Orientation-Selective Functional Magnetic Resonance Imaging Adaptation in Primary Visual Cortex Revisited

Sarah Weigelt,^{1,2,3*} Katharina Limbach,^{1,2,4} Wolf Singer,^{1,2}
and Axel Kohler^{1,2,5}

¹Department of Neurophysiology, Max Planck Institute for Brain Research, Deutschordenstr 46,
60528 Frankfurt am Main, Germany

²Brain Imaging Center Frankfurt, Schleusenweg 2-16, 60528 Frankfurt am Main, Germany

³Department of Brain and Cognitive Sciences and McGovern Institute for Brain Research,
Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

⁴Department of Psychology, Justus Liebig University Giessen, Otto-Behagel-Str. 10F,
35394 Giessen, Germany

⁵Department of Psychiatric Neurophysiology, University Hospital of Psychiatry, University of Bern,
Bolligenstr. 111, 3000 Bern 60, Switzerland

Abstract: The processing of orientations is at the core of our visual experience. Orientation selectivity in human visual cortex has been inferred from psychophysical experiments and more recently demonstrated with functional magnetic resonance imaging (fMRI). One method to identify orientation-selective responses is fMRI adaptation, in which two stimuli—either with the same or with different orientations—are presented successively. A region containing orientation-selective neurons should demonstrate an adapted response to the “same orientation” condition in contrast to the “different orientation” condition. So far, human primary visual cortex (V1) showed orientation-selective fMRI adaptation only in experimental designs using prolonged pre-adaptation periods (~40 s) in combination with top-up stimuli that are thought to maintain the adapted level. This finding has led to the notion that orientation-selective short-term adaptation in V1 (but not V2 or V3) cannot be demonstrated using fMRI. The present study aimed at re-evaluating this question by testing three differently timed adaptation designs. With the use of a more sensitive analysis technique, we show robust orientation-selective fMRI adaptation in V1 evoked by a short-term adaptation design. *Hum Brain Mapp* 33:707–714, 2012. © 2011 Wiley Periodicals, Inc.

Key words: functional magnetic resonance imaging; repetition suppression; repetition attenuation; perception; V1

Contract grant sponsor: Max Planck Society and the Federal Ministry of Education and Research in Germany; Contract grant number: BMBF 01 GO 0508.

*Correspondence to: Sarah Weigelt, Massachusetts Institute of Technology, Department of Brain and Cognitive Sciences and, McGovern Institute for Brain Research, 77 Massachusetts Avenue, 46-4141, Cambridge, MA 02139, USA. E-mail: weigelt@mit.edu

Received for publication 4 August 2010; Revised 29 November 2010; Accepted 2 December 2010

DOI: 10.1002/hbm.21244

Published online 21 March 2011 in Wiley Online Library (wileyonlinelibrary.com).

INTRODUCTION

Orientation selectivity of neurons is the most basic and well-studied principle of processing in visual cortex since the seminal work by Hubel and Wiesel [1962]. Studies in nonhuman primates have identified orientation-selective neurons in all early visual regions, predominantly in primary visual cortex [V1; Blasdel and Salama, 1986, Essen and Zeki, 1978]. Psychophysical investigations provide strong evidence that orientation-selective cells also exist in the human visual system [Blakemore and Nachmias, 1971; Gibson and Radner, 1937]. But only recently, columns presumably containing orientation-selective cells have been described in humans with high-field functional magnetic resonance imaging [fMRI; Yacoub et al., 2008]. Orientation selectivity in human visual areas can also be inferred with the aid of multivariate pattern classification [Haynes and Rees, 2005; Kamitani and Tong, 2005] or fMRI adaptation [Boynton and Finney, 2003; see Sapountzis et al. [2010] for a comparison between methods].

In fMRI adaptation, two stimuli—the adaptor and the test—are presented successively. The second stimulus is either a repetition of the first (a vertical grating followed by a vertical grating) or a variation of the first stimulus along one of the stimulus dimensions in this case orientation (a vertical grating followed by a horizontal grating). Assessing the fMRI signal in the two conditions provides a test to which extent a particular brain region is sensitive to the varied dimension. For gratings, early visual areas are expected to show an adapted response with stimulus repetition, but a rebound from adaptation with an orientation change.

