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Ocular dominance plasticity: A binocular combination task finds no cumulative effect with repeated patching

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ABSTRACT

Short-term monocular deprivation strengthens the contribution of the deprived eye to binocular vision. This change has been observed in adults with normal vision or amblyopia. The change in ocular dominance is transient and recovers over approximately one hour. This shift has been measured with various visual tasks, including binocular rivalry and binocular combination. We investigated whether the ocular dominance shift could be accumulated across multiple periods of monocular deprivation over consecutive days. We used a binocular phase combination task to measure the shift in eye dominance. We patched the dominant eye of ten adults with normal vision for two hours across five consecutive days. Our results show no cumulative effect after repeated sessions of short-term monocular deprivation.

1. Introduction

Patching an eye for a few hours increases its contribution to binocular vision. This is observed in human adults after the critical period for visual development. Lunghi, Burr, and Morrone (2011) first showed this effect by patching adults with normal vision for two hours. This effect induces a shift in ocular dominance and lasts for 30–90 min after patching (Lunghi et al., 2011; Zhou, Clavagnier, & Hess, 2013). Psychophysical (Lunghi et al., 2011, 2013; Zhou et al., 2013, 2014; Zhou, 2017), electrophysiological (Lunghi, 2015; Zhou, 2015) and brain imaging (Binda, 2018; Chadnova, 2017; Lunghi, 2015) studies in humans have also demonstrated this short-term patching effect. The contrast gain of the non-deprived eye is reduced and that of the deprived eye increased (Chadnova, 2018; Zhou et al., 2013) during short-term patching. These reciprocal changes occur possibly in layer 4 of the primary visual cortex (V1) (Reynaud, 2018; Tso, Miller, & Begum, 2017; Zhou, Reynaud, & Hess, 2014) and involve binocular neurones tuned to high spatial frequencies (Lunghi, 2016; Zhou et al., 2014). Intrinsic imaging and voltage-sensitive dye imaging in primate studies have shown these effects in V1 (Reynaud, 2018; Tso et al., 2017). Early work suggests that the effect does not show orientation tuning (Zhou et al., 2014). However a subsequent study shows that patching may have multiple effects and exhibit orientation tuning (Baldwin & Hess, 2018). The patching effect is associated with reduced cortical GABA in V1 (Lunghi, 2015). However later stages of visual processing may also be involved during patching (Bai, 2017; Kim, Kim, & Blake, 2017; Ramamurthy & Blaser, 2018). This has been demonstrated with psychophysical studies. For example, Bai et al. showed that short-term patching induces different effects in binocular rivalry and combination tasks (Bai, 2017). Also kaleidoscope manipulation, which does not affect the properties of images, causes one eye to be weaker than the other eye (Ramamurthy & Blaser, 2018). Moreover continuous flash suppression, Kim et al. showed that the patching effect can be induced solely by the suppression of one eye on the other eye without deprivation of visual input (Kim et al., 2017).

The short-term patching effect in normal adults shows that neural plasticity still exists after the critical period. This remaining plasticity can be exploited to potentially recover the binocular function in adults that had been previously lost in childhood. Amblyopia is a developmental disorder of the visual system. About 3 to 5% of children in the general population develop amblyopia and have poor binocular vision (Levi, Knill, & Bavelier, 2015). Several procedures have been developed to harness any residual plasticity in adults. They may help recover function in the amblyopic pathway (Astle, Webb, & McGraw, 2011; Levi & Li, 2009; Li, 2011; Vedamurthy, 2015; Xu, He, & Ooi, 2010) and restore binocular function (Hess & Thompson, 2015).

Shifts in ocular dominance from short-term monocular deprivation could provide a therapeutic benefit. By rebalancing the eyes, short-term patching could restore binocular function. Psychophysical tools such as binocular competition (e.g. rivalry) and combination visual tasks have been used to measure this effect. In binocular rivalry incompatible stimuli are presented to each eye. Since the stimuli are incompatible to

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each other, these inputs from both eyes rather compete than fuse with each other. Changes in ocular dominance plasticity are measured by relative durations for which each stimulus is perceived. In binocular combination tasks, fusible stimuli are presented to each eye. This is a more typical input from an ecological perspective. Subjects perceive the fused percept based on each eye's level of contribution to binocular vision. Various combination tasks including phase combination, motion combination and contrast combination have been used to measure changes in ocular dominance from short-term patching (Lunghi, Burr, & Morrone, 2013). Both binocular rivalry and combination tasks have been used to measure changes in sensory eye balance. However different neural mechanisms may be involved (Bai, 2017; Baldwin & Hess, 2018). Binocular rivalry represents an inhibitory rivalry of non-fusible monocular images. Binocular combination represents the excitatory combination of fusible images. Therefore they may measure different aspects of sensory eye dominance.

