



# Brain activation during dichotic presentations of consonant-vowel and musical instrument stimuli: a $^{15}\text{O}$ -PET study<sup>1</sup>

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## Abstract

Dichotic listening means that two different stimuli are presented at the same time, one in each ear. This technique is frequently used in experimental and clinical studies as a measure of hemispheric specialization. The primary aim of the present study was to record regional changes in the distribution of cerebral blood flow (CBF) with the  $^{15}\text{O}$ -PET technique to dichotically presented consonant-vowel (CV) and musical instrument stimuli, in order to test the basic assumption of differential hemispheric involvement when stimuli presented to one ear dominate over stimuli presented in the other ear. All stimuli were 380 ms in duration with a 1000 ms interstimulus interval, and were presented in blocks of either CV-syllable or musical instrument pairs. Twelve normal healthy subjects had to press a button whenever they detected a CV-syllable or a musical instrument target in a stream of CV- and musical instrument distractor stimuli. The targets appeared equally often in the right and left ear channel. The CV-syllable and musical instrument targets activated bilateral areas in the superior temporal gyri. However, there were significant interactions with regard to asymmetry of the magnitude of peak activation in the significant activation clusters. The CV-syllables resulted in greater neural activation in the left temporal lobe while the musical instruments resulted in greater neural activation in the right temporal lobe. Within-subjects correlations between magnitude of dichotic listening and CBF asymmetry were, however, non-significant. The changes in neural activation were closely mimicked by the performance data which showed a right ear superiority in response accuracy for the CV-syllables, and a left ear superiority for the musical instruments. In addition to the temporal lobe activations, there were activation tendencies in the left inferior frontal lobe, right dorsolateral prefrontal cortex, left occipital lobe, and cerebellum. © 1999 Elsevier Science Ltd. All rights reserved.

## 1. Introduction

The aim of the present study was to compare hemisphere differences in neural activity measured indirectly by the pattern of regional cerebral blood flow (rCBF) to dichotic presentations of consonant-vowel syllables and musical instrument excerpts, using the  $^{15}\text{O}$  Oxygen Positron Emission Tomography ( $^{15}\text{O}$ -PET) technique. Dichotic listening literally means listening to two different stimuli

at the same time, one in each ear. The typical finding for phonological, or language, stimuli is superior report of the right compared to the left ear item (e.g., [1, 2]). When verbal stimuli such as consonant-vowel (CV) syllables [3] or consonant-vowel-consonant (CVC) syllables [4] are used, there is superior report from the right ear input, which is called a right ear advantage (REA). A reverse effect, that is, a left ear advantage (LEA) has been obtained to dichotically presented non-verbal stimuli, e.g., melodies [5]; also see [6]. Similarly, Bryden, Ley and Sugarman (1982) [7], used different tonal sequences as stimuli, and required the subjects to judge the affective valence of tones in different keys. The result was a left ear advantage in the majority of the subjects (cf also Messerli, Pegna and Sordet (1995) [8], studying musicians and non-musicians).

The most generally accepted explanation for the ear advantage effect in dichotic listening is the 'structural model' suggested by Kimura (1967) [9]. The structural

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model assumes that dichotic listening is related to brain asymmetry through suppression of the ipsilateral auditory pathways, and enhancement of the contralateral pathways from the ear to the primary auditory cortex (also see [10]). Since the contralateral auditory brain regions are more activated during dichotic stimulations (e.g., [11–14]), a verbal stimulus presented in the right ear would thus have direct access to processing centers in the left hemisphere, while the left ear stimulus would have to be transferred across the corpus callosum to reach the speech processing areas in the left hemisphere. Similarly, a non-verbal stimulus presented in the left ear would have direct access to right hemisphere processing.

However, dichotic listening (DL) performance data are 'silent' with regard to the underlying neural mechanisms for the ear advantage effect (cf [15]). Thus, empirical validation with other measures of brain function during linguistic and non-linguistic processing is necessary. The classic validation has been to compare DL performance with performance on the sodium-amytal, or Wada-test (see [15–17]). In the sodium-amytal test, a barbiturate is injected into either the right or left internal carotid artery, sedating one hemisphere at a time. When only one hemisphere is functioning, the researcher can test for which cognitive functions are impaired, and which remain intact. The Wada-test is, however, only performed on neurological patients, limiting its value.

Another approach to validation of the DL technique is to use measures of regional changes of cerebral blood flow during the presentation of verbal and non-verbal dichotic stimuli. The first blood flow study of dichotic stimulus presentations was performed by Coffey, Bryden, Schroering, et al., (1989) [18], who used the  $^{133}\text{Xenon}$  inhalation-technique to localize changes in cortical activation when the subject listened to tone-sequences, one in each ear. The findings showed increased activation in the right hemisphere for most LEA subjects, and a tendency for a reversed pattern of activation for the REA subjects. A limitation with the Coffey et al. (1989) [18] study is, however, that the  $^{133}\text{Xenon}$  inhalation-technique only provides average blood flow values over a period of minutes. Secondly, Coffey et al. [18] used a passive resting condition as baseline. This means that attentional and vigilance factors were not controlled for between the two conditions. In a more recent and truly pioneering study, O'Leary, Andreasen, Hurtig, Hichwa, et al. (1996 [19] also see [20]) used the  $^{15}\text{O}$ -PET technique (which has superior temporal and spatial resolution compared to the  $^{133}\text{Xenon}$  technique) when subjects listened to dichotic presentations of words, environmental sounds, and consonant–vowel–consonant (CVC) syllables. The active conditions were contrasted with two baseline conditions with tone-bursts. In the active conditions, the subjects had to indicate with a minimal motor response when they detected a 'target' stimulus that was presented an equal number of times in the right and left ear. In the baseline

condition, they responded with a similar motor response whenever they heard a tone burst. The results showed increased left temporal lobe activity to the CVCs and words, and increased right temporal lobe activity to the environmental sounds. A possible disadvantage, however, also with the O'Leary et al. (1996) study [19] is that the authors instructed their subjects to attend to either the left or right ear during the dichotic stimulus presentations. This may possibly have confounded a bottom-up, stimulus-driven, laterality effect with an instruction-driven, top-down effect. Thus, in the present data the subjects were not given any specific instructions to attend to either the right or left ear input. Instead they were told to monitor both ear inputs on all trials when trying to detect the target stimulus which was presented an equal number of times in the left and right ear.

