevant neural activity (which is, however, not evident from the findings provided here).
Notably, this hypothesis will be tested in a follow-up experiment playing on the finding of functional left-hemispheric dominance (details in 6.2) during auditory signal-in-noise processing (indicating the left auditory cortex to be dominant in inhibiting task-irrelevant neuronal activity compared to the right).

Basically, it remains to be determined exactly which auditory system levels reflect attentional sharpening, and particularly which level is the lowest to do so. From the MEG data measured here, this cannot be concluded. The N1m was generated in non-primary auditory cortex areas [e.g., Pantev et al. 1995; Eggermont and Ponton 2002], implying that attentional sharpening has happened in these areas, but that does not necessarily mean that sharpening could not have happened lower in the system. From a neuroanatomical perspective, attentional sharpening could have happened on any level of the auditory system as low as the basilar membrane, since the auditory efferent pathway (in cat) has been demonstrated to range from cortex as far as to the outer hair cells in the cochlea [e.g., Wiederhold and Kiang 1970; Liberman and Brown 1986]. The silver bullet to assess this issue would be intracranial electric recordings in awake humans, from different auditory system levels, during states of auditory focused attention versus distraction (needless to say that this would be impossible from an ethical point of view). Intracranial electric recordings in animals may provide insight as well, but this approach is limited, since the reliable manipulation of the attentional state of animals is at least problematic, if not impossible. Moreover, findings in animals can certainly not be assigned to humans in a one-to-one fashion. Nevertheless, modulations of receptive field properties in the auditory system of animals have been reported to covary with task demands [e.g., Fritz et al. 2003; 2005] as well as intracranial electrical stimulation [Suga et al. 2002].

In principle, it would be very interesting to investigate effects of attention and signal-to-noise ratio on other auditory evoked responses (particularly steady-state response and sustained field) than N1m during auditory processing. In contrast to the N1m, the steady-state response is known to be generated in primary auditory cortex [e.g., Draganova et al.]
2008], while the sustained field virtually integrates over the whole auditory
cortex [e.g., Pantev et al. 1994]. By means of comparing effects of attention
and signal-to-noise ratio on these components, it would be possible to track
the time course of effects of bottom-up factors and top-down processes on
auditory cortical processing. It could be hypothesized that bottom-up factors
(i.e., the effective signal-to-noise ratio) would dominantly influence processing
on lower levels of auditory cortex (i.e., primary auditory cortex as tracked by
the steady-state response), whereas top-down processes (i.e., attention)
became more and more influential on higher levels of auditory cortex (i.e.,
non-primary auditory cortex as tracked by the N1m and the sustained field).
Theoretically, Experiments 1 and 3 had the potential to address this issue,
because the amplitude-modulated signal presented in these experiments was
intended to evoke the steady-state response in addition to the N1m (and the
sustained field also could have been analyzed). Unfortunately, due to the
relatively larger BEN power compared to the signal power, it turned out to be
impossible to extract steady-state source waveforms. However, a follow-up
experiment utilizing a fixed broadband masker with varying intensity instead
of several BEN maskers of fixed intensity will likely overcome this problem.
Moreover, a recent study [Gutschalk et al. 2008] demonstrated multitone
maskers (that where not correlated with the signal in time and frequency
domains) to permit the development of signal-related transient as well as
middle-latency steady-state responses.

Finally and noteworthy, the sharpening effect of attention on frequency
tuning has been demonstrated here for the population-level only. That does
not imply that all single neurons belonging to the population measured
necessarily must have narrowed their tuning curves. Again, this question
could only be answered by means of single cell recordings.

6.2 Hemispheric lateralization
Overall increased left auditory cortex activity during auditory signal-in-noise
processing has been observed here in all three experiments, as well as in a
previous study by Okamoto et al. [2007b], indicating that this effect is valid and reliable (nonetheless, replication by a different group, preferentially with a different tool like EEG, would provide important corroboration). Notably, a tonal signal presented in isolation [e.g., Kanno et al. 1996] does not seem to cause left hemispheric increments in N1m amplitude, irrespective of whether listeners focus their attention on the signals or not. Hence, the presence or absence of functional hemispheric lateralization during auditory processing seems (among other factors) to critically depend on the effective signal-to-noise ratio.