Zhou, Thompson, and Hess (2013) first showed that adults with amblyopia also exhibited the short-term patching effect with a phase combination task. Recent studies have shown sustained improvements in visual acuity and stereopsis from repeated short-term patching of the amblyopic eye in adults. Lunghi et al. demonstrated this with a binocular rivalry paradigm with physical exercise (Lunghi, 2019) and Zhou et al. (Zhou, 2019) with a binocular combination paradigm. Also Zhou et al. reported marginal improvements in binocular balance. As these studies indicate, when amblyopic eye is patched instead of the fellow eye – as seen in typical therapeutic patching – binocular function may recover. However, this neuroplastic change will provide long-term benefits only if it can get integrated over time within a protocol. A recent study showed with a phase combination measure that there is little or no dependence of ocular dominance plasticity changes on the duration of the monocular deprivation in normal observers (Min, 2018). This suggests that the effects of the deprivation may rapidly saturate, at least for a single "pulse" of deprivation. In this study, we set out to determine whether effects can summate over multiple "pulses" of deprivation. This could be useful clinically, as several short periods of daily monocular occlusion across many weeks might lead to a longer-lasting accumulated benefit.

In this study we used a binocular phase combination paradigm to measure changes in eye balance from short-term patching. We patched normal observers for five consecutive days and found no accumulated changes in ocular dominance. We found no changes in baseline of sensory eye balance across days. This reinforces the notion that there may be no duration dependence in the patching effect (Min, 2018), whether patching occurs within a single or across multiple days, in normal observers. This finding suggests that the dynamics of ocular dominance plasticity changes in normal observers induced by short-term monocular deprivation are of an all-or-none phenomenon.

2. Materials and methods

2.1. Participants

Ten adults (average age = 23, range = 21–25) with normal or corrected-to-normal vision participated in this study. One subject was the listed first author. All other subjects were naïve to the purpose of this study and provided informed consent. This study conformed to the Declaration of Helinski and was approved by the Institutional Review Boards at McGill University.

2.2. Apparatus

We programmed the experiment in Matlab 2012a using PsychToolBox 3.0.9 (Brainard, 1997; Pelli, 1997). We presented dichoptic stimuli on head-mounted goggles with a refresh rate of 60 Hz, resolution of 800 × 600 pixels and a mean luminance of 59 cd/m^2. These had separate screens to present the dichoptic stimuli to each eye. For the first five subjects we used eMargin Z800 pro goggles. Due to equipment failure we replaced these with GOOVIS Cinego G2 for the remaining subjects.

2.3. Binocular phase combination task

In this task, separate horizontal sine-wave gratings were presented to the two eyes in opposite phases: -22.5° for one eye and $+22.5^\circ$ for the other eye. The phase difference between the two eyes was 45°. The gratings were established at a visual angle of $6.6^\circ \times 6.6^\circ$ degrees, spatial frequency of 0.3 cycles/deg, and base contrast of 60%. We used the method of constant stimuli. Subjects were asked to report the phase of the binocularly perceived grating. They located a flanking reference line to where they perceived the center of the dark strip from the fused percept. When two eyes contribute equally to binocular vision, the perceived phase will be zero (the sum of $+22.5^\circ$ and -22.5°). However, when there is relatively stronger input from one eye, this imbalance will bias the fused percept in favour of that eye's stimulus phase.

We showed stimuli at different interocular contrast ratios by increasing the contrast in one eye and decreasing the contrast in the other eye. Modulating the interocular contrast ratio enabled us to find the contrast ratio when two eyes contributed equally (i.e. balance point). When the balance point is reached, the perceived phase is zero. We implemented five interocular contrast ratios ($1/2$, $1/\sqrt{2}$, $1/1$, $\sqrt{2}/1$, $2/1$) for measuring the baseline balance, and three interocular contrast ratios ($1/\sqrt{2}$, $1/1$, $\sqrt{2}/1$) for post-patching balance. We determined how much the interocular contrast ratio had to be changed to reach the balance point before and after deprivation. The change in ocular dominance after deprivation was quantified by the differences in the contrast balance ratio between before and after patching.

A trial of the phase combination task had an alignment and test phase. During the alignment phase, subjects aligned the two halves of a dichoptic cross and four circles (Fig. 1A) using a keyboard. Two circles and one half of the dichoptic cross was shown to each eye. A fused but unaligned percept would be a combination of four circles and a misaligned dichoptic cross. After the align phase, a test phase ensued where a fused horizontal sinusoidal grating was shown. Subjects were asked to report their perceived center of the darkest area in the fused grating by moving a flanking black reference line. After the test phase, the alignment phase returned. Both the alignment and grating stimuli were displayed until each subject completed performing the task. Throughout the task a pixelated binary noise frame was presented around the stimuli to facilitate fusion. Moreover, there were two configurations of the sinusoidal gratings to eliminate positional bias. In the first configuration, the dominant eye was shown with a grating of $+22.5^\circ$ and the non-dominant eye with a grating of -22.5° relative to the center. In the second configuration, the dominant eye was shown with a grating of -22.5° and the non-dominant eye with a grating of $+22.5^\circ$ relative to the center. There were eight trials for every interocular contrast ratio for baseline measurement and five for post-patching measurement. This amounted to 80 trials in the baseline measurement (5 interocular contrast ratios × 8 repetitions × 2 configurations) and 30 in the post-patching measurement (3 interocular contrast ratios × 5 repetitions × 2 configurations). Subjects on average spent 10 min on the baseline task and 3 min on the post-patch task.

