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The cerebral haemodynamics of music perception
A transcranial Doppler sonography study

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Summary
The perception of music has been investigated by several neurophysiological and neuroimaging methods. Results from these studies suggest a right hemisphere dominance for non-musicians and a possible left hemisphere dominance for musicians. However, inconsistent results have been obtained, and not all variables have been controlled by the different methods. We performed a study with functional transcranial Doppler sonography (fTCD) of the middle cerebral artery to evaluate changes in cerebral blood flow velocity (CBFV) during different periods of music perception. Twenty-four healthy right-handed subjects were enrolled and examined during rest and during listening to periods of music with predominant language, rhythm and harmony content. The gender, musical experience and mode of listening of the subjects were chosen as independent factors; the type of music was included as the variable in repeated measurements. We observed a significant increase of CBFV in the right hemisphere in non-musicians during harmony perception but not during rhythm perception; this effect was more pronounced in females. Language perception was lateralized to the left hemisphere in all subject groups. Musicians showed increased CBFV values in the left hemisphere which were independent of the type of stimulus, and background listeners showed increased CBFV values during harmony perception in the right hemisphere which were independent of their musical experience. The time taken to reach the peak of CBFV was significantly longer in non-musicians when compared with musicians during rhythm and harmony perception. Pulse rates were significantly decreased in non-musicians during harmony perception, probably due to a specific relaxation effect in this subgroup. The resistance index did not show any significant differences, suggesting only regional changes of small resistance vessels but not of large arteries. Our fTCD study confirms previous findings of right hemisphere lateralization for harmony perception in non-musicians. In addition, we showed that this effect is more pronounced in female subjects and in background listeners and that the lateralization is delayed in non-musicians compared with musicians for the perception of rhythm and harmony stimuli. Our data suggest that musicians and non-musicians have different strategies to lateralize musical stimuli, with a delayed but marked right hemisphere lateralization during harmony perception in non-musicians and an attentive mode of listening contributing to a left hemisphere lateralization in musicians.

Keywords: music perception; transcranial Doppler sonography; hemispheric lateralization; cerebral haemodynamics

Abbreviations: CBFV = cerebral blood flow velocity; RI = resistance index; SPECT = single photon emission tomography; (f)TCD = (functional) transcranial Doppler sonography

Introduction
The physiology of music perception has been addressed in several studies. In particular, the hemispheric lateralization of music listening has been investigated by different methods such as neuropsychological testing, neuroimaging, EEG and Doppler ultrasound. Three major problems can be found in these studies. First, differences between the subjects, such as musical experience, handedness and gender, have been neglected in some studies. Secondly, the character of music, its similarity to language and the attitude of the subjects towards it have not been considered in other studies. In these studies, the impact of simple musical elements such as intervals, chords and pitch or timbre discrimination on lateralization were examined primarily, and complex musical structures were not looked at. Thirdly, for most of the methods, analysis of dynamic short duration changes during music perception is not possible. The time period necessary to evaluate functional changes is at least a few minutes for modern neuroimaging or neuropsychological testing.

However, despite these difficulties in analysing music perception by neurophysiological and neuropsychological methods, some widely accepted results have been obtained. Already at the beginning of this century, it was suggested from analysis of brain damage cases that there is an asymmetry of the brain for the different aspects of music perception (for a review, see Henschen, 1926). However, the results of the case studies are often too heterogeneous to yield conclusive information on the problem of interhemispheric dominance during music perception (Joseph, 1988). The first controlled studies were neuropsychological investigations on dichotic listening which showed a left hemisphere dominance for language perception and a right hemisphere dominance for melody perception (Kimura, 1961; 1964). The latter finding has also been confirmed for musical chord discrimination (Gordon, 1970) and for tonal sequence discrimination (Zatorre, 1979; Mazzucchi *et al.*, 1981). In these studies, however, no influence of the gender, musical competence or handedness of the subjects could be detected.

Bever and Chiarello (1974) modified these findings by showing that the right hemisphere advantage for melody perception is only true for non-musicians, but not for subjects with musical experience who analyse musical structures with a left hemisphere dominance in a more analytical and non-holistic way than non-musicians. These differences between musicians and non-musicians have been confirmed further by Johnson (1977), Gordon (1978*a*), Peretz and Morais (1980) and Hassler (1990), who all showed a significant difference or a trend to a left hemisphere dominance in subjects with musical experience or with an analytical and attentive way of listening to musical structures. Gaede *et al.* (1978) related this finding to musical aptitude. Furthermore, Messerli *et al.* (1995) suggested that not only the level of musical competence but also the musical features of the stimuli (verbal or non-verbal; complex or not complex) contribute to the lateralization. The hypothesis of a left hemisphere dominance in musicians recently has even been supported by morphological studies with MRI showing a stronger leftward planum temporale in musicians with absolute pitch ability (Schlaug *et al*., 1995). This study by Schlaug *et al.* (1995) corresponds to the recent finding using functional magnetic source imaging of enhanced cortical representation for tones of the musical scale in musicians (Pantev *et al.*, 1998). Besides these differences in musical experience, Hassler (1990) found gender differences in the lateralization of musical processing using dichotic listening tests, suggesting that female subjects in general have a lower dominance of the left hemisphere than male subjects. Cohen *et al.* (1989) excluded an influence of ethnic aspects in their studies on dichotically presented musical stimuli in French-Canadian and Chinese subjects.

