Journal of Neuroscience Methods 254 (2015) 46–59

Contents lists available at ScienceDirect

Journal of Neuroscience Methods

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

Basic neuroscience

AICHA: An atlas of intrinsic connectivity of homotopic areas

Marc Joliot[a,*], Gaël Jobard[a], Mikaël Naveau[a], Nicolas Delcroix[b], Laurent Petit[a], Laure Zago[a], Fabrice Crivello[a], Emmanuel Mellet[a], Bernard Mazoyer[a], Nathalie Tzourio-Mazoyer[a]

[a] GIN, UMR 5296, CNRS, CEA, Bordeaux University, Bordeaux, France
[b] GIP CYCERON, UMS 3408, Caen F-14000, France

HIGHLIGHTS

- AICHA a functional brain ROIs atlas based on resting-state fMRI data acquired in 281 individuals.
- AICHA include a crucial aspect of cerebral organization, namely homotopy.
- Each region having a unique homotopic contralateral counterpart with which it has maximal intrinsic connectivity.
- AICHA is ideally suited for investigating brain hemispheric specialization.

ARTICLE INFO

Article history:
Received 26 February 2015
Received in revised form 17 June 2015
Accepted 7 July 2015
Available online 23 July 2015

Keywords:
Atlas
Brain parcellation
Homotopy
Intrinsic connectivity
fMRI
Resting state

ABSTRACT

Background: Atlases of brain anatomical ROIs are widely used for functional MRI data analysis. Recently, it was proposed that an atlas of ROIs derived from a functional brain parcellation could be advantageous, in particular for understanding how different regions share information. However, functional atlases so far proposed do not account for a crucial aspect of cerebral organization, namely homotopy, i.e. that each region in one hemisphere has a homologue in the other hemisphere.
New method: We present AICHA (for Atlas of Intrinsic Connectivity of Homotopic Areas), a functional brain ROIs atlas based on resting-state fMRI data acquired in 281 individuals. AICHA ROIs cover the whole cerebrum, each having 1—homogeneity of its constituting voxels intrinsic activity, and 2—a unique homotopic contralateral counterpart with which it has maximal intrinsic connectivity. AICHA was built in 4 steps: (1) estimation of resting-state networks (RSNs) using individual resting-state fMRI independent components, (2) *k*-means clustering of voxel-wise group level profiles of connectivity, (3) homotopic regional grouping based on maximal inter-hemispheric functional correlation, and (4) ROI labeling.
Results: AICHA includes 192 homotopic region pairs (122 gyral, 50 sulcal, and 20 gray nuclei). As an application, we report inter-hemispheric (homotopic and heterotopic) and intra-hemispheric connectivity patterns at different sparsities.
Comparison with existing method: ROI functional homogeneity was higher for AICHA than for anatomical ROI atlases, but slightly lower than for another functional ROI atlas not accounting for homotopy.
Conclusion: AICHA is ideally suited for intrinsic/effective connectivity analyses, as well as for investigating brain hemispheric specialization.

1. Introduction

Over the previous ten years, the use of brain parcellation atlases (Evans et al., 2012) has become more frequent with the introduction of resting state functional magnetic resonance imaging (fMRI) connectivity analysis (Biswal et al., 1995). Within this framework, atlas based sets of regions of interest (ROI) are used to compute a brain graph, i.e., a model of the human brain functional connectome (Bullmore and Bassett, 2011). As shown by Craddock et al. (2012), region-based analysis has advantages compared with voxel-based analysis, including better sensitivity, interpretability and computational time. Furthermore, the reduction of the dimensionality of the fMRI data makes the problem statistically manageable by lowering the required number of statistical tests (Zalesky et al., 2012).

Today, several atlases are available, and each atlas has specific properties that should be considered with respect to the user's

* Corresponding author. Tel.: +33 05 47 30 43 97.
E-mail address: marc.joliot@u-bordeaux.fr (M. Joliot).

http://dx.doi.org/10.1016/j.jneumeth.2015.07.013
0165-0270/

needs. The available atlases for functional/intrinsic connectivity and graph analyses can be characterized by the dataset of images that served in their elaboration, the target space that had been chosen for normalization, the neuro-anatomo/functional parameters that drive the parcellation, and the parcellation algorithm.

The datasets involved in atlas creation define their "specific *versus* generic" nature. At one end are the most "specific" atlases, that are built from a single-subject dataset (such as in the AAL case (Tzourio-Mazoyer et al., 2002); at the other end are the most "generic" atlases, that are built from datasets representative of the general population. Note that elaboration of a truly "generic" atlas is out of reach, since it would request datasets for all ages, ethnicities, etc. Rather, available generic atlases are based on samples representative of some specific population, balancing for some given phenotypes, such as sex (Craddock et al., 2012), or conversely, selecting a specific phenotype, such right-handedness (Shen et al., 2013).

Regarding the target space, two main choices are available, namely volume (Ashburner and Friston, 2005) or surface (Dale et al., 1999). While the surface space has been demonstrated to be more accurate (Jo et al., 2007), the volume space is important when one is interested in tissue other than the cortical gray matter mantle, such as white matter or nuclei. The partial or complete parcellation proposed for a given brain tissue class should also be considered in atlas selection. For example, network centrality graph analysis (Bullmore and Bassett, 2011) can be critically affected in the case of partial coverage atlases because such analyses consider the strength of the connection between all graph regions. For example, centrality analysis based on an incomplete parcellation atlas or a complete cortex coverage atlas can lead to discrepant sets of "hub" region identification.

