Original Article

Cortical Representation of Persian Word Production: An fMRI Study

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Abstract:

Background: Neural correlates of single word reading with the use of a functional MRI (fMRI) scan have been widely studied in different languages. These study patterns of cortical activation differ in different languages. In this report we used a similar technique to study cortical activation when reading single Persian words.

Methods: The subjects were comprised of nine healthy right-handed bilingual individuals who performed three consecutive fMRI paradigms.

Results: Our study showed activation of the inferior frontal gyrus (IFG) when single Persian words were read. These results revealed that the pattern of brain activation during word production in Persian has a similar topography to that of English equivalents.

Conclusion: The paradigms selectively activate word production areas and are useful in neurological assessment of the Persian population.

Keywords: Dominant hemisphere - functional MRI - language - Persian - word production

Introduction

Integrity of the left hemispheric function in most healthy individuals is essential in language perception, processing and production. An understanding of the neural correlates of a language is important in clinical neurology as well as in understanding language disorders. Functional Magnetic Resonance Imaging (fMRI) provides a non-invasive and safe tool to study languages in different cultures.[1–3] Most studies have been completed on European languages, demonstrating a common neural substrate including an inferior frontal gyrus (IFG) in word production and word reading.[2] For example, a study of Spanish and English did not show any difference in the cortical activation in true bilinguals.[4] Another study of German and Russian languages used fMRI and ERP, with the conclusion that no substantial differences in cortical activation between these two languages existed.[5] However, there are evidences that different languages cause different patterns of activation in the cerebral cortex. For example, cerebral activation in the Chinese language is characterized by extensive activity of the neural systems, with strong left lateralization of frontal (BAs 9 and 47) and temporal (BA 37) cortices in addition to right lateralization of the visual system (BAs 17–19), parietal lobe (BA 3), and cerebellum.[6,7] This suggests that the left mid-frontal area (BA 9) coordinates and integrates the intensive visuospatial analysis demanded by logographs' square configuration and the semantic (or phonological) analysis required by the Chinese language. In support of this theory, another study compared cerebral activation during Chinese, Spanish, and English language tasks.[8] This study has shown that the Chinese language produced significantly more bilateral hemispheric activation than Spanish and English. This asymmetry was primarily due to a greater activation in the right temporoparietal region in the

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Chinese group, which suggested increased participation of this region in spoken word recognition in Mandarin-Chinese.[8]

Persian, unlike Arabic which is a Semitic language such as Hebrew, is an Indo-European language that differs from English and other Latin-based languages in many aspects. Persian consists of 29 consonants and 6 vowels. Some main differences are that Persian is written from right to left, some of the letters are attached whereas others are detached from one another, and diacritics are only used for beginning readers. Fluent Persian readers are able to read and write with no diacritic specified (Islamic Republic of Iran Academy of Persian Literature, www.persianacademy.ir). It is therefore important to delineate cortical representations of the Persian language for future neuropsychological and clinical studies. The main purpose of the present study is to demonstrate the cortical activation during Persian word reading and production in native Persian speakers using lexico-semantic tasks. To the best of our knowledge, this is the first report of an fMRI study in the Persian language.

Materials and Methods

Subjects and fMRI paradigms

A total of nine healthy right-handed bilingual male university students with an average age of 23 years (20 – 28) participated in this fMRI experiment. The study had the approval of the local Ethics Committee. All subjects were native Persian speakers with no medical problems and were fluent English speakers. Their handedness was determined using the Edinburgh Handedness Inventory.[9] Before running the fMRI examination, the subjects were provided with detailed instructions about the procedure and were allowed to practice a preliminary similar task in order to ensure their capability to perform the designed tasks.

The subjects lay supine in the scanner while looking at a semitransparent screen through a non-magnet mirror above their head. A standard one channeled quadrate head coil was used and the stimuli were projected from the other side of the curtain by a video projector using Presentation™ software.

A simple block-design paradigm was used. This consisted of six blocks (three for rest and three for activation) with a duration of 30 seconds for each block. The stimuli were presented randomly for each subject. The tasks consisted of Word Production (WP) and Reverse Word Reading (RWR) in Persian and Word Generation (WG) in English. Each WP activation block consisted of six word trials.

The stimuli in each activation block of the WP task consisted of five word trials. In each “5-second trial”, the subject was exposed to a four letter Persian word, letter by letter from right to left, in the right sequence. Each letter replaced the previous one with an inter-stimulus interval of one second. Then, the subject was required to read the four letter word silently (without any movement of the vocal organs to minimize jaw movement artifacts) during the five second interval in each trial. Throughout the rest block a neutral symbol such as an asterisk or slash was presented to the subject to subtract visual activation.