The brain asymmetry shown for language and melody perception has not been found in rhythm perception. Dichotic studies showed a trend to a left hemisphere dominance in rhythm perception (Gordon, 1978*b*), but EEG studies did not reveal any significant differences between the activation of the right or left hemisphere during rhythm perception by musicians (Beisteiner *et al.*, 1994). However, the latter study and other EEG studies (Davidson and Schwartz, 1977; Hirshkowitz *et al*., 1978; Breitling *et al.*, 1987; Altenmüller, 1989) confirmed the right hemisphere dominance in the music perception of non-musicians and in producing melodies for all subjects. Studies after hemispheric anaesthesia by intracarotid sodium amobarbital revealed a specific role of right temporal lobe structures in mediating memory for music (Loring *et al.*, 1992; Plenger *et al.*, 1996) and in singing with correct pitch (Bogen and Gordon, 1971; Gordon and Bogen, 1974).

The first PET studies on music perception showed an increased right hemisphere activation of metabolism for timbre discrimination, chord and musical sequence perception and pitch discrimination in musically naive subjects (Mazziotta *et al.*, 1982; Zatorre *et al.*, 1992). Complex tasks of detection of pitch changes in melodic sequences also led to an increase of right hemisphere metabolism as measured by PET (Zatorre *et al.*, 1994). In the most recent study on PET during music perception (Platel *et al.*, 1997), activation was found in the left hemisphere for familiarity of musical structures (left inferior frontal gyrus and superior temporal gyrus), for pitch tasks (left cuneus/precuneus) and for rhythm tasks (left inferior Broca's area), whereas the right hemisphere was activated for timbre tasks (right precentral and inferior frontal gyri). Although a degree of independence among the musical processing components was shown, there was functional evidence in this and similar PET studies for complex cognitive strategies (Sergent *et al.*, 1992). However, PET studies did not reveal the pattern of activation within the first seconds of activation, and complex musical structures with different elements were not investigated. The findings of the early PET studies of music processing could not be reproduced by regional cerebral blood flow measurement with single photon emission tomography (SPECT) (Ryding *et al.*, 1987; Formby *et al.*, 1989).

We performed a study using functional transcranial Doppler sonography (fTCD) of the middle cerebral artery during music perception to investigate hemispheric lateralization and to analyse the impact of the type of music, the musical experience and gender of the subject, and the attention during listening. The fTCD has the advantage of being a non-invasive method with an excellent resolution in time; however, it has a poor resolution in space. Changes of cerebral blood flow velocity (CBFV) even within a few seconds can be detected. Thus, fTCD is more appropriate to evaluate short duration changes than PET, SPECT and functional MRI. The latter methods show a better resolution in space, which is, however, not necessary for analysing hemispheric lateralization. The validity and reliability of fTCD in the investigations of acoustical perception and similar cognitive functions have been shown in several studies on language processing and memory (Droste *et al*., 1989; Hartje *et al*., 1994; Silvestrini *et al*., 1994; Rihs *et al*., 1995; Knecht *et al*., 1996), on mathematical tasks (Droste *et al.*, 1989;

Kelley *et al.*, 1992) and on visual processing (Aaslid, 1987; Conrad *et al.*, 1989; Droste *et al.*, 1989; Kelley *et al.*, 1992; Silvestrini *et al.*, 1994; Rihs *et al*., 1995).

Only one study has been published so far on fTCD during music perception, which did not consider short duration changes of CBFV, differences in musical experience or differences in the type of music (Matteis *et al.*, 1997). In this study, in which the authors only examined non-musicians, melody perception induced a non-significant, and melody recognition a significant increase of CBFV in the right hemisphere. We hypothesize that it is possible to reproduce the recent findings of neuroimaging studies on hemispheric lateralization of music and language perception by fTCD and, furthermore, that it is possible to show dynamic short duration changes (within a few seconds) of CBFV in response to different types of music or to language. In addition, we were interested in the impact of musical experience, age and gender of the subjects on the hemispheric lateralization.

Methods

We designed a prospective study with healthy subjects to assess bilateral fTCD of the middle cerebral artery during music and language perception. Previous mapping studies have shown that most brain parts supplied by the middle cerebral artery are involved in the processing of music perception and production (for a review, see Sergent, 1993). Therefore, we did not insonate the anterior and the posterior cerebral arteries. In the data analysis, the impact of the following major variables on cerebral haemodynamics was considered: the type of music or language; gender of the subject; musical experience of the subject; mode of listening (attentive versus non-attentive); and short changes in tempo during music perception. In a pre-test, the equipment and the procedure (Doppler ultrasound tubes; administration of the tubes; music application via earphone; software) were tested and optimized. None of the pre-test subjects were enrolled in the final study.

Subjects

We used 24 healthy subjects (12 male, 12 female) in the final data analysis. Three further subjects had no appropriate ultrasound temporal skull window; in two further subjects, tubes moved during the examination and their data were not included. None of the subjects had any symptoms of a neurological, psychiatric or internal disease, and had not taken any medication on the day of examination and for at least 3 days before. No subject showed impairment of auditory acuity as tested by audiometry. All subjects were right-handed (inclusion criterion) according to the criteria of the Edinburgh inventory (Oldfield, 1971). The mean age of the subjects was 26.2 $\pm$ 3.3 years (range 22–33). There were no significant differences in age between male and female subjects or between subjects with and without musical experience. All subjects gave informed consent prior to the first investigation. The study was approved by The Ethics Committeee of The Faculty of Medicine, University of Münster, Germany.

