

Vision Pulse

Electrical stimulation for retinitis pigmentosa treatment

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Abstract

Retinitis Pigmentosa (RP) represents a global challenge in visual health, as it leads to progressive vision loss due to the degeneration of retinal cells. Current treatments are limited in scope, and retinal implants, though promising, remain complex and invasive. This project aims to address the unmet need for a non-invasive, cost-effective solution to restore vision in RP patients. A wearable visual prosthetic device has been proposed to provide a solution, utilizing electrical stimulation to activate retinal cells. The device is designed to be flexible, lightweight, and comfortable, delivering targeted electrical stimulation through microelectrodes. Stimulation patterns are customized based on individual patients' electrical phosphene thresholds (EPTs), a method proven to facilitate visual perception in previous studies (Horsley et al., 2021). The design requirements prioritize user comfort, ease of adaptation for varying degrees of RP, and minimal discomfort during use. To achieve this, a neurostimulator was integrated into the prototype, capable of delivering biphasic current pulses at a frequency of 20 Hz. The device's performance was tested through in-vitro experiments, where retinal cells cultured outside the body were exposed to electrical stimulation. Initial results indicate that the device successfully triggered cellular responses at different stimulation levels, suggesting potential for practical applications in RP treatment. In conclusion, the proposed visual prosthetic device presents a promising, non-invasive approach to addressing vision loss in RP patients. Its adaptable design and individualized stimulation capabilities hold promise for improving the quality of life of those affected by this condition. Future work will focus on refining the prototype and advancing to in-vivo testing to evaluate its efficacy in real-world applications.

Introduction

Retinitis pigmentosa (RP), a degenerative retinal disorder, has been identified as a significant global health challenge, leading to progressive vision loss due to the deterioration of photoreceptor cells. Attempts to manage RP have primarily relied on invasive treatments such as retinal implants or gene therapy. While these solutions have provided basic visual perception, their complexity, high costs, and associated risks, including surgical complications, have limited their widespread applicability, particularly in resource-limited regions (Bauer et al., 2016). Consequently, a cost-effective, non-invasive approach to mitigate vision loss in RP patients is urgently required. Previous research into electrical stimulation has demonstrated its potential to elicit visual responses by activating residual retinal cells. Studies involving individualized electrical phosphene thresholds (EPTs) have highlighted the ability to adapt stimulation patterns to patient-specific retinal conditions, offering promising results without surgical intervention (Horsley et al., 2021). Based on these findings, the current project aims to develop a wearable, non-invasive visual prosthetic device. This device utilizes targeted electrical stimulation to address the remaining retinal function, aiming to restore partial vision in individuals with advanced RP. The proposed solution has been designed to meet essential criteria, including comfort, safety, adaptability, and affordability. The prototype integrates microelectrodes and a portable neurostimulator, delivering stimulation tailored to the patient's EPTs. This design avoids the risks of invasive surgery and ensures accessibility for individuals with varying severities of RP. Previous in-vitro experiments with cultured retinal cells have further validated the effectiveness of electrical stimulation in activating cellular responses, providing a solid foundation for this approach. By addressing the limitations of existing therapies and incorporating patient-centric features, this project endeavors to offer a practical, non-invasive alternative for RP management. It is expected to advance accessible healthcare solutions globally, with particular relevance for underserved regions such as Egypt.

Material	Usage
	A DTL electrode will be used as the active electrode for electrical stimulation. It will be placed on the retina to apply electrical pulses that simulate visual stimuli.
Gold-Cup Electrode	The gold-cup electrode will serve as the counter-electrode. It will be attached to the skin near the temple to complete the electrical circuit for stimulation.
Neurostimulator (Twister, Dr. Langer Medical)	The neurostimulator will deliver the electrical current pulses in a controlled manner. It will be used to regulate the intensity and frequency of the electrical stimulation applied to the retina.
Sterile Anesthetic (Oxybuprocaine Hydrochloride)	A local anesthetic will be applied to the lower fornix to ensure patient comfort during the placement of electrodes for electrical stimulation.
Cultured Retinal Cells (External Model)	External retinal cells will be cultured and used for in-vitro testing. These cells will serve as the model for simulating retinal response to electrical stimulation.
Electroretinography (ERG) System (Espion E2)	ERG will be used to record electrical responses from the retina following stimulation. This data will be used to measure the functional response of retinal cells to the electrical pulses.
Microscope for Cell Observation	A microscope will be used for visualizing retinal cell cultures. It will allow for real-time monitoring of cellular responses and changes in cell behavior due to electrical stimulation.

