Contralateral White Noise Selectively Changes Right Human Auditory Cortex Activity Caused by a FM-Direction Task

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Behne, Nicole, Henning Scheich, and André Brechmann. Contralateral white noise selectively changes right human auditory cortex activity caused by a FM-direction task. J Neurophysiol 93: 414–423, 2005. First published September 8, 2004; doi:10.1152/jn.00568.2004. Animal and human studies suggest that directional categorization of frequency-modulated (FM) tones (rising vs. falling) is a function of the right auditory cortex (AC). To investigate this hemispheric specialization in more detail, we analyzed both the binaural and monaural representation of FM tones and the influence of contralateral white noise on the processing of FM tone direction. In two fMRI-experiments, FM tones with varied direction, center-frequencies, and duration were presented binaurally or monaurally without contralateral white noise (experiment 1) and with contralateral white noise (experiment 2) while the subjects had to perform the same directional categorization task. In experiment 1, contralateral FM tones led to strongest activation, binaural FM tones to intermediate, and ipsilateral FM tones to weakest activation in each AC. This is in accordance with binaural response properties of neurons in animal AC. In experiment 2, contralateral white noise had no significant effect on the activation of left AC by FM tones, whereas in right AC, it led to a significant increase in activation for ipsilateral FM tones. This result provides further support for the critical role of right AC for directional categorization of FM tones, which for ipsilateral input has to be processed in competition to the excitatory input of white noise via the direct contralateral pathway.

Introduction

Hemispheric lateralizations of auditory cortex (AC) functions have been described mainly from impairments after unilateral lesions and from imaging studies (for a recent review see Tervaniemi and Hugdahl 2003). But exactly which aspects of auditory analysis are lateralized in which hemisphere is still a matter of debate (Poeppel 2003; Zatorre et al. 2002). Monaural or dichotic stimulus presentations provide access to these problems since information reaching the two hemispheres from one ear has a contralateral dominance. This was used in the present fMRI study to further pursue a salient question of pattern recognition in speech prosodies, music, and animal vocalizations, namely whether the right AC is responsible for distinguishing and categorizing the direction of frequency modulations (rising versus falling FM). This hypothesis was suggested by several studies both in animals and humans. In the Mongolian gerbil and in the rat it was found that right but not left AC lesions impaired discrimination learning of rising versus falling FM tones (Syka et al. 2003; Wetzel et al. 1998). Similarly, patients with right brain damage showed poorer performance in directional discrimination of FM tones than patients with lesions in the left hemisphere (Divenyi and Robinson 1989). Furthermore, fMRI results showed enhanced activation in right human AC in a directional categorization task compared with passive FM tone presentation and compared with durational categorization (short versus long) (Brechmann and Scheich in press). A PET-study showed also enhanced activation in right AC compared with tasks involving other stimuli (Poepel et al. 2004).

In a monaural approach several factors may determine the results. A contralateral dominance of stimulus representation in AC is usually explained by binaural response properties of cortical neurons. Neurons in animal AC can be divided into EI, EE, EO, and IE cells depending on their response properties for contralateral and ipsilateral stimulation. Electrophysiological studies mainly in primary areas of AC have shown that EE, EI, and EO cells are most abundant whereas IE cells are rare (Clarey et al. 1992; Reser et al. 2000). Although similar neurophysiological analyses of binaural properties of neurons in nonprimary areas are rare (Schreiner and Cynader 1984), from a bottom-up view of these combinations the resulting activation in each hemisphere should be strongest for contralateral (C) stimuli, intermediate for binaural (B) stimuli and weakest for ipsilateral (I) stimuli (CBI-gradient). It is conceivable that this simple combinatorial scheme primarily interpreted in terms of sound localization (Clarey et al. 1992) may be broken in areas of AC not specifically involved in sound localization. By analogy certain AC regions processing a specific feature of a pattern seem to be largely invariant for the processing of nonspecific features of the same stimuli (Suga 1994). This was shown especially in right posterior AC for level variations of FM tones (Brechmann et al. 2002) and in the posterior superior temporal cortex for variations of word repetition rate (Price et al. 1992). A similar invariance might also hold for the ear of stimulation. Thus assuming that areas of right AC are specialized for the directional categorization of FM tones, the activation could be invariant with respect to the stimulated ear.

