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Optical-neural Stimulation in Non-human Primates: Modulating Brain Function and Behavior*

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Abstract Optical-neural stimulation, which encompasses cutting-edge techniques such as optogenetics and infrared neurostimulation, employs distinct mechanisms to modulate brain function and behavior. These advanced neuromodulation techniques offer accurate manipulation of targeted areas, even selectively modulating specific neurons, in the brain. This makes it possible to investigate the cause-and-effect connections between neural activity and behavior, allowing for a better comprehension of the intricate brain dynamics towards complex environments. Non-human primates serve as an essential animal model for investigating these complex functions in brain research, bridging the gap between the basic research and clinical applications. One of the earliest optical studies utilizing optogenetic neuromodulation in monkeys was conducted in 2009. Since then, the optical-neural stimulations have been effectively applied in non-human primates. This review summarises recent research that employed optogenetics or infrared neurostimulation techniques to regulate brain function and behavior in non-human primates. The current state of optical-neural stimulations discussed here demonstrates their efficacy in advancing the understanding of brain systems. Nevertheless, there are still challenges that need to be addressed before they can fully achieve their potential.

Key words optical-neural stimulation, optogenetics, infrared neurostimulation, non-human primates
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Neuromodulation represents a transformative field in neuroscience and clinical medicine, aiming to manipulate brain activity to treat neurological and psychiatric disorders, as well as to enhance cognitive function. Neuromodulation techniques is to modulate neural activity at various levels, from individual neurons to entire networks, using diverse methods that range from electrical stimulation to chemical agents and, more recently, light-based approaches such as optical-neural stimulation[1]. Classic neurostimulation techniques like deep brain stimulation (DBS) [2], transcranial magnetic stimulation (TMS) [3], and transcranial current stimulation (TCS)[4-5], utilized the targeted application of electrical currents and/or magnetic fields to the brain[6]. However, despite their efficacy in regulating the neural activity, these approaches encounter various challenges, including the ability to selectively target certain neural circuits or cell types, as well as achieving precise spatial resolution within certain brain regions. Optical-neural stimulation has emerged as a potent technique, offering precision in manipulating neural activity with spatial and temporal specificity.

Optical-neural stimulation encompasses several innovative approaches, most notably optogenetics (Figure 1), which involves genetically modifying neurons to express light-sensitive proteins called opsins[7-11]. These opsins respond to specific wavelengths of light, allowing researchers to precisely modulate specific neurons by delivering light to targeted brain regions. In addition to optogenetics, other forms of optical-neural stimulation, such as infrared neurostimulation (Figure 2), utilize different mechanisms to modulate neuronal activity

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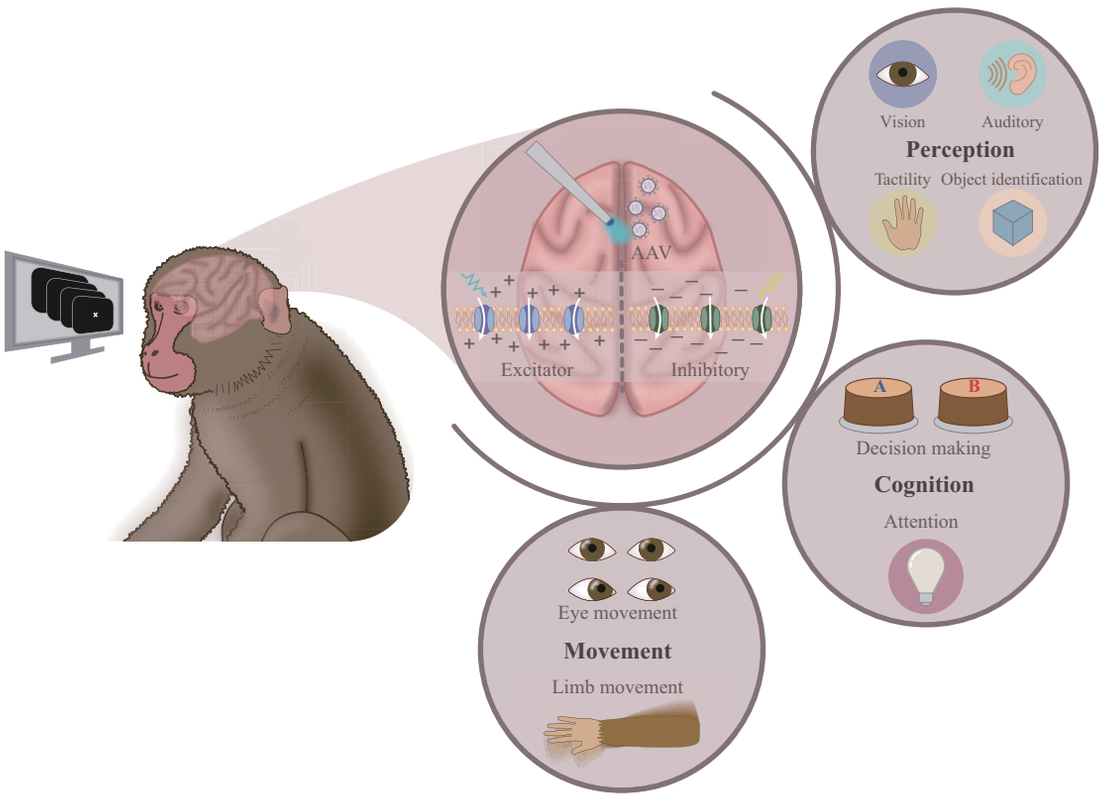