2.4. Procedure

Subjects began the study with baseline measurement. Then their dominant eye was patched for 120 min with a translucent patch. The dominant eye was determined with the Miles test (Miles, 1930). Post-patching tests were performed at 0, 3, 6, 12, 24 and 48 min after patch removal. They repeated this sequence for the next four days at a similar time of the day (Fig. 2).

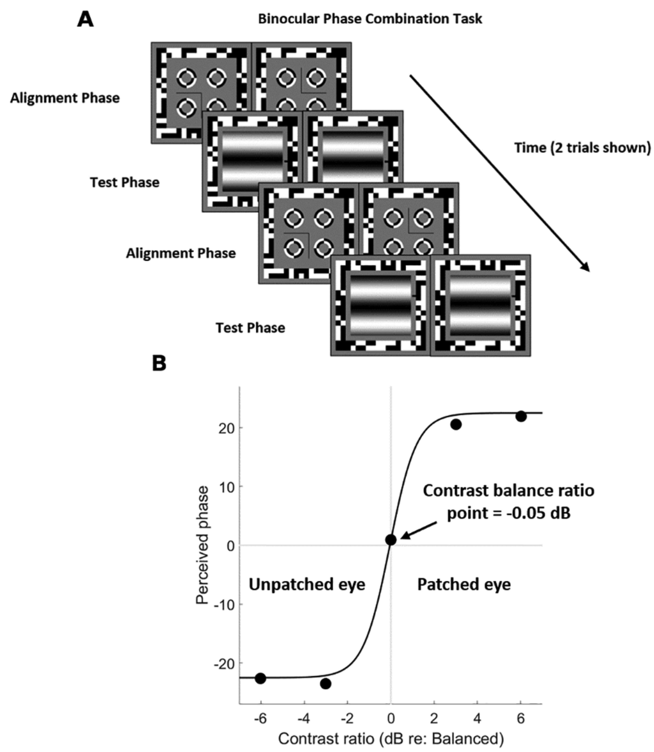

Fig. 1. The binocular phase combination task and a curve fit of perceived phases to a binocular combination model. A) One trial of the binocular phase combination task consisted of an alignment and test phase. There were eighty trials in baseline measurement and thirty in post-patching measurement. Subjects were asked to move the flanking reference line to where perceived center of the darkest area in the fused grating was located. The horizontal sinusoidal gratings had a phase difference of 45°. Pixelated binary noise frames enabled subjects to maintain fusion throughout the task. B) A curve fit of data to a contrast gain control model. We fitted perceived phases at different contrast ratios from the visual task to a contrast gain control model (Ding & Sperling, 2006) to calculate the balance point. A balance point is when two eyes contribute equally to binocular vision (perceived phase = 0°). This figure has been modified from Min (2018).

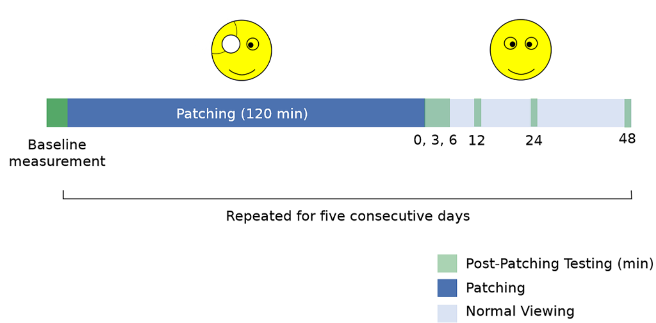

Fig. 2. The protocol for the experiment.

2.5. Data analysis

Perceived phases from two configurations were averaged. The averaged perceived phases were then fitted to a contrast gain control model (Ding & Sperling, 2006); see Fig. 1):

$$\Phi_A = 2tan^{-1}\left[\frac{f(\alpha,\beta,\gamma) - \delta^{1+\gamma}}{f(\alpha,\beta,\gamma) + \delta^{1+\gamma}} tan\left(\frac{\theta}{2}\right)\right], \quad (1)$$

where

$$f(\alpha,\beta,\gamma) = \frac{1+\delta^{\gamma}}{1+\alpha\delta^{\gamma}}, \quad (2)$$

θ denotes the fixed phase difference between the gratings that were presented to both eyes (45°), Φ_A denotes the perceived phase from the two gratings, δ denotes the interocular contrast balance ratio (of the stimuli shown on the screen), α denotes the gain factor which determines the contrast balance ratio between the two eyes when they contribute equally to binocular vision. γ is the parameter that controls the slope of the transition between the left and right eye percepts. We estimated the two free parameters α and γ by fitting our data of perceived phases to the contrast gain model function (Ding & Sperling, 2006). We bootstrapped responses from each trial to generate each measurement's bootstrapped population of α values.

