NEUROSCIENCE

RESEARCH ARTICLE

L. Lyu et al. / Neuroscience 435 (2020) 10–21

Natural-scene-based Steady-state Visual Evoked Potentials Reveal Effects of Short-term Monocular Deprivation

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Abstract—Ocular dominance plasticity beyond the critical period has been demonstrated in adult humans in recent investigations of short-term monocular deprivation (MD). To our knowledge, all previous research adopted non-natural synthetic stimuli in testing perceptual ocular dominance before and after the MD. However, it is recognized that complex natural stimuli may engage cortical mechanisms substantially different from simple synthetic stimuli. Therefore, it remains largely unknown whether reshaping of ocular dominance following MD could be observed during perception of natural scene stimuli without conspicuous interocular competition. Here we used the steady-state visual evoked potential (SSVEP) technique to measure the ocular-specific neural effects of MD with natural scene stimuli where the two eyes' images were tagged with different frequencies. Two hours of MD boosted the neural gain for the deprived eye. During the course of MD, the SSVEP amplitude ratio for the deprived eye compared to the non-deprived eye increased significantly over time, indicating a progressive increase of neural gain for the deprived eye. These findings demonstrate that the effects of short-term MD can manifest when viewing natural scenes, providing a natural case in support of the homeostatic compensation theory of MD. Our work also indicates that the technique of natural-scene-based SSVEP could be particularly useful for future work exploring the neural dynamics during adaptation to natural stimuli.

Key words: ocular dominance, monocular deprivation, Fourier phase, natural scene, steady-state visual evoked potential (SSVEP).

INTRODUCTION

Our brains receive complex information from the natural environment. As consequences of evolution and development, the functions of the visual system may become uniquely adapted to the properties of natural stimuli in the visual environment (Felsen and Dan, 2005). This important nature has been found in visual adaptation, an aspect of experience-dependent neural plasticity (Sharpee et al., 2006). As a particular form of adaptation that can bring insights into adult visual plasticity, short-term MD has recently received substantial attention (Lunghi et al., 2011, 2013, 2015a,b; Zhou et al., 2013, 2014; Lunghi and Sale, 2015; Bai et al., 2017; Binda and Lunghi, 2017; Wang et al., 2017; Yao et al., 2017; Binda et al., 2018; Ramamurthy and Blaser, 2018). In typical MD, input images from one eye are blocked or degraded, while participants are able to view the natural environment or movies during the deprivation. How are neural activities changed in response to natural stimuli following the MD? The answer to this question, unfortunately, remains largely unknown, because all the past work has measured the effects of MD using simple synthetic stimuli (e.g., gratings, white noise). As compared to natural images, synthetic stimuli are statistically much simpler, functionally less relevant, and in some cases less effective for driving visual cortex neurons (Smyth et al., 2003; David et al., 2004; Felsen and Dan, 2005; Felsen et al., 2005; Sharpee et al., 2006; Sonkusare et al., 2019). Thus, the effects of MD estimated with synthetic stimuli may not necessarily apply when the observer is under natural scene stimulation.

By using the SSVEP technique, the present study for the first time tested the neural effects of MD with natural scene stimuli, allowing a more direct measurement of the deprivation effects during perception of natural

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Abbreviations: EEG, electroencephalography; EOI, electrode of interest; FDR, false discovery rate; MD, monocular deprivation; RLS, recursive least square; ROI, region of interest; SNR, signal-to-noise ratio; SSVEP, steady-state visual evoked potential.

https://doi.org/10.1016/j.neuroscience.2020.03.039
0306-4522/

scene stimuli. During the adaptation phases, the non-deprived eye was always presented with movie videos; whereas in the deprived eye, either the mean-luminance or the phase-scrambled images of each movie frame were presented. The former adaptation condition simulated the monocular patching deprivation (Lunghi et al., 2011, 2013, 2015a,b; Zhou et al., 2013; Lunghi and Sale, 2015; Binda and Lunghi, 2017; Binda et al., 2018). The latter condition was also called the “pink-noise” condition in the recent work on monocular phase regularity deprivation (Bai et al., 2017). Before and after 125 min of MD (see Fig. 1A), we conducted an unfiltered SSVEP test including 10 trials where the stimuli in both eyes were identical unfiltered natural movies. Each trial included a top-up adaptation period followed by a contrast-reversed flickering period where the movie images reversed the contrast at 6 Hz in the deprived eye and 7.5 Hz in the non-deprived eye. The unfiltered test stimuli did not involve conspicuous interocular competition, thus could probe the neural effects of MD under the natural viewing condition.

During the MD, four interim tests were conducted at different time points (see Fig. 1B). The interim test stimuli in our initial experiment were kept the same as the MD adapting stimuli, except that the stimuli in the flickering periods were frequency tagged similarly as in the unfiltered pre- and post-tests. This enabled the measurements of visual responses to the inputs that resembled the adapting stimuli most. To fairly compare the interim tests with the pre- and post-tests, the stimuli

