Localization of Broca's and Wernicke's areas with resting state fMRI

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Aims and objectives

Speech is one of the most important functions of the brain and has a profound effect on quality of life. One of the most widely used clinical applications of functional MRI (fMRI) is presurgical brain mapping of motor, sensory and cognitive functions, including speech. The language system of the brain varies in its location across healthy individuals and in many cases of brain damage may reorganize partially or completely to the contralateral hemisphere. Through individual brain mapping fMRI allows to assess a relative position of the eloquent cortex and mass lesion of the brain [1]. The usual approach to pre-surgical mapping of the eloquent cortex is task-based fMRI which involves measurement of the BOLD signal evoked by a given task or condition. However, tasks administered to patients in the scanner are difficult, uncomfortable, or lengthy even for relatively intact individuals. Therefore, fMRI often becomes unreliable and useless for presurgical planning. Resting-state fMRI (rsfMRI) is an alternative approach that has key advantages as it demands less from the participant in terms of task performance, and poses far fewer challenges or barriers to yielding valid data [2]. Thus, rsfMRI potentially might be more effective for localization of speech areas in patients than the conventional task-based fMRI, as it was already proved for the motor system pre-surgical mapping [3]. However, there were only few studies of the effectiveness of connectivity-based localization of the speech areas.

The aim of our research is to assess applicability of the rsfMRI (seed-based component analysis method) for localization of Broca’s and Wernicke’s areas in healthy right- and left-handed Russian-speaking volunteers. We chose the seed-based component analysis (SCA) method which implies the use of the individual regions of interest (ROI) in speech areas, obtained from task-based fMRI, as a seed, and therefore involves less subjective inference than the independent component analysis (ICA) method. We believe that inference from the previous studies using the SCA method may be limited since the interindividual variability was not considered: the same ROI was used for all participants [4] or was derived from the human brain atlas [5]. The left-handed population was specifically addressed since the question of validity of the rsfMRI assessment of the speech system has not been studied in left-handed yet despite of the greater variability in their functional neuroanatomy of speech than that of the right-handed [6].
Methods and materials

1. Participants

Research was carried out at the Radiology Department of Federal Center of Medicine and Rehabilitation in Moscow and was approved by the Interuniversity Ethics Committee of Moscow. Twenty right-handed (16 women and 4 men, mean age 22±2 years) and 13 left-handed (8 women and 5 men, mean age 23.7±3 years) healthy native speakers of Russian without neurological disorders were screened for the MRI contraindications and took part in the study.

2. Procedure

In the scanner participants performed two tasks: covert reading of sentences vs. letter strings for Wernicke’s area localization [7] and covert action-naming for Broca’s area localization, a task requiring participants to respond to a picture of a familiar object with a name of the typical action performed with this object (vs. passive viewing of abstract picture as a control condition) [8]. After these two tasks a resting state session (with eyes closed) was administered to all participants.

Action-naming task. Within an experimental condition block, seven familiar objects were projected onto the screen, one object per 3.24 second. Participants were instructed to covertly name an action that might be performed with the shown object. In a control condition block, abstract pictures obtained as a result of a visual transformation of the same seven objects were projected onto the screen. Participants were instructed to watch these objects passively without naming anything. Experimental and control condition blocks alternated.

Reading task. In experimental condition, 11-word Russian sentences were projected onto the screen word-by-word, one word per 0.92 second. Participants were instructed to read the sentences covertly. In the control condition, words were replaced by letter strings of matching length (each string comprised of several repetitions of one letter, i.e. "aaaa" or "pppppp"). Participants were asked to repeat covertly the presented letter three times. Experimental and control conditions alternated in blocks, 2 sentences or 22 letter strings each.

