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Comments and Controversies

Combining the tools: Activation- and information-based fMRI analysis

Nikolaus Kriegeskorte* and Peter Bandettini

Section on Functional Imaging Methods, Laboratory of Brain and Cognition, National Institute of Mental Health, Bethesda, MD, USA

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We agree with most of Andreas Kleinschmidt's thoughtful comments and historical remarks (Kleinschmidt, 2007-this issue). Activation- and information-based techniques contribute complementary tools to the fMRI analysis toolbox (see Table 1). They should be used in combination as motivated by neuroscientific inquiry. We should clarify that our somewhat provocative title "Analyzing for information, not activation, to exploit hi-res fMRI" (Kriegeskorte and Bandettini, 2007-this issue) was meant to contrast these fundamentally different concepts, not to suggest that activation-based analysis (Worsley et al., 1992; Friston et al., 1994; Friston et al., 1995) has no place in the toolbox for hi-res fMRI.

Hi-res fMRI: a different regime

In his title, Kleinschmidt poses the question: "Different analysis solutions for different spatial resolutions?" We think this question merits serious consideration and would like to maintain that the spatial resolution of the measurement (among many other factors) does need to be taken into account in deciding the analysis strategy. Upon initial consideration, it may appear that moving to high resolution constitutes merely a quantitative change, with the same analyses equally applicable, but yielding more fine-grained maps. In fact, hi-res fMRI puts us in an altogether different regime in terms of both the neuroscientific questions to be addressed and the statistical analyses appropriate.

Most fundamentally for the neuroscientist, hi-res fMRI promises access to columnar-level information. This motivates shifting the goal of analysis from the localization of activated functional regions to the characterization of their intrinsic representations, i.e. from activation to information. More practically, hi-res fMRI confronts us with the four challenges we describe (Kriegeskorte and Bandettini, 2007-this issue). As Kleinschmidt suggests, these challenges seem familiar from standard-resolution fMRI. But they take on a novel quality in hi-res fMRI because of their greater severity and combined effect. To recapitulate: at high resolution, fMRI patterns may not provide accurate images of neuronal activity patterns (challenge 1); the noise (challenge 2) and the number of voxels (challenge 3) are substantially greater; finally, Talairach or a cortex-based common space cannot accurately relate hi-res voxels between subjects for group analysis (challenge 4). Crucially, the conventional method of dealing with the milder versions of these challenges at standard resolution, i.e. smoothing or local averaging, would defy the purpose of hi-res fMRI: smoothing would decrease the effective resolution.

To clarify the core of our argument for the synergy between hi-res fMRI and information-based analysis:

1. Smoothing removes fine-grained pattern information from the data and thus defies the main purpose of hi-res fMRI.
2. Without local combination of single-voxel signals (as provided by smoothing), the four challenges (already substantial at standard resolution) can prove prohibitive in hi-res fMRI.
3. Multivariate statistics summarizing local response-pattern information provide an alternative means of locally combining single-voxel signals without removing the neuroscientifically valuable fine-grained pattern information (as smoothing would).

Combining the tools

Independently of spatial resolution, we think that the widespread 2-step strategy, consisting in a mapping of the entire imaged volume (top 2 rows of Table 1) followed by selective region of interest (ROI) analysis (bottom 3 rows), continues to have great potential. Mapping provides a more exploratory, wider view of the data and can lead to the discovery of new regions involved in a given process. Selective ROI analysis provides a complementary, more hypothesis-driven view of a detail of the functional architecture, focusing statistical power to reveal a given region's functional properties. This 2-step approach can either be based on a single experiment (using independent contrasts for the mapping that defines the ROI and the selective ROI analysis) or on a localizer experiment (for defining the ROI) and a main experiment (to which selective ROI analysis is applied). These two variants are discussed in the exchange between Friston et al. (2006) and Saxe et al. (2006).

* Corresponding author.
E-mail address: kriegeskorten@mail.nih.gov (N. Kriegeskorte).

