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# Time-resolved fMRI of mental rotation

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**TIME-RESOLVED fMRI seeks to elucidate neuronal activity during a single execution of a mental task, which corresponds typically to a timescale of seconds. However, this is also the timescale of the hemodynamic response, which delays and blurs the signal in time. In order to distinguish the temporal characteristics of the neuronal activity from that of the hemodynamic response, which is often vaguely known, we recorded a set of fMRI time courses under conditions of a varying behavioral parameter, and correlated this parameter to the width of the fMRI response. For the task under investigation, the mental rotation of three-dimensional objects, we found that the activation in the parietal lobe is related to an aspect of the task that is described by the reaction time (for example, the very act of mental rotation), and not only to aspects of the task that are constant from trial to trial, such as the visual presentation at the beginning or the decision at the end of the task.**

**Key words**: Functional magnetic resonance imaging; Functional mapping; Mental rotation; Temporal resolution



## Introduction

Conventional steady-state functional magnetic resonance imaging (fMRI) experiments use prolonged task periods involving the continuous and repetitive execution of a task. Typically, the inter-task delay is short relative to the hemodynamic response to neuronal activity, which delays and blurs the signal. Hence the fMRI signal from one individual task cannot be easily resolved, and information on neuronal activity on the timescale of a single task is usually lost. To overcome this problem, tasks can be performed repeatedly, with a long intermittent delay (from a few seconds to tens of seconds), while images are acquired continuously.[1,2] In this manner, neural activity during the execution of a single task can be detected through the hemodynamic response.

The temporal characteristics of the signal induced by a particular task may vary in different areas of the brain because of differences in hemodynamic response functions (which are, in general, dependent on the vascular environment and not well known), or because of actual differences in neuronal activity. In order to separate these two effects for a given task, we proposed previously to record a set of fMRI time courses with a varying behavioral parameter (e.g. the reaction time),[2] and we later demonstrated that sequential neural activity can indeed be obtained during the execution of a single task, without averaging.[3] The essence of our method is that a variable behavioral parameter (for example, a reaction time) is correlated with a temporal aspect of the fMRI time-course (for example, the onset time or width of the activation peak). Such a correlation contains valuable information about the temporal sequence of neuronal events during the execution of a task. For example, if the neuronal activity in a particular area always occurs at the end of the task, the onset time of the corresponding signal will be shifted in time with the reaction time, but the width of the signal will be constant. On the other hand, in areas activated during the entire reaction time following the presentation of the stimulus, the width of the signal will be correlated with the reaction time, but the onset time of the signal will be constant. Since this method allows, in principle, for a temporal resolution better than that superficially suggested by the hemodynamic response function, we will call it 'time-resolved fMRI'.

Time-resolved fMRI is technically demanding. It is of particular importance in cognitive tasks that the evolution of the signal is measured in a single execution of the task and that the fMRI data from individual trials are distinguished from one trial to the next. This is because there exist confounding habituation and learning effects, and often a large spread in reaction times in such tasks. The objective of the experiment is to measure brain activity as it occurs during the performance of a single task; hence the nominal temporal resolution (the time to acquire a single image) must be at least an order of magnitude

shorter than the execution time of the task. Here we demonstrate the application of time-resolved-fMRI to a well-known cognitive task, the mental rotation of three-dimensional objects.[4] While this is a single, well-defined task, most subjects perceive it as 'difficult', compared with many cognitive tasks commonly studied. The execution of this task requires several seconds (in our implementation, between 3 and 15 s), depending on the rotation angle and the individual subject, and is highly variable among trials. As shown here, we were able to measure each single execution of the task by fMRI and correlate a behavioral parameter (the reaction time) to the width and the onset time of the fMRI peak in the corresponding time course.