Moreover, the activation of sensory cortex does not exclusively depend on bottom-up inputs but also on top-down influences of attention, cognition, and memory related processing (Corbetta et al. 1990; Engel et al. 2001; Friston and Price 2001; Stephan et al. 2003). In auditory cortex recent studies have shown that the same acoustic stimuli can lead to different activations depending on the conceptual listening task (Brechmann and Scheich in press; Sussman et al. 2002). This implies...
that using a stimulus in combination with a task that might require the involvement of a specific hemisphere or area may modify the bottom-up activation.

The situation may be further complicated by hemispheric interaction. AC of one hemisphere does not exclusively receive inputs from the ascending auditory pathway but also excitatory and inhibitory callosal inputs from the AC of the other hemisphere (Clarke et al. 1993; Hoptman & Davidson 1994; Musiek and Reeves 1986). However, little is known about the functional interaction except from dichotic listening studies (for reviews see Bryden and Bulman-Fleming 1994; Hugdahl 2000; Zaidel et al. 1990).

The present study investigated the lateralization of auditory information processing in a dichotic approach using a stimulus class in combination with a conceptual listening task presumably involving the right hemisphere. The subjects had to categorize linear FM tones in different frequency ranges according to the direction of modulation (upward versus downward) during presentation to left, to right or to both ears. If AC in one hemisphere or an area therein is not specifically involved in the task of identifying FM tone direction its activation should be mainly influenced by bottom-up inputs, namely activation should be strongest for contralateral FM tones, weakest for ipsilateral FM tones and intermediate for binaural FM tones. Conversely, if FM tone directional processing depends on top-down influences on one hemisphere or an area therein this CBI-gradient may be modified. In a second experiment, in which we presented white noise contralateral to the monaural FM tones, we sought to enhance this top-down influence by complicating task processing.

METHODS

Subjects

Seventeen right-handed subjects (Edinburgh Handedness Inventory) with normal hearing participated in this study. Subjects (12 females, 5 males, between 21 and 35 yr of age, mean age 25 yr) gave written informed consent to the study which was approved by the ethics committee of the University of Magdeburg.

Stimuli and task

Each subject carried out experiment I and II in two separate sessions. 32 different linear frequency modulated (FM) tones with center-frequencies from 1000 Hz to 3200 Hz in steps of 100 Hz were presented binaurally or monaurally to the right or left ear. The FM tones had a duration of 400 ms or 600 ms and a linear rise/fall time of 10 ms. To achieve the same modulation rate of short and long FM tones of the same center frequency \( F_c \) the starting and end frequency of each downward and upward FM tone were calculated by

\[
F_c (Hz) \pm F_c (Hz)/2 \times \text{duration (s)}
\]

One experimental session consisted of 12 stimulus blocks alternating with 13 silence blocks of 46 s each resulting in a total duration of 19 min and 10 s. Blocks with FM tones presented binaurally, monaurally to the right ear or monaurally to the left ear alternated in this order so that each stimulus condition occurred four times. Each stimulus block consisted of 23 downward and 23 upward sweeps (repetition rate, 1 Hz), half of which had a duration of 400 ms. In one of the two sessions continuous white noise was presented contralateral to the ear which was monaurally stimulated with FM tones. Nine subjects started with the experiment without white noise (experiment I) while eight subjects started with the experiment with contralateral white noise (experiment II).

Before the experiments the sound pressure level was adjusted for each subject such that it was about 70 ± 5 dB SPL and equal at both ears. White noise was 2 dB softer than the FM tones.

The subjects had to detect each downward FM tone and report this by pressing a button. For a correct response subjects had to press within 1 s after FM tone onset.

Scanning procedure

Subjects were scanned on a Bruker 3T/60 head scanner equipped with a quadrupolar birdcage head coil. Three slices of 8 mm thickness oriented parallel to the Sylvian fissure were collected covering the superior temporal plane in both hemispheres. In 19 min and 10 s 150 functional volumes were acquired in block-design using a gradient echo sequence (echo time (TE), 31.6 ms; repetition time (TR), 127.8 ms; flip angle, 15°; matrix size, 64 x 60; field of view, 18 cm).

