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TOP-DOWN MODULATION OF THE AUDITORY STEADY-STATE RESPONSE IN A TASK SWITCH PARADIGM

Diplomarbeit im Fach Psychologie
vorgelegt von Nadia Müller
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ABBREVIATIONS

ANOVA	Analysis of Variance
AM	Amplitude Modulation
aSSR	auditory Steady State Response
EEG	Electroencephalography
ERP	Event Related Potential
ERF	Event Related Field
fc	carrier frequency
FFT	Fast Fourier Transformation
fm	modulation frequency
fMRI	Functional Magnetic Resonance Imaging
LI	Laterality Index
MEG	Magnetoencephalography
MLR	middle latency response
ms	milliseconds
nlme	nonlinear mixed effects model
PET	Positron Emission Tomography
SD	standard deviation
SSF	steady-state field
SSR	steady-state response
SSVEP	Steady-State Visual Evoked Potential

ABSTRACT

Our perceptual system is constantly exposed to a huge amount of sensory information. Two main concepts exist which describe how our brain selects the relevant information for further processing: Top-down theories refer to selection processes by higher-order brain areas whereas bottom-up theories characterise data-driven processing. The present study is concerned with the investigation of auditory selective attention, a central top-down mechanism for selection of auditory information. Amplitude-modulated tones (modulated by 20 Hz and 45 Hz respectively) that elicit auditory steady-state responses were chosen as stimuli.

Until now, the impact of selective attention on the auditory steady state response is not well understood and remains to be clarified. In aid of this, a dichotic listening experiment was designed which allowed the study of selective attention within the auditory modality. Fourteen subjects were exposed to binaural stimulation while switching between left and right ear focus. As they had to detect target tones in the prior designated ear they were forced to re-adjust their focus of attention from trial to trial. Thus, the impact of selective attention on the auditory steady-state response could be investigated within the auditory system.

The MEG data of 14 normal-hearing subjects were collected and analysed. Data sets were projected to 8 regional sources, including the two left and the two right temporal sources I was interested in. To disclose attention-mediated effects on the auditory steady-state response, the amplitude of the respective modulation frequencies was identified using a Fast Fourier Transformation. Significant results, revealing an attention-mediated impact on the auditory steady-state response, were found: Selective attention emerged to inhibit the auditory steady-state responses of attended stimuli in the ipsilateral hemisphere. In contrast, no modification of neuronal activity was observed in the contralateral hemisphere. These findings contradict the existing literature which favours an enhancement of neuronal activity due to attention. Task switching within the auditory modality was found to be one of the crucial factors for these surprising results.

I. INTRODUCTION

1.1 Top-down or bottom-up, how does our brain perceive the environment?

1.1.1 Top-down and bottom-up theories in general

Our brain is permanently exposed to an enormous amount of information which our perceptual system has to deal with. The brain, however, has limited processing capacities. Therefore the sensory input has to be selected and structured.

In the past, two main theories have addressed the question of how perceptual processing is realized in the brain.

Before 1950, theories of perception were dominated by the so-called bottom-up approach. Bottom-up refers to data-driven processing, that means that perception is based on the properties of the stimulus, such as colours, light distribution or shape in visual perception. In bottom-up theories the incoming information is supposed to be processed without influence from higher-order brain regions, just on the basis of stimulus features. Thus the sensory input reaches the receptors of the respective sensory system and enters the brain, usually passing brainstem areas, thalamic regions and eventually arrives in the cortex for conscious perception.

In the early 1950s a new perceptual approach, called the *New Look*, became popular as researchers found evidence for cognitive influences on perception.

Bruner and Postman (1949) presented cards to subjects which were either in the expected colour (hearts and diamonds in red) or in the wrong colour (hearts and diamonds in black). They found that subjects took four times longer to identify the manipulated cards in contrast to the original ones. Thus expectations seem to affect the way we perceive objects. Based on these observations a new theory of information processing was developed called top-down processing in contrast to the earlier bottom-up theories. Top-down strategies refer to conceptually-driven processing, that means that higher-order brain areas act on perception already in very early stages. So prior knowledge of the person or a meaningful context in which the stimulus is presented can influence perception quite at the beginning of cognitive processing.

In general, if stimuli are chosen, selection processes have to operate, in such a way that neuronal activity of the relevant stimuli is enhanced and processing facilitated.

According to bottom-up approaches neural activity can be altered due to the salience of the sensory input. Looking at top-down theories, neuronal processing of incoming sensory stimuli is facilitated by the influence of higher-order brain functions that recognize specific sensory information as relevant and actively support processing. Nowadays it is assumed that both approaches are valid and both contribute to perception in most situations. According to this, Sarter and colleagues (2001) emphasize that it is important to see top-down and bottom-up approaches not as distinct theories but as two mechanisms that usually interact and account for an optimized perceptual performance. Thus, if something relevant in our environment happens, which requires our attention, like the dangerous snake in the grass we should be able to fall back on bottom-up processes. In contrast, if we are hungry and have to look for food, top-down mechanisms should direct our gaze to the inconspicuous mushrooms in the grass.

1.1.2 An example of top-down functioning: Auditory selective attention

As mentioned above, our brain somehow has to select some of the vast amount of incoming sensory information for further processing because of its limited capacities. A basic mechanism responsible for extracting crucial information is selective attention. Selective attention refers to mechanisms that either facilitate relevant sensory input or inhibit the irrelevant one. Selective attention mechanisms can work either bottom-up or top-down. According to bottom-up approaches salient stimuli can attract attention automatically without conscious selection. In contrast, top-down selective attention describes active search for stimuli based on knowledge and the aims of a person.

Cherry (1953) was one of the first who conducted behavioural studies of selective attention in the auditory modality. To study underlying mechanisms he used the so-called shadowing technique. Subjects listened to two competing messages in the left and in the right ear through stereo headphones and were asked to repeat the message of one of the ears word by word. This forced them to direct their attention to the designated ear. Cherry showed that subjects are quite good at repeating the message of the attended ear, but cannot report the content of the unattended message. Likewise, they could not decide if the unattended message contained a coherent story or just random words, if it was played backwards or presented in a different language. Subjects could however remember if the words were spoken by a female's or a male's voice or if just a simple tone was presented in the unattended channel. Even in these early studies, it became obvious that selective attention acts on incoming sensory information in a way that attended information is processed differently from the unattended one. It is of importance to notice that these different processing strategies were elicited by task instructions requiring top-down reasoning.

In the following more recent studies concerning selective attention and its correlates in the brain are cited.

1.1.3 Auditory selective attention and its correlates in the brain

Selective attention has been studied with different paradigms and techniques in several modalities. In this part I will consider some of these in the auditory domain. (Hillyard et al. 1973, Näätänen et al. 1978, Woldorff et al. 1993, Tiitinen et al. 1993, Petkov et al. 2004, Debener et al. 2002).

With varying techniques different questions can be addressed. Magnetencephalography (MEG) or Electroencephalography (EEG), for instance, offer a high temporal solution and are known to be good at studying time-courses of cognitive processes, but are not appropriate for mainly spatial questions. For these concerns Functional Magnetic Resonance Imaging (fMRI) or Positron Emission Tomography (PET) are of importance as these techniques allow the researcher to infer specific areas in the brain generating neural activity. These methods are not however suitable for examining temporal processes. Hence, I will provide an assortment of several studies that point to the different approaches and findings. Moreover, I will focus on studies that mainly examine top-down effects on selective attention, what shouldn't lead to the impression that bottom-up effects on selective attention are irrelevant.

Recording of event related potentials has been one of the most popular methods to study auditory selective attention in the past.

Hillyard and colleagues (1973) conducted one of the pioneering EEG experiments examining auditory selective attention. Sequences of tones were presented to the left and right ear while subjects were told to attend to the stimuli in one of the ears. They were asked to count target tones – randomly occurring tones of a different pitch – in the prior designated ear. In the control task subjects had to read a novel while listening to the same auditory input as in the attend-conditions. The stimuli were presented in a rapid rate so that subjects were forced to attend to one ear if they wanted to manage the task in the attend condition. The EEG data showed a negative displacement of the ERP when the attended tones were presented compared with the unattended tones at 80 - 110 ms post stimulus. This is in the time-slot of the N100, an important ERP component for sensory processing. Additionally, a positive component peaking at around 250 – 400 ms post stimulus could be isolated. Thus, it appears that focused auditory attention affects early sensory processing.

Näätänen and colleagues (1978) showed in a similar experimental design with longer interstimulus intervals that the attention-mediated negativity started with 150 ms after stimulus onset and lasted until 500 ms post stimulus. Thus their findings cannot account for an enlargement of the N100 caused by attention, but favour a “superimposition of a negative shift on the evoked potential to the attended stimuli rather than a growth of the real N100 component of the evoked potential” (Näätänen, 1978). Thus, the authors suppose that the negative displacement, they found, represents an additional activity with a different origin and function than just an enhancement of the N100 proposed by Hillyard and colleagues (1973).

Debener and colleagues (2002) studied attentional effects in an auditory oddball-task by the means of EEG. Subjects were exposed to sequences of tones containing frequent tones (80%) and tones of a different frequency that served as target tones (10%). Additionally, a set of novel stimuli (10%) – unique environmental sounds - was included. Subjects were asked to count silently the target tones, a task requiring active selective attention - a top-down process. On the other hand, the novel stimuli were supposed to attract attention passively and to elicit bottom-up brain activity. Subjects were asked to take part in two sessions at an interval of seven days. They compared the P300 event-related potential elicited by the novel stimuli with the P300 caused by the target stimuli. The ERP amplitudes for the novel stimuli declined within the sessions, but not between sessions. The P300, according to the target stimuli, however remained constant during the sessions and declined from one week to another. The authors explain the results as following: Novel stimuli are subject to habituation effects as the ERP amplitude declined during the recording session, but stayed the same compared to the recording session one week later. Target stimuli, in contrast, reflect voluntary aspects of attention as the ERP amplitude decreased between sessions. The authors interpret the decline from one session to another as an adjustment of processing resources because the task became familiar to the subjects. Further, the results are interpreted in such a way that neural activity caused by novel stimuli elicits bottom-up attentional activity and target stimuli represent top-down related attentional effects. This effect becomes apparent in the different activation patterns.

Woldorff and colleagues (1993) combined MEG and fMRI to study selective attention on auditory stimuli. In a dichotic listening task, subjects had to detect target tones in a prior designated ear while ignoring tones of a different pitch in the other ear. Target tones were tones that were 12 dB fainter than the standard ones with 55 dB. Left hemispheric responses were recorded via MEG. The authors circumscribed their reports to brain responses elicited by right ear stimulation – contralateral to the recorded hemisphere. Significantly larger magnetic brain responses were found elicited by the tones in the attended ear. To specify, tones in the attended ear elicited an enlarged event-related field most prominent between 20 - 50 ms and 80 –130 ms after stimulus onset, overlapping with the sensory-evoked M100 response - the counterpart to the N100 wave in EEG. The main sources of these attention-mediated effects were found in the supratemporal plane in the auditory cortex in or slightly lateral to Heschl's gyrus.

Petkov and colleagues (2004) studied activity in the auditory cortex during a selective attention task. They addressed the question of whether selective attention enhances the activity of neurons already activated by the stimulus or activates additional groups of neurons. To do this, they tested subjects using fMRI as this method is able to localize different activation sources because of its high spatial resolution. In the experiment itself, subjects were exposed to sequences of auditory (tones) and sequences of visual (pictures of forms) stimuli which were presented simultaneously, both at a high rate. Two-thirds of the blocks included auditory and visual stimuli and one-third contained stimuli only in one modality, that means either visual or auditory. Both sequences contained the randomly presented stimuli and targets. Targets were sound repetitions in the auditory task and form repetitions in the visual one. The subjects' task was to detect the targets merely in the designated modality and to respond by a button press. If subjects had to attend to the visual sequences, the unattended tones elicited stimulus-dependent activations (SDAs). If, on the contrary, subjects had to attend to the tone sequences, activity according to the attention-related modulations (ARMs) was isolated. SDAs were calculated by subtracting activity during the visual attention task without auditory input from activations in the same task with auditory stimulation. ARMs in turn were isolated by subtracting activations during attend-visual conditions with simultaneous auditory input from the attend-auditory conditions with simultaneous visual input. Comparing the SDAs with the ARMs the attentional impact could be calculated and top-down versus bottom-up influences isolated. Petkov and colleagues found significant activations of the SDAs in superior temporal gyrus, close to Heschl's gyrus and large activations in mesial Heschl's gyrus next to the primary auditory cortex, whereas the ARMs peaked basically in lateral auditory regions. In addition, SDAs showed a much more widespread distribution than the ARMs.

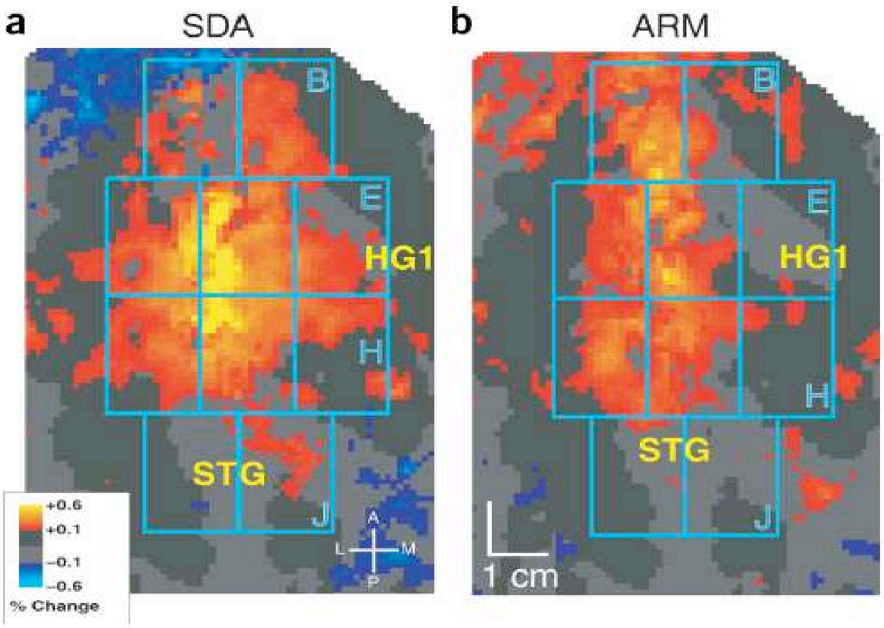

FIGURE 1. 1 Stimulation-dependent activations and attention-related modulations (SDAs and ARMs); Red/yellow colours indicate activation magnitudes. Significant SDAs were obtained in all but the two most posterior grids. Significant ARMs were not observed in any of the mesial grids (B,E,H). Adapted from Petkov et al. (2004).

Furthermore, differences in the tuning of sound frequency and location were found, to that effect that ARMs showed a much broader tuning. Moreover, The ARMs increased with sound repetition whereas the SDAs rapidly adapted.

Thus, a clear distinction in the processing of stimuli and activation sites under attended and non-attended conditions could be demonstrated.

More recently it has been assumed that gamma band activity could play a major role in selective attention. Several studies showed that selective attention to sensory stimuli enhances gamma band activity (Tiitinen et al. 1993, Debener et al. 2003, Sokolov et al. 2004, review: Fell et al. 2003).

Tiitinen and colleagues (1993) used a dichotic listening paradigm to study the effects of selective attention on 40 Hz activity in the brain. The task was to listen selectively to tones in one ear, to detect occasional occurring deviant tones in that ear and to react by a button press. Tones in the other ear were to be ignored. The activity derived from the unattended ear served as the first control condition. In addition, in a second non-auditory control task the subjects had to read a book while the tone sequences were presented. The early evoked 40 Hz activity (beginning 25 ms after stimulus onset) was clearly enhanced in the attend-condition compared with both non-attend conditions. These effects were particularly outstanding at frontal and central electrodes.

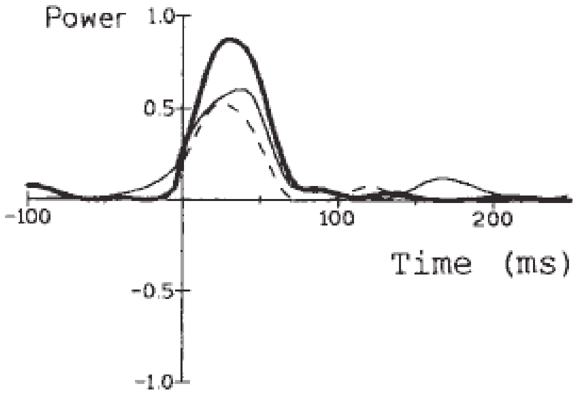

FIGURE 1. 2 40-Hz responses (from electrode Fz) of a representative subject to left-ear 1,000-Hz standard stimuli when attended (thick line), unattended (thin line), and when the subject was reading (dashed line). Selective attention enhances the response to attended stimuli; adapted from Tiitinen et al. (1993).