Activation blocks of RWR consist of 12 word trials. In each RWR task, "2.5-second trial", the subject was presented with a five letter Persian word while letters were presented in reverse order. They were asked to read each word silently during task presentation. The rest blocks were similar to those of the WP.

Finally in the WG test, subjects were asked to generate single English words which began with the presented letter. A single letter was shown to the subjects in the WG paradigm and subjects were instructed to formulate as many words as possible that began with this letter. There were six letters randomly selected for each activation block which lasted for a five second display. The 30 second rest block was the same as in the previous tasks.

Data acquisition and analysis

The fMRI data were obtained using a 1.5-Tesla GE® Signa scanner with a gradient echo/ Echo Planar Imaging (EPI) protocol (TE=60 ms, TR=3000 ms, flip angle=90, field of view=34cm^2, number of slices=15, slice thickness=7mm, gap=1mm and bandwidth= 62.5MHZ). A T1-weighted spin-echo sequence was used to generate high-resolution structural maps of the subject’s brain with the same dimension and orientation of the functional images. Image acquisition included fifteen contiguous axial slices, parallel to the AC-PC line according to the Talairach atlas,[10] beginning from the base of brain. All images were taken immediately after beginning the tasks.

The FMRIB Software Library (FSL) library was used for data analysis.[11]

Pre-statistical analysis

Four preprocessing stages were applied to remove motion artifacts, improve signal-to-noise ratio (SNR), and to remove drifts from raw data. These included: BET to remove non-brain tissue,[12] motion correction using MCFLIRT,[13] spatial smoothing using a Gaussian kernel of FWMH of 5 mm, and high pass temporal filtering with sigma= 45.05s.

Statistical analysis

Time-series statistical analysis was carried out using FILM pre-whitening. The corresponding BOLD-signal was characterized by "Z-stat", being a transformation of *t*-statistics, or dividing the parameter estimate by its standard error.[14] Finally, cluster-thresholding was carried out to reveal clusters that were significantly activated. Only clusters with Z-stat>1.7 (and 2.2), and cluster *P* values less than 0.05 were assumed to be significant (data were analyzed at two different threshold levels). Additionally, group analysis for each task was performed.

Image registration

Z-statistic maps (functional maps) were normalized and registered to the Talairach standard space as well as anatomical MR images, in order to show major activation foci and determine their exact location.[15] This automated intensity-based image registration was carried out using the FLIRT program.[12]

Region of interest and post-statistical analysis

Regions of interest (ROIs) were defined for each subject-task separately, using BrainMap™ databases established by probability density estimates of functional cerebral loci.[16,17] These ROIs were the major cerebral areas known for language processing. Accordingly, in our analysis for each ROI, all clusters with Z-stat>1.7 and 2.2 were selected.

Indices and other statistical analysis

The Lateralization Index (LI) was calculated by density of significantly activated voxels and mean activated voxels in ROIs instead of the whole hemisphere.[18] This equation yields LIs values between +100 (strong left hemisphere dominance) and -100 (strong right hemisphere dominance). LIs were subsequently ranked as left hemisphere language dominant (defined as LI>20), co-dominant (-20≤LI≤+20), or right hemisphere dominant (LI<-20).[19]

Assuming Broca's area as the main ROI, the Cartesian coordinates of the center of gravity of the activation volume were calculated and nominated as the epicenter of Broca's area. Mean Z-stats were calculated for each task separately and then compared. The mean of X, Y, and Z values for three Cartesian coordinates of the epicenters were compared using student *t*-test, and the corresponding Z-stat. A *P* value<0.05 was considered as a validation criteria. Finally, group analysis was performed to reveal the same activated areas among subjects for each task.

Results

All subjects participated in a pre-trial phase in order to be able to perform the task properly. The preprocessing of the data file with FSL yielded a pertinent curve for each activated voxels. The activation results confirmed the Edinburgh Handedness [mean laterality quotient was +53.3 (+35 to +80)] in all subjects who participated in the experiment.

Robust cortical activation was seen in the left IFG and peri-sylvian areas in nearly all subjects during all tasks (9 of 9 in WP and WG and 8 of 9 in RWR). Group analysis was performed and the data suggested the same activated areas for the word production process in both Persian and English (Figures 1 and 2).