## Materials and Methods

FMRI experiments were carried out with a 4 Tesla whole-body MR imaging system (Siemens, Erlangen, Germany; Varian, Palo Alto, CA) with a head gradient insert. Five normal, right-handed female subjects were studied according to the guidelines of the Institutional Review Board of the University of Minnesota. At the beginning of the imaging session, anatomic MR images were acquired with a conventional TurboFLASH method.[5] On the basis of these images, three coronal, 10 mm slices were selected, such that the most posterior slice contained the posterior part of the parieto-occipital sulcus. Hence the 30 mm imaging slab covered parts of the occipital and parietal lobes. For fMRI studies, BOLD-based[6] images were then acquired with an echo-planar imaging sequence at high temporal resolution (repetition time = 197 ms (three slices), echo time = 25 ms, in-plane resolution = 64 × 64 pixels, field of view = 24 × 24 $cm^2$).[2,3]

The computer-generated paradigm was presented to the subject via a rear-projection screen (outside of the magnet) and a mirror above the eyes, attached to the top of the head-gradient set. The paradigm consisted of perspective drawings of three-dimensional objects (Fig. 1), similar to those used in the classic experiment by Shepard and Metzler.[4] The subjects were instructed to give a correct answer in as much time as needed. Each imaging session consisted of 16 trials. At the beginning of each trial, two identical objects at the same orientation were shown. After several dummy scans to avoid transient saturation effects, the acquisition started with the first baseline period (51 images, 10 s). Then, at the onset of the task period, one or both objects were replaced by different ones; this was the signal for the subject to commence execution of the task. The task was to decide whether the two objects were identical (though, in general, at a different perspective, or rotation angle), or mirror images of each other. As soon as a decision was reached, the subject indicated the choice by pressing one of two buttons on a keypad. When the button was pressed, the two objects were again replaced by the original pair, thereby initiating the second baseline period. The length of the task period was therefore variable, depending on the time the subject required to execute the task (reaction time, RT). The total length of each acquisition was 183 images (36 s; Fig. 1).

In each imaging session, two different objects (each having a standard and a mirror orientation) and four different rotation angles (0°, 20°, 60°, 100°) between the objects were used. In eight of the 16 trials, the

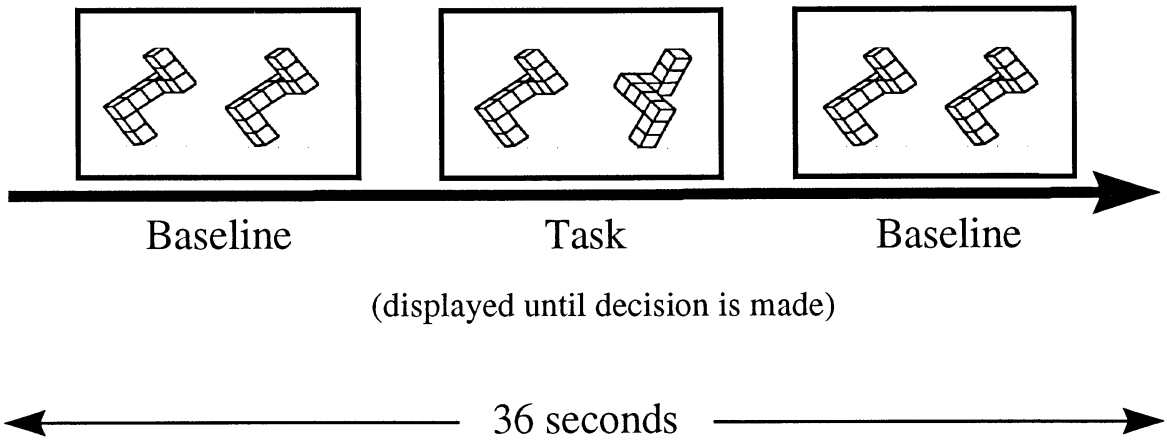



FIG. 1. Schematic depiction of a task. During the first baseline period, two identical objects were shown at the same orientation. The task period started when the display changed to two objects that were, in general, at different orientations. The subject then decided whether the two objects were identical or different and pressed a button on a keypad accordingly. As soon as a button was pressed, the display reverted to the baseline condition.

objects were identical, and in the other eight trials, they were mirror images of each other; the trials were randomized with respect to the identical/mirror image condition and the rotation angle.