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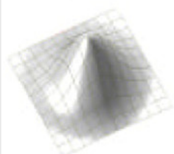
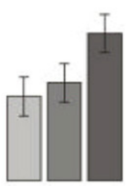
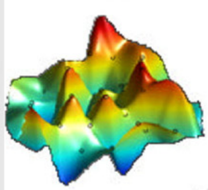
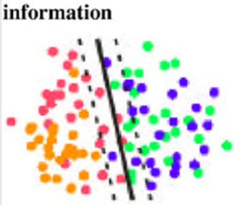
Table 1
Complementary activation- and information-based fMRI analysis tools

	Goal of the analysis	Method	Problems	Promise
Whole-slab mapping	**Finding activated regions** 	Activation-based mapping: univariate statistics applied to smoothed data	Insensitive to fine-grained pattern information	Localization of extended homogeneous activations
	Finding informative regions 	Information-based mapping: multivariate searchlight statistics applied to unsmoothed data	Less sensitive to extended activations	Localization of regions carrying a particular type of fine-grained pattern information
Selective ROI analysis (independent tests only[i])	**Characterizing ROI activation** 	Univariate analyses on ROI-average time courses	Insensitive to fine-grained pattern information	Characterization of the overall "involvement" of a region in a given process
	Visualizing fine-grained ROI activity patterns 	Univariate mapping on unsmoothed data	FMRI patterns may not be accurate images of neural patterns, sensitivity-taxing multiple-comparisons challenge (ROI: ok; whole slab: prohibitive for hi-res)	Visualization of fine-grained activity patterns, characterization of encoding dimensions and columnar spatial organization
	Characterizing ROI information 	Multivariate analysis of unsmoothed data: multivariate pattern-difference testing, classification analysis, multidimensional scaling, etc.	Sensitivity-taxing curse of dimensionality (ROI: ok; whole slab: prohibitive for hi-res)	Characterization of the overall information content of the intrinsic representations of a region

[i] We note that ROI definition is a data preselection process sensitive not only to the effect of interest but also to noise. Independent data are therefore needed to test or visualize any ROI effect related to the mapping contrast the ROI has been defined by.

Kleinschmidt proposes a particular 2-step strategy, in which information-based analysis serves as an exploratory first pass and subsequent univariate mapping provides a means of visualizing the underlying activity patterns. We find this particular 2-step strategy very useful in our own research. For example, an information-based searchlight mapping (Kriegeskorte et al., 2006) can serve to find an informative region in hi-res fMRI data. A univariate mapping on unsmoothed data can then be used to visualize that region's intrinsic activity patterns. (The icon in row 4 of Table 1 shows the response of an anterior temporal region, defined by searchlight mapping, to visual presentation of a particular face photo.) In this context, the univariate mapping benefits from the small size of the ROI to be mapped, alleviating the multiple comparisons problem. Caution is required in interpreting the spatial structure of these fine-grained activity patterns, because hi-res fMRI patterns may not provide accurate images of neuronal activity patterns. Nevertheless a difference between two fMRI patterns does imply a difference between the corresponding neuronal patterns. Such fMRI pattern effects, assessed by multivariate tests and pattern classification analyses, indicate neuronal pattern information distinguishing the contrasted experimental conditions.

Other combinations of multivariate and univariate analysis appear equally promising. Activation- and/or information-based mapping can be used for ROI definition, followed by activation- and/or information-based ROI analyses. The classical 2-step strategy consists in activation-based mapping for ROI definition followed by activation-based ROI analysis. This is still a very useful tool, whenever fine-grained pattern information is not of interest. Hi-res fMRI will not be needed in that case. An example of a region of interest best defined by an activation-based mapping is the fusiform face area (Kanwisher et al., 1997). A separate experiment tapping into the intrinsic representations of the region would lend itself to information-based ROI analysis. As Kleinschmidt suggests, the best strategy will depend on the particulars of the experiment and on the neuroscientific question to be addressed.

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