Fig. 1　Applications of optogenetics to modulate brain function and behavior in non−human primates

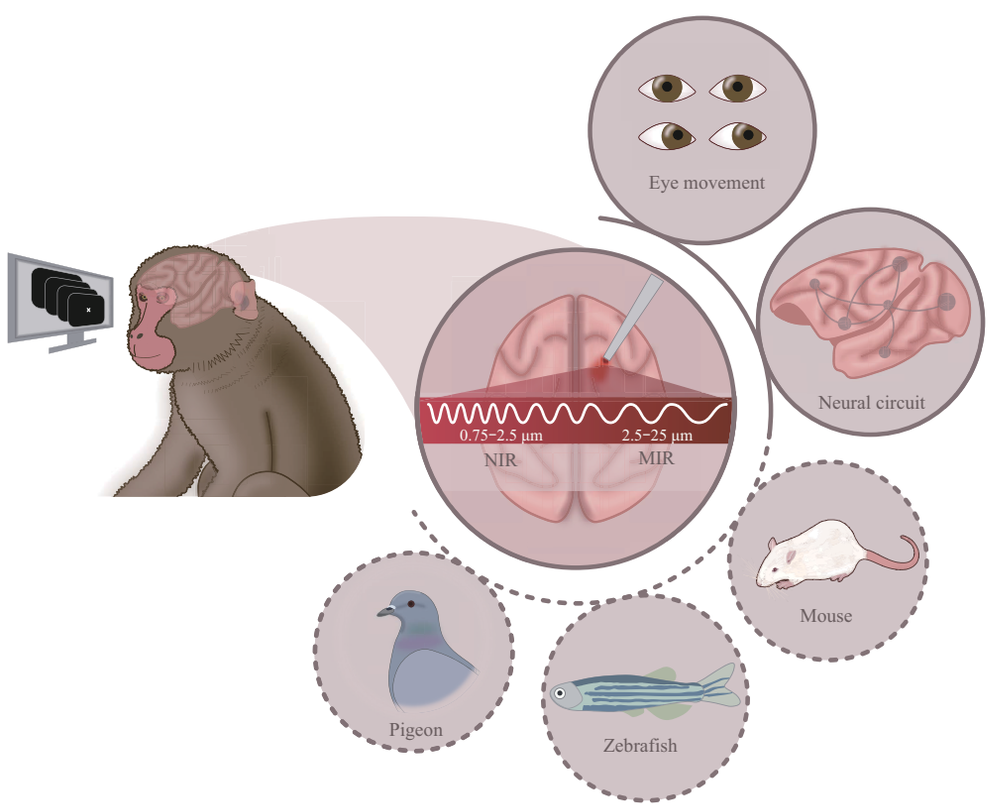

Fig. 2　Applications of infrared neurostimulations to modulate brain function and behavior

NIR, near-infrared stimulation; MIR, mid-infrared stimulation. Solid circles present research in non-human primates. Dashed circles present recent studies from other animal models.

non-invasively[12-13]. These techniques hold promise for applications where genetic modification may not be feasible or desirable, offering alternative approaches to study and potentially treat neurological conditions.