We transformed α into log units with Eq. (3):

$$\alpha_{dB} = 20 \times log_{10}(\alpha_{ratio}), \quad (3)$$

where

$$\alpha_{ratio} = \frac{\alpha_{DE}}{\alpha_{NDE}}. \quad (4)$$

The estimated α_{ratio} represents the contrast balance ratio of each eye's equal contribution to binocular vision in linear units. α_{dB} is the contrast balance ratio in the log scale. We transformed it into the log units to avoid bias in favor of the dominant eye. For example, when the contribution of the non-dominant eye (α_{NDE}) is 2 and that of the dominant eye (α_{DE}) is 1, α_{ratio} is 0.5. However, when the contribution of the non-dominant eye (α_{NDE}) is 1 and that of the dominant eye (α_{DE}) is 2, α_{ratio} is 2. The differences between these balance ratios ($\alpha_{ratio} = 2$, $\alpha_{ratio} = 0.5$) and that when two eyes contribute equally ($\alpha_{ratio} = 1$) should be the same but they are not so in the linear scale. Instead, the difference is larger when $\alpha_{DE} > \alpha_{NDE}$. For this reason, we transformed the contrast balance ratio into log units to avoid bias for the dominant eye. Log transformation of contrast balance ratio has been used in previous studies (Baldwin & Hess, 2018; Min, 2018). We calculated differences in contrast balance ratios between baseline and after patch removal, and plotted them as Δ contrast balance ratio (units in dB). The y-axis (see Fig. 3A, B and C) represents the difference in contrast balance ratios between baseline and post-patching eye balance. The higher the y-axis, the stronger the patched eye's contribution to binocular vision relative to that before patching. We quantified the patching effect over time (0 to 48 min post-patching) by calculating area under the curve between the linear units of time after patching (x-axis in minutes) and log units of Δ contrast balance ratio (y-axis in dB). The areal measures were in the unit of dB minutes (see Fig. 3E and F).

3. Results

We were interested in whether the recovery rate of the patching effect would be similar between the first and later days after repeated sessions of patching (see Fig. 3A–B). We linearly fitted the recovery slopes from all five days on log-log axes and quantified the slope and intercepts of the linear fits for every subject. We conducted a paired *t*-test using RStudio (Team, 2016) between the recovery slopes on day 1 and 5 across all subjects and found no significant difference between both days, t(9) = 0.72, p = 0.49. We also conducted a two-way (factors: day of the study, patching) repeated measures ANOVA; we averaged Δ contrast balance ratio at 0, 3 and 6 min after patching to compute the peak patching effect in the ANOVA. We found that the effect of patching itself was significant, F(1,9) = 17.32, p = 0.002 but not the effect of day, F(4, 36) = 1.542, p = 0.211. Therefore, we found no significant difference in the peak patching effect across days. We were also interested in whether there would be a difference in the immediate effect of patching across days. Fig. 3C shows the averaged changes in the contrast balance ratio relative to baseline across all subjects (individual data figure shown in the Appendix) at 0 min after patch removal. We performed a one-sample *t*-test and found that the patching effect itself was significant at 0 min after monocular deprivation (shown by the asterisks in Fig. 3C) on all days. However we found no significant

