Auditory processing in the brainstem and audiovisual integration in humans studied with fMRI

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Document Version
Publisher's PDF, also known as Version of record

Publication date:
2008

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
Slabu, L. M. (2008). Auditory processing in the brainstem and audiovisual integration in humans studied with fMRI. [Thesis fully internal (DIV), University of Groningen]. [s.n.].

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Chapter 3

The effect of slice orientation on auditory fMRI at the level of the inferior colliculi

L.M. Slabu, R. Renken, J.M. Hoogduin, J.E.C.Wiersinga-Post and H. Duifhuis
Abstract

The aim of this study is to investigate the effect of slice orientation on auditory fMRI measurements in the inferior colliculi. Functional imaging at this level is complicated by heartbeat related motion and by the small size of the inferior colliculi compared with auditory cortex.

Fourteen healthy volunteers listened monaurally to modulated pink noise. BOLD contrast EPI images were acquired at a 3 T MRI system with gradient echo planar imaging, without the use of cardiac gating. Sparse sampling was used (TR = 12 s) to minimize the influence of the scanner noise. Three different slice orientations were compared: approximately parallel, at 45 degrees, and orthogonal to the brainstem.

We calculated the standard deviation, and normalized standard deviation of the residuals, mean signal intensity, effect size, median t-values and number of active voxels to quantify variability in activation between orientations at the inferior colliculi and auditory cortex level.

Our results indicate that the imaging plane at 45 degrees to the brainstem and auditory cortex has the lowest sensitivity to motion (reflected in the standard deviation and normalized standard deviation) and offers the highest spatial accuracy. The orthogonal slice orientation offers the highest effect size but with a reduced spatial specificity.

3.1. Introduction

Functional imaging of the brainstem is complicated due to heartbeat related motion, blood flow, cerebrospinal fluid movement, tissue deformation, and the small size of the auditory nuclei. In spite of a great amount of research dealing with activation of the auditory cortex (AC), limited information exists on functional imaging of the subcortical auditory pathway [Heßelmann et al., 2001]. The subcortical areas involved in auditory information processing are: the cochlear nucleus (CN), the superior olivary complex (SOC), the lateral lemniscus (LL), the inferior colliculus (IC), and the medial geniculate body (MGB). The first study that reported brainstem imaging (IC) using an auditory stimulus with fMRI was by Guimaraes et al. in 1998. They investigated the effect of cardiac gating vs. non-gating in the IC and found that it produces less signal variability while using cardiac gating [Guimaraes et al., 1998].

The IC are the major site of converging projections from both lower and higher brain centers, and are supplied by blood vessels of different shapes and size, resulting in the subject specific motion specificity. The size of the inferior colliculi is approximately 6 x 6 x 4 mm [Hawley et al., 2005].

Motion of the brainstem arises from several correlated factors, such as vasculature (arteries and veins attached to the brainstem which cause a movement with each arterial pulsation) [Marks et al., 1992], cerebrospinal fluid movement,
and tissue deformation. During the systolic (contraction) phase of the cardiac cycle, i.e. - when the vessels pulsate - the brain tissue moves in the finite cranial volume. The sudden pressure increase within the cerebral vasculature causes an intracranial pressure wave that moves along the cerebral arterial tree within a few milliseconds [Feinberg et al., 1987]. As a result, the arteries expand, first in the frontal lobe and subsequently in the more posterior parts of the brain. The force exerted on the parenchyma from the expanding vasculature leads to the expansion of the brain during systole and forces CSF down through the foramen magnum [Poncelet et al., 1992].

