Adaptive changes in visual cortex following prolonged contrast reduction

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How does prolonged reduction in retinal-image contrast affect visual-contrast coding? Recent evidence indicates that some forms of long-term visual deprivation result in compensatory perceptual and neural changes in the adult visual pathway. It has not been established whether changes due to contrast adaptation are best characterized as “contrast gain” or “response gain.” We present a theoretical rationale for predicting that adaptation to long-term contrast reduction should

Compensation hypothesis

In this study, we tested a *compensation hypothesis,* that prolonged exposure to low contrasts results in compensatory changes in the adult human visual system. We examined the effects of prolonged contrast deprivation on contrast coding by having subjects with normal vision view the world through contrast-reducing goggles for 4 hours. Subjects' contrast-discrimination sensitivity and fMRI contrast response were measured in pre- and post-tests. Contrast discrimination thresholds are typically measured by determining the smallest contrast difference required to discriminate two patterns that are identical except for a difference in contrast. The plot of contrast increment threshold (ΔC) vs. baseline (i.e. pedestal) contrast (C) is called the contrast discrimination function or threshold versus contrast (TvC) function. This function has a characteristic 'dipper shape' (Legge & Foley, 1980; Nachmias & Sansbury, 1974). It has been hypothesized that the shape of contrast discrimination functions is accounted for by the form of underlying neuronal contrast response functions (CRF) such that an increment in contrast (ΔC) can be detected only when the increment in the neuronal response increases by some criterion amount (ΔR_c) (Legge & Foley, 1980).

The first goal of the current study was to see whether prolonged exposure to low contrasts brings about any compensatory changes in visual contrast coding. If prolonged contrast reduction results in increased gain of the response in visual cortex—a form of neural compensation—then we would expect to see improved contrast discrimination, i.e. reduced values of ΔC. If the adaptation occurs at the cortical level including binocular neurons, we should observe an interocular transfer effect of the adaptation to the unadapted fellow eye.

Contrast gain or response gain?

Our second goal was to identify the mechanism of the prolonged adaptation. There are two likely mechanisms underlying any adaptive change: increased contrast gain and increased response gain. Often contrast adaptation has been studied on a short time scale of seconds or minutes. Its mechanism has often been described by a contrast-gain model in which the system adjusts the dynamic range of the CRF to be centered near the mean stimulus contrast. But this contrast-gain mechanism may not provide an effective strategy for dealing with prolonged contrast reduction.

To understand why prolonged contrast deprivation might involve a different mechanism from short-term contrast adaptation, consider a simplified characterization as follows. Assume that:

1. the response mechanism (neuron or BOLD) has a limited response range (see Footnote 1) with a maximum value of R_{max}

Linking psychophysical contrast discrimination and fMRI BOLD contrast response

The third goal of this study was to confirm the theoretical linkage between TvC and CRF. Earlier studies have shown good agreement between TvCs and CRFs measured in V1 with fMRI (Boynton, Demb, Glover, & Heeger, 1999; Zenger-Landolt & Heeger, 2003) such that the TvC is approximately proportional to 1 over the derivative of the CRF (see Equation 4 in Linking psychophysics and fMRI BOLD measurements section).

We focused on the early visual areas V1 and V2 for three reasons:

1. There is already evidence linking the CRFs measured with fMRI BOLD signals to psychophysical contrast discrimination data (e.g., Boynton et al., 1999);
2. Higher-level cortical areas such as hV4 and Lateral Occipital Complex (LOC) do not appear to represent contrast faithfully (e.g., Gardner et al., 2005; Murray & He, 2006); and
3. With grating stimuli, BOLD signals can be measured more reliably in early visual areas, increasing the likelihood of finding subtle adaptation effects.

In summary, our empirical predictions are that adaptation will produce:

1. a decrease in contrast discrimination thresholds compared with pre-adapted thresholds;
2. an increase in the gain of fMRI contrast response functions; and
3. a reduction in contrast discrimination thresholds for the unadapted fellow eye.

Confirmation of these predictions would lend support to the compensation hypothesis, and would indicate that the adaptation effects are cortical in origin.