Resting state session. During the scanning participants were lying with their eyes closed. They were instructed to avoid sleep as well as any systematic intellectual activity.
3. Equipment and imaging parameters

Images were acquired using Siemens Magnetom Avanto 1.5T scanner. T1-weighted images were obtained for anatomical reference with MPR sequence (TR/TE/FA 1900/2.9/15), 176 sagittal slices 1 mm thick. Each task was performed in a separate single functional run. T2*-weighted functional images were obtained with EPI sequence (TE 50 ms, FA 90°, TR was 2520 ms for the action naming run, 3050 ms for the run of reading task, and 3560 ms for the resting state session). Functional images covered the whole brain, all slices were oriented parallel to the line connecting anterior and posterior commissures (AC/PC plane) and consisted of 64×64 isotropic voxels. There were 30 slices 3.8 mm thick in the action naming run, 30 slices 4 mm thick in the reading run, and 36 slices 3.6 mm thick in the resting state run. Homogeneity of the magnetic field (a field map) was measured separately for each functional run with a gradient echo sequence (GRE) and had the same slice prescription as the corresponding functional sequence.

4. Data analysis

Task-based functional data were analyzed using SPM12. Functional data obtained during resting state session were preprocessed with SPM12 and further analyzed using Conn v.14. Anatomic data underwent spatial normalization and segmentation into white matter (WM), gray matter (GM), and cerebrospinal fluid (CSF). Preprocessing of the functional data included the following steps: reorientation (in a way that the origin of coordinates was shifted to coincide with the anterior commissure); correction of motion artifacts and magnetic field inhomogeneities (“Realing&Unwarp” SPM procedure); spatial coregistration of functional and structural images; spatial normalization and spatial smoothing with an 8-mm FWHM Gaussian kernel. Resting state data were also slice-time corrected and bandpass filtered (0.008-0.09) to remove physiological noise. For the task-based functional data, a general linear model was further estimated, and one-sided t-contrasts of the task vs. control condition were used for localization of Broca's and Wernicke's areas.

Marsbar 0.44 was used for individual definition of ROIs. To construct a ROI corresponding to Broca's area, the activation from the action naming task in each individual participant was thresholded at p<0.05 (FWE-corrected), and restricted to the activation within the inferior frontal gyrus (IFG) (Figure 1). For the Wernicke's area ROI, the activation from the reading task in each participant was thresholded at p<0.001 (uncorrected), and spatially restricted to the rear upper portion of superior and middle temporal gyri (Figure 2).

Each ROI was used as a seed for the connectivity analysis of the resting-state data from the same participant (Figure 3). The temporal correlation between the BOLD signal in a given ROI and in all other brain voxels was computed and thresholded at r>0.4.
Voxels correlated with the Broca's area seed and located in the rear upper portion of superior and middle temporal gyri were considered as candidates for the Wernicke's area. Vice versa, voxels located in the inferior frontal gyrus and correlated with the Wernicke's area seed were considered as candidates for Broca's area.

To estimate success of speech area localization we used two parameters: 1) efficacy - presence/absence of the seed-correlated voxels in typical anatomical location of the speech area in question; 2) accuracy - percent of overlap of the locations of the speech area estimated from the resting state and task-based data; accuracy was computed according to the formula:

\[
\text{%overlap} = \frac{2 \times \text{Voverlap}}{\text{Vtask} + \text{Vconnectivity}},
\]

where Vtask - volume of task-based localization of the speech area, Vconnectivity - volume of connectivity-based localization of the speech area.
Images for this section:

**Fig. 1:** Forming ROI in Broca's area. Activation from the action-naming task is limited to the voxels in the inferior frontal gyrus.

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**Fig. 2:** Forming ROI in Wernicke's area. Activation from the reading task is limited to the voxels in the rear upper portion of superior and middle temporal gyri.

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Fig. 3: An example of seed-based component analysis. a) An Individual ROI in Wernicke’s area was used as a seed for connectivity analysis, volume that demonstrated seed-correlated activity in the inferior frontal gyrus was considered as a candidate of Broca’s area. b) An Individual ROI in Broca’s area was used as a seed in connectivity analysis, volume that demonstrated seed-correlated activity in the rear upper portion of superior and middle temporal gyri was considered as a candidate of Wernicke’s area.

