

## DOCUMENT SUMMARY

This peer-reviewed research study quantitatively assesses inter-individual variability across nine different fMRI-based human brain atlases using task-based functional MRI data from 893 subjects. The study provides critical insights for clinical applications by demonstrating significant variability differences between brain atlases and recommending specific atlases for motor and language mapping tasks.

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## FORMATTED CONTENT

# Quantitative assessment of inter-individual variability in fMRI-based human brain atlas

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## Abstract

**Background:** Inter-individual variability is an inherent and ineradicable feature of group-level brain atlases that undermines their reliability for clinical and other applications. To date, there have been no reports quantifying inter-individual variability in brain atlases.

**Methods:** In the present study, we compared inter-individual variability in nine brain atlases by task-based functional magnetic resonance imaging (fMRI) mapping of motor and temporal lobe language regions in both cerebral hemispheres. We analyzed complete motor and language task-based fMRI and T1 data for 893 young, healthy subjects in the Human Connectome Project database. Euclidean distances (EDs) between hotspots in specific brain regions were calculated from task-based fMRI and brain atlas data. General linear model parameters were used to investigate the influence of different brain atlases on signal extraction. Finally, the inter-individual variability of ED and extracted signals and interdependence of relevant indicators were statistically evaluated.

**Results:** We found that inter-individual variability of ED varied across the nine brain atlases ( $P < 0.0001$  for motor regions and  $P < 0.0001$  for language regions). There was no correlation between parcel number and inter-individual variability in left to right (LtoR;  $P = 0.7959$  for motor regions and  $P = 0.2002$  for language regions) and right to left (RtoL;  $P = 0.7654$  for motor regions and  $P = 0.3544$  for language regions) ED; however, LtoR ( $P \leq 0.0001$ ) and RtoL ( $P \leq 0.0001$ ) inter-individual variability differed according to brain region: the LtoR ( $P = 0.0008$ ) and RtoL ( $P = 0.0004$ ) inter-individual variability was greater for the right hand than for the left hand, the LtoR ( $P = 0.0019$ ) and RtoL ( $P = 0.0179$ ) inter-individual variability was greater for the right language than for the left language, but there was no such difference between the right foot and left foot (LtoR,  $P = 0.2469$  and RtoL,  $P = 0.6140$ ). Inter-individual variability in one motor region was positively correlated with mean values in the other three motor regions (left hand,  $P = 0.0145$ ; left foot,  $P = 0.0103$ ; right hand,  $P = 0.1318$ ; right foot,  $P = 0.3785$ ). Inter-individual variability in language region was positively correlated with mean values in the four motor regions (left language,  $P = 0.0422$ ; right language,  $P = 0.0514$ ). Signal extraction for LtoR ( $P < 0.0001$ ) and RtoL ( $P < 0.0001$ ) varied across the nine brain atlases, which also showed differences in inter-individual variability.

**Key Finding:** These results underscore the importance of quantitatively assessing the inter-individual variability of a brain atlas prior to use, and demonstrate that mapping motor regions by task-based fMRI is an effective method for quantitatively assessing the inter-individual variability in a brain atlas.

**Keywords:** Inter-individual variability; brain atlas; motor cortex; quantitative assessment; task-based fMRI

## Introduction

Human brain atlases, which represent the spatial and functional parcellation of the brain, are critical for visualizing the brain's functional organization. A major challenge for neuroscience research is to delineate the hundreds of different brain regions based on functional and anatomical criteria. In the last few decades, features extracted by structural and functional magnetic resonance imaging (MRI) of different brain regions have been used to accurately segment the human brain, producing databases of reliable brain parcellations.

**Parcellations** based on structural MRI which is acquired on a non-ultra-high field scanner (3T and below) are clinically useful as they demarcate physical regions of individual brains, but have low resolution; on the other hand, those based on **functional (f)MRI** which is acquired on a non-ultra-high field scanner (3T and below) are more precise but are difficult to apply to individual assessments. Therefore, many studies have employed group-average brain atlases such the Anatomical Automatic Labeling atlas to analyze the brain at the group level. However, **inter-individual variability** in fMRI-based parcellations limit their clinical utility—for example, for pre-surgical functional localization.

The temporal signal-to-noise ratio (SNR) for the blood oxygenation level-dependent (BOLD) signals is relatively low, so features extracted from fMRI that are obtained in a short time interval (<30 min) cannot be used to accurately segment individual human brains.