Method

Apparatus

We used artificial contrast reduction to test normally sighted subjects. Contrast reduction was implemented using a disk-shaped (36 mm in diameter) contrast-reducing filter worn in front of the eye. The filter attenuated contrast by a factor of 3 (0.5 log unit) while minimizing blur (acuity reduction is less than 0.2 logMAR unit). The filter also has a factor of 2 (0.3 log unit) luminance reduction. The filter is one of a series of contrast filters built by Denis Pelli for research purposes (c.f., Pelli, 1987, pp. 134–146) using 0.5 μm diamonds and clear casting acrylic. The contrast reduction factor was controlled by making filters with various concentrations of diamonds (Pelli, personal communication, September 22, 2006). The filters were calibrated psychophysically by measuring contrast sensitivity (Pelli-Robson test) with and without the filter in front of the eye (Table 1). We further confirmed the filter's contrast reduction by comparing the contrast-detection thresholds for the grating patterns used in the Main experiment, for viewing with the contrast-reducing goggles and the luminance matched Neutral Density (ND)-filter goggles. As expected, we observed a three-fold elevation of contrast-detection threshold for the contrast-reducing goggles viewing condition (mean ratio across three subjects of 3.13 ± 0.19).

		S1	S2	S3
Log contrast sensitivity	Without goggles	1.90	2.05	1.65
	With goggles	1.30	1.60	1.15

The filter's blur was also calibrated psychophysically by measuring visual acuity (Lighthouse Distance acuity test) with and without the filter in front of the eye (Table 1). The luminance attenuation of the filter was calibrated with a MINOLTA CS-100 Chroma Meter.

Two types of goggles were used for this study. For one set of goggles, the contrast-reducing filter was worn over the subject's dominant eye, with dominance determined by a subjective alignment test. A translucent occluder, transmitting virtually no pattern information, but matched for overall light transmission, covered the fellow eye. The filter and occluder were mounted in goggles which blocked all light except through the filter apertures. We refer to these goggles as contrast-reducing goggles. For the second set of goggles, a neutral density (ND) filter (optical density = 0.3 log units), matched for luminance attenuation with the contrast-reducing filter, was worn over the dominant eye and the translucent occluder was mounted over the fellow eye. We refer to these goggles as ND-filter goggles.

Subjects

Three subjects participated in this study. All subjects had normal or corrected-to-normal vision, and had normal contrast sensitivity (Table 1). They were experienced psychophysical subjects (three of the authors) and served in both behavioral and fMRI experiments. Written informed consent was obtained in accordance with a protocol approved by the University of Minnesota Institutional Review Board.

Experimental design

This study consisted of three experiments (Main, Control and Interocular-transfer tests). The main experiment examined the effect of prolonged contrast attenuation on contrast coding. Separate days were devoted to the effects of adaptation on behavior (psychophysics) and brain response (BOLD). In both cases, subjects wore the contrast-reducing goggles during pre- and post tests, as well as during the four hours of adaptation (Figure 2).

During the four hours of goggles adaptation, subjects went about their usual daily activities such as reading, working on computers, walking around the building, and eating lunch. We selected four hours of adaptation because pilot testing with two hours revealed effects that were weaker and hard to measure.

A control experiment was identical to the main experiment except that subjects wore the ND-filter goggles, with no contrast attenuation, during the 4-hour adapting period.

Finally, to examine interocular transfer, subjects had four hours of adaptation with the contrast filter over one eye and the translucent occluder over the other eye as in the main experiment. But the pre- and post tests were conducted on the unadapted fellow eye, that is, the eye that wore the translucent occluder during the adapting period. During the pre- and post testing, the unadapted eye viewed the stimulus through the contrast-reducing filter.

In summary, in all three experiments the pre- and post tests for both behavioral and fMRI measurements were conducted while subjects wore the contrast-reducing goggles. The difference between the main and control experiments lies in whether subjects wore the contrast-reducing goggles (main experiment) or ND-filter goggles (control experiment) during the adapting period. The difference between the main and interocular-transfer experiments is whether the adapting eye was tested or the unadapted fellow eye was tested.

Behavioral measurement

Stimuli

The test stimulus was a vertical 2 cycles per degree (cpd) sinusoidal grating placed in an annulus (inner radius, 2°; outer radius 9°, see Figure 3). The edges of the annulus were smoothed using a Gaussian kernel with standard deviation (σ) of 1°. A peripheral annulus grating was used rather than a full-field grating for compatibility with fMRI testing.