Data were analyzed using the in-house software package STIMULATE,[7] and the commercial data analysis program PV-WAVE (Visual Numerics, Boulder, Colorado). Each trial was studied individually; only trials that (a) had an identical pair of objects, (b) had a non-zero rotation angle and (c) were solved correctly were considered valid (hence a maximum of six valid trials per subject). The time-course of each pixel was cross-correlated with a three-dimensional set of trapezoidal reference functions of varying position, width, and rise/fall time. A flat baseline period was appended before and after each trapezoid, such that the length of all reference functions was identical. The size of this set in each of the three dimensions covered all reasonable response functions. The result of this calculation was therefore a set of correlation coefficients; of this set, only the maximum correlation coefficient was retained for each pixel. A pixel was considered active if the maximum cross correlation coefficient, averaged over all valid acquisitions, was at least 0.4. Hence a single activation map was obtained for each subject. The time-course for each trial was then the average time-course of the activated pixels. For each trial, two time-course parameters were calculated. The onset parameter was the onset of the trapezoid that yielded the maximum correlation coefficient with the time course, and the width parameter was the full width at half height of that trapezoid.

## Results

A typical activation map for one subject is shown in Fig. 2, overlaid onto a functional echo planar image (three coronal slices); also shown is the corresponding anatomic image. In agreement with previous studies using a similar paradigm,[8,9] there was activation throughout the parietal lobe. Similar activation was observed in all subjects. In the occipital lobe, activation was generally seen in associative visual areas, but not in the primary visual cortex (presumably because objects were displayed on the screen throughout the experiment). For the purpose of this study, only the parietal lobe was considered further.

In Fig. 3, time-courses of activated pixels from two trials in the same subject are shown. Time index 0 indicates the start of the task period. The reaction times for the two trials were different, as indicated by the arrows. The onset time of the two response peaks is virtually identical; however, the width of the peaks is different, by approximately the same amount by which the two reaction times differ. For quantification, the width parameter was calculated for each trial. In order to compare the width parameters from different subjects with one another, they were normalized as follows: a linear fit of the width parameter as a function of the reaction time was carried out for each individual subject. The $y$-intercept of the fitting function, which is presumably related to the subject- and region-specific hemodynamic response function, was calculated while the slope of the function was set to 1. This is shown for one subject in Fig. 4A. The width parameters were then normalized by subtracting the $y$-intercept. The combined result for all subjects is plotted in Fig. 4B. The normalized width parameter was approximately equal to the reaction time; a linear fit yields $R = 0.88$ and a slope of 0.9. We also compared the offset of the width parameter (the $y$-intercept of the fitting function) for each individual subject (Fig. 5). Among the five subjects studied, the values of this offset varied between 1 and 7 s.