Feinberg et al. (1987), Poncelet et al. (1992), Enzmann et al. (1992), and Greitz et al. (1992) have demonstrated that the upper brainstem shows motion in the rostro-caudal and in the ventro-dorsal directions in the contraction phase of the heart. This pattern of oscillations differs from subject to subject due to variations architecture of the involved blood vessels [Feinenberg et al., 1987, Enzmann et al., 1991, 1992, Poncelet et al., 1992, Greitz et al. 1992]. There is a ventro-caudal motion of the lower brainstem, which precedes systolic CSF flow reversal in the aqueduct, involving the superior structures of the brainstem and hypothalamus, followed by a motion of the upper brainstem [Enzmann et al., 1992].

Reported investigations of changes in shape and motion of the brainstem used rapid imaging sequences. The brainstem moves approximately 0.5 mm with the cardiac cycle and approximately 2 mm with forced inspiration or breath holding. Motion of cerebral cortex (included the AC) with the cardiac cycle is only 10-20% of the brainstem motion [Poncelet et al., 1992, Maier et al. 1994, Cox, 1996]. Therefore, we will focus our attention only on the subcortical areas, where the motion represents a practical limit in imaging.

Figure 3.1. The movement of the brainstem in the rostro-caudal and in the ventro-dorsal planes (A) and the brainstem motion in the sagittal view (B)

One method to compensate for the brainstem motion is to use cardiac gating: image acquisitions are synchronized to the same phase of the cardiac cycle [Vlaardingerbroek and den Boer, 1996]. Guimares et al. (1998) were the first to apply this method to brainstem fMRI experiments. In later studies cardiac triggering is applied consistently in the brainstem fMRI experiments [Melcher et al., 2000, Griffiths et al., 2001, Sigalowsky et al., 2001, 2006, Harms et al., 2002,
Bakes and van Dijk, 2004, Hawley et al., 2005, Krumbholz et al., 2005, Kovacs et al. 2006, Schönwiesner et al., 2006]. In the studies made by Heßelmann et al. (2001), Yetkin et al. (2004) and Langers et al. (2005), the scanning was performed without cardiac gating. Yetkin et al. and Langers et al. scanned in coronal plane orientation. Their experiments showed consistent activation of the MGB and the IC and in a few cases activation of CN, SOC, and LL. The study of Heßelmann et al., using an axial plane orientation, only showed activation of the lower brainstem, SOC and CN.

![Image 1](image1)

**Figure 3.2. The imaging planes for the functional scan sessions: A) parallel, B) orthogonal, and C) at 45 degrees to the brainstem in the sagittal view**

The published studies on the effect of slice orientation at 3T focused on the effects of the reproducibility and the susceptibility artifacts. The first is a motor cortex study which quantifies the variability in activation between orientations (axial, oblique axial, coronal and sagittal) and between subjects [Gustard et al., 2001]. The oblique axial slice orientation offers the highest signal detection accuracy. The second study is on the orbitofrontal cortex. One of the goals of this experiment is to investigate the influence of the tilt angles of the EPI imaging on the BOLD sensitivity maps. The angles are: -45°, -30°, -25°, 0°, 5°, 30° and 45°. The results show that the 30° is a good compromise to study this region of interest [Deichmann et al., 2003]. The third experiment (at 1.5 and 3T) focuses on imaging the amygdala, where there is a pronounced susceptibility effect [Chen et al., 2003]. Based on field gradient measurements and taking the anatomic structure of the human amygdala into consideration, the pseudo-coronal plane is the preferred orientation for this anatomical region. In a previous fMRI study on the amygdala by Merboldt (2001), he proposed a coronal plane. A major difference between imaging these anatomical structures and imaging the brainstem is in the amount of movement.

