Do ontological concepts stand up to a meta-analysis of neuroimaging data?

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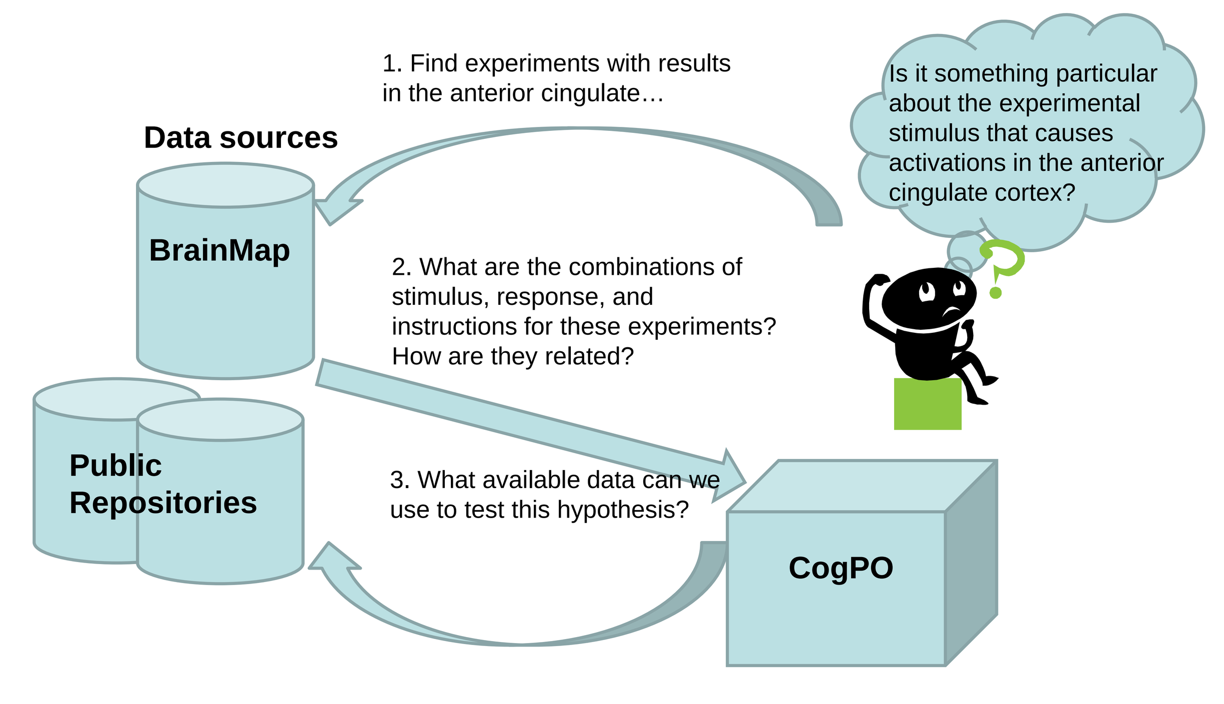
Introduction

The goal of the Cognitive Paradigm Ontology is to provide a basic ontology for the description of cognitive behavioral experiments for use in human PET, fMRI, ERP, and cognitive psychology studies. **Figure 1** below shows an example of a planned use of CogPO (Turner & Laird, 2011). It is not just the description of the experimental methods, but the relationships between different experimental conditions that we aim to represent.



