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Role of optogenetics in pain management

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ABSTRACT

Optogenetics is a biological technique that involves the use of light to control genetically modified neurons to express the channels of light-sensitive Ions. Optogenetics can also be referred to as Optical monitoring of neuronal activity in non-neuronal cells, and control of biochemical pathways. Optogenetics is less invasive than electrical stimulation response time in optogenetics is comparatively faster than other treatments. Chronic pain affects one-third of the population, and current treatments cause limited relief and serious side effects. An alternative approach to pain reduction would be the direct modulation of somatosensory pathways using optogenetics. Optogenetic treatment can be a very effective way to relieve chronic pain while avoiding conventional pain medicine's side effects. The use of optogenetics in pain management has greatly accelerated over the last decade. This review discusses the versatility of different optogenetic tools and its effective applications in the field of medicine.

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INTRODUCTION

Optogenetics is a biological technique involving the use of light to manipulate genetically engineered neurons to transmit the channels of light-sensitive ions. Optogenetics can also be referred to as Optical monitoring of neuronal activity and the control of biochemical pathways in non-neuronal cells. Neural control is done with optogenetic actuators, e.g. channelrhodopsin, halorhodopsin, archaerhodopsin, however visual neuronal activity should be taken into consideration by using optogenetic sensors, e.g. calcium, vesicular discharge (Synaptophluorin), synapses or layer voltage. During the period from 2004 to 2009, Optogenetics was developed. Researchers worldwide then started using optogenetics, and thousands of scientific findings have been published.

Optogenetics technology works in several steps. First, special genes from single-celled organisms. For example, certain algae and bacteria are adapted for use as tools to study specific behaviours in animals. Such single genes, known as microbial opsins, generate proteins that function as light-sensitive ion channels or pumps, trigger or prevent the output of electric current in cells by controlling the passage of charged ions in response to light through the cell membrane. Second, advanced genetic tools are being used to target certain cells with opsin

genes. Targeting ensures that the products of the genes (opsin proteins) are formed only in different cell types. For example, cells in the brain that are not intended to receive opsin genes will not produce opsin proteins; therefore, the non-target brain cells will not be responsive to direct light. There were several microbial opsins found in nature, and some were genetically modified in the laboratory. Clinically inspired discoveries have also helped shed light on cellular activities associated with conditions like epilepsy, Parkinson's disease, Huntington's disease, stroke, chronic pain, obsessive-compulsive disease, drug addiction, depression, social dysfunction, and anxiety. Optogenetics is a very powerful neuroscience method. This approach works from the bioengineered light-sensitive proteins. Optionally it can stimulate or silence specific types of cells and neuronal circuits with millisecond temporal accuracy. This method allows for a more temporal resolution to analyze a particular neural circuit operation in various diseases. Newly found opsins are sensitive to higher wavelengths (Mahmoudi *et al.*, 2017). Cumulative research from both humans and animals indicates that anterior cingulate cortex (ACC) is critical for pain-related perception and therefore, a possible focus for pain-related therapy (Gu *et al.*, 2015). Patients with interstitial cystitis/bladder pain syndrome suffer from chronic pain that severely affects the quality of life. While the underlying pathophysiology is not well known, pain is temporarily relieved by suppression of sensory afferents to the bladder. Cellular approaches, combined with the latest optogenetics, enable the various techniques like activating inhibitor immunoglobulin concentration and goitre (Samuel and Devi, 2015). Latest innovations that provide optogenetic proteins that use light to problems include heart attack, stroke, asthma and immune deficiency on neuronal engraving techniques originating from stem cells, optogenetic regulation of physical function to enhance reinnervation and muscle power (Dave and Preetha, 2016; Abigail, 2019). Studies have shown that the autonomic hepatic nervous system plays a key role in controlling hepatic lipid homeostasis, inflammation and fibrosis. However, there is increasing evidence that Optogenetics, which has the ability to activate neurotrophic factors, may modulate both stages of non-alcoholic fatty hepatic disease (Choudhari and Jothipriya, 2016). Here, the study explores the possibility that optogenetic inhibition of nociceptive sensory afferents could be used to modulate bladder pain (Samineni, 2017).

Mechanism of Optogenetics

Genes for triggered ion channels were added to the cell population by a human genetically modified virus, in which cells produce these light-responsive channels based on the promoter area of the inserted DNA series (Zhang and Cui, 2015). Cells which contain a promoter that can recognise the promoter sequence which express these channels while cells that lack a promoter-specific for the sequence will not express. Once the genes have been inserted, it can take 1-2 weeks to be fully expressed. The studies showed that a fibre optic cable is surgically attached to the top of the skull or inserted near the brain area of interest depending on how close it is to the surface of the brain. The channels can now be powered by light from the optic cable and in effect, the neurons in which they are embedded. Channelrhodopsin gene can be used to excite the nerve when the light hits the nerve. Using halorhodopsin can inhibit the nerve when light hits the nerve (Hegemann and Möglich, 2011). Severe onychocryptosis can be successfully treated with optogenetics. The response of contingent optogenetics helps to discover the mechanisms that can influence onychocryptosis (Iyer *et al.*, 2019).