Auditory neuroimaging is becoming an increasingly important area and for this to be successful requires robust and accurate methods for imaging the subcortical auditory system. In the current auditory fMRI study we investigate the effect of slice orientation on the measured activity at the level of the colliculi and auditory cortex, and ignore the possible effect of cardiac gating. During cardiac gating image acquisition is synchronized with the same heart phase of the cardiac
cycle [Vlaardingerbroeck and den Boer, 1996, Guimaraes et al., 1998]. In the present study the images acquired are not all measurements of a single phase of the cardiac cycle. Therefore, displacement of the brainstem, respectively of the IC from image to image is expected. We hypothesized that cardiac gating can be omitted if the slice orientation is chosen to minimize sensitivity to movement [see fig. 3.1]. Three different slice orientations with respect to the sagittal view were used: orthogonal to the brainstem and to the rostro-caudal direction of the brainstem motion – called orthogonal, parallel with the brainstem and perpendicular to the sagittal plane – named parallel, and at 45 degrees to the brainstem and to the previous one defined – called 45 degrees [see fig. 3.2]. We expected that the motion of the brainstem is the least reflected in the 45 degrees orientation plane. A comparison with auditory cortex was also performed, where the motion is minimal.

3.2. Materials and methods

3.2.1. Subjects and task

Fourteen subjects participated in this study that was approved by the Medical Ethical Committee Groningen. All subjects had normal hearing (hearing loss < 20 dB). Data sets from 4 out of the 14 subjects were excluded because of excessive head motion (translation > 6 mm; rotation> 4 degrees) during the long scanning session (approximately 1.5 hours). The remaining data from ten subjects (age 23 to 33; 6 females; 1 left-handed) were analyzed. The light was dimmed during the experiment and the subjects were blindfolded to reduce visual stimulation.

The stimuli consisted of dynamic ripples generated by modulation of pink noise in the temporal and spectral domain. The stimuli were delivered separately to the left and the right ears, with duration of 8 s. The ripples can be characterized by four parameters: the spectral modulation density of 1 c/o (cycle per octave), the temporal modulation frequency of 8 Hz, the modulation amplitude of 80 %, and an upward drift direction [cf. Langers et al., 2003, Langers et al., 2005].

Stimuli were generated using a computer (PC) equipped with a DA converter. The output of the DA converter was connected to the standard sound system of the MRI [cf. sec 3.2.3]. At the start of each experiment, the sound pressure level was measured with the Brul Kjaer artificial ear Type 4153 equiped with a condenser microphone (Brul Kjaer 4190) connected to a preamplifier (Brul Kjaer ZC0026). The microphone and preamplifier were connected to a Brul Kjaer Modular Precision Sound Analyzer Type 2260 through a 10 m long extension cable (Brul Kjaer AO0442). Stimuli were presented at 75 dB SPL, after a reduction of sound level (max. 31 dB) by using earplugs. Due to technical modifications of the scanner, sound was delivered at 69 dB SPL for the last 6 subjects. The subjects had to report if the stimuli were perceived in the left or right
ear. The response was recorded (all subjects attained > 90\% correct response) using an optically wired response box (fORP system; Current Designs Inc.). Stimuli were presented in pseudo random order and the numbers of right vs. left stimuli were balanced.

3.2.2. fMRI design

A sparse sampling [Hall et al., 1999] fMRI design (TR = 12s) was used, with a delay from the end of image acquisition until the beginning of the stimuli presentation of 1.5 s. The paradigm contained two stimuli (left and right), followed by a silent baseline (REST) condition [cf. Renken, 2004], resulting in a series of 60 stimuli (30 right, 30 left), and 30 REST periods (fig. 3.3).

![Figure 3.3. fMRI design](image)

*Figure 3.3. fMRI design: the acoustic stimuli (black bars), were presented between two volume acquisitions (gray bars).*

3.2.3. Data acquisition

Anatomical structures were identified using landmarks visible on the reference scan. The scanning planes intersected the CN, SOC, IC, MGB, and the AC.

Images were collected using a 3T Philips Intera scanner equipped with an 6-channel SENSE head coil. Each session included three functional scans and 3 anatomical scans each containing 41 slices oriented parallel, orthogonal and at 45 degrees to the brainstem (see fig. 3.2). The IC having the size approximately of 6 x 6 x 4 mm, usually covers 3 or 4 slices.