Non-human primates (NHPs) play a pivotal role in neuroscience research, providing valuable insights into the fundamental workings of the brain, and offering potential avenues for improving human health and well-being[14-15]. NHPs exhibit significant genetic, anatomical, and physiological similarities to humans, making their brain structures and functions more akin to humans than any other animal model. This similarity enables researchers to investigate complex cognitive functions, behaviors, and neurological disorders that are challenging to replicate in simpler organisms. In this review, we explore recent studies on the effects of optical-neural stimulation in non-human primates, examining its diverse applications, mechanisms, challenges, and future directions. By leveraging light to probe and modulate the intricate neural networks of the brain, optical-neural stimulation could drive forward the frontiers of neuroscience research and clinical innovation.

1 Optogenetics

Optogenetics combines optics with genetics, employing viral transfection and transgenic techniques to elicit the expression of light-sensitive proteins, or opsins, on the membranes of targeted cells[16]. Opsins respond to specific wavelengths of light (typically blue or yellow) by either opening or closing ion channels in the cell membrane. Upon activation by light, these channels can either depolarize (excite) or hyperpolarize (inhibit) neurons, enabling fine manipulation of neural activity with exceptional spatial and temporal precision. Commonly utilized photosensitizing proteins include channelrhodopsin-2 (ChR2) [17], archaorhopsins[18], halorhodopsins[19], and others[20-21].

1.1 Pioneer studies of optogenetics in monkeys

One of the earliest studies utilizing optogenetic neuromodulation in monkeys was conducted by Han *et al*.[22] in 2009. In this landmark study, researchers used adeno-associated virus (AAV) to express channel retinoid-2 in the frontal lobe of awake rhesus monkeys, and neural activity was excited by blue-light stimulation. Their results showed precise control of movement-related neural circuits using optical stimulation, marking a significant milestone in the application of optogenetics to non-human primates.

Over the next several years, researchers devoted their efforts to improving the efficiency of genetic tools for use in NHPs[23-28]. Optogenetic stimulation has been demonstrated to have a comparable effect to electrical stimulation, while offering greater specificity in targeting specific neuron types or regions. Optogenetic stimuli had a smaller effect on response latency and eye movement trajectories, suggesting that the perturbation of cortical activity induced by optogenetic stimuli was more localized[29]. Recently, sophisticated hardware devices were developed to facilitate optogenetics in NHPs, such as microelectrodes[30-31], transparent meningeal windows[32], advanced illuminator[33]. These studies have laid a solid foundation for the continued development and application of optogenetics in NHPs.

1.2 Research on the regulation of movements

1.2.1 Eye movements

During nature viewing, we shift our gaze to align objects of interest within the foveae. The eye movement system processes numerous visual information and is responsible for motor control, making it a crucial model for understanding the transition from sensation to movement[34]. Optogenetics stimulation in specific brain regions in the eye movement system produced different effects on eye movements. Saccade is an extensively researched mode of eye movements, its underpinning neural circuit contained several brain regions, including frontal eye field (FEF), supplementary eye field (SEF), caudate nucleus (CN), substantia nigra pars reticulata (SNr), and superior colliculus (SC). The FEF received projections from the SEF, and transmitted projections *via* the FEF-CN-SNr and the FEF-SC pathways[35].

Stimulating the FEF with optogenetic has the ability to modulate neural activities in the SC[36]. Optogenetic inhibition of SC shifted the endpoint position during monkeys visual-guided saccades. The saccadic eye movements exhibited reduced velocity along with delayed reaction time [37]. Alternatively, optogenetic activation of the FEF axon terminals within the SC resulted in shortened saccade latencies towards the response fields corresponding to the stimulation sites in the SC, while increased saccade

latencies away from the response fields[36, 38]. Through optogenetic inactivation of FEF neurons in monkey, researchers demonstrated that FEF activity during each epoch (the visual, delay and motor periods) was necessary for memory-guided saccade execution[33].