Fourteen subjects had musical experience as defined before enrolment (inclusion criterion) and they were students or postgraduates of the Department of Musical Education, University of Dortmund. They had to be able to play at least two instruments, one of which they had played for at least 10 years. Daily practice of the instruments for at least 2 h was a further inclusion criterion for the subjects with musical experience. Ten subjects had no musical experience. The only formal musical experience allowed was primary school musical education. They had never played an instrument and did not listen to music regularly. In the text, the subject groups are called musicians and non-musicians. Subjects further were asked to rate their normal mode of music listening according to two statements: (i) listening to music as background music without analysing musical structures; and (ii) listening to music attentively and analysing musical structures. Fifteen subjects rated themselves as background listeners (eight of them being musicians) and nine rated themselves as attentive listeners (six of them being musicians). There was no significant coincidence of musicians and attentive listeners ($\chi^2 = 0.41$; $P < 0.521$).

Doppler ultrasound recording

Transcranial Doppler ultrasound was performed with a TC 2-64B device (EME company, Überlingen, Germany). Two 2 MHz transducer probes were attached to a headband and placed at a temporal skull window bilaterally. The middle cerebral arteries were insonated at a depth of between 45 and 55 mm. The technique, and in particular the correct identification of the middle cerebral artery, was performed according to the literature (Ringelstein *et al.*, 1990).

The envelope curves of the Doppler frequency spectrum in the middle cerebral artery were recorded continuously bilaterally. Mean CBFV, resistance index (RI) (calculated as systolic CBFV minus diastolic CBFV divided by diastolic CBFV) and pulse rate were registered separately for every cardiac cycle bilaterally. In order to avoid artefacts caused by displacement of the probes induced by coughing or by head moving, cardiac cycles with mean CBFV values outside the range of 20–200% of the total period mean CBVF were rejected. Calculation of the values and averaging processes (see Procedure) were performed using a software program developed by one of the authors (D.R.).

Music presentation

The main constituents of music are harmony/melody (both depending on timbre and pitch discrimination), rhythm and language. Therefore, we chose a total of three different pieces which were presented to the subjects in random order. Each of the pieces was dominated by one of the constituents mentioned above. The ‘language’ piece was a mixture of

Table 1 *Mean CBFV (in cm/s) with simple standard deviation during different periods of music perception presented separately for the total subject group, for musicians and non-musicians, and for both hemispheres*

	Total group (n = 24)		Musicians (n = 14)		Non-musicians (n = 10)	
	Left	Right*	Left†	Right	Left†	Right‡
Baseline	60.6 ± 11.9	60.9 ± 13.0	64.7 ± 10.0	64.7 ± 10.1	55.0 ± 12.0	55.6 ± 14.6
Language perception	61.1 ± 11.1	60.4 ± 12.8	65.0 ± 9.8	64.0 ± 10.5	55.6 ± 10.5	55.5 ± 14.0
Rhythm perception	61.3 ± 11.6	61.5 ± 12.8	65.5 ± 10.0	65.1 ± 10.1	55.5 ± 11.3	56.5 ± 14.3
Harmony perception	60.6 ± 12.0	61.7 ± 13.0	64.9 ± 9.9	65.0 ± 10.1	54.5 ± 12.1	57.0 ± 14.9

Comparison between the different kinds of music perception was carried out by univariate variance analysis with repeated measures and between groups by the Mann–Whitney U-test. *A significant difference ($P < 0.019$) within the different values on the right hemisphere; †a significant difference ($P < 0.037$) between the left hemispheric values of the musicians versus non-musicians; ‡a significant difference ($P < 0.026$) within the different values on the right hemisphere.

known famous radio news items in the German language consisting of four excerpts of ~30 s duration recorded in a serious male voice without a break by one of the authors (J.D.). The 'rhythm' piece was a composition of the German rock band 'Einstürzende Neubauten'. It was selected from the song 'ZNS' from the album 'Halber Mensch' (1983). This piece consists of similar but non-repetitive electronic rhythms without melodies or harmonies, with some noises and electronic effects added. The 'harmony/melody' piece (in the following text referred to as 'harmony') was the four-voice madrigal 'Praesidium sara' composed in 1568 by Orlando di Lasso (1532–1594). It is one of the characteristics of Lasso's music that the harmony modulations predominate over the rhythm. The text is in Latin and can hardly be understood. Each piece lasted ~2 min. None of the pieces was known to any of the subjects. Although a piece with language presentation is included, all pieces are termed 'music pieces' in the subsequent text.

The three pieces were pressed on a digital computer disk and presented via earphones bilaterally by a commercial CD-player (Philips CD482). Before the procedure, the order of the pieces was randomized using the shuffle function of the CD-player.

Procedure

All subjects were examined in the afternoon in a dark and air-conditioned room. They were placed lying down. After application of the headband with the bilateral Doppler ultrasound probes and the earphones, subjects were asked to rest for ~10 min and not to speak, cough or chew during the whole examination. A baseline registration with no acoustical signal was performed for 2 min and then the three periods of music were presented in random order, each presentation lasting 2 min. A break of 20 s was introduced between each item. During the whole procedure of ~10 min, the CBFV of the middle cerebral arteries was registered bilaterally and continuously. Patients did not get an acoustical feedback of the ultrasound signals. The data obtained during this procedure were analysed by our software system and then by a statistical software program (SPSS).

