Transcranial random noise stimulation and exercise do not modulate ocular dominance plasticity in adults with normal vision

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Short-term deprivation of one eye by monocular patching causes a temporary increase in the contribution of that eye to binocular vision when the eye patch is removed. This effect, known as ocular dominance plasticity, provides a model of neuroplasticity within the human binocular visual system. We investigated whether physical exercise and the non-invasive brain stimulation technique transcranial random noise stimulation (tRNS), two interventions that may increase visual cortex neuroplasticity, enhance ocular dominance plasticity when delivered individually or in combination. Ocular dominance was measured using a grating rivalry test and a dichoptic letter contrast polarity judgment test. We observed robust ocular dominance changes for both outcome measures following 2-hour monocular deprivation; however, the magnitude of the effect was not influenced by exercise or tRNS. Ocular dominance plasticity may already be maximal after 2 hours of monocular deprivation in those with normal vision and therefore cannot be augmented by interventions designed to enhance neuroplasticity.

Introduction

Patching one eye (monocular deprivation [MD]) for a short period of time alters eye dominance in human adults. Lunghi, Burr, and Morrone (2011) were the first to demonstrate this effect, now referred to as ocular dominance plasticity, by measuring binocular rivalry using dichoptic gratings (grating rivalry) before and after 2.5 hours of MD. They found that, after MD, the deprived eye exhibited increased dominance during grating rivalry. This effect has been independently replicated in individuals with normal vision and those with amblyopia using grating rivalry tasks (Finn, Baldwin, Reynaud, & Hess, 2019; Lunghi, Burr, & Morrone, 2013; Lunghi & Sale, 2015; Lunghi et al., 2011; Sheynin, Chamoun, Baldwin, Rosa-Neto, Hess, & Vaucher, 2019), global motion coherence tasks (Zhou, Clavagnier, & Hess, 2013), binocular phase combination tasks

Citation: Chen, X., Hall, K., Bobier, W. R., Thompson, B., & Chakraborty, A. (2022). Transcranial random noise stimulation and exercise do not modulate ocular dominance plasticity in adults with normal vision. *Journal of Vision*, *22*(10):14, 1–13, https://doi.org/10.1167/jov.22.10.14.

https://doi.org/10.1167/jov.22.10.14 Received March 30, 2022; published September 15, 2022 ISSN 1534-7362

(Bai, Dong, He, & Bao, 2017; Chen et al., 2020; Min, Baldwin, Reynaud, & Hess, 2018; Sheynin, Chamoun et al., 2019; Zhou, Clavagnier, & Hess, 2013; Zhou, Reynaud, & Hess, 2017; Zhou, Thompson, & Hess, 2013), binocular orientation combination tasks (Spiegel, Baldwin, & Hess, 2017), and electrophysiological recordings (Chadnova, Reynaud, Clavagnier, & Hess, 2017; Lunghi, Berchicci, Morrone, & Di Russo, 2015; Zhou, Baker, Simard, Saint-Amour, & Hess, 2015). In these studies, MD duration ranged from 30 minutes to 5 hours, and the ocular dominance plasticity effect lasted from approximately 30 minutes to 1 hour. Together, the results of ocular dominance plasticity studies indicate that MD modifies a fundamental component of binocular vision.

Increased neural activity in response to visual stimulation of the deprived eye has been observed using both functional magnetic resonance imaging (Binda, Kurzawski, Lunghi, Biagi, Tosetti, & Morrone, 2018) and steady-state visual evoked potentials (Zhou et al., 2015). Along with psychophysical observations (Baldwin & Hess, 2018; Sauvan et al., 2019; Zhou, Clavagnier et al., 2013), these findings suggest that ocular dominance plasticity arises from an upregulation of contrast gain for deprived eye inputs to the visual cortex. The observation that MD causes a reduction in gamma-aminobutyric acid (GABA) levels in the primary visual cortex (Lunghi, Emir, Morrone, & Bridge, 2015) suggests that reduced cortical inhibition may enable the associated contrast gain changes.

Several interventions have been identified that may enhance neuroplasticity within the visual cortex. These include systemic drugs (Gratton, Yousef, Aarts, Wallace, D'Esposito, & Silver, 2017; Silver, Shenhav, & D'Esposito, 2008), exercise (Cassilhas, Tufik, & de Mello, 2016; Hötting & Röder, 2013), video games (Bediou, Adams, Mayer, Tipton, Green, & Bavelier, 2018; Föcker, Cole, Beer, & Bavelier, 2018), and non-invasive brain stimulation techniques (such as transcranial random noise stimulation [tRNS]) (Fertonani, Pirulli, & Miniussi, 2011; Sabel et al., 2020; for a review, see Thompson, 2021). Studies involving some of these interventions have used ocular dominance plasticity as a neuroplasticity index. For example, Sheynin, Proulx, and Hess (2019) investigated the effect of cholinergic potentiation, which counteracts GABAergic inhibition, on ocular dominance plasticity, hypothesizing that it might enhance the effect of MD. Contrary to their hypothesis, they found that donepezil, a cholinesterase inhibitor, reduced ocular dominance plasticity in adults with normal vision. In another study, participants played different genres of video games during monocular deprivation to test the hypothesis that attentionally demanding games would enhance ocular dominance plasticity (Chen et al., 2020). No effect of videogame play was observed. However, in a different study where participants either completed an attentive jigsaw task or passively stared at a plain curtain, Wang, McGraw, and Ledgeway (2021) found greater ocular dominance plasticity following the attentive task, suggesting that attention may still play a role in the effect of MD. Moreover, inspired by evidence from animal studies that physical exercise enhances neuroplasticity by reducing GABAergic inhibition (Baroncelli et al., 2012; Kaneko & Stryker, 2014), several groups have explored the effect of exercise on ocular dominance plasticity. The results have been mixed. Lunghi and Sale (2015) demonstrated that physical exercise (i.e., cycling) increased the magnitude of the ocular dominance plasticity. Other groups, however, failed to replicate this effect (Finn et al., 2019; Zhou et al., 2017). Thus, despite these attempts, an effective protocol for enhancing human neuroplasticity indexed by increased ocular dominance plasticity has not yet been identified.