A second potential drawback with regard to the evaluation of localization of brain activity during phonological and non-phonological stimulus presentations in the O'Leary et al. [19] study is that a rather complex stimulus structure was used also for the simple stimuli. As pointed out by Hugdahl et al. [15], words and CVCs involve semantic components in addition to phonological components. Many recent dichotic studies of laterality for phonology thus stay with the simpler CV-syllable task, with a single vowel /a/ paired with the six stop consonants /b/, /d/, /g/, /p/, /t/, /k/. Thus, we found it important to perform a PET blood flow validation study using phonologically simpler stimuli, and contrasting a hypothesized left hemisphere laterality effect for CV-syllables, with a hypothesized right hemisphere effect for musical stimuli (cf [6, 21]).

## 2. Methods

### 2.1. Subjects

Twelve right-handed male subjects between 20–30 years of age participated in the study. Handedness was checked with the Edinburgh Handedness Inventory [22]. All subjects had Danish as their native language, and the CV-syllables did not represent any real words. Informed consent was obtained according to the Declaration of Helsinki II and the study was approved by the local ethics committee of Copenhagen (KF 01-171/93).

### 2.2. Stimuli

All stimuli were digitized and presented from a PC equipped with a Creative Laboratories SoundBlaster 16 board. Stimulus presentations were controlled from software written in the MEL2 (Micro Electronic Laboratory, [23]) programming language. After digitization, the stimuli were temporally aligned for simultaneous onset in the

left and right channels with the help of a sound editing program equipped with stereo channel editing (Goldwave Software). All stimuli were aligned at the initial energy release as closely as possible (within 1–5 ms range).

Pairs of consonant-vowel (CV)-syllables and excerpts from musical instruments were presented through earphones in a dichotic listening situation. All stimuli had a duration of 380 ms, with an onset-to-onset interstimulus interval of 1000 ms (+/–200 ms). The two classes of stimuli were matched with regard to the parameters duration, intensity, and interstimulus interval. The CV-syllables were /ba/, /da/, /ka/, and the musical instrument sounds were /harpichord/, /guitar/, and /organ/. Thus, three CVs and three musical instrument excerpts were used. In addition, binaural presentations of three simple tones (800, 1200 and 1600 Hz) served as baseline conditions (repeated twice) for subtraction with the CV-syllables and musical instrument conditions.

Half the subjects had the /da/-syllable as the target; the other half of the subjects had the /ka/-syllable as target. For the musical instruments, half the subjects had the /harpichord/ as target, the other half of the subjects had the /organ/ as target. The order of presentation of the CV-syllable and musical instrument stimuli was counter-balanced across subjects, with half the subjects starting with the CV-syllable stimuli, and the other half of the subjects starting with the musical instrument stimuli.

There were 96 trials for each scan, 64 target-trials and 32 non-target trials. For half of the 64 target-trials, the target stimulus appeared in the right ear channel ( $n = 32$ ), and for the other half of the trials it appeared in the left ear channel ( $n = 32$ ). Thus the target stimulus appeared equally often in the right and in the left ear channel. The non-target and target-trials were randomly distributed across the 96 trials. There were also 96 trials for the baseline conditions.

### 2.3. PET scanning and image analysis

Positron emission tomography (PET) scans were obtained with an 18 ring GE-Advance scanner operating in 3D acquisition mode, producing 35 image slices with an interslice distance of 4.25 mm. The total axial field of view was 15.2 cm with an approximate in-plane resolution of 5 mm. The technical specifications have been described elsewhere [24]. Each subject received 12 intravenous ‘slow bolus’ injections<sup>2</sup> of 200 MBq (5.7 mCi) of  $H_2^{15}O$  over 15 s. The interscan interval was 10–12 min. A 10 min transmission scan was performed for attenu-

ation correction. Head movements were limited by head-holders constructed by thermally moulded foam. Images were reconstructed with a 4.0 mm Hanning filter transversally and a 8.5 mm Ramp filter axially. The resulting distribution images of time integrated counts were used as indirect measurements of regional neural activity [25]. Each scan had a duration of 90 s.

### 2.4. Procedure

In the active, experimental, conditions, the subjects were instructed that they would hear two different sounds, one in each ear, and that they should be attentive to both ears and press the button whenever they detected the ‘target’ sound. For each of the experimental conditions, they were also specifically instructed before each scan whether they should listen to CV-syllables or musical instruments. The order of presentation of the CV-syllable and musical instrument stimuli was counter-balanced across the subjects. In the baseline conditions, the subjects were instructed that they would hear three different tones, with ‘high’, ‘medium’, and ‘low’ pitch, and that they should press the response key whenever they heard a tone (thus no discrimination between the tones was required). The subjects also had a few test-trials for each condition before the actual stimulus presentation began. The baseline conditions were presented in the first and last PET scans, and the data for the baseline subtraction from the active conditions were the mean of the first and last scans.