Major activated areas in addition to the left IFG pars opercularis and triangularis (Brodmann's area 44 and 45) including (Table 1):

1-Left supplementary motor area (SMA) in Brodmann's area 6

2-Left middle frontal gyrus (MFG) in Brodmann's area 6

3- Paracingulate gyrus bilaterally

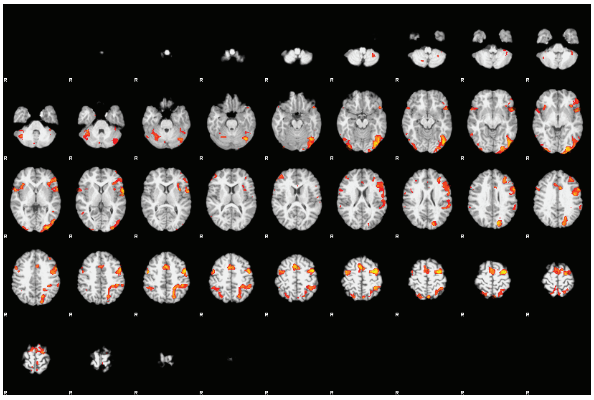
4- Left supramarginal gyrus and left superior parietal lobule

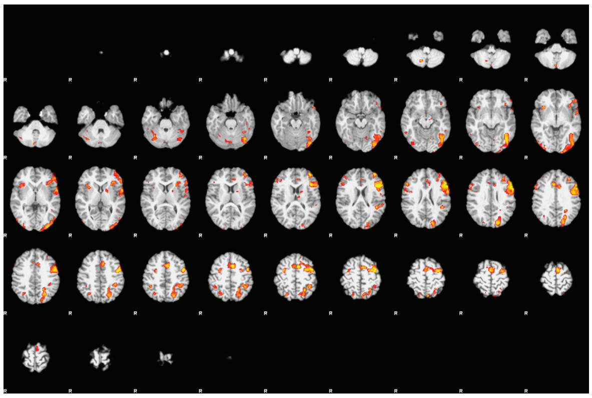
5- Lateral occipital cortex and precuneus area bilaterally

6- Left precentral gyrus

7- Left inferior temporal gyrus (ITG)

The Laterality Indices for different Z-stat were calculated. Our results demonstrated that a higher threshold would lead to higher LI.





Figures 1 and 2. Typical activations during Word Production and Word Generation tasks. Axial sections of fMRI from a single subject registered to the T1 standard space image with FSL software [WP (Figure 1) and WG (Figure 2) with analysis threshold of Z-stat>2.2]. Results show prominent activation of language related areas in the left hemisphere. Concomitant activations in other brain areas also noted in Table 1 include PMC, SMA and Broca's homologous in the right hemisphere. These images show that the same topographic areas are used for the single word production process in both Persian and English.

Table 1. Details of activated cerebral areas in all subjects. **Note that other activated regions such as scattered areas in the cerebellum and right hemisphere are also observed in some subjects. Subject number 4 shows an unexpected pattern of activation with right hemisphere dominance.** **This section should be placed under the table, not as the title.

Subject	Age	Activated area in WP with Z>1.7 (In addition to left IFG)	Broca volume (cluster size in cm^{13})	LImag (Z> 1.7)	LImag (Z> 2.2)	Activated area in RWR with Z>1.7 (In addition to left IFG)	Broca volume (cluster size in cm^{23})	LImag (Z> 1.7)	LImag (Z> 2.2)
1	22	Left PMC Left SMA Bilateral lateral occipital	84.5	+48	+55.5	Left PMC Left ITG	105	+58	+77.5
2	24	Left ITG Left PMC	32	+43.5	+48.5	Bilateral lateral occipital Left ITG	21.5	+34	+45
3	21	Right IFG Bilateral lateral occipital	35.5	+47	+41	Bilateral ITG Left PMC Prefrontal	47	+36	+53
4 *	23	Bilateral temporal Right IFG	5	-38	-40.5	Right IFG Right temporal No activation in left IFG	—	-57	-44
5	28	Bilateral lateral occipital Superior parietal lobule	33	+34.5	+36.5	Left SMA Left temporal	26.5	+29	+48
6	21	Left ITG Left SMA	20.5	+43	+49	Prefrontal Right IFG	25	+34	+40
7	20	Bilateral lateral occipital Superior parietal lobule	29	+42.5	+44	Bilateral lateral occipital	18	+38.5	+50
8	26	Left ITG Left SMA Right IFG	110	+56.5	+70	Bilateral temporal Right IFG	101	+55	+65
9	21	Left ITG Bilateral lateral occipital	68	+56	+53.5	Left PMC	74	+60	+68

The topographic epicenter of the word production area was obtained for each subject/task separately and mapped on a two-dimensional Talairach grid. The epicenters of WP activation in nine subjects and RWR in eight subjects are shown on the Talairach grid (Figure 3). As shown in this figure, the results indicate an inter-subject variation for Persian native speakers.