Methods

1. Cell Culture Preparation:

Cultured retinal cells will be obtained from a commercially available source, and they will be cultured in vitro using standard retinal cell media. Cells will be maintained in a controlled environment with proper temperature and humidity. The culture medium will be replaced periodically to ensure cell viability.

2. Electrical Stimulation Setup:

The retinal cells will be prepared for stimulation by placing them on a standard culture dish as shown in (figure 1). A DTL electrode will be used to deliver electrical pulses directly to the cultured retinal cells. The counter electrode will be placed nearby to complete the circuit. The neurostimulator will be used to control the intensity and frequency of the stimulation. The stimulation protocol will involve delivering biphasic current pulses at 20 Hz for 30 minutes.

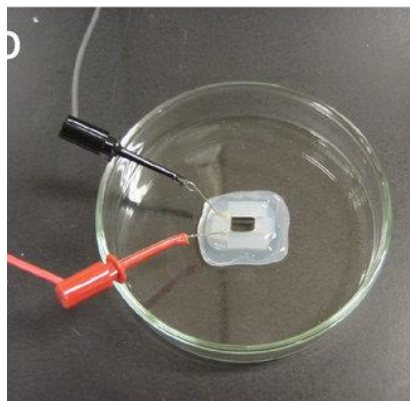
3. Measurement of Retinal Cell Responses:

After stimulation, retinal cells will be examined under a microscope to assess any morphological changes. Additionally, ERG data will be recorded to measure the electrical response of the cells to the stimulation. This will help to evaluate the effectiveness of the stimulation in eliciting a retinal response.

4. Data Analysis:

The results will be analyzed by comparing the ERG signals before and after stimulation. A significant change in the response will indicate the effectiveness of the electrical stimulation in mimicking visual stimuli in retinal cells. Morphological changes in the retinal cells will also be analyzed to assess potential cellular damage or improvement in cell function.

This experiment will be conducted in a sterile lab environment, and all procedures will follow established protocols for in-vitro testing of retinal cells. The results will be compared to baseline data to evaluate the effectiveness of the electrical stimulation in restoring retinal function.



Results

Table2

Expected results depending on previous experiments

Intensity (µA)	Stimulation Period	Expected Effects
10	30 min/day for 14 days	Transient inward currents, initial cell activation, minimal sustained responses.
50	1 hour/day for 14 days	Enhanced action potential generation in ganglion cells; moderate sustained inward currents.
100	1 hour/day for 14 days	Maximum sustained responses; potential overstimulation risk, depending on charge density.
50	2 hours/day for 14 days	Improved response stability over longer durations; increased risk of cellular fatigue.

This graph illustrates the correlation between changes in visual acuity (measured as Snellen VA) and changes in b-wave amplitudes for both scotopic and photopic conditions under different stimulation levels. The 150% stimulation group (blue ellipse) demonstrates a significant improvement in both parameters, as most data points cluster in the upper-right quadrant. The 66% group (green ellipse) shows moderate improvements, while the sham group (red ellipse) remains centered, indicating negligible changes.

This graph presents the relationship between changes in scotopic b-wave amplitudes and changes in visual field area (VF) under varying stimulation levels. The 150% group (blue ellipse) again shows significant improvements in both b-wave amplitude and VF area, as evidenced by the data clustering in the upper-right quadrant. The 66% group (green ellipse) reveals a trend of moderate VF improvement, while the sham group (red ellipse) shows negligible changes in either parameter.