Before scanning began, the earphones were put in place in the subjects’ ears. A 10 min transmission scan was performed during which time the subjects were familiarized with the different experimental conditions. The subject pressed the right or left button of a computer mouse positioned on an armrest to the right of the subject, whenever a target was detected. Finally, eyepads were placed over the subjects’ eyes to eliminate distracting light stimuli.

Each activation scan started with the listening task followed by an injection after a delay of 10 s. Data acquisition was started 25 s later, and ended after 90 s. A trial began by presenting the target stimulus 10 times with an interstimulus interval (ISI) of 1200 ms, to familiarize the subject with the target stimulus. Following a delay of 5 s, 96 dichotic stimulus pairs were then presented.

### 2.5. Data analysis

The dichotic listening accuracy scores were statistically evaluated in an analysis of variance (ANOVA), in a two Stimulus (CV-syllables vs Musical instruments)  $\times$  2 Ear (Left vs Right) factorial design. Thus, the design was a complete within-subjects design, with all subjects measured on all levels of the independent variables.

<sup>2</sup>The study involved a total of 12 scans, of which four scans are reported. The active scans that are reported in the present paper occurred first in the scan sequence. The other scans involved detecting target stimuli among simple tones, and passive listening conditions without key-pressing (which does not control for motor activity confounds).

PET image analysis was performed using Statistical Parametric Mapping software (SPM-96, MRC Cyclotron Unit, London, U.K.; [26]). All intra-subject images were aligned on a voxel-by-voxel basis using a 3-D automated six parameters rigid body transformation (AIR software; [27]), and transformed into the standard stereotactic atlas of Talairach and Tournoux (1988 [28], (via Friston et al., (1995) [29]). Before statistical analysis, the images were filtered with a 16 mm isotropic Gaussian filter to increase the signal to noise ratio and to accommodate residual variability in morphological and topographical anatomy that was not accounted for by the stereotactic normalization process. Differences in global activity were removed by proportional normalization of global brain counts to a value of 50. Areas with a statistically significant change in normalized counts (rNC) were determined using the *t*-statistic on a voxel by voxel basis. The resulting set of *t*-values constituted the statistical parametric map (SPM) [24, 30].

Planned comparisons were performed, comparing the CV-syllables and musical instruments vs baseline (see Table 1). Voxels were considered significant if their *Z*-score exceeded a threshold of  $P < 0.05$  corrected for multiple independent comparisons. This level corresponded to threshold values of  $Z > 4.71$  and  $Z > 4.59$  for the comparisons for CV-syllables and musical instruments vs baseline, respectively. The threshold values were subsequently dropped to a value of  $P < 0.001$  ( $Z > 3.09$ ) uncorrected for multiple comparisons to observe activation tendencies. These activation tendencies are commented on in the Discussion to the extent that similar activations have been found in other studies. For both sets of comparisons, single significant activation foci were found in the left and right superior temporal gyri (see the Results section). From the coordinates defined at the

peak voxels of these foci (Table 1), the regional normalized counts (rNCs) were sampled and used as raw scores in a factorial analysis of variance (ANOVA), comparing homologous areas in the left and right hemispheres. The ANOVA allowed for comparisons of hemispheric differences in brain activation to the CV-syllable and musical instrument stimuli. The rNC data were evaluated in a similar  $2 \times 2$  factorial design as the DL data.

The magnitude of the predicted ear advantage for each stimulus condition was moreover correlated with the corresponding rNC asymmetry on a within-subjects basis. This was done to evaluate the relationship between rNC change and the DL ear advantage effect. A difference score in the predicted direction was obtained for the DL data by subtracting the left ear score from the right ear score for the CV-syllables conditions, and by subtracting the right ear score from the left ear score for the musical instruments condition. Similarly, a difference score in the predicted direction was obtained for the rNC data by subtracting right hemisphere activation from left hemisphere activation for the CV-syllables condition, and left hemisphere activation from right hemisphere activation for the musical instruments conditions.

### 3. Results

#### 3.1. DL response accuracy

The ANOVA showed a significant interaction between stimulus (CVs vs musical instruments) and ear of presentation,  $F(1, 11) = 16.43$ ,  $MS_{\text{error}} = 21.09$ ,  $P = 0.002$ . Figure 1 (upper panel) shows that the interaction was due to better reports for the right ear for the CV-syllables

Table 1

Peak voxel coordinates in the *x*-, *y*-, and *z*-axis for significantly activated clusters seen in Figs 2 and 3. The quoted *P*-values were corrected for multiple independent comparisons. The coordinates are given in the standard stereotactic space (Talairach and Tournoux 1988 [28]) in mm for the maximally significant pixel in each area in the order *x*, *y*, *z*; *x* is the lateral displacement from the midline (– for the left hemisphere and + for the right hemisphere); *y* is the anterior-posterior displacement relative to the anterior commissure (AC) (– for positions posterior to the commissure); *z* is the vertical displacement relative to the AC–PC (posterior commissure) midline (– for positions inferior to the midline)

Comparison	<i>x</i>	<i>y</i>	<i>z</i>	<i>Z</i> -score	<i>P</i> -value	Anatomical localization
Consonant-vowels minus simple tones	–62	–28	8	7.45	<0.05	Left superior temporal gyrus
	64	–18	2	6.79	<0.05	Right superior temporal gyrus
	32	22	2	5.06	<0.05	Right inferior frontal gyrus
	–38	24	4	4.05	0.37	Left inferior frontal gyrus
	–30	–58	–42	4.30	0.17	Left cerebellum
Musical instruments minus simple tones	64	–24	8	5.33	<0.05	Right superior temporal gyrus
	–56	–26	6	4.55	0.07	Left superior temporal gyrus
	40	24	26	4.15	0.27	Right dorsolateral prefrontal cortex
	–22	–82	–8	4.57	0.06	Left occipital lobe
	–32	–54	–44	4.55	0.07	Left cerebellum

