Effects and mechanisms of reward on short-term monocular deprivation effects

Authors: Song FangxingThe user, Feng Guang, Bao Min, Song Fangxing, Bao Min

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Abstract

Ocular dominance plasticity is a hot topic in the field of brain plasticity research. Studies of short-term monocular deprivation have shown that adults still exhibit ocular dominance plasticity. At present, how to effectively reshape ocular dominance in adults remains an urgent issue to be resolved, and this is closely related to the treatment of adult amblyopia. Reward can modulate brain plasticity, and the combination of reward and training can enhance learning efficiency and promote neural rehabilitation. However, it is not yet clear whether reward can be combined with short-term monocular deprivation to facilitate the reshaping of ocular dominance in adults, and its underlying mechanisms remain unknown.

The present study plans to use behavioral measures and EEG to reveal, at the levels of perceptual and neural ocular dominance, the phenomenon of reward-enhanced monocular deprivation effects; to elucidate the mechanisms of reward-enhanced monocular deprivation effects by integrating behavioral testing, fMRI, and TMS techniques; and to compare short-term monocular deprivation paradigms with and without reward, thereby verifying the corrective effect of reward-based monocular deprivation on adult amblyopia. The findings will help deepen our understanding of brain plasticity and promote methodological innovation in adult ocular dominance reshaping and amblyopia correction.

Full Text

The Impact and Mechanism of Reward on Short-term Monocular Deprivation Effects

SONG Fangxing[1], **FENG Guang**[1], **BAO Min**[2],[3]
([1] School of Mental Health and Psychological Sciences, Anhui Medical Univer-

sity, Hefei 230032, China)
([2] CAS Key Laboratory of Behavioral Science, Institute of Psychology, Chinese Academy of Sciences, Beijing 100101, China)
([3] Department of Psychology, University of Chinese Academy of Sciences, Beijing 100049, China)

Abstract

Ocular dominance plasticity represents a prominent research topic in the field of brain plasticity. Studies on short-term monocular deprivation have revealed that adults retain considerable ocular dominance plasticity. However, effectively reshaping ocular dominance in adults remains an urgent challenge, closely linked to the treatment of adult amblyopia. Reward can modulate brain plasticity, and combining reward with training enhances learning efficiency and promotes neurorehabilitation. Nevertheless, it remains unclear whether reward can be integrated with short-term monocular deprivation to facilitate the remodeling of adult ocular dominance, and the underlying mechanisms are poorly understood. This study will employ behavioral measures and EEG to uncover the phenomenon of reward-enhanced monocular deprivation effects from both perceptual and neural ocular dominance perspectives. Furthermore, we will combine behavioral, fMRI, and TMS techniques to elucidate the mechanisms through which reward enhances monocular deprivation effects. Finally, we will compare short-term monocular deprivation paradigms with and without reward to validate the therapeutic efficacy of reward-enhanced monocular deprivation for adult amblyopia. The findings will enrich our understanding of brain plasticity and drive methodological innovation in adult ocular dominance remodeling and amblyopia correction.

Keywords: reward, ocular dominance, plasticity, monocular deprivation, attention

1. Research Significance

Brain plasticity is crucial for individual survival and development, serving as the foundation for learning and memory while enabling functional recovery through neural pathway reorganization after injury and maintaining neural system stability and balance (Axelrod et al., 2023). Ocular dominance plasticity provides an important window for investigating brain plasticity and plays a significant role in amblyopia treatment. Classic neuroscience research has traditionally held that ocular dominance plasticity exists only during critical periods of growth and development (Wiesel & Hubel, 1963). Recent studies on short-term monocular deprivation, however, have demonstrated that adults retain considerable ocular dominance plasticity (Castaldi et al., 2020). Moreover, this short-term monocular deprivation effect also exists in adult amblyopia patients (Lunghi, Sframeli, et al., 2019; Zhou et al., 2019), offering new avenues for adult amblyopia correction. Nevertheless, the mechanisms underlying this short-term ocular dominance plasticity remain incompletely understood, and how to enhance the short-term monocular deprivation effect represents a key challenge limiting its clinical application.

Traditional short-term monocular deprivation research primarily manipulates monocular visual input to influence ocular dominance plasticity (Lunghi et al., 2011; Zhou et al., 2014). However, recent findings reveal that, beyond visual input, attention can also modulate short-term ocular dominance plasticity (Song et al., 2023; Song, Dong, et al., 2024; Song, Lyu, et al., 2024), opening a new chapter on how high-level cognitive functions influence ocular dominance plasticity. Top-down cognitive feedback modulation may serve as an effective means to enhance short-term monocular deprivation effects. Reward can regulate attention, and numerous studies have shown that reward can function as a teaching signal to guide attentional selection (Anderson et al., 2021; Song et al., 2020; Song et al., 2021). Therefore, a critical scientific question emerges: Can reward enhance short-term monocular deprivation effects? Based on reward' s guidance of attention and attention' s modulation of ocular dominance plasticity, we propose that reward may influence short-term monocular deprivation effects by regulating attention. Additionally, research indicates that reward can affect visual processing of the rewarded eye independently of conscious attention (Dong et al., 2022). Thus, reward may also directly modulate short-term monocular deprivation effects without relying on attention.

