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Exploration of Sex Differences in the Brain based on Structure and fMRI Techniques

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Abstract

There are significant differences in the physiological structure and function of male and female human brains. Sex-related changes in human brain structure have been widely discussed in many studies, and the research results are inconsistent. This paper mainly uses Voxel-Based Morophometry (VBM) and Functional Connectivity (FC) methods. The MRI data images of 5 healthy men and 5 healthy women from USTC were processed and analyzed. Format conversion, origin correction, segmentation, smoothing, statistical difference analysis and other processing steps were carried out successively to find the different brain regions of different genders. Secondly, the functional image data was preprocessed, and Regions of Interest (ROI) were extracted from the differential brain regions sought by VBM to make functional connections, and then statistical analysis was carried out to obtain the difference map. There are two resting state functional connectivity networks in the prefrontal cortex: one is related to aPFC and DLPFC; The other is related to language areas (including IFG and STG). Studies have shown that there are significant differences in the structure and function of the human brain between the sexes, with the medial frontal cortex larger in males and the dorsolateral prefrontal cortex larger in females. In the whole measured cortex, especially in the aPFC+DLPFC region, males show stronger spontaneous wave power than females. Men also showed stronger intra-network connections in the aPFC+DLPFC region. In contrast, women showed stronger internetwork connections between the language area and the aPFC+DLPFC area. In addition, gender differences were shown in both the spatial distribution of spontaneous fluctuation power and the functional connectivity of resting states.

Keywords

Male and Female Brain Sex Differences; Voxel-based Morphological Analysis; Functional Connectivity; Dial Prefrontal Lobe.

1. Introduction

In the cutting-edge research of medicine and neuroscience, the study of gender differences in the brain has always been a central topic attracting significant attention. With the rapid development of modern imaging technologies, such as magnetic resonance imaging (MRI), computed tomography (CT), positron emission tomography (PET), and single-photon emission computed tomography (SPECT), powerful technical support has been provided for in-depth exploration of the mysteries of the brain [1 - 4]. These technologies are constantly being updated and upgraded, enabling researchers to analyze the differences between male and female brains from multiple dimensions, including structure, function, and metabolism, which has greatly promoted the research progress in this field.

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The brain, as the most complex and crucial organ in the human body, has gender differences that involve multiple disciplinary fields, such as biology, psychology, and sociology [5 - 7]. Past studies have found that there are significant differences between men and women in cognitive abilities, emotional expressions, and behavior patterns [8 - 10]. For example, men tend to perform better in spatial cognition tasks, while women may have an advantage in language expression and emotion recognition [11 - 13]. The neural mechanisms behind these differences have attracted many scholars to conduct in-depth exploration. In terms of brain structure, the average volume of the male brain is usually slightly larger than that of the female brain, while the hippocampus and language-related regions in the female brain are relatively more developed [14 - 16]. At the functional level, functional magnetic resonance imaging (fMRI) studies have revealed significant differences in the functional connectivity patterns of the default mode network (DMN), executive control network, and emotional processing network between men and women [17 - 19].

The functional magnetic resonance imaging (fMRI) technology occupies an important position in brain research due to its outstanding advantages, such as non-invasiveness, high temporal and spatial resolution [20]. It is based on the blood oxygen level-dependent mechanism, which can accurately measure the hemodynamic changes caused by neuron activities, and thus conduct an in-depth analysis of the functional characteristics of the brain. This technology has been widely applied in many fields, including basic research, cognitive science, disease diagnosis and treatment, and brain-computer interfaces [20].

In this paper, we used voxel-based morphometry (VBM) and functional connectivity (FC) methods to systematically analyze the MRI data of 5 healthy male and 5 healthy female subjects from the University of Electronic Science and Technology of China. The aim is to further explore the characteristics of gender differences in the brain and provide valuable references for subsequent related research.

2. Materials and Methods

2.1. Subject Investigated

Subjects from the University of Electronic Electronics collected structural and fMRI raw image data from five healthy adult men and five healthy adult women. All subjects had no psychiatric or neurological disease history and were willing and eligible to participate in the fMRI study. They all had normal vision or normal corrected vision. After a full explanation of the study purpose and protocol, all subjects signed their written informed consent. This study was approved by the ethical review committee of the University of TC.