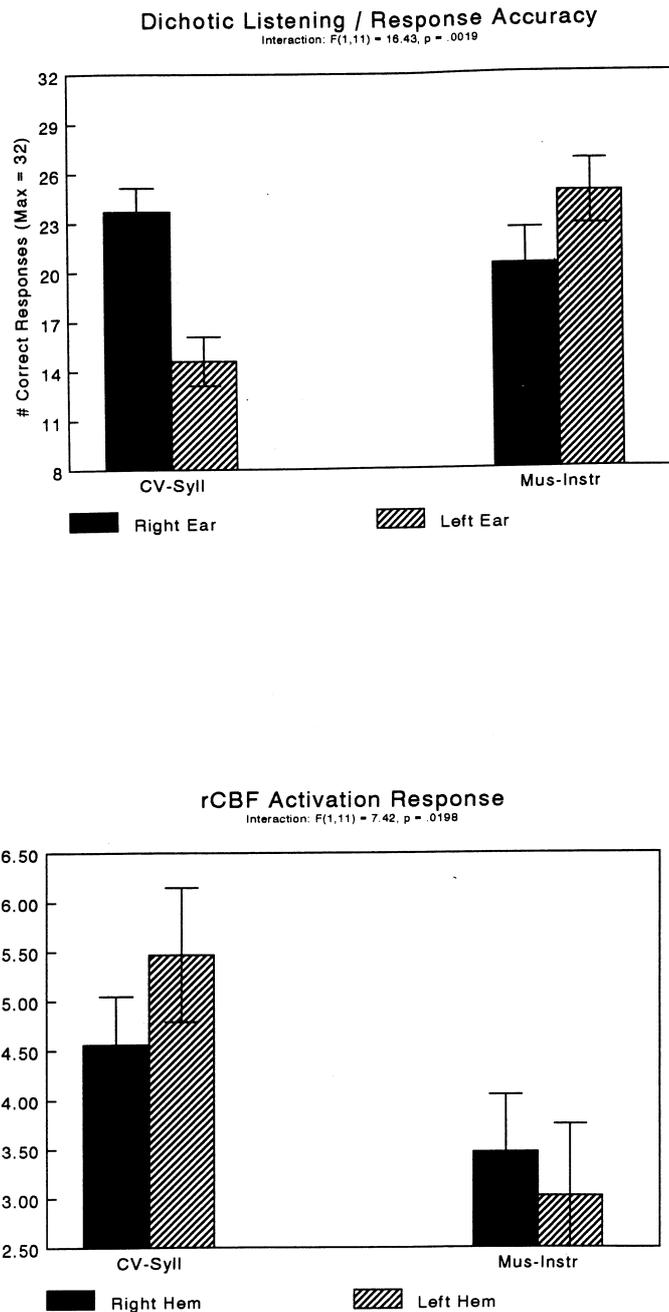


Fig. 1. Dichotic listening response accuracy scores (upper panel), and rNC activation expressed as increase in regional counts (lower panel) in the active conditions compared to the baseline conditions. CV-syll = Consonant-vowel syllables stimuli; Mus-Instr = Musical instruments stimuli. rNC values are derived from activation in the left ( $x,y,z = -62/-28/8$ ) and right ( $x,y,z = 64/-24/8$ ) superior temporal gyri.

stimuli, and better reports from the left ear for the musical instruments stimuli. This was confirmed with tests for significant simple main-effects, using Tukey's LSD-test [31], which showed a significant right ear advantage for the CV-syllables ( $P = 0.006$ ), and a significant left ear advantage for the musical instruments stimuli ( $P = 0.041$ ).

rNC changes were evaluated with the Statistical Parametric Mapping (SPM) software. Significant rNC

increases were mainly located in the posterior part of the superior temporal gyrus, shown in Fig. 2 (sagittal plane) and 3 (axial plane) plotted onto reference MRI images transformed into the Talairach space [28].

For the CV-syllables, the SPM-96 analysis showed significant rNC increases in the left and right superior temporal gyri ( $Z$ -values = 7.45 and 6.79, respectively; see Fig. 2). The corresponding Talairach and Tournoux [28] coordinates were:  $(x,y,z) = (-62, -28, 8)$ , and