Debener and colleagues (2003) examined top-down effects on the early auditory evoked gamma band activity as well. They used an oddball paradigm in which rare target tones occurred with a probability of p = 0.10 and standard tones with p = 0.80. The target tones and standard tones were sine tones of 350 or 650 Hz respectively. Furthermore, they presented unique irrelevant sounds with a probability of p = 0.10. The activity caused by the rare target tones was associated with top-down attentional control as the subjects' task was to attend to these tones and to count them. In contrary, the unique irrelevant sounds were supposed to cause bottom-up related activity as they were unexpected occurring new stimuli entering the brain and clearly stimulus driven. Applying this paradigm, Debener and colleagues could separate top-down from bottom-up influences on evoked gamma band activity. According to their hypothesis, they found an enhanced gamma activity for the rare target tones, favouring a top-down influence on the auditory evoked gamma band activity caused by selective attention. The irrelevant novel stimuli did not however result in enhanced gamma activity. Thus it seems that the augmented evoked gamma activity is associated with top-down attentional processes and not with bottom-up related perception of auditory stimuli.

In conclusion, the attentional impact on brain responses was shown for a diversified assortment of studies which investigated different kinds of neuronal activity (e.g. ERPs, gamma activity) with various imaging techniques. Selective attention definitely seems to affect brain activity. To note, the temporal cortex turned out to be involved in selective attention so that it appears reasonable to concentrate on temporal regions for the study of auditory selective attention.
Furthermore, MEG emerged to be an important tool to show the attention-mediated influence on brain activity (elicited by auditory stimuli).

1.2 The steady-state response

In the following I will discuss the auditory steady state response which is a kind of neuronal activity in the gamma range as well, but, in contrast, elicited by special kinds of stimuli.

Measuring brain activity by imaging techniques like Electroencephalography (EEG) and Magnetencephalography (MEG) requires methods by which the tiny signals superimposed by the background-noise become visible. The most common method to solve this problem are the event related potentials (ERP) or event related fields (ERF). That is the EEG/MEG signal is time-locked to a particular stimulus or task which is repeated several times. By averaging many trials the small signal can be extracted and analyzed.

Another possibility to separate the relevant brain activity from the inevitable noise is to use stimuli that elicit a steady state response. The steady state response is elicited by rhythmic stimulation and appears in the EEG/MEG signal as an oscillating activity at a specific frequency. It can be analyzed even for a single trial.

In the following, the nature, the important parameters and the application of the auditory steady state response are explained in more detail.

1.2.1 The nature of the auditory steady-state response

Steady states are elicited when stimuli are presented at a sufficiently high rate to induce an overlapping of the responses with those elicited by subsequent stimuli (Regan, 1982). Accordingly, steady-states are evoked by rapid stimulus sequences in contrast to transient evoked responses. The resulting oscillating response can be recorded in EEG or MEG and is called the steady state response. Originally, steady-state responses were measured in the visual domain as it was difficult to record the smaller amplitude of the auditory steady-state responses. Galambos and colleagues (1981) were one of the first recording steady states in the auditory domain. Until now, however, the nature of the auditory steady state response is not completely understood. There is a clear agreement that the steady state response follows the time-course of the stimulus that means that the measured activity is phase-locked to the stimulus rhythm. Usually steady states are elicited by sequences of clicks (Galambos et al. 1981), amplitude modulated tones (Picton et al. 1987) or tone pulses (Pantev et al. 1996). The most common way to evoke auditory steady states is the sinusoidal amplitude-modulation of a tone. In this context two kinds of frequencies seem to be important. First, the carrier frequency which is defined by the frequency of the presented tone, perceived as the pitch of the tone. Second, the modulation frequency which describes the frequency by which the amplitude of the tone is varied.

Galambos and colleagues (1981) showed that the steady state response is remarkable significant at stimulus rates of 40 Hz. As the peaks of single transient responses usually occur after 25 ms, the superposition of many transient responses would be most significant at a stimulation rate of 40 Hz. Therefore they supposed that the 40 Hz potential is a result of the superposition of transient middle-latency responses (MLRs). That means that it is nothing else than the sum of the responses of each of the presented stimuli. Hence, it should be possible to predict the steady-state response from the activity of transient responses. Azzena and colleagues (1995) tested this hypothesis. Their results were contradictory as the steady states could not be predicted accurately from the superposition of the transient responses at stimulus rates higher or lower than 40 Hz. Likewise Santarelli and Conti (1999) found deviations of the measured brain response from the one predicted by the superposition of the MLRs. They pointed to an additionally occurring fast oscillating response which could not be explained by the superposition of the MLRs. This activity is assumed to be related to auditory cortical neurons responsible for rapid oscillations. Furthermore, Pantev and colleagues (1996) compared the neural sources of the auditory steady states and the middle latency responses in order to detect the relationship between these components. They found an opposite tonotopic organisation of these two activity patterns what entails the neurons responsible for the steady states being independent of the neurons generating the middle latency responses. In addition the N1m source was located more posterior than the aSSR. These results are inconsistent with the theory of superposition because different neuron groups seem to be involved. Thus there is some evidence against the theories of simple superposition of the MLRs.

An alternative approach interprets the steady-state response as resonating activity of neurons in the auditory cortex. The corresponding neural circuits are supposed to resonate at the frequency of stimulation (Herdmann, 2002) which results in an augmented amplitude of the recorded activity. Neurons that are responsible for the steady-state response seem to have an intrinsic rhythm and resonate best at their

eigenfrequency. According to this, the outstanding steady-state response at 40 Hz is supposed to arise from the stimulation of neurons in the auditory cortex by a rate of 40 Hz.
The results provided by Azzena, Santarelli and Conti or Pantev and colleagues support the idea of resonance. Yet, most of the 40 Hz responses can be explained on the basis of the transient responses as well and the evidence for the steady states as a resonance phenomenon is not sufficient. Likewise Gutschalk and colleagues (1999) could not replicate the findings of Azzena and colleagues. That is, they did not find an effect of stimulus rate on the recorded brain response and could still explain the steady-state response as the superposition of middle latency responses. In conclusion, more research is needed to solve the controversy about the nature of the auditory steady state response.

Another important question is where the sources of the aSSRs are located in the brain. In general there are two main models: the model of focal sources that supports either cortical or subcortical sources and the distributed model which supposes a subcortical-cortical interaction. The model of focal cortical sources is favoured by source-localization studies utilising MEG (Pantev et al. 1996, Gutschalk et al. 1999). Pantev and colleagues modelled a single moving dipole in the superior temporal gyrus responsible for the activity elicited by 40 Hz stimulation. Similarly, sources in the supratemporal plane were identified by Gutschalk and colleagues (1999). These results are in accordance with the recent evidence provided by Ross and colleagues (2005), who showed that the primary auditory cortex is the main source of the aSSRs However, John and Picton (2000) studied latencies of auditory steady states and found similarities to the wave five of the auditory brainstem response by stimulating with high frequencies what supports the assumption that subcortical sources are involved. In addition, Herdmann and colleagues (2002) presented their subjects with 1000 Hz tones with modulation frequencies of either 39 or 88 Hz. For the high frequency stimulation they reported generators of the aSSR basically in the brainstem. For the 39 Hz stimulation they found generators in the brainstem and in the cortex. Reyes and colleagues (2005) analyzed sources of the aSSR by means of PET in order to clarify the question of source localization of the aSSR. They could locate six sources mainly in the right hemisphere including temporal, frontal and parietal regions as well as regions in the brainstem and the cerebellum.

Ross and colleagues (2005) conducted a MEG experiment to test laterality effects on brain responses. Therefore they exposed subjects to amplitude-modulated tones monaurally and binaurally. Source localization revealed the primary auditory cortex as a main source of the aSSR whereas transient response components were found in more lateral regions. Moreover they found a right hemispheric dominance of the auditory steady state response in contrast to the transient responses.

In conclusion, it seems that there is evidence for a main generator in the primary auditory cortex and various additional sources in cortical and subcortical regions. Moreover some evidence exists for right lateralization of the aSSR.

1.2.2 Parameters of the aSSR and its application in research

The steady state response is determined by its phase and amplitude. Most researchers focus on the amplitude of the steady state response which is interpreted in a similar way as the ERP amplitude. Phase data has often been used in order to test reliability of the measurement by studying the phase coherence but seldom to get to know more about the cognitive processes lying behind. John and Picton (2000) suggested to use the phase data for detecting latencies of brain responses and studying time courses of brain activity. Anyway a direct transformation from phase to latency is associated with problems as various processes in the auditory system like filtering processes and ambiguities in the recorded data are inevitable (John & Picton 2000).

Concerning stimulus rates it is widely accepted that the steady state response generally decreases with increasing stimulus rate, at least for modulation frequencies above 40 Hz. The response is notably enhanced in the frequency range of 40 Hz and less but also enhanced at stimulus rates around 90 Hz in comparison to the supposed decline (see figure 1.3).

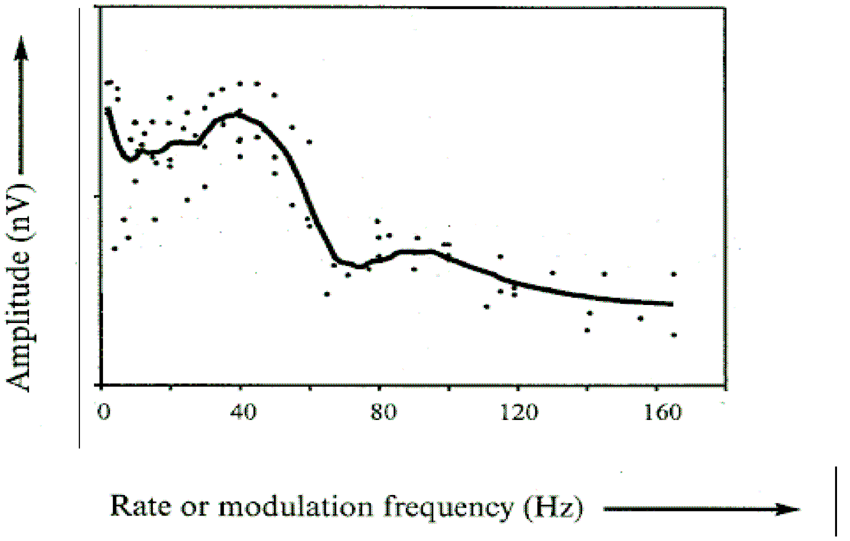

FIGURE 1. 3 The human auditory steady state response. Adapted from Picton et al. 2003.

Concerning the intensity of stimulation, there is evidence that with higher intensity phase and latency are shortened and the amplitude is increasing.

Steady states have some advantages measuring brain responses. The recorded activity is frequency-specific in contrast to transient responses that contain a wide range of frequencies. Accordingly, sinusoid amplitude-modulated tones only possess energy at the carrier frequency and at two sidebands separated from the carrier frequency by the modulation frequency. Multiple steady states can be measured at the same time if the presented stimuli are associated with different modulation frequencies.

Steady-state responses are analyzed by extracting frequency-specific amplitudes or phases from the recorded brain signal. Therefore, the amplitude has to be estimated, for instance, by Fast Fourier Transformation or Wavelet Transformation. Both mathematical processes give complex numbers for specific frequencies. So for each frequency-bin, the amplitude (from the absolute value of the complex number) and the phase can be given.

The Fast Fourier Transformation returns values valid for a prior defined time domain. That means it can be used to assign a frequency spectrum to a time-referenced signal. In the case of steady states elicited by amplitude-modulated tones the components of the waveform can be separated by the different modulation frequencies. Thereby, the recorded activity belonging to specific modulation frequencies can be extracted and the accordant amplitudes and phases calculated. Compared to the Fast Fourier Transformation, the Wavelet Transformation additionally takes into account the time component of the signal. The Wavelet analysis deals with the fact that it is impossible to know the exact frequency and the exact time of occurrence of this frequency in a signal due to Heisenberg's uncertainty principle. Therefore, a "window" is shifted along the signal and for every position the spectrum is calculated. Then this process is repeated many times with a slightly different window for every new cycle. In the end a collection of frequency-time representations of the signal is obtained. So, for instance, an amplitude value for a given frequency at a given time point can be estimated. It has to be noticed that the outcome of a Wavelet Analysis always is a compromise between time and frequency resolution.

By using steady state information in research it seems to be essential to know about the parameters by which this oscillating activity is influenced or altered. Likewise steady states are influenced for example by sleep (Linden et al., 1985) and the application is discussed to be special with children (Maurizi et al. 1990). The relationship of the aSSR to attention is still unclear as discussed in the following chapter.

1.3 The steady-state response and attention

1.3.1 Steady-states and attention in different modalities

Concerning top-down influences on the auditory steady state response there is still a controversy whether or not this oscillatory activity is affected by attention.

In the visual domain, however, controlled studies exist supporting an attention-mediated influence on the steady state response (Morgan et al. 1996; Müller et al. 1998; Chen et al. 2002). Recently, even in the somatosensory field an effect of attention on the somatosensory steady-state response was found (Giabbicconi et al. 2004).

Visual selective attention can be studied focusing on different aspects. On one hand, selective attention can be interpreted in a location-based manner, that means that we direct our attention to a specific location in the visual field –often referred to as “the spotlight of attention”. On the other hand, attention can be directed to a specific object in the visual field – termed as the object-based approach. Morgan and colleagues as well as Müller and colleagues focused on the location-based approach of selective attention whereas Chen and colleagues studied the impact of object-based selective attention on the steady-state visual evoked potentials (SSVEPs).

In the EEG experiment by Morgan and colleagues (1996) subjects were asked to attend to a stream of letters in one visual half-field while ignoring the simultaneously presented one in the other visual half-field. Subjects had to respond to an occasionally occurring digit. The letter sequences were superimposed on a background which was flickered by either 8.6 Hz in one visual half-field or 12 Hz in the other one in order to generate the corresponding SSVEPs. Thus the authors could compare the amplitude of the different steady state responses and infer attentional effects. They found a clear augmentation of the SSVEPs in the attended location compared to the unattended one. This effect was more prominent in the right hemisphere.

Müller and colleagues (1998) presented their subjects with flickering bars modulated by different frequencies of either 20.8 Hz in the left visual half-field and 27.8 Hz in the right one. Each bar contained five LEDs that usually were in red colour. Randomly, two of them changed their colour into green. A target was defined as the simultaneous change into green of the top and the bottom LED. Before each trial a cue was presented to indicate the side to which the subjects should attend to. The subjects’ task was to detect colour-changes of the bars in the to-attend visual half-field during the 10-seconds-period of one trial. Afterwards the brain responses according to the different attention-conditions could be compared. Data was recorded via EEG. The authors could show a significant increase in amplitude of the SSVEPs elicited by the attended visual field versus the ignored one. This effect was most prominent in the hemisphere contralateral to the attended field in the posterior cortex.

Chen and colleagues (2002) presented two superimposed images flickering with different frequencies (7.41 Hz or 8.33 Hz). The image consisted of horizontal or vertical bars in either red or green colour. Subjects were told to attend either to the horizontal or vertical bars in either red or green colour. Their task was to detect changes in the width of any of the bars in the to-attend-image. The SSVEPs, recorded by the means of MEG, were significantly enlarged in the frequency range corresponding to the attended image compared to the unattended one. Interestingly, in the second task different results were found as, this time, the subjects had to attend just to the middle bar of the image. Here the responses to changes in the attended image were diminished in comparison to the unattended image what points to an effect of suppression.

In conclusion, the SSVEPs seem to be affected by selective attention concerning the object-based concept as well as the location-based one.

Finally, Di Russo and Spinelli (2002) focused on attention-mediated differences in latencies of the SSVEPs. Subjects were confronted with sinusoidal gratings flickering with frequencies between 6 Hz and 10 Hz and had to attend to temporal frequency changes in the attend condition, detect target letters in the unattended condition and fixate on the central spot in the passive condition. The authors hypothesized that in the attended condition stimuli are processed faster in early stages and so latencies should be shorter. According to their hypothesis they found shorter latencies and higher amplitudes of the steady state responses of the EEG in the attend condition.
In conclusion, in the visual domain appears to exist clear evidence favouring an effect of selective attention on the steady state responses.

