

Long-term effects of monocular deprivation revealed with binocular rivalry gratings modulated in luminance and in color

Claudia Lunghi

Department of Neuroscience,
Università Degli Studi di Firenze, Firenze, Italy
Institute of Neuroscience, CNR – Pisa, Pisa, Italy



David C. Burr

Department of Neuroscience,
Università Degli Studi di Firenze, Firenze, Italy
Institute of Neuroscience, CNR – Pisa, Pisa, Italy



M. Concetta Morrone

Department of Translational Research on
New Technologies in Medicine and Surgery,
Università di Pisa, Pisa, Italy
Scientific Institute Stella Maris, Pisa, Italy



During development, within a specific temporal window called the *critical period*, the mammalian visual cortex is highly plastic and literally shaped by visual experience; to what extent this extraordinary plasticity is retained in the adult brain is still a debated issue. We tested the residual plastic potential of the adult visual cortex for both achromatic and chromatic vision by measuring binocular rivalry in adult humans following 150 minutes of monocular patching. Paradoxically, monocular deprivation resulted in lengthening of the mean phase duration of both luminance-modulated and equiluminant stimuli for the deprived eye and complementary shortening of nondeprived phase durations, suggesting an initial homeostatic compensation for the lack of information following monocular deprivation. When equiluminant gratings were tested, the effect was measurable for at least 180 minutes after reexposure to binocular vision, compared with 90 minutes for achromatic gratings. Our results suggest that chromatic vision shows a high degree of plasticity, retaining the effect for a duration (180 minutes) longer than that of the deprivation period (150 minutes) and twice as long as that found with achromatic gratings. The results are in line with evidence showing a higher vulnerability of the P pathway to the effects of visual deprivation during development and a slower development of chromatic vision in humans.

Introduction

The developing sensory brain is highly plastic (Pascual-Leone, Amedi, Fregni, & Merabet, 2005), allowing it to self-calibrate and to adapt to the environment. Plasticity in humans, and indeed in all mammals, is regulated within a clearly defined *critical period* (Wiesel & Hubel, 1963): Early visual deprivation, such as early untreated congenital cataracts, provokes permanent deficits in both basic visual functions, such as visual acuity, and high-level functions, such as shape and depth perception (Fine, Smallman, Doyle, & MacLeod, 2002; Fine et al., 2003; Levi, McKee, & Movshon, 2011; Maurer, Lewis, & Mondloch, 2005; Ostrovsky, Andalman, & Sinha, 2006). Plasticity in young infants is so profound that in the congenitally blind other sensory modalities invade the visual cortex, which starts to respond to tactile (Sadato et al., 1996) and auditory (Roder, Stock, Bien, Neville, & Rosler, 2002) stimulation. Competition between the monocular inputs is a crucial factor contributing to the plasticity of the developing visual system: Binocular deprivation affects the visual cortex organization of animals less than monocular deprivation (Wiesel & Hubel, 1965), and humans with unilateral cataracts show more severe deficits than those with bilateral cataracts (Lewis, Maurer, & Brent, 1995).

Citation: Lunghi, C., Burr, D. C., & Morrone, M. C. (2013) Long-term effects of monocular deprivation revealed with binocular rivalry gratings modulated in luminance and in color. *Journal of Vision*, 13(6):1, 1–15, <http://www.journalofvision.org/content/13/6/1>, doi:10.1167/13.6.1.

It has been generally assumed that after closure of the critical period, the brain becomes relatively hard-wired with little or no experience-dependent plasticity (Berardi, Pizzorusso, & Maffei, 2000; Fine et al., 2003; Hensch, 2004; Maurer et al., 2005). Recent evidence, however, has questioned this assumption, and the degree of neuroplasticity in adult mammals is now a debated issue. In adult animals, ocular dominance plasticity can be restored by increasing excitation or by decreasing inhibition in the central nervous system (Harauzov et al., 2010; Maya Vetencourt et al., 2008), confirming the importance of the excitation-inhibition balance in determining visual cortical plasticity. Although in adult humans there is no evidence of ocular dominance plasticity, the adult visual cortex shows a residual plastic potential as demonstrated for fine properties of vision, such as perceptual learning (Karni & Bertini, 1997), orientation tuning (Bao & Engel, 2012; Zhang, Bao, Kwon, He, & Engel, 2009), contrast discrimination (Kwon, Legge, Fang, Cheong, & He, 2009), multisensory processing (Merabet et al., 2008), and binocular fusion (Klink, Brascamp, Blake, & van Wezel, 2010).

The few published studies on recovery from deprivation also suggest residual plasticity in human adults. On late removal of unilateral cataracts (Elleberg, Lewis, Maurer, Brar, & Brent, 2002), some visual recovery was observed, mainly involving higher cognitive functions, such as global motion perception, probably mediated by the associative cortex, rather than basic visual sensitivity mediated by the primary visual cortex. On the other hand, preserved visual parsing is observed after late removal of bilateral congenital cataracts (Fine et al., 2002; Ostrovsky, Meyers, Ganesh, Mathur, & Sinha, 2009); this is in line with evidence showing that the effects of binocular deprivation (which does not drive neural competition) are less severe and less durable than those of monocular deprivation (Wiesel & Hubel, 1965). Also, short binocular deprivation in adults can reveal some residual neural plasticity in human vision. For example, Kwon et al. (2009) showed a slight improvement in contrast sensitivity thresholds after four hours of contrast reduction, correlated with an increased blood-oxygen-level-dependent (BOLD) signal in V1 and V2. Boroojerdi et al. (2000) observed an increase in excitability of the primary visual cortex (transcranial magnetic stimulation phosphene thresholds decreased, and the BOLD signal in V1 was enhanced) after a few hours of binocular blindfolding, confirming the important role of intracortical inhibition and excitation balance for plasticity. This was also supported by results from the same lab demonstrating that benzodiazepine administration completely annuls the effect of light deprivation on cortical excitability (Boroojerdi, Battaglia, Muellbacher, & Cohen, 2001). Zhang et al.

(2009) showed that four hours of selective attenuation of a specific orientation slightly improved discrimination thresholds of the deprived orientation.

We recently introduced a novel technique to study plasticity in adult humans: We combined *binocular rivalry* with *monocular deprivation*—the classic paradigm used to investigate ocular dominance plasticity—to demonstrate that the adult human visual cortex retains a surprisingly high degree of neural plasticity (Lunghi, Burr, & Morrone, 2011). When two incompatible images are displayed separately to the eyes, they do not merge into a single percept, but compete for visual awareness, resulting in ineluctable perceptual alternations with only one image dominating perception at a time, only to be supplanted by the previously suppressed one. This form of bistable perception, called *binocular rivalry* (Blake & Logothetis, 2002), probably reflects reciprocal inhibition of the two rival images (Tong, Meng, & Blake, 2006), making it an optimal tool to study visual competition in early visual processing (Haynes & Rees, 2005). In our previous study, we demonstrated that a short period of monocular deprivation (150 minutes) had important consequences for the dynamics of binocular rivalry between luminance-modulated gratings: Following monocular deprivation, the deprived eye strongly dominated visual perception over the nondeprived eye with an effect being measurable for up to 90 minutes following reexposure to binocular vision.

Here, we extend this technique to study the effects of deprivation on binocular rivalry on *equiluminant* chromatic stimuli, modulated in color (to favor the parvocellular system), and compare these effects to those with luminance-modulated grating (reanalyzed from data of Lunghi et al., 2011). As equiluminant gratings are known to strongly excite P-cell and poorly excite M-cell responses, testing the effect of monocular deprivation on the dynamics of binocular rivalry between equiluminant stimuli allows us to investigate a differential susceptibility between the P and M pathways. Given the evidence of a higher susceptibility of the P pathway to the effect of visual deprivation in animals (Horton & Hocking, 1997), we expected a longer-lasting effect of monocular deprivation on the rivalry between equiluminant stimuli, likely to involve structural neural modification of P pathway. Moreover, recent evidence (Denison & Silver, 2012) has demonstrated a different contribution of the M and P pathways in driving the dynamics of binocular rivalry, showing that the M stream is more involved in eye rivalry, the P stream more in stimulus rivalry. That the P pathway is more involved in mediating stimulus rivalry suggests that it has a role in sustained perceptual stability and could possibly show different retention of the effects of monocular deprivation. We show that monocular deprivation affects the dynamics of binoc-

ular rivalry for both luminance- and chromatic-modulated stimuli but more for chromatic stimuli, with which it biases rivalry in favor of the deprived eye for at least three hours after two and a half hours of monocular deprivation. Brief periods of deprivation (30 minutes) have very little effect on rivalry for luminance-modulated stimuli.