2.2. Image Data Acquisition

Brain imaging data for all subjects was collected on a 3T MR scanner, GE DISCOVERY MR750 (General Electric, Fairfield Connecticut, USA), with an eight-channel head coil. Functional MRI BOLD images were imaged by echo plane sequence and collected with the following parameters: TR = 2000 ms, TE = 30ms, matrix size = 64 X 64, FA = 90°, FOV = 240 x 240 mm^2, resolution = 3.75 mm 3.75 mm 3.2 mm, number of layers = 43, no spacers, thickness = 3.2mm.

2.3. Data Analysis Method

2.3.1. Voxel-based Morphometry

Voxel morphometry (VBM) is a newly developed method that applies voxel-level comparisons of the whole brain to objectively detect regional gray matter abnormalities. Previous studies have used VBM for brain morphometric studies in different populations, but with different results. The core principle of VBM is to reveal neuroanatomical changes by automatically analyzing and comparing subtle differences in brain structure between different individuals or

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groups. This method, which quantitatively analyzes brain MRI images in voxels, can detect density or volume changes in gray matter, white matter and cerebrospinal fluid, thus reflecting local characteristics of brain structure. Before processing the data with VBM, we will preprocess the data in the following steps:

(1)Origin correction: In the process of data acquisition, the orientation varies between the brain, so the origin is needed to correct the data, correct the image by using THE SPM display, and then set the origin on AC, and make AC-PC in the same horizontal line.

(2)Spatial standardization: the structure of the human brain and the original images of functional MRI are spatially standardized, and the magnetic resonance images of the brain structure of each individual studied are standardized into the same stereo space.

(3)Image segmentation: the spatially standardized images for image segmentation, and an image is divided into several parts or subsets according to certain rules. These subsets do not cross each other, and each subset meets the consistency of a specific region.

(4)Image smoothing: segmentation after segmentation image smoothing processing, using three-dimensional Gaussian kernel and image discrete convolution operation, Gaussian kernel for isotropic, namely three direction smoothness, so as to improve the signal-to-noise ratio, make subject comparison in a reasonable spatial scale range, easy to be the average between subjects.

2.3.2. VBM Statistical Analysis

First using the SPM system on the data of two-sample T test get sex brain gray matter sex difference figure, in the brain gray matter volume change specific area, age, gender, double sample gray matter volume T test three variables as covariates for regression, and then use AlphaSim correction ($p < 0.05$) brain gray matter difference area between the men and women. The correlation of Pearson's correlation analysis scale was used to calculate the gray matter volume in the difference region and observe the difference region between men and women to judge the sex difference of the magnetic resonance imaging of human brain structure.

2.4. Whole Brain Functional Connectivity

2.4.1. Preprocessing of the fMRI Data

Before using the fMRI system to calculate the data results analysis, we need to preprocess the data, the process is as follows:

(1)Remove time point: it is the adaptation process of the machine just started running or the subject just lying in. Due to the many time points, this paper removes the first ten time points, so that the machine can better adapt to the environment.

(2)Time layer correction (Slice Timing): magnetic resonance brain imaging data is scanned by layer to correct and align the remaining images in time to eliminate pseudoregression or topological effects caused by the difference in the acquisition time of different slices and keep the acquisition time of all voxels throughout the brain.

(3)Head motion correction (Realign): The images collected at different time points are corrected to the reference position to eliminate the effect of slightly moving the head during the scan. In this paper, the parameters describing the head movement are set as 3 translation parameters and 3 rotation parameters.

(4)Standardization (Normalize): Use EPI standard meningeal version, DARTEL, T1 image data to match the corrected data from the original space to the EPI template in the standard space of Montreal Neurology Institute (Montreal Neurological Institute, MNI), and resample to 3333, so that the spatial location and orientation of the data are consistent.

(5)Regression covariates (Nuisance Covariates Regression): using the whole brain signal, regression to exclude physiological noise, white matter, cerebrospinal fluid signals, and head movement processing.

(6)Linear drift (Detrend): There is a linear trend in the accumulation of time. Therefore, the delinear drift is adopted to achieve the adaptive environment.

(7)Smoothing (Smooth): To enhance the signal to noise ratio of the data, a Gaussian smoothing kernel is selected. This smooth nucleus size is 2-3 times the size of the voxel, [8 8 8].