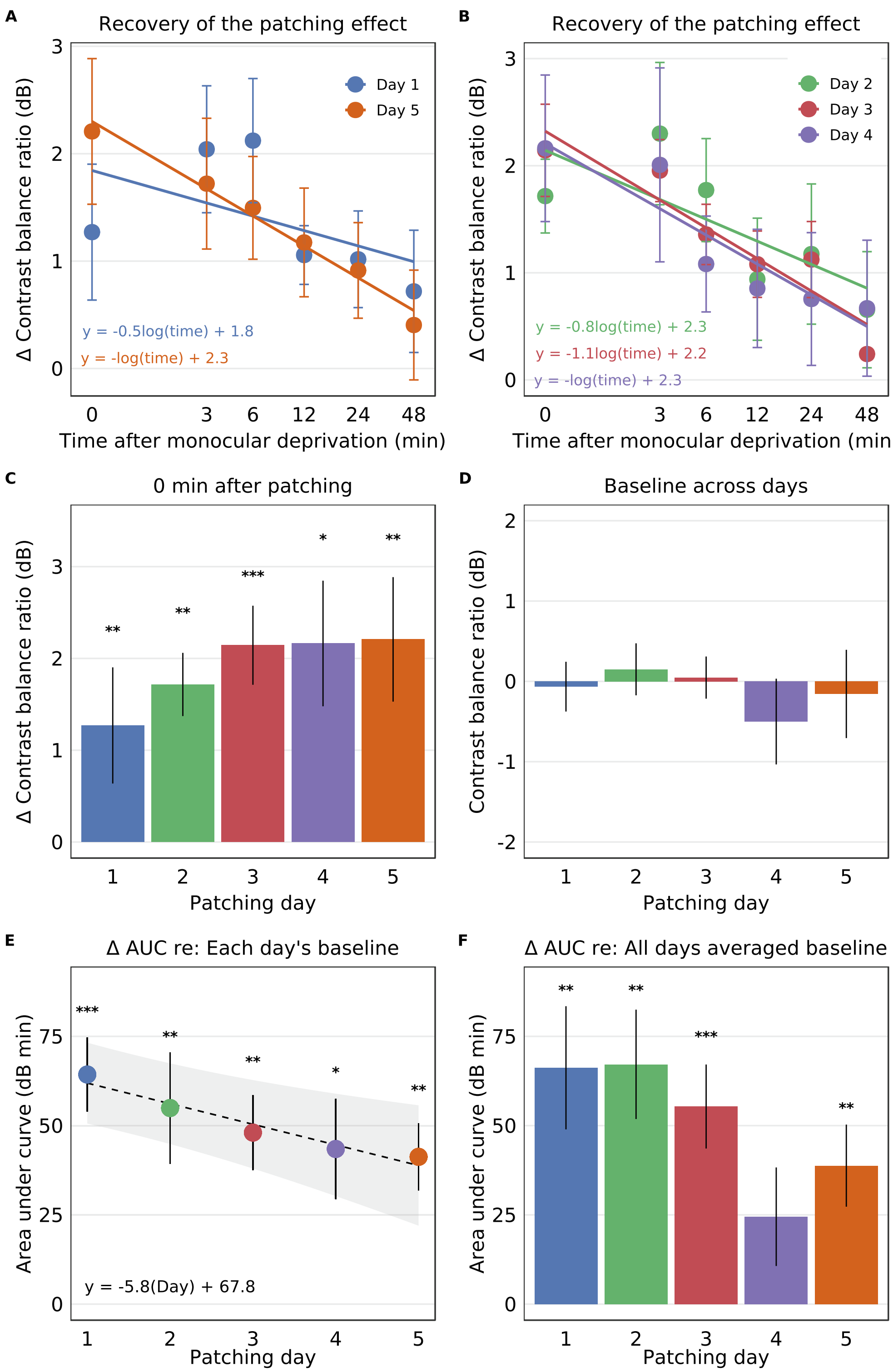

Fig. 3. Averaged results across ten adults with normal vision. A-B) The averaged recovery rate of the patching effect on log/log scaled axes from day 1 to 5 of the study (individual recovery plots shown in the Appendix). Each point represents changes in sensory eye balance as a function of the time after monocular deprivation. The error bar shows standard errors. Each color represents different day of the study. C) Averaged changes in contrast balance ratio relative to baseline from each day across all subjects. The error bars show standard errors. The changes in contrast balance ratio on all days are significantly different from baseline (*p < 0.05, **p < 0.01, ***p < 0.001) according to a one-sample *t*-test. D) The baseline of each day before each session. Each bar represents baseline from each day averaged across all subjects. The error bars represent standard errors. E) Area under a curve (AUC) reflecting changes of ocular dominance relative to each day's baseline over the established timepoints after patching. This areal measure captures how sensory eye balances changes as a function of time after patch removal; it provides a single number to represent the ocular dominance effect from patching over time. AUC contrast balance ratio of 0 represents no change in eye dominance relative to the averaged baseline across all subjects over time. AUCs relative to each day's baseline is significant (*p < 0.05, **p < 0.01, ***p < 0.001) according to a two-tailed one sample *t*-test. The error bars represent standard errors of the AUCs across all subjects. The dashed line represents the averaged linear slope and intercept across all subject over days; linear regression for each subject was performed across AUCs from five days of the study. The shaded error bar (in grey) indicates the range of standard errors from the slopes of best fitted lines for each subject. F) AUC reflecting changes of ocular dominance relative to averaged baseline across all days. AUCs on all days except day 4 are significantly different from the averaged baseline according to a two-tailed one sample *t*-test.

difference in the immediate patching across days from a one-way repeated measures ANOVA ($p > 0.05$).

We wanted to investigate whether the baseline of binocular balance would vary across days after repeated patching. Fig. 3D shows the averaged baselines across subjects (individual data figure shown in the Appendix). We performed a one-way repeated measures ANOVA and found no significant difference in baseline across days, $F(4,36) = 0.88$, $p = 0.48$. We found no indication of accumulation. According to a two-tailed one sample *t*-test, we found that the averaged baseline across subjects from each day were not significantly different from zero (contrast balance ratio when each eye contributes equally to binocular vision), suggesting that no significant imbalance had been induced by repeated patching.

We quantified the effect of patching over time by computing the area under a curve (AUC; units in dB minutes) between the log y-axis of the normalized contrast balance ratio (relative to baseline) and linear x-axis of the established timepoints after monocular deprivation (individual data figure shown in Appendix; see Fig. 3E for a averaged data figure). The areal measure would equal zero when patching had not induced a shift in sensory eye balance over time relative to baseline. We also wanted to assess whether the magnitude of the areal measure on each day was significantly different from baseline. A two-tailed one sample *t*-test revealed a significant difference on all days (see Fig. 3E). Moreover, we examined whether the magnitude of AUC varied across days. A one way repeated measures ANOVA showed no significant difference in the magnitude of each day's AUC across days, $F(4, 36) = 0.65$.