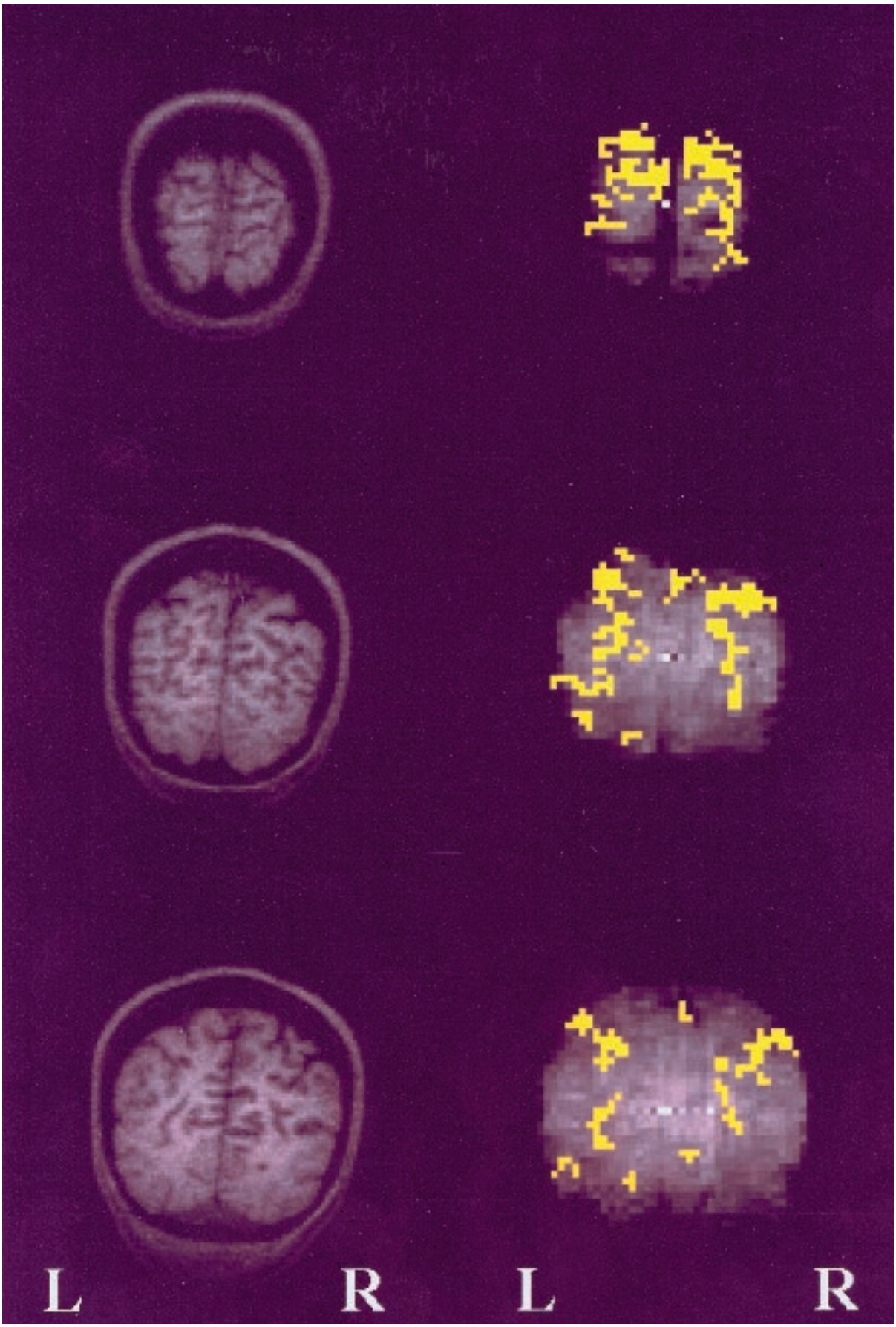
We found no correlation between the onset parameter and the reaction time. We also compared the mean onset parameters among subjects; within experimental error, the mean onset times of all subjects were not different.

## Discussion

In this experiment, we studied a cognitive task by time-resolved fMRI. We observed the execution of a single task without averaging; hence behavioral parameters, which are in general not the same from one execution of the task to the next, can be correlated with parameters characterizing the fMRI time course.

In the mental rotation task, the width of the peak in the fMRI time course in the parietal lobe was equal to the reaction time (except for a subject-specific offset), and the onset time in the fMRI was not correlated to the reaction time. We will assume that the hemodynamic response is a linear function of the neuronal activity.[10,11] Our findings suggest then (but do not prove) that the parietal lobe is active during the entire period of mental rotation. The measured parietal lobe activity originates, at least in part, from an aspect of the task that varies with the reaction time, and not from aspects of the task that are constant between trials, like the motor response at the end of the task.

