Linking visual perception with human brain activity

David J Heeger

The past year has seen great advances in the use of functional magnetic resonance imaging (fMRI) to study the functional organization of the human visual cortex, to measure the neuronal correlates of visual perception, and to test computational theories of vision. Activity in particular visual brain areas, as measured with fMRI, has been found to correlate with psychophysical performance, with visual attention, and with subjective perceptual experience.

Addresses
Department of Psychology, Jordan Hall, Building 420, Stanford University, Stanford, California 94305, USA;
e-mail: heeger@stanford.edu

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Abbreviations

d′	discriminability index
fMRI	functional magnetic resonance imaging
MT+	human homolog of monkey MT; also called V5
V1	primary visual cortex

Introduction

The vast majority of neuroimaging experiments have focused on which parts of the brain respond to a particular sensory stimulus or are active during the performance of a particular cognitive or perceptual task. Although this has been an important first step, perception and cognition depend not only on which brain areas are active, but also on how neuronal activity within each of those areas varies over space and time. Functional magnetic resonance imaging (fMRI) is now being used routinely to measure variations in the level of brain activity with a spatial resolution of several millimeters and a temporal resolution of several seconds. This technological advance is enabling a new era of computational neuroimaging research [1••], complementary to electrophysiology in awake behaving monkeys [2•], for exploring the relationship between brain and behavior in humans. Here, I review quantitative fMRI methods and summarize some recent results that illustrate the promise of this new approach.

fMRI methods

Two main paradigms have been adopted for computational neuroimaging experiments: periodic and event-related. I will use examples from my lab to demonstrate the reliability and sensitivity of these two types of measurement.

Periodic paradigm

In the periodic paradigm, the modulation of brain activity is measured as the stimulus or task alternates between two states. A sequence of functional images is acquired during each scan. For a given fMRI voxel, corresponding to a small (e.g. $1 \times 1 \times 4$ mm) brain volume, the image intensity changes over time and comprises a time-series of data. The fMRI responses are quantified by making three calculations: first, dividing each voxel's time-series by its mean intensity to convert from arbitrary (image intensity) units to units of fractional signal change; second, averaging the resulting time-series over the set of voxels corresponding to a predefined visual area (see below); and then, third, calculating the amplitude and phase of the best fitting sinusoid with a period equal to that of the stimulus/task alternations (Figure 1a).

To control for a subject's attentional state, they are typically required to perform a series of trials of a difficult perceptual task throughout each fMRI scan. Each trial of the task might consist of two brief (e.g. 500 ms) stimulus intervals followed by a brief (e.g. 750 ms) response interval. Alternating brief stimulus presentations with blank intervals in this way has the added benefit of minimizing any effects of adaptation by visual neurons.

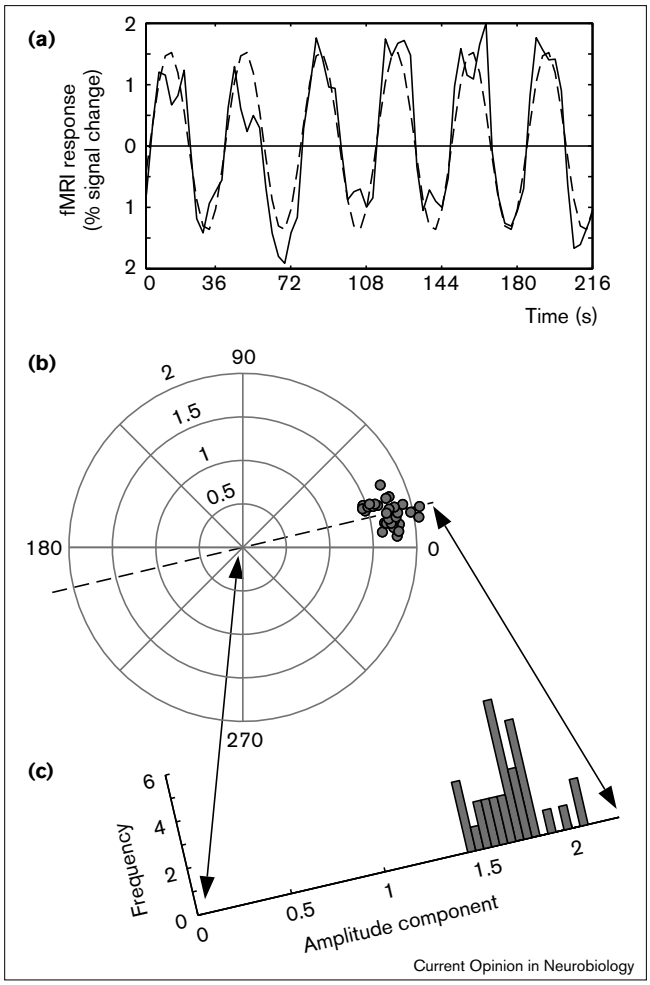
The data in Figure 1, for example, represent modulations in brain activity in primary visual cortex (V1) while a subject viewed stimuli that alternated between high and low contrasts. Throughout each scan, the subject performed a contrast discrimination task, first discriminating between stimuli with contrasts of 90% and 92%, and then discriminating between a uniform gray field (0% contrast) and a 0.8% contrast stimulus. Figure 1a shows that the fMRI signal increases for the higher contrasts, and then decreases for the lower contrasts. This is to be expected because the responses of most V1 neurons increase monotonically with contrast. Parts b and c of Figure 1 plot 30 repeated measurements in the same subject, and under identical conditions. The resulting fMRI data are reliable, tightly clustered and well characterized by a normal distribution.