Recently, in the somatosensory domain, Giabbicconi and colleagues (2004) could demonstrate an effect of selective attention on the steady-state somatosensory evoked potential by the means of EEG. Subjects were asked to attend to one hand and to ignore the other one while both index fingers were concurrently stimulated at frequencies of 20 Hz and 26 Hz. Their task was to detect targets in the stimulation of the to-attended side. The amplitude of the steady state response according to the attended finger was significantly augmented.

Hence, the steady-state response seems to be affected by attention in different modalities. In the auditory domain, however, the outcomes are still ambiguous. In the following, the two most important studies showing the controversy of attentional effects on the auditory steady state response are described.

1.3.2 The auditory steady-state response and attention

In the original work of Linden and colleagues (1987), examining the auditory steady-state response and attention, no attention-mediated effect was found. Yet, more recently, Ross and colleagues (2004) could detect an effect of attention on the auditory steady state response.

Linden and colleagues (1987) were one of the first studying attentional influences on human steady states in general. They used amplitude-modulated tones with modulation frequencies of 37 Hz and 41 Hz and carrier frequencies of 500 Hz and 1000 Hz. Subjects had to perform a dichotic listening task while their brain activity was recorded via EEG. They were asked to attend to tones in one ear in order to detect frequency changes while ignoring the tones presented to the other ear. Although the authors found clear changes in the late auditory evoked potentials caused by selective attention, they reported no attention-related effects on the amplitude and phase of the human auditory steady state response.

Ross and colleagues (2004) criticised the tasks used by Linden and colleagues as they required no specific attention to the stimulus rhythm eliciting the 40 Hz aSSR and as they could not separate between cortical and sub-cortical sources of the activity by using EEG. Hence, Ross and colleagues developed a task in which subjects had to attend to changes in the modulation frequency in the attend condition. Consequently the subjects were forced to focus particularly on the modulation rhythm of the presented tones which is supposed to be more specific for the aSSR generation than the detection of frequency changes. In the control task subjects were asked to count the pictures presented in a slideshow. To note, subjects were stimulated with 500 Hz tones, modulated by 40 Hz, at the right ear. The obtained MEG data showed clear evidence for attentional effects on the aSSR in temporal regions. The aSSR amplitude was significantly augmented in the time interval between 200 ms and 500 ms after stimulus onset in the to-attend condition as clarified in the figure below. The aSSR response was larger in the right hemisphere, ipsilateral to the side of stimulation. The effect of attention on the aSSR, however, was more prominent in the left hemisphere, contralateral to stimulation.

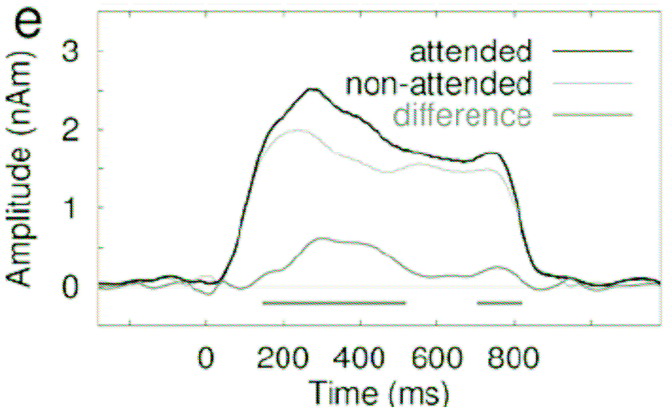

FIGURE 1.4: Attention and the ASSR.

Time-course of the ASSR amplitudes.
(Horizontal bars denote significant amplitude differences).

Adopted from Ross et al. (2004).

In addition, the main sources of the auditory steady state responses could be inferred by using MEG. As a result, primary auditory cortex in Heschl's gyrus appeared to be crucial for the aSSR generation.

The results of Ross and colleagues clearly support an attention-mediated influence on the auditory steady state response. However, the findings are limited in various aspects. That means, one cannot rule out the possibility of a simple effect of alertness on the aSSR in the setting used by Ross and colleagues as the different conditions used in their experiment are not comparable in terms of the required attentional effort. The steady state response may be affected by attentional changes that are not specific to the processed information but could result from more general changes in arousal or alertness. Moreover, selective attention within the auditory domain could not be investigated as the control task just demanded attention in the visual domain. Furthermore, no statements can be made concerning the hemispheric asymmetry of auditory steady-states and attention as just one ear was stimulated. Hence, the relationship between attention and the aSSR still has to be solved and investigated more precisely.

The present experiment aims at investigating how selective attention acts on the amplitude of the auditory steady state response.

To achieve this, the dichotic listening paradigm used in the experiment of Linden and colleagues was combined with the improvements concerning the task and the stimuli itself in the experiment of Ross and colleagues. The dichotic listening technique allows the investigation of selective attention independent of any changes in arousal and within one modality (Hillyard et al., 1973). To define targets as changes in modulation frequency (Ross et al., 2004) instead of changes in carrier frequency (Linden et al., 1987) turned out to be successful to reveal attention effects in relation with auditory steady-state responses (see above). Thus, a dichotic listening experiment was designed that forced the subjects to attend to changes in modulation frequencies in the prior designated ear.

1.3 Hypotheses

The first two hypotheses are concerned with the characteristics of the auditory steady-state response in the temporal cortex regardless of the attentional impact. On one hand, this was done to confirm the assumptions on that I will base the investigation of attentional effects in the second part. On the other hand to replicate prior observations of aSSR parameters. The third hypothesis addresses the main question of the present study: If and how is the aSSR altered by attention?

Hypothesis 1

The auditory steady-state response should be enhanced in the frequency-bins corresponding to the modulation frequencies in the temporal cortex (Picton et al. 2003). As I stimulated dichotically with two different tones solely varying in modulation frequency (SLOW=20 Hz vs. FAST=45 Hz), the amplitude of the steady-state responses should be enhanced for modulation frequencies of 20 Hz and 45 Hz. Furthermore, the aSSR is supposed to be additionally enhanced in the hemisphere contralateral to stimulation. This hypothesis was based on the neurophysiology of the human auditory system: Neurons mostly cross towards the hemisphere contralateral to the stimulation when ascending to the cortex. Thus, most fibres that reach the auditory cortex stem from the contralateral ear. For instance, Pantev and colleagues (1986) conducted a MEG experiment with tone burst stimulation and found enlarged neuronal responses in the hemisphere contralateral to stimulation. Likewise, Scheffler and colleagues (1988) used fMRI and reported an augmentation of the neuronal responses in the hemisphere contralateral to the presented tone pulses eliciting the neuronal activity. Thus, some evidence exists favouring the contralateral dominance of neuronal activity. To sum up, the amplitudes of the aSSRs of 20 Hz and 45 Hz should be enhanced and the aSSR in the hemisphere contralateral to the side of stimulation additionally augmented. For clarification see table 1.1.

	THE TWO DIFFERENT STIMULI	
	SLOW/FAST	FAST/SLOW
LEFT TEMPORAL	**FAST** SLOW	**SLOW** FAST
RIGHT TEMPORAL	**SLOW** FAST	**FAST** SLOW

TABLE 1.1 Frequency bins with enhanced amplitude. FAST (45 Hz) and SLOW (20 Hz) refer to the different modulation frequencies. Dashed printed indicates that the amplitude should be additionally enhanced. The auditory input of stimulus one was composed of a slowly modulated tone presented to the left side and a fast modulated tone to the right side. For stimulus two it was the other way round.

Hypothesis 2

According to Ross and colleagues (2005), the auditory steady-state response is augmented in the right hemisphere compared to the left one. Studies investigating steady-states in the visual domain support a right lateralization of steady-state responses as well (Morgan et al. 1996). Thus, the auditory steady-state response for both modulation frequencies should be enhanced in the right hemisphere compared to the left one (see table 1.2).

	MODULATION FREQUENCIES	
	SLOW	FAST
LEFT TEMPORAL	–	–
RIGHT TEMPORAL	+	+

TABLE 1.2 Expected hemispheric differences of the amplitude of the aSSR.

Hypothesis 3

As outlined in part 1.2.5, the debate about whether and how the aSSR is modulated by selective attention is still proceeding. Thus the aim of the current study was to investigate the impact of selective attention on the auditory steady-state response within the auditory modality.

According to Ross and colleagues (2004) the aSSR is enhanced when the corresponding tone is attended compared to when it is unattended. Source localisation revealed temporal regions as being primarily involved in the effects (Ross et al. 2004, Woldorff et al. 1993). Moreover, studies investigating the attentional impact on steady-state responses in other modalities, showed that attention enhances the steady-state response (Giabbicconi et al. 2004 & Müller et al. 1998).

Transferred to my design, attending to a tone in one ear should result in an enhancement of the steady-state amplitude of the accordant modulation frequency. The effect is supposed to be found in temporal regions. For an illustration see table 1.3.

	ATTENTION	
	LEFT	RIGHT
STIMULI: FAST / SLOW (45 Hz) (20 Hz)	**45 Hz** ↑	**20 Hz** ↑
SLOW / FAST (20 Hz) (45 Hz)	**20 Hz** ↑	**45 Hz** ↑

TABLE 1.3 Expected attentional impact on the amplitude of the aSSR. Modulation frequencies of attended stimuli are supposed to be enhanced.

II. MATERIALS AND METHODS

2.1 Subjects

16 subjects who reported normal hearing were included in the current study (7 women; mean age ± standard deviation: 25 ± 3.28). All participants were right handed according to the Edinburgh Handedness Inventory (Oldfield 1971) and free of psychiatric or neurological disorders according to the M.I.N.I. (Mini International Neuropsychiatric Interview, German Version 5.0.0). Subjects were informed about the experimental procedure approved by the Ethical Committee of the University of Konstanz and signed a consent form before participating. After the experiment they were paid for participation. Two subjects were excluded from data analysis because of two many artefacts in the MEG data.

2.2 Stimuli

Subjects were exposed to amplitude-modulated tones created in MATLAB (Version 6.5.0 on Mac OS 9.2). Therefore, four different kinds of steady-state tones were generated: Two “pure tones” whose amplitude was manipulated by either 45 Hz (fm1) or 20 Hz (fm2). And two so-called “change-tones” that altered their modulation frequency in between. That means that their amplitude was manipulated by either 45 Hz (fm1) or 20 Hz (fm2), changed in between to 25 Hz (fm1’) or 12.5 Hz (fm2’) respectively and went back to their initial position. See figure 2.1 for an illustration.

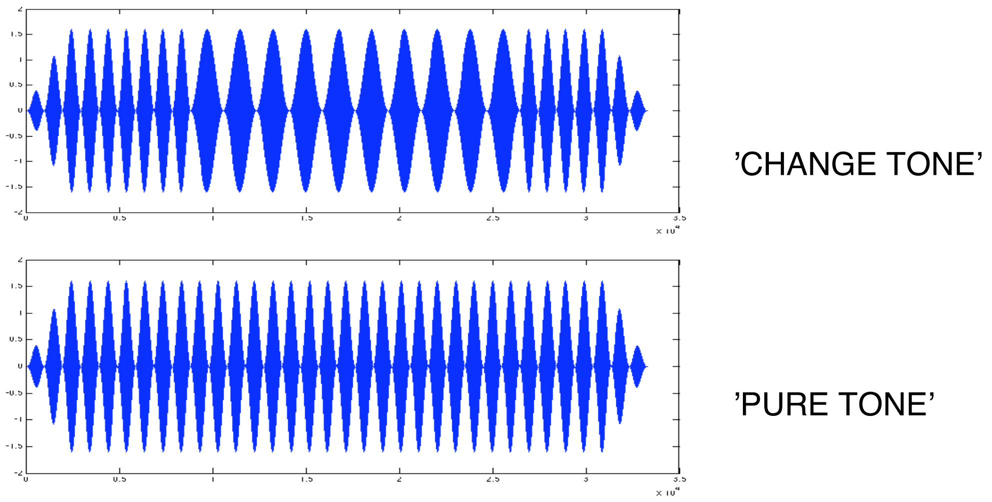

FIGURE 2.1 An example of a target (“change“) tone (45Hz-25Hz-45Hz) and a pure tone (45 Hz).

The remaining parameters were identical for each of the tones: Every stimulus was presented with a stimulus duration of 800 ms (t). The carrier frequency (fc) was set to 655.146 Hz and remained the same for all stimuli. The tones were presented with a sampling rate (Fs) of 44100 Hz and a modulation depth of 100%. To avoid clicks at the on- and offset of the stimuli a 50 ms fade-in period at the beginning of the tone and a 50 ms fade-out period at the end of the tone were included.
The following formula was used for the creation of the tones:

$$\text{signal} = \sin(2*\pi*fc/Fs*n).*(1-\cos(2*\pi*fm/Fs*n))$$

To provide the same subjective loudness to each ear and each person, tones were adjusted to the individual hearing level in both ears separately. In the experiment itself, however, subjects were stimulated binaurally. That means, different amplitude-modulated tones were given on the left and right ear simultaneously. Hence, four distinct stimuli result: Two stimuli without change in modulation frequency (pure tones on both ears) and two stimuli that contained a target tone (1 change tone and 1 pure tone). To note, just pure tones were presented to the unattended-ear, whereas pure and change tones could appear in the attended ear. For an illustration of the stimuli see table 2.1.

	STIMULUS 1	STIMULUS 2
PURE TONES	FAST/SLOW (45 Hz) (20 Hz)	SLOW/FAST (20 Hz) (45 Hz)
CHANGE TONES	FAST-CHANGE/SLOW (45Hz-25Hz-45Hz) (20 Hz)	SLOW-CHANGE/FAST (20Hz-12.5Hz-20Hz) (45 Hz)

TABLE 2. 1 The different kind of stimuli. Pure tones on both sides (90%) and the respective targets: change tones included (10%)

Pure and change tones were presented in a randomised manner, however trials with change-tones (targets) being 10 % and trials with pure tones on both sides being 90 % of the altogether two hundred trials.

2.3 Experimental Design

A 2 x 2 design was chosen for the main experiment: Two attentional conditions and two conditions resulting from the different modulation frequencies (fm1 and fm2) of the steady-state tones. For the attentional manipulation a task-switch paradigm was used. Subjects saw an arrow pointing randomly to the left or to the right that told them to shift their attention to the designated ear. Subjects' task was to detect target tones (10%) which were defined as tones altering their modulation frequency in between presentation (= "change") in the to-attended ear. Trials with target tones were later excluded from statistical analysis. The following four conditions result from this experimental design:

Experimental Design		STIMULI (fm1 and fm2 in to-attended ear)	
		fast / slow (45 Hz) (20 Hz)	slow / fast (20 Hz) (45 Hz)
TASK (attention to…)	"right" →		
	"left" ←		

TABLE 2. 2 The Experimental Design – The four conditions.

The different conditions were equally weighted and a total of 200 trials presented during the course of the main experiment. Trials were selected randomly. Each trial commenced with a cross in the middle of the screen that subjects had to fixate for 1 to 1.5 seconds. Subsequently, an arrow, pointing to the right or left side, was shown to indicate the focus of attention. After 1 to 1.5 seconds subjects were exposed to the auditory stimulus. Directly afterwards the question for the task ("Hat sich was verändert?") was displayed in the screen whereupon subjects had to respond with a right-hand button press; left key meant "change" and right key "no-change". Consequently, if the tone in the designated ear altered its modulation frequency in between presentation subjects had to respond by pressing the left button, otherwise by the right button. The interstimulus interval (ISI) varied between 2.5 and 3.5

seconds. During the ISI, subjects were exposed to a pair of eyes that encouraged them to blink so that blinking was avoided during task performance. The time intervals, which the fixation cross, the arrow or the pair of eyes appeared in, differed slightly in a randomised manner to prevent expectation effects. The design is illustrated in figure 2.2.

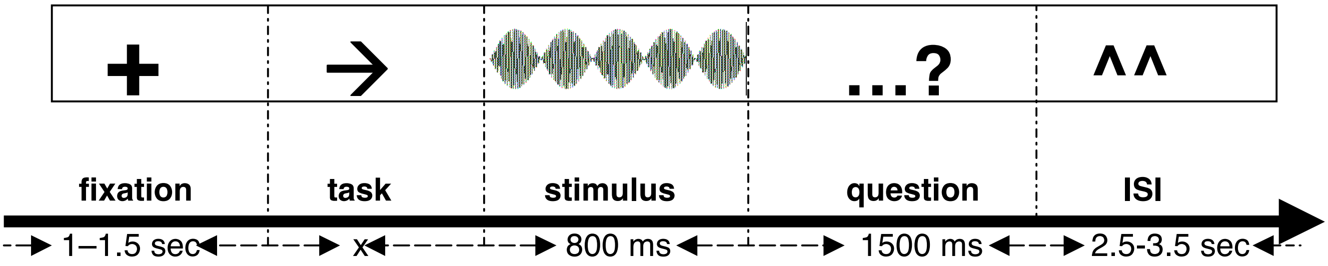

FIGURE 2. 2 The Experimental Design - Procedure of one trial.