Cognitive paradigms in biomedical research

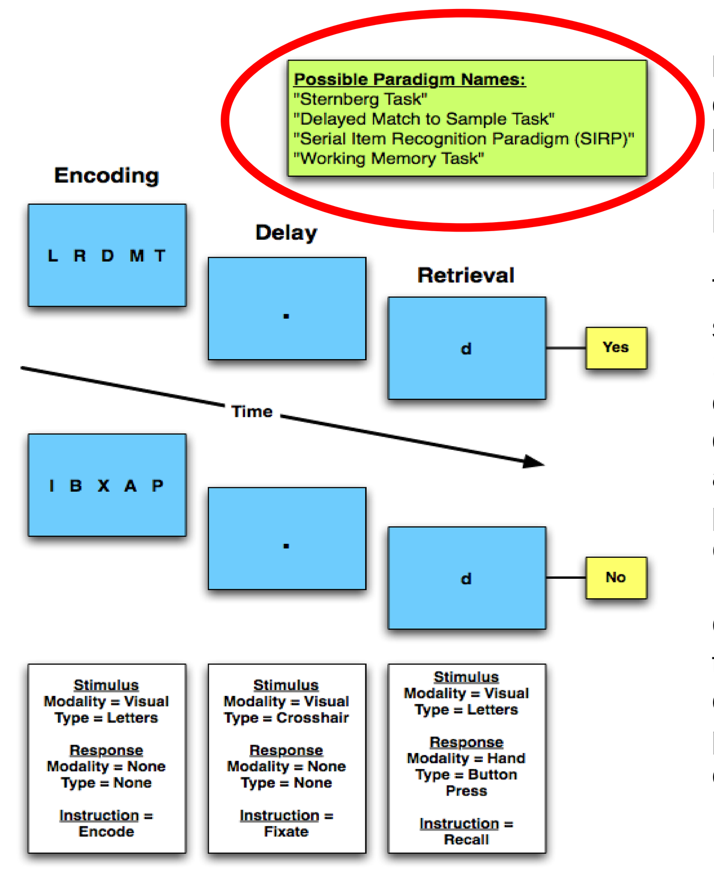


Figure 2. The same paradigm may be called different names in the literature, leading to confusion in interpreting the neural circuitry being activated during task performance.

The BrainMap repository of neuroimaging studies (www.brainmap.org) now has nearly 10,000 experiments stored. Any ontology of cognitive experiments must be able to describe all of these behavioral paradigms, as well as those underlying the datasets in public repositories like XNAT Central, CogAtlas, and the BIRN Data Repository.

Other ontologies can be used to describe the subject populations and their characteristics, or the neuroimaging or physiology methods involved in the experiments.

BrainMap

The BrainMap schema has been in development and use for almost 20 years (Fox et al., 2005). Categorization of paradigms according to the **stimulus**, **response**, and **instructions** which make up each experimental **condition** allows advanced searching for similarities and contrasts.