In summary, to clarify whether reward can modulate short-term monocular deprivation effects and the underlying cognitive neural mechanisms, this study designs a reward-integrated short-term monocular deprivation paradigm and investigates it using EEG, fMRI, and TMS techniques. This research holds significant theoretical and practical value. Theoretically, it will reveal how bottom-up visual input (monocular deprivation) and top-down cognitive modulation (reward) jointly regulate ocular dominance, thereby refining our understanding of the mechanisms underlying short-term ocular dominance plasticity. Understanding this interaction will help us better comprehend how the brain adjusts its functions according to external environments and internal cognitive states, enriching our knowledge of human vision and brain plasticity. Practically, adult amblyopia treatment has always faced major challenges, as existing clinical interventions are only effective for young children while proving largely ineffective for adult patients. This study' s integration of reward with short-term monocular deprivation promises to more effectively reshape adult ocular dominance, thereby driving methodological innovation in adult amblyopia treatment.

2.1 Short-term Monocular Deprivation Reshapes Adult Ocular Dominance

During visual information processing, the human binocular system exhibits functional asymmetry. Generally, the brain' s response to visual stimuli from one eye is stronger than that from the other, a phenomenon known as ocular dominance, with the eye producing stronger responses called the dominant eye (Porac

& Coren, 1976). An extreme pathological manifestation of ocular dominance is amblyopia, a visual disorder caused by abnormal visual experience such as anisometropia, strabismus, or form deprivation, resulting in impaired visual cortex neurodevelopment without organic ocular lesions (Holmes & Clarke, 2006). Amblyopia typically manifests as physiological changes in the visual pathway of one eye accompanied by decreased visual acuity, reflecting a series of neural, perceptual, oculomotor, and clinical functional abnormalities arising from disrupted normal visual development during early life (Levi, 2020; McConaghy & McGuirk, 2019). Currently, amblyopia treatment exhibits clear time sensitivity, achieving optimal efficacy during the critical period, with therapeutic effects declining significantly with age. Adult amblyopia patients show limited treatment effects and low compliance, making it clinically urgent to explore more effective and scalable intervention strategies.

Ocular dominance is not static but shifts in response to external visual experience, demonstrating plasticity. For instance, in Wiesel and Hubel’ s classic study, suturing the eyelid of one eye (the deprived eye) in kittens for several weeks prevented visual input. After several months, they observed atrophy of the lateral geniculate nucleus (LGN) representing the deprived eye, reorganization of ocular dominance columns in V1, and a shift in ocular dominance toward the non-deprived eye, with only a few neurons still responding to the deprived eye (Wiesel & Hubel, 1963). Utilizing this long-term ocular dominance plasticity induced by monocular occlusion, prolonged patching of the fellow eye in amblyopic children during the critical period can significantly improve visual acuity in the amblyopic eye, effectively treating amblyopia (Levi, 2020; McConaghy & McGuirk, 2019). Additionally, Wiesel and Hubel performed three months of monocular suturing in adult cats and found no change in binocular neural ocular dominance (Wiesel & Hubel, 1963), indicating that ocular dominance plasticity has maximal potential during developmental critical periods, with adult ocular dominance remaining relatively stable thereafter. However, Lunghi et al. (2011) discovered that after short-term (2.5 hours) monocular occlusion deprivation in adults [Figure 1: see original paper], the deprived eye dominated for longer periods in binocular rivalry tasks while the non-deprived eye’ s dominance time correspondingly shortened, indicating a shift in ocular dominance toward the deprived eye. This short-term monocular deprivation effect demonstrates that the adult visual cortex retains considerable plasticity.

The short-term monocular deprivation effect is modulated by multiple factors. First, image properties of visual input prove to be important factors influencing this effect. Research shows that even without completely blocking visual input to the deprived eye, merely stripping partial information can also induce monocular deprivation effects, which are influenced by the degree and type of visual information removed (Bai et al., 2017; Lyu et al., 2020; Wang et al., 2017; Yao et al., 2017). For example, reducing contrast in the deprived eye to 20% can induce ocular dominance shifts, but reduction to 40% cannot (Zhou et al., 2014); depriving high spatial frequency components induces ocular dominance shifts, while depriving low spatial frequency components does not (Zhou et al., 2014). Beyond image energy information, phase information of deprived images can also produce monocular deprivation effects, with differential manifestations in binocular phase integration tasks versus binocular rivalry tasks (Bai et al., 2017; Lyu et al., 2020; Zhou et al., 2014). We have previously detailed the influence of image properties on short-term monocular deprivation effects in a review article (宋方兴 et al., 2023), which this paper will not reiterate. Second, exercise represents another potential modulating factor. Inspired by animal studies showing that physical activity can modulate visual cortex plasticity (Baroncelli et al., 2012; Baroncelli et al., 2010; Sale et al., 2007), Lunghi and Sale (2015) investigated the role of exercise during monocular deprivation in adults. Results showed that intermittent cycling during deprivation enhanced monocular deprivation effects compared to sedentary conditions. However, subsequent studies using different ocular dominance measurement paradigms (such as dichoptic surround suppression, binocular integration, and interocular suppression) failed to replicate these results (Baldwin et al., 2022; Finn et al., 2019; Zhou et al., 2017), indicating that exercise' s facilitative effect on adult short-term ocular dominance plasticity requires further verification. Additionally, research has found that individual physiological states also affect short-term monocular deprivation effects. For instance, studies show that monocular deprivation effects gradually weaken with increasing body mass index (BMI) (Lunghi, Daniele, et al., 2019). After bariatric surgery, ocular dominance plasticity can be restored in obese individuals (Daniele et al., 2021). Recent research further indicates that sleep significantly modulates short-term monocular deprivation effects (Menicucci et al., 2022). Specifically, entering a sleep state immediately after monocular deprivation can sustain deprivation effects for over six hours, far exceeding the typical duration of 30 minutes to one hour. Moreover, animal studies have found that brief dark exposure can enhance cortical plasticity (Mitchell et al., 2016; Mitchell & Maurer, 2022). Inspired by these findings, researchers investigated whether brief dark exposure could enhance adult ocular dominance plasticity (Min et al., 2023). The study found that dark exposure alone did not induce ocular dominance changes, but brief dark exposure before monocular deprivation significantly enhanced subsequent deprivation effects, indicating that dark exposure can increase adult ocular dominance plasticity. Beyond these exogenous factors, internal neural states may also influence short-term monocular deprivation effects. Research has shown that opening versus closing eyes in darkness induces significantly different brain activity patterns (Boytsova & Danko, 2010). Based on this, researchers manipulated eye opening/closing of the deprived eye during monocular deprivation to investigate internal state effects (Chen, Gao, et al., 2023). Results showed that monocular deprivation effects are influenced by internal states, with larger effects when the deprived eye remains open. In summary, short-term ocular dominance plasticity is not solely driven by visual input itself but is jointly regulated by multiple exogenous factors and internal neural states, reflecting its complex modulation mechanisms.