Challenges faced in Optogenetics

Optogenetics is less invasive than electrical stimulation. Response time in optogenetics is comparatively faster than other treatments. To activate or stop certain groups of neurons in the circuit requires a precise electrophysiology technique. Although optogenetics can achieve high spatial resolution and localisation on the order of certain stimulation, it does so at the expense of genetic modification of cells. Optogenetic methods may also be limited by the specificity of wavelengths and the difficulty of light guidance to specific neurons. There are several challenges faced by optogenetics to improve the necessary aspects like transfection method, improvement of optogenetic tools, improvement of appropriate light sources (Huang *et al.*, 2016). For different signs, such as skin diseases, cancer or neonatal jaundice, light-based therapies have been calculated (Timothy *et al.*, 2019). Advances in optogenetics also play a significant role in the diagnosis of jaundice (Harsha, 2015). Experts use optogenetics to activate people with physical deficiencies (David *et al.*, 2019).

Optogenetics in pain management

A third of the population is afflicted by chronic pain and existing therapies provide little relief and significant side effects. An alternative approach to pain reduction would be the direct modulation of somatosensory pathways using optogenetics (Beaudry, 2017). Optogenetics is an exciting possibility for future treatment of chronic pain,

but there are many questions that remain to be answered (Gu *et al.*, 2015). For example, it's unclear if patients can receive light medication for their entire lives or whether optogenetics after a few treatments might cure their chronic pain for good. Chronic pain is a clinically increasingly big problem and we rely only on opiates for many years. It's difficult to treat because of tolerance, which means that dosages need to be increased, leading to severe side effects. Optogenetic treatment may be a very effective way to alleviate chronic pain while reducing conventional pain medication side effects. The theory of optogenetic manipulation and its use in pain study using animal models, and the possibility of using optogenetic stimulation in the future treatment of migraine headache (Liu, 2019). Biological differences in sensory perception between human and model organisms may pose major obstacles in the treatment of chronic pain (Beaudry, 2017). Such obstacles may include functional differences in target receptor pharmacology and signalling or fundamental differences in neuronal physiology (Mickle and Gereau, 2018). Optogenetics affords the opportunity to non pharmacologically control neuronal activity in pain pathways. Implementation of optogenetics for pain control will require both a light activatable ion channel and a light source that is small and compatible with biological tissues (Vogt, 2015).

Improvement of Optogenetics

The optogenetic approach offers enormous potential for basic research for the future because high precision neural stimulation and attempting to silence can indeed be performed merely by light in a reversible manner. The benefits of light stimulation offer promising potential for gene therapy (Hegemann and Möglich, 2011). The optogenetic approach presents new possibilities for the study of neural networks. This can be accomplished by developing nerve cells cultivated on a micro or nanopatterned substrates. Cells can simply be stimulated or silenced by a light-beam with spatial precision. Electrode devices are needed only for the recording of the light-evoked signals. Immediately after having established that ChR2 can be used for remote neuron control, Several laboratories have begun projects to map the brain in living animals (Zhang, 2011).

Opttogenistry is useful not only in Migraine research and pain management but also in creating a potential approach for the treatment In the various fields of dentistry. Optogenetic methods were often used for mapping neural pathways and modern neuropharmacology but are seldom used in the field of acupuncture analgesia science. Optogenetics provides a high spatial resolution, as sensors can be combined with motifs and targeted to specific types of cells and subcellular heart domains. Wireless optogenetics guards against obesity by promoting thermogenesis of non-canonical fats (Baheerati and Devi, 2018). Thyroid functions tests are intended to separate hyperthyroidism and hypothyroidism from the euthyroid state. Optogenetic control of apoptosis in Xenopus laevis Embryos Targeted Tissues (Fathima and P, 2016).

Benefits of optogenetics

In the future, gene therapy with optogenetic tools appears possible besides the application of drugs. Deep Brain Stimulation (DBS) can treat Parkinson's disease (PD). Tests on inadequate photoreceptor mice have indicated that light-evoked possibilities in the visual cortex after the transduction of the ON-bipolar cells with ChR2 in the retina. This suggests that the animals' retina recovered photosensitivity, which is conveyed to the brain via the optic nerve. Trajectories of animal movement in the dark and in the light clearly have increased activity in the light as it is obtained for animals of wild type (Häusser, 2014). Habitual snoring, a prominent symptom of sleep-disordered breathing with Optogenetics, can be treated by controlling neuronal activity (Shruthi and Preetha, 2018).

Various optogenetic stimulus strategies have been studied for their effects on sleep design and overall sleep volumes (Ilankizhai and Devi, 2016). Sleep Apnea and sleep adenoids can be treated with optogenetic Auto-CPAP (Devi and Sethu, 2018). Optogenetics can treat acupuncture and narcotics pain medications (Swathy and Sethu, 2015). In the brainstem, there is neuronal regulation of the respiratory rhythms (Renuka and Sethu, 2015). The utilisation of optogenetics was principally inside the field of neuroscience, the method before long got pertinent to other sensitive tissue existing optogenetic instruments and approaches and examined their appropriateness. Only a small number of studies were included. There are many properties for optogenetics that are not included here. Thus optogenetics can be developed and utilized if it was clearly studied and understood.

