Capturing high-order interactions in neuroimaging data

Abstract No:

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Introduction:

Unsupervised data analysis approaches have been widely used in recent years and have become instrumental in establishing new research directions impossible with more traditional supervised approaches, such as the study of the default mode network of the brain (Raichle and Snyder, 2007). Growing interest in unsupervised analysis of multi-modal data, multi-subject studies, whole brain activity and other datasets involving multiple interacting variables, have increased demand for multivariate unsupervised techniques (Sui et al., 2011). However there is still relatively little work on the examination of the full relationships among interacting variables in an unsupervised fashion. In this work, we propose a novel approach to address the problem of identifying these higher-order interactions and demonstrate it with an application to a large multi-task fMRI dataset.

Methods:

The crux of our approach is to partition random variables into "factors" based on the mutual information among these variables. Roughly, the approach fills a niche between simpler pairwise clustering and complex graphical models (see Figure 1). To tackle the combinatorial difficulty of searching for high-order interactions, we present a practical method by making choices different from those of graphical models (GM): no detailed structure, approximate independence of factors, and a smoothed objective. We aim at capturing various types of interdependencies among random variables including three cases in the lower part of Figure 1. Since each resulting factor contains random variables that are mutually coregulated, and the whole approach is enabled by a spectral decomposition of the hypercube, we call our approach coregulation analysis via spectra of a hypercube (CASH).

Results:

We extracted features from three well-known paradigms: an auditory sensorimotor task, a Sternberg working memory task and a auditory oddball task using GLM from 68 patients with schizophrenia and 86 controls as part of the Mind Clinical Imaging Consortium (MCIC) study. All details about the tasks and data collection and processing are summarized in Kim et al. (2010). Each of the subject had 29 spatial ICA components which we used as features to factor. When using datasets comprised of complete subject sets for patients as well as for controls, we obtained a factoring of features displayed in Figure 2. Bootstrap analysis of CASH convergence trajectories as well as the dispersion of solutions for the groups of patients and controls show stable and significant difference between these groups (Figure 3). Lower objective values for patients meaning tighter relationship between features supports previous findings of "more similar" activations in schizophrenia patient than controls (Calhoun et al., 2006; Michael et al., 2009) but goes well beyond previous work by incorporating a much richer set of features. For example, a notable feature is that in the patients temporal lobe is grouped with motor areas (factor 1 in Figure 2), whereas in controls it is grouped with the higher cognitive areas (factor 3 in Figure 2). Although we are not working with the data from actively hallucinating subjects, the lack of higher cognitive control over temporal areas in the patients may be indicative of schizophrenia. In controls high-level intrinsic networks co-acting with temporal lobes may be controlling perception of the internal voice (van Lutterveld et al., 2011).

Conclusions:

We have developed a framework for capturing arbitrarily complex, multi-way interactions among random variables based on information theory. Our results are consistent with and extend known findings from univariate and second order-based methods, thus arguing for approaches such as CASH that can capture true higher-order dependencies in datasets from complex domains such as neuroscience.

Modeling and Analysis Methods:

Multivariate modeling

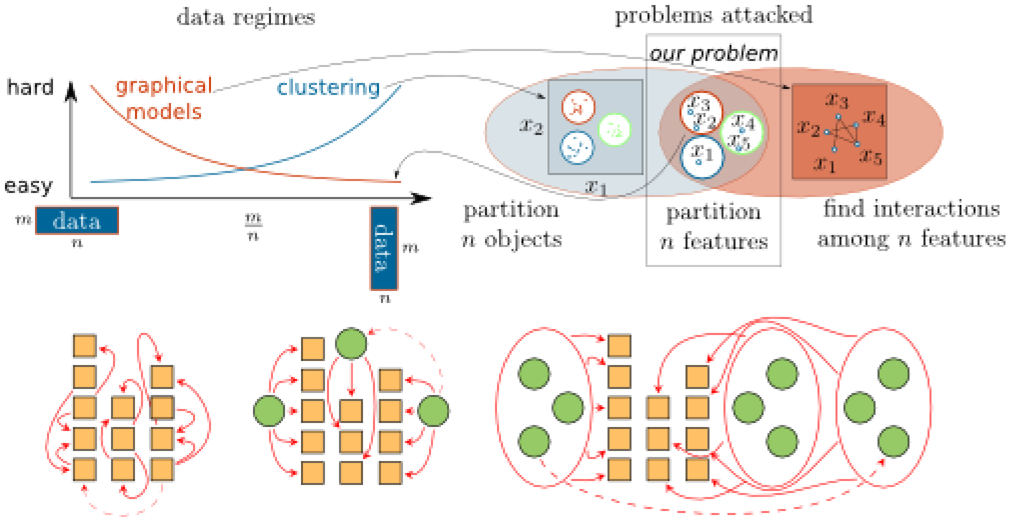


Fig.1: On the top is the niche of our method in the space of clustering and graphical models (GM). The bottom diagrams show Scenarios of interdependence among random variables which are covered by our model. A directed graphical model is shown as an example only and it may as well be an undirected or a mixed type relationship. Solid and dashed arrows denote strong and weak statistical interactions respectively. Squares are the observed random variables and circles are the hidden variables