For each atlas, there are some neuro-anatomo-functional parameters that guide the parcellation scheme and constrain the definition of landmarks that constitute the boundaries of the atlas regions. Three types of landmarks are used for gray matter parcellation, including sulci (anatomical landmarks, Tzourio-Mazoyer et al., 2002; Kennedy et al., 1998), borders of cytoarchitectonic areas (Caspers et al., 2006) or limits defined from functional properties, such as the borders of spatially coherent regions of homogeneous functional connectivity (Craddock et al., 2012). Note that the homogeneity in the regions of interest of a given atlas will depend on the parameters that guide its parcellation scheme.

The atlas building constraints that are explicitly or implicitly associated with the parcellation scheme, such as the choice of the landmarks, has a strong impact on the topology of the parcellation in terms of the shape and number of parcels and thus on the atlas' final resolution.

The aim of the present work was to design an atlas suitable for functional/intrinsic connectivity and graph analysis that would consider and benefit from a major characteristic of brain organization, namely homotopy. Homotopy corresponds to the fact that the two hemispheres have comparable organization regarding macroscopic anatomy, cytoarchitecture and large-scale functional organization (Fuster, 1998; Mesulam, 1990) and are for the most part connected to each other by the white matter tracts of the corpus callosum, which originate from and terminate in the 4th cortical layer. As a consequence, almost all areas from identical cortical structures and with identical hierarchical levels are connected through the corpus callosum in a mirroring way. However, this cortical symmetry is not perfect because of the global torsion of the brain, the Yaklovian torque, which makes difficult a point-to-point correspondence between cortical areas that are functionally homotopic (Toga and Thompson, 2003). In addition, the torque goes along with asymmetries in sulcus depth and position in relation to differences in asymmetries in neighboring cortices (Lyttelton et al., 2009); the largest sulcal and cortical asymmetries in newborns and adults are located at the termination of the Sylvian fissure and at the superior temporal sulcus (Hill et al., 2010). These gross morphological differences across hemispheres increase the difficulty in defining homotopic regions in the temporal and inferior parietal areas. For example, in order to calculate regional asymmetries, one must define what is meant by homotopic regions. This definition can be based either on anatomical atlases, such as AAL (Tzourio-Mazoyer et al., 2002), which use a rough spatial metric based on the position of the regions relative to the sulci, or on a cytoarchitectonic atlas based on both anatomical symmetry in position and differences in the cortical lamination patterns (Caspers et al., 2006). In functional atlases, criteria based on the functional characteristics of the regions of the atlas areas have not yet been proposed to define homotopic areas. However, it is common to observe homotopic-like patterns in resting data analysis using seed based analysis (van den Heuvel and Hulshoff Pol, 2010; Jo et al., 2012) or network decomposition methods (Beckmann et al., 2005; Naveau et al., 2012; Yeo et al., 2011). Furthermore, Stark et al. (2008) have reported that the highest mean functional connectivity is observed between inter-hemispheric symmetrical areas compared with other inter-hemispheric or intra-hemispheric connections. These observations support that homotopic organization is a fundamental feature of the functional organization of the cortex and plead for the definition of homotopic areas based on functional, rather than anatomical, criteria.

The Atlas of Intrinsic Connectivity of Homotopic Areas (AICHA) we propose here is thus a population-level, cerebrum gray matter brain atlas of homotopic regions based on a time correlation structure of the resting brain. We designed AICHA based on the following properties: 1—a large dataset of 281 healthy participants balanced for handedness and gender; 2—volumetric MNI space of normalization to cover the gray matter of the whole cerebrum, including the sub-cortical gray nuclei; 3—time correlation structure of the functional resting state signal (intrinsic connectivity) as the basis for landmark definition; and 4—choice of an algorithm that permits a homotopic parcellation to maximize the weight of the functional signal at the final step. We describe the AICHA atlas building, its dataset regional functional homogeneity (i.e., the intra-regional similarity level of the voxel blood oxygen level dependent time-series), compare it to four existing atlases, and provide the intra- and inter- hemispheric intrinsic connectivity patterns at different thresholds of regional connection strength.

2. Materials and methods

2.1. Participants

Two hundred eighty-one healthy adults (137 women, 144 men) aged 18–57 years (25 ± 6 years, mean ± SD) were included in this study. Subject handedness was self-reported, and their manual preference strength was measured using the Edinburgh score (ES, mean ± σ, (Oldfield, 1971). 133 subjects were right-handed (66 women, ES = 94 ± 10; 67 men, ES = 91 ± 13) and 148 subjects were left-handed (71 women, ES = -63 ± 39; 77 men, ES = -63 ± 41). All subjects provided informed written consent, and the local ethics committee (CPP de Basse-Normandie, France) approved the study.

2.2. Data acquisition and pre-processing

2.2.1. Imaging methods

Imaging was performed on a 3 Tesla MRI scanner (Achieva Philips, Best, The Netherlands). Spontaneous brain activity was monitored using blood oxygen level dependent (BOLD) fMRI while the participants performed an 8-min resting state condition (T2*-EPI, sequence parameters: 240 volumes; TR = 2 s; TE = 35 ms; flip