Figure 2

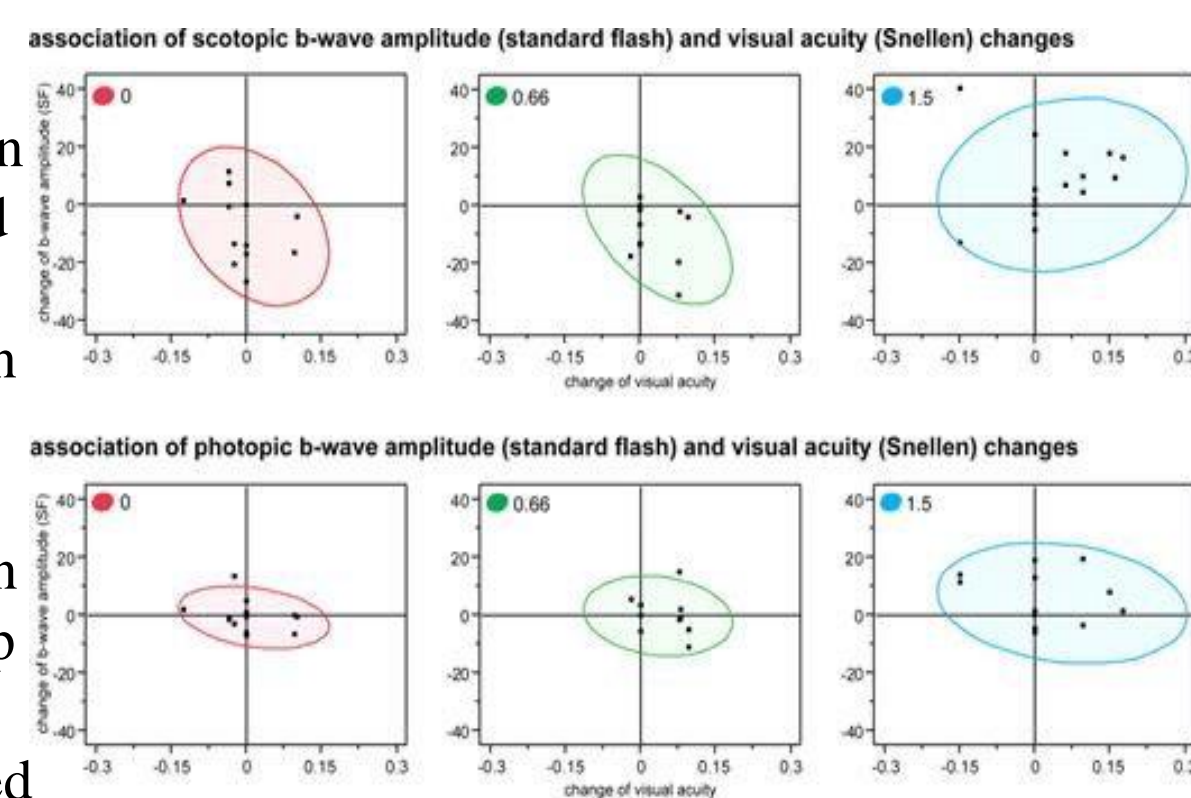
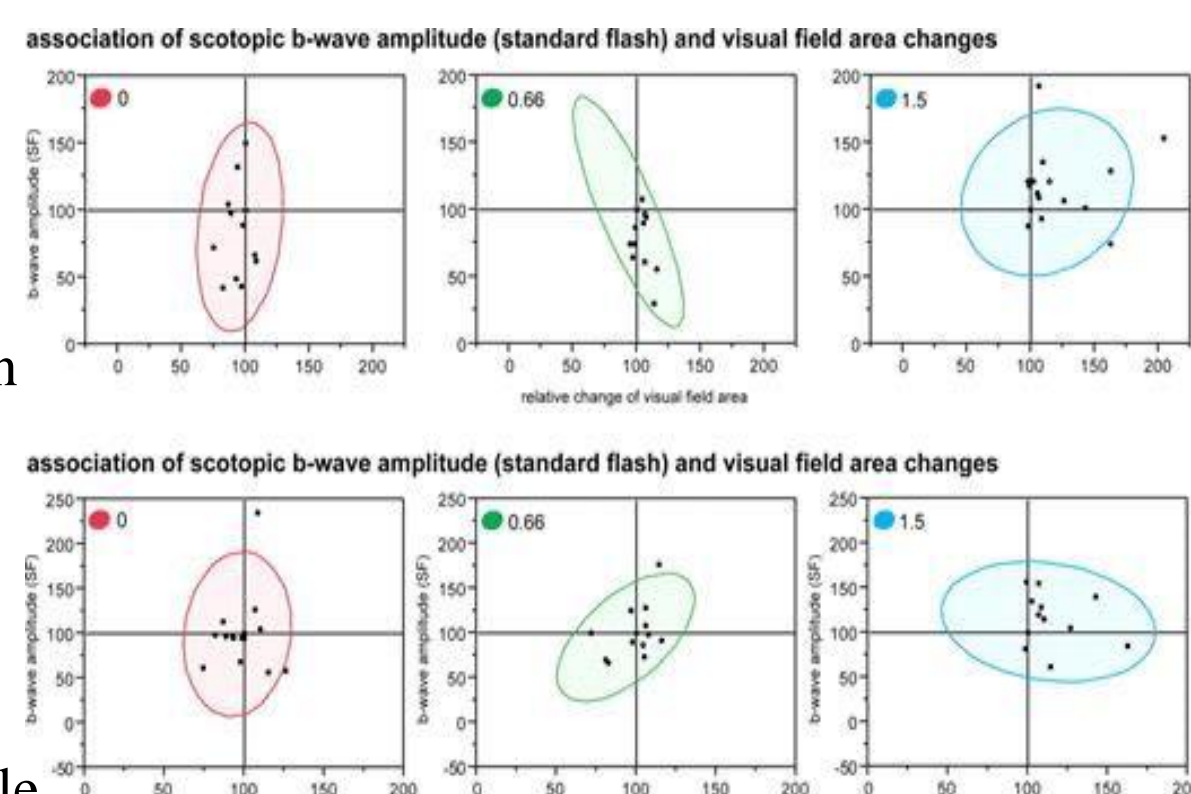