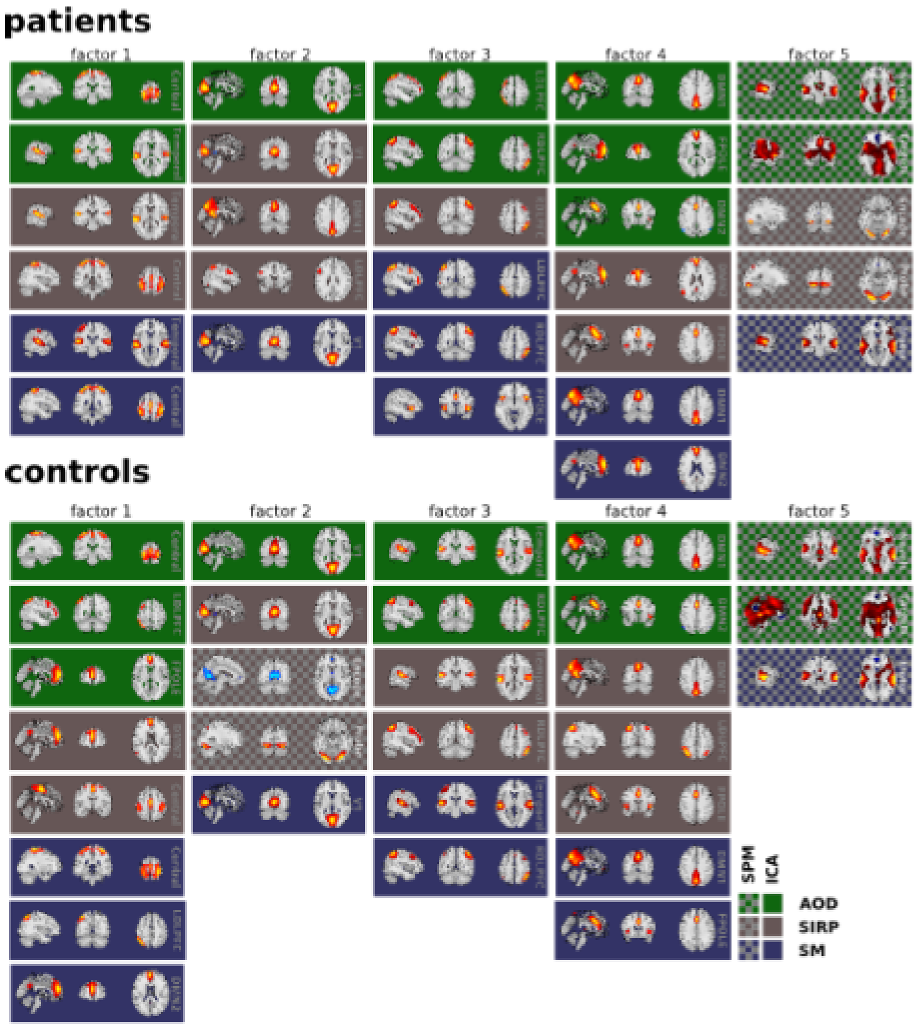
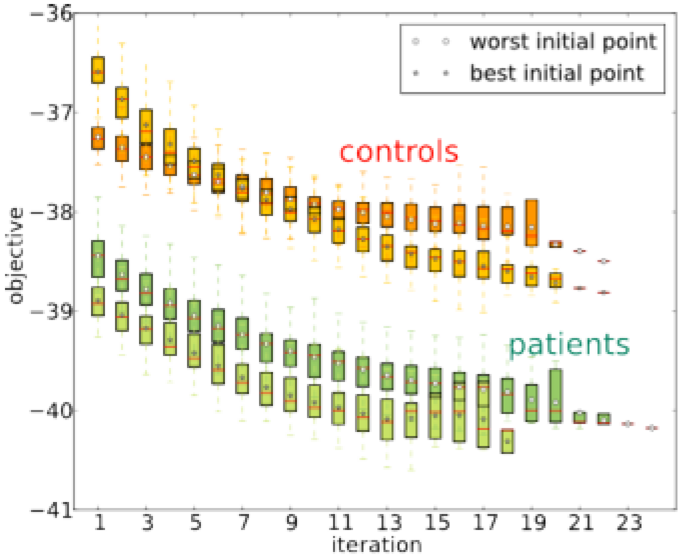


Fig.2: CASH factoring of the 29 features for two groups. Each of the three tasks is denoted with its own color. The solid background denotes features coming from the ICA analysis, and the checkerboard background denotes a feature coming from the SPM analysis.



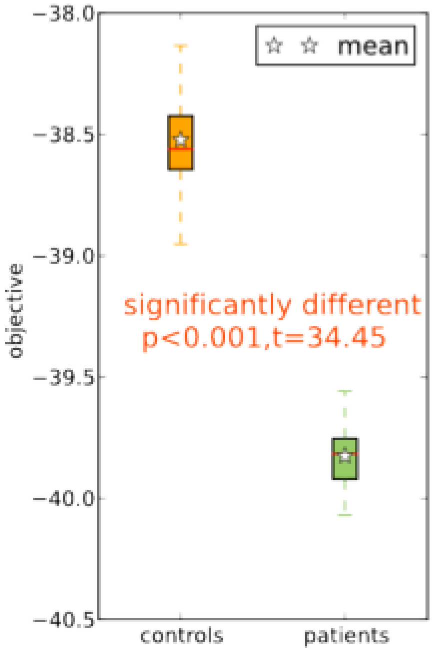


Fig.3: Distribution of the CASH objective values (lower is better) on the multi-task feature dataset - box and whisker (1.5IQR) plots. Top figure summarizes results of the bootstrap analysis of the same dataset re-sampling subjects with replacement 50 times. Trajectories for only two starting points are shown for each group: one that converged to the best solution in the experiment of bottom figure, and one that converged to the worst (the highest objective value). Bottom figure shows distributions of objectives at 50 local minima found by running the algorithm with 50 random starting points using complete datasets

Abstract Information

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