

# Transient Vision Restoration Training Using a Unique Virtual Reality Platform in Glaucoma

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## Research article

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# Abstract

## Background

To evaluate the efficacy of transient vision restoration training (tVRT) with an augmented virtual reality platform in glaucoma patients.

## Design:

A self-control, prospective study.

## Methods

This study recruited subjects with glaucoma. All participants were treated with tVRT which based on an augmented virtual reality platform for 20 minutes. The intraocular pressure (IOP), the best-corrected visual acuity (BCVA), global mean defect (MD) values, global indices mean sensitivity (MS) were evaluated and compared before and after treatment.

## Results

While the IOP and BCVA after tVRT did not change obviously compared to baseline. However, the global MD significantly reduced, consistently the global MS changed better in the treated patients.

## Conclusions

The glaucomatous optic neuropathy remains potentially neuroplasticity. And the training based on an augmented virtual reality platform may have a positive impact on vision restoration.

## Background

Glaucoma is the leading cause of irreversible blindness worldwide. In 2013, there were 64.3 million people with glaucoma among aged 40–80 years worldwide, which will reach 76 million by 2020 and 111.8 million by 2040[1–3], of whom a sixth dwell in China[4]. Glaucoma is characterized by retinal ganglion cells (RGCs) damage, optic atrophy and results in visual field (VF) defects.

Neuron damage was long considered as permanent and unchangeable, especially in the visual system as its retinotopic organization and highly specific cortical organization. However, a series of experimental[5–8] and clinical evidence demonstrated neuroplasticity or neuron restoration, even in adult visual system [9–12].

Some efforts had been made to restore the residual vision for optic neuritis, ischemic neuropathy, glaucoma, photoreceptor degeneration, trauma and other neuropathies[10, 13–16]. Besides, very few reports have been published that visual restoration in patients with glaucoma may be achieved using the repetitive transorbital alternating current stimulation (rtACS)[17–19]. For interested in optic neuroplasticity, further prospective or clinical study is needed.

In this study, glaucoma patients with visual field defects were trained with tVRT which is based on an augmented virtual reality platform for 20minutes, and the efficacy was then estimated.

## Methods

### Participant recruitment

This is a prospective study. The Medical Ethics Committee of Beijing Shijitan Hospital approved the prospective study protocol. Informed consent was obtained from all patients and from guardians for minor patients prior to enrollment. The study was approved and monitored by clinical practice guideline, adhered to the Declaration of Helsinki, and registered in the Chinese Clinical Trial Registry (registration number: ChiCTR1900027909).

Identified diagnosed glaucoma participants underwent a full ophthalmologic examination including BCVA, the anterior segment examination by a slit lamp, IOP by Canon TX-10 noncontact tonometer, fundus image, optical coherence tomography (OCT) image of optic nerve head (ONH) and VF test. Besides, clinical and medical history were also recorded.

The inclusion criteria included that the patients with stable glaucoma without monocular or binocular blindness, and had sufficient experience in Octopus 101 perimeter (Haag-Steit AG, Koeniz-Berne, Switzerland) standard automated perimetry to minimize the learning effect. The damage of ONH and retinal nerve fiber layer defect (RNFLD) were confirmed by both OCT and fundus image. The VF tests were classified as reliable if the false-positive response rate was <15%, and the false-negative response was <25%[20].

The exclusion criteria were defined with the history of any other optic neuropathy, any retinal or macular disease, optic media opacities, spherical refractive error greater than  $\pm 6$  diopters, and astigmatism greater than  $\pm 3$  diopters[20]. Presence of any chronic-degenerative disease of the nervous system, motor disturbance, neglect, nystagmus or other forms of impairments to fixate, amblyopia, photosensitivity, history of trauma, any other ocular disease or ocular surgery at least one year prior to recruitment or expected ocular surgery within the six months after study entry.