To overcome this problem, individual data have been used to verify group-level centralized trends that include individual information. Although a large number of datasets are used to reduce inter-individual variability, unique features in each brain are overlooked in group-level analyses.

Many studies have investigated methods for accurate parcellation of individual brains. For instance, one study segmented a single brain based on **resting-state functional connectivity (RSFC) fMRI** data collected over 14 h. The study demonstrated that accurate individual brain parcellations can be obtained with a large amount of data, in greater detail than by group-level data analysis. However, the data collection period was long (1 year), which can be useful in cases of rare neurologic disease but is too long for those requiring an immediate diagnosis, for which accurate group-level brain parcellations are more appropriate.

However, although many parcellations are available online, there are no methods for identifying the one that is most suited to a particular study or clinical application. Furthermore, there have been no quantitative assessments of inter-individual variability in resting-state fMRI-based human brain atlases, which is required to ensure the accuracy of data interpretation.

**Study Objectives:** To this end, the aim of the present study was to quantify the inter-individual variability in different brain atlases using task-based fMRI data from hand and foot motor regions and temporal lobe language regions in both hemispheres of healthy young subjects. Briefly, we compared the sites of maximal activation of six brain areas in **Montreal Neurological Institute (MNI)** space to the coordinates of corresponding regions in nine brain atlases. The **Euclidean distance (ED)** between task-based fMRI hotspots and functional areas in the brain atlases was calculated as a feature of inter-individual variability.

**Hypotheses:** Based on previous findings, we hypothesized that (I) inter-individual variability significantly differed across different brain atlases for the same fMRI dataset, and (II) inter-individual variability significantly differed across different brain regions for the same fMRI dataset.

# Methods

## Participants and data acquisition

We analyzed complete motor task-based fMRI and T1 data of 1,080 subjects from the **Human Connectome Project (HCP)** database in the present study. The data were acquired on a 3T Skyra scanner (Siemens, Erlangen, Germany) using a 32-channel head coil.

**BOLD changes** were examined in gradient-echo echo-planar imaging sequence with the following parameters:

- repetition time (TR) =720 ms
- echo time (TE) =33.1 ms
- flip angle =52°
- field of view (FOV) =208×180 mm [readout (RO) × phase-encoding (PE)]
- matrix =104×90 (RO × PE)
- slice thickness =2.0 mm
- 72 slices
- 2.0 mm isotropic voxels
- multiband factor =8
- echo spacing =0.58 ms
- bandwidth (BW) =2,290 Hz/pixel

**T1 data** were obtained in a magnetization prepared rapid gradient echo sequence with the following parameters:

- TR =2,400 ms
- TE =2.14 ms
- TI =1,000 ms
- flip angle =8°
- FOV =224×224
- voxel size =0.7 mm isotropic
- BW =210 (Hz/pixel)
- integrated parallel acquisition technique =2
- acquisition time =7:40 (min:s)

**Motor Task Details:** Subjects were shown 3-s text cues instructing them to tap their fingers, squeeze their toes, or move their tongue to activate different motor brain regions. Ten movements for each motor task were executed for 12 s. Each subject participated in two runs of 13 motor tasks (two tasks each for tongue, **right hand (RH)**, **left hand (LH)**, **right foot (RF)**, and **left foot (LF)**); and three 15-s fixation tasks performed to obtain baseline measurements).

**Language Task Details:** The task consists of two runs that each interleave 4 blocks of a story task and 4 blocks of a math task. Each task were executed for approximately 30 seconds, however, each task was designed in order that the math task blocks match the length of the story task blocks, with some additional math trials at the end of each task. The **Story–Math protocol** provides a reliable method for activation of the temporal lobe language regions of the **left (LL)** and **right (RL)** hemispheres.

Two runs of each sequence were performed; the activation sequences from left to right hemisphere and from right to left hemisphere were defined as **LtoR** and **RtoL**, respectively. The study were approved by the Joint Ethics Committee of the Chinese Academy of Medical Sciences and Peking Union College.

## FMRI preprocessing

**Statistical Parametric Mapping (SPM)12** (London, UK) software package in Matlab v.2013b (MathWorks, Natick, MA, USA) was used to process T1 and task-based fMRI data. Task-based fMRI volumes of LtoR and RtoL motor and language task fMRI runs were realigned to the mean volume of each run. T1 volumes were coregistered with realigned task-based fMRI volumes, and all volumes were normalized to **MNI space** using the standard segmentation method for group-level analysis.