The relatively slow conventional fast low angle shot (FLASH) sequence was modified by using long gradient-ramp rise time (2500 μs), which reduced the scanner noise to approximately 54 dB SPL at the ear. In contrast to echo planar imaging (EPI) sequences that acquire a complete functional image during each repetition, the gradient echo sequence acquires one line in k-space during one repetition (TR). High T1-contrast imaging to obtain anatomical landmarks immediately followed the fMRI. The head of the subjects was fixed with a vacuum-cushion with attached ear muffs containing the fMRI compatible headphones (Baumgart et al. 1998).

Data analysis

Each functional data-set was subjected to a quality check: Subject’s 3D-movement was monitored using the AIR package (Woods et al. 1998). Continuous movements exceeding one voxel in at least one direction were used as criteria for data exclusion. The mean gray value of the temporal lobe defined in two slices was computed for each volume. Images with percentage deviation of gray values from the mean gray value larger than 2.5% were excluded from further analysis. Images were corrected for 2D-movement using the AIR package.

The functional data were analyzed with the software-package KHORFu (Gaschler et al. 1996). The matrix size of 64 x 64 was increased to 128 x 128 by pixel replication followed by smoothing with a Gaussian filter (FWHM = 2 pixel (2.8 mm), Kernel = 5 pixel (7 mm)). For each subsequent scan of the same slice, the mean intensity was computed and then scaled to the mean slice intensity averaged over all volumes. Each voxel series was temporally smoothed using a moving averaging filter with kernel width of two time points. Functional activation was analyzed by correlation analysis to obtain statistical parametric maps. A simple trapezoid function served as correlation vector, roughly modeling the expected BOLD response. The first image of each stimulus and silence block was set to half-maximum value. The remaining images acquired during the silence blocks were set to minimum values and the remaining images acquired during the stimulus blocks were set to maximum values. Activated voxel \((P < 0.05; \text{min. clustersize } = 8)\) were assigned to one of the four territories TA, T1, T2, and T3 which were defined by individual landmarks (Brechmann et al. 2002). For each voxel the average BOLD signal intensity, i.e., the percentage change in image signal between stimulus and silence blocks were determined. The intensity weighted volume (IWI) as the product of number of activated voxels and their mean BOLD signal intensity change was computed.

Contralaterality index of activation (IWI) in each AC was determined as activation by contralateral FM tone stimulation minus

\[ \text{IWI}_{\text{contra}} - \text{IWI}_{\text{contra}} \]

where \( \text{IWI}_{\text{contra}} \) is the intensity weighted volume of the contralateral AC and \( \text{IWI}_{\text{contra}} \) is the intensity weighted volume of the contralateral AC. The contrast between 

\[ \text{IWI}_{\text{contra}} - \text{IWI}_{\text{contra}} \]

was computed and then scaled to the mean slice intensity averaged over all volumes. Each voxel series was temporally smoothed using a moving averaging filter with kernel width of two time points. Functional activation was analyzed by correlation analysis to obtain statistical parametric maps. A simple trapezoid function served as correlation vector, roughly modeling the expected BOLD response. The first image of each stimulus and silence block was set to half-maximum value. The remaining images acquired during the silence blocks were set to minimum values and the remaining images acquired during the stimulus blocks were set to maximum values. Activated voxel \((P < 0.05; \text{min. clustersize } = 8)\) were assigned to one of the four territories TA, T1, T2, and T3 which were defined by individual landmarks (Brechmann et al. 2002). For each voxel the average BOLD signal intensity, i.e., the percentage change in image signal between stimulus and silence blocks were determined. The intensity weighted volume (IWI) as the product of number of activated voxels and their mean BOLD signal intensity change was computed.

Contralaterality index of activation (IWI) in each AC was determined as activation by contralateral FM tone stimulation minus
activation by ipsilateral FM tone stimulation divided by the sum of both conditions.

Statistical analysis of the data were performed using the nonparametric test for matched pairs by Wilcoxon (Wilcoxon matched-pairs signed-rank test).

**Definition of territories**

We used an empirical landmark-oriented approach to systematize across individuals the separate clusters of activated voxels in the auditory cortex which are regularly seen with imaging parallel to the Sylvian fissure. This scheme has proven useful for regional comparison since a functional parcellation of human auditory cortex is not yet available (for discussion see Brechmann et al. 2002).

