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Measuring individual morphological relationship of cortical regions

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HIGHLIGHTS

- A new metric was proposed to quantify individual morphological relations of regions.
- The new metric is indexed as the similarity of different morphological distributions.
- We estimate the morphological distribution from individual MRI image.
- The metric seemed to have potential application to individual differences studies.

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ABSTRACT

Background: Although local features of brain morphology have been widely investigated in neuroscience, the inter-regional relations in brain morphology have rarely been investigated, especially not for individual participants.
New method: In this paper, we proposed a novel framework for investigating this relation based on an individual's magnetic resonance imaging (MRI) data. The key idea was to estimate the probability density function (PDF) of local morphological features within a brain region to provide a global description of this region. Then, the inter-regional relations were quantified by calculating the similarity of the PDFs for pairs of regions based on the Kullback–Leibler (KL) divergence.
Results: For illustration, we applied this approach to a pre-post intervention study to investigate the longitudinal changes in morphological relations after long-term sleep deprivation. The results suggest the potential application of this new method for studies on individual differences in brain structure.
Comparison with existing methods: The current method can be employed to estimate individual morphological relations between regions, which have been largely ignored by previous studies.
Conclusions: Our morphological relation metric, as a novel quantitative biomarker, can be used to investigate normal individual variability and even within-individual alterations/abnormalities in brain structure.

1. Introduction

Most studies on brain morphology have focused on local morphological features with either voxel/vertex-based or region-based approaches (e.g., Ashburner and Friston, 2000). These local features have been considered to reflect clinical conditions (Li et al., 2012), development (Franke et al., 2012), plasticity (Wei et al., 2013), and individual differences in various tasks (Kanai and Rees, 2011). However, inter-regional relations of local brain morphology (referred to as the morphological relations) in individuals have seldom been explored, although they could provide exclusive useful information about the inter-regional associations that are not evident from local morphological measures.

Thus far, several approaches have been proposed for quantifying morphological relations, all of which are based on the co-variance of regional gray matter morphology with magnetic resonance

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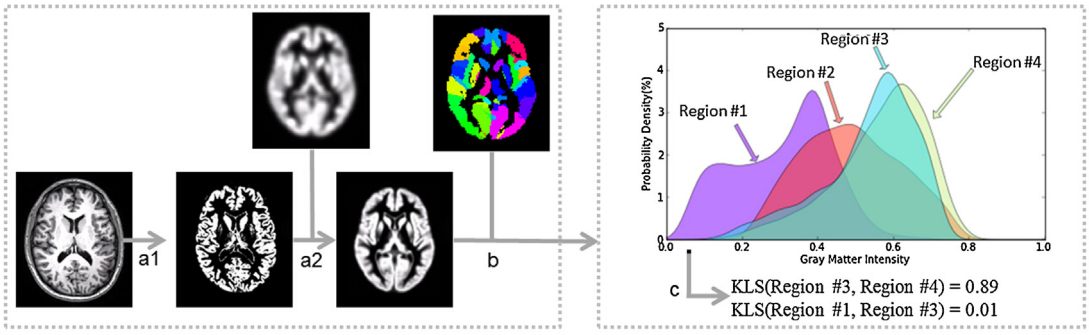

Fig. 1. Flowchart for the estimation of inter-regional morphological relation using gray matter measures from individual MRI data. (a1) MR images were segmented to create gray matter (GM) images. (a2) GM images for each individual were normalized to the standard template in MNI152 space, and then modulated and smoothed for further analysis. (b) Brain parcellation and estimation of regional probability density functions (PDFs). (c) Similarity between PDFs from different brain regions was quantified with KLS.

imaging (MRI) scans. For instance, the relations are characterized by considering the co-variance between averaged regional morphological measures (i.e., cortical thickness or volume) across participants (Mechelli et al., 2005). However, this method can only be used when we have relatively large number of participants, which limits its application to investigating normal individual variability and, particularly, to identifying within-individual brain structural alterations or abnormalities related to morphology. More recently, Tijms et al. (2012) have proposed an insightful method that allows the construction of morphological relations for a single participant. In such an approach, morphological relation is defined as the correlation between two sets of 27 voxels separately from two rigid cubes. However, this approach does not take into account the complexity of the cerebral cortex structure, which often exhibits remarkable variability across participants in terms of the shape and size of a particular region. More importantly, the rigid extraction of those small cubes might not optimally correspond to functionally/anatomically homogeneous regions of the brain (Tijms et al., 2012).