We observed that the magnitude of AUC decreased across days (see Fig. 3E). We wanted to investigate whether the decreasing trend was significantly different from the slope of zero. We linearly fitted the areal measures across days for every subject and calculated the slope and intercept for each linear fit (i.e. each subject). We then performed a two-tailed one sample *t*-test with the linear slopes across all days found that the decreasing trend (averaged linear slope and intercept shown in Fig. 3E) was not significantly different from zero, $t(9) = -1.87$, $p = 0.095$. The range of standard errors from the slopes of the linear fits is shown as grey shade (see Fig. 3E). We realized our sample size could have been too small to detect any significance. To avoid from making a type II error, we performed power analysis for one-sample *t*-test and found that we would need fifteen more subjects to reach statistical significance (power = 0.39). Fig. A3 (in the Appendix) shows that seven subjects showed a decreasing trend of AUCs from day 1 to 5.

Since the baseline was not significantly different across days (see Fig. 2D), we averaged the baselines across all days for every subject and calculated AUC relative to the averaged baseline across days (see Fig. 3F; individual data figure in the Appendix). We wanted to investigate whether AUC on each day relative to the averaged baseline varied significantly from zero. So we performed a two-tailed one sample *t*-test and found that each day's AUC was significantly different from zero except the one from day 4. We were also interested in whether the AUCs relative to the averaged baseline differed across days. So we performed a repeated measures one-way ANOVA and found no significant effect across days, $F(4, 36) = 1.69$, $p = 0.174$.

4. Discussions

We reported in a previous study that the patching duration (15–300 min) does not affect the magnitude and the recovery rate of the patching effect in adults with normal vision (Min, 2018). Therefore we suggested that the patching effect is an all-or-none phenomenon. In this study, we examined whether ocular dominance changes could be accumulated across repeated sessions of patching in normal adults. We found that the patching effect does not accumulate after five consecutive days of deprivation. This finding suggests that the patching effect from any one period of deprivation is not long lasting in normal adults. Furthermore, the baseline of eye balance was not different across days after repeated patching for five days. This is quite different from the plasticity effects produced by transcranial magnetic stimulation which, at least in terms of amblyopic observers, are short lived after a single period of stimulation (Thompson, 2008) but do accumulate across separate periods of stimulation on five consecutive days (Clavagnier, Thompson, & Hess, 2013).

Both this study and the aforementioned study on the effects of patching duration suggest that the patching effect is an instantaneous, all-or-none homeostatic mechanism with fast dynamics in normal adults (Min, 2018; Turrigiano & Nelson, 2004). However, it is important to note that both of these studies used a phase combination task as a primary measure for sensory eye balance. Findings reported in this and the previous study may not be observed in other measures such as binocular rivalry. A future work is necessary where other measures are used. Findings from one measure may not be generalized to others because different neural mechanisms may be involved during different psychophysical tasks (Baldwin & Hess, 2018). For instance, binocular rivalry displays two incompatible stimuli to both eyes. Separate neuronal populations with different preference of orientation will get activated. Conversely, binocular combination shows compatible stimuli to both eyes and therefore activates a common neuronal population (i.e. same preference of orientation) in the primary visual cortex. A recent study found no correlation between parallel and cross-oriented masking after patching in adults with normal vision (Baldwin & Hess, 2018). A parallel mask ensures that the spatial properties of the visual stimulus are identical in both eyes, whereas a cross-oriented mask is orthogonally rotated to the visual target. The former represents binocular combination whereas the latter binocular rivalry. Likewise the levels of changes in ocular dominance after monocular deprivation may be task-specific (Baldwin & Hess, 2018). Moreover, future studies should also investigate the test-retest reliability of various psychophysical tools for measuring sensory eye balance. Recent studies have shown opposite effects of exercise on the patching effect using binocular rivalry measures (Finn, 2018; Lunghi & Sale, 2015).

In adults with normal vision, a fast-homeostatic mechanism after visual disruption is expected. For example, if changes from visual disruption such as patching are accumulated in normals, their binocular balance can be lost. Therefore, a homeostatic mechanism that returns eye balance back to baseline soon after abnormal visual experience will be beneficial in normals. If a similar hemostatic mechanism occurs in adult amblyopes as observed in normals, short-term patching may be an unsuitable therapeutic intervention because long-lasting neuroplastic changes are necessary to recover binocular function of adults with amblyopia. However the nature of the homeostatic mechanism may be different between normals and amblyopes. For instance, both Lunghi et al and Zhou et al demonstrated with binocular rivalry (coupled with physical exercise) (Lunghi, 2019) and binocular combination (Zhou, 2019) respectively that the visual acuity and stereopsis improvements could be sustained after repeated patching. This result suggests that changes in ocular dominance may be longer lasting after visual disruption in adult amblyopes than normals. However it should be noted that the changes in ocular dominance that we report here for normals are for a stimulus of low spatial frequency where we have sufficient spatial resolution to make accurate phase measurements. The spatial loss in amblyopia is limited to high spatial frequencies, so future studies of the cumulative effect of monocular patching in amblyopia should target high spatial frequencies. To do this another approach whose accuracy is not compromised at high spatial frequencies will have to be undertaken, such as the recently developed orientation combination task (Wang, 2019).