When ChR2 was expressed in the primary visual cortex (V1) to modulate neural activities, monkeys shifted their gaze towards the receptive fields of the ChR2-expressing neurons[39]. Using optogenetic stimulation to inhibit V1 GABAergic neurons, researchers found that monkeys were unable to reliably fixate on the target during a visually guided saccade task. Additionally, the monkeys failed to recognize the target in a contrast detection task, even when the target appeared inside the receptive fields of the stimulated neurons[40].

In a self-activated saccade task, optogenetics was employed to suppress cortical inputs from the SEF to the thalamus. The optical stimulation accurately caused temporal and spatial changes in thalamic neural activity that were related to the saccade task. This indicated that corticothalamic projections might play a role in shaping thalamic neural activity associated with goal-directed behavior. However, some thalamic neurons exhibited non-specific changes in their activity throughout the light stimulation period, which could potentially be attributed to the thermal effects of light exposure[41].

Purkinje cells are the main channels of information output in the cerebellar cortex, it plays an essential role in guiding saccades[42-43]. The optogenetic activation of Purkinje cells located in the contralateral oculomotor vermis (OMV) primarily impacted the deceleration phase of saccadic eye movements, eliciting a compensatory reacceleration response. In contrast, the activation of Purkinje cells within the ipsilateral OMV predominantly influenced the acceleration phase of saccadic eye movements, initiating a reacceleration of the eye movements, yet ultimately giving rise to hypermetria. These results suggested that the contralateral OMV played an important role in the active control of eye movements, while the ipsilateral OMV was involved in providing feedback control. These two mechanisms work together to regulate the accuracy and stability of eye movements[44].

1.2.2 Limb movements

Limb movements could be a straightforward and immediate readout of the effectiveness of optogenetic stimulation, eliminating the need for complex experimental paradigms in NHPs. However, previous studies faced obstacles in directly eliciting body movements in monkeys using optogenetics[25]. One study reported that optogenetic stimulation was capable of inducing sustained narrowband gamma local field potentials (LFPs) oscillations within the motor cortex of monkeys. Furthermore, the study indicated that autonomous motor behavior could override these optogenetic-induced gamma oscillations in regions where gamma oscillations propagated beyond the light stimulus area[45].

Significant advancements were achieved in 2019 and 2020, researchers successfully controlled limb movements using optogenetics in marmosets[46] and rhesus monkeys[47]. Optogenetic stimulation was applied in the primary motor cortex (M1) of rhesus monkeys and forelimb movement was effectively induced. Combining cerebellar optogenetic stimulation with 7T fMRI, researchers investigated the stimulation effects on brain networks. They observed strong activation at the stimulation site and the contralateral cerebellum. Additionally, cerebellar activity generated by stimulation within different M1 regions (distal forelimb, proximal forelimb, and hindlimb) displayed a somatosensory topological arrangement[48].

The success in regulating neural activity in motor control regions might be related to two main factors. First, the selection of appropriate genetic tools to ensure high transfection efficiency and expression levels of photosensitive proteins within the targeted brain region. Second, the use of optimal optical equipment and stimulation parameters to enable sufficient light stimulation. In short, both factors must ensure a sufficient number of activated neurons to elicit limb movements[46-48].

1.3 Research on the regulation of cognition

1.3.1 Decision making

Value-based decision making is a common type of decision making, where choices are frequently informed by learning from discrepancies between predicted and realized outcomes, namely, prediction errors[49]. It is believed that midbrain dopamine (DA) neurons encode these reward prediction errors[50-51], which are determined by subjective rather than objective values[52]. In 2016, researchers achieved specific expression of ChR2 in dopaminergic neurons

by injecting two different viral vectors into the midbrain of macaque monkeys. When two identical rewards were given, monkeys tended to choose the option that was accompanied by stimulation of dopaminergic neurons. This result provided further evidence for the role of dopaminergic neurons in reward learning[53]. A recent study in 2023 found that substantia nigra (SN) dopaminergic neurons in monkeys were significantly activated when environmental context was related to reward. Results of optogenetic stimulation of amygdala-SN pathway showed amygdala could induce tonic activity changes in DA neurons through GABAergic neurons in SN. This study suggested regulations of amygdala on DA neurons under reward related environment context[54].