Stimuli were displayed on a uniform gray field (46 cd/m^2) at a viewing distance of 55 cm. The stimuli were generated and controlled using Matlab (version 7.0) and Psychophysics Toolbox extensions (Mac OS X) (Brainard, 1997; Pelli, 1997), running on a Power Mac G5 computer (model: M73). The display was a SONY Trinitron color graphic display (model: GDM-FW520; refresh rate: 85 Hz; resolution: 1024 $\times$ 768). Stimuli were rendered with a video card with 8 bit input resolution and 14 bit output resolution using Cambridge Research System Bits++. Luminance of

made the duration of each scan 238 sec (approximately 4 min).

To equate for attentional demand, we measured subjects' contrast response functions while they did a moderately demanding fixation task, rather than doing the contrast discrimination task. During scanning, the fixation point changed to a cross (either vertical or 45 degree tilted) every 2 sec. The cross lasted 400 ms, then changed back to the fixation point. Subjects were asked to press one of the two buttons to indicate the orientation of the cross. Subjects performed this fixation task throughout the scanning period (i.e., for both stimulus and blank intervals). Subjects were given a series of practice trials outside the scanner.

We followed the standard retinotopic mapping method (Engel, Glover, & Wandell, 1997; Sereno et al., 1995). Rotating wedge scans served to map boundaries between visual areas and expanding ring scans served to map the visual representations at different eccentricities. Each scan of annuli and wedge lasted 190 sec and 286 sec respectively.

An independent scan was used to define the regions of interest (ROI). Subjects passively viewed images of a contrast-reversing (10 Hz) high-contrast sine grating annulus (inner radius 2°; outer radius 9°) centered at fixation. The grating annulus was presented in 20 sec stimulus blocks, interleaved with 20 sec blank blocks. Each block type was repeated 5 times in the scan, which lasted 200 sec.

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function with an exponent of m. The typical values of n and m are 2 and 0.4 respectively, so that the function is expansive ($C^{2.4}$) at low contrasts and compressive at high contrasts ($C^{0.4}$) (Legge & Foley, 1980).

The fits were achieved using a simplex search method (Lagarias, Reeds, Wright, & Wright, 1998) to search for the optimal fit producing the least squares error.

Psychophysical contrast increment thresholds can be predicted from a CRF (Equation 2) by assuming that a contrast increment is detectable when the response R increases by a criterion amount (Legge & Foley, 1980). That is, the predicted threshold, ΔC satisfies:

$$R'(C + \Delta C) - R'(C) = \Delta R_c, \quad (3)$$

where ΔC is the threshold contrast increment and ΔR_c is the criterion response increment. Equation 3 can be solved numerically for various pedestal contrast C

and on fMRI response as *(post fMRI BOLD response) − (pre fMRI BOLD response)*. If there is no change in either thresholds or BOLD responses between pre- and post-tests, the difference values would be zero. If there is any

Fixation orientation task in the scanner

Subjects' CRFs were measured while they were doing a fixation orientation task demanding attention (see details in Method section). Our results show that subjects' performance on the fixation task stayed nearly constant across different conditions: mean accuracy collapsed across contrast levels was 85 ± 7% for pre-test and 87 ± 10% for post-test in the main experiment; 84 ± 8% for pre-test and 80 ± 13% for post-test in the control condition.

A 2 (test condition: pre vs. post) × 4 (contrast) repeated measures ANOVA with test condition and contrast as within-subject factors was conducted on fixation orientation performance. For both main and control experiments, we did not observe any significant main effect of test condition, contrast nor test condition by contrast interaction effect (all $p > 0.13$).