### Procedure

The training device had been mentioned in the previous study, which included: a computer with a polarized 3 dimension (3D) monitor, and 3D polarized glass[21]. Visual field, IOP, and fundus images were examined at baseline and 20 min after transient vision restoration training on the same day.

## Visual field measurements

To determine the visual field changes between pre- and after-tVRT. The Octopus 101 perimeter was used for all tests with the EyeSuite software (Haag-Streit AG, Koeniz-Berne, Switzerland). The G2 test of the central 30° VF was tested with normal strategy. Ametropia was corrected, and the right eye was tested first in all cases.

All participants were practically well in automated perimetry. We estimated visual function through VF which measured in dB.

## Statistical analysis

Statistical analysis was performed using SPSS 21.0. Normal distribution was tested using the one-sample Kolmogorov-Smirnov test. Normally distributed parameters were analyzed using paired-sample t-Test. Nonparametric parameters were analyzed using the rank-sum test for the paired-samples t-test.  $P \leq 0.05$  was considered as statistically significant.

## Results

Thirteen men and women (13 right eyes) aged 15–71 were enrolled in this study. The IOP was  $14.2 \pm 1.3$  mmHg and  $14.6 \pm 1.4$  mmHg at pre- and post- tVRT respectively without significant difference, and the BCVA didn't change obviously either. During the training period, no subjects complained of discomfort.

The distribution of the patients' global pre- and post-training MS, MD are presented in Table 1.

Table 1  
The distribution of MD and MS data

	pre-MS	post-MS	pre-MD	post-MD
Subject1	25.9	26.3	3.7	3.3
Subject2	18	21	9.8	6.8
Subject3	6.9	6.9	21	20.9
Subject4	17.8	18.3	9.8	9.3
Subject5	23.8	24.2	2.5	2.2
Subject6	24.9	24.2	2	2.8
Subject7	2.8	23	6.1	4
Subject8	15.4	16.5	11.6	10.5
Subject9	19.5	17.8	7.4	9.2
Subject10	25.2	25	3.9	4.1
Subject11	14.6	15.5	12.2	11.3
Subject12	9.9	11.8	18.7	16.8
Subject13	24.4	25.2	2.8	2

### Changes in MD

The median change in MD was  $-0.6$  dB (IQR  $-0.9$  to  $-0.3$ ; Fig. 2). The MD decreased significantly, which consistent with the MS elevation (Fig. 1).

### Global MS and MD changes

The median global MS was  $17.5$  dB (IQR  $11.1$  to  $29.8$ ) and  $19.8$  dB (IQR  $15.1$  to  $24.3$ ) at pre- and post-VRT respectively, which increased significantly. The median global MD was  $8.0$  dB (IQR  $3.0$  to  $12.1$ ) and  $19.8$  dB (IQR  $3.0$  to  $11.1$ ) at pre- and post-VRT respectively, which decreased significantly (Fig. 2).

## Discussion

We enrolled 13 individuals in this study. The results showed that there were no subjects with any complaint of discomfort. The IOP and BCVA were not obviously changed. The global MD was improved significantly, consistently the global MS increased after training. And we may conclude that optic nerve damage due to glaucoma had potential plasticity.

Serious optic nerve damage, which resulting from optic neuritis, ischemic neuropathy, glaucoma, photoreceptor degeneration, and trauma, was generally considered irreversible. In the latest decades,

more and more studies reported that the nervous system even mature mammalian showed astonishing adaptability, which was known as “neuroplasticity” or “neurological rehabilitation”[11, 12]. In the 1980s, a famous deafferentation study introduced that topographic cortical representations are maintained dynamically throughout life in primates[8]. Lately, spinal cord injury patients with disabilities standing up were reported by several different research teams[22–24].