Visual search for high-value objects contributes to more survival resources for animals in the natural environment. Previous studies have shown that this process is related to the connection from the tail of the caudate nucleus (CDt) to SC through SNr[55-56]. In 2020, Amita and colleagues[57] probed specific neural processes in this pathway by optogenetically stimulating CDt. They found that light activation at different projection sites of CDt elicited direct inhibition of caudal-dorsal-lateral SNr (cdlSNr) and indirect activation of SNr *via* the caudal-ventral part of the external globus pallidus (cvGPe). However, only the stimulation of CDt-cdlSNr pathway elicited SC activation, which in turn facilitated saccades to contralateral high-value objects. Addationally, value signals associated with high-value objects were transmitted through the inhibitory CDt-cdlSNr-SC pathway, facilitating saccades to high-value objects during visual search. Using a similar paradigm, with photomodulation of central nucleus of amygdala (CeA) and SNr, they additionally showed that the amygdala activates in response to viewing dangerous and/or resource-rich scenes, which in turn elicited inhibition of SNr and de-suppression of SC, thus facilitated saccades towards the contralateral side[58]. These results suggested that SNr might play a role in integrating information in value-based decision making.

Decision making always comes with risks, and changes in neural activity could affect decision making. When the middle temporal (MT) area was inhibited by light, monkeys' orientation choices deviated from the preferred orientation of neurons, and their confidence in decision making was also affected. Furthermore, the effect of inhibition of neural activity in MT on behavioral choices diminished over time, suggesting that compensatory changes might occurred in the readout downstream from MT neuronal activity[59]. In a recent study, optical modulation of the pathway from ventral tegmental area (VTA) to ventral Brodmann area 6 (area 6V) altered risk-dependent decision making in rhesus monkeys. Area 6V consists of ventral (6VV) and dorsal (6VD) parts. Activation of the VTA-6VV pathway enhanced the alpha-band response in area 6VV, which was associated with the high risk-high return (HH) option, and promoted the selection of the HH option. While activation of the VTA-6VD pathway had the opposite effect. These effects might be related to the short-term modulation of dopaminergic synapses, since most of the regulated neurons in the VTA are dopaminergic[60].

1.3.2 Attention

Visual attention enables monkeys to select from a vast array of information, prioritizing what is most pertinent to the current behavioral context[61]. Hüer *et al*. [62] explored the role of FEF in attentional modulation by optogenetically inhibiting FEF-MT pathway in rhesus monkeys. They found that suppression of FEF input reduced firing rates in MT neurons, resulting in enhancement of target stimuli and reduction of distractor suppression by approximately one-third. However, monkeys' behavior remained unaffected, which suggested that direct FEF input could impact attentional modulation component of MT neurons. The lack of behavioral change might be stem from the experimental design, which maximized neural effects on spatial attentional modulation but posed less challenge to behavior. Another study explored whether attention and working memory share the same neural mechanisms. This study found that optogenetic inhibition of bilateral posterior lateral prefrontal cortex (LPFC-p) led to a significant decrease in task performance during the test period (sustained feature attention). While during the delay period (working memory maintenance), inhibition of LPFC-p had no effect on task performance. These findings suggested that LPFC-p played a key role in feature attention but was not involved in working memory maintenance, indicating dissociable neural substrates for feature attention and working memory at neuronal and regional levels[63].

1.4 Research on the regulation of perception

1.4.1 Vision

A previous study has demonstrated that CamK-specific optogenetic activation of the lateral geniculate nucleus (LGN) konio neurons induced selective feedforward activation in the super-granular layers of V1, which was comparable with the approach of electrical microstimulation[64]. In a study exploring the integration of visual information using optogenetics, researchers found that if neural populations had proximal function, they would integrate their activity for visual perception, and if their function was distal, they would keep their activity independent. Optogenetic stimulation and visual stimuli were used to drive two neural populations with overlapped receptive field. Improvement in the detection of visual stimuli was observed only if optogenetic activated neurons that were tuned to visual stimuli. This study further found that noise correlation was closely linked with functionally proximal neural populations that were both optogenetically and visually activated[65].