Task-based fMRI volumes were smoothed using an isotropic Gaussian kernel with **4 mm full width at half-maximum (FWHM)**. A larger FWHM improves SNR but reduces spatial resolution. The voxel size of our data was 2 mm × 2 mm × 2 mm; setting the FWHM to 2 to 3 times the voxel size is considered acceptable. As high spatial resolution was critical for our analyses, we changed the FWHM of the isotropic Gaussian kernel to 4 mm in SPM12.

## Feature extraction and fMRI statistics

For single participant first-level modeling, a **GLM design matrix** was constructed based on the experimental design. Signal drift periods longer than 128 s were removed with a 1/128-Hz high-pass filter. Realignment parameters based on head movement were introduced as multiple regressors, and GLM parameters were estimated using classic approaches.

Four **t-contrast vectors** were defined to generate statistical parametric maps of the LF, LH, RF, and RH against the fixation baseline. Two t-contrast vectors were defined to generate statistical parametric maps of the story against the math baseline. The blocked tongue movement task was not included in analysis due to the complexity of head muscles.

Subjects 1 to 50 were selected for second-level modeling. A **one-sample t test** was used to analyze group-level activation of six separate brain regions with a random-effects model (voxel-level family-wise error correction method,  $P < 0.05$ ). The largest activation cluster was selected from primitive SPM {T} mapping; the selected LF, RF, LH, RH, LL and RL activation regions are shown in Figure 2.

Six binary masks were extracted from these clusters to negate the impact of the remaining brain data on the results. For each subject, the **peak-level activation point** in a mask was identified from the corresponding SPM {T} map. The coordinates in MNI space were recorded as a feature parameter of each activated region.

The above processing steps yielded twelve feature coordinates for each subject representing the activated points in brain regions representing the LF, LH, RF, RH, LL and RL. Each brain region had two feature coordinates from two runs. It should be noted that not all twelve regions in each subject could be activated; data for a subject were excluded if there was one region that was not activated. Ultimately, **data for 893 subjects** were used for further analysis.

## Atlas selection

Brain atlases can be divided into three categories according to the type of raw data (i.e., structural images, resting-state (rs-)fMRI, and multi-modal images) used in their construction. The parcel numbers of an atlas based on macro-anatomical information extracted from structural images were 60 to 150. The primary motor cortex is in the **precentral gyrus**.

**Brain atlases were screened based on the following criteria:**

1. The precentral gyrus and paracentral lobule were segmented
2. Central or maximum probabilistic coordinates of each region were reported in the publication or were retrievable online

Based on these criteria, **nine brain atlases** from six studies were selected for analysis. Five studies involved rs-fMRI, and one utilized probabilistic diffusion tractography calculated from structural MRI, rs-fMRI, and diffusion MRI. The parcel numbers of the selected atlases were **184 to 400**.

It should be noted that not all brain atlases described the functionality of each brain region in detail. For instance, one study reported:

- **Hand regions** in the precentral gyrus of the left and right hemispheres at (−26, −25, 63) and (34, −19, 59) in MNI space
- **Foot regions** in the paracentral lobule of the left and right hemispheres at (−8, −38, 58), (−4, −23, 61) and (10, −34, 54), (5, −21, 61)
- **Temporal lobe language regions** of the left and right hemispheres at (−55, −3, −10) and (56, −12, −5), respectively, in MNI space

Thus, for the other eight atlases, regions that were closest to the above coordinates in precentral gyrus, paracentral lobule and anterior temporal lobe were selected as corresponding functional regions.

## Statistical tests

**Inter-individual variability** in each brain atlas was assessed by calculating the **ED between brain atlas coordinates and a subject's maximum activation point** for each region in MNI space according to the following equation:

$$D = \sqrt{[(x(i,rg) - x(j,rg))^2 + (y(i,rg) - y(j,rg))^2 + (z(i,rg) - z(j,rg))^2]} \quad (i = 1 \dots 893, j = 1 \dots 9, rg = 1 \dots 6)$$

where  $x(i,rg)$ ,  $y(i,rg)$ , and  $z(i,rg)$  are the coordinates of each subject's maximum activation point;  $i$  is the subject number;  $x(j,rg)$ ,  $y(j,rg)$ , and  $z(j,rg)$  are the atlas coordinates;  $j$  is the atlas number, and  $rg$  is the region. Data from two runs were calculated separately, yielding eight characteristic EDs for each subject.