An early study using fMRI adaptation to study orientation selectivity in human visual cortex found effects in early visual areas V2 and V3, but not in V1 [Boynton and Finney, 2003]. Boynton and Finney as well as other groups who replicated their findings [Fang et al., 2005; Murray et al., 2006] used adaptors with a short duration (1 s or less) in an event-related design, in which the immediate adaptation (short-term) from the adaptor to the test image was tested. Only when experimental designs involving long-term adaptation were used, orientation-selective fMRI adaptation was also reliably detected in V1 [Engel, 2005; Fang et al., 2005; Jurcoane et al., 2009; Larsson et al., 2006; Liu et al., 2007; Montaser-Kouhsari et al., 2007; Sapountzis et al., 2010; Tootell et al., 1998]. Critically, these studies used a long pre-adaptation phase (from 20 s up to 150 s), in which one orientation was shown continuously, followed by a sequence of so-called top-up stimuli and test stimuli, in which the top-up stimulus had the same orientation as the pre-adaptation stimulus (cf. Fig. 1B). Together, this led to the puzzling notion that V1, in contrast to V2 and V3, might not show robust orientation-selective short-term fMRI adaptation.

The present study aimed at re-evaluating this question by testing three differently timed adaptation designs to investigate the effect of the pre-adaptation phase and the

top-up adaptor. We demonstrate robust orientation-selective fMRI adaptation in V1 evoked by a short-term adaptation design. Furthermore, we replicate previous findings that a long-term adaptation design elicits orientation-selective adaptation in V1 and provide first indications for differences between the adaptation approaches.

MATERIALS AND METHODS

Subjects

Ten human subjects (age range, 20–27 years; mean age, 24.3 years, 6 female) participated in three adaptation experiments and a retinotopic-mapping experiment. All had normal or corrected-to-normal vision. Subjects gave their written informed consent; the study was approved by the Ethics Committee of the University Clinics of Frankfurt.

Stimuli

Stimuli were created and presented using PsychToolbox [Brainard, 1997, Pelli, 1997] for Matlab (The MathWorks, Natick, USA). Stimuli were Gabors at 100% Michelson contrast, with a gray center, a spatial frequency of 1.3 cycles per degree, counter-phase flickering at 2 Hz, subtending 22.5° visual angle, on a gray background (Fig. 1A). Gabors were created by the difference of two Gaussians (4.1 and 7.5° FWHM) modulating a sinusoidal black-and-white grating either rotated 45° clockwise or counter-clockwise. Stimuli were delivered via a video-goggle system (VisuaStim Digital Glasses, Resonance Technology, Northridge, USA).

Experimental Procedure

Each subject underwent three different experimental designs (pre-adaptation, top-up, and random, Fig. 1B) in individual scanning sessions, which were at least separated by 1 week. The order of experimental designs was balanced across subjects.

The pre-adaptation design (Fig. 1B, upper row) started with 10 s of fixation followed by a 40-s pre-adaptation phase. During the pre-adaptation phase, one Gabor was continuously shown for 40 s. A short fixation period of 2 s followed. Then, 30 trials (20 experimental trials and 10 fixation trials) each lasting 7 s were presented. An experimental trial included the presentation of a top-up adaptor for 4 s followed by a 500-ms interstimulus interval and the presentation of the test stimulus for 1 s and ended with a 1.5-s intertrial interval. The orientation of the top-up adaptor was the same as for the pre-adaptation phase, whereas the test stimulus was either again the same orientation or a different (orthogonal) orientation. During fixation periods, only a red fixation dot was presented. Fixation trials were used to jitter the stimulation timing, which is a prerequisite for a deconvolution analysis. The pre-adaptation

Figure 1.

Illustration of the stimulus and the three different experimental designs. **A:** Our stimulus was a Gabor subtending 22.5° visual angle, presented on a gray background at 100% Michelson contrast, with a gray center, a spatial frequency of 1.3 cycles per degree. The Gabor was either rotated 45° clockwise or counter-clockwise and had a counter-phase flicker at 2 Hz. **B:** Upper row: “pre-adaptation design” that contained a 40-s pre-adaptation phase and a top-up adaptor (4 s) that had the same orienta-

tion as the pre-adaptation phase throughout a run, middle row: “top-up design” with a top-up adaptor (4 s) that had the same orientation throughout a run, and lower row: “random design,” whose adaptor (4 s) was randomly selected from the two possible orientations. The test stimulus (1 s) was always either of the same orientation as the adaptor or of the different (orthogonal) orientation. Between adaptor and test stimulus was a 0.5 s blank interval and between trials was a 1.5 s blank interval.

design closely resembles previously used long-term designs that have been reliably shown to elicit orientation-selective fMRI adaptation in V1 [Fang et al., 2005; Jurcoane et al., 2009; Larsson et al., 2006; Liu et al., 2007; Montaser-Kouhsari et al., 2007; Sapountzis et al., 2010]. It has been argued that the pre-adaptation phase adapts the cortex to a particular orientation and that the top-up stimulus supports the maintenance of the adapted level.