Methods

Observers

Five observers (two males, mean age 24 ± 0.8 years), including author CL, participated in the experiment with chromatic gratings, and seven observers (one male, mean age 26.7 ± 2 years, all different except CL) participated in the experiment with achromatic gratings. Four participants (one male, mean age 24.5 ± 0.7 years, two who did not participate in other studies) participated in the short-term deprivation experiment. All had normal or corrected-to-normal vision, normal stereo acuity (Frisby stereotest; Sasieni, 1978), normal color vision, and no strong eye preference. Participants gave informed consent and were reimbursed for their time at the rate of €7 per hour. The experiments were carried out along the principles laid down in the declaration of Helsinki and the paradigm approved by the ethics committee of the Scientific Institute Stella Maris, and observers gave written informed consent.

Apparatus and stimuli

The experiment took place in a dark and quiet room. Visual stimuli were generated by the ViSaGe (CRS, Cambridge Research Systems) housed in a PC (Dell) controlled by Matlab programs. Equiluminant chromatic stimuli were displayed on a linearized monitor (Barco CDCT 6551, Barco Federal Systems, LLC, Duluth, GA) driven at a resolution of 987×777 pixels with a refresh rate of 120 Hz. Achromatic stimuli were displayed on a 20-inch Clinton Monoray (Richardson Electronics Ltd., LaFox, IL) monochrome monitor, driven at a resolution of 1024×600 pixels with a refresh rate of 120 Hz. Observers viewed the display at a distance of 57 cm through CRS Ferro-Magnetic shutter goggles (Cambridge Research Systems, Ltd., Rochester, Kent, UK) that alternately occluded the two eyes each frame. Responses were recorded through the computer keyboard. The eye-patch was made of a translucent plastic material that allowed light to reach the retina (attenuation 15%) but no pattern information as assessed by the Fourier transform of a natural world image seen through the eye-patch. During the patching period, observers

were free to perform their normal activities, such as working, reading, walking outside, and having lunch.

Chromatic stimuli were equiluminant sinusoidal gratings, made by summing magenta and cyan sinusoidal gratings of equal but opposite contrast, oriented obliquely at $\pm 45^\circ$ (size: 2° , spatial frequency: 1.5). They were displayed on a uniform gray background (luminance: 32 cd/m^2 , CIE: 0.341 0.368) in central vision with a central black fixation point: a common squared dark gray frame (size 2.5°) to facilitate dichoptic fusion. Given that the blue gun was kept constant at 1, the ratio of the red luminance to the sum of the red and green luminance ($R/[R+G]$) was used to determine the subjective equiluminant point of the subjects, evaluated by standard minimum flicker photometry. Points of equiluminance varied between 0.48 and 0.5 for the five observers. To avoid local chromatic adaptation, we randomly shifted the phase of the visual gratings in one or the other direction at a rate of 0.3–0.5 Hz. The background was set at the mean value of the individual guns of the equiluminant grating; equiluminance between the gratings and the background was measured with the photometer (Konika Minolta, Inc., Tokyo, Japan).

Achromatic stimuli were two Gaussian-vignetted sinusoidal gratings (Gabor patches), oriented either vertically or horizontally (size: $2\sigma = 1.5^\circ$, spatial frequency: 3 cpd, contrast: 75%), presented on a uniform background (luminance: 37.4 cd/m^2 , CIE: 0.442 0.537) in central vision with a central black fixation point and a common squared frame to facilitate dichoptic fusion.

For the equiluminant stimuli, luminance and CIE coordinates were 32 cd/m^2 and CIE: 0.363 0.272 for the magenta grating and 32 cd/m^2 and C.I.E: 0.297 0.581 for the cyan grating. Cone contrasts along the axes were LM axis: $L = 8.5\%$, $M = 13.5\%$; S axis: $S = 77\%$ (Smith & Pokorny, 1975). The chromaticities of the visual stimuli in a cone excitation space (MacLeod & Boynton, 1979) were $L/(L+M) = 0.61$ and $S/(L+M) = 0.002$ for the red grating and $L/(L+M) = 0.7$ and $S/(L+M) = 0.01$ for the green grating. Presentations were alternated at the frequency of the shutter goggles, so each eye was presented with only one of the two stimuli. Monocular deprivation was achieved by having observers wear the translucent eye-patch for 150 minutes for the two main experiments and for 30 minutes in the short-term deprivation experiment.

To test the effect of monocular deprivation on the achromatic and chromatic visual pathways, we used visual stimuli that elicited maximum responses of the two systems, high-contrast achromatic Gabor patches with a spatial frequency of 3 cpd and equiluminant magenta/cyan oriented gratings with a spatial frequency of 1.5 cpd, because responses to equiluminant sinusoidal gratings show low-pass characteristics (Kaplan, Shapley, & Purpura, 1988) (A diagram of the

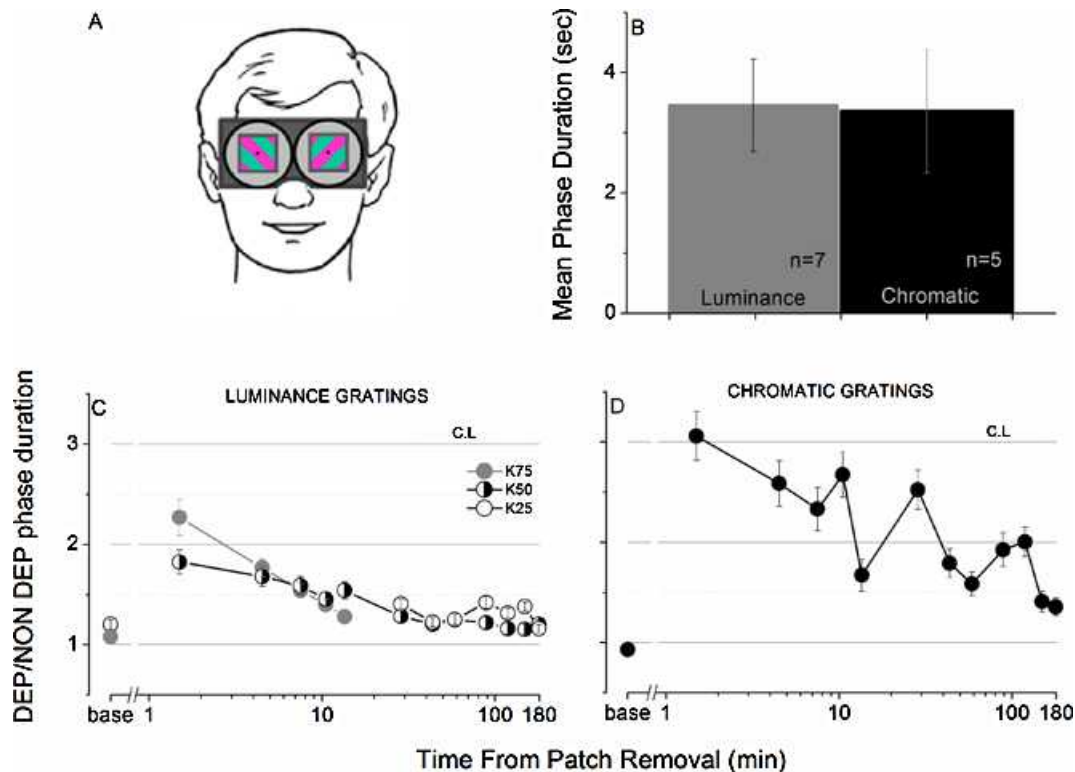


Figure 1. Mean phase durations of the different visual stimuli before and after monocular deprivation. (A) Orthogonally oriented equiluminant gratings (S.F. 1.5 cpd, orientation $\pm 45^\circ$) modulated only in chromaticity along the L/M axis and achromatic Gabor patches (S.F. 3 cpd, orientation 0° – 90°) modulated only in luminance contrast (75%) were presented separately to the eyes through FE-shuttering goggles. (B) Group baseline mean phase durations did not differ for the two visual stimuli tested, independent sample t test: $N = 12$, $t(10) = 0.07$, $p = 0.95$. (C, D) The average ratio between the mean phase durations of stimuli presented to the deprived and nondeprived eyes of four measurements of a single observer (preferred eye-patched) is plotted as a function of time elapsed from the removal of the eye-patch. (C) When luminance-modulated gratings with different contrast (25%, 50%, 75%) were tested after the first 15 minutes following eye-patch removal, the ratio between the deprived eye and the nondeprived eye mean phase durations did not statistically differ from baseline measurements. (D) When equiluminant stimuli were tested, the ratio between deprived and nondeprived eye durations significantly differed from the baseline for the whole period tested after monocular deprivation (180 minutes). Error bars represent ± 1 SEM.

equiluminant visual stimuli is reported in Figure 1A). The baseline mean phase duration of the two types of visual stimuli was comparable for the group average (Figure 1B).

Task and procedure

In the experiment with luminance and chromatic gratings, each observer was measured separately eight times, patching each eye four times in pseudo random order. Each individual patching session was separated by at least 24 hours. We also measured baseline conditions for each observer before patching, yielding eight separate measurements. After patch removal, we measured binocular rivalry continuously for 15 minutes, giving a short break every three minutes. For luminance gratings, we measured a three-minute block of rivalry again at 90 minutes from patch removal; for

chromatic gratings, we measured three-minute blocks at 30, 45, 60, 90, 120, 150, and 180 minutes. For short deprivation, the procedure was the same, but we measured only the first 15 minutes.