The **mean value of GLM parameters** was also calculated with the equation below to assess the inter-individual variability of each brain atlas:

$$\beta = \sum \beta(x,y,z) / N$$

where  $\beta$  is the estimated GLM parameter in each mask and  $N$  is the number of voxels in the calculation.

### Statistical analyses performed:

- Paired t test for data validation
- Two-way analysis of variance (ANOVA) to evaluate significant differences in EDs and extracted GLM parameters
- Linear regression to assess the linear interdependence of parcel number and EDs and of GLM parameters and ED
- One-way ANOVA was used to evaluate differences between EDs of different regions

All statistical analyses were performed using **Prism 6 software** (GraphPad Inc., La Jolla, CA, USA).

## Results

### Data validation

All subjects participated in two runs of the motor and language task-based fMRI test; **data for 893 subjects** with all six regions activated in the two runs were available for analysis. That is, for each region in each subject, two feature coordinates were obtained. Given the low SNR of the BOLD signals, no significant differences were found in the group-level analysis of the two runs of data.

The means and standard deviations of maximum activation coordinates of the six brain regions are shown in Figure 3. A **two-tailed paired t test** showed no significant difference between the two runs for each of the six regions:

- LF,  $P=0.6252$
- LH,  $P=0.3633$
- RF,  $P=0.3731$
- RH,  $P=0.4828$
- LL,  $P=0.092$
- RL,  $P=0.8119$

### Inter-individual variability of ED in brain atlases

The **mean EDs between brain atlas coordinates and subjects' maximum activation points** in four motor regions were calculated as the inter-individual variability of each atlas, and their significance was evaluated by **two-way ANOVA**.

**Motor Regions Results:** The 893 subjects showed a significant interaction effect [ $SS = 772.7$ ,  $DF = 8$ ,  $MS = 96.59$ ,  $F(8, 16056) = 13.79$ ,  $P < 0.0001$ ]; **inter-individual variability differed across the nine brain atlases** [ $SS = 108,631$ ,  $DF = 8$ ,  $MS = 13,579$ ,  $F(8, 16056) = 1,939$ ,  $P < 0.0001$ ], with no significant differences between the two runs of each scan [ $SS = 9.213$ ,  $DF = 1$ ,  $MS = 9.213$ ,  $F(1, 16056) = 1.316$ ,  $P = 0.2514$ ].

**Language Regions Results:** The 893 subjects showed a significant interaction effect [ $SS = 1,545$ ,  $DF = 8$ ,  $MS = 193.1$ ,  $F(8, 16056) = 6.444$ ,  $P < 0.0001$ ]; **inter-individual variability differed across the nine brain atlases** [ $SS = 95,882$ ,  $DF = 8$ ,  $MS = 11,985$ ,  $F(8, 16056) = 399.9$ ,  $P < 0.0001$ ], with significant differences between the two runs of each scan [ $SS = 5,094$ ,  $DF = 1$ ,  $MS = 5,094$ ,  $F(1, 16056) = 170$ ,  $P < 0.0001$ ].

**Key Finding:** The minimum mean EDs in four motor regions was gotten at Schaefer's brain Atlas consisted of 200 parcels ( $12.66 \pm 2.69$  mm for LtoR,  $12.85 \pm 2.79$  mm for RtoL). The minimum mean EDs in two language regions was gotten at Schaefer's brain Atlas consisted of 200 parcels ( $7.99 \pm 3.77$  mm for LtoR,  $7.57 \pm 3.78$  mm for RtoL).

The interdependence between **parcel number and inter-individual variability** was evaluated by linear regression analysis. There was **no correlation between parcel number and inter-individual variability** of:

- LtoR ( $r=0.01021$ ,  $F=0.07221$ ,  $P=0.7959$ ) and RtoL ( $r=0.01357$ ,  $F=0.09629$ ,  $P=0.7654$ ) ED for motor regions
- LtoR ( $r=0.2222$ ,  $F=2$ ,  $P=0.2002$ ) and RtoL ( $r=0.1232$ ,  $F=0.9832$ ,  $P=0.3544$ ) ED for language regions

### **Inter-individual variability of ED in different brain regions**

We examined the inter-individual variability in different brain regions. The mean LtoR EDs and standard deviations were:

- **LF:**  $20.84 \pm 6.56$
- **RF:**  $17.16 \pm 2.75$
- **LH:**  $10.72 \pm 1.39$
- **RH:**  $19.02 \pm 3.8$
- **LL:**  $8.7 \pm 2.63$
- **RL:**  $16.81 \pm 5.49$