Clusters of activation were scrutinized in a three-dimensional analysis of both hemispheres of individual brains in relation to the prominent anatomical landmarks insular sulcus, first transverse sulcus, Heschl’s sulcus, and superior temporal sulcus. First, clusters of activation centered to and following the course of Heschl’s sulcus were attributed to T2. Clusters on Heschl’s gyrus anterior to T2 and posterior to first transverse sulcus were attributed to T1. Clusters on planum polare anterior to first transverse sulcus were attributed to TA. Clusters posterior to T2 on planum temporale including the anterior part of gyrus supramarginalis were defined as T3.

**RESULTS**

**Behavior**

The sensitivity index (d’), used as an index for task performance in the directional categorization task of experiment I without white noise, was 2.87 ± 0.22 for left aural FM tones, 2.69 ± 0.22 for binaural FM tones and 2.88 ± 0.21 for right aural FM tones. The sensitivity index in experiment II was 2.78 ± 0.20 for left aural FM tones with right aural white noise, 2.80 ± 0.24 for binaural FM tones and 2.69 ± 0.22% for right aural FM tones with left aural white noise. There was no significant difference of sensitivity index between the two experiments or within the experiments between different conditions.

**Activation in experiment I**

Contralateral monaural stimulation with FM tones (contraFM) led to strongest global activation in both AC, binaural stimulation (binFM) to intermediate and ipsilateral monaural stimulation (ipsiFM) to weakest activation (Fig. 1). In both AC the activation difference was significant between contraFM and ipsiFM (P < 0.01). In left AC activation was also significantly stronger during binFM than during ipsiFM (P < 0.01). In the right AC this activation difference was not significant but showed a trend in this direction (P < 0.1). The contralateral index which compares contralateral with ipsilateral stimulation (Fig. 6) shows that relative activation was not different between left and right AC. Thus to a first approximation the results are comparable with a CBI-gradient in both hemispheres.

The stronger global activation of each AC by contraFM than by ipsiFM was mainly caused by activity in the territories left and right T1 (P < 0.05), left and right T2, and left T3 (P < 0.01) (Fig. 2).

The stronger global activation of left AC by binFM than by ipsiFM was mainly caused by left T2 and T3 (P < 0.01). In the right AC this activation difference was only signifi-
Comparison of activation in the two experiments

A direct comparison of activations in the two experiments revealed significant differences exclusively in the right hemisphere. Global activation of right AC ($P < 0.01$) as well as activations of the territories T1, T2, and T3 ($P < 0.05$) were significantly stronger during ipsilateral FM in combination with contralateral noise in experiment II than during ipsiFM without contralateral noise in experiment I.

To test for side by condition effects we additionally subjected the contralateral index of each territory in both experiments to an ANOVA with factors hemisphere and condition (contralateral noise or not). An interaction between factors condition and hemisphere was not significant for any of the areas. We only found significant main effects of hemisphere in T2 ($P = 0.001$), T3 ($P = 0.022$), and whole AC ($P = 0.024$) and of condition in T1 ($P = 0.016$), T2 ($P = 0.006$), T3 ($P = 0.021$), and whole AC ($P = 0.001$). However, posthoc t-test (2-sided) revealed the condition effect to be significant exclusively in right auditory cortex areas (T1: $P = 0.001$; T2: $P = 0.003$; T3: $P = 0.009$) but not in left auditory cortex areas (T1: $P = 0.185$; T2: $P = 0.665$; T3: $P = 0.722$). The significant difference of contralaterality index between the two experiments in the right AC is also revealed by Wilcoxon test ($P < 0.01$) and shown in Fig. 6.


discussion

It has been suggested from animal and human studies that right AC is critically involved in the distinction and categorization of FM tone direction (Brechmann and Scheich in press; Divenyi and Robinson 1989; Poeppel et al. 2004; Syka et al. 2003; Wetzel et al. 1998). The specific point of departure for the present experiments was the previous finding with upward and downward modulated FM tones that right posterior AC areas selectively increased activation during directional categorization over mere exposure to the same FM tones and over durational categorization of FM tones (short versus long) using exactly the same stimuli as in the present study (Brechmann and Scheich in press). Furthermore, activity in right posterior AC inversely correlated with task performance in the directional categorization task. This suggested task-dependent top-down influences on right hemisphere activation. The present results support this lateralization hypothesis by two types of dichotic approaches with varied hemispheric demands on FM tone directional categorization. Thereby the similar CBI-gradient of global activation in the two hemispheres obtained with the first task in the absence of noise served as a baseline. There was, however, a local hemispheric exception to this global gradient, namely that activations in right posterior AC (T3) were invariant with respect to the stimulated ear. In the second experiment the baseline CBI-gradient was reverted in the right AC and prominently in posterior areas when FM tones competed with noise from the contralateral ear. In both experiments task performance of subjects was independent of stimulated ear. This can be taken to indicate that the special activations in right posterior AC are signs of successful coping with varied demands on the right hemisphere.