Event-related paradigm

In an event-related experiment, a particular stimulus is presented for a short period of time (e.g. 500 ms), the subject makes a perceptual judgement based on the stimulus presentation, and then remains idle for a time period (e.g. 14.5 s) sufficient to allow the fMRI signal to subside before the next trial. Two or more different trial types are randomly interleaved during each scan. The data are analyzed by, first, dividing each voxel's time-series by its mean intensity, second, splitting the resulting time series at each voxel into a collection of shorter (e.g. 15 s) epochs that each correspond to a particular trial, and finally, averaging over all repeats of each of the trial types and over all voxels within one of the identified visual areas.

Figure 2 plots V1 responses from a contrast detection experiment: on half the trials (randomly interleaved), a

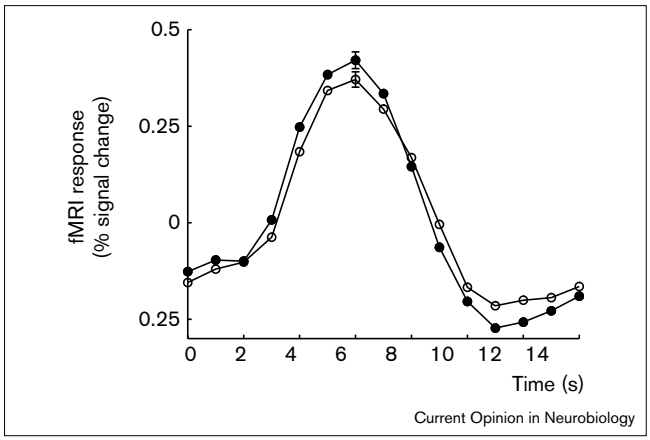
Figure 1



Periodic paradigm. **(a)** The solid curve represents the time-course of V1 brain activity from one fMRI scan. The dashed curve represents the best fit sinusoid. Stimuli were contrast-reversing grating patterns that alternated (36 s/cycle) between high (90–92%) and low (0–0.8%) contrasts. **(b)** V1 responses from 30 repeated scans across three separate scanning sessions. Response amplitude (percent MR signal modulation) is indicated by the radial distance from the origin, and response temporal phase is indicated by the angle from the horizontal axis. The thick dashed line passes through the vector mean of the 30 data points. Slight counterclockwise phase-shift of the fMRI responses relative to the horizontal axis is attributable to the temporal lag that is characteristic of the hemodynamic delay [5,6•,61,62,63•]. **(c)** fMRI response amplitude components, computed as the orthogonal projection of each data point in the polar plot onto the dashed line that accounts for the hemodynamic delay.

low-contrast target pattern was presented; on the other half, no target was presented. The subject pressed one of two buttons to indicate whether or not they saw the target. The target, when present, was just barely detectable ($d' = 1$). The trials were sorted according to whether or not a stimulus was presented. There are two notable results. First, there was a reliable increment in response when the just-noticeable stimulus was presented. Second, the response was surprisingly large even when no stimulus was presented. From control experiments in which the subject passively viewed the same stimulus, we know that these responses were largely driven by the subject's engagement in the task (see below for further discussion of such attentional effects).