The experimental design was implemented in Psyscope X, Version Dep. 37 (Cohen et al., 1993). Triggers were generated in Psyscope and sent to the data acquisition system via the trigger box of the MEG.

2.4 Pilot-study

As targets defined as changes in modulation frequency during tone presentation have not been used in any experimental design before, a pilot-study was conducted to figure out the characteristics of such an experimental manipulation. In other words, it seemed necessary to find out if the detection of changes in modulation frequency is in principle possible and how big these changes should be. Consequently, the modulation frequencies of the tones were adjusted so that the stimuli were still detectable, but, at the same time difficult enough to make the subjects exerting.

Therefore eight subjects were recruited to take part in the pilot-study. The subjects were six females and two males with an average age of 27 years (SD= 1.96).

The pilot-study was conducted in the MEG scanner to provide as similar conditions as possible as in the main experiment. This seemed to be necessary as the sound transmitted by the sound system of the MEG varies from the sound provided by common earphones. Presentation of the stimuli, tasks and instructions were similar to the procedure in the later experiment.

2.5 Procedure

On arrival at the MEG laboratory, subjects were first introduced in the MEG chamber and were then asked to fill in the questionnaires and to sign the consent form. Then each subject was prepared for the MEG recording. The actual experiment was divided into a practice part and the main experiment. Both parts were conducted in the MEG chamber so that the training conditions were as similar as possible. The training session was included in the experimental procedure to make the subjects familiar with the stimuli and to be certain that they are able to distinguish the target tones from the pure tones in the main experiment.

Prior to the training part the loudness of the tones was adjusted. The hearing threshold for each ear was determined by identifying the still noticeable loudness of a standardised steady-state tone. In the experiment, auditory stimuli were presented with 50 dB above Hearing Level, so that perceived loudness was the same for all subjects and each ear.

Afterwards subjects were briefed orally on the task and the training session with the monaural stimulation commenced. In contrast to the main experiment the auditory stimuli in the practice part were presented monaurally, subjects got feedback after each trial and had to respond via mouse click instead of the subsequent used response pad. In the first part of the training session subjects had the possibility to listen to each of the tones separately and were asked to test them as far as they were able to figure out the differences between pure tones and targets.

The training session consisted of 10 trials on each ear, “change” and “pure” tones presented in a randomised manner.

After completing the training session the preparations for the MEG recordings were completed, while subjects were briefed on the task in the main experiment.

Following this, the second very short practice period of 8 trials was conducted. It was exactly the same procedure as in the main experiment and was included to make the subjects familiar with the binaural stimulation. This was done as the binaural stimulation in the present experiment is more difficult and for the first trials confusing as figured out in the pilot-study. Subjects received feedback after this training session from the experimentator who gave a standardised feedback (“already quite good but important to attend to the designated ear further on”) to motivate the subject to do its very best in the main experiment.

Then the main experiment and the MEG recording started. After the main experiment subjects were put out of the scanner and asked how they could manage the task and especially how they managed to attend to one ear. Finally they were paid for participation.

2.6 Stimulus presentation and data acquisition

Stimulus presentation and presentation of the instructions was programmed using Psyscope X (Version Dep 37 on Mac OS X, Version 10.3.9). Auditory stimulation was carried out by a tubing sound delivery system. Tones are generated outside of the magnetic shielded chamber (ASG-BTI) and send to the subject’s ear via the flexible plastic tubes of the sound system with its approximately linear filter properties.

Instructions and visual stimuli were generated by a video beamer (JVCTM, DLA-G11E) outside of the MEG chamber and projected to the ceiling in the MEG chamber by the means of a mirror system. To answer subjects used a response pad that recorded the responses separately. The MEG recordings were accomplished with a 148-channel magnetometer system (MAGNESTM 2500 WH, 4D Neuroimaging, San Diego. USA), installed in a magnetically shielded chamber (Vakuumschmelze Hanau). MEG signals were recorded with a sampling rate of 678.17 Hz and a hard-wired high-pass filter of 0.1 Hz.

2.7 Data pre-processing

For most of the data sets a noise-reducer was applied to minimize the impact of interfering fields. In two data-sets, however, the noise-reducer rather amplified the noise instead of reducing it. This can be due to the fact that the noise reducer needs a minimum of noise to work properly. In these two cases probably the noise was too little to make the noise reducer working. Therefore we decided to use the raw data for these two data sets.

Afterwards, noisy channels were interpolated and the ecg-artefacts corrected using BESA® (Brain Electric Source Analysis http://www.besa.de).

2.8 Data analysis

2.8.1 Behavioural data

Behavioural data was recorded via the MEG system. For each trial in the experiment a trigger was sent indicating if the “yes” or “no” button was pressed. The data was analyzed using Matlab R2007a. Over all trials and subjects the percentage of right and wrong answers was identified. Additionally, t-tests were performed to check the possible influence of the different modulation frequencies fm1 and fm2 on subjects’ behaviour, to figure out differences in behaviour between left and right ear performance, and to reveal differences in performance between subjects.

2.8.2 MEG data

After the data was preprocessed the signal of the 148 channels of the MEG was projected to eight regional sources: Two temporal sources, the left and right temporal plane around the Heschl's gyrus, two prefrontal sources (left and right), two parietal ones (left and right), one in the posterior region (midline), and one medial source in the region of the anterior cingulum, that is located between the parietal and the prefrontal sources.

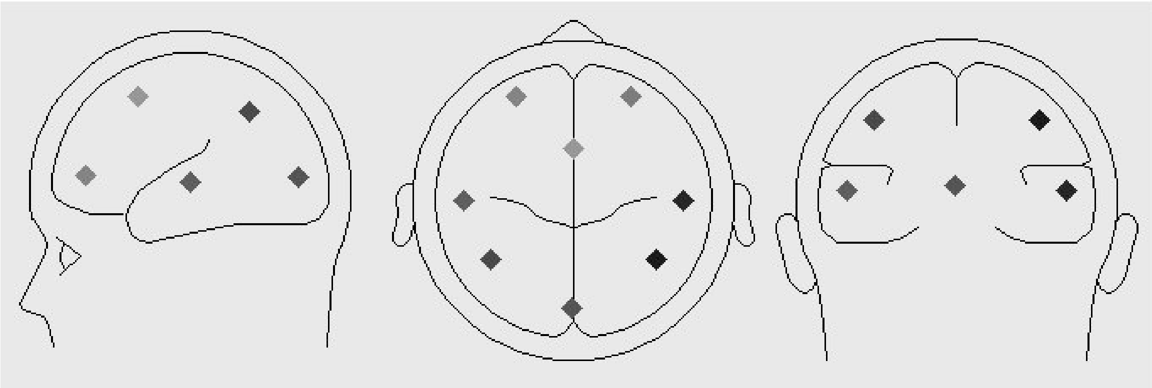

FIGURE 2.3 Illustration of the source-montage used in the current study.

Source-space projection was done using BESA.

Afterwards the data sets were further processed in MATLAB® (version 6.5. MATLAB R2006a). First, the data sets had to be inspected for big artifacts caused by motion or eye blinks. Therefore, they were screened using a criterion that deleted trials with outliers that were so salient that they weren’t likely to be due to attentional effects and just distorted the data. A 200 nAm peak-to-peak amplitude was chosen as threshold level.

As subjects were asked to restrain blinking to the interstimulus intervals and not to move during the experiment, the artefacts that had to be corrected were limited.

For each subject four different frames were created according to the four different conditions (2 stimuli x 2 attention - conditions) resulting in 56 data frames. For each trial a time interval of 500 ms during tone presentation, 200 ms after stimulus onset and 100 ms before stimulus offset, was cut out of the data set. So each of the data frames consisted of a 3-dimensional matrix of 339 data points, 16 sources and the number of trials. Trials with change tones were excluded from statistical analysis.

Evoked activity was then analyzed using a Fast Fourier Transformation (FFT). Therefore, the trials of each data frame were condensed so that an average value for each condition, person and source could be identified. For further analysis only temporal sources were taken into account. A FFT was then applied to each of these averaged data frames. This was done to obtain amplitude values for each frequency.

Afterwards, the Fast Fourier Transformed data sets were normalised. Therefore, for each subject, the data sets were divided by the individual mean, defined as the mean power of the data sets of the corresponding subject over all conditions and temporal sources.

2.8.3 Statistical analysis

For statistical analysis data sets were exported to R - a statistical software environment (http://www.r-project.org, Version R.2.4.1–A Language and Environment 2006). Two packages were added as they were necessary for analysis: Package R.matlab (Version 0.59, Bengtsson & Henrik 2005) for reading the data sets created in MATLAB and the Package nlme (version 3.1-65, Pinheiro & Bates 2000) to calculate a nonlinear mixed effects model. Nonlinear mixed effects models involve both fixed effects and random effects. Thereby it is possible to account for the fact that subjects are randomly selected from the whole population.

A 2 x 2 Analysis of Variance (ANOVA) was performed using a nonlinear mixed effects model. The factors ‘hemisphere’ and ‘modulation frequency’ were defined as fix factors, whereas the factor ‘subject’ represented the random factor. So the amplitudes of the steady-state responses in dependence of the hemisphere (left vs. right) and modulation frequency (45 Hz vs. 20 Hz) were analysed. Ipsilateral and contralateral sources were regarded separately, so that there was one nonlinear mixed effects model for the ipsilateral and one for the contralateral sources. Additionally, Student’s t-tests were performed for a post-hoc verification of the effects.

To reveal the asymmetric activations of the two hemispheres, laterality indices were calculated following Ross and colleagues (2005). The authors defined the laterality index as the difference of right hemispheric amplitude (R) and left hemispheric amplitude (L) divided by the sum of the amplitudes: $LI = (R-L) / (R+L)$. Thus, the LI was +1 for a perfectly right lateralized steady-state response and –1 for a perfectly left lateralized one. To note, it was unconvertible to specify a single laterality index in the present experimental design due to the binaural stimulation with different tones on the left and right ear. Thus, four laterality indices were calculated according to the two modulation frequencies (20 Hz vs. 45 Hz) and the two stimulation sides (left ear vs. right ear). Additionally, to compare the lateralization between varying modulation frequencies respective Student’s t-tests were accomplished.

To analyse the attentional effects, the factor ‘attention’ was added to the nonlinear mixed effects model described above and a nonlinear mixed effects statistic was calculated. Ipsilateral and contralateral activations were again considered separately. Attention was defined as attention to a special modulation frequency. A post-hoc test was calculated to verify the results of the mixed effects statistic.

III. RESULTS

3.1 Behavioural data

Figure 3.1 illustrates the behavioural results. Over all subjects and trials 74 percent of the answers turned out to be correct. Subjects showed the same behavioural performance for the fast (mean±standard deviation: 0.76± 0.18) and the slow tones (0.72±0.23). Likewise, attending to the left (0.73±0.20) or to the right ear (0.76±0.18) did not affect the respective response patterns. The equivalence was confirmed statistically by the appropriate Student's t-tests. Both tests verified the absence of differences between means (each $p > 0.5$).

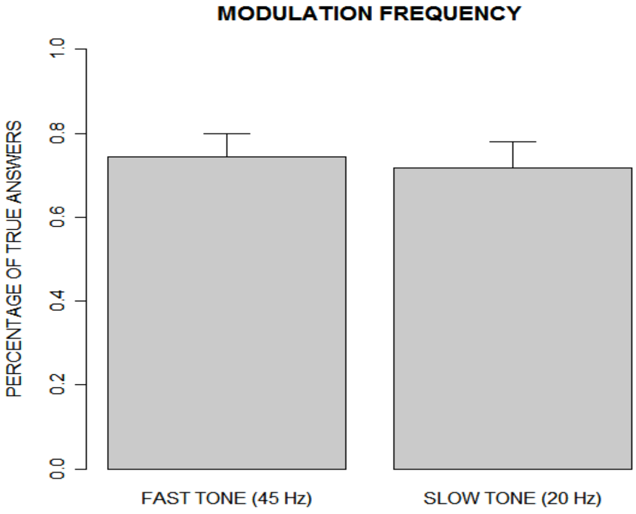

Fig 3.1a Illustration of the averaged behavioural performance over all subjects for the fast tone (45 Hz) compared to the slow tone (20 Hz). Arrow bars indicate the standard error of the mean.

Fig 3.1b Illustration of the averaged behavioural performance over all subjects for attention to the right ear vs. attention to the left ear. Arrow bars indicate the standard error of the mean.

The interindividual differences of performance became significant with a p-value < .001 (t=14.73,df=13).

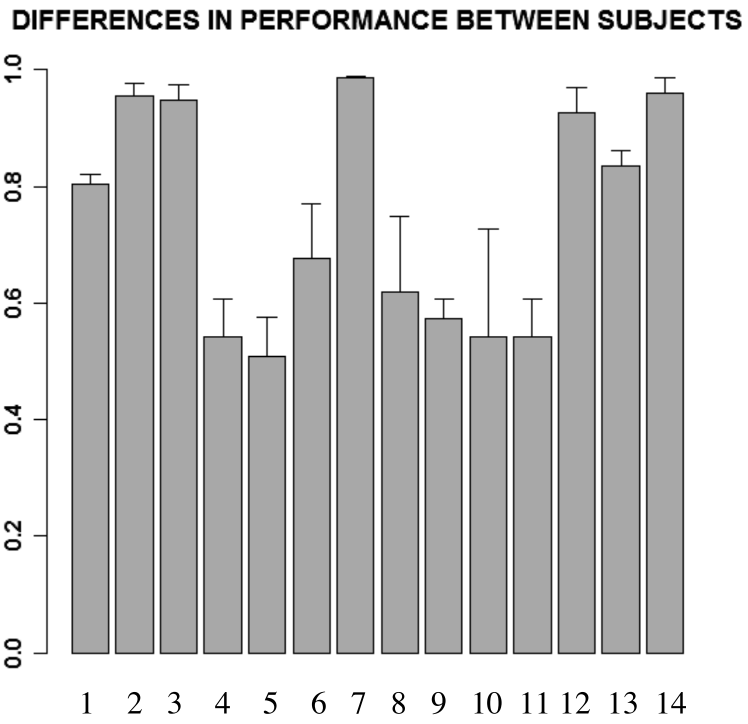

FIGURE 3.2 Interindividual differences among the 14 subjects. Arrow bars indicate the standard deviations.

3.2 MEG data

3.2.1 The auditory steady-state response without the impact of attention

3.2.1.1 The pattern of the auditory steady-state response

The auditory steady-state responses emerged to be significantly enhanced in the frequency bins of modulation. Thus, neuronal activity elicited by the respective modulation frequencies (20 Hz and 45 Hz) was considerably increased.

Moreover, the steady-state responses were additionally exposed in the hemisphere contralateral to stimulation. This was statistically validated by a Student's t-test (p<0.001, t= -9.52). For an illustration of the frequency spectrum see figure 3.3.