Dependence of activation on stimulation side

In experiment I, AC activation of each hemisphere was strongest by contralateral FM tone input, intermediate by binaural and weakest by ipsilateral FM tone input. This CBI-gradient may be explained by the large proportions of EE, EI, and EO cells found in primary-like areas of animal AC that respond with excitation to contralateral input and with inhibition or not at all to ipsilateral input (Clarey et al. 1992; for review). Consequently, the relative contribution of inhibition to the combined input increases from contralateral over binaural to ipsilateral stimulation. Thus the CBI-gradient for the global AC activation of each hemisphere derived in the present experiment I is explicable by bottom-up inputs.

Several imaging studies with fMRI, MEG or PET investigated contralateral activity in human AC by comparing activation by ipsilateral and contralateral stimulation with only a few using binaural stimulation as a control condition. Most of these studies presented stimuli not involving any task (Celesia 1976; Khosla et al. 2003; Loveless et al. 1994; Mäkelä et al. 1993; Pantev et al. 1986; Pantev et al. 1998; Reite et al. 1981; Suzuki et al. 2002; Tiihonen et al. 1989) showing that in both hemispheres activation on contralateral stimulation is stronger than on ipsilateral stimulation. The same contralateral dominance was shown in studies in which the subjects had to perform a task e.g., to indicate a target word (Jäncke et al. 2002b; Kushner et al. 1987), to repeat words (Greenberg et al. 1981; Hirano et al. 1997) or to detect deviant stimuli (Woldorff et al. 1999). Consistent with our results in experiment I these studies also reported stronger activation from contralateral than from
ipsilateral stimulation in both hemispheres. Thus despite the
task demand, no modulations of contralaterality by top-down
effects were evident in these studies. However, such a top-
down influence was demonstrated in two studies which inde-
pendent of stimulation side revealed a larger left than right
activity in posterior superior temporal cortex during a tonal
memory task for subjects using analytic strategies (Mazziotta
et al. 1982) and a larger left than right activity in Heschl’s
gyrus during a pitch identification task (Devlin et al. 2003).
This implies that an ipsilateral subdominance of activation can
be changed by top-down demands of tasks. However, neither
study tested whether activation in either hemisphere was stron-
ger for contralateral than for ipsilateral stimulation despite the
overall left lateralized activation.

During task performance in our experiment I, an effect of
similar activation independent of stimulation side was not
observed in the global activation of AC in the hemispheres but
in one of the four territories of AC. Activation of right T3 was
similar for the three conditions (contraFM, binFM, and ip-
siFM) and thus did not correspond to the bottom-up based
CBI-gradient. It revealed that the stronger global AC activation
during contraFM compared with ipsiFM was mainly caused by
the auditory territories left and right T1, left and right T2, and
left T3. This suggests that the activation of T3 in contrast to

**FIG. 3.** Auditory cortex activation of an individual subject in experiment I (1) and in experiment II (2) during FM tone presentation to the left ear (a) and
to the right ear (b). In experiment I activation of each auditory cortex was stronger during contralateral FM tone presentation. In experiment II in each hemisphere
the activation was stronger during right than during left FM tone presentation. Thus despite the reduced overall activation in experiment II in this single subject
the change in contralaterality between the two experiments is representative for the group results.
other areas was more affected by the task-related information of the stimuli than by the pathway and mechanisms by which the information reached the right posterior areas.