To evaluate the role of the pre-adaptation phase, we used a top-up design (Fig. 1B, middle row) that was equivalent to the pre-adaptation design, but did not include a pre-adaptation phase. Instead, it started with 20 s of fixation. Importantly, as in the pre-adaptation design, the top-up adaptor retained the same orientation throughout the entire run. We hypothesized that the top-up adaptor alone might be sufficient to build up adaptation during the course of the run.

The random design (Fig. 1B, lower row) was equivalent to the pre-adaptation design and the top-up design in terms of timing, but did not include a pre-adaptation phase or a top-up adaptor. In contrast, the orientation of the adaptor stimulus in the random design varied throughout the run. One of the two possible orientations was randomly assigned to each trial, but each orientation was presented equally often throughout the run. The random design

closely resembles previously used short-term designs that have been shown *not* to elicit orientation-selective fMRI adaptation in V1 [Boynton and Finney, 2003; Fang et al., 2005; Murray et al., 2006], but for the length of the adaptor stimulus, which was 4 s in our design. Note that by using the term “short-term,” we refer to the immediacy of the adaptation effect between adaptor stimulus and test stimulus, not necessarily to the duration of the adaptor stimulus.

Behavioral Task

Because fMRI adaptation effects have been shown to be susceptible to attention [Weigelt et al., 2008], subjects performed a very demanding luminance discrimination task (increase or decrease) on the red fixation dot to control and equate attentional load across conditions. The dot had a mean luminance of 9.3 cd/m^2 . Luminance changes by $\pm 2.1 \text{ cd/m}^2$ occurred randomly, but on average every 1.4 s, and lasted 200 ms. Responses were recorded via a fiber-optic response box. We analyzed percent-correct values (% correct) and reaction times (RT) performing ANOVAs with the factors “design” (pre-adaptation, top-up, and random) and “experimental condition” (fixation,

same orientation, and different orientation). For % correct, there was a main effect of condition [$F(2,18) = 7.267$, $P = 0.022$, and $\epsilon = 1.08$]; post hoc pairwise t -tests revealed that subjects performed marginally more accurately during fixation ($M = 73.10$, $SD = 12.43$) than during “orientation” trials (“same orientation,” $M = 70.55$, $SD = 12.99$, $p = 0.098$; “different orientation,” $M = 70.17$, $SD = 13.33$, $p = 0.053$). Most importantly, however, there was no difference in accuracy between “same orientation” and “different orientation” trials ($P = 0.363$). With regard to RT, neither main effects nor the interaction reached significance. We conclude that subjects’ attention was successfully diverted from the stimulus and that differences between experimental conditions cannot be attributed to the task.

fMRI Data Acquisition

Each scanning session started with a point-spread-function sequence for distortion correction [Zaitsev et al., 2004] and included 10 functional runs of the adaptation experiment and one anatomical run. Blood-oxygenation-level-dependent (BOLD) fMRI was performed on a 3 T scanner equipped with a four-channel head coil (Siemens, Erlangen, Germany) at the Brain Imaging Center Frankfurt. For the adaptation experiment, a gradient-recalled echoplanar-imaging sequence was used with the following parameters: number of slices, 20; repetition time (TR), 1,000 ms; echo time (TE), 25 ms; flip angle (FA), 70°; slice thickness, 4.5 mm with a gap of 0.45 mm; in-plane resolution, $3.3 \times 3.3 \text{ mm}^2$. The slices were oriented to reach a complete coverage of the occipital lobe. Each functional run comprised the acquisition of 242 volumes in the top-up and random designs and 274 volumes in the pre-adaptation design. Each scanning session included the acquisition of a high-resolution MP-RAGE sequence for co-registration of the functional data and reconstruction of the cortical hemispheres (TR, 2,250 ms; TE, 4.38 ms; FA, 8°; voxel size, $1 \times 1 \times 1 \text{ mm}^3$).