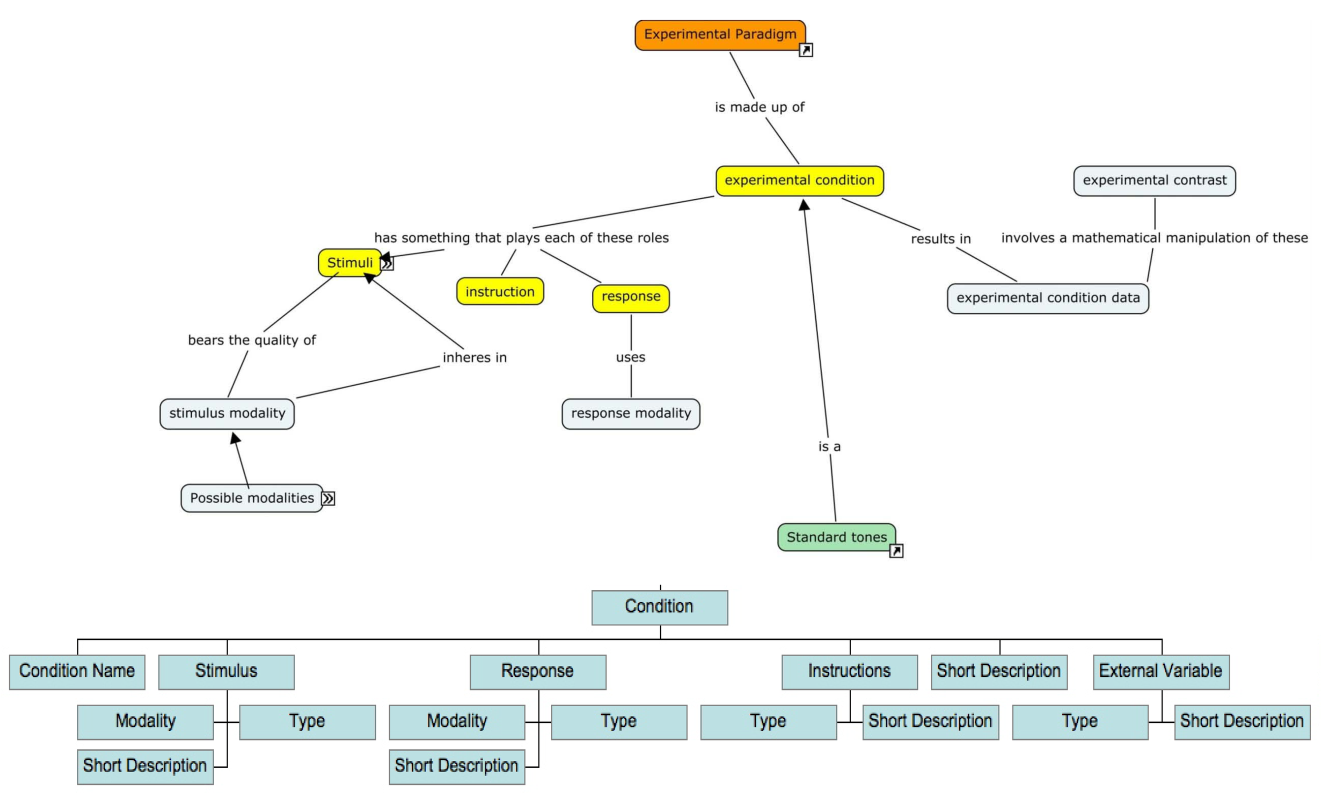


Figure 3. The BrainMap schema for describing each condition within an experiment includes a menu of possible terms for Stimulus Type and Stimulus Modality, and free text for a Short Description. Response and Instructions also have a combination of pre-set terms and free text. The terms allowed in BrainMap are the basis for CogPO.

We used the ontological categorizations in conjunction with meta-analysis of the neuroimaging activation patterns in the BrainMap repository to identify where the ontology provided meaningful categorizations of neuroimaging data, and to highlight concepts and relationships that need refining.

Intrinsic Connectivity Networks

Methods. Peak coordinates from 8,637 published experiments in the BrainMap repository were smoothed using a Gaussian distribution (FWHM=12 mm) to accommodate spatial uncertainty; these smoothed maps provided experiment images as the initial data. Independent component analysis was applied to this 4D data (space X experiment-ID) using MELODIC (Beckmann et al., 2005) in FSL (Smith et al., 2004; Woolrich et al., 2009) to decompose the experiment images into spatially independent components, which represent the major modes of co-activation across the experiments represented in the BrainMap database.