It has been suggested that areas processing specific aspects of a stimulus pattern might be largely invariant for the processing of nonspecific aspects of the same pattern (Brechmann et al. 2002; Frackowiak 1994; Suga 1994). With respect to FM it was previously shown that exposure to different levels of FM tones similar to those in the present study led to systematically weaker level dependence of activation in right compared with left AC (Brechmann et al. 2002). This level-tolerance is considered as a prerequisite of neuronal selectivity for a particular information bearing sound element because biologically important sounds must be interpreted independent of sound pressure levels (Suga 1994). Consequently, the invariance of activation in the present experiment I with respect to the stimulated ear might be interpreted in favor of a specific role of right T3 in the processing of FM-direction. If this were the case it would provide an explanation for the similar performance (d') of subjects independent of ear.

Influence of contralateral white noise on the representation of monaural FM tones

The activation of left AC in experiment II was similar to that in experiment I. ContraFM with ipsilateral white noise (ipsiWN) led to strongest activation, binFM to intermediate activation and ipsiFM with contralateral white noise (contraWN) led to lowest activation. Surprisingly, despite the additional presentation of noise the result in left AC was in accordance to the CBI-gradient for FM tones alone in experiment I. This suggests that noise when presented contralateral to the FM tones has a weak effect on the overall activation of the left AC.

However, we found area-specific differences. In left T1 (covering primary AC) the two combinations contraFM with ipsiWN and ipsiFM with contraWN caused similar activations. This may be expected from a bottom-up view in nonspecific areas if neuron clusters respond to FM tones (e.g., Horikawa et al. 1998; Nelken 2002; Ohl et al. 2000; Rauschecker 1997) and other clusters respond to wideband noise (e.g., Caird et al. 1991; Phillips et al. 1985) or to FM tones and wideband noise. Consequently, contralateral excitation and ipsilateral inhibition may be found in response to both ear combinations of FM tones and noise. How in this way a tonal stimulus at one ear and noise at the other ear produce excitatory-inhibitory interactions in a tonotopic map with mixed responsiveness of neurons was shown in inferior colliculus by a classical 2-deoxyglucose experiment (Webster et al. 1984). Since in our experiment the two combinations of contraFM with ipsiWN and contraWN with ipsiFM led to similar activations in the primary area the underlying net activations of neuronal population must have been comparable. Our results indicate that the situation is very different in the more posterior areas T2 and T3 in left AC. There the responses followed the CBI-gradient suggesting that noise responsiveness and FM tone responsiveness are not comparable in strength or do not interact in a fashion similar to the primary areas. Imaging studies showed that noise mainly produced activation in primary AC (Hirano et al. 1997) and also to some extent in nonprimary auditory regions (Binder et al. 2000; Jäncke et al. 2002a; Patterson et al. 2002). Consistent with our results in left AC the fMRI-study by Binder et al. (2000) showed that binaural noise caused similar activation compared with binaurally presented tones with stepwise varying tone frequencies in primary AC but weaker activation in auditory regions around primary AC. Conversely, two other studies showed that frequency modulated tones compared with unmodulated tones generate greater activation...
in nonprimary auditory regions than in primary auditory cortex (Hall et al. 2002; Hart et al. 2003).

While these are all bottom-up arguments a more speculative top-down argument may also account for the weak influence caused by noise in contrast to FM in secondary AC regions, namely that white noise in contrast to the FM tones did not carry any information important for the task.

The global activation of right AC in experiment II was different from left AC and markedly different from right AC in experiment I. IpsiFM with contraWN led to strongest activation whereas contraFM with ipsiWN led to weakest activation causing a reversal of the CBI-gradient and a significant difference in contralaterality index between the experiments I and II. As seen in a comparison of experiment I and II this reversal of activation was mainly due to a stronger activation by ipsiFM with contraWN compared with ipsiFM without WN. Regional analysis of the contralaterality indices showed that T1, T2, and T3 contributed to this reversal. Comparing the contralaterality indices in right AC with that of the left AC areas in experiment II revealed that the reversal of the CBI-gradient in right AC was mainly caused by T2 and T3, whereas the contralaterality index of right T1 was similar to that of left T1.

In summary, the influence of WN on activation in right AC and most sensitively in posterior areas was stronger than in left AC. The most remarkable effect seems to be that right posterior areas were more strongly activated when contralateral noise was added to ipsilateral FM tones than with ipsilateral FM tones alone while there was no difference on the left side. Supposing similar conditions of responsiveness to FM tones and noise as discussed for left AC these effects cannot be explained by bottom-up considerations of the results.