Author's contribution

S.M collected, analyzed and visualized the data. All authors contributed to the experimental design and the writing of the manuscript.

Declaration of Competing Interest

The authors declare no competing interests.

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Appendix. Dotplots of individual data

Figs. A1–A3

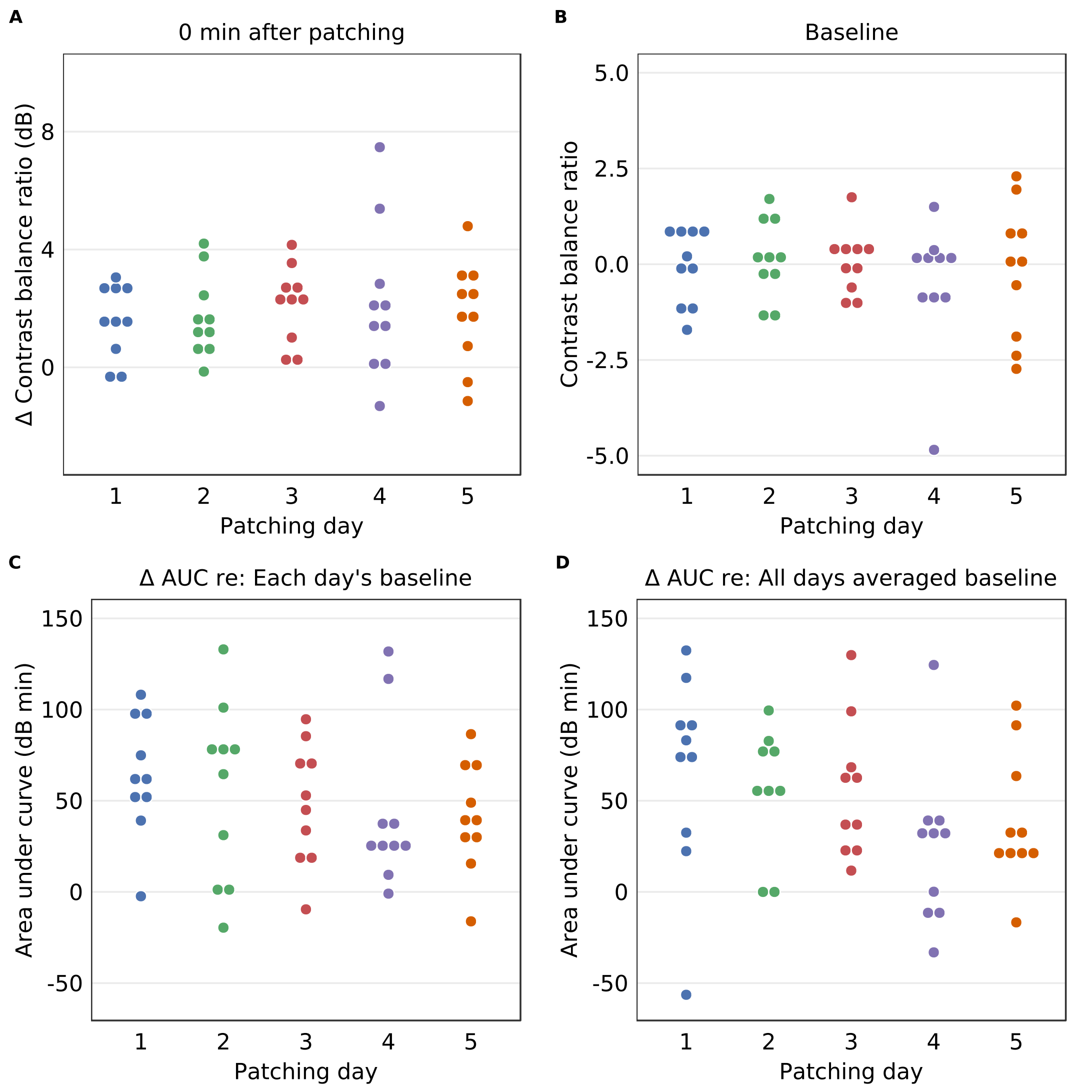

Fig. A1. Dot plots of individual data. A) Each subject's differences in contrast balance ratios between 0 min after patching and baseline across five days. B) Each subject's baseline of contrast balance ratio across five days. C) Each subject's area under the curve relative to each day's baseline. D) Each subject's area under the curve relative to the averaged baseline of all days.