Beyond perceptual-level ocular dominance shifts, short-term monocular deprivation can also induce changes in ocular dominance in primary visual cortex (V1) at the neural level, shifting toward the deprived eye. Specifically, EEG studies have found that after short-term monocular deprivation, the amplitude of the earliest component (C1) of visual evoked potentials increases for the deprived eye while decreasing for the non-deprived eye (Federici et al., 2023; Lunghi, Berchicci, et al., 2015). In the time-frequency domain, alpha desynchronization (>200ms) amplitude significantly increases in the deprived eye while showing a decreasing trend in the non-deprived eye (Federici et al., 2023). Steady-state visual evoked potential (SSVEP) studies similarly found increased SSVEP amplitude in occipital regions for the deprived eye after deprivation (Lyu et al., 2020; Zhou et al., 2015). Furthermore, fMRI studies confirmed that short-term monocular deprivation enhances blood oxygen level-dependent (BOLD) signal responses to the deprived eye in V1 while suppressing BOLD responses to the non-deprived eye (Binda et al., 2018). Notably, short-term monocular deprivation-induced ocular dominance shifts are accompanied by changes in intracortical excitation/inhibition balance: after monocular deprivation, gamma-aminobutyric acid (GABA) concentration (measured by magnetic resonance spectroscopy in V1) decreases (Lunghi, Emir, et al., 2015), and the amplitude of slow pupil oscillations increases (Binda & Lunghi, 2017), indicating involvement of cholinergic and noradrenergic systems. Recently, researchers discovered that beyond V1, the human visual thalamus also exhibits this short-term plasticity (Kurzawski et al., 2022). Using 7T fMRI to investigate activation changes in the lateral geniculate nucleus and pulvinar nucleus before and after monocular deprivation, they found that short-term monocular deprivation enhances BOLD responses to the deprived eye in the ventral pulvinar nucleus while suppressing responses to the non-deprived eye, with these changes showing significant positive correlation with perceptual ocular dominance changes. Subsequently, researchers further investigated the relationship between functional connectivity between the pulvinar nucleus and V1 and monocular deprivation effects (Acquafredda et al., 2025), finding that pre-deprivation connectivity from the pulvinar nucleus to V1 showed significant negative correlation with perceptual ocular dominance changes, indicating that subjects with stronger pulvinar influence on V1 exhibited lower plasticity. These results highlight the role of thalamocortical circuits in short-term ocular dominance plasticity.

More importantly, studies have found that after 2.5 hours of monocular deprivation in adult amblyopia patients, ocular dominance of the deprived eye (the amblyopic eye) is enhanced (Zhou et al., 2013), indicating that short-term ocular dominance plasticity also exists in the amblyopic visual system. Since this approach involves patching the amblyopic eye rather than the fellow eye, contrary to conventional amblyopia treatment, researchers have termed this short-term monocular patching method “inverse occlusion” (Zhou et al., 2019). Notably, as early as the 1950s, researchers employed inverse occlusion methods that patched the amblyopic eye for amblyopia treatment (Bangerter, 1953), but this approach was gradually abandoned due to weaker therapeutic effects compared to conventional fellow-eye patching. In contrast to long-term inverse occlusion, short-term monocular deprivation can be effective in adult amblyopia patients, opening new avenues for adult amblyopia correction. Subsequent studies have further demonstrated that short-term monocular deprivation’ s therapeutic effects on amblyopia exhibit significant cumulative effects over time (Lunghi, Sframeli, et al., 2019; Zhou et al., 2019). Lunghi et al. administered six sessions of short-term monocular deprivation training to amblyopia patients over four weeks and found significant improvements in amblyopic eye visual acuity after training. Zhou et al. conducted daily training for two months and found not only significant improvements in amblyopic eye visual acuity but also marked improvements in binocular balance and stereopsis after training. These findings suggest that if each short-term monocular deprivation effect can be enhanced, the therapeutic efficacy of short-term monocular deprivation for amblyopia could be significantly improved. Therefore, how to enhance and prolong short-term monocular deprivation effects constitutes a key issue that must be addressed for applying this approach to amblyopia treatment.