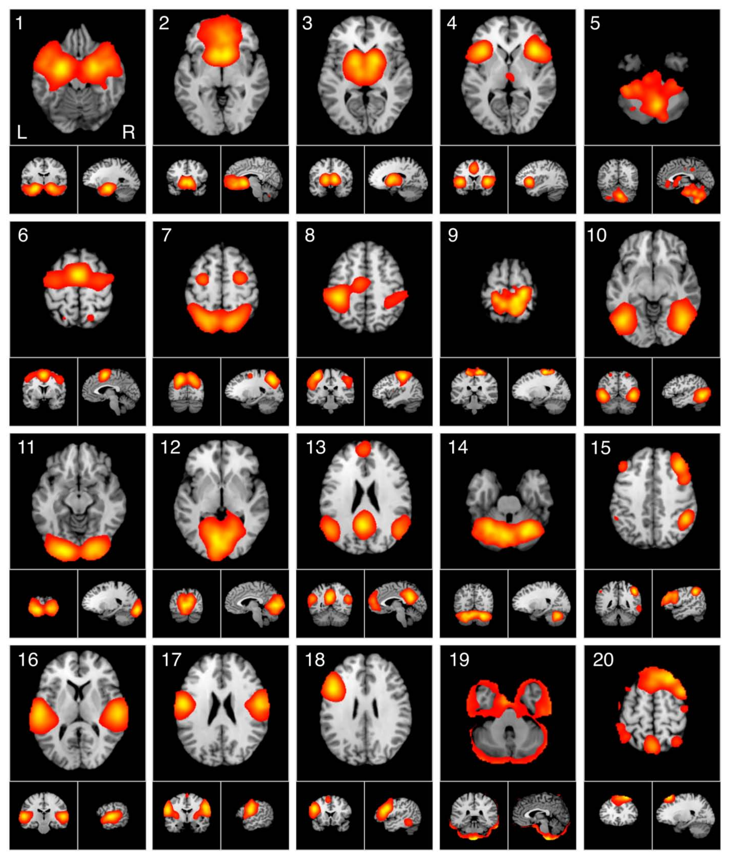


Figure 4. The 20 spatially independent components described in Laird et al., 2011. ICA maps were converted to z statistic images via a normalized mixture-model fit, thresholded at $z > 4$, and viewed in standard (Talairach) brain space.

Along with each spatial map, a corresponding experiment-ID vector was generated that describes how strongly a given component relates to each of the original 8,637 experiment images. Each of the original experiment images were annotated with CogPO terms; the strength of the relationships between different CogPO concepts and the spatial maps was explored through clustering analyses on the weighting coefficients across the experiment images.

Cluster analysis. We present the previous analyses from Laird et al. 2011 for comparison. Those analyses included all 8,637 experiments over all meta-data values and explored Behavioral Domain and Experimental Paradigm as hierarchical clustering variables. For these analyses, a final dataset of 754 combinations of stimulus, stimulus modality, response, response modality, and instructions were included in the hierarchical clustering analyses. Each of these experimental conditions represented the value across the 20 ICNs averaged over as few as one to as many as 73 experiments. Hierarchical cluster analysis (in MATLAB; using 1- Pearson's r as the distance metric, complete linkage using the furthest distance as the clustering method) was performed across both experimental condition and ICN. We then explored the distribution of stimulus types (S), response types (R), Instruction (I), and SxR, SxI, and SxRxI combinations across the clusters.