In all three experiments carried out here, the attentional state of the listeners was manipulated. Moreover, in all three experiments listeners were supposed to focus attention on the signal(s) at least in one experimental condition. Finally, in all three experiments listeners were supposed to perform an active target detection task at least in one experimental condition. In contrast, in the study of Okamoto et al. [2007b], subjects listened passively to the signals, were not supposed to attend to the sounds, and were not required to perform any active task. The fact that the overall increased left auditory cortex activity has been observed in all four experiments suggests that this effect is strongly bottom-up driven, even though Experiment 3 indicated that this lateralization may be modulated by top-down processes in certain circumstances.

An important question that has to be addressed regards the direction of the functional lateralization effect observed here, i.e., why was the overall activity increased in the left hemisphere instead of the right? Several eventualities have to be taken into consideration. (i) Against the background of an increasing number of studies demonstrating left-hemispheric dominance for temporal acoustic signal feature processing [e.g., Zatorre and Belin 2001; Jamison et al. 2006] it can be hypothesized that auditory signal-in-noise processing as investigated here may particularly require temporal processing resources of the brain. This assumption is in line with works demonstrating ‘temporal coherence’ to be a crucial factor in extracting auditory signal from
noise [Barbour and Wang 2002]. If that was the case, adding noise to an auditory signal that would be dominantly processed in the left hemisphere if presented in isolation due to prominent temporal features, should amplify the leftward lateralization, because of an increasing demand for temporal processing resources. Likewise, adding noise to an auditory signal that would be dominantly processed in the right hemisphere if presented in isolation due to prominent spectral features, should reduce, cancel, or even reverse the rightward lateralization. However, this remains an empirical question to be answered. (ii) Considering the fact that only right-handers have been measured in all three experiments carried out here as well as in the study from Okamoto et al. [2007b] points into the direction of the concept of hemispheric language lateralization. It is well-known that right-handers show left-hemispheric language lateralization with a very high likelihood [e.g., Knecht et al. 2000], indicating that most (if not all) of the subjects investigated here were left-lateralized with regard to language. However, this was not tested. In order to assess the role of hemispheric language lateralization for the functional lateralization observed during auditory signal-in-noise processing, it would be necessary to compare listeners with left- versus right-hemispheric language dominance. This is an interesting and solvable task, since hemispheric language lateralization can meanwhile be estimated non-invasively and economically by means of functional Doppler sonography [e.g., Lohmann et al. 2005].

Another question to be answered is whether the increased activity in the left auditory cortex during auditory signal-in-noise processing reflects a functional dominance, or rather a functional inferiority. Apparently, this question could only be answered on the behavioral level. Experiment 3 theoretically had the potential to address this issue, since a monaural auditory signal had been used. Most of the nerve fibers of the ascending auditory pathways cross, and therefore monaural auditory signals are dominantly processed in the contralateral hemisphere. Hence, functional left-hemispheric dominance during auditory processing could be associated with a behavioral
right-ear advantage, as would be suggested by earlier studies demonstrating a right-ear advantage during speech processing [e.g., Hugdahl and Anderson 1986; Asbjørnsen and Hugdahl 1995]. Unfortunately, the demonstration of this behavioral right-ear advantage failed (cf. Experiment 3). However, in order to consolidate the interpretation that the present findings reflect a functional dominance of the left auditory cortex, the right-ear advantage should be demonstrated, preferentially in a carefully designed follow-up behavioral experiment.