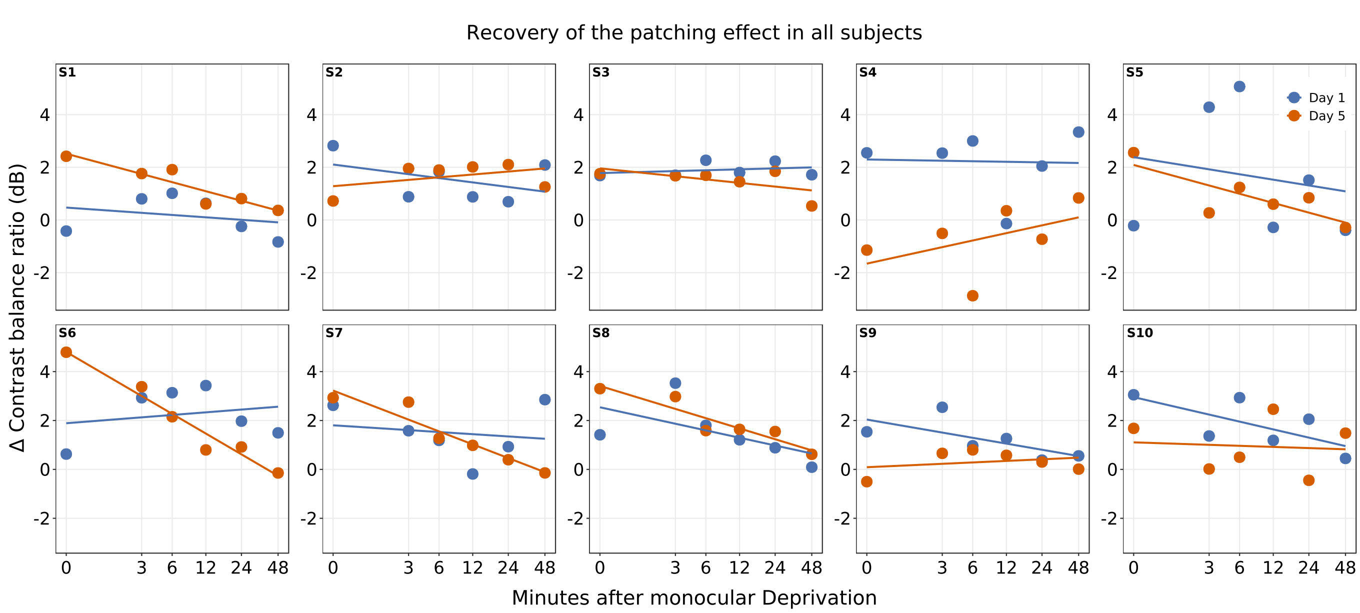

Fig. A2. Each subject's recovery slope after monocular deprivation on day 1 and 5.

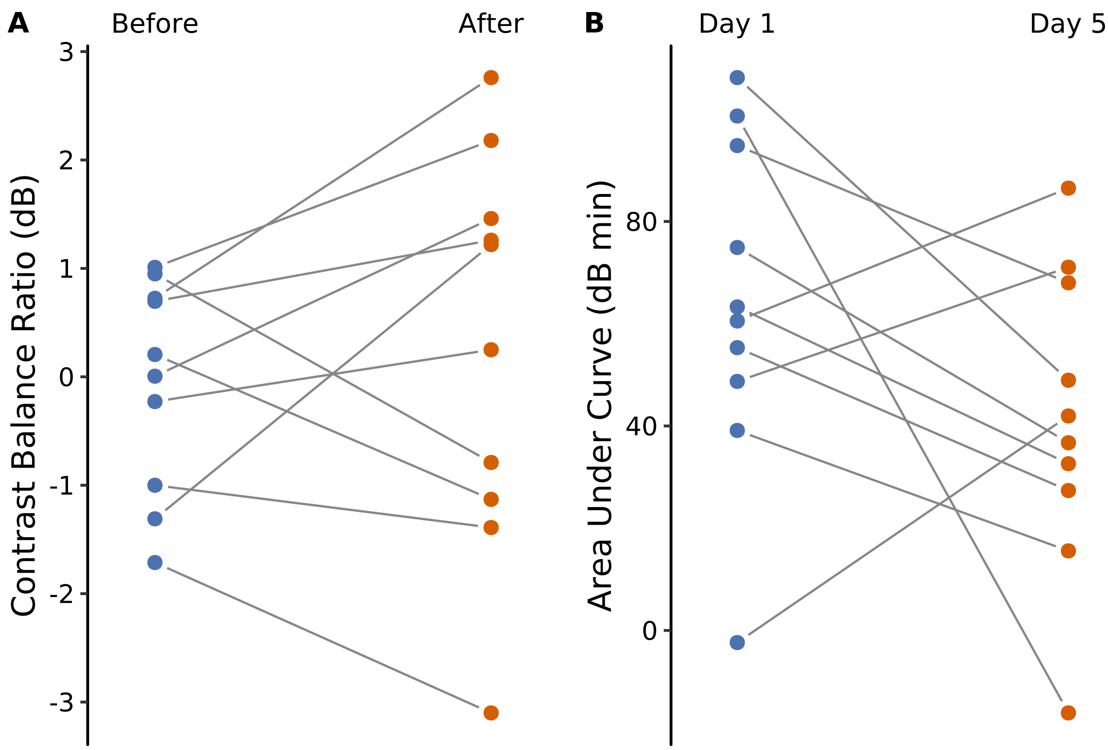

Fig. A3. Each subject's changes in eye balance between day 1 and 5. A) Contrast balance ratio of each subject from before (i.e. baseline on day 1) to after the study (48 min after patching on day 5). B) Area under the curve for each subject on day 1 and 5.

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