Traditionally, for glaucoma patients, the major choice was to control IOP including medical or surgical treatments. Besides, there have been auxiliary treatments such as eye yoga exercise which had been mentioned with limited outcomes recently[14]. Based on the new understanding of neural plasticity, we found that after the vision restoration training period, the global MD improved significantly, and the global MS also changed better in this study. It was supported by the report that primary open angle glaucoma (POAG) with visual field defects was improved by systematic vision stimulation, even in the training-free intervals[18]. Further research also demonstrated that significant detection accuracy gains, faster reaction time, health-related quality-of-life mental health domain increased in glaucoma patients[19].

Except the glaucoma-related visual damage, neuropathy induced by other diseases also can be improved. Patients with retro-chiasmatic injuries underwent visual rehabilitation training, the visual reaction time was significantly shortened, and visual improvement was significant[25, 26]. Sabel and his colleagues reported a 27 years old patient with massive facial injury and brain damage. Only 10% visual field index (VFI) left in his left eye, after neurological rehabilitation training, VFI finally improved to 74%[16].

An obvious question was, why mature neurons remain had the ability of neuroplasticity? The mechanism remained elusive. In glaucoma patients, the retinal region corresponding to the scotoma of the visual field, viable RGCs exist with irregular or swollen cell bodies, smaller and shorter dendritic processes[27], which may retain their dendritic plasticity[28]. In the optic nerve crush model, 70 ~ 90% of RGCs underwent degenerative changes, few cells retained, however approximately 80 ~ 90% of vision function restored within 2 ~ 3weeks[29]. And further research demonstrated these surviving cell bodies moderately enlarged which may undergo neural remodeling[29, 30]. Besides, Sabel had proposed the “residual vision activation theory” which meant that in the damaged visual pathway, in addition to normal and dead RGCs there were some “dormant” nonfunctional living cells[31]. These dying cells unable to produce clinically visible functional activity, may have the ability to modulate peripheral sensory-motor neural networks, providing an anatomical basis for functional remodeling[24]. In this study, the global MD improved significantly, and the global MS also changed better, mainly because of the visual stimulation located at the visual field damage or its border region[17–19].

After the tVRT, none of these participants complained of uncomfortable during the training period. Sabel and his colleague applied the rtACS to restore residual vision[19]. In their study, some adverse events such as transient vertigo, mild headache, cutaneous sensation, back pain and stiff neck occurred, and a few participants dropped out of the study[9]. Besides, trans-corneal electrical stimulation was also used in patients with ischemic optic neuropathy[10], but it was mostly preferred in animal experiments[32–34]. In this study, the subjects were trained with a computer terminal based on an augmented virtual reality

platform without any invasive stimulation, which was much safer than rtACS or other trans-corneal electrical stimulation. And it had been successfully displayed in children with intermittent exotropia and normal population without eye diseases[35, 36].

## Conclusion

In summary, we showed a very interesting and amazing result that the computer terminal based on an augmented virtual reality platform was a safe and effective vision restoration training, which may provide a new treatment strategy for the neuropathy induced by glaucoma.

## Declarations

Ethics approval and consent to participate

The Medical Ethics Committee of Beijing Shijitan Hospital approved the prospective study protocol. The study was approved and monitored by clinical practice guideline, adhered to the Declaration of Helsinki, and registered in the Chinese Clinical Trial Registry (registration number: ChiCTR1900027909). Written informed consent from participants will be obtained after the nature and the purpose of the study are explained.

Consent to publication

Not applicable.

Availability of data and materials

The datasets analyzed in this study are available from the corresponding author (Yan Lu, louiselu@163.com) upon reasonable request.

Competing interests

The authors declare that there is no competing interest regarding the publication of this article.

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Authors' contributions

LXX, and LY conceived and designed the analysis. LXX were the major contributors in writing the manuscript. CH and YL provided the platform for inspection and training. All authors have read and

approved the manuscript.