tRNS, which involves the delivery of an alternating current with randomly varying frequencies to targeted brain areas via head-mounted electrodes (Terney, Chaieb, Moliadze, Antal, & Paulus, 2008), has the potential to enhance visual cortex neuroplasticity and enhance ocular dominance plasticity. Cortical excitability can be modulated using tRNS (Herpich, Contò, van Koningsbruggen, & Battelli, 2018), and several studies have reported that high-frequency tRNS (hf-tRNS; frequency range, 100–640 Hz) to the visual cortex improves vision task performance. To illustrate, delivering hf-tRNS to the visual cortex for 22 minutes resulted in significantly better performance in an orientation discrimination task compared with sham stimulation (Fertonani et al., 2011). In addition, visual cortex hf-tRNS increased the rate and magnitude of visual perceptual learning for a global motion detection task in both healthy participants and patients with cortical blindness (Herpich, Melnick, Agosta, Huxlin, Tadin, & Battelli, 2019). In patients with amblyopia, hf-tRNS to the visual cortex coupled with 2 weeks of perceptual learning significantly improved the visual acuity of both trained and untrained eyes (Campana et al., 2014; Moret et al., 2018). Possible mechanisms for tRNS effects include modulation of voltage-gated sodium channels leading to faster depolarization and the induction of stochastic resonance by adding noise to stimulated neural areas which results in a higher signal-to-noise ratio, a higher probability of positive response, and thus an improvement in signal detection (Moret, Donato, Nucci, Cona, & Campana, 2019; Pavan, Ghin, Contillo, Milesi, Campana, & Mather, 2019; van der Groen, Mattingley, & Wenderoth, 2019; van der Groen & Wenderoth, 2016). There is also evidence that tRNS induced a reduction in GABAergic inhibition when applied to the motor cortex (Chaieb, Antal, & Paulus, 2015) or the prefrontal cortex (Sánchez-León, Sánchez-López, Gómez-Climent, Cordones, Cohen Kadosh, & Márquez-Ruiz, 2021). Therefore, it is possible that tRNS may interact with MD to enhance deprived eye contrast gain and augment ocular dominance plasticity.

Based on their potential to modulate neural excitability and GABA-mediated inhibition within the human visual cortex, we explored the effects of physical exercise and occipital hf-tRNS on ocular dominance plasticity in adults with normal vision. We further explored whether any effects of these two interventions were additive. Because ocular dominance plasticity may arise from reduced visual cortex inhibition, we hypothesized that hf-tRNS and exercise would each enhance the magnitude of eye dominance changes compared with monocular deprivation alone. We also predicted larger increases in ocular dominance plasticity when both interventions were combined. Deprived eye dominance was measured using two binocular rivalry tests—one that was a traditional rivalry test involving dichoptic gratings (hereafter referred to as the grating rivalry test) to measure periods of dominance of the component grating percept of each eye (Finn et al., 2019; Lunghi & Sale, 2015; Sheynin, Chamoun et al., 2019; Sheynin, Proulx et al., 2019) and the other involving dichoptic letters with opposite contrast polarities (hereafter referred to as the letter-polarity test). The letter-polarity test was recently proposed by Bossi, Hamm, Dahlmann-Noor, and Dakin (2018). Compared with other psychophysical eye dominance tests, the letter-polarity test is a relatively easy task for participants to perform and has the potential to be used in clinical settings; therefore, we wanted to assess whether this test can measure eye dominance changes. Our secondary outcome was the duration of grating rivalry mixed percepts. An increase in mixed percepts (perceiving the images of both eyes during grating rivalry) indicates a reduction of interocular inhibition (Kang & Blake, 2011). Because any changes in visual cortex inhibition induced by tRNS and/or exercise would be general (i.e., not specific to one eye), we anticipated that mixed percept durations might increase following these interventions.

With monocular deprivation alone, we successfully induced ocular dominance plasticity; that is, there was a significant increase in the deprived eye dominance for both eye dominance tests. However, we observed no additional effect of visual cortex hf-tRNS or exercise, or their combination, on ocular dominance plasticity. We also found no significant changes in mixed percept duration for any intervention.