Behavioral Paradigms vs Intrinsic Connectivity Networks

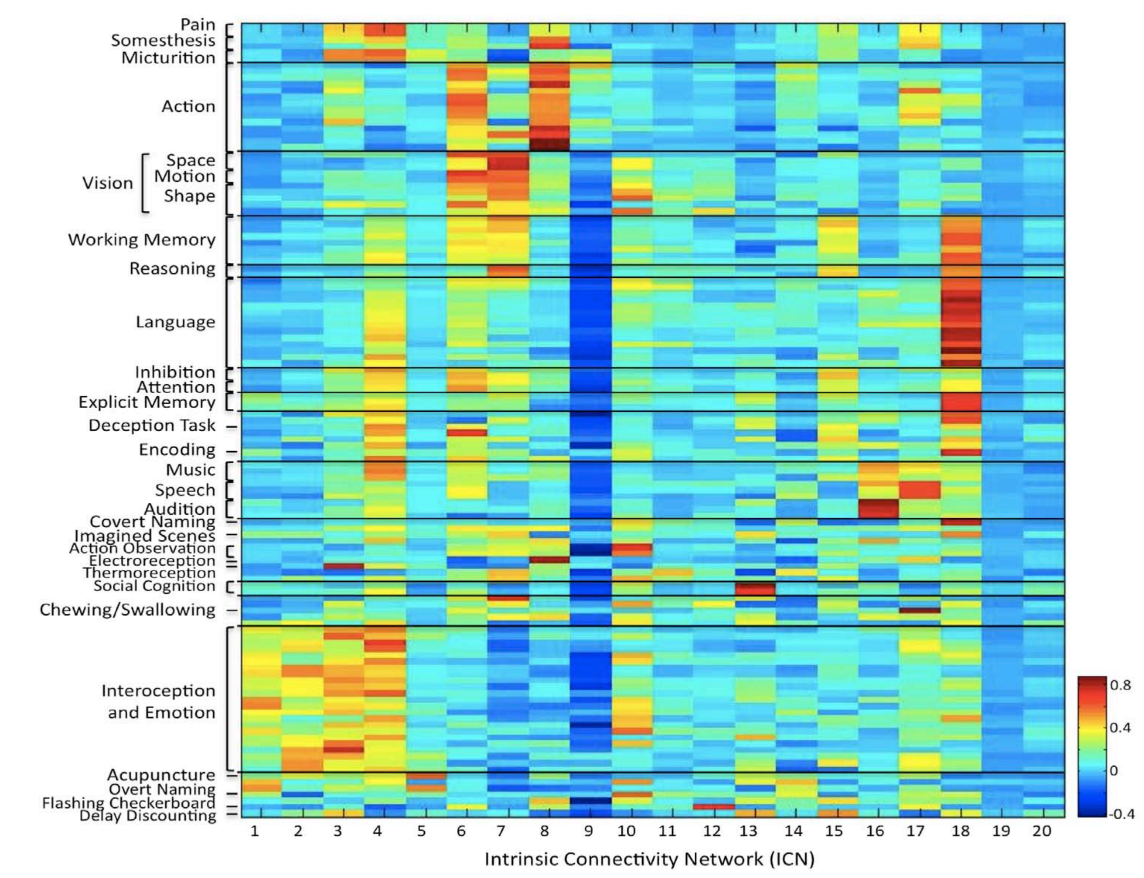
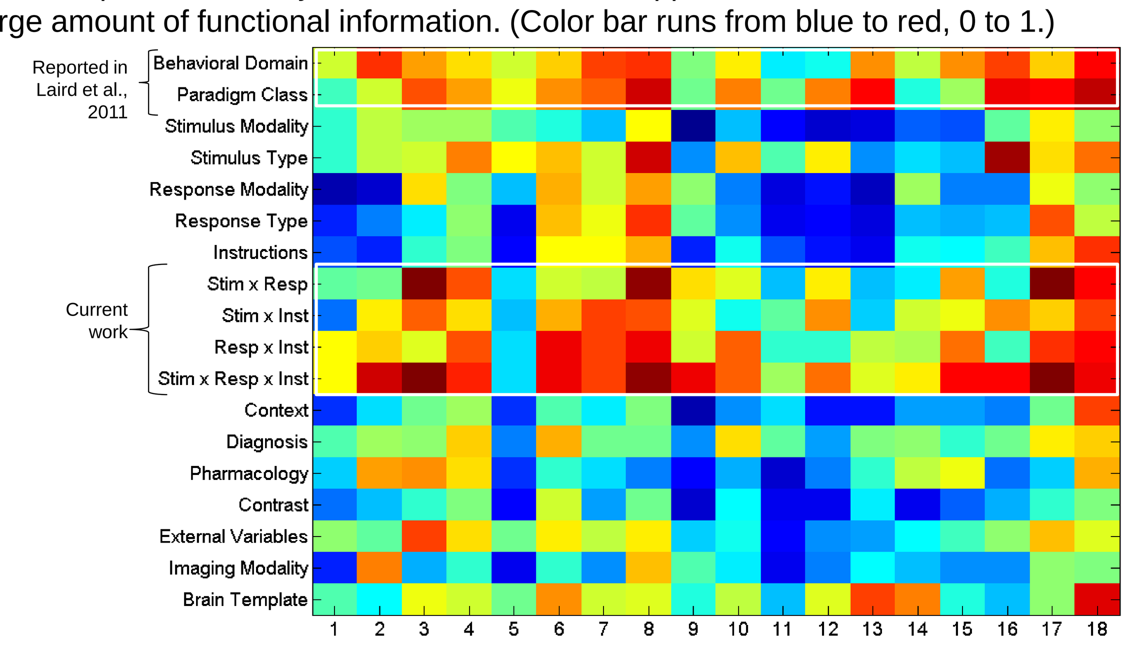


Figure 5 (above). (From Laird et al., 2011). The concatenated metadata matrix for behavioral domains and paradigms, ordered to reflect the groupings set forth by the behavioral- and network-driven hierarchical clustering results.

