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Pattern classification precedes region-average hemodynamic response in early visual cortex

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ABSTRACT

How quickly can information about the neural response to a visual stimulus be detected in the hemodynamic response measured using fMRI? Multi-voxel pattern analysis (MVPA) uses pattern classification to detect subtle stimulus-specific information from patterns of responses among voxels, including information that cannot be detected in the average response across a given brain region. Here we use MVPA in combination with rapid temporal sampling of the fMRI signal to investigate the temporal evolution of classification accuracy and its relationship to the average regional hemodynamic response. In primary visual cortex (V1) stimulus information can be detected in the pattern of voxel responses more than a second before the average hemodynamic response of V1 deviates from baseline, and classification accuracy peaks before the peak of the average hemodynamic response. Both of these effects are restricted to early visual cortex, with higher level areas showing no difference or, in some cases, the opposite temporal relationship. These results have methodological implications for fMRI studies using MVPA because they demonstrate that information can be decoded from hemodynamic activity more quickly than previously assumed.

Introduction

Although the neural activity in visual cortex associated with a visual task such as category recognition begins within a few hundred milliseconds after stimulus presentation (Rust and Dicarlo, 2010), associated change in blood flow measured with functional magnetic resonance imaging (fMRI), known as the hemodynamic response (HR), begins seconds later, and evolves over the course of several seconds, originating in a constrained spatial region, and spreading outward from that point while rising in amplitude (Shmuel et al., 2007). The complex spatiotemporal dynamics of the HR make it difficult to predict when the maximum amount of information about neural activity should be recoverable from the signal. Moreover, the time at which maximal information about brain activity is recoverable may not be the same in different types of analyses or different brain regions. Because knowledge of when maximal information is recoverable from fMRI data is of great utility for optimizing experimental designs and analyses, we undertook a systematic investigation of the timecourse of information availability in the HR.

There are two types of analyses commonly performed on fMRI data: univariate and multivariate. In univariate analyses, a general linear model (GLM) is applied to each voxel individually. By contrast, multivariate pattern analyses (MVPA) of fMRI data take into account relationships in the activity of multiple voxels. Several recent reports have begun to investigate the timecourse of MVPA classification accuracy during a range of cognitive tasks, showing that although the MVPA timecourse roughly tracks the region-average HR timecourse, classification accuracy can have temporal dynamics that differ from the region-average HR (Bode and Haynes, 2009; Greenberg et al., 2010). In fact, under certain conditions, accurate classification can persist even after the region-average HR has returned to baseline (Harrison and Tong, 2009).

We hypothesized that the reverse might also be the case, namely that HR patterns between voxels in a region would be able to support MVPA classification *prior* to a significant rise in the region-average HR. We will call this the "early onset" hypothesis. This hypothesis could be true if the HRs of individual voxels deviated reliably from baseline early in the timecourse, without being uniform enough to cause the region-wide average to deviate from baseline. Similarly, we hypothesized that peak classification would not always occur at the same time as the peak of the region-average HR. We will refer to this as the "early peak" hypothesis. In univariate analyses, peak region-average HR will by definition yield the largest difference between conditions and hence the largest effect size, but this is not the case for MVPA, where HR patterns could potentially contain more information about experimental conditions at timepoints before (or after) the peak region-average HR. This could be the case,

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for example, if the patterns were made less informative by the spatial spreading of blood through the capillary bed that may occur as the HR approaches its peak.

We tested early onset and early peak hypotheses in a number of functionally defined regions in visual cortex. In order to characterize the timecourse of the region-average HR and classification accuracy as precisely as possible, we collected fMRI data over the occipital and temporal lobes at a high temporal resolution (one acquisition = 739 ms), using a slow event-related design, while participants viewed pictures of faces and houses. We analyzed stimulus category classification at each acquisition and compared classification accuracy to the region-average HR within each predefined ROI. We find that both the onset (first above-chance classification) and peak (most statistically significant classification) of the MVPA analysis precede the onset (first significant deviation from baseline) and peak (most statistically significant increase from baseline) of the region-average HR in V1, but not in other visual areas.

Methods

Participants

11 participants (mean age = 26.5, five female) were recruited from Dartmouth College. All participants had normal or corrected-to-normal vision and, prior to participating, gave written, informed consent under a protocol approved by the Dartmouth Committee for the Protection of Human Subjects.

Experimental design

During each experimental run, participants viewed images of human faces and houses (10 of each) from the stimulus set used by Haxby and colleagues (Haxby et al., 2001). Of the 10 faces, five were males. All pictures were presented foveally within a 7.6° (degrees of visual angle) by 8.3° rectangular window. On average, house stimuli were ~6.0° wide by ~3.8° tall, and face stimuli were ~4.5° wide by ~7.6° tall.