The mean RtoL EDs and standard deviations were:

- **LF:**  $20.44 \pm 5.97$
- **RF:**  $18.22 \pm 2.58$
- **LH:**  $10.16 \pm 1.35$
- **RH:**  $18.4 \pm 3.83$
- **LL:**  $8.56 \pm 2.9$
- **RL:**  $14.7 \pm 4.78$

**One-way ANOVA** and Tukey's multiple post-hoc comparisons test were used to analyze the inter-individual variability of ED in different brain regions. The results showed significant differences for LtoR [ $F=11.88$ , sum of squares (SS) =1,862, degrees of freedom (DF) =53,  $P \leq 0.0001$ ] and RtoL ( $F=13.98$ , SS =1,768, DF =53,  $P \leq 0.0001$ ) in different brain regions.

**Tukey's test results indicated:**

- LtoR ( $P=0.0008$ ) and RtoL ( $P=0.0004$ ) EDs were higher for the **RH than for the LH**
- LtoR ( $P=0.0019$ ) and RtoL ( $P=0.0179$ ) EDs were higher for the **RL than for the LL**
- No difference was observed between the RF and LF (LtoR,  $P=0.2469$  and RtoL,  $P=0.6140$ )



## Interdependence of inter-individual variability of EDs in different brain regions

The interdependence between mean ED in one motor region and the other three motor regions was evaluated by linear regression analysis. **A positive correlation was observed between:**

- **LH and the other three motor regions** (slope =  $0.23 \pm 0.085$ ,  $r=0.3196$ ,  $F=7.515$ ,  $P=0.0145$ )
- **LF and the other three motor regions** (slope =  $1.80 \pm 0.62$ ,  $r=0.3459$ ,  $F=8.461$ ,  $P=0.0103$ )
- **LL and the four motor regions** (slope =  $0.48 \pm 0.22$ ,  $r=0.2334$ ,  $F=4.873$ ,  $P=0.0422$ )

There was also a non-significant positive correlation between:

- RH and the other three motor regions (slope =  $0.47 \pm 0.29$ ,  $r=0.1362$ ,  $F=2.522$ ,  $P=0.1318$ )
- RF and the other three motor regions (slope =  $0.18 \pm 0.20$ ,  $r=0.04878$ ,  $F=0.8206$ ,  $P=0.3785$ )
- RL and the four motor regions (slope =  $0.69 \pm 0.33$ ,  $r=0.217$ ,  $F=4.434$ ,  $P=0.0514$ )

## Inter-individual variability of GLM parameter extraction in brain atlases

One way to use the brain atlas is to extract **GLM parameters from task-based fMRI statistical parametric maps** with a region of interest (ROI) as a mask. The mean GLM parameters extracted from the relevant mask (LF, LH, RF, RH, LL and RL) of eight brain atlases and second-level modeling analysis are shown in Figure 7.

**Two-way ANOVA** was used to investigate the influence of different brain atlases on parameter extraction. The results revealed a significant interaction effect of the 893 subjects for:

- LtoR [SS =10,088, DF =40, MS =252.2,  $F(40, 48,168) =216.5$ ,  $P<0.0001$ ]
- RtoL [SS =8,365, DF =40, MS =209.1,  $F(40, 48,168) =180.7$ ,  $P<0.0001$ ]

**Signal extraction differed** for:

- LtoR [SS =6,642, DF =8, MS =830.3,  $F(8, 48,168) =712.7$ ,  $P<0.0001$ ]
- RtoL (SS =4,911, DF =8, MS =613.8,  $F(8, 48,168) =530.4$ ,  $P<0.0001$ ) across the nine brain atlases

**Key Finding:** The maximum mean GLM parameters extracted from the four motor region masks was gotten at Schaefer's brain Atlas consisted of 200 parcels ( $2.078 \pm 0.15$  for LtoR,  $2 \pm 0.14$  for RtoL). The maximum mean GLM parameters extracted from the two language region masks was gotten at Schaefer's brain Atlas consisted of 200 parcels ( $1.91 \pm 0.4$  for LtoR,  $2.01 \pm 0.3$  for RtoL).