fMRI Analyses

fMRI data were analyzed with BrainVoyager QX (version 1.10.4, BrainInnovation, Maastricht, The Netherlands). Because of scanning artifacts (signal jumps) that resulted from a temporarily malfunctioning head coil, we excluded 18 runs of 300 from further analyses (7 of 100 in the pre-adaptation design, 8 of 100 in the top-up design, and 3 of 100 in the random design). The first two volumes of each run were discarded because of T1-saturation effects. Pre-processing included slice-scan-time correction, 3-D motion correction, linear de-trending, and temporal high-pass filtering based on a general-linear-model approach with a Fourier basis set (up to two cycles per time course). Functional data were co-registered with the anatomical data, and both were normalized to Talairach coordinate space [Talairach and Tournoux, 1988].

Figure 2.

Definition of regions of interest. We defined regions of interest (white circles) for each subject at the overlap (“overlap map” shown in purple) of retinotopically defined early visual areas V1, V2, and V3 (“retinotopic map” shown in blue) and a general “activation map” (shown in red) based on the adaptation experiment with the contrast [“same orientation” + “different orientation”] > “fixation” (see Methods section for more information).

Definition of regions of interest

We defined regions of interest (ROIs) in early visual cortex with a two-step approach illustrated in Figure 2. We first identified regions V1, V2, and V3 in each subject with standard retinotopic mapping performed in a different scanning session. Briefly, each individual’s high-resolution anatomy was used to reconstruct the cortical surfaces. Standard polar angle mapping [Muckli et al., 2006] was performed to delineate early visual regions V1, V2, and V3 in each subject (Fig. 2, “retinotopic map” shown in blue). Second, we computed for each subject a general “activation contrast” for the adaptation experiment ([same orientation + different orientation] > fixation) across all three experimental designs and superimposed the resulting map onto the retinotopic map (Fig. 2, “activation map” shown in red). We then defined six ROIs (Fig. 2, white circles) per hemisphere per subject at the overlap (Fig. 2, “overlap map” shown in purple) of the activation map and the retinotopic map: V1 ventral/dorsal, V2 ventral/dorsal, and V3 ventral/dorsal at roughly the same eccentricity for each visual area. Note that this ROI definition does not bias our subsequent analysis with regard to the adaptation effects. The “activation contrast” is based on all three different designs and the two adaptation conditions “same orientation” and “different orientation” occur equally often in all of them. Furthermore, we chose ROIs to contain a constant number of 200 voxels each to allow for a fair comparison between visual areas. We then pooled

data across hemispheres and ventral/dorsal partitions for each subject.

Deconvolution analyses

We used a deconvolution approach to analyze our event-related data [Glover, 1999]. In event-related designs, the closely spaced events result in a substantial overlap of the hemodynamic responses. A deconvolution analysis has the advantage of estimating rather than assuming the hemodynamic response function and is therefore less biased and more able to reveal complex waveforms that occur with fast designs that use closely spaced trials [cf. Serences, 2004]. There are several important prerequisites to using a deconvolution analysis: we balanced the order of our experimental conditions (“same orientation,” “different orientation,” and “fixation”) within each run such that trials from each condition were preceded (two trials back) equally often by trials from each other condition. Also by introducing fixation trials, the onset of responses was jittered. A fast (TR = 1,000 ms) imaging sequence allowed us to measure multiple points of the hemodynamic response.

In our deconvolution analysis, 20 stick predictors were defined to cover the temporal extent of a typical hemodynamic response. We extracted the deconvolved signal time courses for the two conditions for each subject and each region in each design. The time courses were adjusted to a zero baseline by subtracting the mean of the first three time points for each subject and condition separately. For the deconvolution-based general linear model, single-subject data were prepared in the following manner: the time course of a voxel or region of interest was normalized, such that the mean signal value was transformed to a value of 100 and the individual time-point values fluctuated around the mean as percent signal deviations (computed on the raw data). A time-point value of 102 would therefore indicate an increase of two percent relative to the mean in the original data. In this way, the reported beta values of the deconvolution analysis directly provide an estimate of the actual percent signal change.

Note that we did not include an experimental condition in which only the adaptor stimulus was shown (but no test stimulus). Although it might have been interesting to fully disentangle the response toward the adaptor stimulus from that of the test stimulus, we chose not to include such an experimental condition to avoid additional expectancy effects toward the appearance or nonappearance of the test stimulus, as these have been shown to impact adaptation effects considerably [Summerfield et al., 2008].