Eye dominance was assessed operationally from binocular rivalry baseline recordings with the dominant eye being the one that prevailed. Immediately after the removal of the eye-patch, observers sat in front of the monitor wearing the shuttering goggles, and the first experimental session began. After a countdown, the binocular rivalry stimuli appeared. Subjects reported their perception (clockwise or counterclockwise for the equiluminant gratings and horizontal or vertical for the achromatic gratings) by continuously pressing with the right hand one of two keys (left or right arrows) on the computer keyboard. As assessed in pilot studies and in debriefing sessions, mixed percepts were very rare and occurred for only very brief periods between perceptual transitions, and their frequency remained constant

across conditions even after deprivation. Neither subject nor experimenter knew which stimulus was associated with which eye until the end of the session when it was verified visually.

Results

Two groups of subjects wore translucent patches for 150 minutes. After removal of the eye-patch, binocular rivalry was tested at regular intervals with luminance- or chromatic-modulated gratings. Data from observers tested with luminance-modulated gratings have been reported briefly (Lunghi et al., 2011) and were reanalyzed in this paper to allow a direct comparison with data from the new group of observers tested with chromatic gratings. Figure 1 shows the results for one exemplary subject who performed both experiments (author CL). For both luminance- (Figure 1C) and color- (Figure 1D) modulation, a two and a half hour deprivation strongly affected dominance, biasing perception in favor of the deprived eye. In this subject, the effects were stronger and more long-lasting for the chromatic than for the luminance gratings: On patch removal, binocular rivalry for chromatic gratings was three times more prevalent in the deprived than in the fellow eye, and the effect lasted for at least 180 minutes. Luminance gratings also biased rivalry toward the deprived eye, initially by a factor of two, lasting for about 30 minutes after patch removal.

As detailed in the methods section, the equiluminant gratings had lower cone contrast than the luminance gratings: 25% compared with 75%. To assess the importance of contrast, we remeasured the effect with luminance-modulated gratings of 50% and 25% contrast. As the results of Figure 1C show, contrast had very little effect on the bias in rivalry, in either the amplitude or the longevity, effectively ruling out reduced contrast and, therefore, adaptation strength as an explanation for the longevity of the effects with color gratings.

Figure 2A shows the average results for all subjects (seven subjects for the luminance condition, five for color). These average results are similar to those of the example subject of Figure 1. For luminance gratings (gray symbols), the mean phase duration of the deprived eye increased by 56% on eye-patch removal while that of the nondeprived eye decreased by 28%, a 2.3-fold difference between the eyes. Chromatic gratings (black symbols) were similar: a 56% increase in the deprived eye, a 27% decrease in the nondeprived eye, yielding a factor of 2.3. The baseline measurements do not differ from 1, implying perfect balance between the eyes, t tests: luminance: $N = 7$, $t(6) = 0.82$, $p = 0.44$; color: $N = 5$, $t(4) = 0.14$, $p = 0.89$. Furthermore, baseline

measurements for luminance and chromatic gratings did not differ from each other, independent samples t test: $N = 12$, $t(10) = 0.7$, $p = 0.49$. Following 150 minutes of monocular deprivation, the ratio between the deprived and nondeprived eye mean phase durations was significantly biased in favor of the deprived eye, paired t tests: luminance: $N = 7$, $t(6) = 6.28$, $p \leq 0.001$; color: $N = 5$, $t(4) = 4.19$, $p = 0.014$. The effect of monocular deprivation was comparable for the two types of visual stimuli tested during the first three minutes following eye-patch removal but followed different dynamics for luminance and chromatic visual stimuli. When luminance-modulated gratings were tested, the effect of monocular deprivation on mean phase durations was only significant for data recorded during the first 15 minutes following reexposure to binocular vision; data recorded 90 minutes after eye-patch removal clearly show that balance between the eyes was restored, paired t test: $N = 7$, $t(6) = 0.35$, $p = 0.73$. For chromatic gratings, rivalry was significantly biased in favor of the deprived eye for at least three hours following reexposure to binocular vision, paired t test: $N = 5$, $t(4) = 2.81$, $p \leq 0.05$. At 180 minutes after removal of the eye-patch, the mean phase duration of the deprived eye was 38% longer than that of the nondeprived eye. In addition, the difference between phase durations for luminance- and chromatic-modulated stimuli recorded 12 minutes following reexposure to binocular vision was statistically significant, t test: $t(10) = 2.29$, $p \leq 0.05$, a difference that was also confirmed for data recorded 90 minutes after eye-patch removal, t test: $t(10) = 2.93$, $p = 0.015$. The data are well fitted by a power function of the form

$$y = 1 + \left(\frac{a}{\log(t+1)} \right)^b, \quad (1)$$

where y is the magnitude of the effect, t is time expressed in log, and a and b are free constants determining, respectively, amplitude and decay time. The goodness of fit was $R^2 = 0.87$ for luminance-modulated stimuli, and $R^2 = 0.79$ for color. The half-life of the effect, defined as the time at which the fitting curve reaches one half of the initial effect (value 1.6, indicated by the gray dashed line in Figure 2) was 3.7 minutes for luminance-modulated gratings and 27.2 minutes for gratings modulated in chromaticity, showing that the decay of the effect was slower for chromatic stimuli by a factor of 7.3. The decay of the effect of monocular deprivation expressed by the constant b given in Equation 1 was systematically lower for chromatic gratings: Figure 2B shows the average decay rate obtained by fitting the individual observers' data with Equation 1; the decay rate is significantly higher for luminance gratings, t test: $N = 12$, $t(10) = 3.95$, $p = 0.0027$, indicating a faster decay of the effect compared with chromatic gratings.

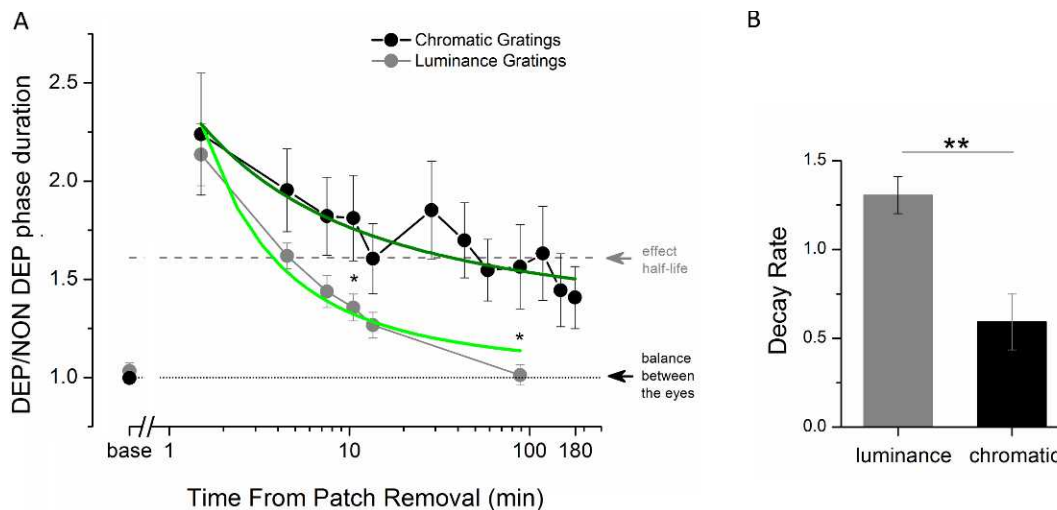


Figure 2. Effect of monocular deprivation on binocular rivalry mean phase durations. (A) The ratio between mean duration of the deprived and nondeprived eyes is plotted as a function of time elapsed from the removal of the eye-patch for luminance (gray symbols, average of 52 measures, eight repetitions times seven observers; only the preferred eye was patched for one observer, data taken from Lunghi et al., 2011) and chromatic (black symbols, average of 40 measures, eight repetitions times five observers) gratings. Error bars represent ± 1 SEM. The dashed line represents balance between the two eyes. Following 150 minutes of monocular deprivation, the phase duration is strongly unbalanced in favor of the deprived eye. The data are well fitted by a function of the form given in Equation 1. (B) The average value of the parameter b (the decay rate) of Equation 1 for fitting the equation to individual data separately for luminance and chromatic gratings.

To rule out the possibility that the effect of deprivation could be caused by retinal adaptation, therefore saturating quickly and requiring short adaptation durations, we tested a third group of observers with only 30 minutes of deprivation with luminance-modulated gratings. This brief deprivation had little effect on rivalry (Figure 3). During the first three minutes, perception was significantly biased toward the deprived eye, paired t test: $N = 4$, $t(3) = 4.72$, $p \leq 0.05$, but the effect was much less than after 150 minutes of patching: a factor of only 1.26 compared with 2.3. Furthermore, the effect was significant only during the first three minutes after patch removal: Data recorded later did not differ from baseline measurements, t test: $N = 4$, $p > 0.05$. This result indicates that the long-lasting effect of monocular deprivation that we observed is likely mediated by plastic neural modifications at the cortical level.