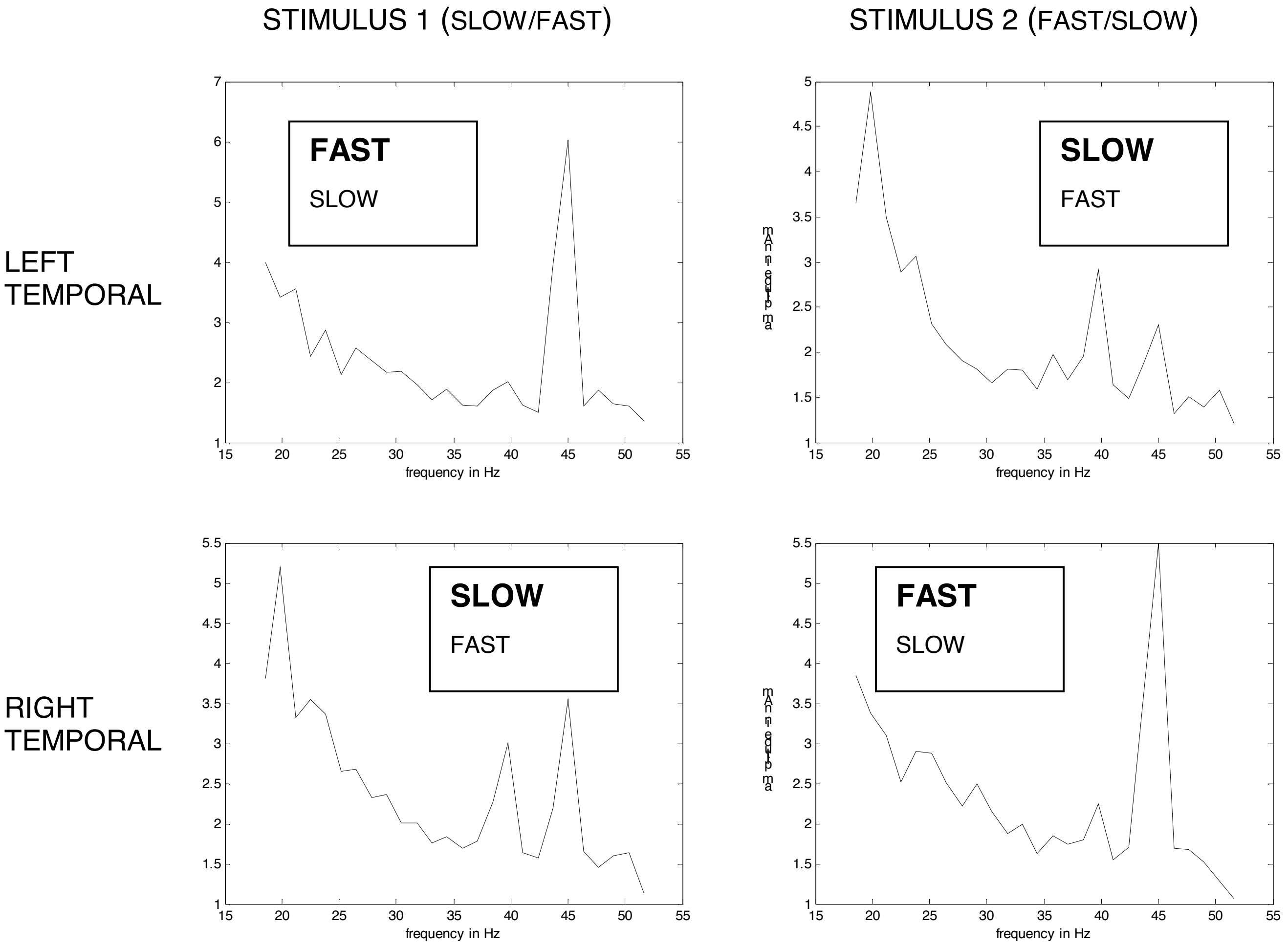

FIGURE 3.3 Auditory steady-state responses in temporal regions.

In order to investigate the lateralization of the ASSR more precisely, the following four laterality indices, averaged between subjects, were revealed (see table 3.1). Each of the four laterality indices deviated significantly from zero (each $p<0.01$), pointing to a clear lateralization towards one hemisphere.

Laterality Indices	right ear stimulation	left ear stimulation
45 Hz	- 0.24	0.39
20 Hz	- 0.14	0.22

TABLE 3.1 Laterality Indices calculated according to Ross et al. (2005) for the 4 different conditions averaged between subjects: A value of –1 means perfect left lateralization, whereas a value of +1 points to a perfect right lateralization.

When looking at the single laterality indices, the principle of contralaterality becomes obvious: By stimulating the right ear, the accordant laterality indices appeared to be both of negative value, pointing to a significant left lateralization. Presenting tones to the left ear, however, produced positive values throughout, denoting a significant dominance of the right hemisphere. Thus, the aSSR turned out to be left-lateralized for right-ear stimuli and right-lateralized for left-ear stimuli, verifying again the dominance of contralateral activations.

3.2.1.2 Right lateralization of the auditory steady-state response

The results concerning the right lateralization of the auditory steady-state responses however appeared to be more ambiguous.

Regarding ipsilateral and contralateral activations separately, different activation patterns could be identified. Accordingly, the mixed effects statistic for contralateral activations did not reveal hemispheric differences (see table 3.3). To note, neither a main effect for hemisphere nor an interaction between hemisphere and modulation frequency could be disclosed.

However, the mixed effects statistic, regarding the ipsilateral sources, showed a significant main effect for hemisphere, pointing to a right lateralization. In addition, the interaction between hemisphere and frequency became significant. The detailed results of the mixed effects statistic for the ipsilateral sources are shown in table 3.2.

IPSILATERAL ACTIVATION	numDF	denDF	F-value	p-value
(Intercept)	1	207	106.46576	<.0001
Hemisphere	1	207	8.83601	0.0033
Frequency	1	207	3.16723	0.0766
Hemisphere x Frequency	1	207	8.14860	0.0047

TABLE 3.2 Nonlinear mixed effects model of ipsilateral activation. Numerator degrees of freedom (NumDF), denominator degrees of freedom (denDF), F- and p-values are displayed for the entire model.

A post-hoc one-tailed paired t-test (left vs. right hemisphere, ipsilateral activation) confirmed the main effect for the right hemisphere (p<0.01, t= -2.85). The mean power values, demonstrating right lateralization of the ASSR for the ipsilateral activations are illustrated in figure 3.4.

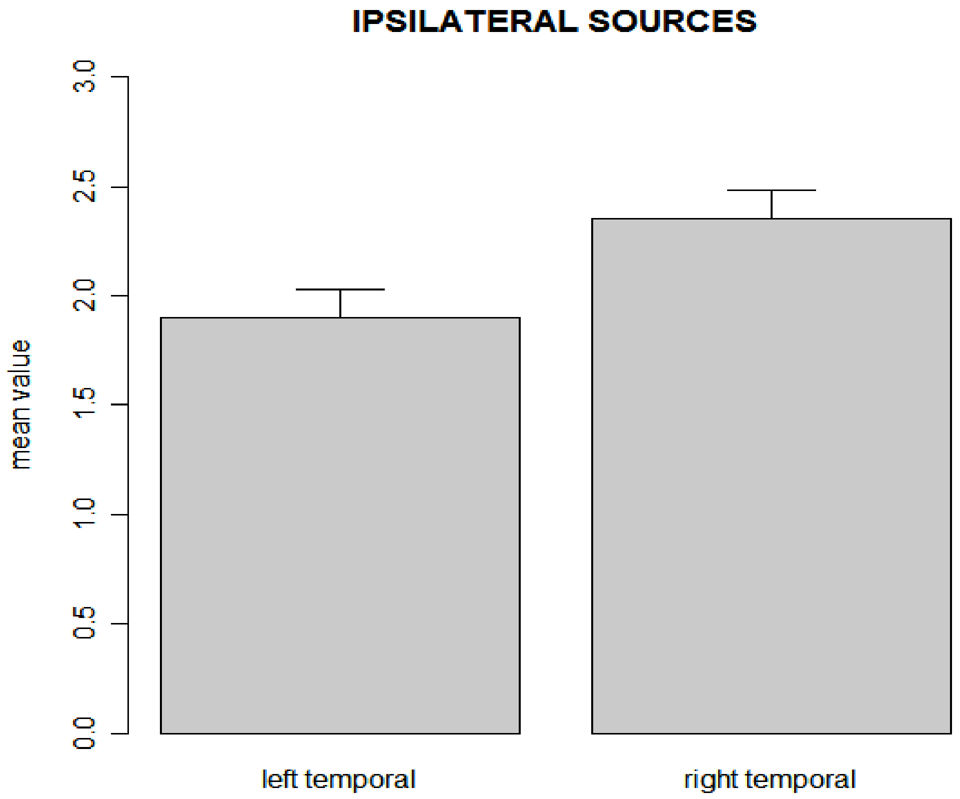

FIGURE 3.4 Right lateralization of the ASSR for ipsilateral sources. The mean power values are displayed. Arrow bars indicate standard errors.

To get a clearer impression of left versus right lateralization, it has to be noted that in addition to the main effect for hemisphere, a significant interaction between hemisphere and modulation frequency was revealed for ipsilateral activations (p<0.01, F=8.42). Thus, it turned out to be reasonable to regard laterality with respect to the different modulation frequencies. Likewise, a significant right hemispheric dominance of the 45 Hz response was disclosed, in contrast to the 20 Hz response which did not show lateralization to the left or right hemisphere. The interaction between hemisphere and modulation frequency (ipsilateral activations) is illustrated in figure 3.5.

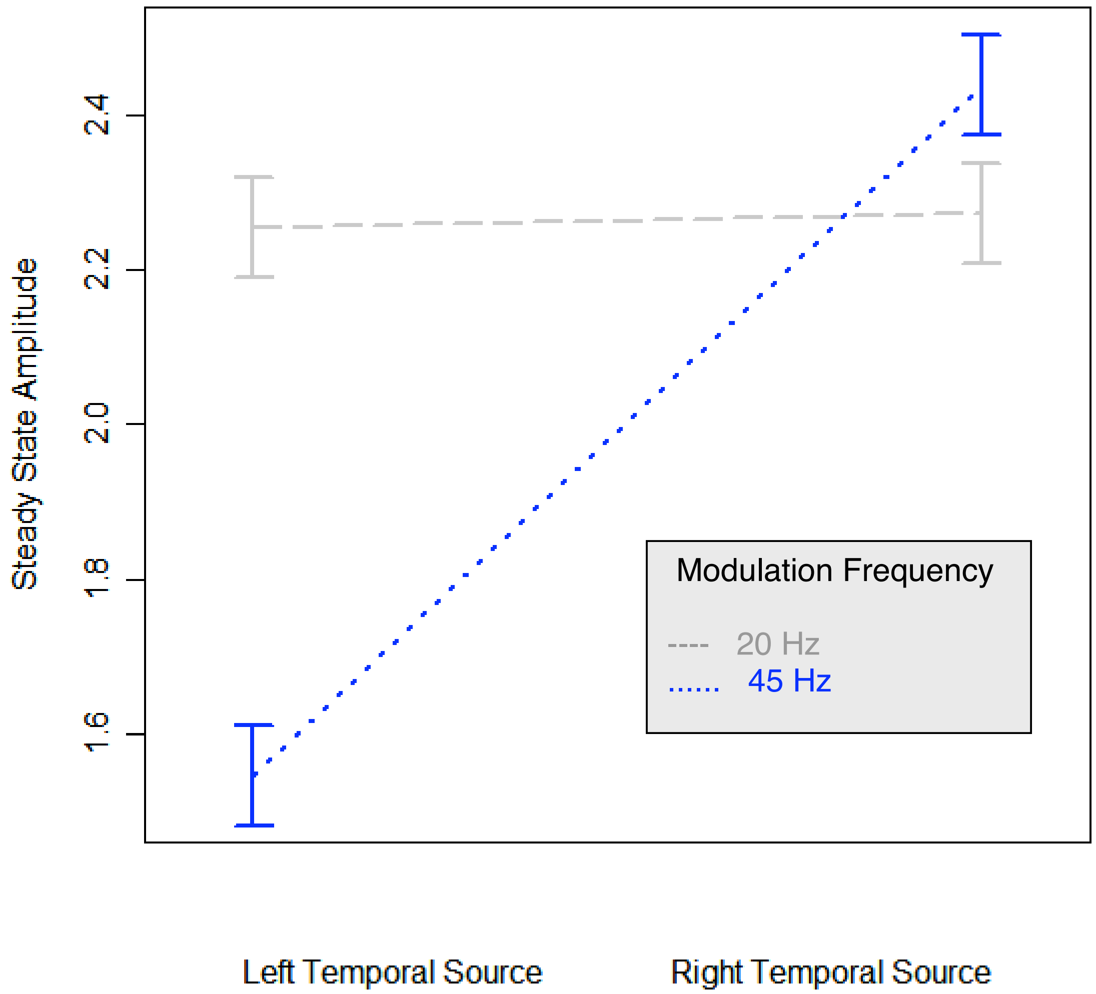

FIGURE 3.5 Interaction of the ASSR between hemisphere and modulation frequency. Mean power values are displayed. Error bars indicate the standard errors of the mean.

Regarding the respective laterality indices, the diverging results between 20 Hz and 45 Hz auditory steady-state responses were confirmed as follows: Differences between the absolute values of right versus left ear stimulation pointed to distinct activations of the left and right hemisphere additionally to the principle of contralaterality. Differences between the absolute values, revealed for both modulation frequencies separately, were verified by accomplishing the respective Student's t-tests. Accordingly, for the 45 Hz responses, a clear right lateralization could be revealed (t= -2.00, p=0.048), whereas for the 20 Hz response no significant lateralization was identified (t= -1.51, p=0.13). For an illustration of the laterality indices see figure 3.6.

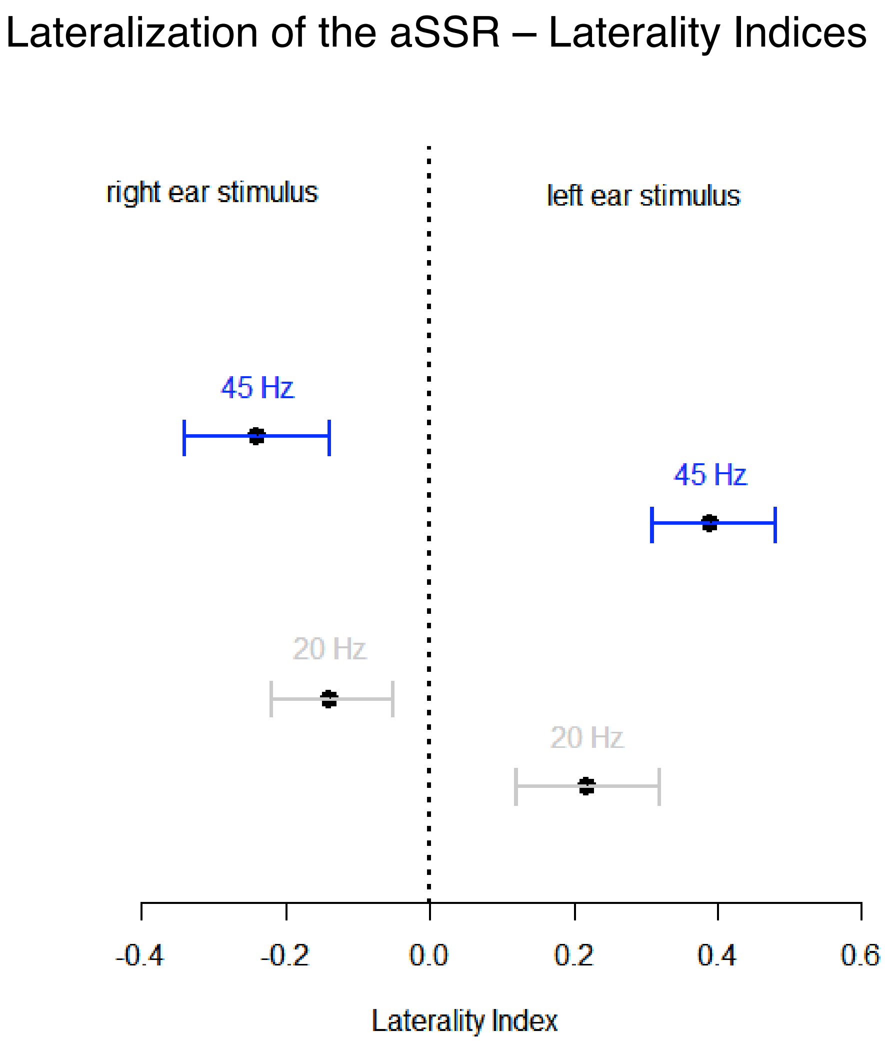

FIGURE 3.6 Laterality Indices averaged between subjects. Arrow bars indicate the 95 percent confidence intervals.

3.2.1.3 Influence of the modulation frequency on the amplitude of the aSSR

Regarding the temporal sources together, the amplitudes of the aSSR did not seem to vary with modulation frequency. However, analyzing contralateral and ipsilateral sources separately, the 45 Hz response turned out to be significantly enhanced for contralateral sources. Likewise the mixed effects model and a post-hoc one-tailed paired t-test (t= -2.03, p=0.02) for contralateral sources could identify a main effect for modulation frequency. Looking at the ipsilateral activations no significant difference between the amplitudes of the respective modulation frequencies could be identified. The results of the mixed effects statistic for the contralateral sources are shown in table 3.3. For an illustration of power differences related to the respective modulation frequencies (20 Hz & 45 Hz) see figure 3.7.