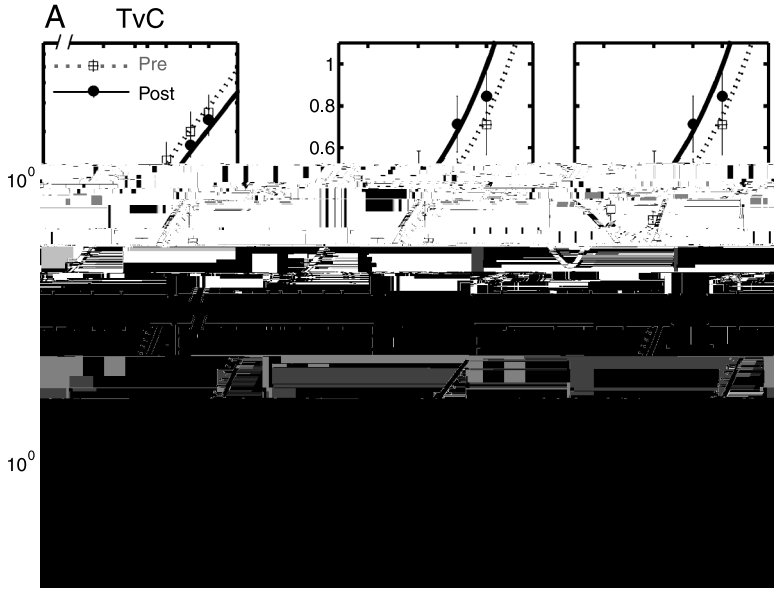
These results help us to rule out changes in attentional modulation as an explanation for the increase in cortical contrast response following adaptation.

Identifying mechanisms of the adaptation effect

Figure 7A shows contrast increment thresholds, averaged across subjects, plotted as a function of filtered pedestal contrast in log-log coordinates. Figures 7B and 7C show fMRI BOLD signal changes (%) in V1 and V2, averaged across subjects, as a function of filtered stimulus contrast in linear-log coordinates. The patterns of results from individual subjects were similar. We used the simultaneous fit to TvC and CRF data (see Linkage between TvCs and fMRI CRFs section) to identify the mechanism underlying the adaptation effect.

We did so by examining the parameter changes in Equation 2 and interpreted these changes to distinguish between contrast gain and response gain: an increase of R_{max} in the post-test signifies response gain; a decrease of C_{50} signifies contrast gain.

Changes in the parameters were studied with the nested model test (see Footnote 3) with a lattice of six models (the full and reduced models, and four intermediates). The nested model test is often used to identify the model that best accounts for the given data with the fewest parameters (c.f., Li, Lu, Tjan, Dosher, & Chu, 2008). We used the following procedure: in the full model, all four parameters of the model Equation 2 (i.e., R_{max}, C_{50}, n, m) are changed between the pre- and post-test conditions. That is, there are eight free parameters in the model. In the reduced model, the pre- and post-test conditions share all four parameters of the model equation. Thus, there are four free parameters in the reduced model. In intermediate models, some but not all



four parameter values are shared between pre- and post-test conditions. For instance, the R_{max} is forced to be identical for the pre- and post-test conditions while other parameters are allowed to vary. Note that the fixed parameter values between pre- and post-test conditions are allowed to vary in the optimization method.

In a nutshell, the response-gain model is the one where only R_{max} is allowed to vary between pre- and post-test but the other parameters are forced to have the same values. The contrast-gain model is defined as the one in which only C_{50} is allowed to vary between pre- and post-test with others being identical. The *n-m* model is one with only *n* and *m* parameters being allowed to vary between pre- and post-test.

The nested model test showed that the best fitting model is the response-gain. The model, shown as smooth curves in Figure 7, accounts for 75.39% (V1) and 74.29% (V2) of the variance in the data. This model is statistically superior to the reduced model ($F_{(2,20)} = 30.64$, $p < 0.01$; $F_{(2,20)} = 28.90$, $p < 0.01$ for V1 and V2 respectively), and as good as the full model ($F_{(6,14)} = 0.95$, $p = 0.30$; $F_{(6,14)} = 1.04$, $p = 0.24$). In comparison, neither the contrast-gain model nor *n-m* model is significantly different from the reduced model (all $p > 0.1$). Both are significantly inferior to the full model, as are the intermediate model that includes R_{max} (all $p < 0.01$).