The functional scans consisted of $T_2^*$ weighted EPI images (TR = 12 s, TE = 20 ms, flip angle = 90°, FOV = 192 mm, matrix scan 96 x 96, matrix reconstruction 128 x 128, SENSE factor = 2.3, 41 ascending slices, 2 mm slice thickness). The phase encoding was always in the right-left direction. The scan duration was 2015 ms per volume. Total number of volumes was 90. The scan parameters for the three anatomical images were: TR = 25 ms, TE = 20 ms, flip angle = 30°, FOV = 256 mm, matrix size 256 x 256, 41 slices, 2 mm thickness, no
slice gap. The acquisition order of the 3 orientations was randomized for each subjects in each imaging session to balance the effects of in-plane susceptibility influence, fatigue and habituation.

3.2.4. Data analysis

Individual EPI time series were processed using the Statistical Parametric Mapping (SPM99, www.fil.ion.ucl.ac.uk/spm/1) software. The preprocessing steps included: realignment and motion correction using an isotropic 3-mm Gaussian kernel. Data were not normalized. After applying the general linear model, the following contrasts were made: left stimuli vs. REST and right stimuli vs. REST. The t-maps were overlaid on top of the mean – realigned EPI images after applying a threshold of $t \geq 3.21$ (corresponding to $p < 0.001$, uncorrected for multiple comparison).

By applying the threshold mentioned above, besides the activation of the IC, and AC, the significantly active voxels to left or right stimulus presentation were also: for the 45 degrees orientation plane in 5 out of 10 subjects for CN, 5/10 for SOC, and 1/10 for MGB, for the parallel orientation plane 7/10 for CN, 5/10 for SOC, and 5/10 for MGB, and for the orthogonal orientation plane in 6/10 for CN, 6/10 for SOC, and 2/10 for MGB. We focus the analysis on the IC and AC. The results of the analysis of CN and SOC are presented in chapter 4.

Four regions of interest (ROI) were defined based on the activation clusters from the left and right ear stimulation for the left and right IC using the MarsBar toolbox for SPM (http://marsbar.sourceforge.net). Furthermore, the union of the four ROIs defined above was used as an additional ROI. Specific anatomical landmarks were used to identify the location of the activation clusters of the superior and inferior colliculi, the cerebral aqueduct, the pontomesencephalic junction, the posterior commissure and the midline. Sketches from Duvernoy (1995) were used to help identify the location of this activation cluster in relation to the above-mentioned anatomical landmarks (see fig. 3.4).

To identify differences in scanning plane orientations, the data were analyzed using the parameters: mean signal intensity ($I$), number of activated voxels ($N$), effect size ($Es$), standard deviation (SD) and normalized standard deviation (NSD=$SD/I$) of the residuals (ResMS images). The residuals reflect the variance in the data that is not explained by the model and can reveal regions that are sensitive to the brainstem motion. The $I$, N, SD, and NSD were calculated on the union of the ROIs. The $Es$ and the median t-values were analyzed separately for each ROI. The data were mean-corrected, i.e. for each subject the mean of the three orientations was subtracted before the average over subjects was calculated. For a simple graphical representation of a probability distribution, we present the median and interquartile range (IQR) of the mean-corrected data. The IQR is the range

---

1 We used SPM99 because of the implemented MarsBar toolbox for defining the region of interest.
between the third and first quartiles and is a measure of statistical dispersion. This interval covers the central 50% of the data.

To determine whether the distribution differs significantly between the orientations we used the two-sample Kolmogorov-Smirnov test (KS test). Orientations are considered different if the probability, called p value, falls below 0.05 and differences are considered marginal if it is between 0.05-0.09. The significance level shows the probability to obtain a fall positive answer. KS test is a non-parametric test, easy to apply because there are no restrictions for the distribution. To demonstrate the difference between the three orientation planes, we applied the KS and also the repeated-measures ANOVA tests with the same p = 0.05, used by the statistic theory for the group analysis using the SPSS 14.00 software. The KS test for two independent samples is applied for the ordinal and continuous data. The statistic of the test is:

\[ D = \max \left| F_1(x) - F_2(x) \right|, \]

where \( F_i \) measure the cumulate frequency in the \( i \) sample. For the used KS, the number of the degrees of freedom is \( df = 9 \) and the decision of the test is independent of the volume of the two samples.