Data analysis

First, data were analysed for the whole presentation period of 2 min. Mean CBFV, RI and pulse rate were averaged for each of the three single periods and for the baseline period. Differences between baseline and presentation periods were analysed by *t*-test for paired samples. The lateralization, i.e. differences in mean CBFV between the right and the left middle cerebral artery, was evaluated by univariate variance analysis. The main analysis was performed as a univariate variance analysis with three factors (type of music, gender and musical experience) using repeated measures to evaluate their impact on lateralization and interaction of the factors. The mean CBVF was chosen as the dependent variable. The analysis was completed by a *post-hoc* Scheffé test of the interaction between gender and musical experience. We also performed a univariate analysis with two factors (type of music; attention to music), with the mean CBFV as the dependent variable to evaluate the influence of attention on lateralization. This analysis was also completed by a Scheffé test of the interactions between the type of music and the attention to music. The last analysis of the averaged values was performed as a univariate variance analysis with the type of music as the independent variable with repeated measures, and with RI and pulse rate as dependent variables. Direct comparison between musicians and non-musicians was performed by the Mann–Whitney *U*-test in this subanalysis.

Secondly, we analysed the dynamic changes of mean CBFV separately for both hemispheres and for musicians versus non-musicians during the presentation of the different types of music. The mean CBFV was evaluated at every second and averaged for all subjects in each subgroup. The difference between baseline and the increase or decrease of mean CBFV was calculated for every second and presented as a function of time over a period of 1 min. The mean time taken to reach the peak of mean CBFV on the dominant hemisphere, which was also the peak of the interhemispheric difference of mean CBFV, was evaluated, and a comparison between musicians and non-musicians was made by the Mann–Whitney *U*-test.

All tests were two-tailed and the significance level was set at $P = 0.05$.

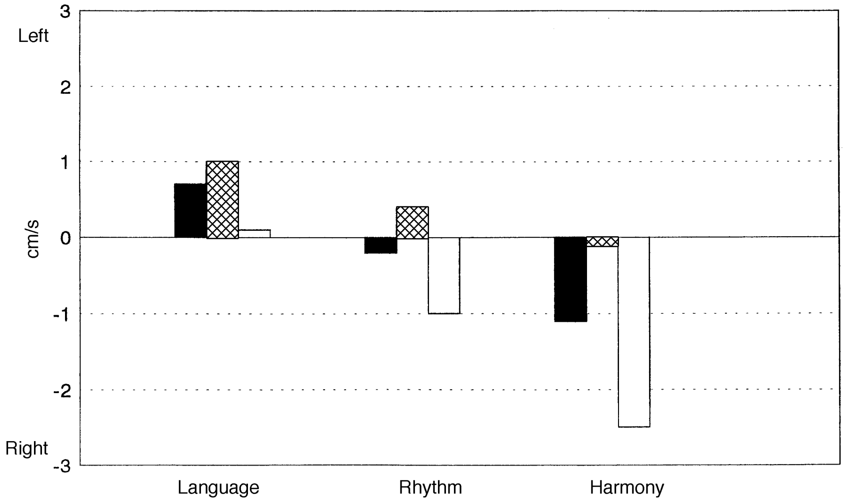

Fig. 1 Interhemispheric changes of mean CBFV in cm/s separately presented for the total subject group (black columns, $n = 24$, $P < 0.019$), musicians (cross-hatched columns, $n = 14$) and non-musicians (open columns, $n = 10$, $P < 0.026$). Statistical comparison within one group by univariate variance analysis with repeated measures (for further explanation, see text).

Results

We first tested the impact of the order of presentation on the differences in mean CBFV. All changes of mean CBVF were independent of the order of presentation of the different pieces of music in a univariate variance analysis. Therefore, the subsequent data analysis included all recordings of the 24 subjects in any one sample.

The impact of musical experience, type of music and gender on lateralization

In Table 1, the arithmetic mean CBFV (with 1 SD) of all periods is presented separately for the right versus left hemisphere, for musicians, non-musicians and the total group. The main result evident from this table is that the mean CBFV within the left hemisphere is very stable and that significant differences occur predominantly within the right hemisphere. There was a difference in mean CBFV between musicians and non-musicians of ~8–10 cm/s for all periods. For the left hemisphere, this difference was significantly greater in musicians than in non-musicians ($P < 0.037$); for the right hemisphere, the difference was not significant.

In the total subject group and in the group of non-musicians, the mean CBFV increased during harmony perception and decreased during language perception in the right hemisphere when compared with the baseline. These results are in contrast to those obtained in the left hemisphere where mean CBFV was unchanged during harmony perception and increased during language perception. The comparison with baseline revealed a significance level of $P < 0.003$ for these differences in both groups in the right hemisphere; this comparison was possible because no significant baseline differences between the right and the left hemisphere could be found in the total group ($P < 0.808$). In the univariate analysis of interhemispheric differences with the factors gender, type of music and musical experience, the increase during harmony perception and the decrease during language perception in the right hemisphere were significant for the total group ($P < 0.019$) and for the non-musicians ($P < 0.026$). The rhythm perception did not induce a significant lateralization in any group. The changes in the different subject groups are presented in Fig. 1, showing a left hemispheric lateralization for language perception in the total group and in the musicians, and a right hemispheric lateralization for harmony perception in the total group and in the non-musicians.