Figure 2



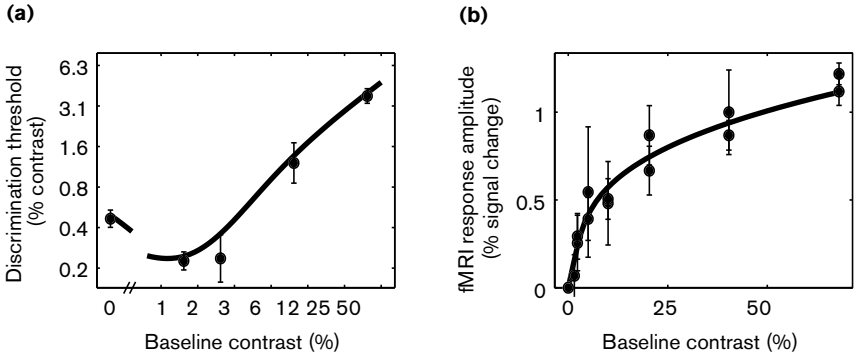
Event-related paradigm. V1 responses from a total of 440 trials in 24 scans across three separate scanning sessions, while a subject performed a series of contrast detection trials. The filled symbols represent the average time-course of response for trials on which a just noticeable (0.9% contrast, restricted to a peripheral annulus of the visual field) target pattern was presented. The open symbols represent average response for trials on which no pattern was presented. The error bars indicate typical standard error of the mean response at each time point.

Some event-related fMRI experiments have been performed with very brief inter-trial intervals, thereby avoiding the long idle periods between trials [3,4•]. The analysis then relies on an assumption that the fMRI signal linearly sums the responses to closely spaced trials — that is, it assumes that the fMRI signal is proportional to the local average neuronal activity, averaged (or blurred) over a period of time. There is empirical support for this assumption in some brain areas [5], but other brain areas may well violate this assumption, particularly for brief inter-trial intervals [6•].

Defining visual brain areas

Both the periodic and event-related paradigms require that the visual brain areas be predefined. Methods are well established for routinely defining several visual brain areas, such as the early, retinotopically organized brain areas (V1, V2, V3, V3A, V4v, and V8) [1••,7,8], area MT+ (also called V5), which is a motion-sensitive area that may be homologous to monkey areas MT, MST and FST [1••], and an area in the ventral occipital lobe that responds strongly to pictures of faces [9–13]. Most studies have concluded that this latter brain area is specifically and selectively involved in face recognition, but recent evidence suggests otherwise [14,15•]. A variety of additional visual brain areas have been identified, but standardized methods for routinely localizing these areas have not yet been established.

Figure 3



Neuronal correlate of visual pattern discrimination. **(a)** Contrast discrimination thresholds for one subject, measured psychophysically using a conventional two-alternative, forced-choice paradigm. Error bars, standard error of the mean of several repeated threshold measurements. **(b)** fMRI responses in V1 for the same subject, as a function of baseline contrast. Each data point is the result of a single scan. Error bars, estimates of the standard error of the mean response for each scan. Smooth curves, simultaneous fit to fMRI and psychophysical data. Adapted from [24•].

Neuronal correlates of psychophysical performance

The quantitative methods described above have been adopted to correlate brain activity with performance in various visual discrimination tasks, including color discrimination [16••], reading [17,18,19•], motion discrimination [17,19•,20,21,22••], and pattern discrimination [23,24•].

Early psychophysical studies [25] and electrophysiological studies in anesthetized cats and monkeys (see [2•]) provided indirect evidence that pattern discrimination judgements are limited by neuronal signals in early cortical visual areas (e.g. V1). To establish a firmer link between pattern discrimination and brain activity, we used a combination of fMRI and psychophysics to measure perceptual performance and brain activity in the same subjects [24•]. The psychophysical experiments measured contrast discrimination thresholds (i.e. contrast changes that were just barely detectable). The fMRI experiments measured response as a function of stimulus contrast for the same stimuli.