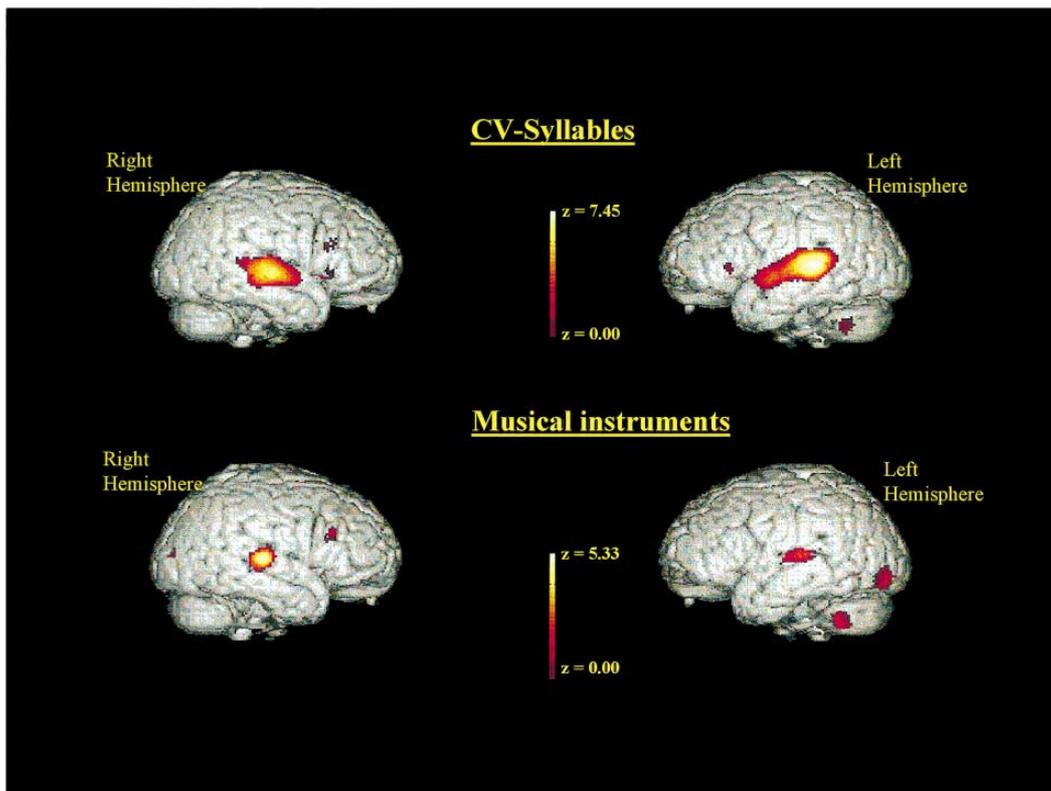


Fig. 2. Clusters of significant rNC increases in the active conditions after subtraction with the mean of the two baseline conditions. Data were transformed to Z-scores in the SPM-96 analysis software and plotted onto lateral views of an MRI-brain template. The images were thresholded at a significant level of  $P < 0.001$  ( $Z > 3.09$ ) uncorrected for multiple independent comparisons.

$(x, y, z) = (64, -18, 2)$ . The significant temporal lobe activation areas are also seen in the axial plane in Fig. 3, revealing significant activation patterns bilaterally in the posterior parts of the temporal lobes, including the primary and secondary auditory cortex (planum temporale).

In addition to the large rNC increases in the temporal lobe areas to the CV-syllables, there were also significant activations in the right inferior frontal gyrus (coordinates:  $(x, y, z) = (32, 22, 2)$ ), with a Z-value of 5.06. Activation tendencies below threshold were found in the left hemisphere where the CV-syllables activated an area in the cerebellum (coordinates:  $(x, y, z) = (-30, -58, -42)$ ), with a corresponding Z-value of 4.30 ( $P = 0.17$ ). Furthermore, activation tendencies were found in a small area in the left inferior frontal gyrus (coordinates:  $(x, y, z) = (-38, 24, 4)$ ), with a corresponding Z-value of 4.05 ( $P = 0.37$ ).

For the musical instruments, the SPM-96 analysis showed a significant rNC peak in the superior temporal gyri, with Z-value = 5.33 for the rNC increase in the right hemisphere, and Z-value = 4.55 immediately below the significance threshold ( $P = 0.07$ ) for the corresponding increase in the left hemisphere. The Talairach

and Tournoux [28] coordinates were:  $(x, y, z) = (64, -24, 8)$ , and  $(x, y, z) = (-56, -26, 6)$ , for the right and left hemispheres, respectively. As for the CV-syllables stimuli, the musical instruments also showed activation tendencies below the significance threshold in other brain areas outside the temporal lobes. As can be seen in the lower panels of Fig. 2, there was a small activation in the left occipital lobe ( $(x, y, z) = (-22, -82, -8)$ ), with a corresponding Z-value = 4.57 ( $P = 0.06$ ), and an activation focus in the right dorsolateral prefrontal cortex (DLPFC)  $(x, y, z) = (40, 24, 24)$ , with the corresponding Z-value = 4.15 ( $P = 0.27$ ). Activation tendencies were furthermore seen in the cerebellum  $(x, y, z) = (-32, -54, -44)$ , with a Z-value = 4.55 ( $P = 0.07$ ). The Talairach and Tournoux [28] coordinates that corresponded to peak activation voxels in significant clusters are summarized in Table 1.

### 3.2. PET rNC data ANOVA

The ANOVA showed a significant main effect of type of stimulus,  $F(1, 11) = 10.73$ ,  $MS_{\text{error}} = 3.48$ ,  $P = 0.007$ . As can be seen in Fig. 1 (lower panel), blood