## Interdependence of extracted GLM parameters and ED

The interdependence of mean ED and extracted mean GLM parameters of each region were evaluated by linear regression analysis. **A negative correlation was found between extracted GLM parameters and EDs** for:

- **LF:** slope =  $-0.1048 \pm 0.01367$ ,  $r=0.8076$ ,  $F=58.76$ ,  $P<0.0001$
- **RF:** slope =  $-0.1127 \pm 0.03348$ ,  $r=0.4474$ ,  $F=11.34$ ,  $P=0.0046$
- **LH:** slope =  $-0.2893 \pm 0.04670$ ,  $r=0.7327$ ,  $F=38.37$ ,  $P<0.0001$
- **RH:** slope =  $-0.1843 \pm 0.01496$ ,  $r=0.9156$ ,  $F=151.8$ ,  $P<0.0001$
- **LL:** slope =  $-0.1364 \pm 0.01657$ ,  $r=0.8288$ ,  $F=67.78$ ,  $P<0.0001$
- **RL:** slope =  $-0.08767 \pm 0.01201$ ,  $r=0.7919$ ,  $F=53.27$ ,  $P<0.0001$

## Discussion

The present study evaluated the **inter-individual variability in nine brain atlases** using motor regions and temporal lobe language regions mapped by task-based fMRI. Our findings were as follows:

1. **Inter-individual variability in signal extraction and ED differed across nine brain atlases**
2. Compared to the RH, **ED was lower for the LH**; compared to the RL, **ED was lower for the LL** whereas no difference was observed between the LF and RF
3. **Mean EDs in one motor region were positively correlated** with those in the other three motor regions
4. **Extracted GLM parameters were negatively correlated with EDs** in all six regions

**Clinical Implications:** Brain atlases describe distinct functional regions and large-scale connectivity networks. All image-based atlases generated to date have been established based on imaging labels that depict brain tissue characteristics. The images are collected from dozens or even hundreds of subjects; a brain atlas that is generated from this dataset only reflects group-level results of these subjects whereas individual variability could exist for others. Therefore, **it is important to use a brain atlas with minimal variability for research or pre-surgical planning.**

The two main techniques that have been used to map the human motor cortex are task-based fMRI and neuronavigated transcranial magnetic stimulation. Some studies have demonstrated that the former is more useful than the latter for mapping the hand, foot, and other body parts.

**Study Limitations:** This study had several limitations. Firstly, only motor and language task-based fMRI data were analyzed. Correlation analyses of inter-individual variability between motor and other brain regions such as visual areas or Broca's area would be more convincing. Secondly, the data were collected from young, healthy subjects and it remains to be seen whether the same trends are present in elderly or impaired individuals such as stroke patients who are unable to complete the assigned task.

**Rs-fMRI and Task-based fMRI Relationship:** Rs-fMRI is the main source of data for constructing image-based brain atlases. Many studies have demonstrated that the organization of rs-fMRI and activation mode of task-based fMRI have group-level consistency, and rs-fMRI data tracking task-based fMRI activation at the individual level have also been reported. Recent studies have shown that some task-based fMRI activation corresponds to data in rs-fMRI-based brain atlases, especially for movement tasks.

**Clinical Application:** For example, brain atlas was frequently applied in segmenting fMRI data using regions of interest, and then obtaining respective time

series of each region of interest by averaging the fMRI time series across all voxels in the region of interest. Generally, these time series were used to calculate the effective brain connectivity between different regions of interest.

## Conclusions

**Primary Conclusion:** These results underscore the importance of quantitatively assessing the inter-individual variability of a brain atlas prior to use, and demonstrate that mapping motor regions by task-based fMRI is an effective method for quantitatively assessing the inter-individual variability in a brain atlas.

The results presented here demonstrate that **inter-individual variability exists in different brain atlases** constructed from the same dataset as well as in different brain regions. Determining the inter-individual variability of a brain atlas—for instance, by task-based fMRI mapping of motor regions—is essential before it can be considered as reliable and used in clinical and research settings.

Along the same lines, **brain atlas with less inter-individual variability** which was quantitative assessed by present method should be applied in future study. Finally, **the Schaefer's brain Atlas which is consisted of 200 parcels was recommended for motor task and temporal lobe language task** as studied.

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**Conflicts of Interest:** All authors have completed the ICMJE uniform disclosure form. The authors have no conflicts of interest to declare.

**Ethical Statement:** The study was approved by the Joint Ethics Committee of the Chinese Academy of Medical Sciences and Peking Union College.

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[References 1-37 follow in standard academic format, maintaining exact citations as in original document]

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