(8)Filter (Filter): In this paper, the BOLD signal frequency at 0.01-0.08Hz is used to suppress or eliminate the high-frequency components to reduce the noise.

(9) Delete time point (Scrubbing): Because functional connectivity analysis is sensitive to confounding movements of head movements, the time point with head displacement of more than 0.5mm and the previous and last two time points of the point were removed.

2.4.2. Statistical Analysis of the Functional Connectivity Analysis

The medial prefrontal lobe of the human brain was used as the seed point for the functional connectivity calculation, and its functional connectivity to the whole brain was calculated for each seed point. The fMRI data collected by men and women were two-sample T-test, age and sex were regressed as covariates, and GRF (corrected for functional connectivity results at P <0.05). Pearson's correlation analysis of the results was conducted to observe the difference in brain functional connectivity between men and women, thus analyzing the differential characteristics of brain functional connectivity between men and women.

3. Experimental Result

3.1. Morphological Differences in the Male and Female Brains

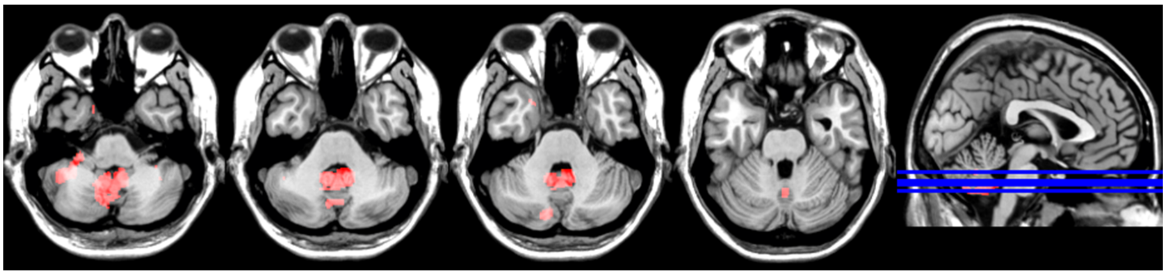

Figure 1. Double T difference plot of gray matter volume between men and women (Mricron slice chart)

According to VBM calculation and statistical analysis, comparing the gray matter volume between men and women, we can find that the gray matter area of temporal lobe and parietal lobe is denser in men, and the lower temporal lobe and prefrontal lobe is more concentrated in women. Significant difference result analysis can be obtained by two-sample T-test, as shown in Figure 1 and Table 1.

3.2. Functional Connectivity Differences between Male and Female Brains

We selected male and female medial prefrontal lobe as seed point, the area of interest for two-sample T test, differential analysis of functional connectivity, as shown in Figure 2 and table 2, we can get that male medial frontal cortex is larger, while female dorsolateral prefrontal cortex, the connection between prefrontal and limbic system, which is related to its sensitivity and ability in empathy and social interaction.

The results suggest that areas in the brain associated with mood and anxiety, prefrontal cortex, and limbic regions are more active, while in men, areas responsible for vision and coordination are more active. According to single-photon emission computed tomography measurements, blood flow in different brain regions at rest and during cognitive tasks.

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Table 1. Table of regional differences in brain gray matter between men and women

region	MNI coordinate (X,Y,Z)	voxel size	T price
Right Brainstem // Medulla // Cerebelum_9_R (aal)	(1.5,-48,-51)	2660	5.0311
Right Cerebrum // Temporal Lobe // Middle Temporal Gyrus // White Matter // Temporal_Mid_R (aal)	(54,-33,-7.5)	14279	-11.12
Left Cerebrum // Temporal Lobe // Sub-Gyral // White Matter // Temporal_Mid_L (aal)	(-49.5,-25,-21)	6910	-8.202
Right Cerebrum // Frontal_Inf_Orb_R (aal)	(49.5,28.5,-16.5)	849	-4.87
Left Cerebrum // Limbic Lobe // Parahippocampa Gyrus // White Matter // araHippocampal_L (aal)	(-21,-33,-13.5)	717	-4.165
Inter-Hemispheric // Cuneus_L (aal)	(1.5,-99,15)	1602	-7.07
Left Cerebrum // Temporal Lobe // Superior Temporal Gyrus // White Matter // Temporal_Pole_Sup_L (aal)	(-43.5,6,-16.5)	246	-3.983
Frontal_Inf_Orb_L (aal)	(-30,39,-19.5)	2496	-8.262
Left Cerebellum // Cerebellum Anterior Lobe // Culmen // Lingual_L (aal)	(-16.5,-52.5,-10.5)	306	-4.829
Right Cerebrum // Temporal Lobe // Superior Temporal Gyrus // Gray Matter // brodmann area 22 // Temporal_Sup_R (aal)	(63,1.5,3)	551	-3.555
Left Cerebrum // Parietal Lobe // Postcentral Gyrus // Gray Matter // brodmann area 3 // Postcentral_L (aal)	(-33.-31.5,51)	429	6.053
Left Cerebrum // Frontal Lobe // Superior Frontal Gyrus // Gray Matter // brodmann area 6 // Paracentral_Lobule_L (aal)	(-3,-15,79.5)	463	-4.868