Rivalry is traditionally characterized by phase-duration distributions, which have a characteristic asymmetrical distribution, usually well approximated by a two-parameter (r , λ) *gamma distribution* of the form

$$g(x) = \frac{\lambda^r x^{r-1}}{\Gamma(r)} e^{-\lambda x}, \quad (2)$$

where Γ is the *gamma function*, r is the shape parameter, and λ is the scale parameter (Levelt, 1967). Figure 4 shows the phase-duration distributions of the deprived (black) and nondeprived (orange) eyes (nor-

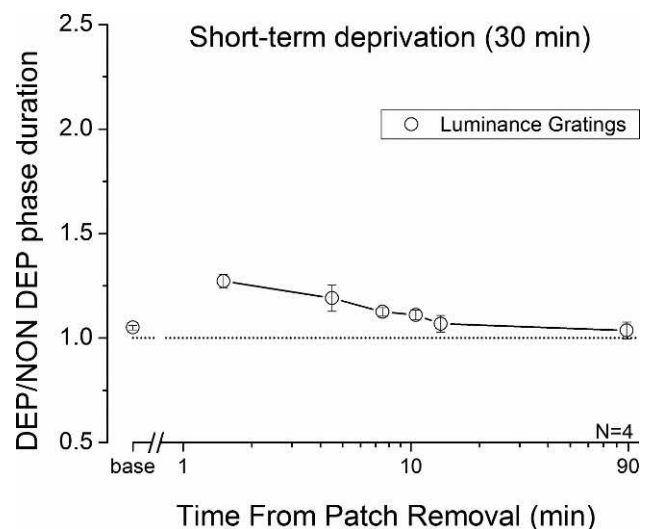


Figure 3. Effect of short-term monocular deprivation on binocular rivalry mean phase durations. The ratio between the mean phase durations of the deprived and nondeprived eyes is plotted as a function of time elapsed from the removal of the eye-patch for luminance-modulated gratings (average of 28 measures, eight repetitions times four observers; only the preferred eye was patched for one observer). The dashed line represents equal balance between the two eyes. Following 30 minutes of monocular deprivation, the phase duration is slightly unbalanced in favor of the deprived eye only during the first three minutes following eye-patch removal. Error bars represent ± 1 SEM.

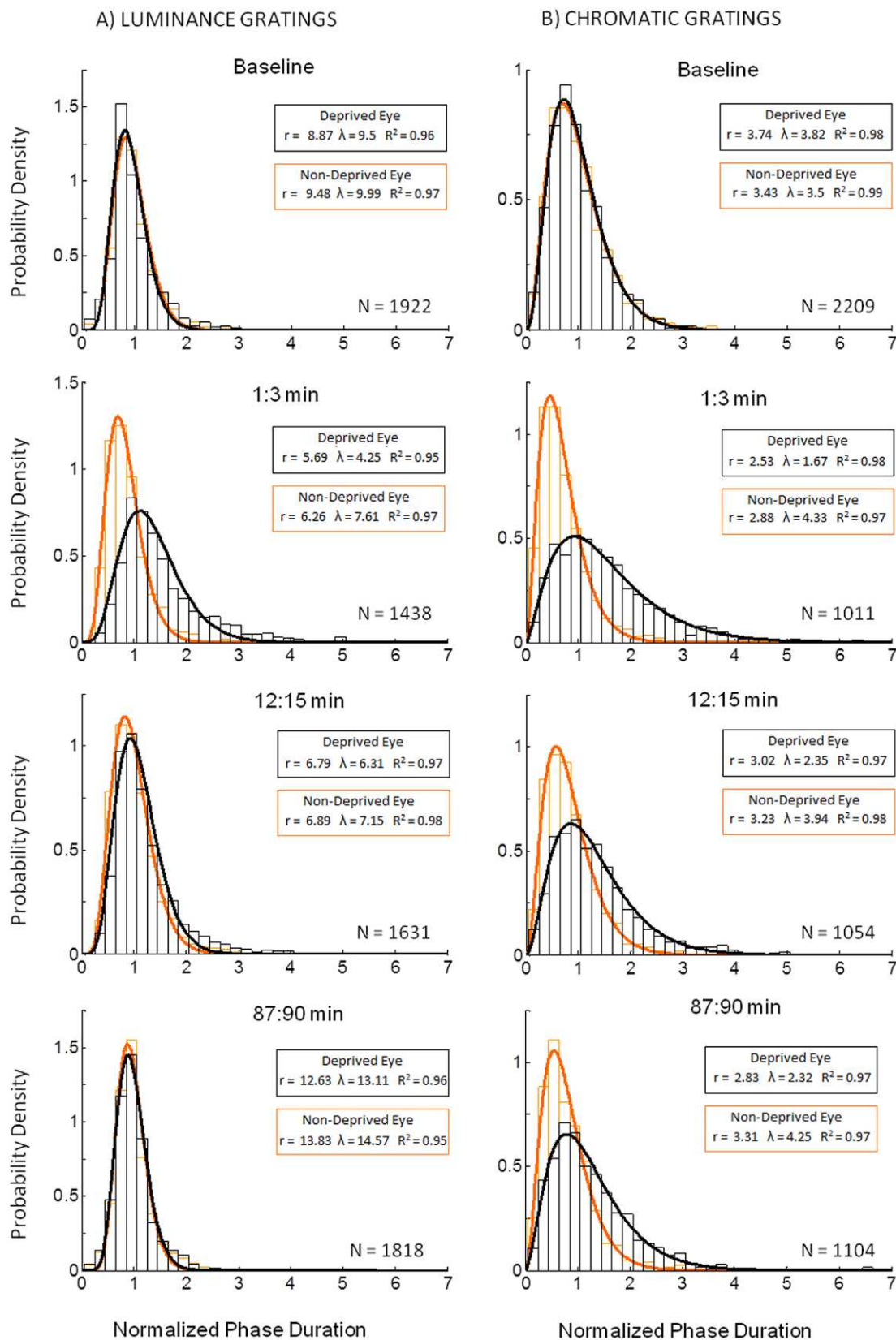


Figure 4. Phase-duration distributions of the deprived (black) and nondeprived (orange) eyes, plotted separately for different three-minute experimental blocks for luminance (A, data taken from Lunghi et al., 2011) and chromatic (B) gratings after monocular deprivation. Phase durations were normalized to the mean baseline phase duration for each subject because of the great interindividual variability in mean phase duration (from 1 to 9 s for luminance gratings, from 2 to 6 s for chromatic gratings). Phase-duration distributions are well fitted by a two-parameter (λ , r) gamma distribution of the form given in Equation 2.

malized for each observer to the baseline mean phase duration of that eye) and the relative gamma-distribution fits for several three-minute experimental blocks for luminance (Figure 4A) and chromatic (Figure 4B) visual stimuli. The baseline distributions (top panels) are very similar for the two eyes with similar values of r and λ . After monocular deprivation, the phase-duration distributions of the deprived eye became broader and shifted toward the right, indicating that, on average, all phase durations were longer, and the opposite held for phase-duration distributions of the nondeprived eye, indicating that, on average, phase durations were shorter. Nonetheless, the distributions maintained typical gamma-like characteristics and were well fit by the gamma distribution (see inserts of Figure 4 for goodness of fit). The separation between the phase-duration distribution of the deprived and that of the nondeprived eye was greater for chromatic than for luminance stimuli: 90 minutes after eye-patch removal, phase-duration distributions of the two eyes were identical for luminance-modulated gratings (bootstrap sign test: $p = 0.24$) while they clearly remained different for chromatic gratings (bootstrap sign test: $p < 0.0001$). When we directly compared phase duration distributions recorded 90 minutes following eye-patch removal for chromatic and luminance gratings, we found that deprived-eye phase-duration distributions were, on average, longer for chromatic gratings (bootstrap sign test: $p < 0.0001$), and phase durations for the nondeprived eye were, on average, shorter for chromatic gratings (bootstrap sign test: $p < 0.0001$). The phase duration distribution results show that the effect of deprivation is both increased phase durations of the deprived eye and curtailed phase durations of the nondeprived eye and that, despite the twofold unbalance between the eyes (Figure 2), the dynamics of binocular rivalry were normal after deprivation.

Figure 5 plots the ratio of r to λ separately for the deprived eye (filled symbols) and the nondeprived eye (open symbols) as functions of time from eye-patch removal. In line with the literature on the dynamics of binocular rivalry (De Marco, Penengo, & Trabucco, 1977), in the baseline measurements, λ and r of the same eye distribution were virtually identical, approximating unity. Monocular deprivation affected λ and r differently, particularly for chromatic gratings (black symbols): The shape parameter r remained basically unaltered while the scale parameter λ decreased for the deprived eye and increased for the nondeprived eye. This effect was just as prevalent 120 minutes after removal of the eye-patch. For luminance-modulated gratings (gray symbols), the differential effect on the two parameters was mostly apparent for the deprived eye while for the nondeprived eye a slight difference between the two was noticeable only during the first six minutes of binocular vision.