We consider the repeated-measures ANOVA test for the “orientation plane” variable with three values: 45 degrees, parallel and orthogonal, to check the equality of the dispersions. Where the three means are not equal from ANOVA, we looked at the simple contrasts to compare each pair of values: 45 degrees vs. parallel, 45 degrees vs. orthogonal and parallel vs. orthogonal.

### 3.3. Results and discussion

Figure 3.4 illustrates an example of an activation pattern of a single subject in one slice of the IC and one slice of AC using the comparison left stimuli vs. REST and right stimuli vs. REST (overlaid on top of the anatomical images) for the three orientation planes.

In table 3.1 we present the peak t-values and N for the union of the four ROIs [cf. sec 3.2.4] for the 10 subjects. The four ROIs are: left IC left stimulation, right IC left stimulation, left IC right stimulation, and right IC right stimulation. From table 3.1 we notice the inter-subjects asymmetry in peak t-values and the number of active voxels. Even though the scan planes intersect the arteries and veins at different angles and blood vessels occupy different proportions of a given voxel, the median and interquartile range of I and N did not reveal inter-orientation differences at the IC (fig. 3.5).

The comparison between the orientations revealed no significant difference for the range of the mean-corrected t-values at the IC. The t-values are proportional to Es divided by residual noise. To study both parameters separately, we investigated the SD and the NSD of the residuals and the Es (fig. 3.6). In the 45
degrees orientation, the SD and NSD have the lowest values. This indicates that the 45 degrees orientation is least sensitive to the ventro-dorsal and to the rostro-caudal motions.

Figure 3.4: fMRI activation maps of one slice of the IC (white arrows) and AC obtained by applying the contrast left stimuli vs. baseline (REST) or right stimuli vs. REST, using the three orientations overlaid on top of the anatomical images. The threshold for activation was $t \geq 3.21$ ($p < 0.001$, uncorrected for multiple comparisons).
Table 3.1. Peak t-values and the number of activated voxels (N) for the union of the four ROIs. The number of degrees of freedom is 72, $t \geq 3.21$ (corresponding to $p < 0.001$ uncorrected for multiple comparisons).

<table>
<thead>
<tr>
<th>Subjects</th>
<th>45 degrees</th>
<th>parallel</th>
<th>orthogonal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>t</td>
<td>N</td>
<td>t</td>
</tr>
<tr>
<td>1</td>
<td>5.53</td>
<td>12</td>
<td>5.25</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>-</td>
<td>3.79</td>
</tr>
<tr>
<td>3</td>
<td>4.30</td>
<td>11</td>
<td>3.33</td>
</tr>
<tr>
<td>4</td>
<td>6.10</td>
<td>25</td>
<td>6.44</td>
</tr>
<tr>
<td>5</td>
<td>3.78</td>
<td>1</td>
<td>3.74</td>
</tr>
<tr>
<td>6</td>
<td>4.05</td>
<td>4</td>
<td>4.67</td>
</tr>
<tr>
<td>7</td>
<td>3.70</td>
<td>35</td>
<td>4.38</td>
</tr>
<tr>
<td>8</td>
<td>3.94</td>
<td>5</td>
<td>4.45</td>
</tr>
<tr>
<td>9</td>
<td>3.95</td>
<td>13</td>
<td>3.54</td>
</tr>
<tr>
<td>10</td>
<td>4.53</td>
<td>3</td>
<td>3.37</td>
</tr>
<tr>
<td>Mean</td>
<td>12</td>
<td>11.8</td>
<td>21.2</td>
</tr>
</tbody>
</table>

Figure 3.5. The median and IQR of the mean-corrected intensity, mean-corrected number of activated voxels and mean-corrected t-values across subjects at the IC level.
In contrast with the results in fig. 3.6, the mean-corrected Es has the highest value in the orthogonal orientation (fig. 3.7) [see also table 3.2].