Methods

Participants

Inclusion criteria were best-corrected visual acuity of at least 20/20 in each eye. Exclusion criteria were (a) inability to fuse dichoptic images; (b) high baseline eye dominance (ED $>$ 0.7), as determined by our computerized eye dominance tests described below; and (c) common safety considerations for transcranial electrical stimulation, including a history of epilepsy or seizures, pacemakers or metal implants within the skull, pregnancy, mental illness or psychiatric conditions, and psychoactive medication. Participants were asked to avoid any recreational drugs within 24 hours before their visits. This study conformed with the tenets of the Declaration of Helsinki and was approved by the ethics committee of Midwestern University (Downers Grove, IL). Written informed consent was obtained from all participants prior to their participation.

Eye dominance tests

Eye dominance was measured using two tests: the grating rivalry test and the letter-polarity test. Visual stimuli for both tests were presented on a light-emitting diode monitor (ROG PG278QR, ASUSTek Computer, Inc., Taipei, Taiwan) against a gray background (48 cd/m^2). The refresh rate of the monitor was 60 Hz, and the resolution was 1920 $\times$ 1080 pixels. The stimuli for the grating rivalry test were generated on a Windows computer (Intel Core i7-8700K, 16-GB RAM) using MATLAB R2019a (MathWorks, Natick, MA) with Psychtoolbox 3.0.15 extensions. The stimuli for the letter-polarity test were generated on the same computer via the PsychoPy module in Python 3.6.6. Participants viewed left and right stimuli dichoptically through a mirror stereoscope. The viewing distance was 108 cm. A chin rest was used to stabilize participants' head position.

In the grating rivalry test (Figure 1), two stationary, orthogonally oriented (+45° and –45°) circular gratings (2° diameter, 2 cycles per degree [cpd], 100% Michelson contrast) were dichoptically presented. Participants continuously reported their perception using a keyboard while fixating a central cross. Specifically, participants were instructed to press one of four keys to indicate exclusive perception of the –45°grating, exclusive perception of the +45° grating, perception of a uniform plaid pattern ("superimposition"), or perception of patches of the orthogonal gratings ("piecemeal"). Six 1-minute trials were presented. Percept durations were summed and averaged across trials. We subsequently added superimposition and piecemeal durations together to calculate the duration of total "mixed" percept (d_M). Half of the mixed percept duration was added to each exclusive percept (deprived, d_D; non-deprived, d_{ND}) to calculate eye dominance. This was done to include the contribution of each eye to mixed percept within the equation. Thus, deprived eye dominance was $\mathrm{ED}_{\mathrm{rivalry}} = \frac{dD + \frac{1}{2} * dM}{dD + dND + dM}$. Eye dominance results ranged from 0 to 1, with a larger value indicating more dominance from the deprived eye. This calculation is mathematically equivalent to the ocular dominance index ($\mathrm{ODI} = \frac{dp - dnp}{dp + dnp + dm}$) used in

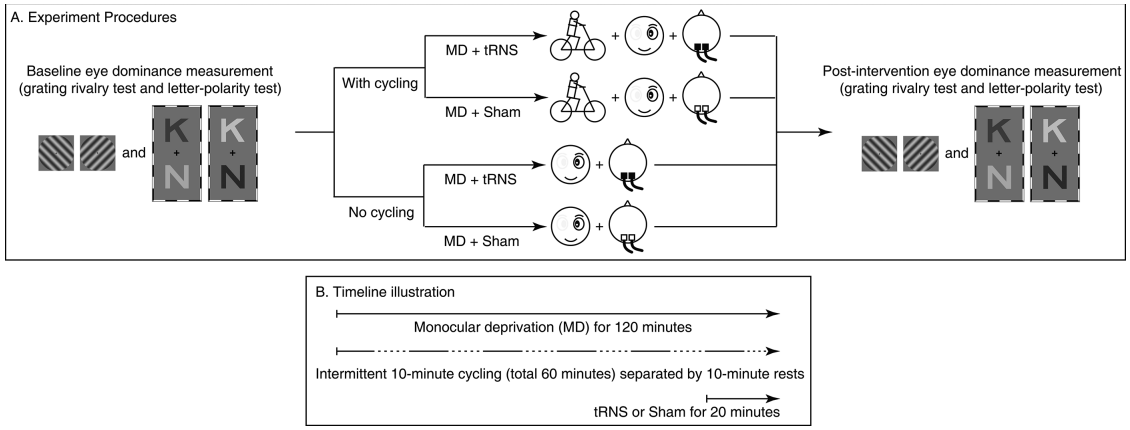

Figure 1. Illustration of experimental procedures and timeline. In all four conditions, participants received MD of their dominant eye for 2 hours. During the final 20 minutes of MD, participants received either tRNS or sham stimulation. In two conditions, participants performed a cycling task for a total of 60 minutes (10-minute blocks of cycling separated by 10-minute rests). Participants wore a heart rate sensor while cycling and were asked to maintain 60% of their maximum heart rate. Eye dominance was measured using two computerized tests before and after MD. Please refer to the main text for further details.

Min et al. (2021) (i.e., $ED_{rivalry} = \frac{1}{2} * ODI + \frac{1}{2}$). The rate of perceptual alternations (i.e., alternation rate) was calculated as the average number of alternations per second.

