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Neural architecture underlying classification of face perception paradigms

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ABSTRACT

We present a novel strategy for deriving a classification system of functional neuroimaging paradigms that relies on hierarchical clustering of experiments archived in the BrainMap database. The goal of our proof-of-concept application was to examine the underlying neural architecture of the face perception literature from a meta-analytic perspective, as these studies include a wide range of tasks. Task-based results exhibiting similar activation patterns were grouped as similar, while tasks activating different brain networks were classified as functionally distinct. We identified four sub-classes of face tasks: (1) Visuospatial Attention and Visuomotor Coordination to Faces, (2) Perception and Recognition of Faces, (3) Social Processing and Episodic Recall of Faces, and (4) Face Naming and Lexical Retrieval. Interpretation of these sub-classes supports an extension of a well-known model of face perception to include a core system for visual analysis and extended systems for personal information, emotion, and salience processing. Overall, these results demonstrate that a large-scale data mining approach can inform the evolution of theoretical cognitive models by probing the range of behavioral manipulations across experimental tasks.

Introduction

As more resources are being developed and deployed for the management, sharing, and meta-analysis of “big data” in neuroimaging, the development of knowledge representation systems has likewise accelerated to enable objective and succinct descriptions of these data, including neurotechnological, neuroanatomical, and cognitive parameters. However, cognitive data descriptors are relatively underdeveloped compared to those from the neurotechnological and neuroanatomical domains. That is, as a community we are relatively more confident regarding data annotations differentiating sub-class or type of *MRI scan* (e.g., T2* or EPI images) or *brain structure* (e.g., hippocampus or amygdala) than in differentiating data that relates to *memory* (e.g., episodic or working). Nevertheless, semantic representation of cognitive and perceptual mental processes is a necessary component of large-scale, community-wide, and consensus-based mapping of structure–function correspondences in the human brain. Such a representation must include the full and robust definitions of mental processes; however, the identification and standardization of terms we use to describe the multitude and diversity of cognitive and perceptual functions is an inexact science. As a result, many alternative and often competitive terminologies exist. With the rise of high profile, high-impact projects such as the Human Connectome Project (Van Essen et al., 2013; Toga et al., 2012), the BRAIN Initiative (BRAIN Working Group, 2014), the Human Brain Project (Markram, 2012), and the RDoCs framework (Insel et al., 2010), the need for knowledge representations of cognitive aspects of neuroscience data has reached a critical point. Our community goal of mapping the human brain will surely require definition and standardization of the terms that are used to describe human thought and mental processes, as well as the behavioral tasks used to elicit them during neuroscience experiments.

Here, we propose and validate a strategy for deriving a classification system of functional neuroimaging paradigms using a proof-of-concept

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application. Our aim was to develop a meta-analytic data mining approach for paradigm classification based on neurobiological evidence provided by functional activation patterns, with the intent that such a strategy may mitigate the challenges associated with a lack of paradigm-related semantic consensus within a given domain. The overall premise of this work is that differences in activation patterns across studies should be captured and leveraged as they indicate meaningful segregations in brain function. Under this premise, tasks activating similar brain networks should be grouped as functionally similar in a cognitive schema, while tasks demonstrating differential activation patterns should be classified as functionally distinct.

As an exemplar domain, we demonstrate our approach in the context of face discrimination, as this category of neuroimaging tasks is highly heterogeneous and commonly employed across numerous perceptual, cognitive, and affective studies in both healthy and diseased populations. These studies broadly include visual stimulus presentation of human faces in which participants passively view faces or actively discriminate one or more aspects or features of face presentation (e.g., old/new, male/female, and happy/sad/angry/fearful). Faces can be used as stimuli for classical conditioning, lip-reading, and naming tasks, or to cue autobiographical memory retrieval, emotion induction, or social processing. Given the wide scope of face tasks in the literature, our aim was to establish a neuroinformatics procedure capable of objectively decomposing the collective group into meaningful sub-categories. Using meta-analytic data reported across a diverse range of studies archived in the BrainMap database, we sought to determine if multiple functional networks distributed across the brain are differentially recruited for various task paradigms. Our ultimate goal was threefold: to develop a paradigm classification strategy for use by cognitive ontologies, to examine the underlying neural architecture of face perception from a meta-analytic perspective, and, more broadly, to assess whether an evidence-based data mining approach can inform the evolution of existing cognitive models.