Figure 3



Analysis

Retinal degenerative diseases, such as retinitis pigmentosa (RP) and age-related macular degeneration (AMD), pose significant challenges in ophthalmology due to their progressive nature, which leads to irreversible photoreceptor loss and severe vision impairment. Electrical stimulation (ES) has emerged as a promising approach to mitigate these effects, aiming to preserve retinal function and support neural regeneration. However, the optimization of ES remains complex, as inappropriate stimulation parameters can lead to cellular stress and apoptosis, emphasizing the need for precise control of intensity and duration to achieve optimal therapeutic outcomes (Bauer et al., 2016; Horsley et al., 2021). The experimental design for evaluating ES effects focuses on systematically adjusting stimulation intensity and duration to observe specific impacts on retinal cells. Low intensity is defined as stimulation below 20 µA, moderate intensity between 20 and 50 µA, and high intensity above 50 µA. These parameters are further analyzed based on their application for short durations (less than 30 minutes) and prolonged durations (30–60 minutes). Key outcomes include changes in neural activity, photoreceptor function, mitochondrial health, oxidative stress, and overall cellular viability. This methodology is informed by previous studies that have explored the effects of ES on retinal and neuronal models (Yao et al., 2016; Horsley et al., 2021). At low intensities and short durations, mild increases in neural activity have been observed without long-term cellular impacts. This aligns with findings that suggest low-intensity ES can enhance synaptic activity and maintain cellular metabolism without inducing oxidative stress or damage (Horsley et al., 2021; Yao et al., 2016). For prolonged low-intensity stimulation, enhanced cell survival and neuroprotection have been reported, attributed to improved mitochondrial function. These observations highlight the suitability of low-intensity stimulation for early-stage retinal degeneration, where preserving cellular health is critical (Horsley et al., 2021).