The letter-polarity eye dominance test was originally described by Bossi et al. (2018). Briefly, two pairs of inverse polarity letters were presented dichoptically (Figure 1). Each pair in the top and bottom rows contained a dark letter (with a negative contrast coded as a minus value) and a bright letter (with a positive contrast coded as a positive value). The contrasts of the two letters presented to each eye always summed to zero. Participants fused the fixation cross and the fusion-lock boarder of the stimuli to superimpose the positive and negative contrast versions of the same letter. Participants reported whether the top or bottom letter was whiter. When rivalry was experienced, participants were asked to compare the whiteness of the positive contrast upper and lower letters. To measure the "balance point" of the interocular contrast difference at which the left eye and right eye letters had an equal probability of dominance, we implemented the method of constant stimuli. Twenty repeats of nine letter contrasts (from 0.3 to 0.7, in steps of 0.05, producing interocular differences ranging from 0 to 0.4) were tested in a random order for a total of 180 trials. With a given contrast value c, the contrasts in each letter pair were either c and $-(1 - c)$ or $-c$ and $(1 - c)$. These two pairs of contrasts were randomly assigned to the top or bottom row of the stimulus. For full details of the manipulation of letter contrasts, please refer to Bossi et al. (2017) and Bossi et al. (2018). We subsequently used a Logistic function to fit these data and calculated the point of subjective equality as the balance point. This balance point was used to indicate deprived eye dominance (ED_{letter}). A value greater than 0.5 indicated greater dominance of the deprived eye; a value smaller than 0.5 indicated greater dominance of the non-deprived eye.

Cycling

In two visits, participants completed six 10-minute blocks of cycling on a stationary bike separated by 10-minute rest blocks (Finn et al., 2019; Lunghi & Sale, 2015) during the 2-hour monocular deprivation period (Figure 1). Participants wore a Polar H10 heart rate monitor (Polar Electro, Helsinki, Finland) to monitor their heart rate, and they were able to read their heart rate from a mobile app. While they were cycling, participants were asked to maintain their heart rate at 60% maximal heart rate. This maximal heart rate was calculated based on the Tanaka formula ($HR_{max} = 208 - 0.7 \times age$) (Tanaka, Monahan, & Seals, 2001). A 1-mile walk test was used to estimate participants' maximal oxygen consumption (VO_{2max}) (Kline et al., 1987). VO_{2max} was used to ensure that participants were of average cardiovascular fitness for their age so that the heart rate estimation was valid.

Transcranial random noise stimulation

During the final 20 minutes of the 2-hour monocular deprivation period, hf-tRNS (100–640 Hz) was delivered to the visual cortex using a battery-driven stimulator (neuroConn DC-Stimulator PLUS; neuroConn GmbH, Ilmenau, Germany). Two electrodes were placed over O_1 and O_2 as identified using the international 10/20

electrode positioning system. These sponge electrodes (35 cm^2) were soaked in saline to reduce impedance. The electrodes were kept in place with elastic bands. A 1-mA current was applied to the visual cortex for 20 minutes, including 20 seconds for ramping up and 20 seconds for ramping down. For sham stimulation, the electrodes were placed over the same region of the cortex. The current ramped up for 20 seconds and then ramped down for 20 seconds. The stimulator was kept behind participants with its screen covered so that participants would not see it. The experimenter occasionally checked the screen as if real stimulation were being delivered.

Procedures

This study employed a within-subjects design and involved four laboratory visits (Figure 1). During each visit, participants first completed both eye dominance tests to measure their baseline eye dominance and then wore a translucent eye patch over their dominant eye as determined by the grating rivalry test (MD) for 2 hours. The eye patch allowed only diffuse light transmission. Participants were asked to keep their deprived eye open while using their other eye to watch a movie randomly picked from the *Harry Potter* franchise.

During the final 20 minutes of monocular deprivation, participants received either tRNS or sham stimulation of their visual cortex. In two of the four visits, participants were also asked to perform a cycling task while one eye being deprived. Thus, the combinations of interventions were (a) cycling + MD + tRNS; (b) cycling + MD + sham; (c) MD + tRNS; and (d) MD + sham (Figure 1). The sequence of these four conditions was randomized. Immediately after MD, eye dominance was measured again. Because the grating rivalry test was our primary measure of eye dominance, participants always completed this test before the letter-polarity test.

Data analysis

Data were analyzed using SPSS Statistics (IBM Corp., Chicago, IL) and JASP. A p value < 0.05 was considered statistically significant. Normality of data was assessed using Shapiro–Wilk tests. Outcome changes across conditions were compared using a two-way repeated-measures analysis of variance (ANOVA) with a within-subjects factor of condition (four conditions as described above) and a within-subjects factor of time (pre- vs. post-intervention). A one-way repeated-measures ANOVA was also performed on the differences from baseline scores for each eye dominance test. Effect sizes were reported using omega squared (ω^2). Deprived eye dominance from each test, mixed percept duration, and alternation rate were analyzed separately.