Using the KS test, we also checked if these differences are significant. The results were the same for the NSD and the Es between the different slice orientations [see table 3.2]. From table 3.2, except the conclusions marked with * and †, we can enunciate that the variables I, mean-t and N do not depend on the orientation plane; while SD and NSD are variables which depend on the orientation plane.
Table 3.2. The significance values of the KS and ANOVA tests on the mean-corrected data between the three orientation planes for the IC.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>The significance values of the test</th>
<th>45 degrees vs. parallel</th>
<th>45 degrees vs. orthogonal</th>
<th>parallel vs. orthogonal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>KS test</td>
<td>ANOVA</td>
<td>KS test</td>
<td>ANOVA</td>
</tr>
<tr>
<td>SD</td>
<td>0.085†</td>
<td>0.06†</td>
<td>0.07†</td>
<td>0.08†</td>
</tr>
<tr>
<td>NSD</td>
<td>0.005*</td>
<td>0.115</td>
<td>0.03*</td>
<td>0.02*</td>
</tr>
<tr>
<td>N</td>
<td>0.996</td>
<td>0.89</td>
<td>0.095</td>
<td>0.19</td>
</tr>
<tr>
<td>I</td>
<td>0.55</td>
<td>0.36</td>
<td>0.86</td>
<td>0.30</td>
</tr>
<tr>
<td>t-values</td>
<td>0.84</td>
<td>0.47</td>
<td>0.17</td>
<td>0.43</td>
</tr>
<tr>
<td>Es</td>
<td>0.83</td>
<td>0.41</td>
<td>0.00*</td>
<td>0.155</td>
</tr>
</tbody>
</table>

*the probability of the Kolmogorov-Smirnov Z and ANOVA statistic is significant below 0.05;
†the probability of the Kolmogorov-Smirnov Z and ANOVA statistics is marginal, between 0.05-0.09.

Because the effect sizes and t-values are the only parameters that were calculate on the union of the ROIs, for a better understanding of the data we also calculated in table 3.3 these values separately, for the left IC (IC-L)-left stimulation, IC-L -right stimulation, right IC (IC-R) -right stimulation, and IC-R-left stimulation.

For the IC, the differences between the Es for the three orientation planes were significant only for the inferior colliculus on the side controlateral to the stimulation. From figure 3.7 we can conclude that the mean-corrected Es has the highest value in the orthogonal orientation. The t-values are significantly different only for the right IC, left stimulation between 45 degrees vs. parallel and orthogonal.

Table 3.3. The significance values of the of KS test on the mean corrected data for the effect sizes for the ICL and ICR.

<table>
<thead>
<tr>
<th>Parameters at the IC-R level</th>
<th>Left Stimulation</th>
<th>Right Stimulation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>45 vs. parallel</td>
<td>45 vs. orthogonal</td>
</tr>
<tr>
<td>Es</td>
<td>0.01*</td>
<td>0.00*</td>
</tr>
<tr>
<td>t-values at the IC-R</td>
<td>0.01*</td>
<td>0.00*</td>
</tr>
<tr>
<td>t-values at the IC-L</td>
<td>0.70</td>
<td>0.33</td>
</tr>
</tbody>
</table>

*the probability of the Kolmogorov-Smirnov Z statistic is significant below 0.05.
By visual inspection of the data we observed that, using the scan plane orthogonal to the brainstem, activation occurs also in immediate vicinity of the colliculi and for the 45 degrees orientation plane the activation is laying directly on the IC [see fig. 3.8]. We used the anatomically-defined ROIs. In table 3.4 we present the number of active voxel in the exterior of the IC for the 45 degrees and orthogonal planes.