CONCLUSION

The use of optogenetics in pain management has greatly accelerated over the last decade. The versatility of different optogenetic tools allows extensive modulation of the morphology, direction, duration and location of cellular membranes and its effective applications in the field of medicine and dentistry.

Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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REFERENCES

Abigail 2019. Evaluation of Muscular Endurance among Dentists. *Indian Journal of Public Health Research & Development*, 10(10):258–261.

Baheerati, M. M., Devi, R. G. 2018. Obesity in relation to Infertility. *Research Journal of Pharmacy and Technology*, 11(7):3183–3185.

Beaudry, H. 2017. Will optogenetics be used to treat chronic pain patients? *Pain Management*, 7(4):269–278.

Choudhari, S., Jothipriya, M. A. 2016. Non-alcoholic fatty liver disease. *Research Journal of Pharmacy and Technology*, 9(10):1782–1785.

Dave, P. H., Preetha 2016. Pathogenesis and Novel Drug for Treatment of Asthma-A Review. *Research Journal of Pharmacy and Technology*, 9(9):1519–1523.

David, *et al.* 2019. Physical Fitness among the Dental Physician, Dental Undergraduates and Postgraduates Students. *Indian Journal of Public Health Research & Development*, page 223.

Devi, R. G., Sethu, G. 2018. Evaluation Of Adenoids By Oronasal And Nasal Spirometry. *Asian Journal of Pharmaceutical and Clinical Research*, 11(10):272–274.

Fathima, F., P, P. 2016. Evaluation of Thyroid Function Test in Obese Patients. *Asian Journal of Pharmaceutical and Clinical Research*, 9(9):353–355.

Gu, L., *et al.* 2015. Pain inhibition by optogenetic activation of specific anterior cingulate cortical neurons. *PloS one*, 10(2):117746.

Harsha, L. 2015. Systemic Approach to Management of Neonatal Jaundice and Prevention of Kernicterus. *Research Journal of Pharmacy and Technology*, 8(8):1087–1092.

Häusser, M. 2014. Optogenetics: the age of light. *Nature Methods*, 11(10):1012–1014.

Hegemann, P., Möglich, A. 2011. Channelrhodopsin engineering and exploration of new optogenetic tools. *Nature Methods*, 8(1):39–42.

Huang, K., Dou, Q., Loh, X. J. 2016. Nanomaterial mediated optogenetics: opportunities and challenges. *RSC Advances*, 6(65):60896–60906.

Ilankizhai, R. J., Devi, R. G. 2016. Role of environmental factors on sleep patterns of different age groups. *Asian Journal of Pharmaceutical and Clinical Research*, 9(6):124–126.

Iyer, P. K., Devi, R. G., Priya, A. J. 2019. A Survey Study on Causes, Treatment and Prevention of Onychocryptosis. *Indian Journal of Public Health Research & Development*, 10(8):807.

Liu, S. 2019. Potential Application of Optogenetic Stimulation in the Treatment of Pain and Migraine Headache: A Perspective from Animal Studies. *Brain Sciences*, 9(2):26.

Mahmoudi, P., Veladi, H., Pakdel, F. G. 2017. Optogenetics, Tools and Applications in Neurobiology. *Journal of Medical Signals and Sensors*, 7(2):71–79.

Mickle, A. D., Gereau, R. W. 2018. A bright future? Optogenetics in the periphery for pain research and therapy. *Pain*, 159(9):65–73.

Renuka, S., Sethu, G. 2015. Regeneration after Myocardial Infarction. *Research Journal of Pharmacy and Technology*, 8(6):738–741.

Samineni, V. K. 2017. Optogenetic silencing of primary afferents reduces evoked and ongoing bladder pain. *The Preprint Server for Biology*.

Samuel, A. R., Devi, M. G. 2015. Geographical distribution and occurrence of Endemic Goitre. *Research Journal of Pharmacy and Technology*, 8(8):973–978.

Shruthi, M., Preetha, S. 2018. Effect of Simple Tongue Exercises in Habitual Snorers. *Research Journal of Pharmacy and Technology*, 11(8):3614–3616.

Swathy, S., Sethu, V. G. 2015. Acupuncture and lower back pain. *Research Journal of Pharmacy and Technology*, 8(8):991–993.

Timothy, C. N., Devi, R. G., Priya, A. J. 2019. Evaluation of Peak Expiratory Flow Rate (PEFR) in Pet Owners. *Indian Journal of Public Health Research and Development*, 10(8):803–806.

Vogt, C. C. 2015. Systemic gene transfer enables optogenetic pacing of mouse hearts. *Cardiovascular Research*, 106(2):338–343.

Zhang, F. 2011. The microbial opsin family of optogenetic tools. *Cell*, 147(7):1446–1457.

Zhang, K., Cui, B. 2015. Optogenetic control of intracellular signalling pathways. *Trends in Biotechnology*, 33(2):92–100.