NeuroImage 150 (2017) 177–190

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

Cross-cultural consistency and diversity in intrinsic functional organization of Broca's Region

Yu Zhang[a,b,l], Lingzhong Fan[a], Svenja Caspers[d,f,j], Stefan Heim[d,i,j], Ming Song[a,b], Cirong Liu[g], Yin Mo[h], Simon B. Eickhoff[d,e], Katrin Amunts[d,f,j], Tianzi Jiang[a,b,c,g,k,*]

[a] *Brainnetome Center, Institute of Automation, Chinese Academy of Sciences, Beijing 100190, China*
[b] *National Laboratory of Pattern Recognition, Institute of Automation, Chinese Academy of Sciences, Beijing 100190, China*
[c] *CAS Center for Excellence in Brain Science and Intelligence technology, Institute of Automation, Chinese Academy of Sciences, Beijing 100190, China*
[d] *Institute of Neuroscience and Medicine (INM-1), Research Centre Juelich, 52425 Juelich, Germany*
[e] *Institute for Clinical Neuroscience and Medical Psychology, Heinrich-Heine-University Düsseldorf, 40225 Düsseldorf, Germany*
[f] *C. and O. Vogt Institute for Brain Research, Heinrich-Heine-University Düsseldorf, 40225 Düsseldorf, Germany*
[g] *Queensland Brain Institute, The University of Queensland, QLD 4072, Australia*
[h] *The First Affiliated Hospital of Kunming Medical University, Kunming 650032, China*
[i] *Department of Psychiatry, Psychotherapy and Psychosomatics, Medical Faculty, RWTH Aachen, 52074 Aachen, Germany*
[j] *JARA-BRAIN, Juelich-Aachen Research Alliance, 52425 Juelich, Germany*
[k] *Key Laboratory for NeuroInformation of Ministry of Education, School of Life Science and Technology, University of Electronic Science and Technology of China, Chengdu 625014, China*
[l] *Department of Neurology and Neurosurgery, McGill University, Montreal, Quebec H3A 2B4, Canada*

A R T I C L E I N F O

Keywords:
Broca's region
Resting-state
Functional connectivity
Cultural impacts
Chinese
German

A B S T R A C T

As a core language area, Broca's region was consistently activated in a variety of language studies even across different language systems. Moreover, a high degree of structural and functional heterogeneity in Broca's region has been reported in many studies. This raised the issue of how the intrinsic organization of Broca's region effects by different language experiences in light of its subdivisions. To address this question, we used multi-center resting-state fMRI data to explore the cross-cultural consistency and diversity of Broca's region in terms of its subdivisions, connectivity patterns and modularity organization in Chinese and German speakers. A consistent topological organization of the 13 subdivisions within the extended Broca's region was revealed on the basis of a new in-vivo parcellation map, which corresponded well to the previously reported receptor-architectonic map. Based on this parcellation map, consistent functional connectivity patterns and modularity organization of these subdivisions were found. Some cultural difference in the functional connectivity patterns was also found, for instance stronger connectivity in Chinese subjects between area 6v2 and the motor hand area, as well as higher correlations between area 45p and middle frontal gyrus. Our study suggests that a generally invariant organization of Broca's region, together with certain regulations of different language experiences on functional connectivity, might exists to support language processing in human brain.

Introduction

As one fundamental domain in cultural variations, language diversity has been reported in almost every linguistic aspect (Evans and Levinson, 2009; Fitch, 2011; Nettle, 1999). For instance, as a typical logographic language, Chinese maps each graphical character directly into one syllable using orthography-to-phonology transformation. Whereas, alphabetic languages like German segment each word into letters and then translate into a phonetic sequence following the grapheme-to-phoneme conversion rules (Tan et al., 2005a). Besides, Chinese has the unique characteristics of many varieties of spoken dialects assigned to the same writing systems, and using tones to distinguish between irrelevant characters. Additionally, homophones are more common in Chinese languages due to fewer distinct syllables than common written characters. The topic of how language diversity shapes the brain has attracted numerous researchers to study the underlying neural basis of language (Berwick et al., 2013; Friederici, 2011; Gomez et al., 2014; Musso et al., 2003; Nakamura et al., 2012). It has been widely reported that different language experiences were associated with various brain activations during processing of language