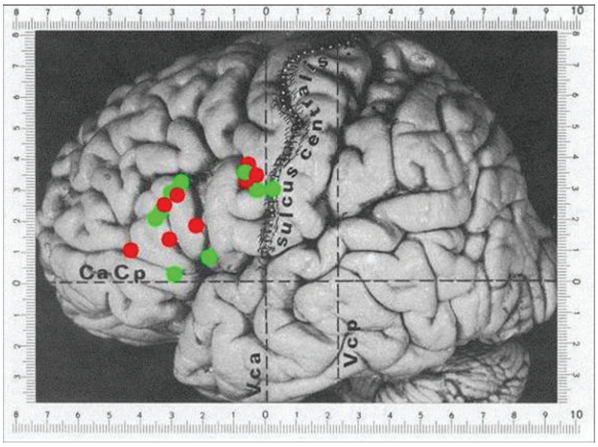


Figure 3. Scatter diagram of epicenters of activated peri-opercular regions superimposed to the standard Talairach grid (red circles for reverse word production task, and green circles for reverse word reading task). Note the distribution of the epicenters behind and in front of the fontal operculum.

Assuming Broca's area as the main ROI, the mean epicenter coordinates for WP were -44, 20, 22, RWR (-38, 22, 24), and WG (-40, 22, 22) according to the Talairach space. A comparison of the epicenters showed that both Persian tasks together with WG in English activated the same topographic areas with slightly different mean Z-stat ($P<0.05$). The analysis of Z-stats in the main ROI revealed that the Persian tasks yielded higher mean Z-stats in comparison to WG (2.70 for WP, 2.58 for RWR and 2.35 for WG). Also Persian tasks lead to higher mean LIs in comparison to English at the same Z-stat (+63, +58, and +50 for WP, RWR, and WG, respectively with Z-stat>2.2; Table 1).

Discussion

Persian, unlike Arabic which is a Semitic language such as Hebrew, is an Indo-European language that differs from English and other Latin-based languages in many aspects. Some of the main differences are that Persian is written from right to left, some letters are attached while others are detached, and diacritics are only used for beginning readers. Fluent Persian readers are able to read and write with no diacritic specified. Dissimilarities in cortical representations of different languages are probable, necessitating development of specific tasks in Persian, with satisfactory test re-test reliability. The capability of a native task for lateralization and localization of language critical areas is also vital for some surgical planning strategies.

Previous studies that examined word production in different Western languages such as English, Dutch and French suggested that the performance of a language task in different languages activates the same cerebral areas.[20] For example in German, the proposed area is the left IFG including Broca's area that might be involved in sub-lexical conversion of orthographic input strings into phonological output codes.[21] In addition, the pattern of brain activation during the WP task may be different in Eastern languages such as Chinese, in which an extensive activation of both hemispheres are seen.[7]

Our study shows that Persian language activates cerebral areas that closely resemble Western languages. Difference between Persian and English such as the requirement for more orthographic to phonologic transformation processing appears to have no significant effect on the activation of a common neural substrate but leads to higher BOLD signal in Persian tasks as assessed by Z-stat. This is supported by the observation that WP and RWR tasks in Persian and WG in English activated the left hemisphere language related areas, particularly the left IFG (Broca's area) with high intensity (Z-stat >2.2) and little inter-individual variability $P<0.05$. We propose that that in Persian the process of orthographic to phonologic transformation occurs at a sub-lexical level. Broca's area plays a critical role in this transformation, potentially by supporting effortful sub-lexical phonological analysis.[21–24] This robust transformation process leads to higher signal intensities in the left IFG during the performance of Persian tasks.

A number of potential problems may have affected our study. Simultaneous activation of multiple areas makes it rather difficult to tease apart specific areas involved in specific language processing. Inter-individual spatial variability during similar paradigms may also cause difficulties in the location of a language process.[25–29] Choice of improper tasks may also affect the occurrence of "multiple simultaneous activations".[29] This may cause ambiguity and uncertainty in the differentiation of eloquent and silent brain regions.[29–31] We employed the group analysis method to minimize simultaneous activations in this study. Moreover, the tasks implemented in this study required a high level of orthographic to phonologic transformation for the production of a single word that lead to robust activation in the left IFG. By using improved rest conditions in future studies (for example production of meaningless vs. meaningful words in WP) would possibly minimize the semantic component of the task and differentiate semantic vs. phonological processes. Also the comparison between different tasks (these paradigms with custom paradigms) allows us to understand the optimized protocol for word production in the Persian population.

Conclusion

Our study showed that Persian language activates cerebral areas similar to the English language with higher BOLD signal intensities. It is proposed that this is partly due to the fact that Persian is an Indo-European language, but the orthographic to phonologic transformation process in Persian requires more effort. More detail studies are required to analyze the neural substrate during different steps of language processing in the Persian language.

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