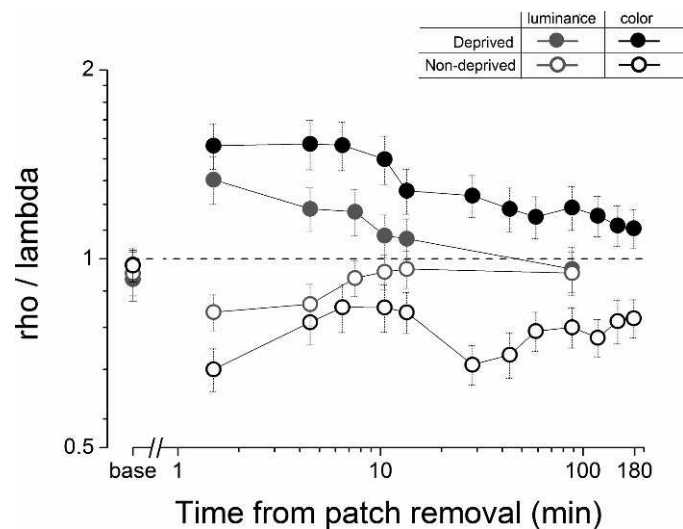


Figure 5. Phase duration distribution parameters. The ratio between the shape (r) and scale (λ) parameter of the gamma distribution fits (Equation 2), plotted as a function of time elapsed from removal of the eye-patch, for luminance (gray symbols, data taken from Lunghi et al., 2011) and chromatic gratings (black symbols) and the deprived (filled symbols) and nondeprived (open symbols) eyes, respectively. Error bars represent ± 1 SEM.

The analysis of mean phase durations and phase-duration distributions is standard in binocular rivalry. A more dynamic way of approaching the analysis of bistable perception is to track the probability of perceiving one or another stimulus over time (Lunghi et al., 2011; Mamassian & Goutcher, 2005). The advantage of this method is that it describes the dynamics of rivalry, providing a time course of visual perception, while the analysis of phase durations does not take into account the order of the events during a period of observation (because of the assumption that phase durations are independently and stochastically distributed). This is important because it has been demonstrated that at least two different processes with different characteristics operate during binocular rivalry: one at the onset of rivalry and one during sustained observation (Carter & Cavanagh, 2007).

We therefore computed the probability of perceiving the visual stimulus presented to the deprived eye (averaged over 6 s bins) as a function of time elapsed from rivalry onset for each three-minute experimental block. Figure 6 shows the time course of the probability of seeing the stimulus presented to the deprived eye for luminance-modulated (Figure 6A) and for chromatic gratings (Figure 6B). The baseline probabilities oscillate constantly around chance level, indicating that the stimuli presented to each eye were equally likely to be perceived. Monocular deprivation affected both the onset of rivalry and the sustained level of rivalry but in different ways for luminance and chromatic stimuli.

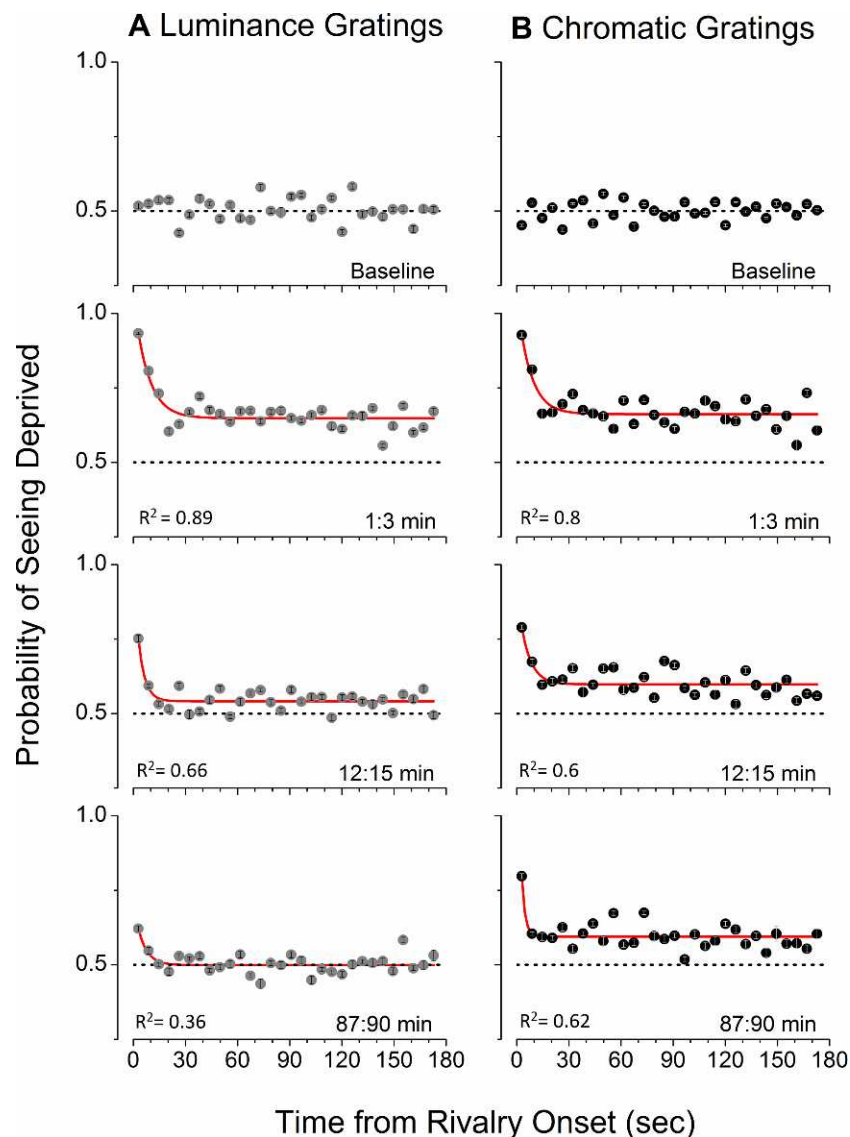


Figure 6. Average proportion of reported deprived-eye dominance. The probability of perceiving the stimulus presented to the deprived eye expressed as a function of time elapsed from the onset of different three-minute experimental blocks for luminance (A, data taken from Lunghi et al., 2011) and chromatic (B) gratings. The probability traces were computed by calculating the frequency of deprived-eye dominance (sampling rate = monitor refresh rate, 120 Hz) in 6 s bins for every experimental session recorded (52 for luminance gratings, 40 for chromatic gratings). The average probabilities across sessions are well fit by an exponential decay function given in Equation 3. Error bars represent ± 1 SEM for every 6 s bin. The average parameters of the fitting functions are reported in Figure 7.

The probabilities recorded after deprivation are well fit by an exponential decay function of the form

$$y = Ae\left(\frac{t}{\tau}\right) + y_0, \quad (3)$$

where y is the magnitude of the effect, A is the maximum amplitude, τ is the decay constant, and y_0 is a lower asymptote. After an initial exponential decay, the probability asymptotes to a level (y_0) above chance for all the testing sessions following deprivation when chromatic gratings are tested (Figure 6B) while for luminance-modulated gratings the probability decays

to chance level 90 minutes after eye-patch removal, and only the bias on onset rivalry is present. When we directly compared the probabilities recorded 90 minutes after reexposure to binocular rivalry for chromatic and luminance gratings, we found that for chromatic gratings the probability of seeing the stimulus presented to the deprived eye was systematically higher than for luminance gratings: Taken together, both the probabilities recorded during the first 25 s of viewing (onset effect) and those recorded during the following 155 s (sustained effect) were significantly higher for chromatic gratings (bootstrap sign test: 1,000,000 repeti-

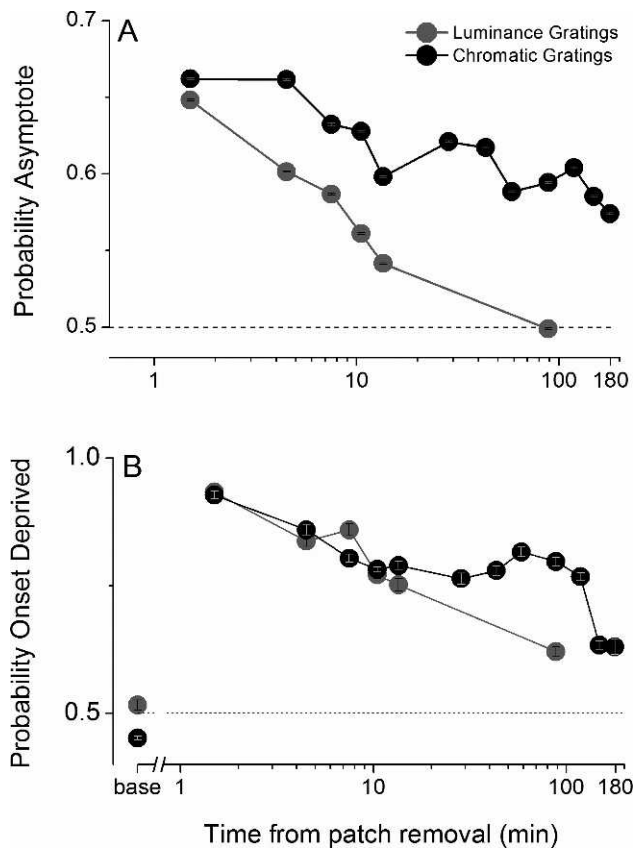


Figure 7. Probability trace asymptote and onset bias. (A) The asymptote of the effect of deprivation, corresponding to the fitting parameter y_0 of Equation 3 as a function of time elapsed from eye-patch removal. Error bars represent ± 1 SEM. (B) The probability of seeing the stimulus presented to the deprived eye at the onset of rivalry. In both cases, gray symbols refer to luminance and black symbols to chromatic gratings. The dashed lines in both graphs represent chance level, that is, no effect. Error bars represent ± 1 SEM (for luminance gratings, data taken from Lunghi et al., 2011).

tions, H_0 : chromatic \leq luminance, $p < 0.001$ for the onset effect, and $p < 0.05$ for the sustained effect).