Recent studies have found that attention can influence ocular dominance and ocular dominance plasticity, providing new theoretical foundations for improving traditional visual input-based monocular deprivation paradigms. Before elaborating on this research, we must first distinguish between attention’ s modulatory effects on ocular dominance versus ocular dominance plasticity. Ocular dominance is a real-time state—for instance, if one eye dominates conscious perception for longer durations than the other during binocular rivalry tasks, that eye is considered dominant. Attention’ s influence on ocular dominance refers to inducing ocular dominance changes through specific paradigms that manipulate attention. In contrast, attention’s influence on ocular dominance plasticity refers to attention’ s effect on changes in ocular dominance. For example, this study focuses on ocular dominance changes induced by short-term monocular deprivation (i.e., the short-term monocular deprivation effect). Within this framework, attention’ s influence on ocular dominance plasticity manifests as attention affecting the monocular deprivation effect produced by short-term deprivation. Next, we will discuss research progress on both aspects.

2.2 Attention’ s Influence on Ocular Dominance

In classic short-term monocular deprivation paradigms, researchers achieve form deprivation by completely blocking visual input to one eye. However, this paradigm offers limited potential for further enhancing short-term monocular deprivation effects at the visual input level. Notably, during monocular deprivation, beyond the asymmetry in visual input, attentional resource allocation between the two monocular pathways is also unbalanced. Therefore, an important question arises: Can attention itself modulate ocular dominance? Addressing this question, researchers have recently conducted a series of studies yielding important advances.

First, studies have investigated attention’ s influence on ocular dominance by manipulating spatial structural relationships of visual input (Wang et al., 2021). In this research, identical images were presented dichoptically to both eyes, but a Porro prism placed before one eye caused that eye to view inverted images. Since upright images have greater biological significance, researchers hypothesized that subjects would selectively attend to upright images, creating differential attention allocation between the eyes. Results showed that after 2.5 hours of attention training, ocular dominance of the eye receiving inverted images was enhanced, suggesting that eye-based attention may induce ocular dominance shifts. However, this study did not directly measure whether attention was preferentially allocated to upright images, and inverted images created mismatched contour information between the two eyes, necessitating further research on attention' s role in ocular dominance shifts.

Recently, we designed a novel dichoptic video adaptation paradigm to investigate eye-based attentional modulation of ocular dominance (Song et al., 2023). In this paradigm, subjects watched normally playing video images with one eye (the attended eye) while the other eye viewed the same video played in reverse (the unattended eye). Since reversed videos are meaningless and lack logical coherence, subjects would subjectively allocate more attention to the attended eye to better comprehend the plot, creating differential attention allocation between the eyes. This paradigm can maintain largely consistent image content between the two eyes while guiding subjects to actively allocate more attentional resources to one eye (the eye viewing normally playing video). The study found that after sustained attention to one eye, ocular dominance shifted toward the unattended eye, demonstrating that eye-based attention can induce ocular dominance plasticity. Furthermore, we combined fMRI and TMS techniques to investigate the neural mechanisms underlying eye-based attentional modulation of ocular dominance and provided direct causal evidence (Song, Dong, et al., 2024). In fMRI experiments, we compared brain activation between dichoptic conditions (one eye viewing forward video, the other viewing reversed video) and binocular conditions (both eyes viewing forward video), finding stronger activation in the dorsal attention network regions responsible for top-down attentional control—including the frontal eye field (FEF), intraparietal sulcus (IPS), and superior parietal lobule (SPL)—in dichoptic versus binocular conditions, indicating greater attentional engagement in dichoptic conditions. In subsequent TMS experiments, we applied continuous theta-burst stimulation (cTBS) to inhibit FEF, IPS, and a control target (vertex), finding that only FEF inhibition eliminated ocular dominance changes induced by dichoptic reversed video, providing causal evidence for FEF' s critical role in controlling eye-based attentional modulation of ocular dominance. Additionally, to explain attention-induced ocular dominance shifts, we proposed an ocular opponency neuron adaptation mechanism based on the binocular rivalry ocular opponency-neuron model (Said & Heeger, 2013) (Song et al., 2023). This mechanism posits that during dichoptic reversed video viewing, opponent neurons receiving excitation from the attended eye and inhibition from the unattended eye remain activated longer, thereby generating stronger adaptation than opponent neurons receiving excitation from the unattended eye and inhibition from the attended eye, resulting in greater activity reduction. During subsequent binocular rivalry tasks, this imbalanced opponent neuron adaptation leads to weaker feedback inhibition for the unattended eye than the attended eye, enhancing the unattended eye' s ocular dominance. Subsequently, we employed SSVEP technology, using interactive modulation frequency SSVEP responses as an index reflecting opponent neuron activity, providing direct neural evidence for the opponent neuron adaptation mechanism (Song, Lyu, et al., 2024). In summary, these studies provide evidence that attention can induce ocular dominance plasticity, opening the curtain on research into high-level cognitive functions influencing ocular dominance plasticity. The combination of visual input' s feedforward influence and high-level cognitive feedback modulation may represent an effective approach for enhancing short-term ocular dominance plasticity, though this requires further investigation.

