Auditory processing in the brainstem and audiovisual integration in humans studied with fMRI
Slabu, Lavinia Mihaela

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

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.]

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the “Taverne” license. More information can be found on the University of Groningen website: https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment.

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Download date: 28-07-2024
Chapter 4

Cochlear nucleus and superior olivary complex responses using different slice orientations in auditory fMRI

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 at the lower brainstem - the cochlear nucleus and superior olivary complex. This chapter is an extension of the previous one, using the same analysis.

Fourteen healthy volunteers listened monaurally to modulated pink noise. BOLD contrast EPI images were acquired at a 3 T MRI system. Sparse sampling was used (TR = 12s) to minimize the influence of the scanner noise. Three different slice orientations were compared: approximately parallel, at 45 degrees and orthogonal to the brainstem in the sagittal view.

In this study, we present the numbers of active voxels, effect size, median t-values and mean signal intensity, standard deviation and normalized standard deviation of the residuals to quantify variability in activation between orientations for the cochlear nucleus and superior olivary nuclei.

Our results do not show differences in using three imaging planes regarding the scanning of the cochlear nucleus and superior olivary complex.

4.1. Introduction

Movement is unavoidable in living human subjects, and since the fMRI BOLD effects are relatively small (1-5% signal changes), even small motions are important [Cox, 1996]. This chapter focuses on how the different slice orientation in imaging the lower brainstem is expressed in the fMRI data. We used the same data sets and analysis as in the previous chapter on different anatomical structures - cochlear nucleus (CN) and superior olivary complex (SOC).

The CN is located in the medulla and contains three major divisions, each having a tonotopic organization: dorsal, anteroventral, and posteroventral nuclei. Ventral and dorsal CN are located at the dorsolateral surface of upper medulla, and the posterior border of cochlear nucleus complex is outlined by the foramen of Luschka. [Gebarski et al., 1993, Yetkin et al., 2004]. The SOC is located in the pons and is divided in three components: medial, lateral and the nucleus of trapezoid body. The SOC receives inputs primarily from the antero-ventral CN, and together these structures form the pathway for the horizontal location of sounds [Martin, 2003]. The size of CN is approximately 3x3x7 mm and of SOC is 2x2x5 mm [Hawley et al., 2005]. In humans, the largest nucleus of the SOC, the medial superior olive, has a rostrocaudal extent of about 2.6 mm and a dorso-ventral extent of 1.8 - 2.4 mm [Bazwinsky et al., 2003, Krumbholz et al., 2005].

Feinberg et al. (1987), Enzmann et al. (1991, 1992), Poncelet et al. (1992) and Greitz et al. (1992) described the motions of the entire brainstem in the rostrocaudal and in the ventro-dorsal directions in the contraction phase of the heart. Greitz et al. (1992) investigated the amplitude and time of the motion in 1.0 T and 1.5 T MRI scanners, using a spin-echo sequence. According to this study, the entire
brainstem moves in the ventro-caudal direction, especially due to the arterial expansion [fig. 4.1]. Caudal and ventral motions increased towards the foramen magnum and midline, as if the spinal cord pulls at the brainstem in the systolic phase of the cardiac cycle.

A more detailed study about the brainstem motion was performed by Enzmann et al. (1992) using phase-contrast cine MR pulse sequence and cardiac triggering with a 1.5 T imager. They focused on the displacement of the brain rather than the velocity, and presented the mean values from 10 healthy volunteers. Generally, the central structures showed caudal motion shortly after the systolic phase of the cardiac cycle. The caudal displacement occurs first in the cerebellar tonsil (69% of cardiac cycle), followed by displacement in the medulla, pons, midbrain and hypothalamus. The lower brainstem (medulla) has smaller amplitude in the mean-displacement compared with the upper brainstem (midbrain). The ventro-dorsal direction showed a similar cephalic progression of the motion from the medulla to the midbrain, but smaller in amplitude. The medulla (CN) moves in directions opposite to those of the pons (SOC) and the midbrain (IC) late in the systolic phase of the cardiac cycle (94% of cycle). An additional difference and “somewhat surprising” from Enzmann et al. (1992) point of view is that cerebellar tonsils and lower brainstem have an earlier caudal motion than the upper brainstem (midbrain) and hypothalamus. Based on these findings [Enzmann et al., 1992; Greitz et al., 1992], that the motion of the CN and SOC is earlier and has lower amplitude from the IC motion, we expected that these differences are reflected in the fMRI data using the three planes orientation compared with the upper brainstem.

![Figure 4.1. The direction of the forces during systole in axial (a), sagittal (b) and coronal planes (c) [Greitz et al. 1992].](image)

Our main experiment varied the imaged slice orientations with the two main directions of the brainstem motion (rostro-caudal, ventro-dorsal) and 45 degrees. We examined the resulting fMRI activation and residuals in the lower brainstem nuclei, CN and SOC.
4.2. Materials and methods

The material and methods were the same as in previous chapter [see chapter 3, section 3.2]. The three orientations used were presented in figure 4.2.