Figure 6 (below). The maximum across classes of the average loading value within the class was computed for every metadata field, as an approach to determine which fields captured a large amount of functional information. (Color bar runs from blue to red, 0 to 1.)



Experimental Conditions by ICN

Figure 7. Heatmap and dendrogram showing the clusters of ICNs (columns) and experimental conditions (rows). The numbering of the components is as shown in Figure 4 (left). Red indicates positive standardized weightings, green indicates negative. The Experimental Condition clusters are labeled A-H for ease of reference, with colored bars indicating the boundaries.

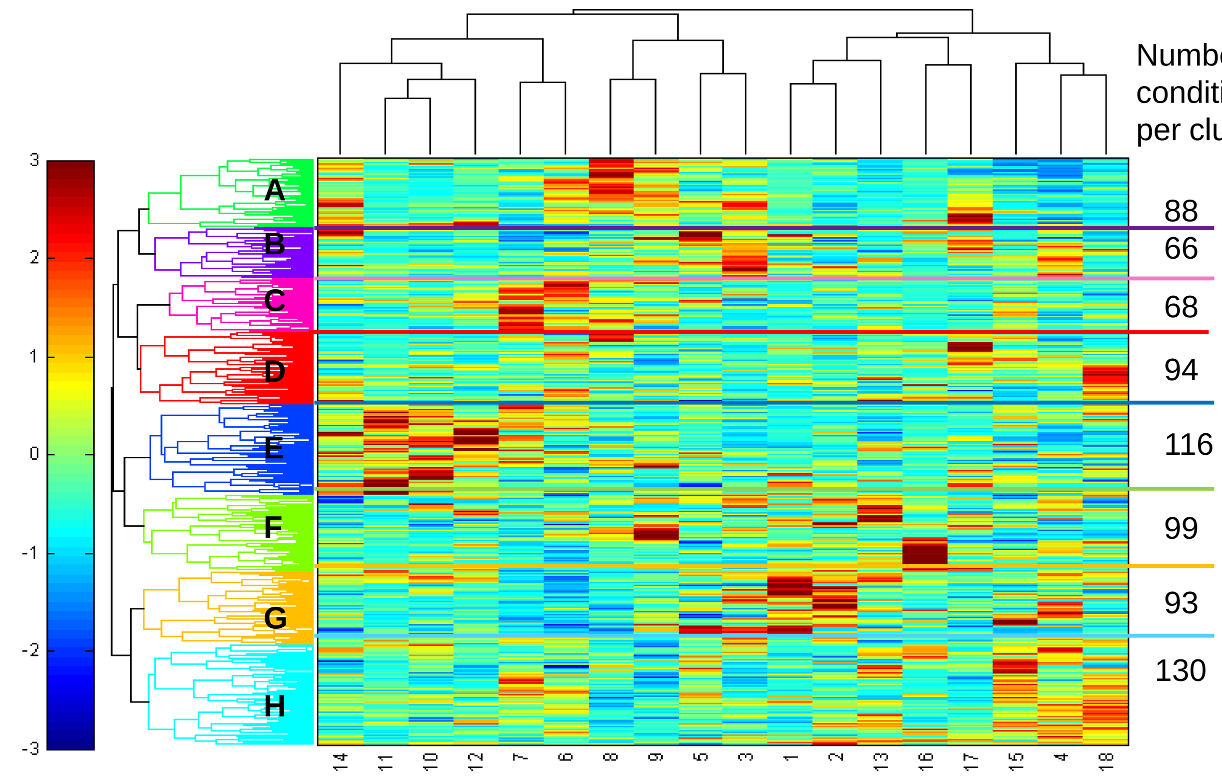


Figure 8. The spatial maps from Figure 4 are arranged by their distance based on experimental conditions. An anatomical arrangement resulted, even though the images themselves were not included in the analysis.