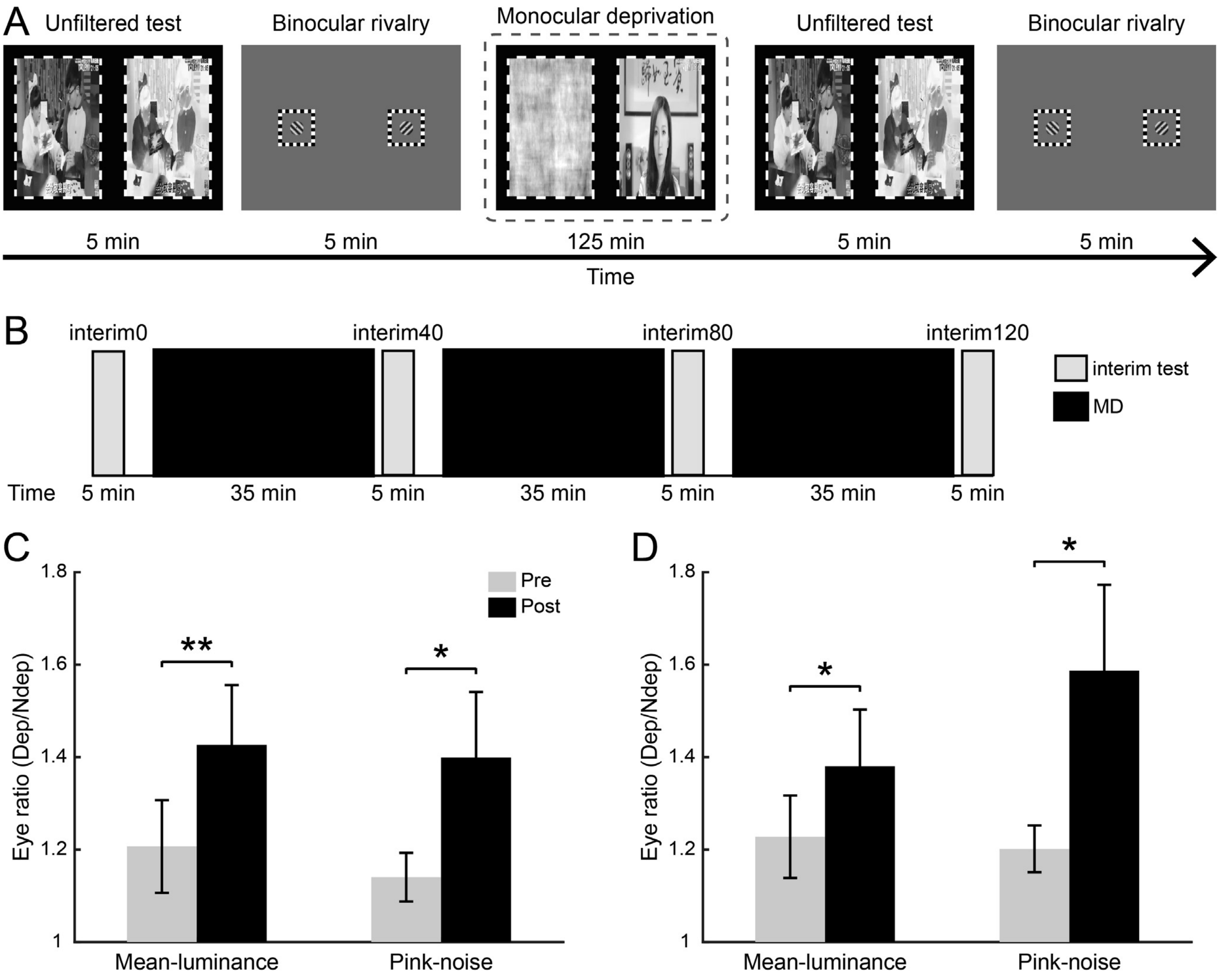

Fig. 1. Experimental design and psychophysical measures of binocular rivalry. **(A)** One experimental session consisted of a pre-adaptation unfiltered SSVEP test followed by a pre-adaptation behavioral measure of binocular rivalry. After 125 min of monocular deprivation, a post-adaptation unfiltered SSVEP test was conducted again followed by a post-adaptation binocular rivalry test. The movie images were compressed in the horizontal dimension so that subjects could see more movie contents within the limited field of view for each eye when viewing through the stereoscope. **(B)** The 125 min of monocular deprivation consisted of three 35-min MD periods (dark bars) and four interim tests (gray bars). **(C)** Grand average eye ratio indices for the pre- and post-adaptation binocular rivalry tests for the mean-luminance and pink-noise adaptation conditions in the initial experiment. Asterisks represent significant differences between the post-test and the pre-test, as evaluated with paired *t*-test. $^{*}p < 0.05$, $^{**}p < 0.01$. **(D)** Grand average eye ratio indices for the pre- and post-adaptation binocular rivalry tests for the mean-luminance and pink-noise adaptation conditions in the second experiment. Error bars represent standard errors of means.

of the interim tests in our second experiment were replaced with unfiltered stimuli during the flickering periods but remained identical to the adapting stimuli during the top-up adaptation periods.

EXPERIMENTAL PROCEDURES

Data and code availability statements

The data and analysis scripts used in this article will be made publicly available via *Mendeley Data* after manuscript acceptance.

Participants

A total of twenty subjects (16 females, 4 males; age range 18–28 years) participated in the initial experiment. Six of them and fourteen new subjects (9 females, 11 males; age range 19–28 years) participated in the second experiment. All subjects were not aware of the experimental hypotheses, and had normal or corrected-to-normal vision. Informed consents were obtained from all the subjects prior to participation. Experimental procedures in the present study were approved by the Institutional Review Board of the Institute of Psychology, Chinese Academy of Sciences. The work was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Apparatus

Stimuli were presented on a gamma-corrected 21-inch Dell P1130 CRT monitor (800 × 600 pixels resolution at the refresh rate of 60 Hz), and programmed in MATLAB and Psychtoolbox (Brainard, 1997; Pelli, 1997). The mean luminance of the CRT monitor was 44.7 cd/m^2. Stimuli were viewed at a distance of 70 cm in a dark room through a mirror stereoscope. A chin-rest was used to help minimize head movement.

MD for 125 min

Stimuli. In the binocular rivalry task, the visual stimuli comprised a pair of dichoptically presented sine-wave grating disks (orientation: ±45°, diameter: 1°, spatial frequency: 3 cpd, Michaelson contrast: 80%), whose edges were smoothed with a Gaussian envelope. They were presented foveally with a central red fixation point (0.07° in diameter) and a high contrast checkerboard “frame” (size: 2.5°× 2.5°; 0.25° thick) that facilitated stable binocular fusion.

During the adaptation phases, the stimuli were achromatic video images (Fig. 1A) that were presented dichoptically and surrounded by a high contrast checkerboard “frame” (size: 11.66° × 18.54°; 0.37° thick). The frame rate of the video was 30 Hz. The original video images were always presented to one of the two eyes (i.e. the non-deprived eye). The video images presented to the other eye (i.e. the deprived eye) had been offline processed separately for two different adaptation conditions. In one adaptation condition, each image was replaced with its mean luminance. Thus this condition was called the mean-luminance condition, which simulated the monocular patching deprivation (Lunghi et al., 2011, 2013, 2015a, b). The other adaptation condition was referred to as the pink-noise condition in which the video images were replaced with pink noises. The power spectra of the pink noises were exactly the same as those of the video images (their difference was less than 10^{-5}%). However, the phase spectrum of a pink noise was derived from that of a white noise (randomly selected from 30 pre-defined white noises every 2–5 s).

