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Describing functional diversity of brain regions and brain networks

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ABSTRACT

Despite the general acceptance that functional specialization plays an important role in brain function, there is little consensus about its extent in the brain. We sought to advance the understanding of this question by employing a data-driven approach that capitalizes on the existence of large databases of neuroimaging data. We quantified the *diversity* of activation in brain regions as a way to characterize the degree of functional specialization. To do so, brain activations were classified in terms of task domains, such as vision, attention, and language, which determined a region's *functional fingerprint*. We found that the degree of diversity varied considerably across the brain. We also quantified novel properties of regions and of networks that inform our understanding of several task-positive and task-negative networks described in the literature, including defining functional fingerprints for entire networks and measuring their functional assortativity, namely the degree to which they are composed of regions with similar functional fingerprints. Our results demonstrate that some brain networks exhibit strong assortativity, whereas other networks consist of relatively heterogeneous parts. In sum, rather than characterizing the contributions of individual brain regions using task-based functional attributions, we instead quantified their dispositional tendencies, and related those to each region's affiliative properties in both task-positive and task-negative contexts.

Introduction

Advancing our understanding of neuroscience centrally depends on characterizing how structure and function are related in the brain. The idea of functional specialization has led to major success stories in neuroscience, as exemplified by the elucidation of the organization of the visual system. Building on the findings of Hubel and Wiesel, work in the 1970s and 1980s described the visual system as comprising (at the time) 10–15 separate regions exhibiting a fair degree of specialization, including regions with selectivity for motion, color, and object processing (Zeki, 1993). The apparent success of the functional specialization framework is not confined to vision, but extends to other sensory modalities, as well as motor control and cognition, as examination of standard textbooks will attest. More recently, functional neuroimaging has also contributed to our understanding of functional specialization in the brain, and has led to some stark examples of purported selective processing tied to face processing and "place" processing, for example (Kanwisher, 2010).

Neuroscience also recognizes that brain regions are not islands but communicate with and influence each other. In particular, characterization of the connectivity of the prefrontal cortex with other parts of the brain helped solidify the idea that brain architecture might support "parallel distributed networks" (Goldman-Rakic, 1988). In the past decade, work in neuroimaging has also highlighted functional integration, and current techniques of network science are popular in characterizing regional interactions. Yet, given the observed degree of interaction, understanding functional specialization becomes considerably more complex. Acknowledging these issues in structure–function mappings, Passingham et al. (2002) proposed the idea of a *functional fingerprint*, namely a multidimensional representation of area function based on a small set of "dimensions". In the case of the motor areas they investigated, they employed dimensions such as "motor coupling", "movement/muscle", and "proprioceptive/cutaneous".

In the present study, we sought to advance the understanding of functional specialization by employing a data-driven approach that capitalizes on the existence of large databases that summarize human neuroimaging findings. This type of data has been used in a growing number of meta-analytic studies (Laird et al., 2011; Yarkoni et al., 2010). Like Passingham et al. (2002), we determined functional fingerprints as a way to characterize the roles of brain regions in a *multidimensional* manner. Related approaches have been described by Fox and collaborators in studying specific brain regions (Narayana et al., 2012; Robinson et al., 2012), as well as Poldrack et al. (2009) in performing whole-brain analysis. Here, functional activations were classified in terms of task domains as defined in the BrainMap database (Laird et al., 2005). The functional fingerprint for a given region thus represented both the set of domains that systematically engaged the region and the relative degree of engagement. From these fingerprints, we calculated a *diversity index* to further characterize the degree of *functional diversity*. A brain region with high

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diversity would be one engaged by tasks in many of these domains, whereas a low-diversity region would be engaged by a few domains. Furthermore, quantification of functional fingerprints allowed us to probe properties of brain networks, including the degree to which they are composed of regions with similar functional fingerprints. In general, the proposed approach permits a nuanced exploration of both local function and functional cooperation in networks, opening – we hope – new avenues for future work.

Materials and methods

Functional fingerprint and diversity analysis

To estimate functional fingerprints and diversity, we analyzed studies from the BrainMap database (Laird, et al., 2005). As there are no widely accepted ontologies of mental processes (Price and Friston, 2005; Yarkoni, et al., 2010), we employed the BrainMap taxonomy, which has undergone considerable refinement in the past decade (Fox and Lancaster, 2002; Fox et al., 2005a, 2005b; Laird et al., 2009b). Twenty task domains were considered, spanning perception, action, cognition, and emotion, an approach similar to that employed in recent studies (e.g., Laird et al., 2009a; Smith et al., 2009). All studies considered involved healthy adults and used a within-subjects, whole-brain, univariate design. That is, brain activity during an experimental task was observed over the whole brain and compared voxelwise to activity observed in the same participant during a control task. Here, we use the term "observation" to refer to the pairing of a reported activation and a task domain. For example, for an experiment filed in the database under both "emotion" and "vision" domains (due to the task manipulation), each reported activation would count as two observations (one per domain) at its activation site.