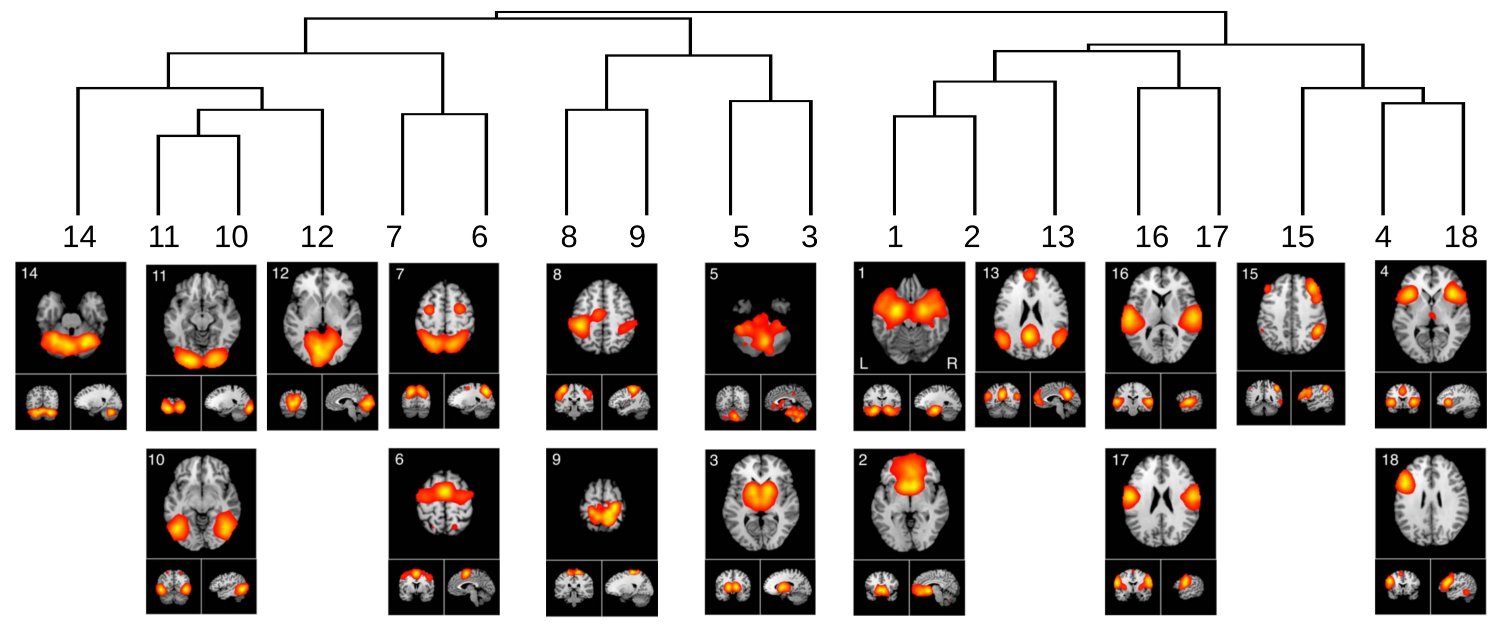
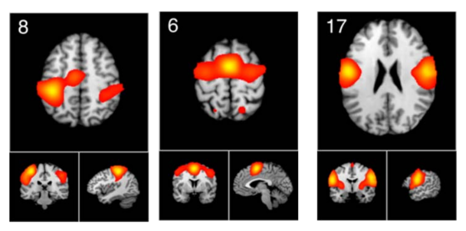
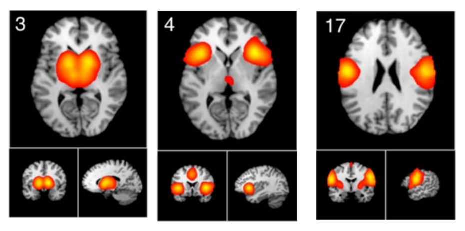


Figure 9. The most heavily weighted spatial components per cluster, along with their most frequent metadata from Stimulus modality, Stimulus, or the SxR, SxI, or RxI combinations. The percent of conditions in that cluster with that metadata value are given. Group E in particular did not have a predominant S, R, or I type, or combinations; its more consistent subclusters should be explored.