Procedure. Binocular rivalry test. A binocular rivalry task was used to measure the perceptual eye dominance psychophysically both prior to and after the 125 min of adaptation phase (Fig. 1A). Each binocular rivalry test consisted of 5 trials. In each trial, the rival gratings were presented for 55 s, followed by a 5-s blank interval. The orientation associated to each eye was kept constant within a trial, but randomly varied across the trials. Participants were required to report their perception (clockwise, counterclockwise, or mixed) by holding down one of the three keys (Left, Right, or Down Arrow) on the keyboard.

Before the formal experiment, participants had to practice the binocular rivalry task for 3–4 days to ensure that they had been familiar with the task and achieved a relatively stable performance for estimating the perceptual eye dominance. They practiced four tests per day, with a 10-min break in between (except a 5-min break between the first two tests). The measured perceptual eye dominance has been shown to fluctuate widely in the first several trials of a day (Suzuki and Grabowecky, 2007). Therefore, the first test served as a warm-up test, which only included five trials. The data of the first test were not analyzed. The three subsequent tests each consisted of 16 trials. For the formal experiment, as in the practice, participants also completed a 5-min warm-up test (the data of which were not included for analysis) and a 5-min break before the pre-adaptation unfiltered SSVEP test.

SSVEP test. Before and after the 125 min of adaptation phase, subjects completed an unfiltered test in which both eyes were presented with the original video images (Fig. 1A). This aimed to explore any effects of short-term MD during perception of natural scene stimuli without conspicuous interocular competition.

During the adaptation session, there were four interim tests where the original video images were presented to the non-deprived eye and the mean-luminance or pink-noise images were presented to the deprived eye (Fig. 1B). The interim tests were performed at 0 min, 40 min, 80 min and 120 min after the beginning of the adaptation phase, which tracked the changes of neural ocular dominance as the deprivation progressed.

Each SSVEP test consisted of 10 trials. Each trial lasted for 30 s, including a 24-s top-up adaptation period and a 6-s contrast-reversed flickering period (for three subjects we adopted 22 s of top-up adaptation and 8 s of contrast-reversed flickering to increase the signal-to-noise ratio (SNR) in their data). The flickering frequency was 6 Hz for the deprived eye and 7.5 Hz for the non-deprived eye. Participants were instructed to watch the video and minimize eye blinks during the flickering periods. All SSVEP tests used the same ten video clips to avoid any difference of electroencephalography (EEG) signals caused by the video content.

Experimental design. A diagram of the experimental procedure is further shown in Fig. 1A. The responses to the unfiltered test and performance of binocular rivalry were measured before and after 125 min of MD. During the deprivation (see Fig. 1B), the four interim tests were interleaved with the three MD periods. Each MD period lasted for 35 min. During each test and MD period, subjects were instructed to put their heads on the chin-rest so that head movements were minimized. Each SSVEP test was followed by a 5-min break to allow the subject to rest, during which subjects took their head off the chin-rest to relax while kept eyes closed. Every time subjects put their head back to the chin-rest, they were required to confirm the fusion. It took about 3 h to complete a whole session of experiment. Each subject finished one session for each adaptation condition on a separate day, with the sequence for the adaptation condition counter-balanced. The dominant eye was always deprived and the eye dominance was determined by the last three practice sessions with the dominant eye being the one that showed longer summed phase duration.

Behavioral data statistical analysis. We computed the summed phase durations of the exclusively monocular percepts and mixed percepts respectively across all the trials of a test. To quantify the perceptual eye dominance, we calculated an eye ratio index as $(T_{Dep} + T_M/2) / (T_{Ndep} + T_M/2)$, where T_{Dep}, T_{Ndep}, and T_M represented the summed phase durations for perceiving the stimulus in the deprived eye, the stimulus in the non-deprived eye, and mixed percepts respectively.

The eye ratio indices for the pre- and post-adaptation binocular rivalry tests were compared with paired t-test.

EEG data acquisition and statistical analysis. EEG data were recorded using a 64-channel Neuroscan Synamps2 system (Compumedics Neuroscan) with a band-pass filter from 0.05 to 100 Hz and an additional notch filter at 50 Hz, and digitized at 1000 Hz. A 64-channel Ag-AgCl electrode cap was used, but only collected data from 21 electrodes (we collected data from all electrodes in four subjects to have a more comprehensive knowledge of the whole brain topography), including CB2, O2, Oz, O1, CB1, PO8, PO6, PO4, POz, PO3, PO5, PO7, P8, P6, P4, P2, Pz, P1, P3, P5 and P7. All electrodes were referenced to a REF electrode between Cz and CPz.

Off-line analysis was conducted using customized MATLAB code. Raw EEG data were resampled to 1024 Hz and band-pass filtered between 1 and 30 Hz. Next, a surface Laplacian spatial filter was used to minimize common noise (Hjorth, 1975); signals from three to five electrodes surrounding the center electrode were averaged then subtracted from the signal from center electrode. The resultant was then processed with different types of analyses.

EEG data quality control. Reasonably high SNR was required to extract the power of frequency-tagged signals. Electrode impedances were always kept below 5 KΩ. Given the short duration of the flickering period of a single trial (6 or 8 s), the frequency resolution was very low (1024/6144 = 0.167 or 1024/8192 = 0.125). To obtain a higher frequency resolution, for each test and each electrode, EEG signals from the flickering periods of the 10 trials were first connected in series over time, and then a fast Fourier transform was applied to a 60-s or 80-s time window. The SNR was computed as the ratio of the power at the frequency of interest to the average power of the 20 neighboring frequency bins (Zhang et al., 2011). Another 13 subjects failed to participate in the formal experiments because of low SNR (less than 15 for any target frequency).

Extraction of amplitude. For each test and each electrode, EEG signals from the flickering periods of the 10 trials were first averaged in the time domain, and then the amplitude of the tagged frequencies was extracted by using an adaptive recursive least square (RLS) filter (Tang and Norcia, 1995). Similar to Zhang et al. (2011) work, the amplitude was calculated by using a pair of sine and cosine matched filters within a 1.2 second window, and adaptively updated by sliding the window point by point over time. To avoid the start-up transient of the adaptive filter, we excluded the first 2.4 seconds of the amplitude data. Thus a 3.6-s or 5.6-s amplitude time course was obtained. The average of the amplitude data was calculated for each individual participant.