RESULTS

To investigate which specific design parameters are necessary to elicit orientation-selective fMRI adaptation in V1, we tested three differently timed adaptation designs (see Fig. 1). We used a “pre-adaptation design” that has been

shown to reliably elicit orientation-selective fMRI adaptation in V1 [Fang et al., 2005; Jurcoane et al., 2009; Larsson et al., 2006; Liu et al., 2007; Montaser-Kouhsari et al., 2007; Sapountzis et al., 2010]. We compared this pre-adaptation design to a “top-up design” that was identical to the pre-adaptation design with regard to the use of the top-up adaptor and the trial timing, but did not contain a pre-adaptation phase and a short-term or “random design,” which matched the two previously described designs in terms of the trial timing, but did not contain a pre-adaptation period or a top-up adaptor.

ROIs in visual areas V1, V2, and V3 were identified in each subject based on standard retinotopic mapping (see Definition of regions of interest section). We extracted the deconvolved signal time course for the experimental conditions “same orientation” and “different orientation” from each subject, each region, and for each of the three different experimental designs. Figure 3 shows the time courses averaged across subjects. Our experimental design led to bimodal hemodynamic responses with two peaks (first peak at time points 5 and 6 s, and second peak at time points 7 and 8 s after stimulus onset). Because adaptor stimulus and test stimulus were only separated by 500 ms, both peaks reflect the response to both stimuli. More precisely, while the first peak mainly reflects activation to the adaptor stimulus, it already contains the rising BOLD response to the test stimulus. Accordingly, the second peak mainly reflects the response to the test stimulus, but still contains the falling BOLD response to the adaptor stimulus. Therefore, we included both peaks in the analyses. We first computed an overall four-way repeated-measures ANOVA with factors “design” (pre-adaptation, top-up, and random), “area” (V1, V2, and V3), “peak” (first peak and second peak), and “orientation” (same and different).

The four-way ANOVA revealed main effects for “peak” [Hotelling = 8.55, $F(1,9) = 76.98$, $p < 0.001$, $\eta^2 = 0.90$], “area” [Hotelling = 5.38, $F(2,8) = 21.50$, $p = 0.001$, $\eta^2 = 0.84$], and “orientation” [Hotelling = 2.41, $F(1,9) = 21.65$, $p = 0.001$, $\eta^2 = 0.71$], but no main effect for “design” ($p = 0.09$). These effects were expected, reflecting an overall higher signal for the second peak, a signal dropoff from V1 to V2 and V3, and a lower signal for the repeated stimulus (“same”), respectively. One two-way interaction, “peak” $\times$ “design,” also reached significance [Hotelling = 1.28, $F(2,8) = 5.12$, $p = 0.04$, $\eta^2 = 0.56$]. Collapsing across areas and orientation, the interaction was driven by a stronger BOLD increase from peak 1 to peak 2 for the pre-adaptation design compared to the other designs (pre-adaptation: $\Delta\text{BOLD} = 0.39$, top-up: $\Delta\text{BOLD} = 0.26$, random: $\Delta\text{BOLD} = 0.22$). In addition, two significant three-way interactions were found in the analysis (other interactions $p > 0.12$). The interaction “design” $\times$ “area” $\times$ “orientation” [Hotelling = 4.14, $F(2,8) = 6.20$, $p = 0.03$, $\eta^2 = 0.81$] reflected the fact that, collapsing across peaks, numerical differences between the “same” and “different” conditions were less homogeneous across areas in the top-up design compared to the other designs. Most importantly, the interaction “peak” $\times$ “design” $\times$

Figure 3.

Main results. BOLD signal time courses estimated by a deconvolution analysis and averaged across subjects for each design, separately for regions V1, V2, and V3. Error bars correspond to SEM. Shaded regions mark $p < 0.025$, paired two-tailed t -tests across subjects on the average of time points 5 and 6 s (first peak) and 7 and 8 s (second peak) after stimulus onset.

“orientation” [Hotelling = 1.65, $F(2,8) = 6.61$, $P = 0.02$, $\eta^2 = 0.62$] showed that, collapsing across areas, the differences between the orientation conditions developed differently across peaks for the three designs. To further characterize this three-way interaction pattern, we computed two-tailed paired t -tests across subjects for each area and each design, testing for a lower BOLD signal in the “same orientation” condition in contrast to the “different orientation” condition separately for the two peaks (see Fig. 3).