* Corresponding author at: Brainnetome Center, National Laboratory of Pattern Recognition, Institute of Automation, Chinese Academy of Sciences, Beijing 100190, China.
E-mail address: jiangtz@nlpr.ia.ac.cn (T. Jiang).

http://dx.doi.org/10.1016/j.neuroimage.2017.02.042
Received 21 October 2015; Accepted 15 February 2017
Available online 16 February 2017

(Paulesu et al., 2000; Tan et al., 2005a; Wu et al., 2012) and perception (Tan et al., 2008; Xue et al., 2006), diverse structural basis for dyslexia (Jednorog et al., 2015; Paulesu et al., 2001; Siok et al., 2008; Siok et al., 2004), as well as other distinct cognitive abilities (Salillas and Carreiras, 2014; Zhu et al., 2007). However, despite these cultural influences on brain mapping, a common language brain network has been revealed (Bolger et al., 2005; Paulesu et al., 2000; Tomasi and Volkow, 2012). As a core language region, Broca's region is involved in language processing across a variety of studies, for instance, during learning of new languages in both infants and adults (Dehaene-Lambertz et al., 2002, 2006; Gomez et al., 2014; Musso et al., 2003), and performing various language tasks across linguistic domains (Bolger et al., 2005; Price, 2012; Tan et al., 2005a). A consistent activation pattern in Broca's region has also been discovered for the processing of differential language systems, such as signed and spoken languages (Campbell et al., 2008; Neville et al., 1998; Soderfeldt et al., 1997), as well as native and second languages (Clahsen and Felser, 2006; Illes et al., 1999; Perani and Abutalebi, 2005). This study aimed to reveal the cross-cultural consistency in the intrinsic organizational principles of Broca's region as well as the characteristics of neural plasticity in terms of different language experiences.

However, talking of “Broca's region” disregards the fact that it is a heterogeneous region in many respects. Its intrinsic architecture has been studied using histological anatomy, whereby the subdivisions were distinguished by significant changes in laminar patterns of cell bodies (cytoarchitecture) (Amunts et al., 1999; Brodmann, 1909) or in distributions of transmitter receptors (receptor architecture) (Amunts et al., 2010). More recently, neuroimaging studies have also revealed the non-homogeneity of Broca's region by showing different activations of its subregions in various language tasks, for instance area 44 v was involved in syntax processing while the inferior frontal sulcus was associated with working memory (Clos et al., 2013; Makuuchi et al., 2009). Distinct anatomical (Anwander et al., 2007; Neubert et al., 2014) and functional connectivity profiles (Goulas et al., 2012; Klein et al., 2007) of the subdivisions in Broca's region have also been reported, for instance the engagement of area 44 in the dorsal language pathway by projecting to posterior superior temporal gyrus and the involvement of area 45 in the ventral language pathway by connecting with the anterior superior temporal gyrus. In light of the subdivisions, it is still unclear how far the fine-grained organization of Broca's region is affected by linguistic diversity.

Resting-state fMRI (rs-fMRI), which measures spontaneous fluctuations in BOLD signals, provides important insights into the core organization of the brain (van den Heuvel and Hulshoff Pol, 2010; Zhang and Raichle, 2010) and is therefore a useful tool to address the question of the cross-cultural consistency and diversity in the intrinsic organization of Broca's region. In this study, multi-center rs-fMRI data was used to test our hypothesis, including two datasets acquired in Chinese Han and Bai ethnic populations, who speak different Chinese dialects, and the other two datasets obtained from two local German groups, who are native speakers of German. We explored the cross-cultural consistency and diversity in the functional organization of Broca's region, including the topology of its subdivisions, functional connectivity patterns and modularity organization.