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Results

In the right-handed group the Broca's area, obtained from the action-naming task, was localized in the left inferior frontal gyrus in 65% and in both inferior frontal gyri in 35% participants. In the left-handed group, the Broca's area was localized in the left hemisphere in 54% cases, in right hemisphere in 15% cases, and had bilateral localization in 27% cases (Table 1).

Table 1. Localization of individual ROI in Broca's area. Broca's area was obtained from activation of the action naming task.

<table>
<thead>
<tr>
<th>Broca's area ROI (Hemisphere)</th>
<th>Number of participants (%)</th>
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<tbody>
<tr>
<td></td>
<td>Left-handed</td>
</tr>
<tr>
<td>Left</td>
<td>7 (54%)</td>
</tr>
<tr>
<td>Right</td>
<td>2 (15%)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>4 (27%)</td>
</tr>
</tbody>
</table>

The Wernicke's area, obtained from the reading task, was localized in the left temporal lobe in 65% and 62% in the right-handed and left-handed group respectively. Wernicke's area was localized bilaterally in 35% and 38% participants in the right-handed and left-handed group respectively (Table 2).

Table 2. Localization of individual ROI in Wernicke's area. Wernicke's area was obtained from activation in the reading task.

<table>
<thead>
<tr>
<th>Wernicke's area ROI (Hemisphere)</th>
<th>Number of participants (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Right-handed</td>
</tr>
<tr>
<td>Left</td>
<td>13 (65%)</td>
</tr>
<tr>
<td>Right</td>
<td>-</td>
</tr>
<tr>
<td>Bilateral</td>
<td>7 (35%)</td>
</tr>
</tbody>
</table>

Individual ROI of each speech area was used as a seed for the connectivity analysis. Success of Broca's area localization (Figure 4) in the right-handed group was as following:
1) When, according to the task-based data, the Wernicke’s area was localized in the left hemisphere, efficacy of Broca’s area localization in the left hemisphere was 92%. The scatter of accuracy values was from 0% to 62% (mean value 22±18%). Efficacy of the Broca’s area localization in the right hemisphere was 69%. The scatter of accuracy values was 0%-30% (mean value 10±17%).

2) When, according to the task-based data, the Wernicke’s area had bilateral localization, efficacy of Broca’s area localization was 75% in the left hemisphere and 63% in the right hemisphere. Accuracy of Broca’s area localization fluctuated from 0% to 36% in the left hemisphere (mean value 12±15%) and from 0% to 14% (mean value 3±6%) in the right hemisphere.

Success of Broca’s area localization in the left-handed group was as following:

1) Efficacy of Broca’s area localization was 68% in the left hemisphere and 71% in the right hemisphere when the seed in Wernicke’s area was localized in the left hemisphere. The scatter of accuracy was 0-31% in the left hemisphere (mean value 13±17%) and 0% in the right hemisphere.

2) With the bilateral localization of the seed in Wernicke’s area, efficacy of Broca’s area detection was 33% in the left hemisphere and 50% in the right hemisphere. The value of accuracy was 0-16% in the left hemisphere (mean value 5±8%) and 0-31% in the right hemisphere (mean value 10±14%).

Success of Wernicke’s area localization (Figure 5) in the right-handed group was the following:

1) When the seed in the Broca’s area was localized in the left hemisphere, efficacy of the Wernicke’s area localization was 77% in the left hemisphere and 92% in the right hemisphere, the accuracy fluctuated from 0% to 43% in the left hemisphere (mean value 17±16%) and equaled to 5% in the right hemisphere in the only one participant.

2) With the bilateral localization of the seed in the Broca’s area, efficacy of Wernicke’s area localization in the left and right hemispheres was 86% and 57% respectively. Accuracy value fluctuated from 0% to 43% (mean value 14±16%) in the left hemisphere and from 0% to 48% in the right hemisphere (mean value 16±20%).