In figure 3.8 the activation of the IC is presented in one slice for the 45 degrees and orthogonal directions for the ten subjects applying the comparison left stimuli vs. baseline (REST) for subjects 1, 2, 3, 5, and 6 or right stimuli vs. baseline (REST) for subjects 4, 7, 8, 9, and 10. For an easier visualization of the IC in the 45 and orthogonal planes, we present the sagittal views. The choice between left or right stimuli vs. baseline was based on the maximal activation of orthogonal plane. The activation areas are larger in case of an orthogonal orientation to the brainstem (the probability of KS test is 0.03). The scan plane orthogonal to the brainstem is oriented perpendicular to the direction of the vessels nearby the colliculi (e.g. the vein of Galen) and expected to be less sensitive to the in-plane flow of the veins near the colliculi [Krings et al., 1999]. The parallel and 45 degrees acquisition planes were oriented more parallel to the direction of the vessels and suffer from through-plane flow. Therefore, the acquisition time to image the vessel is longer than in the 45 degrees case, making the acquisition more sensitive to vessel motion during the heart beat.

**Table 3.4. Number of activated voxels outside of the IC, \( t \geq 3.21 \) (corresponding to \( p < 0.001 \) uncorrected for multiple comparisons).**

<table>
<thead>
<tr>
<th>Subjects</th>
<th>45 degrees</th>
<th>orthogonal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9</td>
<td>16</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>20</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>18</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>24</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>7</td>
<td>27</td>
<td>9</td>
</tr>
<tr>
<td>8</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>42</td>
</tr>
</tbody>
</table>

The probability of KS test 0.03

Assuming that the maximum displacement of the brainstem in the cardiac cycle is 500 \( \mu m \), and the velocity of the brainstem is less than 2 mm/s, so the time in which the brainstem reaches the displacement is 0.25 s. Since the acquisition time per slice is approximately 50 ms and the slices were acquired in the ascending way, in the opposite direction of the IC motion, it could not mean that the same physical brain tissue is acquired twice in the same slice or that a piece of the brain tissue is completely missed. The relations between through-plane and in-plane motions between the plane orientations are:
through-plane motion for the: 45 degrees > parallel > orthogonal; 
in-plane motion for the: 45 degrees < parallel < orthogonal.

Figure 3.8. fMRI activation maps of the IC in one slice applying the comparison left stimuli vs. baseline (REST) or right stimuli vs. REST, using the imaging plane orthogonal and 45 degrees to the brainstem for the ten subjects (overlaid with mean EPI images, using a threshold for activation of $t \geq 3.21$ (corresponding to $p < 0.001$ uncorrected for multiple comparisons); left/right stimulation for the sagittal view.
In other words, the acquisition plane at 45 degrees has the highest through-plane motion and the orthogonal plane orientation has the highest in-plane motion.

To observe if there are any differences between IC and AC, a structure that moves only with approximately 0.05 - 0.1 mm [Cox, 1996], we calculated the same parameters for the AC. We can conclude from the results presented in fig. 3.9 that the SD and NSD are the lowest for the 45 degrees and highest for the orthogonal
plane. The number of active voxels are the highest using the 45 degrees orientation plane. For the E’s, the highest values are for the orthogonal plane.

KS’s and ANOVA’s revealed significant effects on the studied parameters for the AC. From table 3.5 we can conclude that the variables SD, NSD, N, I, mean-t values, and the E’s depend on the orientation plane for the AC. Checking the means for the cases when the two tests give the different results, we accept the solution in direction of our hypothesis (the orientation planes is significant) [see table 3.6].

Compared with the brainstem there is less motion at the AC level, so we expected less orientation effect for the SD and NSD [see table 3.6].