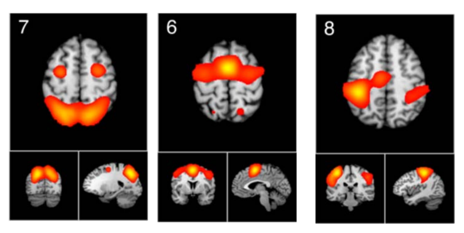
Group A. Hand (49%); Flexion-Ext/Move (15%)



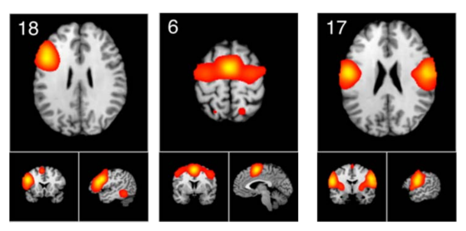
Group B. Heat (9%); No Resp/Attend (18%)



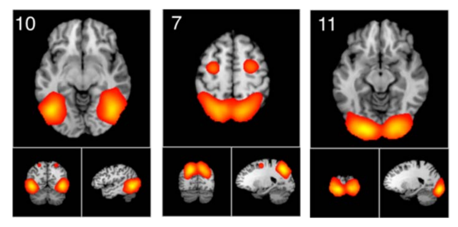
Group C. Visual (84%); Move (42%); Shapes/Button Press (10%)



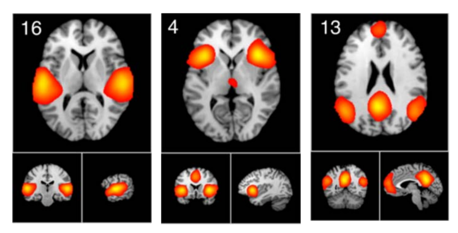
Group D. Speech (39%); Speech/ Generate (8.5%)



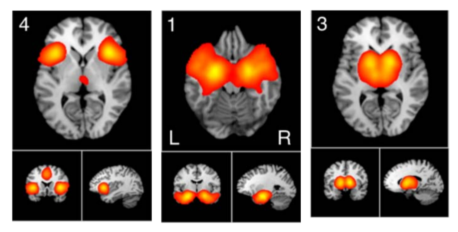
Group E. Visual (84%); Digits/Speech (4%)



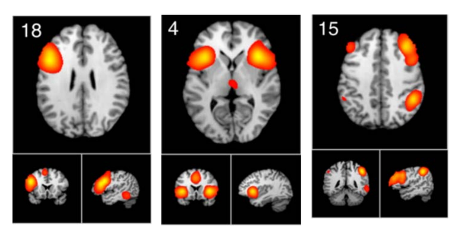
Group F. Auditory (48%); No Resp/Attend (12%)



Group G. Words/Button Press (7%); Button Press/Attend (7%)



Group H. Button Press/Discriminate (10%); Words/Speech (7%)



Conclusions

While the behavioral domain loads heavily on the ICNs, grouping by SRI combinations indicates novel relationships. 1) Including stimulus and response modality as a grouping factor clusters the ICNs by anatomical regions. 2) When SRI combinations are tightly correlated with behavioral domain, the clusters with ICNs are similar (e.g. Move Instructions in Action studies). In behavioral domains in which the SRI combinations are more variable, this level of clustering identifies highly diverse clusters of experimental conditions which load on similar ICNs. This potentially can allow very different experimental paradigms to be related through their experimental conditions.

Citations

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