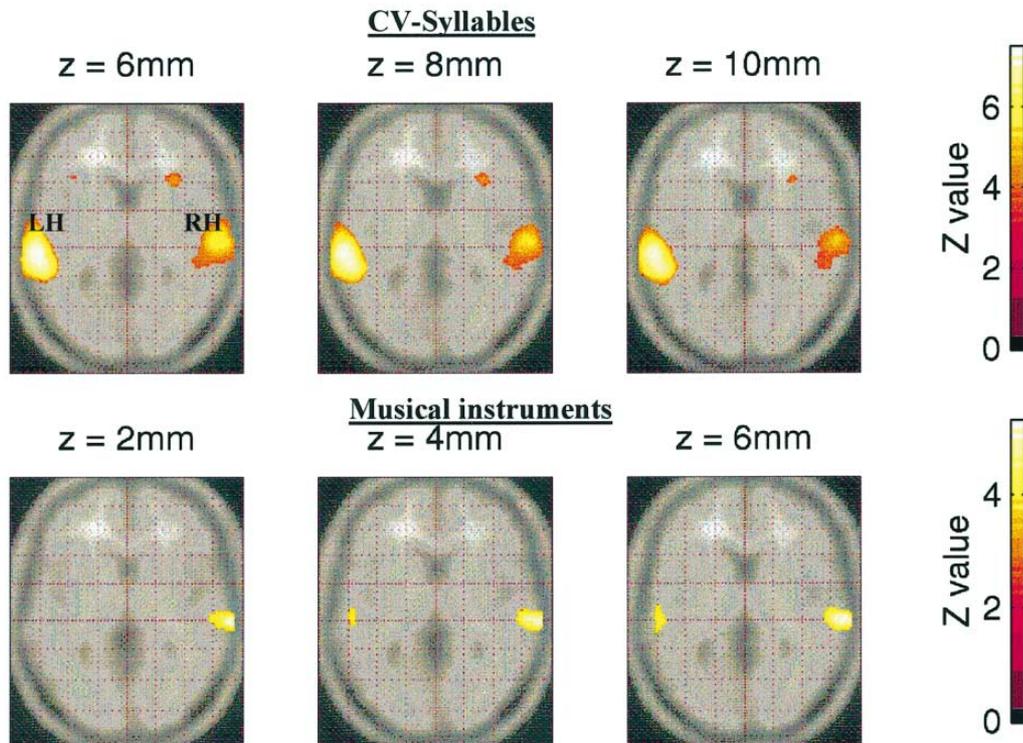


Fig. 3. Same as for Fig. 2 but data are plotted on axial plane templates in three different vertical slices 2 mm apart. The images were scaled to the maximal Z-value of the respective comparisons.

flow increased to a greater extent in both hemispheres to the CV-syllables compared to the musical instruments stimuli. However, the significant main effect was accompanied by a significant interaction between type of stimulus and hemisphere activation,  $F(1, 11) = 7.45$ ,  $MS_{\text{Error}} = 0.756$ ,  $P = 0.019$ . The significant interaction was followed-up with Tukey's LSD-test, which revealed significantly greater activation in the left compared to the right temporal lobe during the CV-syllables stimuli ( $P = 0.026$ ), with a trend for greater brain activation in the right temporal lobe areas for the musical instruments stimuli, although the test for simple main effects only showed a borderline significance ( $P < 0.10$ ) (see Fig. 1, lower panel, for means).

The within-subjects correlations between predicted magnitude of the ear advantage effect and CBF change resulted in non-significant correlations. Thus, there were no significant trends in the data with regard to the magnitude of change for either type of stimuli. The correlation

coefficients were  $r = -0.29$  and  $r = 0.01$  for the CV-syllable, and musical instrument stimuli, respectively.

#### 4. Discussion

To sum up the major findings, both the DL performance data and the PET data showed asymmetry effects of the dichotic mode of stimulus presentations. The rNC increases were in general bilateral, but with greater left hemisphere activation to the CV-syllables, and tendency for greater right hemisphere activation to the musical instruments (see Figs 2 and 3). A second characteristic was the overall greater activation to the CV-syllables compared to the musical instruments (Fig. 1). This latter observation may lend some support to the view that the auditory cortex, and particularly the planum temporale in the superior temporal gyrus is specifically tuned to phonological processing. Dyslexic

subjects, with an auditory phonological decoding deficit, have reduced, or reversed, planum temporale asymmetry [32]; also see [33]. It is, however, difficult to draw firm conclusions about absolute specialization for a brain area from the few activation conditions used in the current study. Moreover, Shaywitz et al. (1995) [34], and Fiez (1997) [35], have suggested that phonological processing also may be subserved by the inferior frontal lobe (also cf Petersen et al., 1988 [36]). As seen in Table 1 and Fig. 2, the CV-syllables in the present study activated below threshold a small area in the left inferior frontal lobe, possibly supporting the Shaywitz et al. [34] study.

In the CV-syllables condition, more correct items were reported from the right ear, with corresponding greater rNC activation in the left temporal lobe. In the musical instruments stimulus condition, more correct items were reported from the left ear, with corresponding greater rNC activation in the right temporal lobe. There was a 38% right ear advantage for the CV-syllables condition, with a corresponding 17% left hemisphere advantage in the rNC measure. For the musical instruments condition, there was a 17% left ear advantage, and a 13% right hemisphere rNC advantage. Thus, the asymmetry in regional changes in brain blood flow in response to the two types of stimuli were closely mimicked by the asymmetry in response accuracy of the stimulus items presented in the left compared to the right ear. The structural model of dichotic listening performance [9, 10], stressing the role of hemispheric specialization for the processing of verbal versus non-verbal stimuli, thus seems to be supported in the present study. Since the subjects did not receive specific instructions regarding deployment of attention, any observed asymmetry effects are most likely due to 'stimulus-driven' bottom-up processes rather than to attention-driven, top-down processes, instructing the subjects to specifically focus their attention to only one ear at a time, and to report only the items presented in that ear.

Taken together, the present rNC changes in the left and right hemispheres confirm previous lesion studies (e.g., [16, 37]) that the right ear advantage (REA) in dichotic listening to CV-syllables is related to increased neural activity in the left hemisphere, particularly temporal lobe areas. The present results also fit the findings reported by O'Leary et al. [19] that listening to CV-syllables activates the left and right superior temporal gyri asymmetrically, without disentangling the effect of attention from the effect of hemispheric specialization. The data indicate that listening to dichotically presented syllables result in greater left-sided activation, caused by a 'bottom-up' or 'stimulus-driven' asymmetry effect, since our subjects did not have specific instruction to focus attention to either side.