To focus our analysis on the electrodes showing sufficiently strong visual responses, for each electrode we compared the average SSVEP amplitude for both eyes with the grand mean amplitude across all the electrodes and subjects by using a one-sample t-test. Only electrodes showing significantly (one tailed, $p < 0.05$) larger SSVEP amplitude than the grand mean were selected as electrodes of interest for further analysis (Huang et al., 2018). The SSVEP amplitudes were then averaged within the electrodes of interest for statistical comparisons. A normalization index was then computed by dividing the average amplitude of the signal for the deprived eye by that for the non-deprived eye.

The normalization indices for the pre- and post-unfiltered tests were compared with paired t-test. A linear trend analysis was used to evaluate any changes of the normalization indices across the four interim tests.

Progressive changes

Stimuli. The same stimuli as in the initial experiment were used.

Procedure. The procedures were similar to those in the initial experiment with only a few exceptions. First, during the 6-s contrast reversed flickering test of interim tests, the deprived eye was presented with the intact image instead of mean luminance or pink noise. Second, only one subject adopted 22-s top-up adaptation and 8-s contrast reversed flickering test.

Behavioral and EEG data analysis. The same parameter setting was used for the EEG data acquisition. We collected data from all electrodes in fourteen subjects in the second experiment. An inspection of the whole-brain topographical patterns for the grand average SSVEP amplitudes for these fourteen subjects suggested that these whole-brain topographical patterns were generally consistent with the 21-electrode topographical patterns of all the twenty subjects (Figs. 2 and 4). The behavioral and EEG data analysis were also similar to those in the initial experiment and 9 other subjects failed to participate in the formal experiments in the second experiment because of low SNR.

RESULTS

MD for 125 min

Perceptual ocular dominance was measured psychophysically before and after 125 min of MD (see Fig. 1A) by using a binocular rivalry task. In our initial experiment, MD boosted the perceptual dominance of the deprived eye as reflected by an increase of the eye ratio index (paired *t*-tests; mean-luminance: $t(19) = 3.74$, $p = 0.001$, $d = 0.84$; pink-noise: $t(19) = 2.55$, $p = 0.020$, $d = 0.57$, see Fig. 1C), a replication of the findings in the previous work (Lunghi et al., 2011, 2013; Bai et al., 2017). To quantify our results, an eye ratio index was calculated as $(T_{Dep} + T_M/2)/(T_{Ndep} + T_M/2)$, where T_{Dep}, T_{Ndep}, and T_M represented the summed phase durations for perceiving the stimulus in the deprived eye, the stimulus in the non-deprived eye, and the mixed percepts respectively. T_M remained similar before and after deprivation for the pink-noise adaptation condition ($p > 0.1$), whereas it showed a reduction for the mean-luminance adaptation condition (paired *t*-tests; $t(19) = 1.95$, $p = 0.066$, $d = 0.44$). To select electrodes, we compared the average SSVEP amplitude for both eyes on each electrode with the grand mean amplitude across all the electrodes and subjects by using a one-sample *t*-test. Only electrodes showing significantly (one tailed, $p < 0.05$) larger SSVEP amplitude than the grand mean were selected as electrodes of interest for further analysis (Huang et al., 2018). The electrodes of interest were mainly found around the central occipital and right occipito-temporal regions (see Table 1). SSVEP responses at the central occipital electrodes are more related to early visual processing (Di Russo et al., 2007; Norcia et al., 2015); whereas the responses at the right occipito-temporal electrodes have been found to relate with face processing (Rossion and Boremanse, 2011). The SSVEP amplitudes were then averaged within the electrodes of interest for subsequent analyses.

Strikingly, the SSVEP amplitude ratio index increased after the MD, suggesting that the neural ocular dominance changed in correspondence with the perceptual ocular dominance (see Table 2 and Fig. 2A, mean-luminance: $t(19) = 5.12$, $p < 0.001$, $d = 1.14$; pink-noise: $t(19) = 2.90$, $p = 0.009$, $d = 0.65$, paired *t*-tests). We conducted the Spearman's correlation analysis between the change of eye ratio index (post/pre) and the change of SSVEP amplitude ratio index (post/pre), and found no significant correlation (all rs < 0.1, *p*s > 0.8). However, it was puzzling that the amplitude ratio indices for the interim tests did not change significantly (linear trend tests, all *p*s > 0.47, see Table 2 and Fig. 3), which appeared to contradict the results for the pre- vs. post-tests (see Fig. 2A). We speculated that the interim test stimuli could mask the effects of MD. In the dichoptic presentation of the interim tests, the unfiltered video images had substantially higher contrast than the mean-luminance images, and contained much richer contour information than the pink-noise images. This may cause strong interocular suppression of the deprived eye by the non-deprived eye (Kovacs et al., 1996; Baker and Graf, 2009) and obvious reduction in amplitude for the deprived eye (see small amplitude ratio indices in Fig. 3). Alternatively, stimuli with low contrast energy or poor contour information are ineffective in driving cortical neurons in the primary visual cortex or extra-striate visual cortex (Dumoulin et al., 2008). Therefore, it is reasonable that neurons would not show increases when they are not being driven strongly and are likely suppressed. As a result, any changes of neural ocular dominance would be overridden in this paradigm.

Progressive changes

To remove the strong influence of interocular suppression, we used the unfiltered frequency tagged stimuli for the interim tests in our second experiment. As in our initial experiment, we observed a shift of perceptual ocular dominance in favor of the deprived eye after deprivation (see Fig. 1D; mean-luminance: $t(19) = 2.27$, $p = 0.035$, $d = 0.51$; pink-noise: $t(19) = 2.54$, $p = 0.020$, $d = 0.57$), as well as a shift of neural ocular dominance towards the deprived eye (see Table 2 and Fig. 2B; mean-luminance: $t(19) = 4.42$, $p < 0.001$, $d = 0.99$; pink-noise: $t(19) = 3.04$, $p = 0.007$, $d = 0.68$). Here a significant correlation between the perceptual and neural shift in ocular dominance was found for the pink-noise condition ($r = 0.59$, $p = 0.0069$). Similar to the initial experiment, the summed phase duration of mixed percepts showed a significant reduction after deprivation for the mean-luminance adaptation condition (paired *t*-tests; $t(19) = 2.31$, $p = 0.033$, $d = 0.52$) while showed no change for the pink-noise adaptation condition ($p > 0.1$). Importantly, the amplitude ratio indices for the interim tests increased gradually over time for the mean-luminance condition (see Table 2 and Fig. 4, mean-luminance: $t(19) = 3.07$, $p = 0.006$, $d = 0.69$), suggesting that the strength for the deprived eye was progressively promoted during the MD. This phenomenon was not observed for the pink-noise condition (see Table 2 and Fig. 4; pink-noise: $t(19) = 1.70$, $p = 0.105$, $d = 0.38$).