We performed an additional subanalysis of differences between males and females. In the interaction analysis between gender and musical experience, we obtained a significantly higher mean CBFV in the right hemisphere of female subjects when compared with males ($P < 0.026$). A *post-hoc* Scheffé test (critical value = 2.57) revealed that female non-musicians contributed most to this difference (difference = 3.45), suggesting that this subgroup has the highest degree of lateralization to the right hemisphere during music perception independent of the type of music. No further differences were observed between male and female subjects.

Attentive versus background listening

In Table 2, the arithmetic mean CBFVs (± SD) are presented separately for the attentive listeners and the background listeners. There were no significant differences in the left hemisphere measurements for music pieces when compared either with those for baseline or with those for the right hemisphere. However, the analysis of the interaction between the type of music and the type of listening in the right hemisphere revealed a significantly higher mean CBFV for harmony perception than for language perception in

Table 2 *Mean CBFV in cm/s with simple standard deviation during different periods of music perception presented separately for attentive and background listeners (for definition, see text) and for both hemispheres*

	Attentive listeners (n = 9)		Background listeners (n = 15)	
	Left	Right*	Left	Right*
Baseline	62.4 ± 11.5	62.1 ± 15.7	59.6 ± 12.0	60.2 ± 11.0
Language perception	62.6 ± 10.9	62.3 ± 16.2	60.1 ± 11.2	59.3 ± 10.1
Rhythm perception	63.2 ± 11.8	62.5 ± 15.9	60.2 ± 11.3	60.9 ± 10.5
Harmony perception	61.5 ± 13.1	62.5 ± 16.0	60.0 ± 11.3	61.2 ± 10.7

Comparison between both listener groups was carried out by univariate variance analysis with repeated measures. *A significant difference ($P < 0.049$) within the right hemisphere of attentive listeners as compared with the right hemisphere of background listeners (for explanation, see text).

background listeners ($P < 0.049$). A *post-hoc* Scheffé test (critical value = 0.86) revealed that all interactions of the background listeners contributed to this difference (all values above 1.11 except the interaction between harmony and rhythm perception with a value of 0.22). This means that in background listeners, the right hemisphere is activated more than in attentive listeners during harmony perception when compared with baseline. In addition, there was an overall trend for increased mean CBFV in attentive listeners (62.4 ± 13.9 cm/s versus 60.2 ± 11.0 cm/s; $P < 0.107$).

Time course of lateralization

The time course of lateralization was evaluated separately for musicians and non-musicians during the three different music periods. In Fig. 2, six different graphs are presented illustrating the left hemisphere lateralization of language perception in both subject groups and the right hemisphere lateralization of harmony perception in non-musicians. Musicians reached the peak of CBFV increase over baseline (in most cases identical to the peak of interhemispheric lateralization) after 5.3 ± 2.0 s (language perception), 6.9 ± 2.7 s (harmony perception) and 7.0 ± 2.4 s (rhythm perception). Non-musicians showed the respective increases after 7.2 ± 3.1 s (language perception), 14.4 ± 3.7 s (harmony perception) and 13.1 ± 4.2 s (rhythm perception). The difference between musicians and non-musicians in the time taken to reach the peak of lateralization was significant both for harmony perception ($P < 0.021$) and for rhythm perception ($P < 0.032$) as measured by the Mann–Whitney *U*-test.

RI and pulse rate changes

In Table 3, the RI values are presented as arithmetic means (± SD for all periods separately for the musicians and non-musicians. All mean values are between 1.42 and 1.46, with standard deviations ranging from 0.04 to 0.09. No significant differences could be detected. Table 4 shows the pulse rates during the different periods separately for the musicians and non-musicians. During music perception, there was a significantly lower pulse rate in the non-musicians; this difference was not significant at baseline. The low pulse rate in the group of non-musicians was influenced by the inclusion of two athletes with a resting pulse rate of ~40 beats/min. However, during harmony perception, the pulse rate decreased in the group of non-musicians and increased in the group of musicians. This difference was significant in a univariate variance analysis ($P < 0.021$). During rhythm and language perception, no significant differences could be observed between the two groups.

Discussion

On one hand, our study confirms previous findings on the cerebral dominance of music perception. On the other hand, we obtained new results adding further information on different cognitive strategies during music perception. These results will be discussed in terms of the different factors influencing the lateralization and dynamics of music perception.

Influence of musical experience, mode of listening and gender

In our total group and in the subgroup of non-musicians, we observed a significant right hemisphere lateralization during harmony perception and a significant left hemisphere lateralization during language perception. Rhythm perception did not induce any lateralization in either group. A right hemisphere lateralization for harmony perception in non-musicians was first suggested by Beaver and Chorale (1974) and then confirmed by Johnson (1977), Gordon (1978*a*), Peretz and Moraiss (1980) and Hassler (1990) using dichotic listening tests, and by Mazziotta *et al.* (1982) and Zatorre *et al.* (1992, 1994) using PET techniques. However, in the only previous TCD study on music processing (Matteis *et al.*, 1997), melody perception led to an increase of CBFV in both hemispheres. This conflicting result is most probably due to the different subject groups in the two studies. In the study by Matteis *et al.*, subjects were not selected on the