With regard to the first peak, we found significant orientation-selective fMRI adaptation in the pre-adaptation design in all three regions [V1: $t(1,9) = 3.66$, $p = 0.005$; V2: $t(1,9) = 2.96$, $p = 0.02$; V3: $t(1,9) = 2.77$, $p = 0.02$]. No other design reached significance [top-up design, V1: $t(1,9) = 1.37$, $p = 0.20$; V2: $t(1,9) = 0.58$, $p = 0.58$; V3: $t(1,9) = 1.75$, $p = 0.12$; random design, V1: $t(1,9) = 2.10$, $p = 0.07$; V2: $t(1,9) = 1.69$, $p = 0.13$; V3: $t(1,9) = 1.77$, $p = 0.11$].

With regard to the second peak, we found significant orientation-selective fMRI adaptation in the pre-adaptation design in V1 [$t(1,9) = 3.31$, $p = 0.009$]. Most interestingly, however, V1 also showed orientation-selective fMRI adaptation in the top-up design [$t(1,9) = 2.78$, $p = 0.02$] and in

the random design [$t(1,9) = 4.95$, $p = 0.001$]. Region V3 showed orientation-selective fMRI adaptation in the top-up design [V2: $t(1,9) = 2.16$, $p = 0.06$; V3: $t(1,9) = 3.95$, $p = 0.003$] and both V2 and V3 in the random design [V2: $t(1,9) = 3.85$, $p = 0.004$; V3: $t(1,9) = 3.59$, $p = 0.006$]. However, no effect was seen in the pre-adaptation design for V2 and V3 [V2: $t(1,9) = 0.94$, $p = 0.37$; V3: $t(1,9) = 1.17$, $p = 0.27$].

In summary, for all designs, orientation-selective fMRI adaptation effects could be demonstrated in V1, V2, and V3, but differences in the BOLD signal seem to emerge earlier in time for the pre-adaptation design compared to the short-term designs.

DISCUSSION

Although replicating previous findings that orientation-selective fMRI adaptation can be elicited with long-term adaptation designs [Fang et al., 2005; Jurcoane et al., 2009; Larsson et al., 2006; Liu et al., 2007; Sapountzis et al., 2010], we show robust orientation-selective fMRI adaptation evoked by a short-term adaptation design that did not

require a long pre-adaptation phase nor a top-up adaptor. Furthermore, our results demonstrate that the pre-adaptation design leads to an early onset of orientation-selective fMRI adaptation, while the top-up and random designs show orientation-selective fMRI adaptation later in the response.

The apparent lack of short-term orientation-selective fMRI adaptation in human V1 has always been especially puzzling, because robust short-term adaptation effects have been described in cat and monkey V1 using unit recordings [Bonds, 1991; Nelson, 1991; Müller et al., 1999]. In addition, position-selective short-term fMRI adaptation has been demonstrated in V1 in several studies [Kourtzi and Huberle, 2005; Murray et al., 2006; Weigelt et al., 2007]. On the basis of the results of the present study, however, we conclude that V1 has no special status with respect to orientation-specific short-term fMRI adaptation.

Why were we successful in finding orientation-selective fMRI adaptation in V1 with a short-term adaptation approach, while others [Boynton and Finney, 2003; Fang et al., 2005; Murray et al., 2006] were not? First, even for the short-term design, we used an adaptor duration (4 s) that was equivalent to the top-up adaptor durations usually used in long-term adaptation designs and longer than the ones used by other studies (1 s maximum). We used this adaptor duration, so that designs did not vary in their stimulus durations, but only with respect to the presence or absence of a pre-adaptation phase and/or a top-up adaptor. Second, we used a very sensitive method—deconvolution—to estimate the complex BOLD time course that emerges as a consequence of closely spaced trials in event-related designs. Using deconvolution, we can nicely demonstrate the bimodal waveform of the BOLD signal elicited by our adaptation sequence. Third, we used a fast repetition time for the acquisition of the BOLD signal ($TR = 1,000$ ms), providing us with more time points to precisely estimate the BOLD time course. Fourth, we measured a high number of trials per experimental condition per design providing us with very reliable estimates of the average BOLD responses. These four methodological modifications might have provided the high sensitivity required in detecting orientation-selective short-term adaptation effects.