CONTRALATERAL SOURCES	numDF	DenDF	F-value	p-value
(Intercept)	1	207	90.00197	<.0001
Hemisphere	1	207	0.06579	0.7978
Frequency	1	207	5.25899	0.0228
Hemisphere x Frequency	1	207	1.19097	0.2764

TABLE 3.3 Nonlinear mixed effects model of contralateral sources. Numerator degrees of freedom (NumDF), denominator degrees of freedom (denDF), F- and p-values are displayed for the entire model.

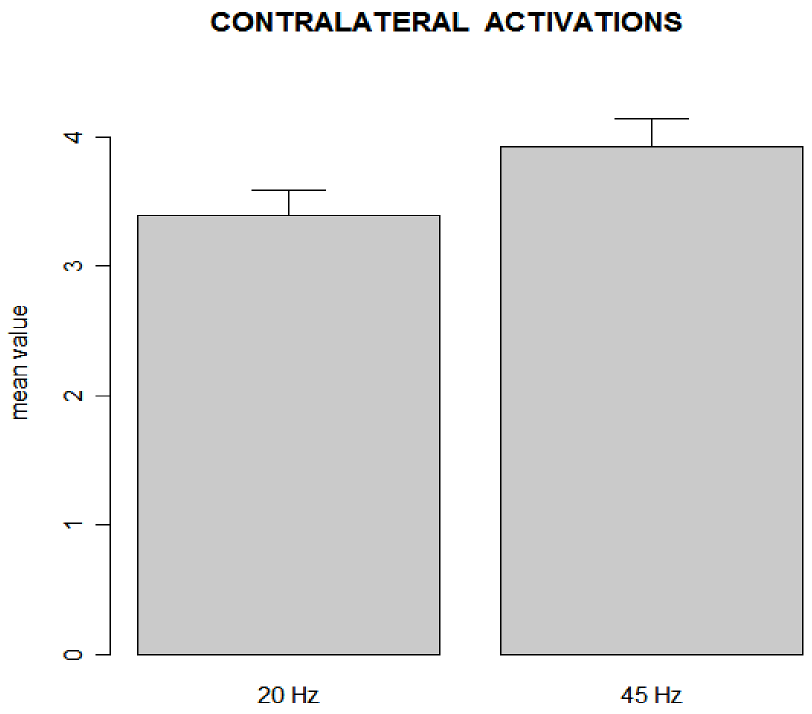

FIGURE 3.7 Effects of modulation frequency on the amplitude of the aSSR for contralateral activations. Mean power values are displayed. Arrow bars indicate standard errors.

3.2.2 The impact of selective attention on the auditory steady-state response

Looking at contralateral sources no differences due to the varying attentive conditions could be found as figured out by the respective mixed effects statistic. However, the mixed effects statistic for the ipsilateral sources disclosed a significant attention main effect (F=4.85, p=0.03). The Nonlinear mixed effects statistic for ipsilateral activations is shown in table 3.4.

IPSILATERAL SOURCES	numDF	denDF	F-value	p-value
(Intercept)	1	203	106.46576	<.0001
Attention	1	203	4.85278	0.0287
Hemisphere	1	203	9.12873	0.0028
Frequency	1	203	3.27215	0.0719
Attention x Hemisphere	1	203	1.32237	0.2515
Attention x Frequency	1	203	2.31781	0.1295
Hemisphere x Frequency	1	203	8.41855	0.0041
Atten. x Hemi. x Frequ.	1	203	2.36462	0.1257

Table 3.4 Mixed effects model of ipsilateral sources. Numerator degrees of freedom (NumDF), denominator degrees of freedom (denDF), F- and p-values are displayed for the entire model.

Thus, the amplitudes of the aSSRs ipsilateral to stimulation turned out to be clearly diminished when the respective stimulus was attended (p=0.03, see tab 3.4). This attention main effect was verified by a post-hoc two-tailed t-test (p=0.04, t= -2.05). Accordingly, the means of power values, illustrating the attention-mediated effect in the ipsilateral hemisphere are displayed in figure 3.8.

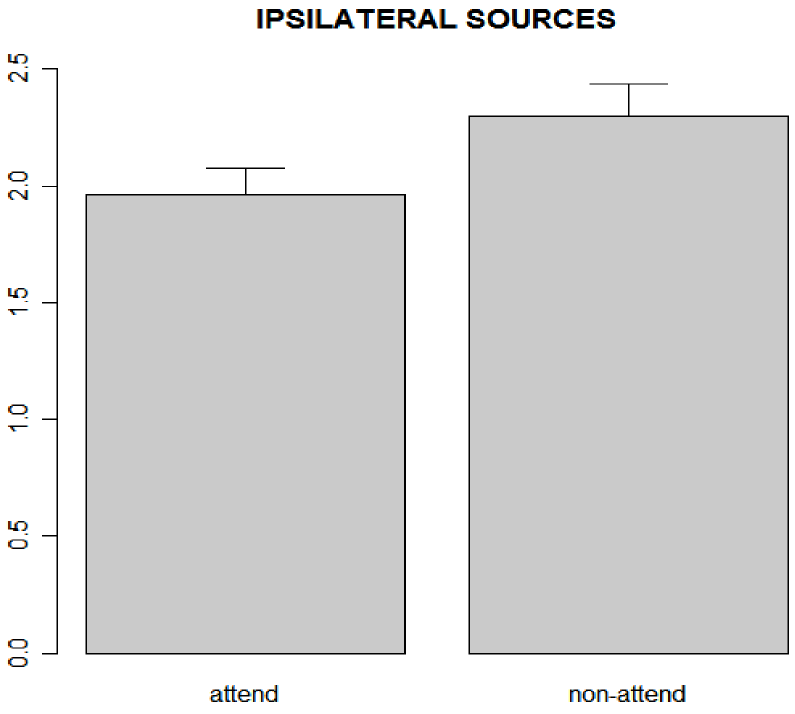

FIGURE 3.8 Auditory steady-state responses and attention. Mean power values are displayed. Arrow bars indicate standard errors.

III. DISCUSSION

4.1 Behavioural data

Behavioural data was analyzed to ensure that no behavioural effects were responsible for the present results. Subjects' performance was compared for the two different stimuli with distinct modulation frequencies and for left versus right ear stimulation. As expected no differences were found concerning modulation frequency or right versus left ear stimulation. Subjects answered correctly at an average of 74 per cent, suggesting that they were not struggling with the task but still exerting. However, interindividual differences in performance were quite high. From the fourteen subjects five subjects answered correctly less than 60 % of the time, barely above chance level, and seven subjects answered correctly in over 80 percent of the trials. Performance of the other subjects was in between. It is questionable if the five subjects who performed just over chance level really tried to manage the task and directed their attention to the designated ear. It is likely that the task was too hard for them and that they gave up after a while or did not make an effort at all. This is problematic for the interpretation of the attention task, as the experimental manipulation only works with motivated subjects. Thus, the outcomes that are concerned with the investigation of attention could be even clearer with exclusively motivated subjects.

4.2 The shape of the auditory steady-state responses

4.2.1 Frequency spectrum of the auditory steady-state responses

To ensure that our experimental stimulation with two simultaneous tones, just differing in modulation frequency, worked, I investigated the frequency spectrum of the auditory steady-state responses in the auditory cortex. The two different frequencies of modulation are supposed to be exposed in both hemispheres, with the one contralateral to the stimulation side over-represented. This hypothesis was based on the neurophysiology of the human auditory system: Neurons of the auditory pathway ascend separately from both ears to the brainstem. There most of the fibres cross toward the hemisphere contralateral to the stimulation side and ascend further on to the auditory cortices. Thus, a combination of numerous crossing and less noncrossing fibres reaches the auditory cortex. Therefore, the 20 Hz and 45 Hz steady-state responses in the temporal cortex should be enhanced in both hemispheres and additionally augmented in the hemisphere contralateral to the stimulation. This hypothesis was confirmed as illustrated in figure 3.3 in the results part. Figure 4.1 shows a typical frequency spectrum obtained from the FFT.

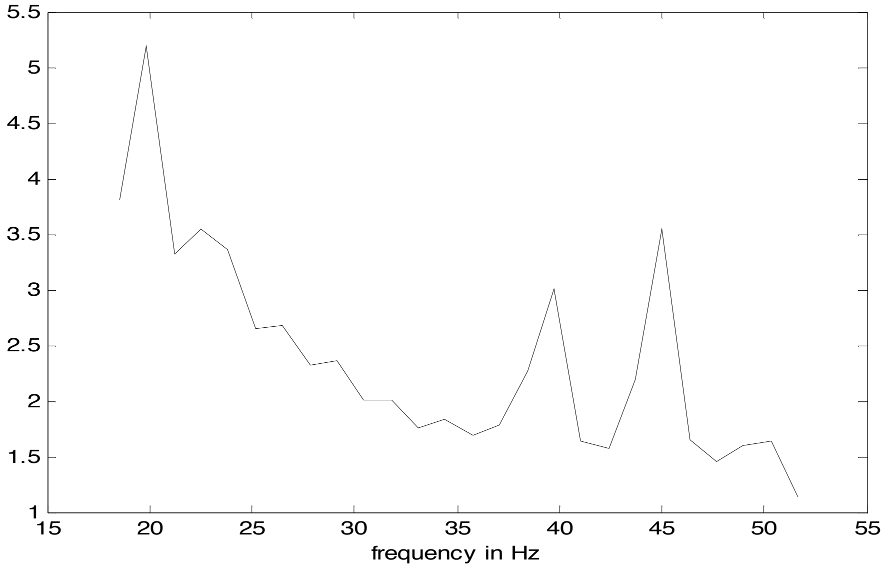

FIGURE 4.1 A typical frequency spectrum of the ASSR. Right temporal sources. Stimulus1 (SLOW/FAST). The 20 Hz, 40 Hz (first harmonic) and 45 Hz responses are enhanced. The 20 Hz response is additionally augmented. The ordinate shows the amplitude in nAm.

The figure clearly depicts the enhanced frequencies: 20 Hz and 45 Hz. It also indicates that the response seems to be increased at 40 Hz besides the expected 20 Hz and 45 Hz augmentations. When looking at the frequency spectra in different hemispheres (see figure 3.3) it is remarkable that the 40 Hz enhancement is especially outstanding in case of a concurrent 20 Hz enhancement. A plausible explanation is that the 40 Hz response reflects the first harmonic of the 20 Hz response. Thus, if the amplitude of the 20 Hz response is elevated, the amplitude of the first harmonic of the 20 Hz response is also enhanced and becomes detectable.

All in all, the principle of contralaterality was confirmed. However, for the sake of completeness, it has to be remarked that the results of Ross and colleagues (2005) differ from the present findings, when comparing the revealed laterality indices. Each of the four calculated laterality indices in the present experiment favour the principle of contralaterality. In contrast to this, Ross and colleagues reported a contralateral dominance of the auditory steady-state response only for left ear stimulation and did not reveal a lateralization for right ear stimulation. When looking at the diverging results, it has to be remarked that the experimental manipulations were quite different. Ross and colleagues used two different designs. In the first one, amplitude-modulated tones were presented monaurally and thus the respective neuronal responses could be investigated separately for both ears. In their second paradigm, they presented amplitude-modulated tones, both modulated by 40 Hz, to the left and right ear simultaneously. Looking at the present experimental design, however, tones were always presented binaurally and the respective modulation frequencies differed with right versus left ear stimulation. For an illustration of the varying findings see figure 4.2.

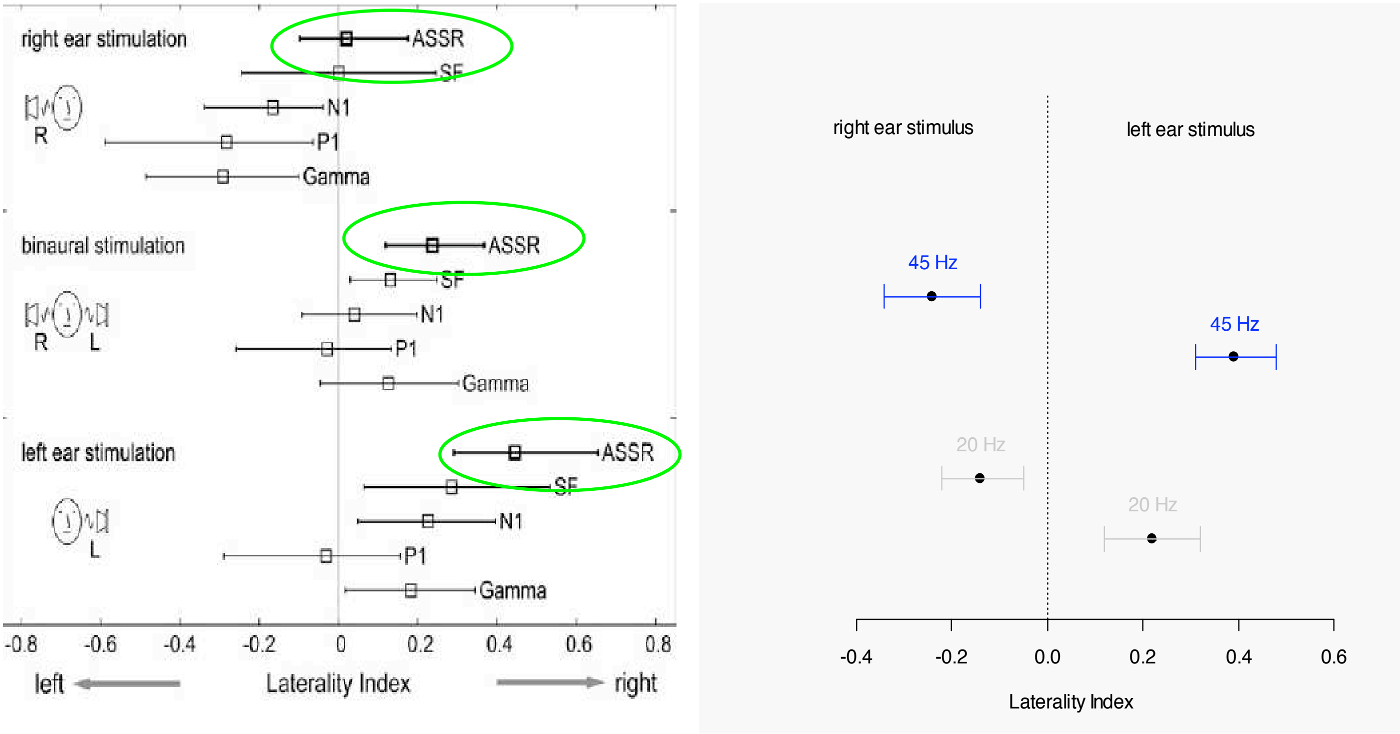

FIGURE 4.2 Group mean laterality Indices revealed by Ross et al. 2005 (left) and by the present study (right). Error bars denote the 95 % confidence intervals for the mean.

Neither of the two designs utilized by Ross and colleagues (2005) can be easily compared to the present experimental design. Therefore, it is likely that the respective laterality indices vary as they cannot be directly compared. As stated above, the neurophysiology of our auditory system favours the principle of contralaterality and therefore it still seems likely that the contralateral neuronal activity is enhanced as revealed by the present results.

All in all, the auditory steady-state response was enhanced in the frequency-bins corresponding to the modulation frequencies in the temporal cortex, the principle of contralaterality is accomplished, the dichotic stimulation was successful and the resulting data is therefore credible for further analysis.

4.2.2 Right lateralization of the auditory steady-state response

Concerning right lateralization of the ASSR, the findings of Ross and colleagues (2005) were only partly replicated. As stated above, the absolute values of the laterality indices of right-ear versus left-ear stimulation were compared to reveal a possible right hemispheric dominance. Two main findings emerged from this:

On one hand, a significant right lateralization of the 45 Hz response could be disclosed. This is in accordance with the results of Ross and colleagues who suggested a right lateralization of the ASSR for frequencies of 40 Hz. Thus, the right lateralization of modulation frequencies around 40 Hz could be verified.

On the other hand, however, the 20 Hz response did not appear to be lateralized to either hemisphere, what is in contrast to the results revealed by Ross and colleagues (2005). Indeed, Ross and colleagues showed right lateralization of the ASSR exclusively for the 40 Hz response and therefore the diverging results are not contradictory. When regarding the literature, it becomes clear that the ASSR does not show consistent activations according to varying modulation frequencies.

Plausible explanations emanate from studies with PET and fMRI. Devlin and colleagues (2003) studied lateralization of auditory processing in the primary auditory cortex by the means of fMRI. Stimuli were sinusoidal amplitude-modulated tones of 250 or 4000 Hz. The stimuli were modulated by 5 Hz and presented monaurally in a pseudo-randomized manner. The authors observed a prominent left lateralization of the sSSRs. Thus, modulating by other frequencies can lead to different observations.