The offset of the width of the response peak (the $y$-intercepts shown in Fig. 5) was, in general, different among subjects. This parameter is related to differences in hemodynamics, caused by different vascular architecture. We also observed differences in onset or width of the response peaks for the same subject in different pixels of the parietal lobe sporadically in our experiments; this may be due to poor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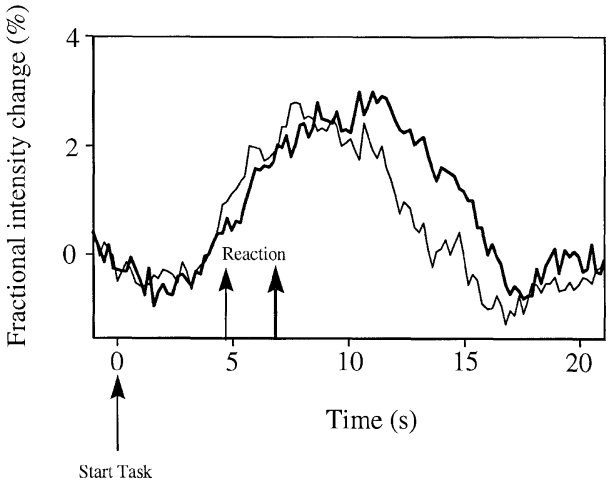


FIG. 3. Timecourses of two trials. In this case, the reaction times differ by approximately 2 s. The arrows indicate the reaction times for the two tasks. The peaks show similar onset time, but the peak corresponding to the longer reaction time (thick line) is wider.

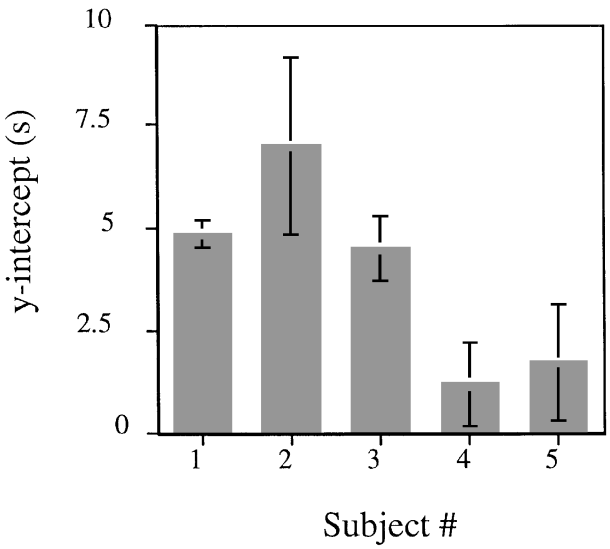


FIG. 5. Offsets of the width parameters (shown in the *y*-offset at Fig. 4A) for the five individual subjects. The offsets are in general different from one another. Bars indicate errors of the curve fit.