Note: MNI, Montreal Neurological Institute, X, Y, Z, MNI space;

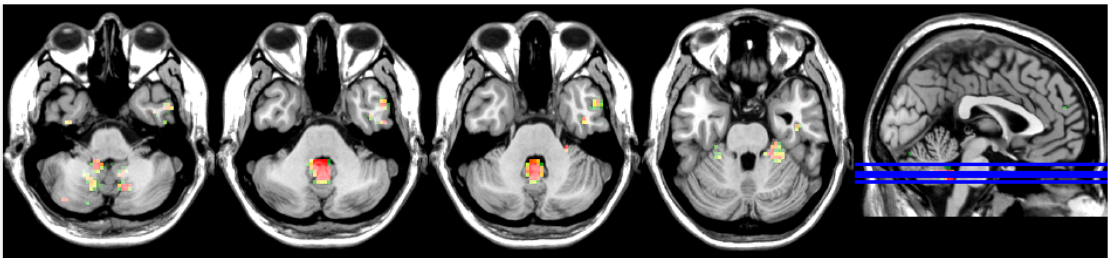

Figure 2. Double T difference map of medial prefrontal functional connectivity between men and women (Mricron slice)

Table 2. Table of regional differences between men and women

Connection area	**MNI coordinate (X, Y, Z)**	**voxel size**	**T price**
Right Cerebellum // Cerebellum Anterior Lobe // Nodule // Vermis_9 (aal)	(3, -54, -36)	302	-7.46
Left Cerebrum // Frontal Lobe // Inferior Frontal Gyrus // White Matter // Frontal_Inf_Tri_L (aal)	(-45,21,15)	245	6.3212
Left Cerebrum // Frontal Lobe // Medial Frontal Gyrus // White Matter // Supp_Motor_Area_L (aal)	(-9,15,48)	273	6.36

The medial prefrontal lobe was selected as the seed point because it is a key node in the default network in the resting state. The default network of the brain includes discrete, bilateral and symmetrical cortical regions, medial and lateral parietal lobe, medial prefrontal lobe and lateral temporal lobe. Through the connection of the whole brain function can make the brain signal

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better transmission, in the functional cognition and disease examination can better continue to that you give differential monitoring, the data effect is more clear and intuitive. By calculating the correlation and spatiotemporal characteristics of brain region activity, we can reveal the functional connections and information transfer mode between different brain regions.

4. Summary and Outlook

The experimental study in this paper reveals the gender differences of magnetic resonance imaging in human brain images. Through this experiment, we used VBM and whole brain functional connectivity to process the structure and functional MRI of human brain and obtain the gender difference images. Several studies have shown that men and women have significant differences in brain structure, mainly in the overall brain volume, cortical thickness, and the volume of specific brain regions. For example, male brain average are slightly larger than females, where the hippocampus and language-related regions are generally more developed than males. The fMRI studies have revealed differences in functional connectivity patterns between the sexes, especially in the default mode network (DMN), executive control networks, and emotion processing networks. The connectivity within the female brain seems to be more extensive and dense, while the male brain shows more localized connectivity advantages. Gender differences are associated with specific cognitive abilities, such as language processing, spatial ability, and emotion recognition. These differences are partly attributed to the inconsistency between brain structure and function, but also emphasize the influence of environmental and social factors.