Likewise, Giraud and colleagues (2000) explored steady-state responses in the human cortex in dependence of the modulation frequency via fMRI. They found different regions including brainstem and cortical areas responding preferentially to AM-sounds. Furthermore, these different regions could be subdivided according to a particular sensitivity to special modulation frequencies. Taken together, different modulation frequencies seem to elicit different amplitudes depending on the brain structure and therefore might also have different effects on lateralization.

In the present experiment, the impact of different modulation frequencies on the steady-state amplitude is also reflected in the interaction between frequency and hemisphere for the ipsilateral activations. As illustrated in figure 3.5, the 45 Hz response is significantly lateralized with the right-hemispheric response being more than 50 % stronger than the left hemispheric one. The 20 Hz response, however, is not lateralized at all. Thus, it appears that the different modulation frequencies cause different activation patterns concerning laterality, at least in our experimental design.

As it was not the main goal of the present study to investigate laterality effects, the experimental design is not adequate to draw final conclusions about laterality and the relation between laterality and modulation frequencies. Further studies are required that are able to shed light on the lateralization of the ASSR in dependence of varying modulation frequencies.

4.2.3 Influence of the modulation frequency on the amplitude of the ASSR

Most studies investigating auditory steady-state amplitudes in dependence of different modulation frequencies propose that the respective responses peak at frequencies around 40 Hz. Looking at the present study the ASSR for the 45 Hz modulation frequency is significantly enhanced compared to the 20 Hz response, however only for contralateral sources. A more prominent amplitude of the 45 Hz aSSR is in accordance with our expectations. In contrast, regarding the ipsilateral sources, no difference in amplitude between the 45 Hz ASSR and the 20 Hz ASSR could be identified.

However, the results concerning the amplitude of different modulation frequencies are not so clear cut. Picton and colleagues (2003) assembled the results of nine studies. For an illustration see figure 4.3.

Figure 4.3: Effects of stimulus rate – the comparison of 9 studies:

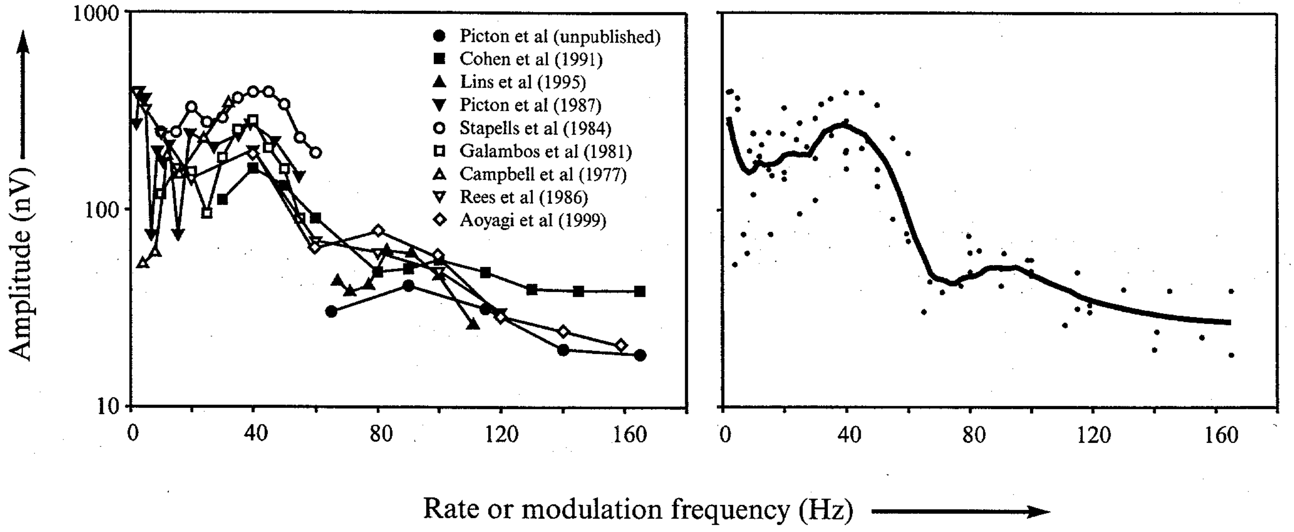

Figure 10. Effects of stimulus rate. The left graph shows data from nine different studies wherein the rate of stimulation or the modulation frequency was manipulated. The stimuli were all AM tones, except for the Galambos study, which used clicks, and the Stapells study, which used tone-bursts. Stimulus intensity varied between 55 and 70 dB HL. The data were made comparable using the following procedures. Peak-to-peak amplitudes have been halved to make them equivalent to baseline-to-peak measurements. The amplitudes of the responses to binaural stimuli have also been halved. The binaural effect varies with different stimulus rates, with binaural responses being about 200% of the monaural responses at rapid rates (Lins et al, 1995) and 150% at slow rates (Rees et al, 1986). Responses measured by visual analysis in the time domain are usually larger than measured by computer analysis in the frequency domain, because the peaks in the time domain are enhanced by superimposed activity at other frequencies. Responses measured in the time domain were therefore multiplied by 0.75 to make them equivalent to those recorded in the frequency domain. Most of the results at frequencies less than 60 Hz are for waking subjects. If the subjects were asleep, these amplitudes would probably be reduced by a factor of 2 or 3 (Cohen et al, 1991). The actual stimuli in each of the experiments were: Picton et al (unpublished), AM tones at 60 dB SPL (measurements combined over multiple carrier frequencies); Cohen et al (1991), 55 dB HL tones, AM, binaural; Lins et al (1995), 1000-Hz AM tone at 60 dB SPL; Picton et al (1987c), 70 dB nHL AM 1000-Hz tones; Campbell et al (1977), 500-Hz AM tone; Stapells et al (1984), 60 dB nHL tone-bursts of 500 Hz; Galambos et al (1981), clicks of unspecified intensity; Rees et al (1986), 60 dB SL AM 1000-Hz tones; Aoyagi et al (1999), 50 dB HL AM 1000-Hz tones. The right graph plots the general trend of the various data sets plotted above. Each point on the smooth curve was fitted using a window of 22 points, with the points weighted using a bisquare function of the distance from the point being smoothed, and with the lines between the smoothed points interpolated using a second-degree polynomial.

Adopted from Picton et al. (2003).

As displayed in the figure above different stimuli and techniques produced different results. For instance, Stapells and colleagues (1984) revealed comparable amplitudes for modulation frequencies of 20 Hz and 45 Hz.

On the basis of the observations in the part about lateralization, some distortions could also be due to the interaction between frequencies and hemispheres. For instance, looking at the ipsilateral sources, the 20 Hz response is significantly more pronounced than the 45 Hz response in the left hemisphere, but not in the right hemisphere. These effects could explain the different findings due to an interaction between modulation frequency and hemisphere. Thus, if the auditory steady state response is subject to an interaction between hemisphere and modulation frequency, different experimental designs could have led to different results.

To conclude, our data confirmed the dominance of steady-state responses around 40 Hz only in part.

Different studies mentioned in the literature used different designs, different stimuli or different stimulation sides. Thus, no definite conclusions concerning the relation between aSSR power and modulation frequency can be drawn. Nevertheless, the existing literature favours a dominance of the responses around 40 Hz. To sum up, the present experiment was not designed to study these effects and thus the obtained data cannot account for definite conclusions about the varying sensitivity of different modulation frequencies.

Regarding the results of the present study about laterality and modulation frequencies, the characteristics of steady-state responses concerning varying modulation frequencies and hemispheres still have to be investigated more precisely. Thereby, the study of interaction effects between modulation frequency and hemisphere could reveal interesting new results.

4.3 The auditory steady-state response and attention

Concerning the relationship between attention and the auditory steady-state response, the findings of the present experiment favour an attention-mediated impact on the aSSR. As depicted above, the neuronal responses elicited by attended stimuli turned out to be significantly down-regulated in the ipsilateral hemisphere compared to activations elicited by unattended stimuli ($p<0.05$).

4.3.1 The aSSR and attention – present findings and existing literature

As outlined above, the relationship between the auditory steady-state response and attention is still unsolved. Up to now, no study exists which investigates the impact of selective attention on the auditory steady state response with an adequate experimental design – a design that is able to reveal attention effects and to control for misleading influences like alertness at the same time. Therefore, the present experiment represents a new attempt to disclose a possible attentional impact on the aSSR.

So far, only two studies exist investigating the influence of attention on the auditory steady-state response. The one of Linden and colleagues (1987) negates the impact of attention on the ASSR whereas the one of Ross and colleagues (2004) favours an attention-mediated influence on the ASSR.

The results of the present experiment support an attention-mediated impact on the auditory steady-state response, but with different characteristics than supposed by Ross and colleagues. Amplitude-modulated tones elicited smaller steady-state amplitudes in the ipsilateral hemisphere when they were attended compared to when they were unattended. This was true for both modulation frequencies and hemispheres. In the hemisphere contralateral to the attended ear no attention-mediated influence on the auditory steady-state response could be revealed. That means, the aSSR was reduced in the hemisphere ipsilateral to the stimulation side and unaffected in the contralateral hemisphere. In contrast to these results, Ross and colleagues (2004) showed an enhancement of the auditory steady-state response that was more pronounced in the hemisphere contralateral to stimulation. These unequal results are not particularly remarkable as our experimental design was not comparable to the one used by Ross and colleagues concerning the attentional amount or cognitive strategies that were required. Likewise Ross and colleagues stimulated monaurally and chose a visual task as control task. Thus, in the attend-condition, subjects had to detect changes in modulation frequency similar to our experiment, whereas, in the unattend-condition, they had to perform a visual task.

First, the effort required for the visual control task probably differed from the one needed for the auditory task. That means it cannot be ruled out that the results Ross and colleagues found are simply due to more general influences like alertness to the auditory modality. This possibility is excluded in my experimental design.

Second, the two experimental designs varied concerning the mode of stimulation. In the experiment of Ross and colleagues subjects listened to tones merely presented to one ear, whereas subjects in my experimental design were exposed to binaural stimulation. As binaural stimulation elicits competition in the auditory cortex (Brancucci et al. 2004), inhibition processes are likely to occur. Inter-hemispheric competition is illuminated in part 4.3.2.

Third, looking at the different tasks that were chosen, it is likely that they elicit different neuronal mechanisms in the brain. Subjects in the experiment of Ross and colleagues had to attend to the auditory modality for a while and afterwards to switch to the visual modality (or vice versa). Thus, they simply had to concentrate on one aspect, namely detecting targets in the stimulated ear. Subjects in the task I used, however, had to switch within one modality from trial to trial. Thus, high-flexibility and fast switches of attention were demanded. Task-switching was recently related to inter-hemispheric competition (Wylie et al. 2003). Therefore, it seems likely that competition processes associated with inhibition occurred in the present experiment in contrast to the experiment of Ross and colleagues (see part 4.3.4).

Fourth, the tasks differed concerning the attentional demand. Subjects in the experiment of Ross and colleagues had to attend to the auditory modality as a whole, whereas subjects in the present experiment had to focus their attention to a designated ear within the auditory modality. Moreover, the subjects in the present experiment had to ignore simultaneously occurring distractor stimuli, what was not the case for the subjects in Ross' experiment. These different attentional demands, in turn, are likely to elicit distinct neuronal mechanisms. Similarly, strategies for solving different attentional tasks were associated with distinct neuronal processes (Chen et al. 2002). Findings associated with attentional demands and resulting strategies are highlighted in part 4.3.5.

Linden and colleagues could not reveal an impact of attention on the ASSR at all. Various differences between their experimental design and the present experiment can be identified as well. First, Linden and colleagues chose frequency discrimination tasks in the attended conditions. Thus, subjects were not forced to attend to the stimulus rhythm eliciting the aSSR. This was already criticised by Ross and colleagues.

Second, the dichotic listening design used by Linden and colleagues did not include a task switch paradigm as it was used in my experiment. That means subjects simply had to count targets in the designated ear. Thus, subjects did not have to re-adjust their focus of attention from trial to trial as demanded from the subjects in my experiment, but could try to mask the unattended ear for the whole procedure. Therefore again, the task was different in my design and was likely to elicit different neuronal processes (see part 4.3.4).

In the following, I will present studies conducted in other modalities or with different experimental designs that point to the different aspects, I suggested, possibly being responsible for the present results. This is done as I hardly could not seek out any literature investigating the issues directly related to the present experiment. The first section addresses an important principle of the brain, namely competition of neuronal resources. The second part turns to the general view that selective attention is associated with inhibition processes and relates this to the present results. Therefore, one study that revealed similar effects in the somatosensory domain is highlighted. The third part relates competition processes to task-switching. And, finally, the fourth part discusses findings concerning inhibitory effects associated with different attentional demands.

4.3.2 Competition for neuronal resources – a principle of our perceptual system

As outlined above, the results of the present experiment could support an influence of attention on the ASSR, but interestingly did not replicate the enhancement of the aSSR proposed by Ross and colleagues. Instead, an inhibition of the aSSR in the ipsilateral temporal cortex was disclosed. Competition processes especially arise in situations of high rivalry like a dichotic listening situation (Brancucci et al. 2004). Therefore, it seems likely that competition processes took place in the present experiment with binaural stimulation.

Competition of neuronal resources is a basic principle in perception. Reynolds and colleagues (1999) conducted single-cell recordings in the visual cortex of monkeys and showed that selective attention enhances relevant and inhibits irrelevant stimuli due to neuronal competition on the level of receptive fields. In the auditory cortex, lateral inhibition could be shown as well (Suga 1995). Thus, competing for neuronal resources seems to be a basic principle in the organisation of neuronal systems. Competition is found on the single cell level of neurons' receptive fields (Reynolds 1999, Suga 1995), on the intrahemispheric level within modalities (Kastner et al. 1998), between the two hemispheres (Allison et al. 2000, Brancucci et al. 2004, Rykhlevskaia et al. 2006) and between different modalities (Ghatan et al. 1998).

Relating this to the present results, the inhibition of attended stimuli in the ipsilateral hemisphere is supposed to be due to competition processes on the inter-hemispheric level. Inhibition between hemispheres was recently shown by Brancucci and colleagues (2004) within the auditory modality. The authors conducted a MEG experiment to investigate competition effects in dependence of monaural and binaural stimulation. They showed an inhibition of the ipsilateral auditory regions during binaural stimulation, as disclosed by the cortical M100. This inhibition was guided by the contralateral hemisphere. Interestingly, the suppression effects did not appear with monaural stimulation. These findings clearly point to inter-hemispheric interactions in the auditory cortex during dichotic listening. Moreover, Breebart and colleagues (2001) proposed a binaural processing model based on ipsilateral inhibition guided by contralateral structures. Predictions, based on the model were compared to data obtained from diverse experiments. Even if the results were not unambiguous, they supported the model and consequently inter-hemispheric inhibition in the auditory system.

However, it is worthwhile to note that the results of the present experiment postulate an ipsilateral inhibition especially for the attended input. This issue is addressed in the following paragraph.

So far, it was shown that competition is a basic principle of perception occurring at any level and a clarification of inter-hemispheric interaction in the auditory modality was given.

4.3.2 Effects of inhibition due to selective attention

Competition of neuronal resources was highlighted in the prior part. Now, competition is explicitly related to selective attention. As stated above, the findings of the present experiment favour an inhibition of ipsilateral temporal activity due to attention. Attending a tone in one ear led to a significant decrease of the steady-state amplitude in the ipsilateral auditory cortex.

The principle of inhibiting irrelevant information and facilitating the relevant ones is a well-known principle, already proposed by Treisman’s Attenuation Theory in 1964. Treisman based her theory on the behavioural results of the so-called shadowing-experiments, first conducted by Cherry and colleagues (see introduction part). The behavioural results obtained from these experiments showed that attended input is facilitated and still available for the subjects after the experiment, whereas the unattended or irrelevant input is inhibited and only partly available afterwards. Imaging techniques could later relate the behavioural outcomes to neuronal activity in the brain. As outlined in the introduction part, various studies exist revealing an attention-mediated facilitation of neuronal activity in the auditory domain and for steady-states in other modalities (e.g. Woldorff et al. 1993, Tiitinen et al. 1993, Müller et al. 1998, Giabicconi et al. 2004). Studies pointing to an inhibition of information related to attention are available to a lesser extent.