Figures 1 and 2 also show a right hemisphere asymmetry effect for the musical stimuli, both for response accuracy and rNC, with more correct reports from the

left ear, and increased blood flow in the right superior temporal gyrus. This is in agreement with the observations made by Messerli et al. [8] that the right hemisphere is critical for musical processing (particularly in non-musicians). The results may seem, however, somewhat at odds with the findings by O'Leary et al. [19] who observed similar activation in the left and right hemispheres to non-language stimuli, such as environmental sounds and simple tones. The difference in outcomes may, however, be due to the nature of the stimuli used in the two studies, with musical stimuli being more linked to right hemisphere processing than, e.g., simple tones. Such a view is supported by the findings by Zatorre et al. (1994) who reported greater blood flow activation in the right compared with the left anterior superior temporal gyrus when subjects listened to unfamiliar tonal melodic sequences. The tone sequences were contrasted against a baseline condition of noise bursts that were matched to the tones for total amplitude, duration, and amplitude envelope. In a second condition, subjects were required to compare two tones within a melodic sequence. Increasing the memory load in the task showed increased rNC activations in the right inferior frontal cortex, as well as increased activation in the right temporal lobe, above that observed in the passive listening task. The study by Zatorre et al. (1994) [38] is important for the evaluation of the rNC activation patterns to the musical instruments in the present study, since it indicates the importance of working memory activation in order for a right hemisphere asymmetry effect to be revealed to such stimuli. The target detection task in the present study certainly involved a strong memory load because the subjects had to keep all three musical instruments stimuli in memory in order to make the correct discrimination when the specific target instrument appeared. This suggestion is partly supported by the activation tendency in the right DLPFC.

The cerebellar activations seen to both the CV-syllables and musical instruments stimuli (see Fig. 2 and Table 1) were both below the significance threshold, arguing for caution in drawing too firm conclusions regarding the significance of these findings.

In conclusion, the CV-syllables and musical instruments stimuli primarily activated bilateral areas in the superior temporal gyri (see Figs 2 and 3). However, although the rNC activation patterns primarily were bilateral, the analysis of regional normalized counts, corresponding to the peak voxel in the respective temporal lobe activation clusters, showed significant interactions with regard to asymmetry of the magnitude and intensity of activation (see Figs 1–3). Thus, whereas the CV-syllables resulted in greater rNC increase in the left hemisphere, the musical instruments resulted in greater rNC increase in the right hemisphere. The CV-syllables, however, resulted in overall greater rNC changes than the musical instruments stimuli. The rNC changes were

closely mirrored by the performance data which showed a similar right ear advantage for the detection of the CV-syllables target stimuli, and a left ear advantage for the detection of the musical instruments target stimuli. However, the magnitude of the ear advantage difference and magnitude of rNC activation was not significantly correlated on an individual basis, suggesting a more complex, possibly non-linear, relationship between cognitive effort and neuronal activation. In addition, there were rNC activations in the inferior and medial frontal lobes (bilaterally for the CV-syllables, and in the right hemisphere for the musical instruments stimuli), and in the left occipital lobe and cerebellum. Of these activations only the right inferior frontal activation in the CV-syllables task exceeded the significance threshold corrected for multiple independent comparisons. The present study has thus confirmed previous lesion studies when attempting to validate the dichotic listening technique for the study of cerebral asymmetry, by showing asymmetry of rNC increases to different classes of stimuli that were in the same direction as the performance asymmetries. A possible limiting factor in the current study is that the baseline tones may have produced greater neuronal activation in the right, compared to the left hemisphere (cf [38]). As a consequence, using tones as a subtraction baseline condition could have reduced the CBF asymmetry to the musical stimuli, and potentiated the corresponding asymmetry to the CV-syllables. This should be sorted out in future studies.