Detection of visual targets in monkeys could be affected by optogenetic stimulation. Optogenetic stimulation of V1 evoked fMRI BOLD activation within localized and widespread visual cortical areas, including areas of V2/V3, V4, motion-sensitive area MT and FEF, along with optical illusions in monkeys[66]. When visual target was presented simultaneously with a low-power optical stimulus, detection threshold of visual target was significantly elevated. This might be related to sublinear interactions between optogenetic and visually-driven neural responses in V1. This effect was spatially selective, with the effect being maximal when visual target was located on the receptive field corresponding to the stimulated neuron[67].

Neurons in the inferotemporal (IT) cortex were responsible for object perception. Researchers conducted optogenetic stimulation in IT cortex to study the complexity of perceptual alterations caused by the stimulation in IT cortex. They presented monkeys with seed and perturbed images (created by a generative adversarial neural network (GAN)), IT cortex was optogenetically stimulated in 50% trials of presentation of perturbed image. Monkeys were required to detect and report whether trials contained brain stimulation or not. They found that the animal gave correct identification relied on the linkage between hallucinatory percepts and IT stimulation. This research was crucial to develop mechanistic theory of visual perception and visual prosthetic devices[68]. They also found that the detection of IT stimulation was determined by the visibility of presented images, which included saturation, spatial frequency, contrast and size of images. Higher visibility of the image was accompanied by better detection performance. This might be related to two factors, one was that the higher the visibility of the image, the more neural activity is elicited, and the other was that the higher the visibility of the image, the easier the visual distortions produced by the optical stimulus can be detected[69-70].

1.4.2 Auditory

Obara *et al*.[71] used optogenetics and calcium imaging in marmosets to probe neural activity under mismatched negative (MMN) paradigm. They found that the rostral para-genual (RPB) cortex provided prediction error signals feedback to the primary auditory (A1) cortex. When detecting an abnormal tone in the oddball paradigm, RPB neurons exhibited significant offset calcium response, whereas the response to the standard tone was strongly suppressed. Optogenetic inhibition of RPB activity prevented the A1 from detecting abnormal tones. Optogenetic activation of RPB nonlinearly enhanced the response of A1 to standard tones. Thus, the prediction error generated by RPB was critical for the automatic detection of unexpected stimuli in physiological auditory processing and might be analogous to the learning mechanism of backpropagation.

1.4.3 Tactility

Optogenetics could elicit a simulated sense of touch in the monkey brain. When excitatory nerves in the hand/finger region of the somatosensory cortex was optically stimulated, monkeys raised their hands to inspect their faces, rubbed their fingers/palms, or shook their hands. Researchers further trained monkeys with go/no-go task, optogenetic stimulation was delivered in 50% trials during the task and monkeys were required to detect the stimulation and quickly removed their hands. Their results showed that monkeys could reliably detect the optogenetic stimulation. Additionally, sensations elicited by optogenetics might not be the same as mechanical vibration, because monkeys still needed some time to

learn to recognize optogenetic stimuli when the mechanical vibration stimuli of the fingers were replaced by optogenetic stimuli[72].

1.4.4 Object identification

When optogenetic or pharmacologic inhibition was applied in subregions of IT cortex enriched with face (detector) neurons, deficits in the monkey's facial sex-recognition behavior in the contralateral visual field were observed. However, no significant behavioral changes were observed with inhibition applied on other IT cortical regions[73].

Optogenetic stimulation in neurons of the perirhinal cortex made monkeys tend to judge the presented objects as "seen before" (old objects), neurons highly responsive to old objects mainly located in the anterior region of the perirhinal cortex. This study proposed that there might be a threshold in the output of perirhinal cortex, which determined whether an object was recognized as old or not. Optogenetic stimulation enhanced the neurons' output in the perirhinal cortex, making it more likely to reach or exceed this threshold and thus enhancing the monkeys' tendency to judge as old objects[74].