However, there is a control experiment in a study by Kourtzi and Huberle [2005], which used even shorter adaptor and test durations in a short-term adaptation experiment. They used durations of 300 ms for adaptor and test stimulus and an interstimulus interval of 100 ms. They report orientation-selective fMRI adaptation in V1, V2, V3, V4, and the posterior part of the lateral occipital complex. This suggests that an adaptor duration of 4 s as used by us might not even be necessary to elicit short-term orientation-selective fMRI adaptation in V1.

Our second finding – that a long-term pre-adaptation design leads to an early onset of the orientation-selective adaptation effect – might provide a hint toward differences between long- and short-term adaptation mechanisms. It is interesting to note that the use of the top-up adaptor

(without the pre-adaptation phase) was not sufficient to induce early adaptation. Thus, the early adaptation evoked by the pre-adaptation design is dependent on the pre-adaptation phase. There is preliminary evidence from electrophysiology that in motion-sensitive area MT of the macaque, short- as well as long-term adaptation approaches tap into the same neuronal mechanisms, but that the latter effect is quantitatively stronger [Wallisch and Movshon, 2008]. In contrast, in higher-level regions of ventral visual cortex, it has been shown that short- and long-term designs tap into qualitatively different processes. Fang et al. [2007] investigated the representation of faces in the fusiform face area (FFA). With a long-term adaptation approach (similar to our pre-adaptation design), FFA exhibited viewpoint-tuned adaptation, that is, as the angular difference between the adaptor and the test stimulus increased, adaptation evoked by the test stimulus decreased. With a short-term adaptation approach, however, FFA demonstrated a viewpoint-dependent response profile: the signal only adapted when adaptor and test stimulus had the exact same viewpoint. Epstein and colleagues [2008] found a similar effect in the parahippocampal place area. They contrasted two designs that varied in terms of the interval between the adaptor and the test stimulus. A long interval between adaptor and test stimulus of ~ 20 min revealed viewpoint-tuned adaptation in PPA, while a short interval (500 ms; similar to our random design) led to a viewpoint-dependent response profile. Furthermore, Epstein et al. [2008] showed that there was no interaction between the two adaptation effects and suggested that long- and short-interval adaptation effects might be mediated by dissociable neural mechanisms. In addition to different adaptation profiles found in the cited studies, we describe differences in the onset of adaptation effects, adding another factor differentiating long- and short-term designs. More neuroimaging studies are needed to better understand the interaction between sites (early visual vs. higher-level regions) and mechanisms (short vs. long-term) of adaptation. Furthermore, more electrophysiological studies are needed to clarify whether the effects seen in the BOLD signal are also detectable on the single-cell level.

CONCLUSION

In conclusion, the present study provides evidence for orientation-selective short-term fMRI adaptation in V1 revising previous notions about the alleged lack of such an effect. The present study extends our knowledge of fMRI adaptation in early visual areas and reconfirms the potential of the technique.

ACKNOWLEDGMENTS

The authors thank Sandra Anti for help with data acquisition, Karl Gegenfurtner and Volker Franz for helpful discussions and Oliver Döhrmann for comments on earlier versions of the manuscript.