## References

- [1] Bryden MP. Ear preference in auditory perception. *Journal of Experimental Psychology* 1963;65:103–5.
- [2] Kimura D. Cerebral dominance and the perception of verbal stimuli. *Canadian Journal of Psychology* 1961;15:166–71.
- [3] Hugdahl K, Andersson B. A dichotic listening study of differences in cerebral organization in dextral and sinistral subjects. *Cortex* 1984;20:135–41.
- [4] Studdert-Kennedy M, Shankweiler D. Hemispheric specialization for speech perception. *Journal of the Acoustical Society of America* 1970;48:579–94.
- [5] Kimura D. Left-right differences in the perception of melodies. *Quarterly Journal of Experimental Psychology* 1964;16:355–8.
- [6] Bryden MP. An overview of the dichotic listening procedure and its relation to cerebral organization. In: Hugdahl, K. editor. *Handbook of dichotic listening: theory, methods, and research*. Chichester, U.K.: Wiley & Sons, 1988. pp. 1–43.
- [7] Bryden MP, Ley RG, Sugarman JH. A left-ear advantage for identifying the emotional quality of tonal sequences. *Neuropsychologia* 1982;20:83–7.
- [8] Messerli P, Pegna A, Sordet N. Hemispheric dominance for melody recognition in musicians and non-musicians. *Neuropsychologia* 1995;33:395–405.
- [9] Kimura D. Functional asymmetry of the brain in dichotic listening. *Cortex* 1967;3:163–8.
- [10] Hugdahl K. Dichotic listening: probing temporal lobe functional integrity. In: Davidson RJ, Hugdahl K, editors. *Brain asymmetry*. Cambridge MA: MIT Press, 1995:123–156.
- [11] Maximilian VA. Cortical blood flow asymmetry during monaural verbal stimulation. *Brain and Language* 1982;15:1–11.
- [12] Connolly JF. Stability of pathway-hemispheric differences in the auditory event related potential (ERP) to monaural stimulation. *Psychophysiology* 1985;22:87–96.
- [13] Rosenzweig MR. Representations of the two ears at the auditory cortex. *American Journal of Physiology* 1951;167:147–214.
- [14] Majkowski J, Bochenek Z, Bochenek W, Knapik-Fijalkowska D, Kopec J. Latency of average evoked potentials to contralateral and ipsilateral auditory stimulation in normal subjects. *Brain Research* 1971;24:416–9.
- [15] Hugdahl K, Carlsson G, Uvebrant P, Lundervold AJ. Dichotic listening performance and intracarotid amobarbital injections in children/adolescents: Comparisons pre- and post-operatively. *Archives of Neurology* 1997;54:1494–1500.
- [16] Strauss E. Dichotic listening and sodium-amytal: Functional and morphological aspects of hemispheric asymmetry. In: Hugdahl, K. editor. *Handbook of dichotic listening: theory, methods and research*. Wiley & Sons, 1988:117–39.
- [17] Wada J, Rasmussen T. Intracarotid injections of sodium amytal for the lateralization of cerebral speech dominance. *Journal of Neurosurgery* 1960;17:266–82.
- [18] Coffey CE, Bryden MP, Schroering ES, Wilson WH, Matthew RJ. Regional cerebral blood flow correlates of a dichotic listening task. *Neuropsychiatry* 1989;1:46–52.
- [19] O'Leary D, Andreasen NC, Hurtig RR, Hichwa RD, Watkins GL, Boles Ponto LL, Rogers M, Kirchner PT. A positron emission tomography study of binaurally and dichotically presented stimuli: Effects of level of language and directed attention. *Brain and Language* 1996;53:20–39.
- [20] O'Leary DS, Andreasen NC, Hurtig RR, Kesler ML, Rogers M, Arndt S, Cizadlo T, Watkins GL, Boles Ponto LL, Kirchner PT, Hichwa RD. Auditory attentional deficits in patients with schizophrenia. *Archives of General Psychiatry* 1996;53:633–41.
- [21] Esgate A, Burton A, Burton E. Lateral advantages in same-different comparisons of two-note, dichotically presented chords to a successively-presented probe. *Neuropsychologia* 1997;35:177–82.
- [22] Oldfield RC. The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia* 1971;9:97–113.
- [23] Schneider W, Rodgers K, Maciejczyk VK, Zuccolotto A, St. James J. MEL Professional: users guide. Pittsburgh, PA: Psychology Software Tools Inc, 1995.
- [24] DeGrado TR, Turkington TG, Williams JJ, Stearns CW, Hoffman JM, Coleman RE. Performance Characteristics of a whole-body PET scanner. *Journal of Nuclear Medicine* 1994;35:1398–1406.
- [25] Fox PT, Mintun MA. Noninvasive functional brain mapping by chance-distribution analysis of averaged PET images of H<sub>2</sub><sup>15</sup>O tissue activity. *Journal of Nuclear Medicine* 1989;30:141–9.
- [26] Friston KJ. Statistical parametric mapping. In: Thatcher RW, Hallett M, Zeffiro T, Roy John, E, Huerta M., editors. *Functional neuroimaging: technical foundations*. San Diego: Academic Press, 1994:79–93.
- [27] Woods RP, Cherry SR, Mazziotta JC. Rapid automated algorithm for aligning and reslicing PET images. *Journal of Computer Assisted Tomography* 1992;16:620–33.
- [28] Talairach J, Tournoux P. Co-planar stereotaxic atlas of the human brain. 3-D proportional system: an approach to cerebral imaging. Stuttgart and New York: Georg Thieme Verlag, 1988.
- [29] Friston KJ, Ashburner J, Frith CD, Poline J, Heather JD, Frackowiak RSJ. Spatial registration and normalisation of images. *Human Brain Mapping* 1995;2:165–89.
- [30] Friston KJ, Firth CD, Liddle PF, Frackowiak RSJ. Comparing functional (PET) images: The assessment of significant change. *Journal of Cerebral Blood Flow Methods* 1991;11:690–9.

- [31] Kirk RA. editor. *Experimental design: procedures for the behavioral sciences*. Belmont, Ca: Brooks-Cole, 1968.
- [32] Larsen JL, Høien T, Lundberg I, Ødegaard H. MRI evaluation of the size and symmetry of the planum temporale in adolescents with developmental dyslexia. *Brain and Language* 1990;39:255–88.
- [33] Steinmetz H, Volkman J, Jäncke L, Freund HJ. Anatomical left-right asymmetry of language-related temporal cortex is different in left-handers. *Annals of Neurology* 1991;29:315–9.
- [34] Shaywitz B, Shaywitz S, Pugh K, Constable T, Skudlarski P, Fulbright R, Bronen R, Fletcher J, Shankweiler D, Katz L, Gore J. Sex differences in the functional organization for language. *Nature* 1995;373:607–9.
- [35] Fiez JA. Phonology, semantics, and the role of the left inferior prefrontal cortex. *Human Brain Mapping* 1997;5:79–83.
- [36] Petersen S, Fox P, Posner M, Mintun M, Raichle M. Positron emission tomographic studies of the cortical anatomy of single-word processing. *Nature* 1988;331:585–9.
- [37] Lee GP, Loring DW, Varney NR, Roberts RJ, Newell JR, Martin JA, Smith JR, King DW, Meador KJ, Murro AM. Do dichotic work listening asymmetries predict side of temporal lobe seizure onset? *Epilepsy Research* 1994;19:153–60.
- [38] Zatorre RJ, Evans AC, Meyer E. Neural mechanisms underlying melodic perception and memory for pitch. *Journal of Neuroscience* 1994;14:1908–19.