Results

A total of 18 healthy adult participants (13 females) were recruited. One participant was excluded due to unstable fusion, and one participant was excluded due to high baseline eye dominance (ED > 0.7). Six participants withdrew due to personal reasons. Hence, 10 participants (age, 22–30 years; median, 25 years; nine females) completed the study. All participants except two (P01, P03) were naïve to this study. To ensure that grating rivalry dynamics were correctly recorded, we removed any blocks with a total response duration <50 seconds, indicating a failure to hold down a response button or the use of two button simultaneously. As a result, six trials out of the total 480 trials were removed from the analysis. As expected for participants with weak eye dominance, baseline eye dominance varied across sessions and across the two eye dominance tests (Li et al., 2010) (Supplementary Table S1).

Deprived eye dominance shift

Figures 2A and 3A show deprived eye dominance changes (ocular dominance plasticity) as measured by the grating rivalry test. There was a significant increase in deprived eye dominance after intervention, with a significant main effect of time: $F(1, 9) = 13.56$, $p = 0.005$, $\omega^2 = 0.254$. However, there were no significant differences across conditions, with no main effect of condition, $F(3, 27) = 0.113$, $p = 0.952$, $\omega^2 < 0.01$, and no interaction between these two factors, $F(3, 27) = 0.081$, $p = 0.970$, $\omega^2 < 0.01$. Figures 2B and 3B show deprived eye dominance changes as measured by the letter-polarity test. There was a significant increase in deprived eye dominance after intervention, $F(1, 9) = 64.54$, $p < 0.001$, $\omega^2 = 0.657$. However, there were no significant differences across conditions, $F(3, 27) = 0.708$, $p = 0.556$, $\omega^2 < 0.01$, and no interaction $F(3, 27) = 0.811$, $p = 0.452$, $\omega^2 < 0.01$. We also baseline normalized the data for each session for each participant using subtraction and performed a one-way repeated-measures ANOVA for each eye dominance test to check for any differences between conditions. The results remained unchanged: grating rivalry test, $F(3, 27) = 0.081$, $p = 0.970$, $\omega^2 < 0.01$; letter polarity test, $F(3, 27) = 0.811$, $p = 0.452$, $\omega^2 < 0.01$.

Duration of mixed percept and alternation rate

We designed our button press options in the grating rivalry test to distinguish superimposition and

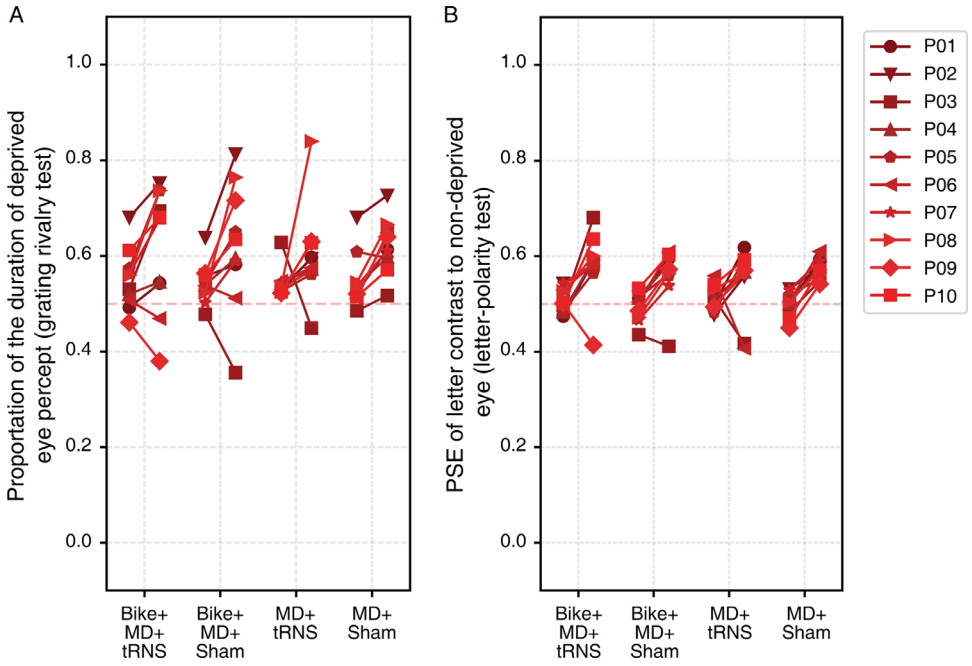

Figure 2. Individual participant deprived eye dominance data at baseline and after each intervention for the grating rivalry (A) and letter-polarity (B) tests. In the grating rivalry test, the proportion of deprived eye percept duration was calculated to indicate deprived eye dominance. In the letter-polarity test, the letter contrast presented to the non-deprived eye at the point of subjective equality (PSE) was calculated to indicate deprived eye dominance. Dashed pink lines represent an eye dominance of 0.5 (i.e., two eyes are perfectly balanced). A value above the dashed lines indicates greater dominance for the deprived eye. On four occasions there was an eye dominance assignment error for participants with weak eye dominance. Therefore, there are four baseline data points slightly below the 0.5 line in panel A. Because the grating rivalry test (A) was used to assign the dominant (deprived) eye, there are many baseline data points below the 0.5 line as anticipated for the letter-polarity test (B).