The asymptotic difference between the deprived and nondeprived eye phase durations (i.e., the offset of the decay, y_0) decayed rapidly for luminance gratings to become insignificant 15 minutes after eye-patch removal (bootstrap sign test, $p = 0.15$) while for chromatic gratings the effect remained significant for the whole three-hour period tested (Figure 7A, bootstrap sign test, $p < 0.0001$). Conversely, the bias in onset rivalry (Figure 7B) followed a similar time course for luminance and chromatic gratings even though the onset bias measured 90 minutes following patch removal was higher for chromatic than for luminance gratings, t test: $t(90) = -2.616$, $p < 0.01$. Moreover, for chromatic gratings, the onset bias was significantly higher than chance level after 180 minutes following patch removal, t test, $t(39) = 2.4655$, $p < 0.02$. These

results indicate that the effect of monocular deprivation decays more rapidly for sustained than for onset rivalry, reinforcing the suggestion that two processes are at work with binocular rivalry (Carter & Cavanagh, 2007), and these are differently affected by monocular deprivation.

Discussion

Within a specific *critical period* (Hubel & Wiesel, 1970; Wiesel & Hubel, 1963), the mammalian visual cortex is highly vulnerable to the effects of visual experience, but it is generally assumed that mammalian adult visual systems, including humans, show little plasticity after closure of this period (Berardi et al., 2000; Fine et al., 2003; Hensch, 2004; Maurer et al., 2005). Our results provide a clear demonstration that the adult human visual system retains a high degree of plasticity, far more than previously thought: Two and a half hours of monocular deprivation dramatically impacts the dynamics of binocular rivalry, causing a twofold dominance of the deprived eye with measurable effects lasting up to 180 minutes, depending on the type of visual stimulation. Although the effect could, in principle, have a subcortical origin, we believe this unlikely, given that the patch was translucent (with a 10% light attenuation and therefore causing no dark-adaptation) and that retinal and geniculate alterations of neuronal discharge show a fast-adaptation time course (Baccus & Meister, 2002; Solomon, Peirce, Dhruv, & Lennie, 2004). In addition, a shorter deprivation of about half an hour produced a just noticeable unbalance between the two eyes while a subcortical origin would have predicted a similar effect to the two and a half-hour deprivation.

The data reported here point to a plasticity of ocular dominance in the adult human visual cortex. Our results stand out from previous evidence reporting long-lasting pattern-adaptation effects, such as the McCollough effect (McCollough, 1965) and the tilt aftereffect (Wolfe & O'Connell, 1986), which probably reflect pattern-sensitive neural changes involving higher associative cortices, including memory structures. Our findings point instead to a plastic reorganization of ocular dominance probably in the primary visual cortex that is and thought to be hard-wired after the closure of the critical period. Monocular deprivation is an effective technique to reveal plasticity as it drives competitive Hebbian-like mechanisms, such as those responsible for the major neural reorganization within the critical period (Mitchell & Sengpiel, 2009). That following monocular deprivation the deprived eye is reinforced and wins the competition for visual awareness, dominating rivalrous perception over the non-

deprived eye, is an unexpected result; long-term monocular deprivation usually results in depression of deprived eye input (Wiesel & Hubel, 1963). Boosting the signal of the deprived eye could be the first response of the visual system to the lack of information provoked by monocular deprivation, an attempt to optimize response to weak stimulation probably by homeostatically modulating contrast-gain mechanisms. Homeostatic bidirectional plasticity has been indeed observed in the mouse visual cortex, where increased responses of both the deprived and nondeprived eyes have been found after monocular deprivation (Mrsic-Flogel et al., 2007). The importance of competitive mechanisms for visual cortical plasticity has been confirmed by recent evidence showing that perceptual learning (when the weak eye is reinforced and contemporarily the strong eye is suppressed) is able to reduce sensory eye dominance and is more effective than a simple reinforcement of the weak eye (Xu, He, & Ooi, 2010).

In our current study, binocular rivalry, which probes neural, inhibition-generated competitive mechanisms (Blake & Logothetis, 2002; Klink et al., 2010; Levelt, 1966; Tong et al., 2006), revealed that even ocular dominance, thought to be plastic only during the critical period, has considerable residual plasticity in young human adults. The effect of monocular deprivation that we found on binocular rivalry shares some characteristics with contrast adaptation, such as the exponential decay (Wark, Fairhall, & Rieke, 2009). However, the effects described here are far more long lasting than those reported for adaptation. Bao and Engel (2012), for example, found that 15 minutes of de-adaptation cancelled the effects of four hours of contrast adaptation; whereas our effects persisted for over three hours, longer than the deprivation period, implicating plasticity mechanisms other than those affected by contrast adaptation. The effects may well be related to contrast adaptation but have characteristics quite different from those reported to date, engaging plastic changes in neural activity that are far more long lasting than previously described.

Our results show that monocular deprivation had more dramatic consequences on the dynamics of binocular rivalry when chromatic- rather than luminance-modulated gratings were tested. Equiluminant gratings are known to reduce the response of M cells in favor of P cells, which are sensitive to chromatic differences (Hubel & Livingstone, 1990; Schiller & Malpeli, 1978). Our results suggest that the parvo pathway is more susceptible to monocular deprivation in adult humans as monocular deprivation produced longer-lasting effects with a slower decay for chromatic than luminance gratings. These results suggest that the parvo system is affected by monocular deprivation for longer periods compared with the magno system,

pointing to plastic structural experience-dependent neural changes. The hypothesis of a leading role of the parvo system in mediating the effect of monocular deprivation on binocular rivalry is in line with evidence showing that during the critical period monocular deprivation has more severe effects on the parvo system with ocular dominance column shrinkage of the macaque primary visual cortex being larger in layer IVc β (Horton & Hocking, 1997). Consistent with this evidence, in humans, visual features associated with the magno system (such as motion perception) are more resistant to visual deprivation, showing spared functions after recovery from blindness (Fine et al., 2003; Maurer et al., 2005; Ostrovsky et al., 2009), indicating that the parvo system is, in general, more vulnerable to the effects of visual deprivation.

Different neural functions, even within the same sensory system, may develop at different rates and have different critical periods. There appears to be a link between the developmental time course of the different visual functions and their vulnerability to abnormal visual experience. The Detroit Model of Levi (2005) proposes that visual functions that develop slowly are more sensitive to the effects of sensory deprivation (i.e., they retain a higher degree of experience-dependent plasticity), following the principle of “last-hired, first-fired.” Achromatic and chromatic vision have different developmental time courses, the first developing fast, the other being a late bloomer in visual development with visual evoked potentials in response to chromatic stimuli developing much later than those to luminance (Morrone, Burr, & Fiorentini, 1990) and not becoming adult-like until 12–14 years of age in humans with latencies not completely mature until 17–18 years of age (Crognale, 2002). As chromatic parsing is mostly associated with P-cell activity (Gegenfurtner & Kiper, 2003; Hubel & Livingstone, 1990; Schiller & Malpeli, 1978), the late development of the chromatic vision in humans suggests that P cells retain a high degree of plasticity even after the closure of the critical period; our results confirmed this spared plasticity.

A recent study by Denison and Silver (2012) has demonstrated that the parvo and the magno systems have different roles in mediating the dynamics of binocular rivalry; the magno system is more involved in *eye rivalry*, and the parvo system is more involved in *stimulus rivalry*. Stimulus rivalry is a particular form of binocular rivalry revealed by the interocular-switching paradigm first proposed by Logothetis, Leopold, and Sheinberg (1996), in which rivalrous images are swapped between the eyes three times per second and can lead to both rapid-regular switches (eye rivalry) or slow-irregular switches (stimulus rivalry). The fact that the parvo system is more involved in mediating stimulus rivalry hints to a role of the parvo pathway in maintaining perceptual stability over prolonged periods

of time. This is in line with our results showing prolonged retention of the effect of monocular deprivation when binocular rivalry between equiluminant gratings is tested.