Instead the reversal of the CBI-gradient might be due to a special role of the right AC in the task, following the hypothesis that right AC and especially posterior areas are specialized to categorically derive the direction of FM tones, independent of frequency. Then the key result, the stronger activation of right AC by ipsiFM combined with contraWN compared with ipsiFM alone needs to be explained in relation to the underprivileged flow of information from the right ear to the right AC during the task. FM tones presented to the right ear mainly arrive in left AC via the excitatory pathway but also in the right AC via the underprivileged ipsilateral pathway. In experiment I without noise the information via the weaker ipsilateral pathway is probably sufficient for the processing of FM direction in the right AC whereas in experiment II information about the sweep direction has to compete with an input of the privileged contralateral noise. According to an hypothesis by Kimura (1961) the information about ipsiFM might have even been suppressed by the contraWN.

Therefore functional neural compensations seems to be required to increase FM tone signal to noise ratio and to enable successful task performance. We offer two explanations how this may occur. First, the FM tone input to right AC via the ipsilateral pathway may be up-regulated by (as yet unknown) top-down mechanisms. But even though descending auditory connections are available this up-regulation of subcortical input is difficult to explain as selective phenomenon only in posterior areas of the right AC. Although the activation of right primary areas (T1) was enhanced for ipsiFM in experiment II compared with experiment I the contralaterality index in right T1 was not significantly different from left T1. Thus the presumed up-regulation of activity in the presence of white noise was similar in left and right primary AC but stronger in right than left posterior areas. The results might therefore be more in favor of a second explanation, namely that FM tone activation from the left AC is transferred to the right AC via the corpus callosum and in this way causes an up-regulation of activity. AC fields have strong homotopic contralateral projections (Budinger et al. 2000; Kaas and Hackett 2000) and left posterior AC areas are activated by FM tones as shown here. Therefore this transfer of information via corpus callosum could be rather area-specific and may lead to an increased activation specifically in right posterior areas. Because in experiment I the CBI-gradient was shown to hold for right AC leading to the weakest activation during ipsiFM stimulation the transfer of FM tone information via the corpus callosum did either not occur or to a lesser degree. The additional presentation of contraWN may lead to an up-regulation of information transfer via corpus callosum such that the level of specific FM activation is increased and discrimination of direction can be performed. This callosal transfer, however, has to be verified by means of imaging methods with higher temporal resolution (MEG, EEG).

**General discussion**

The results of experiment I and II, even though not fully explicable, are compatible with different types of animal and human studies all suggesting that the directional distinction of FM tones (rising versus falling) is a function of the right AC and specifically of right posterior areas. Some recent results support this view and make other possible interpretations less likely. In Mongolian gerbils and rats it was found that right but not left AC lesions impaired discrimination learning of symmetric pairs of rising versus falling FM (Syka et al. 2003; Wetzl et al. 1998). Similarly, human patients with right brain damage showed significantly poorer performance than patients with left brain damage during directional discrimination of FM stimuli (Divenyi and Robinson 1989). An fMRI-study using binaural FM tones with 500 ms duration and the same rate of modulation as in the present study showed a significantly enhanced activation in right posterior areas of AC when the subjects had to categorize the FM tones according to direction compared with a control condition with passive presentation of the same FM tones (Brechmann and Scheich in press).
interesting aspect of this binaural study was that the group activation of these posterior areas during the directional categorization did not show a significant lateralization i.e., stronger right than left activation. A right lateralized activation was only observed for subjects performing the task with a sensitivity index below 1.5 but not for subjects with better task performance like most of the subjects in the present experiment. Nevertheless, the group activation was highly systematic because the activation of the right AC inversely correlated with the task-performance of the subjects. Thus activation became more focused in T3 with better performance. These results explain why subjects in the present experiment I did not show a stronger right than left AC activation in the binaural condition. A second experiment of that study corroborated the selective involvement of right T3 in the directional categorization task. Activation in right T3 was enhanced for directional categorization compared with durational categorization (short versus long) of FM sweeps whereas in left T3 activation was stronger for categorization of duration than for categorization of direction but did not correlate with performance. The authors inferred from this double dissociation that the directional categorization task and not any selective bottom-up representation of the class of FM sweeps per se influences the activation of right posterior AC. Presumably there is no contradiction between the result of a negative correlation of task performance and activation in that study and the present results of an up-regulation of activation during noise interference together with a maintenance of level of task performance. Reduction of activity with proficient task performance can be interpreted as a refinement of processing by limitation to a small network of specialized neurons (Brechmann and Scheich in press; Hasegawa and Miyashita 2002). This reduction of analysis to expert neurons may be counterproductive in the case of noise masking. Instead, the FM tone representation might be enhanced.