2 Infrared neural stimulation

Infrared neural stimulation (INS) is an emerging technique in neuroscience that uses infrared light to modulate neural activity, it emits infrared light directly onto the target brain area *via* optical fibers[12-13,75]. This method offers several advantages over electrical stimulation and optogenetic stimulation. Infrared light can be precisely targeted to small areas, allowing for the stimulation of specific neurons or regions without affecting surrounding tissues. Unlike electrical stimulation, which requires direct contact with neural tissue through electrodes, infrared neurostimulation can be applied without physical contact, reducing the risk of tissue damage and inflammation. Unlike optogenetic stimulation, which needs genetic manipulation or viral transfection, infrared neurostimulation can be introduced directly by turning the light on. In addition, infrared stimulation also circumvents electrical artifacts that can interfere with electrophysiological recordings, providing clearer data for research.

Infrared rays used for neurostimulation can be categorized according to their wavelengths. These include near infrared (NIR, 0.75−2.5 μm), mid infrared (MIR, 2.5−25 μm) and far infrared (FIR, 25−1 000 μm) rays[76-80]. It is commonly believed that infrared neurostimulation primarily involves the process of heating neurons, resulting in changes to their activity through photothermal effects[81]. INS has the potential to produce alternations in neurons, including: (1) neural membrane capacitance[82], (2) the transient receptor potential vanilloid (TRPV) family[83-84], (3) the K^+ channels[77, 85], (4) the intracellular Ca^{2+} storage[86], and (5) concentration of Ca^{2+} and hydrodynamics in astrocytes[87], while the exact mechanisms of INS modulations remain uncertain.

2.1 Near−infrared stimulation

Previous studies have demonstrated that the near-infrared (NIR) stimulation has the ability to excite neural responses both *in vitro*[82, 84, 88-89] and *in vivo*[90-95]. Notably, there are other studies indicating that NIR has the ability to inhibit neural firing[96-99] .

While there have been successful applications of INS in humans[100], there is currently limited study on INS in non-human primates. A previous research utilized NIR within functional magnetic resonance imaging to map the mesoscale connectivity of the brain in monkeys[101]. A fiberoptic array capable of supporting multiple channels for INS[102], together with multimodality-compatible 1Tx/6Rx[103], has been developed for monkeys' research. In 2014, it was revealed for the first time that that infrared light can directly induce and modify function-specific responses in non-human primates. Researchers found that INS could stimulate brain responses that promote neural firing rates *in vivo*. Additionally, they observed that INS delivered through a fiber smaller than 100 μm could directly activate specific functional domains, known asocular dominance columns. The selections of the appropriate of fiber size (100, 200, or 400 μm) for stimulating distinct brain areas highlighted the importance of choosing the right fiber size to regulate the brain function[104].

2.2 Mid infrared stimulation

Mid-infrared (MIR) stimulation is an emerging area of interest in neuroscience, leveraging mid-infrared light with wavelengths ranging from 2.5 to 25 μm to modulate neural activity and investigate brain function. This technique, though less prevalent than near-infrared stimulation, offers unique

advantages and insights into neural modulation.

Recent evidence indicates that the application of MIR with a specific wavelength can have a substantial effect on the firing rates of neurons and on behavioral performances, in brain slices and other small animal models. MIR has the ability to cause non-thermal effects on ion channels, which leads to the regulation of action potentials by injecting currents in the *vitro* slice preparation[77]. MIR with a wavelength of 5.6 μm has the ability to enhance spontaneous neuronal activities[105] and sensory responses[106] in anesthetized rodents. Previous studies have demonstrated that MIR enhances the process of associative learning in mice[105], and controls startle responses in larval zebrafish[77] based on the strength of light powers. A recent study revealed that MIR with a wavelength of 8.6 μm can cause non-thermal and reversible modulations in both neural activity and behavior in awake-behaving pigeons[85]. The researchers found that MIR can cause both excitation and inhibition effects on neural firing in individual neurons, based on ongoing levels of neuronal responses. Additionally, MIR can exert gain regulations of sensorimotor behavior performances in a manner of the strength of visual inputs.

Mid-infrared light with specific wavelengths has the potential to modulate brain function and behavior through processes that differ from those of near-infrared light, including non-photothermal effects and gain modulations that are dependent on sensory inputs. Even today, there is still a deficiency in research of MIR modulation in non-human primates. Thus, MIR in primates is currently in its infancy. Its capacity to bidirectionally modulate neural activity offers valuable insights into brain function and holds significant potential for applications.

