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Individual-specific features of brain systems identified with resting state functional correlations

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ABSTRACT

Recent work has made important advances in describing the large-scale systems-level organization of human cortex by analyzing functional magnetic resonance imaging (fMRI) data averaged across groups of subjects. However, new findings have emerged suggesting that individuals' cortical systems are topologically complex, containing small but reliable features that cannot be observed in group-averaged datasets, due in part to variability in the position of such features along the cortical sheet. This previous work has reported only specific examples of these individual-specific system features; to date, such features have not been comprehensively described. Here we used fMRI to identify cortical system features in individual subjects within three large cross-subject datasets and one highly sampled within-subject dataset. We observed system features that have not been previously characterized, but 1) were reliably detected across many scanning sessions within a single individual, and 2) could be matched across many individuals. In total, we identified forty-three system features that did not match group-average systems, but that replicated across three independent datasets. We described the size and spatial distribution of each non-group feature. We further observed that some individuals were missing specific system features, suggesting individual differences in the system membership of cortical regions. Finally, we found that individual-specific system features could be used to increase subject-to-subject similarity. Together, this work identifies individual-specific features of human brain systems, thus providing a catalog of previously unobserved brain system features and laying the foundation for detailed examinations of brain connectivity in individuals.

1. Introduction

The human cortex is organized into large-scale, spatially-distributed systems. These systems can be described in vivo using a functional magnetic resonance imaging (fMRI)-based technique known as resting state functional connectivity (RSFC), which relies on the observation that in the absence of any task, spatially distant regions of cortex exhibit highly correlated patterns of BOLD activity (Biswal et al., 1995). This is posited to at least partly reflect the statistical history of interactions between regions (Dosenbach et al., 2007). RSFC-based approaches have consistently identified around 10–17 brain systems that replicate across multiple datasets and analysis strategies (Power et al., 2011; Yeo et al., 2011). The spatial characterization of these systems has enabled the identification of plausible links between brain organization and cognitive function by associating specific systems identified during the resting state with sets of regions activated during cognitive processes (Bertolero et al., 2015; Dosenbach et al., 2007; Laird et al., 2011; Smith et al., 2009).

Previous descriptions of cortical systems using RSFC have usually been derived from data averaged across many individuals. While RSFC correlation patterns calculated in single individuals are broadly similar across people (Shehzad et al., 2009; Van Dijk et al., 2010), inter-individual variability can nonetheless be observed in these patterns (Laumann et al., 2015; Mueller et al., 2013; Wang et al., 2015a). This variability has been presumed to reflect individual differences in the strength of communication

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between brain areas. Thus, many investigators test whether measured differences in RSFC relate to group membership or to individual differences in cognitive function. However, an implicit assumption in this approach is that a given section of cortex always represents the same brain area—or at least the same brain system—across individuals (Dubois and Adolphs, 2016; Satterthwaite and Davatzikos, 2015; Wang and Liu, 2014).

Recent work has suggested that this may not be the case. Detailed descriptions of RSFC-derived brain systems in single individuals suggest that inter-subject variability in these systems is not solely driven by varying strengths of network connections. Rather, the topological features of individual-level systems can vary in shape from one individual to the next (Gordon et al., 2015; Langs et al., 2015; Laumann et al., 2015; Wang et al., 2015a), such that, for example, a portion of cortex that is in the Default system in one subject may be more strongly connected to the Fronto-Parietal system in another.

Critically, systems of individuals also tend to have focal topological features that cannot be observed in group-averages (Harrison et al., 2015; Laumann et al., 2015; Wang et al., 2015a). As a result, the brain systems present at a given cortical location can vary dramatically and categorically between an individual and a group-average (Laumann et al., 2015), as well as between one individual and the next (Gordon et al., 2015). These variable brain system features can be consistently observed across many—but not all—individuals (Gordon et al., 2015).