2.3 Attention' s Modulation of Short-term Monocular Deprivation Effects

Beyond whether attention itself can modulate ocular dominance, researchers have gradually begun investigating potential interactions between short-term monocular deprivation and attention, though conclusions remain inconsistent. For example, Chen et al. (2020) investigated whether attention can modulate short-term monocular deprivation effects through action video games. The study designed three experimental conditions requiring subjects to play action video games (such as Honor of Kings), watch action video game videos, or play non-action video games (such as Minesweeper) during monocular deprivation. Results showed that all three conditions produced deprivation effects without significant differences between them, suggesting that attention may not modulate short-term monocular deprivation effects. However, recent studies have further investigated attention' s influence on short-term monocular deprivation effects. For instance, Wang et al. (2025) required subjects to complete an attentional tracking task during monocular deprivation and found that when attention tracking targets matched test gratings in the ocular dominance measurement phase (e.g., both were red-green gratings), larger short-term monocular deprivation effects were produced. Additionally, researchers found that reducing attention to stimuli in the non-deprived eye during monocular deprivation weakened short-term monocular deprivation effects (Chen & Cai, 2025). They established three conditions: in the attention condition, subjects attended to picture types presented in the non-deprived eye and responded; in the non-attention condition, subjects attended to fixation point changes and responded; and in the passive viewing condition, subjects simply viewed pictures passively without additional tasks. Results showed that compared to passive viewing, short-term monocular deprivation effects were significantly weakened in the non-attention condition, while no difference existed between attention and passive viewing conditions. These studies demonstrate that attention can modulate short-term monocular deprivation effects.

Comparing these studies with divergent conclusions reveals respective limitations. First, Chen et al. (2020) presented video images without sound in the video-watching condition, potentially requiring subjects to allocate more attention to the video for better viewing and comprehension. In the Minesweeper game, subjects similarly needed to concentrate and think. Consequently, experimental conditions may not have created significant differences in attentional engagement levels, possibly explaining the absence of between-group differences in deprivation effects. On the other hand, Wang et al. (2025) employed laboratory stimuli requiring subjects to attend only to specific visual features. While this design allowed precise manipulation of attentional resource allocation, only a minimal number of visual neurons were modulated, lacking ecological validity. Meanwhile, Chen and Cai (2025) employed attention reduction to weaken monocular deprivation effects, preventing examination of attention’ s positive modulation of monocular deprivation effects. Therefore, these experimental paradigms face challenges in translation to practical applications (such as amblyopia correction). In summary, current research on attentional modulation of short-term monocular deprivation effects has certain limitations, and whether interactions between visual input and high-level cognition can promote adult ocular dominance remodeling requires further investigation.

2.4 Reward’ s Modulation of Attention and Visual Perception

Reward can modulate brain plasticity, and combining reward with training enhances motor learning outcomes and promotes neurorehabilitation (Johnson & Cohen, 2022). Based on this, combining reward with short-term monocular deprivation may provide a new effective pathway for promoting adult ocular dominance remodeling. Mechanistically, reward’ s modulation of short-term monocular deprivation effects may operate through at least two relatively independent but not mutually exclusive pathways. On one hand, reward may influence short-term monocular deprivation effects by regulating attention. Numerous studies demonstrate that reward significantly affects attentional selection and resource allocation (Anderson et al., 2021). When target stimuli become associated with expected reward, individuals’ processing speed for targets increases substantially (Grignolio et al., 2024; Wang et al., 2019; Wei & Ji, 2021; 王宴庆 et al., 2019), while neural activity in the dorsal attention network (such as the intraparietal sulcus and superior frontal gyrus) also enhances significantly (Etzel et al., 2016). More importantly, once stimuli form associations with reward, they can automatically capture attention even when reward no longer appears, a phenomenon known as value-driven attentional capture (Anderson et al., 2011; Chen, Chen, et al., 2023; Vakhrushev & Pooresmaeili, 2024; 周星 et al., 2023). These results indicate that reward can function as a teaching signal to optimize behavioral performance by modulating attentional selection (Anderson, 2017; Chelazzi et al., 2013). Our preliminary research also supports this view, finding that reward can influence attentional resource allocation (Song et al., 2020; Song et al., 2021; Zhao et al., 2020). Therefore, in short-term monocular deprivation paradigms, if the non-deprived eye becomes associated with reward, reward may indirectly amplify or modulate ocular dominance plasticity by guiding attentional bias toward input in the non-deprived eye.

On the other hand, reward may also directly modulate early visual processing and visual perceptual plasticity independently of attention. As early as 2006, an animal study published in Science found that some neurons in adult rat primary visual cortex could accurately predict reward timing, indicating that the "high-level" cognitive signal of reward prediction can be encoded at early stages of sensory processing (Shuler & Bear, 2006). Recent human studies also provide direct evidence for reward' s modulation of visual perception. For example, Zhang et al. (2018) found that reward can enhance visual perceptual learning, suggesting that reward may promote plasticity by strengthening sensory representations themselves. Further research demonstrates that reward can still influence visual perceptual processing even under unconscious conditions (Cheng et al., 2021; Dong et al., 2022; Lunghi & Pooresmaeili, 2023). For instance, when unconscious stimuli are associated with high reward, stimulus recognition accuracy improves (Cheng et al., 2021), and the speed of stimuli breaking through interocular suppression increases (Lunghi & Pooresmaeili, 2023). Moreover, Dong et al. (2022) found that in a b-CFS task, rewarding one eye enabled stimuli presented in that eye to break through CFS suppression faster, indicating that reward can affect visual processing of the rewarded eye independently of conscious attention. Therefore, during short-term monocular deprivation, reward may directly enhance neural representations of the rewarded eye or related visual input without attentional mediation, thereby altering the magnitude or duration of post-deprivation ocular dominance shifts.