The results demonstrate that neuronal signals appropriate for limiting contrast discrimination performance appear to be present as early as V1. Figure 3a plots the psychophysical contrast discrimination thresholds. Thresholds initially drop slightly at low baseline contrasts and then rise dramatically for higher baseline contrasts, forming the familiar 'dipper function' commonly reported in the literature [25]. Figure 3b plots the V1 responses. The smooth curves were fit simultaneously to both the fMRI and psychophysical data under the hypothesis that a contrast change is detectable when the brain activity increases by a criterion amount. At low contrasts, the slope of the V1 activity is steep, so a small contrast increment evokes a criterion response increment. At high contrasts, a much larger contrast increment is needed to evoke a criterion response increment. Variants of this hypothesis have served as the basis for interpreting psychophysical data for over a century. The fMRI measurements provide additional data that help to constrain the interpretation.

Neuronal correlates of spatial attention

Our ability to perform a visual discrimination task is improved when we are cued to attend, without moving our eyes, toward the spatial location of the relevant stimulus [25,26]. Shifts in attention are correlated with systematic changes in brain activity that have been measured in a number of brain areas using a variety of methods [27–42,43•,44•,45•].

Only within the past year have human neuroimaging [39–42,43•,44•] and monkey electrophysiology [31,32] studies unambiguously demonstrated that spatial attention affects V1 activity. Some theories suggest that attention is mediated entirely by selection very early in the visual pathways. Attentional effects have, however, been notoriously difficult to measure in monkey V1 neurons. Indeed, the attentional effects measured with fMRI in humans are considerably stronger than those measured electrophysiologically in awake behaving monkeys under similar conditions. There are at least five possible explanations for this discrepancy. First, because little is known about the relationship between fMRI responses and the underlying neuronal firing rates (see below), it is possible that the fMRI measurements could be overestimating the effects of attention. Second, small shifts in eye position, equal in size to the V1 receptive fields, present a difficulty for the electrophysiology experiments. If eye position is systematically correlated with shifts in spatial attention, then the responses of individual V1 neurons will modulate as the receptive fields are shifted toward and away from the stimulus [28]. These potential biases can be avoided by carefully accounting for eye position [31], but perhaps at the cost of underestimating the magnitude of the attentional effects. Small shifts in eye position do not present a difficulty in the fMRI experiments because they have a negligible effect on measurements of pooled neuronal activity. Third, it is difficult to train a monkey to perform a threshold discrimination task in which, by definition, they can be correct and get rewarded on only a fraction

(e.g. 80%) of the trials. Therefore, the monkeys in the electrophysiology experiments may not have been performing tasks that were sufficiently demanding to fully engage attention. Fourth, the monkeys may have been overtrained so that the usual attentional mechanisms were no longer needed to perform the task; training can have a critical impact on measurements of attentional modulation [32]. Fifth, there may be genuine species differences.

Neuronal correlates of subjective perceptual phenomena

Quantitative fMRI methods have also been adopted to correlate brain activity with subjective visual experience. First, activity in human MT+ is correlated with the subjective percept of illusory motion in stationary displays [46–49]. Second, activity in several visual brain areas is correlated with the illusory percept of contours in a blank region of the visual field [50,51]. Third, activity modulates with the spontaneously reversing perception of bistable visual stimuli ([52••,53–55]; M Castelo-Brano *et al*., *Soc Neurosci Abstr* 1997, *23*:460). Fourth, particular visual areas respond selectively when subjects simply imagine different kinds of visual stimuli ([56–59,60•]; N Kanwisher, KM O'Craven, *Soc Neurosci Abstr* 1998, *24*:530).

Conclusions

fMRI provides an empirical approach for probing the neuronal basis of perception that complements electrophysiology in awake behaving monkeys. fMRI has limited spatial and temporal resolution compared with electrophysiology. However, the relatively coarse spatial resolution of fMRI allows one to measure activity simultaneously in several different brain areas at once. The sequence of events from neuronal response to fMRI response is complicated and only partially understood [61,62,63•]. With the recent advances in performing fMRI measurements on monkeys, however, we can soon expect to know much more about the relationship between the fMRI signal and the underlying neuronal activity ([64,65,66•]; W Vanduffel *et al*., *Soc Neurosci Abstr* 1998, *24*:11). In addition, human subjects, unlike monkeys, are easily instructed to perform a range of perceptual tasks and can report on their phenomenological perceptual experiences. We are now faced with an unprecedented opportunity in visual neuroscience to move seamlessly from human perception and psychophysics, to fMRI measurements of activity in the human brain and in the more familiar monkey brain, and then to conventional electrophysiological measurements of neuronal activity.

Acknowledgements

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- •• of outstanding interest

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