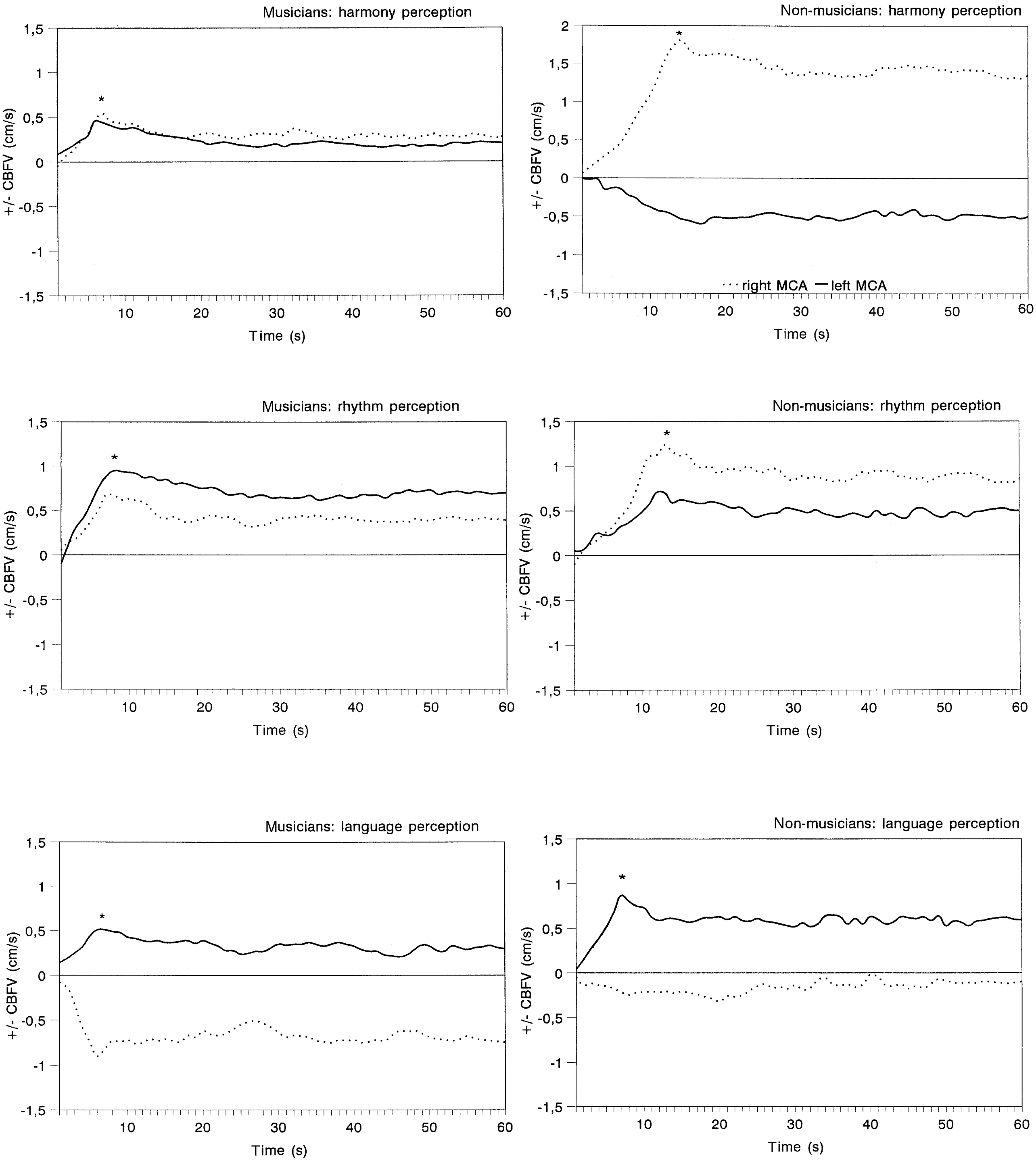

Fig. 2 The time course of mean CBFV increase or decrease presented separately for the right and the left middle cerebral artery over a period of 60 s after stimulus onset (0). Values are given as the difference from the mean baseline value (considered as 0). The asterisk (*) denotes the point at which the maximal interhemispheric difference is reached (for statistical analysis, see text). The six graphs represent musicians or non-musicians during language, harmony or rhythm perception. The dotted line = right MCA; the continuous line = left MCA.

basis of their musical training, whereas we chose strictly separated groups of musicians and non-musicians. The left hemisphere lateralization of language perception which was found in our musician subgroup has been described in several studies on fTCD (Droste *et al.*, 1989; Hartje *et al.*, 1994; Klingelhöfer *et al.*, 1994; Silvestrini *et al.*, 1994; Knecht *et al.*, 1996).

Harmony perception including melody perception (as in

Table 3 *Mean resistance index (RI) with simple standard deviation during different periods of music perception presented separately for musicians and non-musicians and for both hemispheres*

	Musicians (n = 14)		Non-musicians (n = 10)	
	Left	Right	Left	Right
Baseline	1.44 ± 0.05	1.46 ± 0.04	1.42 ± 0.07	1.44 ± 0.08
Language perception	1.44 ± 0.07	1.45 ± 0.05	1.42 ± 0.06	1.43 ± 0.09
Rhythm perception	1.44 ± 0.06	1.46 ± 0.05	1.42 ± 0.07	1.45 ± 0.08
Harmony perception	1.44 ± 0.06	1.46 ± 0.05	1.42 ± 0.08	1.44 ± 0.08

No significant differences were observed.