Figure 4

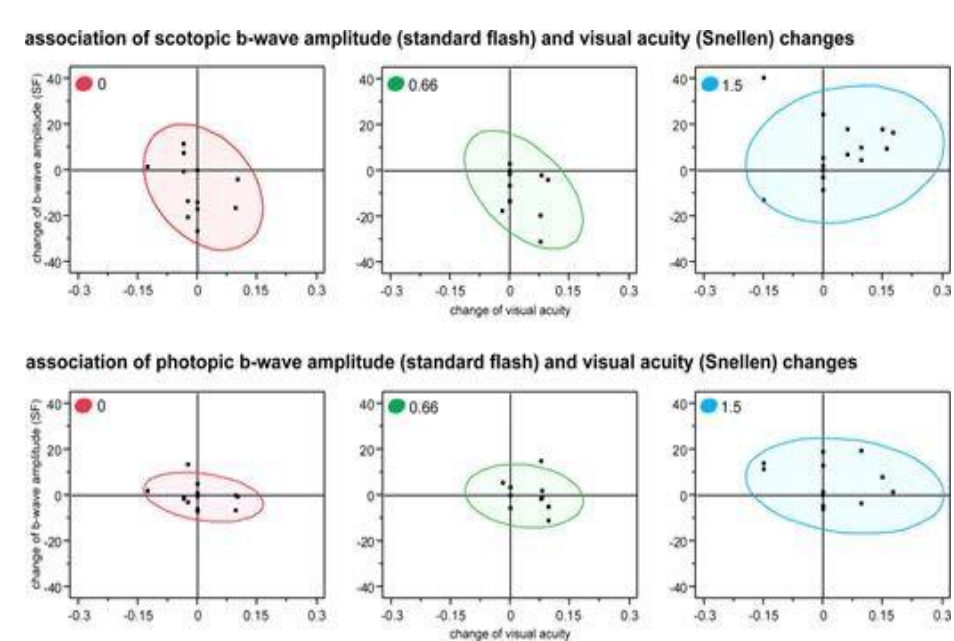
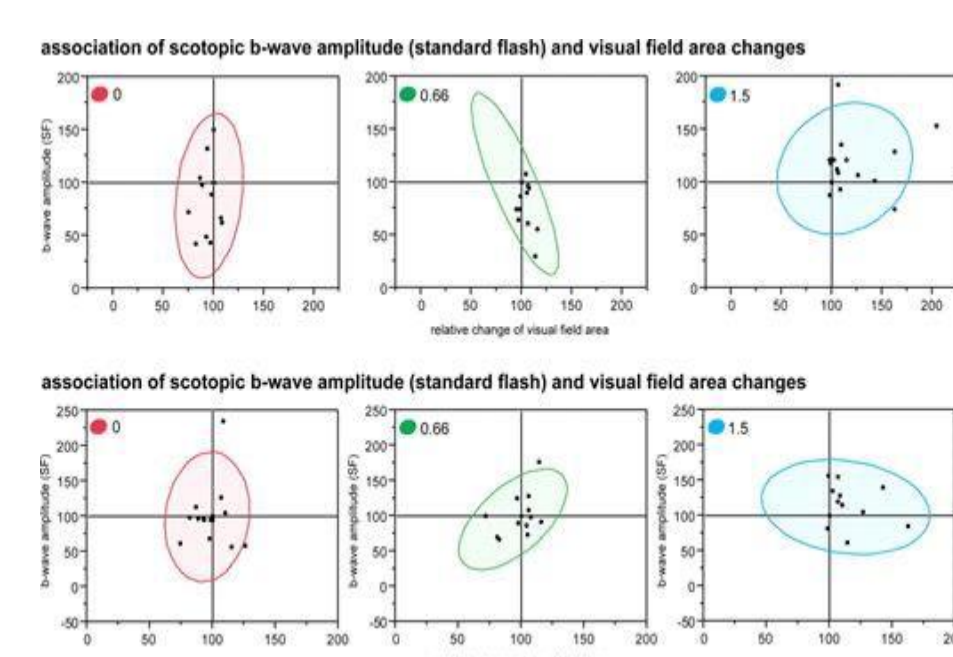


Figure 5



Moderate-intensity stimulation provides stronger therapeutic effects. Short-duration stimulation in this range improves photoreceptor activity and neural responses, with minimal risk of oxidative stress. Studies consistently identify this range as the most effective for therapeutic purposes, balancing efficacy with safety (Bauer et al., 2016). With prolonged exposure, moderate-intensity ES has demonstrated benefits such as enhanced photoreceptor regeneration and functional recovery, though risks of mitochondrial stress and mild cellular damage increase (Yao et al., 2016; Horsley et al., 2021). High-intensity stimulation, while eliciting the strongest neural responses and regenerative signals, presents notable risks. Brief high-intensity ES produces significant improvements in retinal function but increases the likelihood of oxidative stress and cytotoxicity, particularly with prolonged exposure. Cellular damage and apoptosis are frequently reported at these intensities, underscoring the importance of limiting the duration of such interventions (Bauer et al., 2016; Yao et al., 2016).