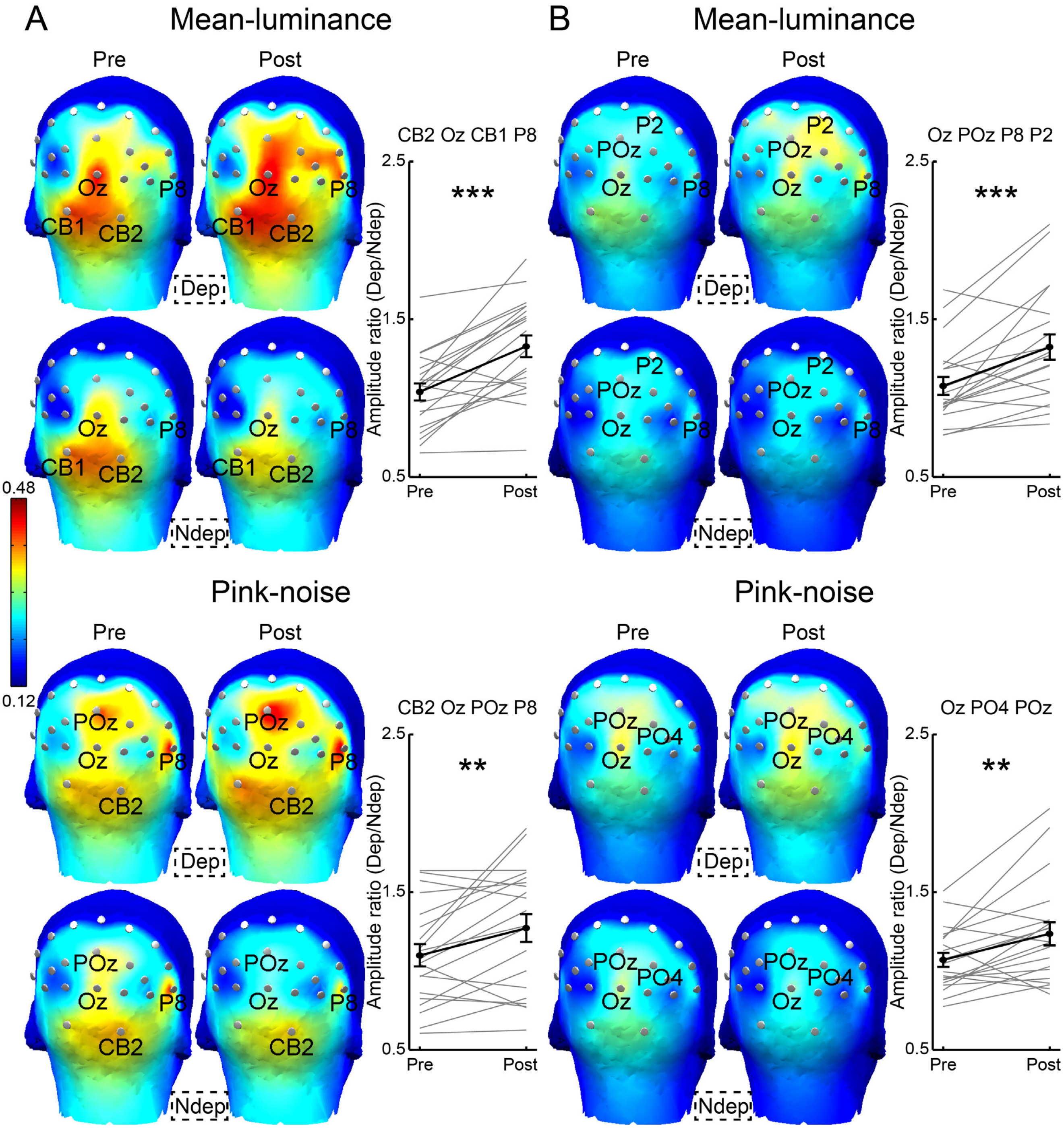

Fig. 2. Effects of deprivation on neural ocular dominance. (A) The topographical maps of grand average SSVEP amplitudes and the amplitude ratio indices for the pre- and post-adaptation unfiltered tests for the mean-luminance and pink-noise adaptation conditions in the initial experiment. Dep and Ndep represent the deprived eye (6 Hz) and non-deprived eye (7.5 Hz). Electrodes of interest, i.e. electrodes with overall significantly larger SSVEP responses than the grand mean amplitude across all the electrodes and subjects, mainly distributed the region of interest (ROI) around the central occipital and right occipito-temporal electrodes. Within each ROI, amplitudes at individual electrodes (large electrode labels) were averaged for statistical comparisons. The gray lines on the dot-line graphs show the amplitude ratios of individual subjects, and the black lines show the group averages. Asterisks represent significant differences between the post-test and the pre-test (paired *t*-test). $^{**}p < 0.01$, $^{***}p < 0.001$. **(B)** The topographical maps of grand average SSVEP amplitudes and the amplitude ratio indices for the pre- and post-adaptation unfiltered tests in the second experiment. Error bars represent standard errors of means.