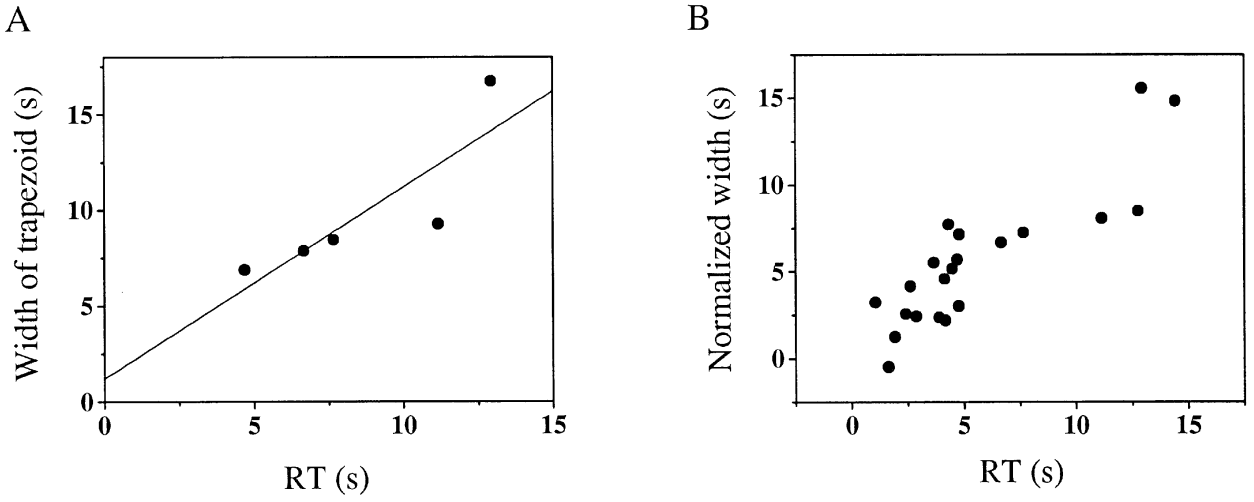


FIG. 4. (**A**) Full width at half maximum of the fMRI time courses for one subject, as a function of reaction time (RT). The *y*-intercept of the fitting function was then subtracted to compare all subjects. (**B**) Normalized full width at half maximum of the fMRI time courses as a function of reaction time (RT) for all subjects. Linear regression yields R = 0.88 and a slope of 0.9.

contrast-to-noise ratio in the single trial data or different vascular environments; however, a systematic, spatially resolved measurement of these parameters is beyond the scope of this report.

Whenever the signal-to-noise or contrast-to-noise ratio is not high enough in a single trial, averaging can and should be performed based on behavioral data such as the reaction time. Averaging without accounting for behavioral differences among trials loses all information correlated with such behavioral parameters and, in this regard, is not better than the conventional way of performing fMRI studies.

## Conclusion

It is possible to observe a single execution of a cognitive task by time-resolved fMRI; this experiment adds one temporal dimension to conventional, steady-state experiments. Since hemodynamic response times are in principle different in different

FIG. 2. Functional maps for one subject. Left: anatomical images of the three coronal slices. The top images correspond to the most posterior slice. Top of images is superior. R, right hemisphere; and L, left hemisphere. Right: corresponding echo planar images, with the functional map overlaid. Activation is seen in associative visual areas and throughout the parietal lobe, but not in the primary visual cortex.

areas and initially unknown, the temporal sequence of neuronal events can often only be determined when a time-related variable, such as the reaction time, is correlated with the fMRI response.

## References


1. Konishi S, Yoneyama R, Itagaki H *et al. NeuroReport* **8**, 19–23 (1996).
2. Kim S-G, Richter W and Ugurbil K. *Magn Reson Med* **37**, 631–636 (1997).
3. Richter W, Andersen PM, Georgopoulos AP and Kim S-G. *NeuroReport* **8**, 1257–1261 (1997).
4. Shepard RN and Metzler J. *Science* **171**, 701–703 (1971).
5. Haase A. *Magn Reson Med* **13**, 77–89 (1990).
6. Ogawa S, Tank DW, Menon R *et al. Proc Natl Acad Sci USA* **89**, 5951–5955 (1992).
7. Strupp JP. *NeuroImage* **3,** S60 (1996).
8. Cohen MS, Kosslyn SM, Breiter HC *et al. Brain* **119**, 89–100 (1996).
9. Tagaris GA, Kim SG, Strupp JP *et al. NeuroReport* **7**, 773–776 (1996).
10. Friston KJ, Jezzard P and Turner R. *Hum Brain Mapp* **1**, 153–171 (1994).
11. Boynton GM, Engel SA, Glover GH and Heeger DJ. *J Neurosci* **16**, 4207–4221 (1996).


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