Figure 4.2. The imaging planes for the functional scan sessions in the sagittal view: A) parallel, B) orthogonal, and C) at 45 degrees to the brainstem.

4.2.1. Data analysis

Individual EPI time series were processed using the Statistical Parametric Mapping (SPM99, www.fil.ion.ucl.ac.uk/spm/) software.

A fixed-effects analysis is done to report single case studies. We applied the realignment and spatial smoothing using an isotropic 3-mm Gaussian kernel. Even after the realignment, there will be residual fluctuations in the fMRI data due to the motion, expressed in the $\varepsilon$ term in the general linear model. The general linear model is an equation that expresses the response variable $Y$ in terms of a linear combination of explained variables $X$ (design matrix) plus an error term (the residual fluctuations) [Friston et al. 1995]:

$$ Y = X\beta + \varepsilon, $$

where $\beta$ represent parameters corresponding to the explanatory variables.

The residuals reflect the variance in the data that is not explained by the model and can reveal regions that are sensitive to the brain motion, respectively brainstem motion. We calculated the standard deviation (SD) and normalized standard deviation (NSD=SD/I) of the residuals, and also consider the mean signal intensity (I), number of activated voxels (N) and effect size (Es).

The contrasts between left or right stimuli vs. REST were analyzed. 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).

The MarsBar toolbox for SPM (http://marsbar.sourceforge.net) was used to define the region of interest (ROI). Since the borders of CN and SOC were not visible on the anatomical images, the ROIs were determined on the activation
clusters and spatial extent of the nearest cluster [Friston, 1997]. Furthermore, the union of the four ROIs defined above was used as an additional ROI. 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. All data were mean-corrected, i.e. for each subject the mean of the three orientations was subtracted before the average over subjects was calculated.

We applied the KS and repeated-measures ANOVA tests on the mean-data of I, N, SD, NSD, t-values and Es to see if there are differences between the slice orientations.

4.3. Results and discussion

CN and SOC activations are presented in table 4.1, by applying the threshold of $t \geq 3.21$ (corresponding to $p < 0.001$, uncorrected for multiple comparison).

One disadvantage of this study is the low detection rate for the activation of the lower auditory brainstem nuclei. Our results show a low detection level of the activation of the CN and SOC similar to the results obtained by Langers et al. at a 1.5 T imager. Their results for the most significantly active voxels were: 1/8 for the left SOC, 6/8 for the right SOC, 0/8 for left CN, and 6/8 of right CN [Langers et al., 2005]. We used a close copy of their paradigm and also used rippled noise as stimulus [Langers et al., 2003]. The weak response in the CN and SOC may be caused by the type of the stimulus used. Furthermore, the size and morphology of these nuclei work against the detection of their activation, even if they were included in the imaged slice [Hawley et al., 2005]. Another cause could be the blood flow at this level different from the inferior colliculi (IC); changes in BOLD signal being well correlated with changes in blood flow. Measurements of the blood flow in the cat brain have revealed the highest level in the inferior colliculus (1.8 cc/gm/min) compared with the other auditory nuclei and auditory cortex [Landau et al., 1955].

Figure 4.3 and 4.4 present the median and interquartile ranges of mean-corrected I (a), N (b), t-values (c), SD (d), NSD (e), and Es (f) at the CN and SOC levels. Figure 4.3 (a, b, c, f) indicates that there are no differences between I, N, t-values, and Es for the CN.

In figure 4.4, the presented parameters indicate comparable results across slice orientations for the SOC, and no significant differences revealed between the three slice orientations.
Table 4.1. The fMRI activations (+) for the CN and SOC at p=0.001 for the 10 subjects.

<table>
<thead>
<tr>
<th>Subjects</th>
<th>45 degrees</th>
<th>coronal</th>
<th>orthogonal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CN SOC</td>
<td>CN SOC</td>
<td>CN SOC</td>
</tr>
<tr>
<td>1</td>
<td>+ +</td>
<td>+ +</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>+ +</td>
<td>+ +</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>+ +</td>
<td>+ +</td>
<td>+ +</td>
</tr>
<tr>
<td>5</td>
<td>+</td>
<td>+ +</td>
<td>+ +</td>
</tr>
<tr>
<td>6</td>
<td>+ +</td>
<td>+ +</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>+ +</td>
<td>+ +</td>
<td>+ +</td>
</tr>
<tr>
<td>8</td>
<td>+ +</td>
<td>+ +</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>+ +</td>
<td>+ +</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>+ +</td>
<td>+ +</td>
<td></td>
</tr>
</tbody>
</table>

A way to quantify this approach it is the KS and repeated-measures ANOVA tests [see chapter 3, subsection 3.2.4]. Table 4.2 presents the significance values of the tests and shows that there are no differences between the three slice orientations.