We used a slow event-related design, in which subjects were presented with a single stimulus for one acquisition (739 ms), which was always followed by an inter-stimulus interval spanning 14 acquisitions (10.3 s). Subjects were instructed to perform a one-back task during which they pressed a button whenever the currently presented stimulus was identical to the previously presented stimulus. This one-back task was employed to ensure that subjects remained alert and awake. All 20 stimuli were shown in a random order once per run, with an additional three being selected randomly for "same" trials, where the stimulus was identical to the preceding stimulus. "Same" trials were excluded from the analysis. With a total of 23 presentations, each run had 360 acquisitions. 10 runs were collected per subject. Stimulus timing and presentation were controlled using MATLAB (The Mathworks; Natick, MA) in combination with Psychophysics Toolbox Version 3 Software (Brainard, 1997; Pelli, 1997). Stimuli were projected onto a screen behind the scanner bore which subjects viewed through a mirror mounted on the head coil.

Data acquisition

Images were acquired with a Philips 3 T Achieva Intera scanner with an eight-channel head coil at the Dartmouth Brain Imaging Center. In order to maximize the temporal resolution of the acquired volumes, we used a rapid scanning protocol, PRESTO-SENSE (Golay et al., 2000), two-shot acquisition scheme with an EPI factor of 17, which allowed us to acquire a partial brain volume every 739 ms (17 axially-oriented slices, 3.0 × 3.0 mm in-plane voxel resolution, 3 mm slice thickness, no gap, interleaved slice acquisition, FOV = 240 × 240 × 51, TR = 21 ms per slice, TE = 14 ms (effective TE = 35 ms), flip angle = 10°, acquired matrix size = 80 × 63, reconstructed matrix size (zero filled) = 80 × 80, P reduction (RL) sense factor of 2, S reduction (FH) sense factor of 1). It should be noted that the acquired matrix size is not what one might expect mathematically. This is because the PHILIPS software attempts to protect the user from SENSE artifacts by enlarging the FOV before SENSE is applied. Without SENSE, the FOV is 240. However, at SENSE R = 2, the value is 129 and not the expected 120 (240/2). Once the image is reconstructed internally, it is cropped to the desired FOV of 240 (instead of 2 * 129 = 258) and the resulting images have a matrix dimension of 63 voxels.

This partial brain volume covered most of the occipital lobes, including all of retinotopic cortex, and parts of the temporal lobes, including lateral occipital cortex (LOC), the occipital face area (OFA), the fusiform face area (FFA), and the parahippocampal place area (PPA). 2 dummy scan acquisitions (~1.5 s) followed by 14 partial volume acquisitions (~10 s) of blank stimuli were collected at the beginning of every scan. High-resolution structural T1-weighted MPRAGE full-brain scans were also acquired for each subject (160 sagittal slices, 0.94 × 0.94 mm in-plane voxel resolution, 1 mm slice thickness, acquired matrix size = 256 × 232, reconstructed matrix size = 256 × 256, FOV = 240 × 240 × 160, TR/TE = 9.9/4.6 ms, flip angle = 8°). This high-resolution scan and scans collected with the same parameters during other sessions were used to construct flattened cortical meshes for retinotopic mapping. A T1-weighted coplanar anatomical image with the same slice orientation as the PRESTO data was also collected. This image was used to aid co-registration of the high-resolution anatomical scan to the functional data.

Localization of regions of interest

We performed retinotopic mapping using 22.5° rotating monochromatic checkerboard bowties. Intact and scrambled objects were used for localizing LOC (Kourtzi and Kanwisher, 2001). In order to localize areas OFA, FFA and PPA, we contrasted short (2 s) dynamic videos of non-translationally moving objects and scenes with analogous videos of faces (Fox et al., 2009). All localization data were acquired during separate scanning sessions using standard fMRI EPI acquisition sequences. Functional mapping was conducted using procedures described previously (Caplovitz and Tse, 2010; Sereno et al., 1995; Slotnick and Yantis, 2003).

Polar angle representation in visual cortex was measured using two symmetrical wedges of a black and white polar checkerboard grating flickering at 8 Hz (Sereno et al., 1995; Slotnick and Yantis, 2003). Each wedge subtended 22.5° of 360° and occupied a given location for one TR (2000 ms) before moving to the adjacent location in a clockwise or counter-clockwise manner (direction alternated across runs). Cortical representation of eccentricity was measured using expanding concentric checkerboard-patterned rings flickering at 8 Hz that each spanned ~1° of visual angle in ring width. For every TR, a given ring was replaced by its outward neighbor, except that the outermost ring was replaced by the innermost ring at the end of the cycle. This process was repeated until the end of the run. For each participant, five runs of each direction were collected for the wedge stimulus and three runs were collected for the concentric rings. Retinotopic areas (V1d, V1v V2d, V2v, V3d, V3v, V4v and V3A/B) were defined as masks on the basis of standard criteria (Sereno et al., 1995), assuming a contralateral quadrant representation for V1d, V1v, V2d, V2v, V3d and V3v, and a contralateral hemifield representation for V4v/VO1 and V3A/B (Tootell et al., 1997). Visual areas V1, V2, V3 and V3A/B were created by merging the dorsally and ventrally defined regions of each respective area. V4v and the hemifield representation just anterior to it, called VO1 (Brewer et al., 2005), were combined because the border between these regions was not distinct in most subjects.

Retinotopic mapping, cortical reconstruction and volumetric segmentation, as well as cortical inflation and flattening, were performed using the FreeSurfer image analysis suite (Dale et al., 1999; Fischl et al., 1999). Once anatomical maps of the occipital lobes were flattened using