In summary, reward' s modulation of short-term ocular dominance plasticity may include both indirect pathways through attentional selection and direct pathways acting on visual processing and ocular dominance plasticity. Distinguishing and clarifying these two mechanisms will not only deepen our understanding of the intrinsic mechanisms underlying short-term ocular dominance plasticity but also provide important theoretical foundations for exploring more effective interventions for reshaping adult ocular dominance.

3. Problem Statement

In summary, although short-term monocular deprivation effects in adults have received considerable attention in recent years, their intrinsic mechanisms remain incompletely understood. How to enhance and prolong short-term monocular deprivation effects remains a key issue limiting clinical application. Despite attempts to enhance short-term monocular deprivation effects through attention, existing research has certain limitations. Considering reward' s modulatory effects on attention and visual perception, reward may become a crucial factor for enhancing short-term monocular deprivation effects. Therefore, this study employs a reward-integrated short-term monocular deprivation paradigm, combining EEG, fMRI, and TMS techniques to investigate reward' s modulation of short-term monocular deprivation effects and its cognitive neural mechanisms.

This research will proceed from three perspectives:

First, can reward modulate short-term monocular deprivation effects? This study will employ behavioral and EEG techniques, rewarding the non-deprived eye during short-term monocular deprivation, and systematically answer whether reward can modulate short-term monocular deprivation effects from both perceptual and neural ocular dominance perspectives by comparing differences between reward and non-reward conditions. We hypothesize that reward can enhance short-term monocular deprivation effects.

Second, how does reward modulate short-term monocular deprivation effects? Considering reward' s influence on attention and visual perception, as well as attention' s modulation of ocular dominance plasticity, we propose a dual-pathway model of reward' s modulation of short-term monocular deprivation effects [Figure 2: see original paper]: On one hand, reward can modulate short-term monocular deprivation effects by regulating attention; on the other hand, reward may directly modulate short-term monocular deprivation effects independently of attention. To validate this model and clarify the potential mechanisms of reward' s modulation, this study will combine behavioral, fMRI, and TMS techniques. First, behavioral experiments will preliminarily investigate whether reward can directly modulate short-term monocular deprivation effects independently of attention. Then, fMRI and TMS techniques will be used to verify the causal roles of reward and attention. If inhibiting reward-related brain regions and attention-related brain regions produces equivalent effects on reward effects, it would indicate that reward only modulates monocular deprivation effects through attention. If only inhibiting reward-related brain regions affects reward effects, it would indicate that reward can only modulate monocular deprivation effects independently. If inhibiting both reward-related and attention-related brain regions weakens reward effects, with the former showing greater effects, it would indicate that both mechanisms operate.

Third, can reward-integrated short-term monocular deprivation more effectively correct adult amblyopia? The primary goal of this study is to investigate reward-integrated short-term monocular deprivation' s reshaping of adult ocular dominance to drive methodological innovation in adult amblyopia treatment. Therefore, after clarifying the mechanisms of reward' s modulation of short-term monocular deprivation effects in healthy populations, we will apply the reward-integrated short-term monocular deprivation paradigm to adult amblyopia populations and compare it with traditional short-term monocular deprivation methods to validate its corrective efficacy for adult amblyopia. We hypothesize that reward-integrated short-term monocular deprivation can more effectively correct adult amblyopia.

4. Research Framework

This study addresses the question of "how to promote adult ocular dominance remodeling" by employing an innovative reward-integrated short-term monocular deprivation paradigm and systematically investigating reward’ s influence on short-term monocular deprivation effects and underlying cognitive neural mechanisms using behavioral, EEG, fMRI, and TMS techniques. The overall framework is illustrated in [Figure 3: see original paper].

4.1 Reward’s Impact on Short-term Monocular Deprivation Effects

Study 1 employs a reward-integrated short-term monocular deprivation paradigm (rewarding the non-deprived eye during monocular deprivation) to investigate whether reward can enhance short-term monocular deprivation effects by comparing differences between reward and non-reward conditions. Study 1 comprises two experiments. Experiment 1 measures perceptual ocular dominance using a binocular rivalry task before and after monocular deprivation, examining reward’ s influence on short-term monocular deprivation effects at the perceptual level. Binocular rivalry stimuli consist of two orthogonal sinusoidal gratings oriented at $±$45°, presented dichoptically at the center of the visual field. Subjects report perceived grating orientation (-45°, +45°, or mixture of both directions) by pressing corresponding keyboard keys (left, right, down keys). To quantify perceptual ocular dominance, we calculate the ocular dominance index (ODI). This index is derived from dynamic perceptual data in binocular rivalry tasks during pre- and post-tests using the formula TDE / (TDE + TNDE), where TDE and TNDE represent total durations of perceiving deprived-eye and non-deprived-eye stimuli, respectively, with scores ranging from 0 (complete non-deprived eye dominance) to 1 (complete deprived eye dominance).

During the monocular deprivation phase, subjects complete a target detection task. The target is a circular blob, and when it appears, subjects must judge the orientation of its notch (left or right). Subjects complete two task sets: reward and non-reward conditions. In the reward condition, subjects receive reward feedback after correct responses to targets, while in the non-reward condition, subjects only receive correct-response feedback without reward. We hypothesize that significant short-term monocular deprivation effects will exist in both reward and non-reward conditions (i.e., post-test ODI > pre-test ODI), with larger effects in the reward condition than the non-reward condition.