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## Figures

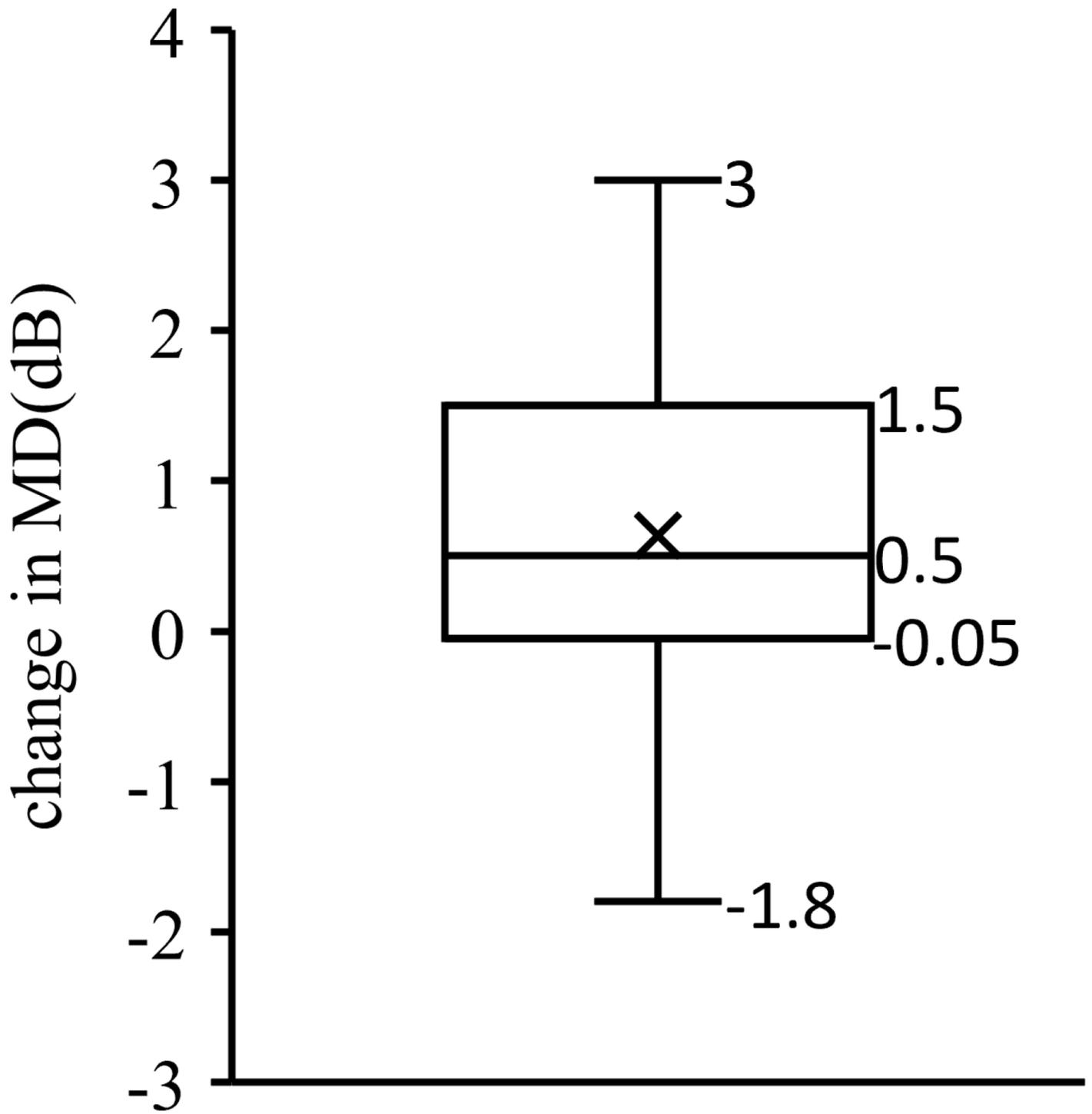
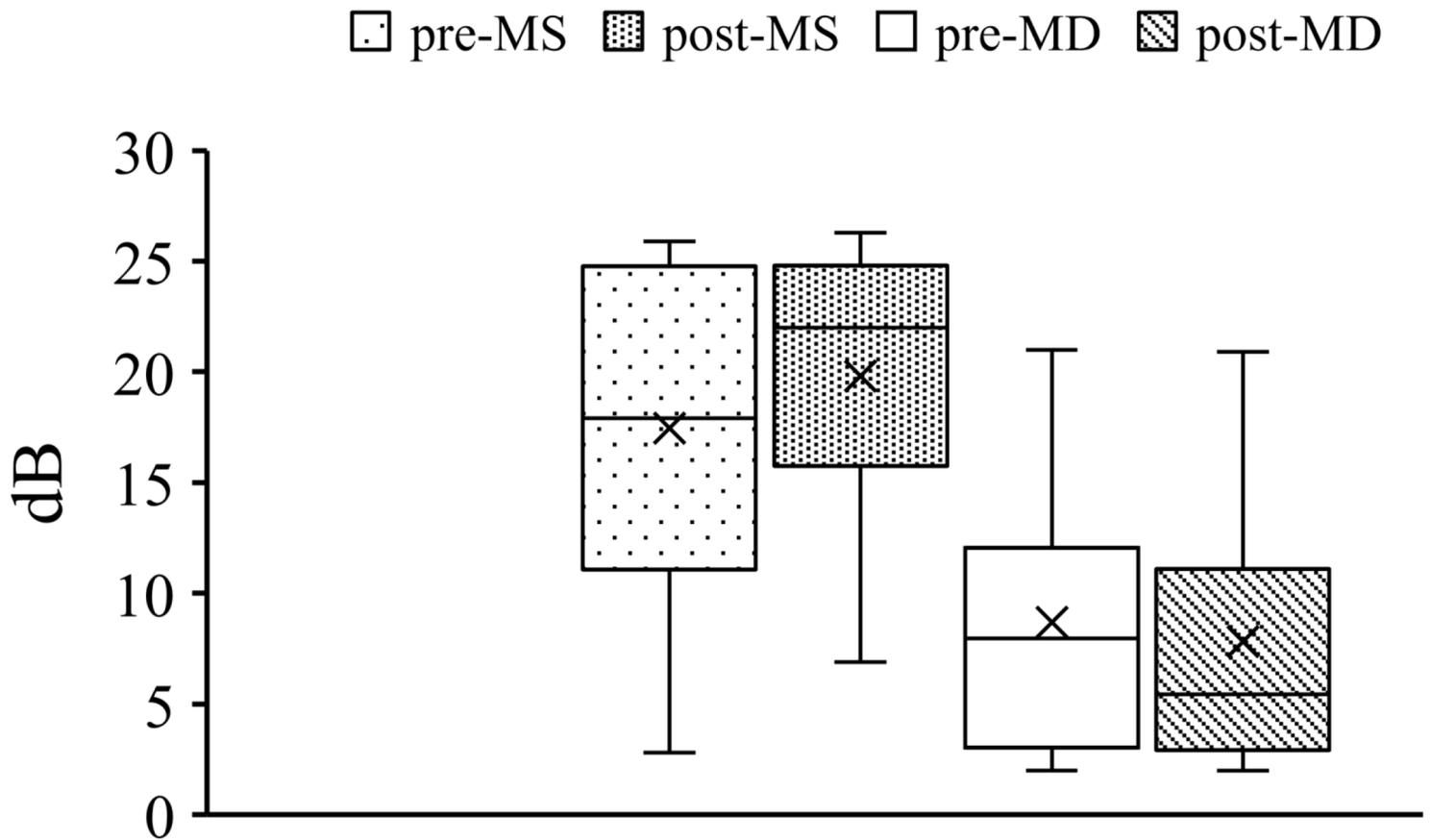


Figure 1

Visual field MD change between pre- and post-training. global mean defect (MD) values, global indices mean sensitivity (MS).



**Figure 2**

Global visual field MS and MD between pre- and post-training. global mean defect (MD) values, global indices mean sensitivity (MS).

## Supplementary Files

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