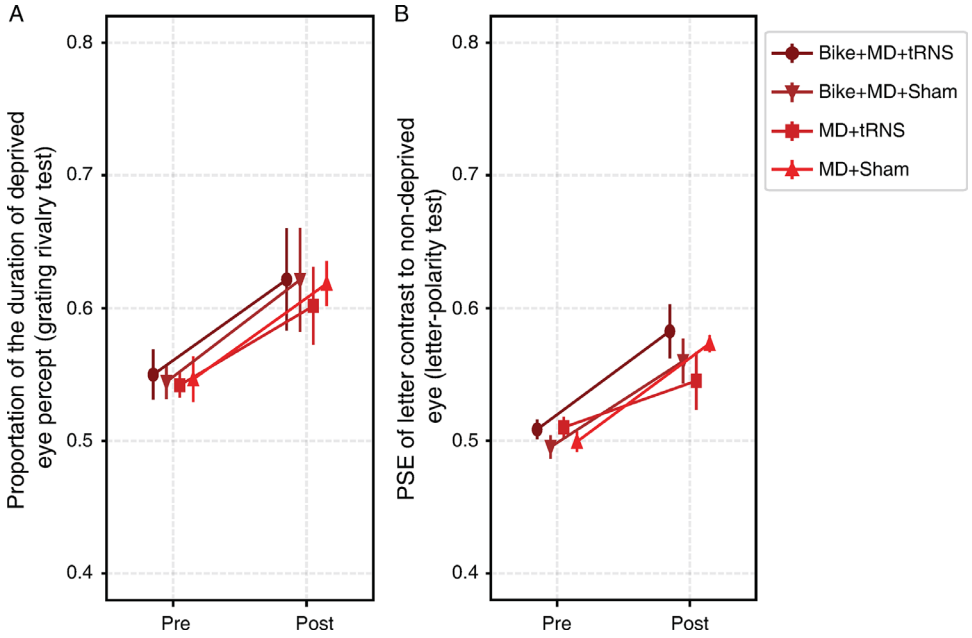

Figure 3. Group mean deprived eye dominance data before (pre-) and after (post-) intervention for the grating rivalry (A) and letter-polarity (B) tests. Error bars denote standard errors of the mean.

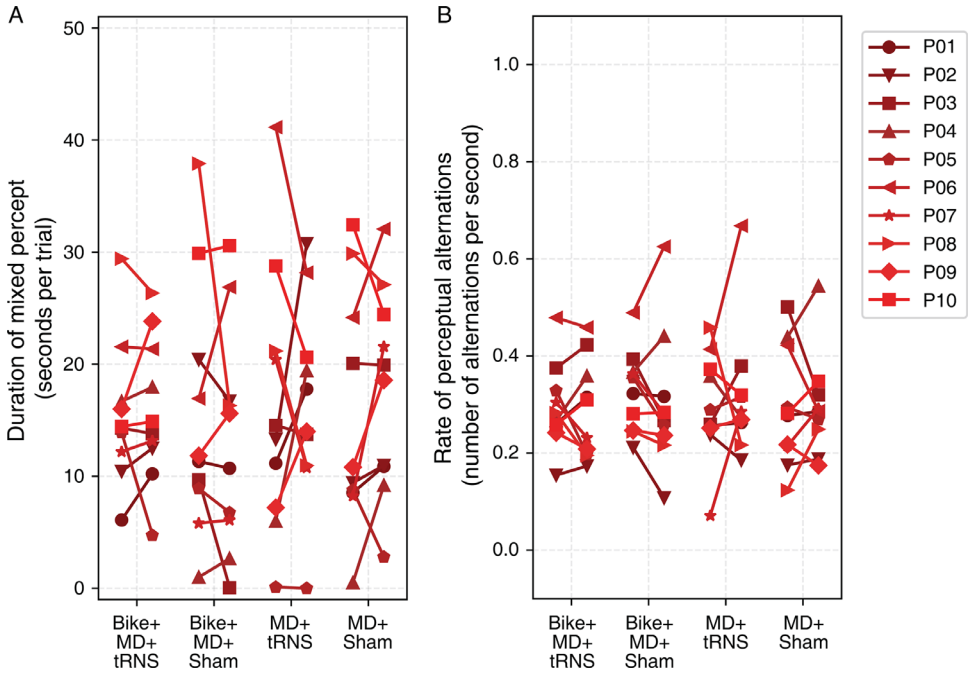

Figure 4. Duration of mixed percept (A) and alternation rate (B) for the grating rivalry measure at baseline and after intervention in each condition. Both the duration of mixed percept and alternation rate were averaged over the six 1-minute trials.

piecemeal percepts, as it was reported that these two percepts could be influenced differently by monocular deprivation (Sheynin, Proulx et al., 2019). However, superimposition was reported by only four participants for an average of 11.6 ± 8.5 seconds. Therefore, we combined the superimposition and piecemeal percept responses to assess mixed percept duration. Figure 4A shows mixed percept duration changes as measured by the grating rivalry test. There were no main effects of time, $F(1, 9) = 0.021$, $p = 0.889$, $\omega^2 < 0.01$, or condition, $F(3, 27) = 0.336$, $p = 0.800$, $\omega^2 < 0.01$, and no interaction, $F(3, 27) = 0.740$, $p = 0.538$, $\omega^2 < 0.01$. Figure 4B shows alternation rate changes as measured by the grating rivalry test. There were no significant differences between pre- and post-intervention, $F(1, 9) = 0.039$, $p = 0.848$, $\omega^2 < 0.01$, or across conditions, $F(3, 27) = 0.406$, $p = 0.750$, $\omega^2 < 0.01$), and no interaction, $F(3, 27 = 0.286$, $p = 0.835$, $\omega^2 < 0.01$.