Looking at the present results, it is of importance to emphasize that attended stimuli led to an inhibition of the steady state response in the ipsilateral hemisphere. That means, if a tone is attended, the respective steady-state response of the ipsilateral hemisphere is inhibited. Relating this to the theories of selective attention, the ipsilateral auditory cortex engages neuronal resources that are required from the contralateral cortex primarily involved in stimulus processing. Thus, the contralateral hemisphere inhibits the ipsilateral hemisphere for a more effective processing of the attended stimulus. To my knowledge, until now, no literature exists that revealed such suppression effects due to auditory selective attention in the ipsilateral hemisphere.

In the somatosensory modality, however, Staines and colleagues (2001) revealed note-worthy results concerning ipsilateral inhibition of relevant information.

The experimental design of Staines and colleagues was similar to the one used in the present experiment. Subjects were exposed to vibrotactile stimuli - vibrating little hammers at a frequency of 25 Hz – and had to detect targets defined as brief changes in frequency. Each index finger was stimulated unilaterally for 20 s, after 20 s the side of stimulation changed and stimulation was applied to the other index finger. This was repeated several times. In contrast to my dichotic listening experiment, the vibrotactile stimuli were presented either to the right or to the left hand and not to both sides simultaneously. However, to rule out simple effects of alertness the authors conducted a second experiment with bilateral stimulation. Neuronal activity was recorded via fMRI. Staines and colleagues could reveal two main effects: A facilitation of activity in the primary somatosensory cortex contralateral to the stimulated hand and an inhibition ipsilateral to the stimulation side. For an illustration of their results see figure 4.4.

Inhibition of activity in the ipsilateral hemisphere:

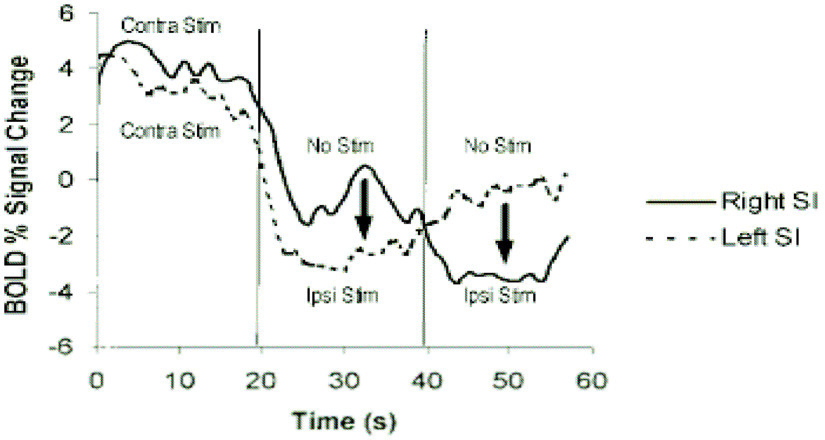

FIG. 1. Group averaged ($n = 6$) time course of BOLD responses for the right (solid line) and left (dashed line) SI in Experiment 1. The time courses have been averaged across repetitions and aligned so that the solid vertical lines separate the task conditions, and the response for the right SI has been shifted by 20 s to facilitate comparison. The stimulation sides are indicated for the right and left SI next to each respective part of the trace. In the first block, task-relevant stimulation was delivered to the contralateral index finger for both the right SI and the left SI. In the second block, stimulation was delivered to the ipsilateral index finger for the left SI (dashed line) and no stimulation occurred for the right SI (solid line). In the third block, the conditions were reversed: stimulation was delivered to the ipsilateral index finger for the right SI (solid line) and no stimulation occurred for the left SI (dashed line). Under task-relevant stimulation conditions, activation in ipsilateral SI was suppressed compared to rest as indicated by the arrows.

FIGURE 4.4 Inhibition and facilitation of neuronal activity. The neuronal activity of attended stimuli is enhanced for contralateral sources and reduced for ipsilateral ones. Adopted from Staines et al. (2001).

However, the results are only circumscribed interpretable. Subjects had to count targets occurring at the index finger that was stimulated and therefore had to direct their attention to the “relevant" hand. Thus, attention was involved in the task. Nevertheless, as the stimulated hand was automatically the to-attended hand as well, an adequate control task for studying selective attention is missing. It was not the authors’ main goal to explicitly study selective attention and so the parallels to my experiment are only in part transferable.

Even if Staines and colleagues found the attention-mediated inhibition of ipsilateral sources for one-sided stimulation and in another modality and, strictly speaking, did not address selective attention, the results strongly support my findings.

Thus, it is likely that in the present experiment the ipsilateral hemisphere was inhibited for attended stimuli due to interaction processes mediated by selective attention.

To sum up, evidence exists favouring an inhibition of neuronal activity of attended stimuli in the ipsilateral hemisphere which definitely supports the present findings.

4.3.3 Task switching and the competition of resources

In this section, inhibition of activity is related to a special demand at selective attention, namely task switching. Competition processes always aim at ameliorating perceptual efficiency by minimising disturbing activity and exposing the relevant aspects of a sensory experience. This seems to be especially relevant in a task switching situation as the attended stimuli have to be separated from the unattended ones from trial to trial. Thus, the perceptual system has to change the focus of attention permanently and should suppress distractor stimuli in an efficient way.

As indicated above one crucial difference between my experimental design and the one used by Ross and colleagues is that subjects had to do exactly this, namely switching between the left and right ear and re-adjusting their focus of attention from trial to trial. Task-switching within one modality was recently related to enhanced competition in neuronal systems. Thus, “a switch of task is accomplished by changing the weights in a competing cognitive system” (Wylie et al. 2003). Related to the present experiment switching between the left and right ear is supposed to lead to an inter-hemispheric competition that could be responsible for inhibition of the ipsilateral hemisphere. The most interfering neuronal activity is supposed to be ipsilateral activity of the attended stimulus. That means, in order to highlight the activity of the attended stimulus and to render task switching efficient, the processing of the attended stimulus should be down-regulated in the ipsilateral hemisphere.

Based on this assumption, competition processes between two hemispheres within one modality would primarily support the present findings. However, it was difficult to find literature dealing with such inter-hemispheric suppression as already stated above. According to Ryklevskaia and colleagues (2006) “it appear(s) that the major limitations of the functional connectivity models currently in use are linked to the properties of existing imaging techniques”. That means, the authors suggest that inter-hemispheric interaction effects are mainly undetected because of lacking methods concerning a sufficient high temporal and at the same time spatial solution. Ryklevskaia and colleagues proposed a new technology, namely the event-related optical signal (EROS; Gratton & Fabiani, 2001) that provides high spatial and temporal resolution at the same time. It is to state that they recently developed a structural equation model that is able to model dynamic functional connectivity on the basis of lagged cross-correlations (lagged CSEM). Ryklevskaia and colleagues (2006) applied the lagged CSEM to inter-hemispheric interactions that appear during task switching. Therefore, they used data from a previous study investigating processes during a spatial stroop task in which subjects had to switch between different dimensions (spatial vs. verbal). Ryklevskaia and colleagues (2006) state that switching between tasks requires both the activation of processing rules that are appropriate for the new task and the inhibition of rules used for the old task. Likewise, the authors suggest that the unprofitable hemisphere is inhibited during task switching processes. Additionally, the authors mention results from their laboratory (Gratton et al., submitted for publication) that favour that inter-hemispheric inhibition is required for successful task switching. As hypothesized, the results showed that the, for the task disadvantaged, hemisphere was inhibited. Transferred to my design, this would mean that for successful task switching the inappropriate hemisphere for the attentional task was inhibited. Thus, if subjects were forced to attend to one ear, the ipsilateral – for the task disadvantaged – hemisphere is supposed to be down-regulated. This is exactly what I found. The results of Ryklevskaia and colleagues (2006) therefore present a plausible explication for the results of the present experiment. However, the different task switching-paradigms are only limited comparable. That means, it is arguable that switching between spatial and verbal tasks in a stroop test can be paralleled to task switching between the left and right ear during a dichotic listening experiment. The first kind of task-switching includes varying assignments of the task itself, whereas the second one requires to switch between different ears.

However, to summarize, inhibiting mechanisms seem to be crucial for realizing the concept of selective attention in the brain. Competition takes place on different levels and is therefore likely to exist in inter-hemispheric interactions, too. Ryklevskaia and colleagues (2006) emphasized the necessity of inhibition in task-switching processes. All in all, this supports the results of the present experiment that point to inhibiting mechanisms during task-switching in the auditory domain.

4.3.4 Inhibition versus facilitation: A result of different attentional demands?

As stated above, the diverging results, that are facilitation in the study of Ross and colleagues (2004) and inhibition in the present experiment, could be due to different attentional demands or tasks. Literature exists that supports different neuronal activation due to varying attentional requests and different focuses of attention. For instance, inhibition versus facilitation mechanisms were found for local versus global tasks (Chen et al. 2002). Just as well, differences in neuronal activity as a function of focused versus divided attention were observed (Hugdahl et al. 2000). To a certain extent, the different experimental paradigms of Ross and the present experiment can be related to global and local forms of attention.

Chen and colleagues (2002) revealed interesting results concerning varying SSVEP amplitudes due to local versus global processing. The experimental design was already described in the introduction part. To briefly recapitulate, subjects were exposed to two overlapping images of seven bars respectively that were flickered with different frequencies. The two different attentional conditions corresponded to the two different task-instructions. In the global condition subjects were asked to respond to width changes in any of the three central bars of the attended image. In the local condition, subjects were asked to respond to width changes only in the central bar of the attended image. MEG data showed an enhancement of the steady-state responses related to the attended image in the global condition compared to the unattended one. However, in the local condition, a relative suppression of the responses corresponding to the attended image compared to the unattended one was observed. For an illustration of the effects see figure 4.5.

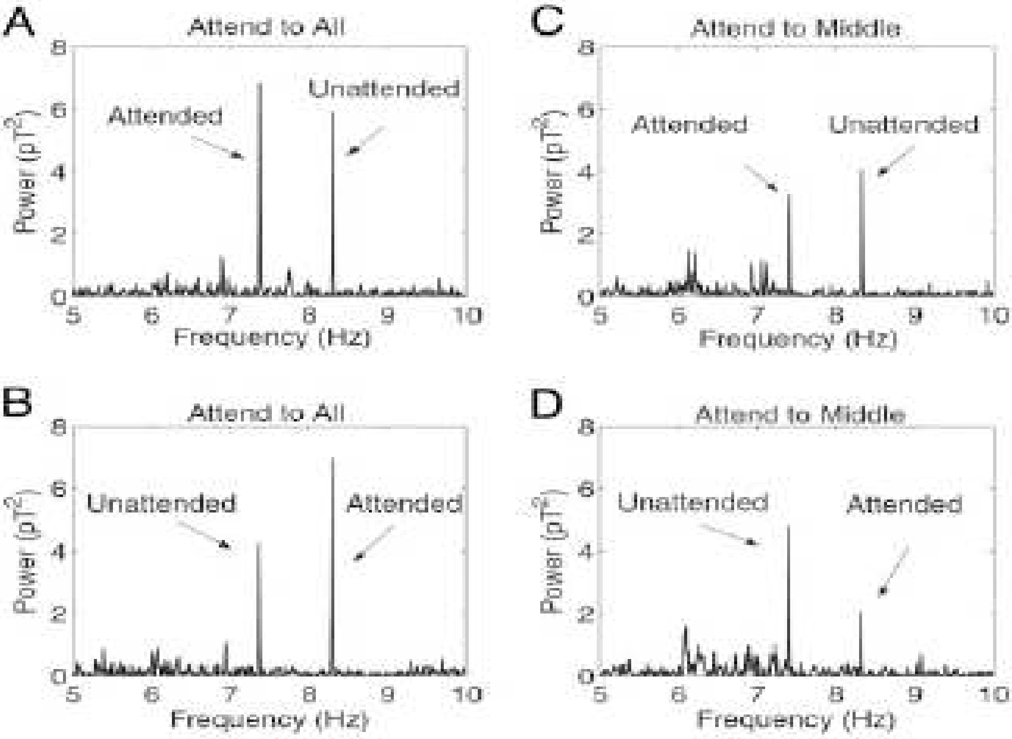

Fig. 3. Power spectra from Channel 127 in one subject (E, Table 2) for four different conditions. In this example, the subject was presented with green-vertical bars flickering at 8.33 Hz and red-horizontal bars flickering at 7.41 Hz. The subject was required to attend to the red bars (*A* and *C*) and to the green bars (*B* and *D*). In *A* and *B*, the subject responded to changes in any of the three central bars (attend-to-all). In *C* and *D*, the subject responded to changes in the middle bar only (attend-to-middle). In the attend-to-all condition, power associated with the attended image was enhanced, compared with that associated with the unattended image. This effect was reversed in the attend-to-middle condition. The units on the ordinate are in picoTesla (pT) (1 pT = 10^{-12} T).

FIGURE 4.5. Steady-state amplitudes in dependence of task-instructions. Adopted from Chen et al. (2003).

To conclude, even if the physical input was the same in the two different conditions, the steady-state responses differed in dependence of task-instructions and attention. Thus, by manipulating the focus of attention (local versus global) different neuronal mechanisms were elicited. This can be paralleled to the results of Ross and colleagues and to the results of the present experiment as follows: Subjects in the experiment of Chen and colleagues had to attend globally to images in the first condition, that means that they had to attend to all of the bars and respond to targets wherever they occurred. This is somehow similar to the conditions in the experiment of Ross and colleagues as subjects had to attend globally to the auditory modality as a whole. In the local condition created by Chen and colleagues, however, subjects were asked to respond to targets in the central bar and ignore changes in the other bars. Thus, in part, they had to suppress distractor targets that they were exposed to. Similarly, in my experimental design, subjects were exposed to two tones simultaneously and had to detect targets only in the designated ear. Again, distractor stimuli from the other ear had to be ignored. However, it has to be remarked that it is problematic to compare the findings, as the dichotic listening task in my experimental design and the more global task in the design of Ross and colleagues (2004) cannot be directly related to the local and global tasks used in the experiment of Chen and colleagues. Furthermore, it is debatable if the results of Chen and colleagues are still valid as a very recent study did not replicate the presented results (Wang et al. 2007). Wang and colleagues found convincing alternative explanations for the results found by Chen and colleagues and did not confirm the inhibition of neuronal activity during the performance of local tasks. Thus, a comparison of local versus global processing and my results could be drawn, even if, strictly speaking, the two experiments are not directly comparable. Furthermore, it remains arguable if the results of Chen and colleagues are still up to date.

4.4 Limitations of the present study

As stated above, the present experimental design represented a new possibility to reveal attention-mediated effects on the ASSR and to control for misleading influences like alertness at the same time. Nevertheless, various weaknesses related to the chosen design have to be mentioned, too.

First, it can be considered as problematic that two amplitude-modulated tones just differing in modulation frequency were presented simultaneously. Up to now, it is not well-defined how simultaneously presented AM-tones of the same carrier frequency are processed in our brain. Some studies point to distortions of the auditory steady-state responses of simultaneously presented tones when carrier frequencies are less than one octave apart from each other (John et al. 2000). Furthermore, most subjects reported after the experiment that they had rather one sensory impression than being able to figure out two different tones in the left versus right ear. Thus, it remains difficult to identify what kind of neuronal activity is produced with binaural stimulation via two amplitude-modulated tones of the same carrier frequency.

Second, the task emerged to be quite difficult and hard to manage for most of the subjects. To my knowledge, the targets (change in modulation frequency during tone presentation) used in the present study have not been utilised somewhere else before. Therefore, the stimuli were tested in a pilot-study and the difficulty adapted so that subjects had to exert themselves but still were able to solve the task. Nevertheless, in the main experiment, it turned out that, for most subjects, the task was marginally difficult. They often seemed to be frustrated after the experiment and sometimes reported that they almost could not figure out the differences between targets and pure tones. Therefore, it remains questionable if subjects tried to manage the task from start to finish or gave up after a while.

4.5 Conclusion

The present study revealed surprising results concerning the relationship between the auditory steady-state response and selective attention: Selective attention seems to down-regulate the auditory steady-state response of attended stimuli in the ipsilateral hemisphere. The existing literature, however, reports an enhancement of neuronal activity in the contralateral hemisphere due to attention.

The present experimental design forced subjects to restrict their attentional focus to the auditory modality while switching between two ears. This turned out to be crucial for the present results emphasizing the role of the ipsilateral hemisphere. Further studies are required to shed light on the mechanisms involved in selective attention and the potentially essential impact of the ipsilateral hemisphere.

If these and other mentioned findings will in fact lead to a ‘switch’ towards an enhanced focus to the ipsilateral hemisphere in the research of attention remains to be seen.

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