Magnetic resonance imaging technology has been continuously improved in the process of scientific progress, combined with structural MRI, fMRI, DTI (diffusion tensor imaging) and other technologies, to provide a more comprehensive map of brain sex differences. To study the changes of inter-individual differences and gender differences in the whole life, considering the interaction of multiple factors such as genetics, environment and lifestyle. This paper is selected the human brain medial prefrontal lobe as the seed point, the connection with the whole brain, the human brain signal and the default network analysis, to get the male and female brain area structure, which reflects the women of social, emotional level of brain organization is more sensitive, men are in the working state has a more sensitive emotional regulation. Due to the experimental sampling experimental data is limited, intelligence, and education factors did not get comprehensive confirmation, with the progress of inspection technology and the continuous improvement of magnetic resonance imaging technology, a variety of other factors will be more involved in medical research, for people to explore the structure and function of the brain characteristics and differences to provide more rigorous and accurate data theoretical basis.

Research on magnetic resonance imaging not only improves our understanding of the human brain, but also provides a scientific basis for clinical diagnosis, personalized treatment, and gender-sensitive policy making. As technological advances and interdisciplinary cooperation deepen, more innovations are expected to emerge in the future.

References

[1] Bushberg JT, Seibert JA, Leidholdt EM, Boone JM. The essential physics of medical imaging. Lippincott Williams & Wilkins; 2012.

[2] Westbrook C, Kaut Z, Ricketts H, Talbot J. MRI in practice. John Wiley & Sons; 2019.

[3] Cherry SR, Sorenson JA, Phelps ME. Physics in nuclear medicine. Elsevier; 2012.

[4] Zanzonico P. Positron emission tomography: a review of basic principles, scanner design and performance, and current systems. Semin Nucl Med; 2004.

ISSN: 2688-8645

[5] Kimura D. Sex differences in the brain: understanding the differences between men's and women's minds. Oxford University Press; 2000.

[6] Baron - Cohen S. The essential difference: men, women and the extreme male brain. Allen Lane; 2003.

[7] Halpern DF. Sex differences in cognitive abilities. Psychology Press; 2012.

[8] Hyde JS. Half the human experience: the psychology of women. McGraw - Hill; 2014.

[9] Maccoby EE, Jacklin CN. The psychology of sex differences. Stanford University Press; 1974.

[10] Geary DC. Male, female: the evolution of human sex differences. American Psychological Association; 2010.

[11] Linn MC, Petersen AC. Emergence and characterization of sex differences in spatial ability: a meta - analysis. Child Development; 1985.

[12] Kimura D. Sex - related differences in the speed of accessing vocabulary. Canadian Journal of Psychology/Revue canadienne de psychologie; 1991.

[13] Hall JA. Gender differences in the expression and perception of emotion. In: Manstead ASR, Wagner H. Handbook of social psychophysiology. John Wiley & Sons; 1991.

[14] Gur RC, Gunning - Dixon F, Turetsky BI, Bilker W, Hughett P, Gur RE. Sex differences in brain gray and white matter in healthy young adults: correlation with cognitive performance. The Journal of Neuroscience; 1999.

[15] Goldstein JM, Seidman LJ, Horton NJ, Makris N, Kennedy DN, Caviness VS Jr, Faraone SV, Tsuang MT. Normal sexual dimorphism of the adult human brain assessed by in vivo magnetic resonance imaging. Cerebral Cortex; 2001.

[16] Shaywitz BA, Shaywitz SE, Pugh KR, Constable RT, Skudlarski P, Fulbright RK, Bronen RA, Fletcher JM, Shankweiler DP, Katz L. Sex differences in the functional organization of the brain for language. Nature; 1995.

[17] Raichle ME. The brain's default mode network. Annual Review of Neuroscience; 2015.

[18] Kelly AM, Uddin LQ, Biswal BB, Castellanos FX, Milham MP. Functional connectivity mapping of the default mode network: a comparison of resting - state fMRI and resting - state PET. Neuroimage; 2008.

[19] Greicius MD, Krasnow B, Reiss AL, Menon V. Functional connectivity in the resting brain: a network analysis of the default mode hypothesis. Proceedings of the National Academy of Sciences; 2003.

[20] Bandettini PA. How does fMRI really work? Nature Neuroscience; 2012.