Table 4 *Mean pulse rate in beats per minute with simple standard deviation during different periods of music perception presented separately for musicians and non-musicians*

	Musicians (n = 14)	Non-musicians (n = 10)	Significance
Baseline	57.4 ± 7.4	48.2 ± 11.5	ns ($P < 0.052$)
Language perception	60.4 ± 11.9	48.9 ± 9.2	$P < 0.012$
Rhythm perception	59.1 ± 10.1	46.7 ± 9.9	$P < 0.014$
Harmony perception	60.7 ± 10.7*	46.0 ± 10.2*	$P < 0.004$

Comparison between musicians and non-musicians for each period was carried out by the Mann–Whitney *U*-test and comparison between differences from baseline by univariate variance analysis with repeated measures. *A significant difference ($P < 0.021$) between musicians and non-musicians in the difference from baseline (no significant difference for language or rhythm perception).

our study) comprises predominantly the timbre and pitch perception of music. For these elements, in particular for timbre discrimination, a right hemisphere advantage has been shown by different methods (Zatorre, 1979, 1992; Altenmüller, 1989; Samson and Zatorre, 1994; Platel *et al.*, 1997). We observed this lateralization in non-musicians but not in musicians, confirming previous results by Bever and Chiarello (1974), Davidson and Schwartz (1977), Johnson (1977) and Peretz and Morais (1979).

Rhythm perception did not lead to significant interhemispheric differences of CBFV but induced an increase of CBFV in both hemispheres. This finding suggests that bilateral structures are involved in the cognitive processing of rhythm perception. Rhythm might be regarded as an acoustical stimulus with both music and language or neither music nor language content. Our rhythm piece consisted of an abstract, non-repetitive rhythm. The nature of this rhythmic material might have caused the lack of lateralization. In the study of Platel *et al.* (1997), an active rhythm task was found to activate only left hemisphere structures, mainly the Broca's area. This has been interpreted in terms of inner speech and as a result of the processing and organization of sequential acoustical stimuli. Several other studies are consistent with a left hemisphere advantage in rhythm perception (Papcun *et al.*, 1974; Gordon, 1978*b*; Mavlov, 1980). However, in all these studies, the active rhythm perception such as rhythm recognition or rhythm comparison was investigated. We studied simple listening to rhythm and, therefore, conclude that this way of rhythm perception also activates right hemisphere structures. A case report on disturbed sensory rhythm processing with unimpaired active rhythm processing in a patient with right hemisphere damage is in concordance with our hypothesis (Fries and Swihart, 1990). During white noise presentation, Klingelhöfer *et al.* (1994) also found a mild bilateral increase of CBFV. This also contributes to the hypothesis that passive acoustical perception without a clear language or music content leads to a symmetrical increase of CBFV.

Lateralization differences between an 'active' (i.e. recognition, comparison, etc.) and a 'passive' mode of listening to musical stimuli were also found in another study on fTCD (Matteis *et al.*, 1997). Active processing includes activation of structures important for mnemic processing of sound material and for short-term memory; these structures are located predominantly in the left hemisphere (Sergent *et al.*, 1992; Zatorre *et al.*, 1994; Platel *et al.*, 1997). Passive listening does not involve these mnemic structures, thus leading to only a mild bilateral increase of CBFV.

This hypothesis is also in agreement with a further result of our study. Background listeners, i.e. subjects with no conscious active processing of musical elements, showed an increased right hemisphere activation during harmony perception when compared with attentive listeners, i.e. subjects who consciously analyse musical elements during listening. This finding was independent of the musical experience or education of the subjects. Attentive listeners, furthermore, showed a trend to increased baseline values of CBFV which was even significant when musicians were compared with non-musicians. Sustained attention during various stimuli processing tasks has been localized to right hemisphere structures (Pardo *et al.*, 1991). Possibly, these structures are necessary to maintain perception of uncommon acoustical stimuli such as harmony perception in non-musicians. Gaede *et al.* (1978) found similar interhemispheric differences in dichotic listening tasks and related these differences to the aptitude and not the experience of music processing. We cannot distinguish between aptitude and experience in our study. Since we did not apply a standardized test to validate the subjects' mode of listening, our findings on the differences caused by the mode of listening remain preliminary.

We found a remarkable gender difference in lateralization of music perception. Female subjects, in particular female non-musicians, showed higher CBFV values in the right hemisphere than males during music perception; this phenomenon was independent of the type of music. Gender differences in hemispheric lateralization have often been postulated, but only a few reliable findings have been reported (Annett, 1980). Droste *et al.* (1989) showed increased bilateral CBFV values for female subjects during distance estimation tasks. Findings of dichotic listening tests suggest that female subjects show higher interhemispheric differences during cognitive tasks independently of the mode of stimulation (Hassler, 1990). Gur *et al.* (1982) demonstrated, in their PET studies, significantly increased activation, in particular of the right hemisphere, during different mental tasks such as solving verbal analogies in female subjects when compared with males. Our data corroborate their assumption of generally higher lateralization effects in female subjects. However, some of the comparable studies on the lateralization of music perception did not show any significant differences between female and male subjects (Hirshkowitz *et al.*, 1978; Messerli *et al.*, 1995) or such a difference was not evaluated (Matteis *et al.*, 1997; Platel *et al.*, 1997).