Materials and methods

Data acquisition and preprocessing

Four rs-fMRI datasets from different centers were used in this study, consisting of a total of 122 healthy right-handed participants. Detailed information regarding these subjects is provided in Table 1. All subjects provided written informed consent to the study protocol as approved by the local ethics committee. The subjects were instructed to rest with their eyes closed, relax their minds, and remain as motionless as possible during the scanning. The first two datasets were acquired from two different Chinese ethnic populations using the same Philips Achieva 3.0 T MRI scanner. The first dataset consisted of 29 subjects of the **Chinese Bai ethnic group** (16 males; age range=20–36 years, mean age=25.0, standard deviation (SD)=4.35), who speak the **Chinese Bai language** which belongs to the Chinese-Tibetan Phylum and has its own written characters (Wang, 2004). The second dataset consisted of 29 subjects of the **Chinese Han population**, who speak **Chinese Mandarin** (14 males; age range=22–34 years, mean age=26.0, SD=2.1). A total of 240 volumes, each covering the entire brain including the cerebellum with 33 axial slices, were acquired using a gradient-echo echo planar imaging (EPI) sequence [repetition time (TR)=2.0 s, echo time (TE)=30 ms, field of view (FOV) =220×220 mm^2, matrix=64×64, slice thickness=4 mm, gap=0.6 mm, flip angle=90°]. A structural scan was also acquired for each participant, using a T1-weighted 3D turbo field echo (TFE) sequence (TR=8.2 s, TE=3.8 ms, FOV=256×256 mm^2, matrix=256×256, number of slices=188, slice thickness=1 mm, no gap, flip angle=7°).

Using a Siemens Tim-TRIO 3.0 T MRI scanner, the third dataset was acquired from 32 native speakers of German (14 males; age range=22–39 years, mean age=29.0, SD=4.82), selected from a sample of 100 subjects at the Research Centre Jülich that has been used in a number of studies (Cieslik et al., 2013; Jakobs et al., 2012; Kellermann et al., 2013; Roski et al., 2013; Rottschy et al., 2013; Eulenburg et al., 2012). This cohort was chosen to match the age and gender of the two Chinese datasets. For each subject, 300 resting state EPI images were acquired using a gradient-echo EPI pulse sequence [TR=2.2 s, TE=30 ms, flip angle = 90°, in plane resolution=3.1×3.1 mm^2, 36 axial slices (3.1 mm thickness) covering the entire brain]. A structural scan was also acquired for each participant, using a T1-weighted 3D magnetization-prepared rapid acquisition with gradient echo (MPRAGE) sequence (176 axial slices, TR=2.25 s, TE=3.03 ms, FOV=256×256 mm^2, flip angle=9°, final voxel resolution: 1 mm×1 mm×1 mm).

The fourth dataset was downloaded from the ‘Leipzig’ dataset in the 1000 Functional Connectome Project website (www.nitrc.org/projects/fcon_1000) (Biswal et al., 2010; Kelly et al., 2012; Tomasi and Volkow, 2012). Thirty-two native speakers of German (13 males; age range = 20–31 years, mean age = 25.0, SD = 3.0), out of 37 healthy right-handed participants were selected in order to match age and gender. For each subject, 195 resting state EPI images were acquired during resting state with fixation on a cross, using a gradient-echo EPI pulse sequence [TR = 2.3 s, TE = 30 ms, flip angle = 90°, in plane resolution = 3.0 × 3.0 mm^2, 34 axial slices (4 mm thickness) covering the entire brain]. A structural scan was also acquired for each participant. More detailed description of this project and other scan parameters are available at http://www.nitrc.org/frs/?group_id=296 and http://www.nitrc.org/docman/view.php/296/719/fcon_1000_ReleaseTable_20100803.xls.

All four rs-fMRI datasets were preprocessed using the same script as described in the 1000 Functional Connectome Project (www.nitrc.org/projects/fcon_1000) (Biswal et al., 2010). The preprocessing steps included: 1) discarding the first ten volumes in each scan series for signal equilibration, 2) performing slice timing correction and motion correction, 3) removing the linear and quadratic trends, 4) band-pass temporal filtering (0.01 Hz < f < 0.08 Hz), 5) spatial smoothing using a 6-mm full-width at half-maximum (FWHM) Gaussian kernel, 6) performing nuisance signal regression [including white matter (WM), cerebrospinal fluid (CSF), the global signal, and six motion parameters], and 7) resampling into Montreal Neurological Institute (MNI) space with the concatenated transformations, including rigid transformation from the mean functional volume to the individual anatomical volume via FLIRT (Jenkinson and Smith, 2001), followed by spatial normalization of the individual anatomical volume to the MNI152 brain template (3 mm isotropic resolution) using FNIRT (Andersson et al., 2007). Finally, a four-dimensional time-series dataset in standard MNI space with 3mm isotropic resolution was obtained for each subject after preprocessing.