Experiment 2 employs an alternating monocular visual stimulus presentation task with simultaneous EEG recording during pre- and post-tests. In this task, visual stimuli are presented separately to each eye by alternately patching each eye, allowing acquisition of visual evoked potentials for each eye individually. Experiment 2’ s monocular deprivation phase task is identical to Experiment 1. ERP and time-frequency analyses will be conducted to measure neural ocular dominance and investigate reward’ s influence on short-term monocular deprivation effects at the neural level. We hypothesize that reward will enhance short-term monocular deprivation’ s modulation of neural ocular dominance.

4.2 Potential Mechanisms of Reward's Modulation of Short-term Monocular Deprivation Effects

Based on reward' s influence on attention and visual perception, as well as attention' s modulation of ocular dominance plasticity, this study proposes a dual-pathway model of reward' s modulation of short-term monocular deprivation effects [Figure 2: see original paper]: On one hand, reward can modulate short-term monocular deprivation effects by regulating attention; on the other hand, reward may directly modulate short-term monocular deprivation effects independently of attention. Study 2 aims to validate this model and clarify the potential mechanisms of reward' s modulation.

Study 2 comprises three experiments. Experiment 3 investigates whether task-irrelevant reward (i.e., attention-independent reward) can modulate short-term monocular deprivation effects, thereby revealing its cognitive mechanisms. Experiment 3' s task and procedure are similar to Experiment 1, differing only in the presentation method of reward stimuli during the target detection task. In Experiment 3, reward stimuli are no longer presented as real-time feedback after key responses but appear randomly in each trial, independent of target stimuli and subject responses. This manipulation decouples reward stimuli from task goals, making the presented reward task-irrelevant. When reward is task-irrelevant, subjects lack motivation to allocate more attentional resources to the task to obtain reward. Therefore, we infer that subjects' attentional states will be similar between reward and non-reward conditions when task-irrelevant reward is presented, though monocular pathways still receive reward signals in the reward condition. According to the dual-pathway model, if reward only influences monocular deprivation effects by modulating attention, Experiment 3 will not observe significant reward effects; if reward can directly modulate monocular deprivation effects independently of attention, Experiment 3 will observe reward effects. If reward effects exist, comparing Experiment 3' s reward effects with those of Experiment 1 can further reveal the relative contributions of attention-dependent and attention-independent pathways.

Experiments 4 and 5 combine fMRI and TMS techniques to verify the causal roles of reward and attention. First, Experiment 4 uses task-state fMRI to investigate which brain regions show stronger activation in reward versus non-reward conditions, thereby identifying the neural basis of reward' s effects. Experiment 4 employs the same target detection task as Experiment 1, using a block design with two conditions: reward and non-reward. Data analysis will be performed using AFNI. Preprocessing includes temporal correction, spatial registration, spatial smoothing, and normalization. Preprocessed data will then be analyzed using general linear models, creating task regressors for each condition (reward, non-reward) by convolving boxcar functions representing task block timing with canonical hemodynamic response functions. Subsequently, regression coefficients or β weights will be extracted for all subjects for group analysis. In group analysis, AFNI program '3dttest++' will be used for paired-sample t-tests comparing differences between reward and non-reward conditions.

The ‘-Clustsim’ option will be used for multiple comparison correction of t-test results (3dClustSim). We hypothesize that compared to the non-reward condition, the reward condition will show stronger activation in reward processing networks (such as vmPFC, OFC) and frontoparietal attention networks (FEF, SPL).

Experiment 5 reveals the causal mechanisms of reward’ s modulation of short-term monocular deprivation effects by applying cTBS to inhibit functions of reward-related and attention-related brain regions and observing changes in reward effects. We plan to use a Magstim Rapid2 stimulator with a 70mm standard figure-8 coil to deliver cTBS. cTBS stimulation will be administered offline using a three-pulse stimulation pattern. The stimulation consists of 267 burst matrices, with each burst containing 3 pulses at 30Hz, repeated at 6Hz frequency, totaling 801 pulses over 44 seconds (Cazzoli et al., 2009; Song, Dong, et al., 2024). To extend the duration of cTBS inhibition, we will administer cTBS twice consecutively to the same target, with a 15-minute interval between stimulations. This stimulation pattern has been shown to extend cTBS effects to over two hours (Goldsworthy et al., 2012; Nyffeler et al., 2006), ensuring that stimulated brain regions remain inhibited throughout the monocular deprivation period. Stimulation intensity will be 80% of individual resting motor threshold (RMT). Based on Experiment 4 results, we plan to select appropriate cortical regions from reward and attention networks showing stronger activation in the reward condition as cTBS targets, such as mPFC and FEF. Additionally, we will apply cTBS to the vertex as a control. To account for individual differences in brain structure, we will use Brainsight 2 neuro-navigation system to map target MNI coordinates onto each subject’ s T1-weighted image. Brainsight 2’ s real-time tracking function enables continuous monitoring of TMS coil position to ensure it remains aligned with target brain regions throughout the experiment. Experiment 5’ s task is identical to Experiment 1, with the addition of cTBS stimulation before the monocular deprivation phase. According to the dual-pathway model, if inhibiting reward-related and attention-related brain regions produces equivalent effects on reward effects, it would indicate that reward only modulates monocular deprivation effects through attention. If only inhibiting reward-related brain regions affects reward effects, it would indicate that reward can only modulate monocular deprivation effects independently. If inhibiting both reward-related and attention-related brain regions weakens reward effects, with the former showing greater effects, it would indicate that both mechanisms operate.