A very exciting finding of Experiment 3 was that top-down attention could apparently modulate the functional dominance of the left auditory cortex during auditory signal-in-noise processing in certain circumstances. This complex and subtle effect manifested as interaction between brain hemisphere, signal-to-noise ratio, and locus of the attention focus, and could only be demonstrated by means of sophisticated experimental manipulation. As evident from all three experiments, signal-to-noise ratio influenced the task-difficulty for the listeners; the instructed locus of the attention focus can be assumed to have signalized the relative importance of precise signal processing to the listeners. As demonstrated, hard task plus importance of precise processing led to a relative decrement in the leftward functional lateralization by an absolute increment of right auditory cortex activity. However, given that the identical dipole had been used as spatial filter for all experimental conditions within hemisphere, and given that the dipole represents the center of gravity of the evoked neural activity and not its extension, it cannot be directly concluded from the data whether the right-hemispheric increment is function-based, structure-based, or both.

6.3 Conclusion
The present project demonstrated that (i) auditory focused attention sharpens population-level frequency tuning in human auditory cortex (and possibly lower auditory levels) in a frequency-specific way, presumably by means of actively suppressing task-irrelevant neuronal activity via inhibitory neural
networks. (ii) Moreover, the left auditory cortex presumably is functionally dominant during auditory signal-in-noise processing. (iii) Even though this leftward lateralization is strongly bottom-up driven and robust, it can be modulated by auditory attention, leading to left hemisphere relief via right-hemispheric backup in particularly demanding conditions. This novel knowledge contributes to the better understanding of auditory processing under natural conditions.


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8 Summary

In everyday life, we are quite often confronted with the challenge to process task-relevant acoustic stimuli (e.g., speech) during the simultaneous presence of task-irrelevant acoustic information (e.g., traffic noise). Usually, the task-relevant stimulus is referred to as signal, while the task-irrelevant information is referred to as noise. The poorer the effective signal-to-noise ratio, the harder it is to process the signal. Oftentimes it is impossible to actively and beneficially influence the signal-to-noise ratio in order to ease signal processing. However, we know from everyday life that auditory signal-in-noise processing is facilitated when we concentrate or focus our attention on the signal, respectively. Despite the apparent relevance of auditory attention for auditory signal-in-noise processing, the effects and mechanisms of attention on the neuronal level remain elusive.

The present thesis reports three experiments that investigated effects of attention on auditory signal-in-noise processing in human auditory cortex. As investigation tool, magnetoencephalography (MEG) was employed. With MEG, the activity of cortical neuronal populations can be measured directly, non-invasively, and without any side effects. The signal-to-noise ratio was manipulated in a simultaneous masking paradigm. Here, sinusoidal tones or amplitude-modulated sinusoidal tones served as signals, while band-eliminated broadband noises were used as maskers. The attentional state of the probands was varied via instructions as well as target detection tasks.

Based on the published literature, the following experimental hypotheses were formulated and evaluated: (i) auditory attention not only amplifies task-relevant neuronal activity, but also sharpens the frequency selectivity of underlying neuronal populations. (ii) These effects of attention are frequency-specific. (iii) Left-hemispheric neuronal activity is overall increased during auditory signal-in-noise processing compared to right-hemispheric activity.
The following main results have been obtained: (i) Experiment 1 demonstrated that auditory attention not only amplifies task-relevant neuronal activity, but also sharpens the frequency selectivity of underlying neuronal populations. (ii) Experiment 2 showed that these effects of attention are frequency-specific. (iii) Experiment 3 showed that signal-related neuronal activity during auditory signal-in-noise processing is increased in the right hemisphere compared to the left, when the signal-to-noise ratio is poor, and the task at the same time indicates the significance of precise signal processing. (iv) All three experiments showed an overall increased left-hemispheric neuronal activity during auditory signal-in-noise processing compared to the right hemisphere.

Based on the current knowledge, these results suggest the following conclusions: (i) it appears likely that the sharpening effect of attention reflects an active suppression of task-irrelevant neuronal activity, which is achieved via efferent, inhibitory neural connections. (ii) The results presumably reflect a fundamental dominance of the left hemisphere during auditory signal-in-noise processing. (iii) This principal functional dominance of the left hemisphere during auditory signal-in-noise processing can be modulated by attentional processes at certain instances.

In sum, the findings obtained in this work significantly contribute to the better understanding of auditory signal processing in natural environments.
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