Changes of reactivity index

In PET and SPECT studies during cognitive tasks, it was shown that the activation of and the subsequent increase in cerebral blood flow is due to neuronal activity in the cortex which is supplied by small resistance vessels (Formby *et al.*, 1989; Zatorre *et al.*, 1994; Platel *et al.*, 1997). On the other hand, there is strong evidence that the diameter of the large cerebral arteries remains constant during cognitive tasks (Aaslid, 1987; Kontos, 1989; Silvestrini *et al.*, 1994). However, in previous fTCD studies during cognitive tasks, evaluation of any kind of RI in order to confirm this hypothesis of dilated small resistance vessels and unimpaired large cerebral arteries was not carried out. We did not observe any changes in RI as calculated in our study (Table 3). During baseline and during all music perception periods, the RI values remained highly constant, with only small standard deviations of ~5%. This finding strongly suggests that changes of large cerebral arteries do not contribute at all to the changes of CBFV during music perception and that regional changes of cerebral blood flow in the cortex cause the increase or decrease of CBFV. We can thus confirm the findings of PET and SPECT studies by means of TCD. Of course, the lack of spatial resolution of fTCD does not allow speculation about the exact region of changes in cerebral blood flow.

Changes of pulse rate

We observed unexpected changes and differences of pulse rate during the different music periods. Although not considered a primary parameter of our study, we will discuss these changes briefly. In previous studies using fTCD during cognitive tasks, either no impact of pulse rate changes on CBFV (Kelley *et al.*, 1992; Silvestrini *et al.*, 1994) or an increased pulse rate mildly correlated to an increased CBFV (Klingelhöfer *et al.*, 1994; Matteis *et al.*, 1997) have been shown. However, different activation patterns which were demonstrated in different cerebral vessel territories monitored simultaneously strongly suggested that changes of pulse rate or blood pressure do not influence the mean CBFV (Aaslid, 1987; Kelley *et al.*, 1992).

In our study, musicians had significantly higher pulse rates than non-musicians during all periods. This difference was mainly a consequence of the inclusion of two athletes in the group of non-musicians who had a resting pulse rate of ~40 beats/min. When their data were excluded from the analysis, no significant difference between musicians and non-musicians during the different periods was observed. However, the changes in pulse rate from baseline to harmony perception are significantly different between musicians and non-musicians. Musicians showed an increased pulse rate during all music periods when compared with baseline. This is in agreement with other fTCD studies on active cognitive tasks. Non-musicians, on the other hand, show a decrease of pulse rate during rhythm and harmony perception, the latter decrease being significant when compared with musicians. This finding can be interpreted as a difference in vegetative activation during 'passive' cognitive tasks of music listening between musicians and non-musicians, meaning a better relaxation effect during passive harmony perception of unknown music in non-musicians. Cardiovascular and endocrine responses to musical perception which have been studied largely show different changes depending on the situation of the subject and the type of musical stimulus (for discussion, see Möckel *et al.*, 1994).

Dynamic aspects

By means of fTCD, it is possible to observe changes of cerebral activation within seconds. This is, apart from the easy and side effect-free mode of administration, the most relevant advantage of fTCD. We demonstrated that the peak increase or decrease of mean CBFV during all periods of music perception is reached after ~5–7 s in musicians and after ~7–14 s in non-musicians (see Fig. 2). During language perception, there was no difference between musicians and non-musicians, but during rhythm and harmony perception non-musicians showed a significantly delayed increase of right hemisphere activation when compared with musicians. The time period until maximal mean CBFV in musicians and in language perception of non-musicians is within the range found in similar studies on fTCD during cognitive tasks (Droste *et al.*, 1989; Klingelhöfer *et al.*, 1994; Rihs *et al.*, 1995; Knecht *et al.*, 1996; Aaslid, 1997). However, non-musicians seem to need more time than musicians for hemisphere lateralization during rhythm and harmony perception. It might be that an unspecific bilateral activation precedes a specific lateral cortical activation during complex acoustical perception of subjects who are not used to this kind of perception or not used to an analytical mode of listening. Conrad *et al.* (1989) found a similar result during complex visuospatial activation, with a maximal interhemispheric difference after ~11 s. Interestingly, we observed a delayed lateralization in those subjects and periods with a predominant right hemisphere lateralization. As the right hemisphere is more involved in sustained attention and preparation (Pardo *et al.*, 1991), one can conclude that non-musicians need a longer period to classify complex acoustical stimuli with musical content and to orientate their attention. Once a lateralization has been determined, however, the amount of lateralization is more pronounced in these subjects than in those with faster lateralization.

Conclusions

Music perception is a complex cognitive process involving different brain structures which is dependent on the type of musical stimulus, musical experience, mode of listening and gender. Musicians and attentive listeners, who are not necessarily identical, show a left hemisphere activation during harmony perception whereas non-musicians and background listeners show a right hemisphere activation relative to baseline. The latter phenomenon is more pronounced in female subjects. Rhythm perception does not induce specific lateralization effects. The cognitive processing leading to lateralized activation seems to be delayed in non-musicians probably due to a delayed involvement of the right hemisphere structures responsible for attentive reactions. In summary, fTCD is an appropriate method to evaluate the group-specific cerebral lateralization of activation during complex cognitive processing; it is superior to other methods in detecting short duration changes of cerebral activation. This general finding will be the basis for further studies using fTCD in order to evaluate the correlation of CBFV with cognitive tasks linked to music perception.

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