Table 3.5. The significance values of the KS and ANOVA tests on the mean-corrected data between the three orientation planes for the AC.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>45 degrees vs. parallel</th>
<th>45 degrees vs. orthogonal</th>
<th>parallel vs. orthogonal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>KS</td>
<td>ANOVA</td>
<td>KS</td>
</tr>
<tr>
<td>SD</td>
<td>0.01*</td>
<td>0.49</td>
<td>0.00*</td>
</tr>
<tr>
<td>NSD</td>
<td>0.055†</td>
<td>0.90</td>
<td>0.00*</td>
</tr>
<tr>
<td>N</td>
<td>0.1</td>
<td>0.15</td>
<td>0.00*</td>
</tr>
<tr>
<td>I</td>
<td>0.00*</td>
<td>0.01*</td>
<td>0.00*</td>
</tr>
<tr>
<td>mean t-values</td>
<td>0.57</td>
<td>0.64</td>
<td>0.03*</td>
</tr>
<tr>
<td>Es</td>
<td>0.00*</td>
<td>0.00*</td>
<td>0.00*</td>
</tr>
</tbody>
</table>

* the probability of the Kolmogorov-Smirnov Z statistic and ANOVA is significant below 0.05;
† the probability of the Kolmogorov-Smirnov Z and ANOVA statistics is marginal, between 0.05-0.09.

Table 3.6. The relational results of KS and ANOVA tests between the three orientation planes combined with the mean values for the AC and IC.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>AC</th>
<th>IC</th>
</tr>
</thead>
<tbody>
<tr>
<td>SD</td>
<td>45 degrees ≈ parallel &lt; orthogonal</td>
<td>45 degrees &lt; parallel ≈ orthogonal</td>
</tr>
<tr>
<td>NSD</td>
<td>45 degrees ≈ parallel &lt; orthogonal</td>
<td>45 degrees &lt; parallel &lt; orthogonal</td>
</tr>
<tr>
<td>N</td>
<td>45 degrees ≈ parallel &gt; orthogonal</td>
<td>45 degrees ≈ parallel ≈ orthogonal</td>
</tr>
<tr>
<td>I</td>
<td>45 degrees &lt; parallel ≈ orthogonal</td>
<td>45 degrees ≈ parallel ≈ orthogonal</td>
</tr>
<tr>
<td>mean t-values</td>
<td>45 degrees ≈ parallel &gt; orthogonal</td>
<td>45 degrees ≈ parallel ≈ orthogonal</td>
</tr>
<tr>
<td>Es</td>
<td>45 degrees &lt; parallel &lt; orthogonal</td>
<td>45 degrees ≈ parallel &lt; orthogonal</td>
</tr>
</tbody>
</table>
On the basis of the existing literature considering the motion of the brainstem vs. AC (Guimaraes et al., 1998), the percent signal intensity shows an increase for the gated AC vs. ungated, but no significant difference for the gated IC vs. ungated. We found that the Es is minimal for the 45 degrees and maximal for the orthogonal orientations plane for the AC, and no difference for the 45 degrees and parallel, and maximal for the orthogonal orientations plane for the IC.

3.4. Conclusions

Although t-values are not significantly different for the IC, the inter-orientation differences are highlighted in the SD, the NSD and Es analyses. The orthogonal slice orientation offers the highest Es, but also the highest SD and NSD. The 45 degrees slice orientation offers the lowest Es and least SD and NSD. We observed that the orientation plane at 45 degrees has the highest accuracy most probably due to the brainstem motion. If accuracy is of less importance the orthogonal direction shows the highest Es. Similarly are the conclusions for the AC which offers the highest values for the N, t-values for the 45 degrees orientation plane, and the lowest values for the SD and NSD, and I. The orthogonal plane offers the highest Es.

3.5. Acknowledgements

The authors wish to thank Anita Kuiper from Neuroimaging Center for the assistance in data acquisition.

3.6. References


Cox RW (1996) Informational notes for the Boson '96 Workshop on fMRI.