Confirming the results using a unified ROI

Given the different ROIs across conditions and experiments in the above analysis, we further validated the results with a unified ROI. Electrodes showing significantly larger SSVEP amplitude than the grand mean amplitude across all the electrodes and subjects

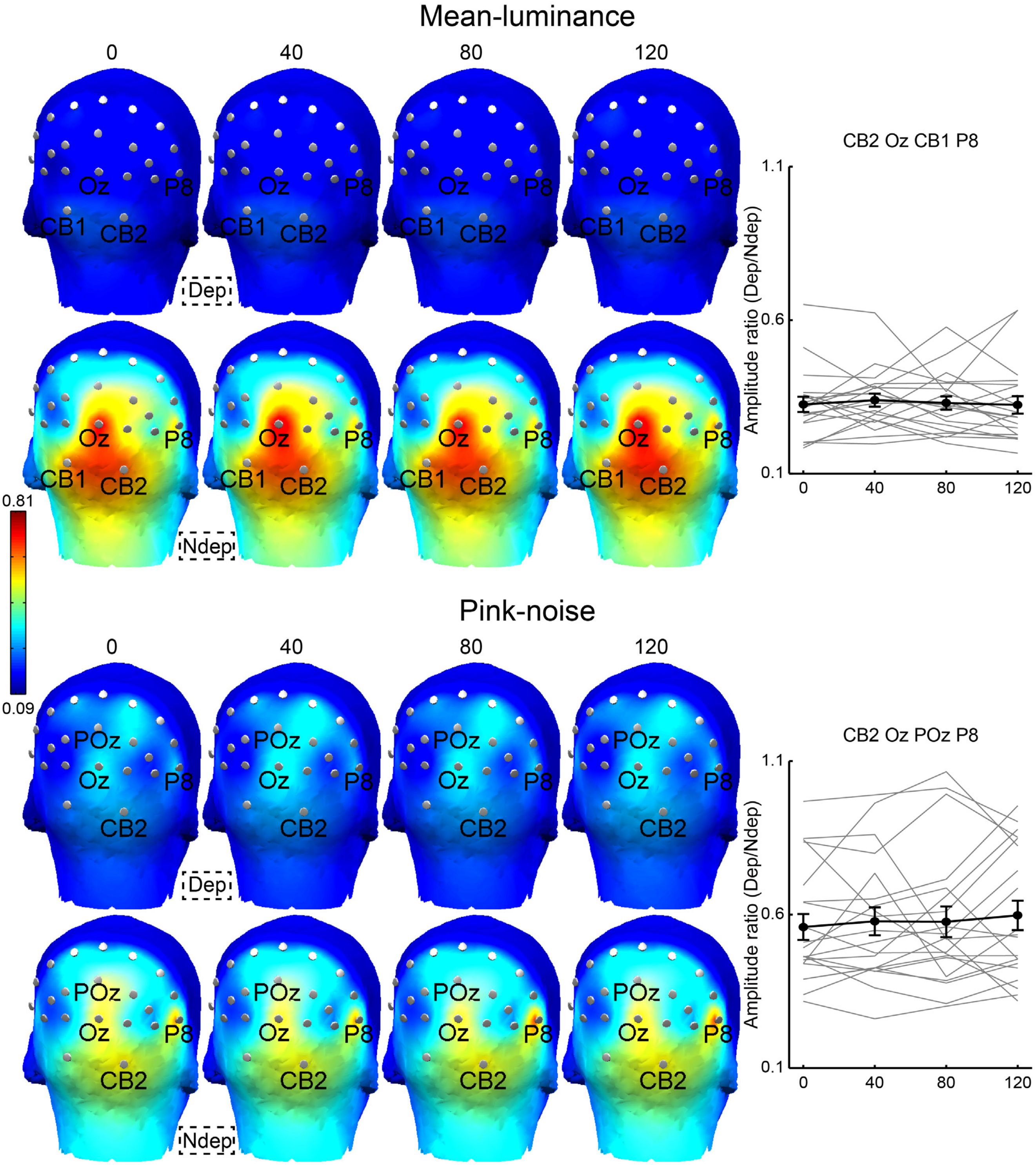

Fig. 3. The changes of neural ocular dominance during the MD (MD for 125 min). Topographical maps of grand average amplitudes and the amplitude ratio indices for the four interim tests in the initial experiment. A linear trend analysis was used to evaluate the changes of amplitude ratio indices across the four interim tests. Error bars represent standard errors of means.

were Oz (4), POz (3), P8 (3), CB2 (2), CB1 (1), PO4 (1), P2 (1) for all experimental conditions. The number in each parenthesis indicated how many times statistical significance ($p < 0.05$) was detected in Table 1 for the corresponding electrode. We then defined an ROI applicable to all experimental conditions by the electrodes which showed statistical significance for at least N times in Table 1. Table 3 showed 4 candidate ROIs selected based on a descending order of N. As shown in each row, shift in neural ocular dominance was consistently observed across conditions and experiments when using a unified ROI. Moreover, the result pattern was consistent across different ROI selections.