One interesting point of our results is that monocular deprivation affected the dynamics of binocular rivalry differently for sustained and onset rivalry, the decay of the effect being slower for onset rivalry. Onset and sustained rivalry show different characteristics (reviewed in Stanley, Forte, Cavanagh, & Carter, 2012); for example, onset rivalry shows a stable and predictable individual bias that varies across the visual field according to the zones of monocular dominance and is therefore linked to (although not totally explained by) ocular dominance while a hallmark of sustained rivalry is the unpredictability of the perceptual switches (for accounts on perceptual memory and onset rivalry see also de Jong, Knapen, & van Ee, 2012; Noest, van Ee, Nijs, & van Wezel, 2007; Pastukhov & Braun, 2008). In general, onset rivalry has been shown to be more sensitive to early visual features than sustained rivalry; for example, small imbalances in contrast and luminance between stimuli strongly affect onset rivalry, leaving sustained rivalry almost unchanged. Equating the strength of the rivalrous images does not annul the stable and consistent bias shown by every observer at the onset of rivalry while balancing stimulus strength equates sustained rivalry dominance (Stanley, Carter, & Forte, 2011). Because of the differences between onset and sustained rivalry, it is likely that the two phenomena are mediated by different mechanisms, and these mechanisms show different susceptibility to the effects of visual deprivation. Indeed, onset and sustained rivalry have been suggested to probe neural adaptation at different time scales (Brascamp et al., 2008).

In our previous brief report (Lunghi et al., 2011), we showed that monocular deprivation also influenced apparent contrast with stimuli presented to the deprived eye appearing, on average, 36% higher in contrast than stimuli presented to the nondeprived eye. The effect of deprivation on the dynamics of binocular rivalry could not be explained by the boost in apparent contrast because, in order to affect mean phase durations in a way similar to deprivation, contrast in one eye had to be higher by a factor of three. We therefore speculated that short-term monocular deprivation acted by increasing the contrast gain of the deprived eye as a first attempt of the visual system to compensate for the lack of information. The fact that monocular deprivation had more severe consequences for equiluminant stimuli could reflect the different contrast gains of M and P cells. While M cell responses rapidly saturate for stimuli above 20% of contrast, most P cells do not show saturating responses to chromatic stimuli even at high chromatic contrasts

(Purpura, Kaplan, & Shapley, 1988; Solomon & Lennie, 2005). If monocular deprivation increases contrast gain of the deprived eye, it is likely to have a greater effect on P-cell responses rather than on M cells, which are limited by saturation.

The gamma-like shape of phase duration distributions has been considered a hallmark of binocular rivalry and bistable perception in general (Carter & Pettigrew, 2003; van Ee, 2005). However, the two parameters defining the gamma distribution usually correlated and are consequently considered redundant (De Marco et al., 1977; Mamassian & Goutcher, 2005). One last interesting result from our data is that monocular deprivation disrupted the correlation between the two parameters defining the gamma distribution used to fit phase duration distributions of the two eyes even though the significance of this finding is uncertain.

Conclusions

In conclusion, we have shown that a brief period of monocular deprivation has drastic consequences on visual perception that are likely to reflect neuroplastic changes at the level of the primary visual cortex. We also showed that the perceptual bias of binocular rivalry was stronger, showing a much slower decay for chromatic than for luminance gratings, lasting for at least 180 minutes after removal of the eye-patch. As equiluminant gratings are known to reduce the responses of M cells, our results suggest that P cells are more susceptible to the effect of visual deprivation and retain a high degree of residual experience-dependent plasticity, resulting in long-lasting retention of the effect of monocular deprivation and being therefore more likely to involve structural neural plastic modification.

That the adult visual system retains a high degree of experience-dependent plasticity is important for understanding neural reorganization following late visual loss and for reconsidering sensitive periods in human vision. Binocular rivalry revealed itself as a sensitive probe for neuroplastic changes and could be a useful noninvasive tool for monitoring plastic changes during occlusion therapy for amblyopia.

Keywords: binocular rivalry, plasticity, visual cortex

Acknowledgments

This research was supported by the Italian Ministry of Universities and Research (PRIN2009) and by ERC project “STANIB” (FP7 ERC). We thank Guido

Marco Cicchini for constant technical help and useful discussions throughout this project.

Commercial relationships: none.

Corresponding author: Claudia Lunghi.

Email: claudia.lunghi@in.cnr.it.

Address: Department of Neuroscience, Università Degli Studi di Firenze, Firenze, Italy; Institute of Neuroscience, CNR – Pisa, Pisa, Italy.

References

- Baccus, S. A., & Meister, M. (2002). Fast and slow contrast adaptation in retinal circuitry. *Neuron*, 36(5), 909–919.
- Bao, M., & Engel, S. A. (2012). Distinct mechanism for long-term contrast adaptation. *Proceedings of the National Academy of Sciences of the United States of America*, 109(15), 5898–5903.
- Berardi, N., Pizzorusso, T., & Maffei, L. (2000). Critical periods during sensory development. *Current Opinion in Neurobiology*, 10(1), 138–145.
- Blake, R., & Logothetis, N. K. (2002). Visual competition. *Nature Review Neuroscience*, 3(1), 13–21.
- Boroojerdi, B., Battaglia, F., Muellbacher, W., & Cohen, L. G. (2001). Mechanisms underlying rapid experience-dependent plasticity in the human visual cortex. *Proceedings of the National Academy of Sciences of the United States of America*, 98(25), 14698–14701.
- Boroojerdi, B., Bushara, K. O., Corwell, B., Immisch, I., Battaglia, F., Muellbacher, W., et al. (2000). Enhanced excitability of the human visual cortex induced by short-term light deprivation. *Cerebral Cortex*, 10(5), 529–534.
- Brascamp, J. W., Knapen, T. H., Kanai, R., Noest, A. J., van Ee, R., & van den Berg, A. V. (2008). Multi-timescale perceptual history resolves visual ambiguity. *PLoS One*, 3(1), e1497.
- Carter, O., & Cavanagh, P. (2007). Onset rivalry: Brief presentation isolates an early independent phase of perceptual competition. *PLoS One*, 2(4), e343.
- Carter, O., & Pettigrew, J. D. (2003). A common oscillator for perceptual rivalries? *Perception*, 32(3), 295–305.
- Crognale, M. A. (2002). Development, maturation, and aging of chromatic visual pathways: VEP results. *Journal of Vision*, 2(6):2, 438–450, <http://www.journalofvision.org/content/2/6/2>, doi:10.1167/2.6.2. [PubMed] [Article]
- de Jong, M. C., Knapen, T., & van Ee, R. (2012). Opposite influence of perceptual memory on initial and prolonged perception of sensory ambiguity. *PLoS One*, 7(1), e30595.
- De Marco, A., Penengo, P., & Trabucco, A. (1977). Stochastic models and fluctuations in reversal time of ambiguous figures. *Perception*, 6(6), 645–656.
- Denison, R. N., & Silver, M. A. (2012). Distinct contributions of the magnocellular and parvocellular visual streams to perceptual selection. *Journal of Cognitive Neuroscience*, 24(1), 246–259.
- Ellemberg, D., Lewis, T. L., Maurer, D., Brar, S., & Brent, H. P. (2002). Better perception of global motion after monocular than after binocular deprivation. *Vision Research*, 42(2), 169–179.
- Fine, I., Smallman, H. S., Doyle, P., & MacLeod, D. I. (2002). Visual function before and after the removal of bilateral congenital cataracts in adulthood. *Vision Research*, 42(2), 191–210.
- Fine, I., Wade, A. R., Brewer, A. A., May, M. G., Goodman, D. F., Boynton, G. M., et al. (2003). Long-term deprivation affects visual perception and cortex. *Nature Neuroscience*, 6(9), 915–916.
- Gegenfurtner, K. R., & Kiper, D. C. (2003). Color vision. *Annual Review of Neuroscience*, 26, 181–206.
- Harauzov, A., Spolidoro, M., DiCristo, G., De Pasquale, R., Cancedda, L., Pizzorusso, T., et al. (2010). Reducing intracortical inhibition in the adult visual cortex promotes ocular dominance plasticity. *Journal of Neuroscience*, 30(1), 361–371.
- Haynes, J. D., & Rees, G. (2005). Predicting the stream of consciousness from activity in human visual cortex. *Current Biology*, 15(14), 1301–1307.
- Hensch, T. K. (2004). Critical period regulation. *Annu Rev Neurosci*, 27, 549–579.
- Horton, J. C., & Hocking, D. R. (1997). Timing of the critical period for plasticity of ocular dominance columns in macaque striate cortex. *Journal of Neuroscience*, 17(10), 3684–3709.
- Hubel, D. H., & Livingstone, M. S. (1990). Color and contrast sensitivity in the lateral geniculate body and primary visual cortex of the macaque monkey. *Journal of Neuroscience*, 10(7), 2223–2237.
- Hubel, D. H., & Wiesel, T. N. (1970). The period of susceptibility to the physiological effects of unilateral eye closure in kittens. *Journal of Physiology*, 206(2), 419–436.
- Kaplan, E., Shapley, R. M., & Purpura, K. (1988). Color and luminance contrast as tools for probing the primate retina. *Neuroscience Research Supplement*, 8, S151–S165.
- Karni, A., & Bertini, G. (1997). Learning perceptual skills: Behavioral probes into adult cortical plas-