REFERENCES

- Blakemore C, Nachmias J (1971): The orientation specificity of two visual after-effects. *J Physiol* 213:157–174.
- Blasdel GG, Salama G (1986): Voltage-sensitive dyes reveal a modular organization in monkey striate cortex. *Nature* 321:579–585.
- Bonds AB (1991): Temporal dynamics of contrast gain in single cells of the cat striate cortex. *Vis Neurosci* 6:239–255.
- Boynton GM, Finney EM (2003): Orientation-specific adaptation in human visual cortex. *J Neurosci* 23:8781–8787.
- Brainard DH (1997): The psychophysics toolbox. *Spat Vis* 10: 433–436.
- Engel SA (2005): Adaptation of oriented and unoriented color-selective neurons in human visual areas. *Neuron* 45:613–623.
- Epstein RA, Parker WE, Feiler AM (2008): Two kinds of fMRI repetition suppression? Evidence for dissociable neural mechanisms. *J Neurophysiol* 99:2877–2886.
- Essen DC, Zeki SM (1978): The topographic organization of rhesus monkey prestriate cortex. *J Physiol* 277:193–226.
- Fang F, Murray SO, Kersten D, He S (2005): Orientation-tuned fMRI adaptation in human visual cortex. *J Neurophysiol* 94:4188–4195.
- Fang F, Murray SO, He S (2007): Duration-dependent fMRI adaptation and distributed viewer-centered face representation in human visual cortex. *Cereb Cortex* 17:1402–1411.
- Gibson JJ, Radner M (1937): Adaptation, after-effect and contrast in the perception of tilted lines. I. Quantitative studies. *J Exp Psychol* 20:453–467.
- Glover GH (1999): Deconvolution of impulse response in event-related BOLD fMRI. *Neuroimage* 9:416–429.
- Haynes JD, Rees G (2005): Predicting the orientation of invisible stimuli from activity in human primary visual cortex. *Nat Neurosci* 8:686–691.
- Hubel DH, Wiesel TN (1962): Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *J Physiol* 160:106–154.
- Jurcoane A, Choubey B, Mitsieva D, Muckli L, Sireteanu R (2009): Interocular transfer of orientation-specific fMRI adaptation reveals amblyopia-related deficits in humans. *Vision Res* 49:1681–1692.
- Kamitani Y, Tong F (2005): Decoding the visual and subjective contents of the human brain. *Nat Neurosci* 8:679–685.
- Kourtzi Z, Huberle E (2005): Spatiotemporal characteristics of form analysis in the human visual cortex revealed by rapid event-related fMRI adaptation. *Neuroimage* 28:440–452.
- Larsson J, Landy MS, Heeger DJ (2006): Orientation-selective adaptation to first- and second-order patterns in human visual cortex. *J Neurophysiol* 95:862–881.
- Liu T, Larsson J, Carrasco M (2007): Feature-based attention modulates orientation-selective responses in human visual cortex. *Neuron* 55:313–323.
- Montaser-Kouhsari L, Landy MS, Heeger DJ, Larsson J (2007): Orientation-selective adaptation to illusory contours in human visual cortex. *J Neurosci* 27:2186–2195.
- Muckli L, Kiess S, Tonhausen N, Singer W, Goebel R, Sireteanu R (2006): Cerebral correlates of impaired grating perception in individual, psychophysically assessed human amblyopes. *Vis Res* 46:506–526.
- Müller JR, Metha AB, Krauskopf J, Lennie P (1999): Rapid adaptation in visual cortex to the structure of images. *Science* 285: 1405–1408.
- Murray SO, Olman CA, Kersten D (2006): Spatially specific fMRI repetition effects in human visual cortex. *J Neurophysiol* 95:2439–2445.
- Nelson SB (1991): Temporal interactions in the cat visual system. I. Orientation-selective suppression in the visual cortex. *J Neurosci* 11:344–356.
- Pelli DG (1997): The VideoToolbox software for visual psychophysics: Transforming numbers into movies. *Spat Vis* 10:437–442.
- Sapountzis P, Schluppeck D, Bowtell R, Peirce JW (2010): A comparison of fMRI adaptation and multivariate pattern classification analysis in visual cortex. *Neuroimage* 49:1632–1640.
- Serences JT (2004): A comparison of methods for characterizing the event-related BOLD timeseries in rapid fMRI. *Neuroimage* 21:1690–1700.
- Summerfield C, Trittschuh EH, Monti JM, Mesulam MM, Eger T (2008): Neural repetition suppression reflects fulfilled perceptual expectations. *Nat Neurosci* 11:1004–1006.
- Talairach J, Tournoux P (1988): Co-Planar Stereotaxic Atlas of the Human Brain, 3-Dimensional Proportional System: An Approach to Cerebral Imaging. New York: Thieme.
- Tootell RB, Hadjikhani NK, Vanduffel W, Liu AK, Mendola JD, Sereno MI, Dale AM (1998): Functional analysis of primary visual cortex (V1) in humans. *Proc Natl Acad Sci USA* 95:811–817.
- Wallisch P, Movshon JA (2008): Dynamics of neuronal adaptation in macaque MT. Program No. 615.9 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience.
- Weigelt S, Singer W, Muckli L (2007): Separate cortical stages in amodal completion revealed by functional magnetic resonance adaptation. *BMC Neurosci* 8:70.
- Weigelt S, Muckli L, Kohler A (2008): Functional magnetic resonance adaptation in visual neuroscience. *Rev Neurosci* 19:363–380.
- Yacoub E, Harel N, Ugurbil K (2008): High-field fMRI unveils orientation columns in humans. *Proc Natl Acad Sci USA* 105:10607–10612.
- Zaitsev M, Hennig J, Speck O (2004): Point spread mapping with parallel imaging techniques and high acceleration factors: Fast, robust, and flexible method for echo-planar imaging distortion correction. *Magn Reson Med* 52:1156–1166.