Discussion

We replicated previous reports of ocular dominance plasticity following MD using both a grating rivalry test and a dichoptic letter-polarity test. Eye dominance shifted significantly in favor of the deprived eye after MD. This effect was not influenced by physical exercise, tRNS, or their combination. We also observed that neither mixed percept duration nor alternation rate during grating rivalry were significantly altered by tRNS, physical exercise, or MD.

We expected physical exercise to increase the magnitude of ocular dominance plasticity. Our hypothesis was mainly predicated on findings indicating that physical activity promotes visual cortex neuroplasticity and enables recovery of vision following early monocular deprivation (Baroncelli et al., 2012; Kaneko & Stryker, 2014) or stroke (Kalogeraki, Pielecka-Fortuna, Hüppe, & Löwel, 2016) in adult rats. In human adults, there has been evidence that physical exercise enhances neuroplasticity, resulting in cognitive function improvement (Cassilhas et al., 2016; Hötting & Röder, 2013). Furthermore, Lunghi and Sale (2015) observed that physical exercise enhanced ocular dominance plasticity. Finn et al. (2019) reanalyzed Lunghi and Sale's data and found that the effect of exercise on ocular dominance plasticity was present when grating rivalry data were analyzed using mean dominance durations but not when using median durations, indicating that the effect was highly variable between subjects. Within their own data, Finn et al. (2019), along with Zhou et al. (2017), did not observe any effect of exercise on ocular dominance plasticity. Moreover, studies using different experimental paradigms to explore exercise-induced neuroplasticity did not observe any effect of exercise on visual perceptual learning (Campana, Fongoni, Astle, & McGraw, 2020; Connell, Thompson, Green, Sullivan, & Gant, 2018). Interestingly, the work of Connell et al. (2018) showed that exercise prior to perceptual learning blocked the learning effect. Here, we observed that exercise did not modulate ocular dominance plasticity. It remains unclear why exercise had an effect

in the study by Lunghi & Sale (2015) but not in other studies.

High-frequency tRNS is a promising non-invasive brain stimulation technique that can modulate cortical excitability. hf-tRNS for as little as 20 minutes is able to reduce phosphene thresholds (increase visual cortex excitability) for up to 1 hour (Herpich et al., 2018). hf-tRNS also strengthens perceptual learning for a variety of visual tasks (Campana, Camilleri, Pavan, Veronese, & Lo Giudice, 2014; Contemori, Trotter, Cottereau, & Maniglia, 2019; Fertonani et al., 2011; Herpich et al., 2019; Moret et al., 2018). In patients with amblyopia, full-frequency tRNS leads to acute improvements in monocular contrast sensitivity and visual acuity (Donkor, Silva, Teske, Wallis-Duffy, Johnson, & Thompson, 2021). Our results did not reveal an effect of hf-tRNS on ocular dominance plasticity.

Our finding that exercise, tRNS, and their combination did not influence ocular dominance plasticity may simply indicate that these interventions have no effect on the homeostatic plasticity processes that are thought to underlie the effects of short-term MD. Another possibility is that there may be a ceiling effect for ocular dominance plasticity in visually normal adults. In fact, as described in the introduction, several groups have tried to augment ocular dominance plasticity by combining MD with different interventions (Chen et al., 2020; Finn et al., 2019; Lunghi & Sale, 2015; Sheynin, Chamoun et al., 2019; Wang et al., 2021; Zhou et al., 2017). Min, Baldwin, & Hess (2019) also examined whether there was any cumulative effect of multiple periods of monocular deprivation on ocular dominance plasticity. Most of these studies did not observe an increase in ocular dominance plasticity, in agreement with our results. On the other hand, there is initial evidence that interventions such as exercise and tRNS may increase ocular dominance plasticity and improve vision in visually impaired populations such as adults with amblyopia (Hess & Thompson, 2013; Lunghi, Sframeli et al., 2019; Perin, Viganò, Piscitelli, Matteo, Meroni, & Cerri, 2020; Sabel et al., 2020; Tuna, Pinto, Brardo, Fernandes, Nunes, & Pato, 2020). Future studies should further explore the use of such interventions in these populations.

Most ocular dominance plasticity studies have adopted 2 to 2.5 hours of MD (Chadnova et al., 2017; Chen et al., 2020; Lunghi & Sale, 2015; Sheynin, Chamoun et al., 2019; Zhou et al., 2017). Min et al. (2018) assessed whether varying the duration of MD from 30 minutes to 5 hours would influence the MD effect. They reported no statistically significant effect of duration; however, there did appear to be a trend for longer MD producing larger effects. In a neuromodulation study, Sheynin, Stolowy et al. (2019) performed both 2-hour and 1-hour MD. Although the authors did not compare these two deprivation durations, it seems, from their data, that 2-hour MD produced ocular dominance plasticity that was two times the magnitude of that induced by 1-hour MD. Given such evidence, we suspect that shorter MD durations (i.e., less than 2 hours) may remove the ocular dominance plasticity ceiling effect in adults with normal vision and reveal enhanced plasticity following interventions such as exercise and tRNS.