- ticity. *Current Opinion in Neurobiology*, 7(4), 530–535.
- Klink, P. C., Brascamp, J. W., Blake, R., & van Wezel, R. J. (2010). Experience-driven plasticity in binocular vision. *Current Biology*, 20(16), 1464–1469.
- Kwon, M., Legge, G. E., Fang, F., Cheong, A. M., & He, S. (2009). Adaptive changes in visual cortex following prolonged contrast reduction. *Journal of Vision*, 9(2):20, 1–16, <http://www.journalofvision.org/content/9/2/20>, doi:10.1167/9.2.20. [PubMed] [Article]
- Levelt, W. J. (1966). The alternation process in binocular rivalry. *British Journal of Psychology*, 57(3–4), 225–238.
- Levelt, W. J. (1967). Note on the distribution of dominance times in binocular rivalry. *British Journal of Psychology*, 58(1), 143–145.
- Levi, D. M. (2005). Perceptual learning in adults with amblyopia: A reevaluation of critical periods in human vision. *Developmental Psychobiology*, 46(3), 222–232.
- Levi, D. M., McKee, S. P., & Movshon, J. A. (2011). Visual deficits in anisometropia. *Vision Research*, 51(1), 48–57.
- Lewis, T. L., Maurer, D., & Brent, H. P. (1995). Development of grating acuity in children treated for unilateral or bilateral congenital cataract. *Investigative Ophthalmology & Visual Science*, 36(10), 2080–2095, <http://www.iovs.org/content/36/10/2080>. [PubMed] [Article]
- Logothetis, N. K., Leopold, D. A., & Sheinberg, D. L. (1996). What is rivaling during binocular rivalry? *Nature*, 380(6575), 621–624.
- Lunghi, C., Burr, D. C., & Morrone, C. (2011). Brief periods of monocular deprivation disrupt ocular balance in human adult visual cortex. *Current Biology*, 21(14), R538–R539.
- MacLeod, D. I., & Boynton, R. M. (1979). Chromaticity diagram showing cone excitation by stimuli of equal luminance. *Journal of the Optical Society of America*, 69(8), 1183–1186.
- Mamassian, P., & Goutcher, R. (2005). Temporal dynamics in bistable perception. *Journal of Vision*, 5(4):7, 361–375, <http://www.journalofvision.org/content/5/4/7>, doi:10.1167/5.4.7. [PubMed] [Article]
- Maurer, D., Lewis, T. L., & Mondloch, C. J. (2005). Missing sights: Consequences for visual cognitive development. *Trends in Cognitive Science*, 9(3), 144–151.
- Maya Vetencourt, J. F., Sale, A., Viegi, A., Baroncelli, L., De Pasquale, R., O’Leary, O. F., et al. (2008). The antidepressant fluoxetine restores plasticity in the adult visual cortex. *Science*, 320(5874), 385–388.
- McCollough, C. (1965). Color adaptation of edge-detectors in the human visual system. *Science*, 149(3688), 1115–1116.
- Merabet, L. B., Hamilton, R., Schlaug, G., Swisher, J. D., Kiriakopoulos, E. T., Pitskel, N. B., et al. (2008). Rapid and reversible recruitment of early visual cortex for touch. *PLoS One*, 3(8), e3046.
- Mitchell, D. E., & Sengpiel, F. (2009). Neural mechanisms of recovery following early visual deprivation. *Philosophical Transactions of the Royal Society - Biological Science*, 364(1515), 383–398.
- Morrone, M. C., Burr, D. C., & Fiorentini, A. (1990). Development of contrast sensitivity and acuity of the infant colour system. *Proceedings of the Royal Society - Biological Science*, 242(1304), 134–139.
- Mrsic-Flogel, T. D., Hofer, S. B., Ohki, K., Reid, R. C., Bonhoeffer, T., & Hubener, M. (2007). Homeostatic regulation of eye-specific responses in visual cortex during ocular dominance plasticity. *Neuron*, 54(6), 961–972.
- Noest, A. J., van Ee, R., Nijs, M. M., & van Wezel, R. J. (2007). Percept-choice sequences driven by interrupted ambiguous stimuli: A low-level neural model. *Journal of Vision*, 7(8):10, 1–14, <http://www.journalofvision.org/content/7/8/10>, doi:10.1167/7.8.10. [PubMed] [Article]
- Ostrovsky, Y., Andalman, A., & Sinha, P. (2006). Vision following extended congenital blindness. *Psychological Science*, 17(12), 1009–1014.
- Ostrovsky, Y., Meyers, E., Ganesh, S., Mathur, U., & Sinha, P. (2009). Visual parsing after recovery from blindness. *Psychological Science*, 20(12), 1484–1491.
- Pascual-Leone, A., Amedi, A., Fregni, F., & Merabet, L. B. (2005). The plastic human brain cortex. *Annual Review Neuroscience*, 28, 377–401.
- Pastukhov, A., & Braun, J. (2008). A short-term memory of multi-stable perception. *Journal of Vision*, 8(13):7, 1–14, <http://www.journalofvision.org/content/8/13/7>, doi:10.1167/8.13.7. [PubMed] [Article]
- Purpura, K., Kaplan, E., & Shapley, R. M. (1988). Background light and the contrast gain of primate P and M retinal ganglion cells. *Proceedings of the National Academy of Sciences of the United States of America*, 85(12), 4534–4537.
- Roder, B., Stock, O., Bien, S., Neville, H., & Rosler, F. (2002). Speech processing activates visual cortex in congenitally blind humans. *European Journal of Neuroscience*, 16(5), 930–936.

- Sadato, N., Pascual-Leone, A., Grafman, J., Ibanez, V., Deiber, M. P., Dold, G., et al. (1996). Activation of the primary visual cortex by Braille reading in blind subjects. *Nature*, *380*(6574), 526–528.
- Sasieni, L. (1978). The Frisby stereotest. *The Optician*, *176*(4544), 7–8, 10.
- Schiller, P. H., & Malpeli, J. G. (1978). Functional specificity of lateral geniculate nucleus laminae of the rhesus monkey. *Journal of Neuroscience*, *41*(3), 788–797.
- Smith, V. C., & Pokorny, J. (1975). Spectral sensitivity of the foveal cone photopigments between 400 and 500 nm. *Vision Research*, *15*(2), 161–171.
- Solomon, S. G., & Lennie, P. (2005). Chromatic gain controls in visual cortical neurons. *Journal of Neuroscience*, *25*(19), 4779–4792.
- Solomon, S. G., Peirce, J. W., Dhruv, N. T., & Lennie, P. (2004). Profound contrast adaptation early in the visual pathway. *Neuron*, *42*(1), 155–162.
- Stanley, J., Carter, O., & Forte, J. (2011). Color and luminance influence, but can not explain, binocular rivalry onset bias. *PLoS One*, *6*(5), e18978.
- Stanley, J., Forte, J. D., Cavanagh, P., & Carter, O. (2012). Onset rivalry: The initial dominance phase is independent of ongoing perceptual alternations. *Frontiers in Human Neuroscience*, *5*, 140.
- Tong, F., Meng, M., & Blake, R. (2006). Neural bases of binocular rivalry. *Trends in Cognitive Science*, *10*(11), 502–511.
- van Ee, R. (2005). Dynamics of perceptual bi-stability for stereoscopic slant rivalry and a comparison with grating, house-face, and Necker cube rivalry. *Vision Research*, *45*(1), 29–40.
- Wark, B., Fairhall, A., & Rieke, F. (2009). Timescales of inference in visual adaptation. *Neuron*, *61*(5), 750–761.
- Wiesel, T. N., & Hubel, D. H. (1963). Single-cell responses in striate cortex of kittens deprived of vision in one eye. *Journal of Neurophysiology*, *26*, 1003–1017.
- Wiesel, T. N., & Hubel, D. H. (1965). Comparison of the effects of unilateral and bilateral eye closure on cortical unit responses in kittens. *Journal of Neurophysiology*, *28*(6), 1029–1040.
- Wolfe, J. M., & O'Connell, K. M. (1986). Fatigue and structural change: Two consequences of visual pattern adaptation. *Investigative Ophthalmology & Visual Science*, *27*(4), 538–543, <http://www.iovs.org/content/27/4/538>. [PubMed] [Article]
- Xu, J. P., He, Z. J., & Ooi, T. L. (2010). Effectively reducing sensory eye dominance with a push-pull perceptual learning protocol. *Current Biology*, *20*(20), 1864–1868.
- Zhang, P., Bao, M., Kwon, M., He, S., & Engel, S. A. (2009). Effects of orientation-specific visual deprivation induced with altered reality. *Current Biology*, *19*(22), 1956–1960.