To evaluate the effect of individual differences on model selection, a statistical bootstrap procedure was performed with the following steps:

1. Sampling with replacement a set of TvC and CRF (either V1 or V2) of both pre- and post-test conditions from three subjects;
2. Averaging the re-sampled TvCs and CRFs ($n = 3$), separately for pre- and post-test conditions;
3. Six variants (i.e., a lattice of six nested models as stated above) of the model Equation 2 was fitted simultaneously to both TvC and CRF. Then the residual sum of squares (*RSS*) of each model was recorded for the nested model test;
4. Using the nested model test, the best fitting model, the one that is not statistically different from the full model but superior to all its reduced models, was selected;

As expected for the cortical site of adaptation, we observed a significant improvement in discrimination sensitivity in the occluded eye following adaptation for all three subjects (Figure 8). The contrast-discrimination results revealed full interocular transfer of the adaptation effect. Discrimination thresholds decreased by an average of 0.14 ± 0.01 log units in the post-tests for the occluded eye, close to the average decrease of 0.12 log units for the adapted eye. A 2 (test condition: pre vs. post) × 7 (contrast) repeated measures ANOVA revealed that the difference in thresholds between pre- and post-tests was significant ($F_{(1,12)} = 39.46$, $p < 0.01$). The difference in thresholds across contrast levels was also significant ($F_{(6,12)} = 153.90$, $p < 0.01$), demonstrating the dependency of discrimination thresholds on pedestal contrast. No significant interaction effect was found ($p > 0.1$).

Our transfer test does not rule out the possibility that monocular occlusion (i.e., adaptation to a field with zero contrast) produces the adaptation effect. This would not be expected, however, if the visual system is adapting in a compensatory way to a change in the contrast characteristics of visible patterns.

Discussion

Our major finding is that four hours of exposure to a low-contrast visual environment produced significant changes in contrast coding demonstrated both behaviorally and in cortical responses. The nature of the changes was consistent with our three predictions from the compensation hypothesis:

1. improvement in contrast-discrimination sensitivity;
2. an increase in the gain of fMRI contrast response functions in visual cortical areas V1 and V2, and
3. interocular transfer of these adaptation effects.

The mechanisms of this adaptive change can be accounted for by the response-gain model. In addition, we also established quantitatively the adequacy of a simple linking hypothesis relating neural response to behavioral contrast-discrimination data (Boynton et al., 1999; Legge & Foley, 1980; Zenger-Landolt & Heeger, 2003).

Linking psychophysical TvC to fMRI BOLD CRF

Our results confirmed the theoretical linkage between

Compensatory changes following contrast deprivation

Our results showed that prolonged exposure to low contrasts lead to compensatory changes in visual contrast coding in both behavioral and physiological domains. We observed that following the prolonged adaptation, discrimination thresholds decreased by an average of 0.12 ± 0.04 log units and the fMRI contrast response in V1 and V2 areas of the brain were increased by average factors of 1.96 and 1.30 respectively.

Nevertheless, it is possible that covert attention could

the contrast-gain mechanism which accounts for short-term adaptation. Our results provide evidence for a response gain mechanism in which the slope of the CRF is steeper near the prevailing contrast following adaptation.

Clinical implications for low-vision

The question of whether there are any compensatory perceptual or neural changes in response to visual deprivation is relevant to low-vision rehabilitation. One possible implication of our findings is that after prolonged experience with eye conditions yielding reduced retinal-image contrast, such as cataract, people might achieve higher discrimination sensitivity for low contrasts compared to people with normal vision. An analogous effect appears in our results. After adapting to low contrasts, subjects' contrast discrimination thresholds were lower than those of subjects wearing the ND filters at least for a certain range of contrast (i.e., 1%, 1.6% and 3.3%) by up to a factor of 1.60.

It remains to be determined if neural compensation takes the form of response gain for cases of contrast deprivation over months or years. Studies of amblyopia hinted a possible role of neural compensation in chronically deprived visual systems (Hess & Bradley, 1980; Simmers, Bex, & Hess, 2003). Hess and Bradley (1980) reported that despite marked contrast deficits at threshold,

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RSS_{reduced} is the sum of squares under the reduced model. When the null hypothesis is true, this statistic has an $F_{d1,d2}$ distribution with $d1 = df_{\text{reduced}} - df_{\text{full}}$ and $d2 = df_{\text{full}}$. The p-value of the test is computed as the probability that an $F_{d1,d2}$ random variable is as large or larger than the observed value of F. In other words, the test evaluates whether the variance accounted for by the added terms in the full model is significantly larger than expected by chance. Using a lattice of nested model, we can select the simplest model which can account best for the data.

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