Methods

Meta-analytic data extraction and pre-processing

The BrainMap database (Fox and Lancaster, 2002; Laird et al., 2005a, 2011a) currently archives brain activation locations from over 11,900 functional magnetic resonance imaging (fMRI) or positron emission tomography (PET) experiments (from over 2,400 journal articles). These experiments have been manually annotated with metadata that describe the experimental design of each archived study. Our study focused on a subset of tasks within BrainMap that were annotated with the paradigm class of “Face Monitor or Discrimination”; the relevant experiments were identified and downloaded for further analysis using the desktop search engine application, BrainMap *Sleuth* (http://www.brainmap.org/sleuth). Search results were filtered to include only face tasks performed by healthy adults to limit any potential bias due to effects of age, disease, or treatment differences. Information about the specific behavioral task performed by participants in each experiment, along with the experiment name, sample size, and stereotaxic coordinates of activation were exported as a tab-delimited text file. Exported coordinates reported in MNI space (Evans et al., 1993; Collins et al., 1994) were transformed to Talairach space (Talairach and Tournoux, 1988) using the Lancaster transform function *icbm2tal* (Lancaster et al., 2007). icbm2tal was developed using global affine transforms to accommodate spatial disparity between Talairach and MNI coordinates as compared to the earlier mni2tal transform (Brett et al., 2001), and to minimize meta-analytic spatial dissonance due to template differences (Laird et al., 2010). Modeled activation (MA) maps were generated by modeling each coordinate of activation as a spherical Gaussian distribution of uncertainty to represent the probability of activation for each voxel, centered upon the experiment's activation foci (Fig. 1, Step 1). The algorithm includes an estimation of the inter-subject and inter-laboratory variability associated with each experiment, and is weighted by the number of subjects included in each experiment (Eickhoff et al., 2009). The per-experiment MA probability maps were converted into feature vectors of voxel values and concatenated horizontally to form an array of size n experiments by p voxels.

Correlation matrix based hierarchical clustering analysis

After generating the n X p matrix of MA probability maps, we employed a pairwise correlation analysis in which correlation coefficients were calculated for each n experiment compared to every other n experiment, to assess similarity of spatial topography across MA maps. Hence, the n X p array of MA maps was transformed into an n X n correlation matrix that captured the similarity of whole-brain modeled activation images across face discrimination experiments (Fig. 1, Step 2). Experiments within the n X n correlation matrix were subsequently grouped into clusters using hierarchical clustering analysis, an agglomerative unsupervised classifier (Fig. 1, Step 3). Previous implementation of correlation matrix based hierarchical clustering of resting state fMRI data (Liu et al., 2012; Keilholz et al., 2010) and hierarchical clustering of BrainMap-based meta-analytic images (Laird et al., 2011b) demonstrated optimal clustering using the *average* linkage algorithm and $1 - r$ as the distance between clusters, where r is the Pearson's correlation coefficient. Following initial testing for optimal performance, these parameters were adopted in the present study. Notably, Pearson's correlation distance maximizes the effects of direction, rather than magnitude, of the two observational vectors, thus identifying correlated MA maps as being topologically similar and anti-correlated MA maps as dissimilar.

The resultant dendrogram was examined to identify sets of experiments that clustered together. Selecting a clustering solution yielding an optimal parcellation of BrainMap experiments relied on two measures. The cophenetic distance between clusters at a specific model order (i.e., number of clusters) describes the dissimilarity between sub-clusters, and is intrinsically higher at low model orders (e.g., a two-cluster solution). Importantly, the relative difference in cophenetic distances when transitioning from model order x to the next highest model order $x + 1$ can be informative when examining if cluster separation results in vastly different solutions. Therefore, we sought to determine the extent to which increasing model order resulted in substantially different activation patterns respective to each cluster by maximizing the relative difference, d_c, in cophenetic distances c_x and c_{x+1}, as model order, x, increased:

$$d_c = \frac{c_{x+1} - c_x}{c_{x+1}}. \tag{1}$$

Related to the above measure of difference in cophenetic distances is the impact that increasing model order has on separating clusters into sub-clusters of proportionate number of variables (e.g., experiments). Increasing the cluster solution could potentially yield a segregation of experiments in which one sub-cluster dominates with a disproportionately large number of experiments. Therefore, we sought to minimize the effect of cluster segregation by calculating the maximum density of experiment separation. Essentially, we aimed to determine if increasing model order resulted in a disproportionate divergence of experiments. For example, if cluster i_0, consisted of n_0 experiments at model order x, and separated into clusters i_1 and i_2, with n_1 and n_2 experiments, respectively, then the density of experiment separation, d_s is calculated as:

$$d_s = \frac{n_1}{n_0}, n_1 \geq n_2. \tag{2}$$