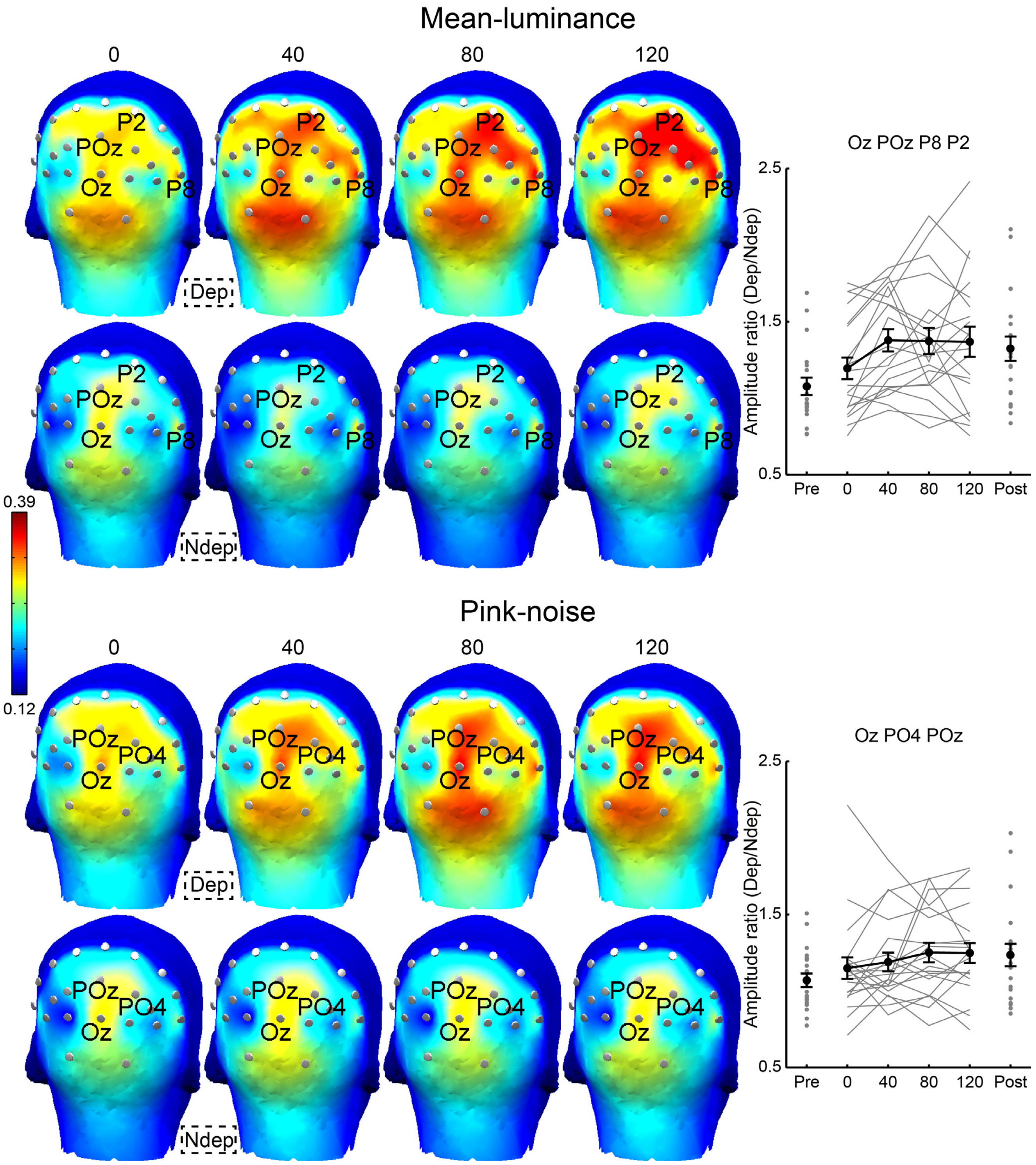

Fig. 4. The changes of neural ocular dominance during the MD (Progressive changes). Topographical maps of grand average amplitudes and the amplitude ratio indices for the four interim tests in the second experiment. A linear trend analysis was used to evaluate the changes of amplitude ratio indices across the four interim tests. Error bars represent standard errors of means.

DISCUSSION

Two experiments consistently showed that the MD for 125 min promoted the neural ocular dominance of the deprived eye under natural scene stimulation without strong interocular competition. These results reflected a homeostatic compensation of the adult visual system (Lunghi et al., 2013, 2015a, b; Binda et al., 2018). This homeostatic compensation may help optimize sensory processing for an eye at a competitive disadvantage under dichoptic adapting conditions, regardless of whether the eye is entirely deprived of input signals (Lunghi et al., 2011, 2013; Zhou et al., 2013), or only deprived of high-order information such as edges and

Table 1. Comparison of the overall SSVEP amplitude on each electrode to the grand mean amplitude across all electrodes. *P* values (one tailed) are listed

Electrode	MD for 125 min Mean-luminance	MD for 125 min Pink-noise	Progressive changes Mean-luminance	Progressive changes Pink-noise
CB2	**0.003**	**0.010**	0.112	0.138
O2	0.159	0.348	0.833	0.777
Oz	**<0.001**	**0.001**	**0.039**	**0.013**
O1	1.000	1.000	0.996	1.000
CB1	**0.004**	0.142	0.202	0.133
PO8	0.973	0.992	0.980	0.976
PO6	0.110	0.778	0.185	0.124
PO4	0.088	0.058	0.057	**0.030**
POz	0.120	**0.039**	**0.033**	**0.044**
PO3	0.902	0.987	0.919	0.626
PO5	1.000	1.000	0.637	0.860
PO7	1.000	1.000	1.000	0.998
P8	**0.012**	**0.001**	**0.025**	0.145
P6	0.369	0.556	0.352	0.376
P4	0.988	0.655	0.877	0.974
P2	0.813	0.156	**0.033**	0.304
Pz	1.000	0.998	0.969	0.824
P1	0.984	0.645	0.307	0.463
P3	0.977	0.986	0.430	0.645
P5	0.999	0.998	0.986	1.000
P7	0.218	0.449	0.734	0.423

Table 2. The deprivation effect of each electrode of interest (EOI) and region of interest (ROI). *P* values are listed and corrected for multiple comparisons using the false discovery rate (FDR) correction method

MD for 125 min Mean-luminance					
EOI	Unfiltered test	Interim test	ROI	Unfiltered test	Interim test
CB2	0.016	0.299	CB2OzCB1P8	< 0.001	0.754
Oz	0.004	0.947			
CB1	0.263	0.947			
P8	0.005	0.790			
MD for 125 min Pink-noise					
EOI	Unfiltered test	Interim test	ROI	Unfiltered test	Interim test
CB2	0.483	0.336	CB2OzPOzP8	0.009	0.471
Oz	0.063	0.718			
POz	0.047	0.247			
P8	0.018	0.460			
Progressive changes Mean-luminance					
EOI	Unfiltered test	Interim test	ROI	Unfiltered test	Interim test
Oz	0.019	0.033	OzPOzP8P2	< 0.001	0.006
POz	0.028	0.673			
P8	0.034	0.195			
P2	0.021	0.195			
Progressive changes Pink-noise					
EOI	Unfiltered test	Interim test	ROI	Unfiltered test	Interim test
Oz	0.086	0.046	OzPO4POz	0.007	0.105
PO4	0.141	0.893			
POz	0.295	0.444			

Table 3. The deprivation effect of each unified ROI. *P* values are listed

ROI	MD for 125 min Mean-luminance		Pink-noise		Progressive changes Mean-luminance		Pink-noise	
	Unfiltered	Interim	Unfiltered	Interim	Unfiltered	Interim	Unfiltered	Interim
Oz	0.001	0.947	0.047	0.718	0.005	0.008	0.029	0.015
OzPOzP8	< 0.001	0.448	0.003	0.627	0.003	0.006	0.007	0.008
OzPOzP8CB2	< 0.0001	0.931	0.009	0.471	< 0.001	0.027	0.001	0.009
OzPOzP8CB2CB1PO4P2	< 0.0001	0.889	0.001	0.416	< 0.001	0.018	< 0.001	0.049

contours (Bai et al., 2017), or presented with uninformative fractionated images (Ramamurthy and Blaser, 2018). However, since monocular stimulation condition was not tested in this study, our results are not considered to reveal any changes at the monocular level.