4.3 Reward-integrated Short-term Monocular Deprivation for Adult Amblyopia Treatment

Adult amblyopia treatment has long been a clinical challenge, with no mature therapeutic protocols established to date. The reward-integrated short-term monocular deprivation paradigm designed in this study promises to more effectively reshape adult ocular dominance, thereby driving methodological innovation in adult amblyopia correction. Therefore, Study 3 directly tests whether reward-integrated short-term monocular deprivation demonstrates superior corrective effects for adult amblyopia.

Study 3 (Experiment 6) plans to recruit two groups of amblyopia patients: one receiving traditional short-term monocular deprivation training, the other receiving reward-integrated short-term monocular deprivation training. Before training begins, visual function pre-tests measuring visual acuity, stereopsis, and perceptual ocular dominance will be administered to all subjects, followed by training. Training will last one week, with two hours of daily training. Subjects in the traditional training group will undergo two hours of daily monocular patching of the amblyopic eye, during which they can engage in free activities. Subjects in the reward training group will complete the target detection task during the two hours of amblyopic eye patching, with the task identical to the reward condition in Experiment 1. Within 24 hours after the entire training period ends, a post-test will be administered, again measuring visual acuity, stereopsis, and perceptual ocular dominance. Additional post-tests will be conducted one week and one month after training completion to monitor the duration of training effects. The effectiveness of reward training will be examined by comparing training outcomes between traditional and reward training groups. We hypothesize that compared to traditional short-term monocular deprivation training, reward training will demonstrate stronger and more sustained training effects.

5. Theoretical Construction and Innovation

Adult ocular dominance remodeling has remained at the forefront of visual plasticity research. This study integrates reward with short-term monocular deprivation and comprehensively employs multimodal techniques including behavioral measures, EEG, fMRI, and TMS to systematically investigate reward' s influence on short-term monocular deprivation effects and their mechanisms, and further examines its application value in adult amblyopia correction.

(1) Constructing a New Theoretical Framework of Joint Regulation of Adult Ocular Dominance by Bottom-up Visual Input and Top-down Cognitive Modulation

Ocular dominance plasticity represents an important entry point for understanding visual system plasticity in adults and has been a hot topic in visual neuroscience in recent years. Traditional views hold that the adult visual system is largely fixed, with plasticity levels significantly lower than during developmental critical periods (Wiesel & Hubel, 1963). However, numerous recent studies based on short-term monocular deprivation have shown that even in adulthood, the visual system retains a certain degree of ocular dominance plasticity (Castaldi et al., 2020). Previous research primarily induced ocular dominance changes by manipulating visual input differences between the two eyes, such as briefly patching one eye or reducing its input strength (Lunghi et al., 2011; Zhou et al., 2014), with core mechanisms mainly stemming from dynamic regulation of excitation-inhibition balance in primary visual cortex (Lunghi, Emir, et al., 2015). However, recent evidence shows that even with completely identical visual input to both eyes, merely changing attention allocation between the two monocular pathways can induce similar ocular dominance shift effects (Song et al., 2023; Song, Dong, et al., 2024; Song, Lyu, et al., 2024). This finding emphasizes the important role of top-down cognitive modulation in ocular dominance plasticity. Based on this, this study proposes a novel theoretical perspective: adult ocular dominance plasticity is not solely driven by visual input but is jointly shaped by bottom-up feedforward input and top-down feedback modulation. To verify this perspective, this study innovatively introduces reward into short-term monocular deprivation paradigms to test whether reward enhances or alters short-term monocular deprivation effects by regulating attention or directly acting on visual processing pathways. This theoretical framework not only refines the mechanisms underlying short-term ocular dominance plasticity but also provides new perspectives for understanding how the brain adjusts its functions according to external environments and internal cognitive states, thereby enriching our understanding of human vision and brain plasticity.

(2) Proposing a Reward-based Intervention Strategy for Short-term Ocular Dominance Plasticity, Providing a New Path for Adult Amblyopia Treatment

Beyond fundamental theoretical significance, ocular dominance plasticity research holds important clinical application value, particularly concerning adult amblyopia intervention. Amblyopia has traditionally been considered a developmental disorder, with clinical interventions focusing primarily on children and adolescents (Holmes & Clarke, 2006). In adulthood, due to significantly decreased visual system plasticity, amblyopia has been widely viewed as "difficult to treat" or even "irreversible." Currently, no mature, effective intervention protocols exist for adult amblyopia. The proposal of short-term monocular deprivation paradigms offers new possibilities for overcoming this dilemma. Existing studies have attempted to apply this paradigm to adult amblyopia populations, observing positive effects on visual function improvement to some degree (Lunghi, Sframeli, et al., 2019; Zhou et al., 2019). These studies demonstrate that even in adulthood, brief interventions can still induce a certain degree of ocular dominance remodeling, thereby improving functional performance of the amblyopic eye. Based on this, how to enhance and prolong ocular dominance plasticity induced by short-term monocular deprivation has become a key issue requiring urgent resolution. The "reward-integrated short-term monocular deprivation" paradigm proposed in this study represents an innovative attempt to address this problem, promising to more effectively reshape adult ocular dominance and thereby drive methodological innovation in adult amblyopia treatment. More importantly, this study not only validates the effectiveness of this paradigm in healthy adults but also further applies it to adult amblyopia populations to directly assess its corrective effects and systematically compare it with traditional short-term monocular deprivation methods, verifying its clinical application potential and providing reference and guidance for future adult amblyopia treatment. In summary, this study not only contributes to advancing fundamental theories of ocular dominance plasticity but also provides a realistically feasible innovative pathway for adult amblyopia treatment, holding significant value for both visual neuroscience and clinical visual rehabilitation fields.

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