We also examined the differential influence of MD, tRNS, and exercise on mixed percept duration. This type of percept is believed to happen when interocular inhibition is relatively low, allowing for a temporary combination of left and right eye images (Kang & Blake, 2011). There are two subtypes of mixed percept: superimposition, which involves binocular combination of both images, and piecemeal, where rivalry still exists in some parts of the stimuli (Alais & Melcher, 2007; Sheynin, Proulx et al., 2019; Skerswetat, Formankiewicz, & Waugh, 2018). The prominence of mixed percepts during rivalry has been linked to GABA-mediated inhibition within the visual cortex. Increased GABA-mediated inhibition reduces mixed percept duration (Mentch, Spiegel, Ricciardi, & Robertson, 2019), whereas MD has been found to increase mixed percept duration (Sheynin, Proulx et al., 2019), presumably due to reduced visual cortex inhibition (Lunghi, Emir et al., 2015). However, not all results are consistent with this model. For example, Abuleil, McCulloch, and Thompson (2021) observed prolonged mixed percept durations following continuous theta burst stimulation to the visual cortex, an intervention that increases inhibition (Franca, Koch, Mochizuki, Huang, & Rothwell, 2006; Sabel et al., 2020). In the same study, no change in mixed percept duration was observed following excitatory anodal transcranial direct current stimulation of the visual cortex (Abuleil et al., 2021).

In our study, mixed percept duration did not change significantly following any of our interventions. One possible explanation for the absence of an effect of MD on mixed percept duration is related to the size and spatial frequency of our grating rivalry stimuli. It has been demonstrated that these parameters influence grating rivalry dynamics whereby large and high spatial frequency stimuli tend to produce longer mixed percepts (Kang, 2009; O'Shea, Sims, & Govan, 1997; Skerswetat, Formankiewicz, & Waugh, 2016). Previous studies of mixed percept duration have used various stimulus parameters for their grating rivalry tests, with sizes ranging from 1 to 6.1 degree of visual angle and spatial frequency ranging from 0.5 to 4 cpd (Abuleil et al., 2021; Bai et al., 2017; Lunghi & Sale, 2015; Lunghi et al., 2011; Lunghi, Morrone, Secci, & Caputo, 2016; Lunghi, Galli-Resta et al., 2019; Lunghi, Sframeli et al., 2019; Min et al., 2021; Sheynin, Proulx et al., 2019). We chose stimuli with a size of 2 degrees and a spatial frequency of 2 cpd because it was the most common combination used by Lunghi et al. in their MD studies

(Lunghi & Sale, 2015; Lunghi et al., 2016; Lunghi, Daniele et al., 2019; Lunghi, Galli-Resta et al., 2019; Lunghi, Sframeli et al., 2019). It is worth noting that, as O'Shea et al. (1997) demonstrated, the combination of 2 cpd and 2° seems to produce nearly maximum exclusive percept (thus minimum mixed percept) compared with other combinations. It is possible that the few reports of superimposition from our participants and our findings of null effect on mixed percept duration may be a result of our combination of stimulus parameters.

Finally, we tested whether ocular dominance plasticity can be measured using the letter-polarity test proposed by Bossi et al. (2018). In their study, the authors compared eight different tests for eye dominance measurement. Their data demonstrated that the letter-polarity test was the most reliable one among those tests. With the use of two-alternative forced choice, this test is likely to be straightforward for participants and therefore achieve good compliance and accurate results (Bossi et al., 2018). Here, with consistent findings from two eye dominance tests, we demonstrated that the letter-polarity test is sensitive to eye dominance changes in adults with normal vision. To our knowledge, this test has not yet been evaluated in visually impaired populations such as adults with amblyopia. Future studies could examine whether this test is also accurate and sensitive for eye dominance measurement in these populations.

Conclusions

Our study demonstrates that neither tRNS nor exercise or their combination affected ocular dominance plasticity after 2 hours of monocular deprivation in adults with normal vision. Our null findings could result from a ceiling effect in our participants. These interventions also do not appear to modulate mixed percept and alternation rate. We also show that the letter-polarity test is sensitive to eye dominance changes following MD in adults with normal vision. Future studies may examine whether exercise and hf-tRNS would affect ocular dominance plasticity with shorter deprivation durations and whether these interventions would enhance ocular dominance plasticity in visually impaired populations.

Keywords: neuroplasticity, monocular deprivation, sensory eye dominance, non-invasive brain stimulation, cycling

Acknowledgments

The authors thank Amy Nguyen, Grant Sealock, Tiffany Tran, and Nicholas Vo for their help with the data collection.

Supported by grants from the Natural Sciences and Engineering Research Council of Canada (NSERC; RGPIN-04404 to WB and RGPIN-05394 and RGPAS-477166 to BT) and the Canadian Foundation for Innovation (34095 to BT), as well as a Midwestern University Faculty Start-Up Seed Grant to AC. BT was also supported by the Hong Kong Special Administrative Region Government and InnoHK. The funders had no role in the conduction of the experiment or in the writing of this manuscript.

Commercial relationships: none.
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