3 Limitations

Optical-neural stimulation has some limitations. Optogenetics and INS impose high demands on experimental equipment, requiring sophisticated instruments for both the generation and delivery of light, as well as advanced genetic tools[10, 13, 107]. Viral transfection is necessary in optogenetic stimulation, which carries potential immunologic risks[108]. NHP has far larger brain size compared with rodents, high viral load is required to achieve effective regulation and modulation[46-48]. In addition, a sufficient size and depth of photostimulation area may result in large neural damage in NHP’s brain, especially for deep brain regions[109]. Recently, researchers employed nanoparticles to convert near-infrared light into locally emitted blue light, enabling effective optogenetic modulation of deep brain regions[110-111]. At present, optical-neural stimulation is mainly used to probe the neural pathways downstream of the stimulation target. A preliminary research reported photosensitive protein transfections in monkeys using retroviral vectors[112], which was claimed as pathway selective optogenetic manipulations. Validating the transfection efficiency in monkeys is a challenge for photogenetic techniques. Although *in vivo* fluorescence imaging was developed to facilitate the validation of transfection efficiency, it was still limited to the superficial brain tissue[113]. Consequently, definitive histological validation of successful transfection becomes imperative, entailing substantial expenses in animal costs.

4 Conclusion

Optical-neural stimulations have dramatically advanced our understanding of the neural mechanisms underlying brain function and behavior in non-human primates. Optical-neural stimulations, in contrast to electrical or magnetic stimulations that would activate neuronal firing and deflect behaviour, can selectively regulate specific cell types through optogenetics, as well as selectively activate or inhibit neuronal responses according to the strength of sensory inputs through infrared stimulations. By enabling precise control over neural circuits and accurate temporal resolution, both optogenetics and infrared stimulations represent promising and versatile techniques to provide invaluable insights into the complex brain functions of primates, including motor control, associative learning, attention, and decision making.

Conversely, the investigation of optical-neural stimulation in non-human primates is still in the early stage and is encountering obstacles on its way. Significant ethical concerns are raised by the utilization of optogenetics in primates. It is imperative to maintain a balance between the scientific benefits and the ethical treatment of animals, ensuring that research is conducted with the standards of animal welfare. The thermal effects and irradiation sizes of infrared stimulations in primates raise safety and

efficacy concerns. In order to explore efficacy and safety of infrared stimulations, further technological and research advancements in primates are necessary. The continuous development and application of these technologies are expected to deepen our understanding of the mechanism of brain activity, and provide new breakthroughs and possibilities for the study of neuropsychiatric diseases, brain-computer interfaces, and other fields. New treatments for neurological disorders such as Parkinson's disease, epilepsy, and depression, may be facilitated by insights obtained from optical-neural stimulation studies in primates. With the progress of the field, optical-neural stimulation will undoubtedly continue to shine light on the intricate workings of the primate brain. Future research that continues to explore the mechanisms, efficacy, and safety, will drive innovations and expand its roles in modulating brain function and behavior.

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非人灵长类的光学神经调控：脑功能和行为的调节*

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摘要　光学神经调控技术，包括光遗传学和红外光神经刺激，可通过不同机制有效调节大脑功能和行为。这些前沿技术能够精确地操控大脑特定区域，选择性地调控特定神经元的活动，从而探究神经活动与行为之间的因果关系，更深入地理解大脑在复杂环境中的动态活动。非人灵长类动物作为研究这些复杂大脑功能的重要模型，起到了连接基础研究与临床应用的桥梁作用。自2009年科学家在猕猴上应用光遗传学进行光学神经调控以来，这些技术已在非人灵长类动物中得到了有效验证和应用。本文综述了近年来利用光遗传学和红外神经刺激技术调节非人灵长类动物大脑功能和行为的最新研究进展，并讨论了当前光学神经调控技术的应用现状，强调了其对于推动解析大脑功能的重要性。同时也探讨了光学神经调控技术在非人灵长类上的进一步研究和应用所面临的挑战。

关键词　光学神经调控，光遗传学，红外神经刺激，非人灵长类

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