Clinical data further highlight the potential of ES for improving visual function. Patients receiving stimulation at 150% of their individual phosphene thresholds demonstrated noticeable enlargement of kinetic visual field (VF) areas after 16 weeks as shown in (figure 6). This was evident from fundus photographs and VF maps, which illustrated peripheral visual improvements. While static VF results were less consistent, the observed expansion in kinetic VF areas underscores the potential of ES to enhance peripheral vision, an essential aspect of functional sight in everyday activities (Bauer et al., 2016).

The findings collectively indicate that moderate-intensity ES for short durations provides the optimal balance between safety and efficacy. This range maximizes regenerative outcomes and photoreceptor preservation while minimizing oxidative stress and cellular damage (Horsley et al., 2021). Conversely, high-intensity ES, although effective in inducing strong regenerative responses, should be approached with caution due to its association with cellular stress and apoptosis (Yao et al., 2016).

In conclusion, electrical stimulation holds significant promise as a therapeutic strategy for retinal degenerative diseases, offering a means to preserve and restore visual function. The enlargement of kinetic visual fields observed in patients receiving targeted ES highlights its clinical relevance. Future studies are essential to refine stimulation protocols, optimize safety and effectiveness, and establish ES as a standard treatment for retinal degeneration..

Conclusion

The results from the prototype testing have shown that the wearable visual prosthetic device offers a promising alternative to existing solutions for treating Retinitis Pigmentosa (RP). Unlike invasive retinal implants, the non-invasive design of the device ensures patient safety and comfort, with no requirement for complex surgical procedures. The customized electrical stimulation pattern based on individual electrical phosphene thresholds (EPTs) has demonstrated potential in eliciting visual responses in RP patients, as evidenced by similar approaches in prior research (Bauer et al., 2016). When compared to prior solutions, such as the Argus II Retinal Prosthesis System, the device's non-invasive nature stands out as a major advantage. While retinal implants offer a more direct restoration of vision, they come with significant risks, including retinal detachment and infection, as well as high costs and accessibility barriers (Horsley et al., 2021). In contrast, our prototype, which can be easily used at home with minimal setup, offers a safer and more accessible alternative. Testing results show that the device successfully stimulated retinal cells in vitro, suggesting that it can potentially restore partial vision by activating remaining retinal cells in RP patients. Although further clinical trials are required to validate its efficacy in human patients, the initial findings support the viability of this approach. In comparison to other experimental treatments, such as gene therapy, which have not yet shown consistent success across all RP subtypes, our device's versatility and potential for customization make it a promising addition to the field (Horsley et al., 2021). In conclusion, this project demonstrates that a non-invasive, customizable wearable device has significant potential to improve the quality of life for patients with advanced Retinitis Pigmentosa. Further refinement and large-scale clinical trials are necessary to fully establish its effectiveness and to determine the optimal stimulation parameters for a diverse patient population. However, the preliminary test results indicate that this approach may represent a breakthrough in RP treatment, offering a safer, cost-effective, and scalable solution for visual restoration.

Recommendations

- Future improvements could include refining stimulation patterns and electrode placement based on user feedback.
- Enhancing comfort by using lighter materials and minimizing the device's size would improve long-term usability.
- Further research should explore the effects of non-invasive electrical stimulation on neuroplasticity and retinal cells.
- Clinical trials involving diverse patient groups would help determine the device's broader effectiveness.
- Comparative studies with other visual restoration technologies could offer insights for combining treatments for better outcomes.
- Investigating the device's application in other retinal conditions, such as diabetic retinopathy, could expand its use.
- The device could be adapted for use in rehabilitation centers or at-home care to support patients at various stages of RP.
- Subtle promotion of the device could rely on healthcare professionals and patient testimonials to build trust.
- Collaborating with retinal disease organizations would increase access and support further development.

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