In this paper, we introduce a novel framework to associate the morphological information of two brain regions without the limitations mentioned above. By estimating the similarity of their morphological distributions, our approach is able to quantify the inter-regional relations within each participant. Technically, morphological distributions can be accurately estimated from the intensity values of voxels within a specified brain region from MRI data. Since the estimated distributions provide a full description of this region, the similarity in the morphological distributions can provide a plausible way of quantifying its inter-regional relations. In this work, the relation was captured via a similarity measurement based on Kullback–Leibler (KL) divergence. This framework can be applied with various local characteristics of the gray matter (e.g., cortical thickness, area, and volume). More importantly, the novel approach has a competitive advantage in that it allows for the quantification of morphological relations for a single participant. Due to this advantage, the method opens up a new avenue for investigating intra- and inter-individual differences in the brain's structural organization with individual MRI data.

In the following sections, we first describe our new method in detail, followed by an illustration of this approach with a pre-post study on the effects of sleep deprivation (SD) on brain structure. Our experiment specifically focused on the morphological relations between the thalamus and multiple ipsilateral association cortical regions. We chose the thalamus because it acts as the gate of nearly all incoming information to the cortex and plays an important role during natural sleep (Blethyn et al., 2006). In addition, a previous study (Liu et al., 2014) has shown that SD has a significant effect on the thalamus.

2. Methods

As shown in Fig. 1, our approach can be summarized in the following three steps:

(a) Computing local morphological features for each voxel in the brain.
(b) Brain parcellation and estimation of the morphological distributions of each region.
(c) Quantifying the relation between the morphological distributions of each pair of compared regions.

As detailed below, Step (a) is done with an automatic neuroimaging technique called voxel-based morphometry (VBM) (Ashburner and Friston, 2000). Steps (b) and (c) are the main contributions of the present paper, and will be described in detail.

2.1. Step a: morphometry computation

The MRI data was preprocessed using VBM (Ashburner and Friston, 2000) implemented in Statistical Parametric Mapping version 8 (SPM8, http://www.fil.ion.ucl.ac.uk/spm/). VBM is an automatic whole-brain neuroimaging analysis technique that allows the quantification of local morphological features from individual MRI data. First, the MRI data for each participant was checked manually by two experienced experts to ensure that it contained no scanning artifacts. Second, gray matter (GM) images were obtained by segmenting individual MRI data using the unified segmentation tools in SPM8. Then, the GM images of each participant were normalized to the study-specific template in MNI152 space using the Diffeomorphic Anatomical Registration Through Exponential Lie Algebra (DARTEL) approach (Ashburner, 2007). Next, to preserve the tissue volume after warping, voxel values in individual GM images were modulated by multiplying the Jacobian determinants derived from the normalization. Finally, all modulated GM images were smoothed individually with an 8-mm full-width at half-maximum (FWHM) Gaussian kernel. Then the smoothed and modulated GM images, consisting of morphological intensity information of each voxel that was comparable across all participants, were used for further analyses.

2.2. Step b: brain parcellation and estimation of regional probability density functions (PDFs)

Regions of interest (ROIs) can be obtained from brain parcellation based on prior atlases. Here, we used the Automated Anatomical Labeling atlas (AAL) (Tzourio-Mazoyer et al., 2002). Additionally, Step (a) gave a scalar quantifying the morphological