A comparison of activation in an FM directional categorization task with tasks involving other stimuli was made in a PET-study by Poeppel et al. (2004). Categorization of FM direction also resulted in enhanced activation in right posterior AC compared with the categorical perception of consonant-vowel syllables and a lexical decision task (Poeppel et al. 2004). Thus in light of these findings the special effects in the present study mainly in the right posterior AC support the view of a specialization of the right posterior AC for directional categorization of slow FM. However, there is another possible interpretation, namely that white noise per se has a different effect on left and right AC. However, neither in a 2-deoxyglucose labeling study in rodent AC (Caird et al. 1991) nor in a fMRI study of human AC (Binder et al. 2000) was binaural noise presentation found to lead to differential hemispheric activation. In light of the literature on contralaterality using various kinds of stimuli (even speech) which all show a stronger response to contralateral than to ipsilateral stimuli in both auditory cortices, a CBI-gradient would also be expected for white noise alone. However, the possibility remains that background noise in interaction with other auditory stimuli leads to an asymmetry of activation. For instance, the MEG mismatch negativity (MMN) elicited by deviant syllables in a series of syllables was found to be decreased in left AC and enhanced in right AC when binaural background noise was added (Shtyrov et al. 1998). In a another study using syllables without deviants additional binaural background noise depressed the dipole moment of the P1m in left AC whereas it enhanced the dipole moment of the P2m in right AC (Shtyrov et al. 1999). These asymmetric effects of noise are difficult to interpret and do not necessarily mean that they are of the same type as observed in our study. Stimuli and noise were presented binaurally and therefore noise served as a binaural peripheral masker of the relevant syllable information. Consequently noise could interact at any stage within the right and left auditory pathway and was not brought to a specific contralateral interaction with relevant stimuli like in our task. From the point of view of mechanisms the result may be more comparable to a masking effect obtained with fMRI when the level of FM tones was considerably below the level of the continuous scanner noise and generated an increased activation in a left AC area (Brechmann et al. 2002).

Although there was no significant difference in performance between the two experiments the directional categorization task might still be complicated by the noise. Behavioral scores do not necessarily reflect the “effort” of the subjects to solve the task. The second experiment may have required more selective attention toward the FM sweeps which compensated for task performance but led to activation differences.

Our findings can be related to more general hypotheses of hemispheric specialization by Zatorre et al. (2002) and Poeppel (2003). Our results are consistent with a right hemispheric specialization for spectral processing (Zatorre et al. 2002) if the directional categorization of FM sweeps is assumed to involve more spectral analysis. But they are also consistent with the hypothesis that the right hemisphere preferentially extracts information from long integration windows (Poeppel 2003) typical for intonation contours in speech prosodies for which frequency modulations are an important acoustic feature.

The hypothesis by Zatorre et al. (2002) is partly based on experiments using nonverbal sounds containing fast or slow frequency transitions. Slow transitions produced bilateral activation during passive stimulation whereas the activation of right AC was reduced during presentation of fast frequency transitions (Belin et al. 1998). The stimuli with fast transition were also shorter in duration. Although the stimuli with long transition are comparable to our FM tones, they did not lead to a difference between left and right global AC activation, as in our study. Further experiments will be necessary to resolve this discrepancy. It will be important to compare relative hemispheric AC activation using short duration FM sweeps which have the same FM rate as the long duration FM sweeps used in this study. The results of such experiments will clarify whether it is the slow FM sweep rate, or whether it is the long duration of our FM stimuli, which led to our results in right posterior AC.

If the hypothesized specialization of right AC for the processing of the direction of long, slow rate FM tones can be substantiated in further experiments, then our paradigm presenting white noise at one ear and a task-relevant stimulus at the other ear may become a general tool for investigations of auditory hemispheric specialization with fMRI. This, however, remains to be tested in future experiments using other stimuli (e.g., FM with short transitions, amplitude modulated tones, speech) and other tasks.
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