MD provides the observer with an unusual visual experience in which one eye views the natural world while the other eye receives a certain type of abnormal inputs. It is known that the human visual system continuously adapts to the natural environment. And visual adaptation has been proposed to be one pervasive form of neural plasticity which happens at different time scales (Kohn, 2007; Bao and Engel, 2012). In other words, adaptation can serve as a general concept to refer to experience-dependent functional changes of the visual system in response to the changes of the visual inputs. The use of this concept can be seen in some recent work on orientation-specific deprivation (Zhang et al., 2009; Bao and Engel, 2012; Haak et al., 2014) and ocular dominance plasticity (Bao et al., 2018), though this does not necessarily mean that different types of adaptation should be based on completely overlapping neural mechanisms. From this perspective, short-term MD can also be considered a particular form of adaptation (e.g. Bai et al., 2017).

By testing with binocular rivalry, the previous work has shown that short-term MD affects mechanisms for resolving interocular conflict (Lunghi et al., 2011, 2013, 2015b; Lunghi and Sale, 2015; Bai et al., 2017; Ramamurthy and Blaser, 2018). These reports are compatible with Said and Heeger's (2013) computational framework of binocular rivalry that involves opponency neurons. Opponency neurons can signal interocular conflict by computing differences between the input signals from the two eyes (Poggio and Talbot, 1981; Said and Heeger, 2013; Katyal et al., 2016, 2018; Li et al., 2017). To achieve this function, they receive excitation from monocular neurons for one eye and inhibition from monocular neurons for the other eye. Accordingly, they are active only when the excitatory signals outweigh the inhibitory signals. Meanwhile, when active, the opponency neurons also inhibit the monocular neurons from which they receive inhibition.

Past results of MD may be explained by the adaptation of opponency neurons. Temporarily depriving one eye of input (i.e. the mean-luminance condition) or contour information (i.e. the pink-noise condition) would activate the opponency neurons that received excitation from the non-deprived eye and inhibition from the deprived eye. Prolonged MD may then have resulted in substantial adaptation of these opponency neurons, thereby reducing their activities. This, in turn, would weaken the inhibition of the deprived eye by those adapted opponency neurons in a subsequent binocular rivalry task, and promoted the predominance of the deprived eye.

Our SSVEP results, however, cannot be accounted for by the effects of adaption of opponency neurons. This is because there was little to no interocular conflict during the unfiltered SSVEP tests of the present study, and so little to no activation of, or adaptation in opponency neurons. Instead, our results show neurophysiological evidence that MD also affects mechanisms that are active when information from the two eyes does not conflict.

It has been shown that short-term MD triggers interocular contrast gain control (Lunghi et al., 2011; Ramamurthy and Blaser, 2018) that is primarily GABA mediated (Sengpiel and Vorobyov, 2005; Lunghi et al., 2015b). By using the unfiltered interim tests, we found in the second experiment that neural ocular dominance changed progressively during the MD for the mean-luminance condition, suggesting that interocular gain control was likely a slowly accruing effect. Previous work has attempted to investigate the time course of MD with psychophysical approaches. For example, Lunghi and colleagues found greater shift of eye dominance for 150 minutes of patching than for 30 minutes of patching in a binocular rivalry task (Lunghi et al., 2013, but see Min et al., 2018), which is in consistent with the neural evidence here. It should be noted that their binocular rivalry tests were performed (before and) after separate adaptation sessions with different adapting durations rather than interspersed within a single adaptation session like our work, because psychophysical tests are relatively time-consuming, and a few minutes of such test may cause non-negligible deadaptation. By contrast, our SSVEP measurements were efficient. Its top-up design also ensured the minimum length of exposure to test stimuli, thus avoiding deadaptation as much as possible.

Our natural-scene-based SSVEP technique provides the first solution for measuring the signal from each eye when two eyes viewed natural scene stimuli without conspicuous interocular competition. Several studies have investigated the neural effect of MD with synthetic stimuli (Lunghi et al., 2015a; Zhou et al., 2015; Chadnova et al., 2017; Binda et al., 2018). However, it is questionable to simply extrapolate from their findings to the situation of natural stimulation. Firstly, synthetic stimuli usually cover limited basic visual features such as retinotopic locations, orientations, and spatial frequencies; whereas natural scene stimuli contain abundant information with particular spatial correlations and space–time statistics (Simoncelli and Olshausen, 2001). Secondly, distinct neuronal activities have been found for synthetic and natural stimulation (Vinje and Gallant, 2000; David et al., 2004; Felsen et al., 2005; Sharpee et al., 2006). As compared to the previous studies on MD, the way we presented the stimuli in the unfiltered SSVEP tests (i.e. binocularly fused natural-scene videos) were more comparable to natural vision. Therefore, the present study tests in a more direct manner whether the neural gain for the deprived eye increases under natural vision or not, and how the brain adapts under the natural viewing conditions.

Another advantage of measuring SSVEP with natural stimuli is to open the possibility for tracking the change of ocular dominance with almost the same stimuli as the adapter. However, no significant changes of the SSVEP amplitude ratio were found in our initial experiment, possibly because the potential effects were masked by relatively large effects of interocular suppression of the deprived eye and a marked weakening of neural responses to the deprived eye. This speculation was supported by the fact that the amplitude ratio during the deprivation in the initial experiment was much smaller than that in the second experiment (Fig. 3 vs. 4). Nevertheless, our method is promising to become a convenient and powerful tool in future work for tracking neural responses to the adapting environment in which no interocular suppression is involved. Application of this method should accord with the ultimate goal of visual neuroscience, namely, to understand how sensory stimuli in the natural environment are processed by neural circuits.

By using natural-scene-based SSVEP technique, the present study provided the first solution for measuring the signal from each eye when two eyes viewed natural scene stimuli without conspicuous interocular competition. Two hours of MD boosted the SSVEP amplitude for the deprived eye relative to the non-deprived eye, supporting the homeostatic compensation theory of MD. Furthermore, our method could be a convenient tool in future work for tracking neural responses to the natural adapting environment, thus may accelerate a deeper understanding of adaptive human brain function.

DECLARATION OF COMPETING INTEREST

No known conflict of interest.

ACKNOWLEDGEMENTS

We thank Ying Wang for her helpful comments. This research was supported by the National Natural Science Foundation of China (31571112, 31871104, 31525011 and 31830037) and the Key Research Program of Chinese Academy of Sciences (XDB02010003 and QYZDB-SSW-SMC030).

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(Received 22 November 2019, Accepted 23 March 2020)
(Available online 27 March 2020)