Success of Wernicke’s area localization in the left-handed group was the following:
1) When the seed in the Broca’s area was localized in the left hemisphere, efficacy of Wernicke’s area localization in the left and the right hemispheres was 57%. Accuracy value varied from 0% to 32% in the left hemisphere (mean value 13±14%) and was 0% in the right hemisphere in just two participants.

2) With the seed in the Broca’s area localized in the right hemisphere (two participants), efficacy of Wernicke’s area localization in the left and right hemispheres was 0% and 50% respectively. In the first participant accuracy value was 0% in both hemispheres. In the second participant accuracy was 0% and 14% in the left and right hemispheres respectively.

3) Efficacy of Wernicke’s area localization was 50% in the left hemisphere and 75% in the right hemisphere with the bilateral seed in Broca’s area. Accuracy value in the left hemisphere was 0% and fluctuated from 0% to 14% in right hemisphere (mean value 6±7%).

A between-group comparison has shown that the success of the Broca's area localization in the left hemisphere was significantly higher with a unilateral Wernicke’s area seed compared to a bilateral seed (90% vs. 54%; Fisher’s exact test F = 0.035, #<0.05). No other difference between seed lateralization or handedness groups reached statistical significance.

Discussion:

Despite of relatively high efficacy of speech areas localization, accuracy of speech areas localization was low (Figure 6). It may be accounted for by suggestion that correlated activities during rest, which form the speech network, may include not only speech areas, but accessory areas as well (for instance, activity in right inferior frontal gyrus) [4]. There are maybe also several technical reasons:

1) In our study, ROI were extracted on the basis of the same p-level statistical threshold for all participants. However, the data variance may also vary across participants depending on their effort or physiological features. An alternative approach of ROI extraction based on the minimal number of voxels may be used.

2) Correlation coefficients in SCA-based analysis were thresholded at 0.4, while changing the threshold may change the accuracy (i.e. degree of overlap with the task-based data).
3) Speech tasks vary in degree of the lateralization of the speech areas revealed in the same participants. So increasing the typical lateralization of the speech areas by using a different task may decrease the proportion of the bilateral ROIs in SCA analysis and, thus, increase the efficacy of the connectivity-based localization.
**Fig. 4:** Efficacy and accuracy of connectivity-based Broca’s area localization in both groups.

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<tbody>
<tr>
<td><strong>Efficacy</strong></td>
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</tr>
<tr>
<td>92%</td>
<td>22±18%</td>
</tr>
<tr>
<td>69%</td>
<td>10±17%</td>
</tr>
<tr>
<td>75%</td>
<td>12±15%</td>
</tr>
<tr>
<td>63%</td>
<td>3±6%</td>
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</tbody>
</table>

- a) in the left hemisphere
- b) in the right hemisphere

**Fig. 5:** Efficacy and accuracy of connectivity-based Wernicke’s area localization in both groups.

<table>
<thead>
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<tr>
<td><strong>Efficacy</strong></td>
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</tr>
<tr>
<td>77%</td>
<td>17±16%</td>
</tr>
<tr>
<td>92%</td>
<td>5%</td>
</tr>
<tr>
<td>86%</td>
<td>14±16%</td>
</tr>
<tr>
<td>57%</td>
<td>16±20%</td>
</tr>
</tbody>
</table>

- a) in the left hemisphere
- b) in the right hemisphere

- 57%  13±14%  0%
- 50%  10±14%  10±14%
**Fig. 6:** An example of overlap of task-based and connectivity-based localizations of speech areas. a) Overlap in Broca’s area. b) Overlap in Wernicke’s area.
Conclusion

1) Efficacy of Broca's area localization with the SCA method in the left hemisphere was high in both right- and left-handed groups when the seed was unilateral. With bilateral seeds, efficacy of connectivity-based Broca's area localization was significantly lower.

2) Efficacy of Wernicke's area localization was relatively high, and it requires further research.

3) Despite of relatively high efficacy of speech areas localization, the accuracy was very low, thus in this stage SCA method for rsfMRI cannot be used yet for the speech areas mapping in clinical practice.
References