A *functional fingerprint* was defined as a 20-dimensional vector, each dimension corresponding to a task domain. Each of the 20 values represented the proportion of local observations in the corresponding task domain (local number of observations divided by the number of observations over the entire database), normalized (i.e., all 20 values summed to 1). See Fig. 1 for illustration of the process. The 20 domains employed were as follows (the term following the hyphen corresponds to the more general domain category): Execution-Action; Imagination-Action; Inhibition-Action; Motor Learning-Action; Observation-Action; Preparation-Action; Attention-Cognition; Working Memory-Cognition; Reasoning-Cognition; Memory-Cognition; Language Semantics-Cognition; Language Other-Cognition; Anger-Emotion; Disgust-Emotion; Fear-Emotion; Happiness-Emotion; Sadness-Emotion; Audition-Perception; Somesthesis-Perception; Vision-Perception.

For cortex, functional fingerprints were calculated in a voxelwise manner using a spherical searchlight. In other words, a spherical region was moved voxel by voxel along cortex, and the resulting fingerprint determined. Because of this, a fair amount of "smoothness" would be expected in the resulting maps, as indeed seen in Fig. 3. Note, however, that despite the overlap between adjacent "searchlights", the results also reveal many zones of considerable "contrast". In other words, the method clearly demonstrates a landscape of "low", "intermediate", and "high" diversity brain regions. Voxel size was 3 mm isotropic. A probabilistic gray matter mask was applied to prevent consideration of activations that fell either outside of the brain or within white matter. Only activations with at least 25% probability of being in gray matter were retained (based on the Talairach atlas provided in the AFNI package; specifically, the TT_caez_gw_18 mask). Any activation observed within the searchlight was considered to contribute to the voxel's functional fingerprint. The results shown here were obtained with a searchlight with a 10-mm radius. Various searchlight radii were investigated and yielded qualitatively similar results for radii ≥ 5 mm. For subcortical regions, all activations within the region (as defined via AFNI's Talairach atlas) were considered. When considering the functional fingerprint of an entire network, the same procedures were applied after pooling the activations of the constituent regions.

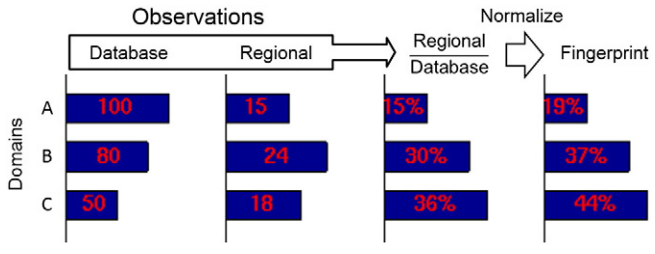

Fig. 1. Determination of functional fingerprints. To illustrate the process, only three task domains are shown. The actual fingerprints used in the paper were 20-dimensional. The label "regional" refers to voxels in cortex (via the searchlight), subcortical regions, or networks. The final normalization step ensures that the fingerprint values all sum to 1.

For the network analyses (see Figs. 5–7), we employed regions of interest (ROIs) from published papers describing several task-positive and task-negative networks (Tables 1 and S1). Initial ROI coordinates were transformed to Talairach space via the icbm2tal routine provided with the BrainMap database (Lancaster et al., 2007). Because having a sufficient number of activations is critical to producing reliable fingerprints, the initial seed coordinates of the ROIs for the networks in Table 1 were automatically shifted to nearby voxels (within 6 mm) that had the highest number of activations.

The literature is replete with measures of diversity, particularly in biology and economics (e.g., Magurran, 2004). The Shannon diversity, H, of a fingerprint was defined as (Shannon, 1948)

$$H = -\sum_{i=1}^{S} p_i \ln p_i$$

where $S = 20$ was the number of task domains and p_i corresponded to the ith domain proportion. As Shannon diversity is negatively biased (i.e., it tends to underestimate diversity), as proposed by Chao and Shen (2003), the correction term $(S-1)/(2n)$ was added to H, where n was the number of observations used in the determination of the fingerprint. This correction is suggested if $n > S$; thus, voxels with fewer than 21 observations were excluded from further analysis.

Functional fingerprint highest density interval

Functional fingerprints and respective diversity values were determined for all voxels/regions with more than 20 observations. Although this threshold allowed us to apply bias correction as described above, not all voxels/regions contained the same number of observations. Consequently, we determined the range of possible estimates of functional fingerprints and diversity via a bootstrapping procedure. For fingerprints, bootstrap resampling was performed on the set of observations defining the fingerprint. Specifically, the observed proportions for each task domain were used to estimate the

Table 1
Network definitions.

Network	Abbreviation	Function/label
Fronto-parietal, seeded from the left intraparietal sulcus as in (Toro et al., 2008)	FrontPar_N	Task-positive
Cingulo-parietal, seeded from the anterior cingulate cortex as in (Toro et al., 2008)	CingPar_N	Task-negative
Dorsal Attention (Yeo et al., 2011)	DorsAtt_C	Goal-directed attention
Ventral Attention (Yeo et al., 2011)	VentAtt_C	Stimulus-driven attention
Control (Yeo et al., 2011)	Control_C	Control
Default (Yeo et al., 2011)	Default_C	Default
Fronto-parietal (Dosenbach, et al., 2007)	FrontPar_D	Rapid adaptive control
Cingulo-opercular (Dosenbach et al., 2007)	CingOper_D	Stable set control