Why do these system features appear in individual data but not in group averages? Laumann et al. (2015) proposed that two factors may account for this observation. First, some features of brain systems may be sufficiently spatially variable (relative to the morphological features of cortex used for cross-subject alignment) that they do not overlap well across individuals. This would cause such features to be "smeared out" when averaged across individuals at each cortical location, creating the appearance of reduced topological complexity in group-average systems. Second, some features of brain systems may be "missing" from some individuals due to specific cortical areas being connected to different brain systems in different individuals. If only a minority of individuals have a strong connection between a brain system and a given cortical area, that connection will not be evident in group-average data.

If this conceptualization of individual variability in brain systems is correct, then it is likely that the system features observed in individuals may represent detailed aspects of the systems-level organization of the brain that, due to reliance on group-average data, have not previously been described. Identifying and characterizing such variable, individual-specific features of brain organization across many individuals would thus advance our understanding of the brain's functional organization.

In the present study we attempted a comprehensive description of the features in individual-specific brain systems that do not emerge in group-average systems. This was accomplished by using a template matching technique (Gordon et al., 2015) to identify features of brain systems in individuals. We first established the within-subject reliability of this technique by examining the consistency of observed brain features across five hours of resting-state fMRI data collected from a single subject. We then identified brain system features that were common across many subjects by applying the technique to many individuals and matching the discrete features of identified brain systems across individuals. We performed several analyses of these commonly-present features. First, we characterized the size, spatial distribution, and frequency of occurrence of each system feature. Second, we determined whether we could observe system features that appeared consistently across subjects, but that were not present in group-average systems. Third, we examined whether these system features reliably emerged across three independent datasets, and whether they reliably emerged when a different set of brain system templates was used for systems definition. Finally, we tested whether matching system features across subjects increased the similarity of functional connectivity patterns.

2. Methods

2.1. Single subject dataset

2.1.1. Subject data was collected from a single healthy, right-handed, young adult male subject, age 34 (author ND)

Informed consent was obtained from the subject. The study was approved by the Washington University School of Medicine Human Studies Committee and Institutional Review Board. These data were previously described in the Supplemental Material of Laumann et al. (2015).

2.1.2. Data acquisition

Imaging was performed on a MAGNETOM Trio Tim 3.0 T Scanner (Erlangen, Germany) with a Siemens 12 channel Head Matrix Coil. Four T1-weighted images (sagittal, 224 slices, 0.8 mm isotropic resolution, TE = 3.74 ms, TR = 2400 ms, TI = 1000 ms, flip angle = 8°) and four high-resolution T2-weighted images (sagittal, 224 slices, 0.8 mm isotropic resolution, TE = 479 ms, TR = 3200 ms) were obtained. Thirty contiguous minutes of resting state data were collected in ten separate sessions, each on a different day (total time = 300 min). The subject visually fixated on a white crosshair presented against a black background. Functional imaging was performed using a gradient-echo EPI sequence (TR = 2.2 s, TE = 27 ms, flip angle = 90°, voxel size = $4 \times 4 \times 4$ mm, 36 slices). In each session, a gradient echo field map sequence was acquired with the same prescription as the functional images.

2.1.3. Distortion correction

Mean field map creation: A mean field map was generated based on the field maps collected in each session, and was then applied to all sessions for distortion correction. See the Supplemental materials and Laumann et al. (2015) for details on this procedure.

2.1.4. Preprocessing

Functional data were preprocessed to reduce artifact and to maximize cross-session registration. All sessions underwent intensity normalization to a whole brain mode value of 1000 and within run correction for head movement. Atlas transformation was computed by registering the mean intensity image from a single BOLD session to atlas space via the average high-resolution T2-weighted image ($n = 4$) and average high-resolution T1-weighted image ($n = 4$). All subsequent BOLD sessions were linearly registered to this first session. Atlas transformation, distortion correction, and resampling to an isotropic 3-mm atlas space (Talairach and Tournoux, 1988) were combined into a single interpolation using FSL's applywarp tool (Smith et al., 2004).

2.2. Washington University (Wash U) dataset

2.2.1. Subjects

Data was collected from 120 healthy young adult subjects during relaxed eyes-open fixation (60 females, mean age = 25 years, age range = 19–32 years). All subjects were native speakers of English and right-handed. Subjects were recruited from the Washington University community and were screened with a self-report questionnaire to ensure that they had no current or previous history of neurological or psychiatric diagnosis. Informed