Our results indicate that the motion of the brainstem is not reflected in the fMRI data obtained with different slice orientations. The values reported in the literature for the displacement and velocity in the caudal direction of the lower and upper brainstem differ from one author to the other. Feinberg et al. (1987) states the brainstem caudal velocity as $-1.3 \pm 0.44$ mm/s and having a parabolic distribution in the ventral direction at the level of the aqueduct. Enzmann et al. (1992) describes the caudal displacement of the lower brainstem as being approximately $0.14 \pm 0.03$ mm and upper brainstem $0.16 \pm 0.02$ mm, respectively, and the peak velocities $1.5 \pm 0.02$ mm/s and $1.5 \pm 0.03$ mm/s. Söellinger et al. (2007) reports that the caudal displacement in the pons is $0.184 \pm 0.021$ mm. Poncelet et al. (1992) shows that the velocity in the midbrain is 2 mm/s caudally with parenchyma displacement not greater than 0.5 mm. The axial motion of the midbrain is subtly asymmetric in the ventro-dorsal direction. Greitz et al. (1992) obtains the maximum anterior velocities 0.3 mm/s in the postero-medial thalamus, 1.5 mm/s in the pons, and 2.3 mm/s in the medulla.
Figure 4.3. The median and interquartile range of mean-corrected $I$, $N$, $t$-values, $SD$, and NSD of the residuals, and $Es$ at the CN.
Figure 4.4. The median and interquartile range of mean-corrected I, N, t-values, SD, and NSD of the residuals, and Es at the SOC.
Table 4.2. The probability of KS and ANOVA tests on the mean corrected values for the three orientations planes for CN and SOC.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>45 degrees vs. parallel</th>
<th>45 degree vs. orthogonal</th>
<th>parallel vs. orthogonal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CN</td>
<td>SOC</td>
<td>CN</td>
</tr>
<tr>
<td>SD</td>
<td>0.13</td>
<td>0.93</td>
<td>0.76</td>
</tr>
<tr>
<td>NSD</td>
<td>0.35</td>
<td>0.425</td>
<td>0.99</td>
</tr>
<tr>
<td>N</td>
<td>0.59</td>
<td>0.25</td>
<td>0.01*</td>
</tr>
<tr>
<td>I</td>
<td>0.40</td>
<td>0.23</td>
<td>0.99</td>
</tr>
<tr>
<td>Mean t-values</td>
<td>0.86</td>
<td>0.67</td>
<td>0.95</td>
</tr>
<tr>
<td>Es</td>
<td>0.999</td>
<td>0.97</td>
<td>0.73</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.
These values are less than the one reported by Meier et al. in 1994, 2-3 mm/sec in the upper brainstem, 5-8 mm/sec in the lower brainstem in the caudal direction. For the lower brainstem a periodic displacement of 1 mm was found. The displacement for the upper brainstem was on the order of 2-3 mm for the rostro-caudal direction when a forced inspiration followed by breath holding (Valsalva maneuver) was experimented. The maximum caudal displacement for the spinal cord is 0.5 - 1 mm, with a velocity of approximately 7 mm/s [Giove et al., 2004].

In summary, the magnitude of the lower brainstem motion in the two directions differs in the literature due to the techniques used or the group/individual data presented, being in the range of 0.11 mm up to 1 mm. The difference in the data regarding the source and the amplitude of the displacement between the upper and lower brainstem remains rather unclear, further studies apparently are needed on this issue. The similarity of all previous studies is the resultant movement of the brainstem which occurred ventro-caudal, the data being presented in the rostro-caudal and ventro-dorsal directions. In our opinion, the lower brainstem, tractable by the spinal cord, has a motion with lower amplitude and earlier in time [Enzmann et al., 1992] than the upper brainstem, which has a higher freedom of motion in the supratentorial space. Our results are most consistently with Enzmann et al. (1992) and Meier et al. (1994) results, which describe the displacement of the brainstem as increasing from the medulla to the midbrain (IC). We consider that this is the main reason why we have no difference for the calculated parameters at the lower brainstem, compared with the upper brainstem. Furthermore, vessel pulsation, cerebrospinal movement, cardiac cycle, and tissue deformation produce fMRI signal variance. The areas exhibiting cardiac-related signal changes are generally proximal to the major arterial and venous structures [Dagli et al., 1999, Krings et al., 1999]. CN and SOC are nuclei that are located lower and deeper in the brainstem, especially SOC, compared to the IC, which can also explain that the motion is not highly reflected at this level and in the fMRI data.

Our main conclusion is that there are no significant difference in using different slice orientation for scanning the lower brainstem, CN and SOC.

4.4. References


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


