



Original Investigation | Neurology

Personalized Visual Perceptual Learning Digital Therapy for Visual Field Defects Following Stroke

A Randomized Clinical Trial

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Abstract

IMPORTANCE Effective treatments for restoring visual field defects (VFDs) in patients with stroke necessitate validation through randomized clinical trials.

OBJECTIVE To evaluate the efficacy and safety of a personalized digital therapeutic based on visual perceptual learning for treating poststroke VFDs.

DESIGN, SETTING, AND PARTICIPANTS A multicenter randomized clinical trial was conducted from October 19, 2022, to November 8, 2023, at 12 hospitals in South Korea. The study included poststroke outpatients 19 years or older with persistent VFDs (>3 months after stroke) and neuroimaging-confirmed stroke lesions in the visual pathway.

INTERVENTION The training group underwent personalized visual discrimination tasks (orientation and rotation) using a mobile virtual reality headset 5 days a week for 12 weeks, with 360 trials per day. The control group received no intervention.

MAIN OUTCOME AND MEASURES The primary outcome was improved visual areas (defined as sensitivity increased by ≥ 6 decibels [dB] during 12 weeks) assessed using Humphrey visual field tests at baseline and 12 weeks.

RESULTS Of 93 enrolled stroke outpatients with VFDs, 82 were included in the final analysis (41 in the intervention group and 41 in the control group; median [IQR] age, 52 [42-65] years; 57 male [69.5%]). As primary measures, the training group, with a high adherence rate, showed significantly greater improvement (sensitivity increased by ≥ 6 dB) in the whole field (median difference, 72 [95% CI, 36-108] degrees squared; $P = .003$; mean [SD], 194.1 [197.3] vs 82.5 [95.0] degrees squared) and defective hemifield (median difference, 72 [95% CI, 36-108] degrees squared; $P = .002$; mean [SD], 158.9 [159.0] vs 72.0 [91.4] degrees squared) compared with the control group. As secondary measures, mean (SD) Humphrey visual field test scores improved after 12 weeks in the training group (whole field: 0.72 [1.55] dB; $P = .005$; defective hemifield: 1.20 [2.08] dB; $P < .001$) but not in the control group (whole field: 0.03 [1.30] dB; $P = .88$; defective hemifield: 0.06 [1.85] dB; $P = .84$).

CONCLUSIONS AND RELEVANCE In this randomized clinical trial of a digital therapeutic for chronic poststroke VFDs, the visual perceptual learning-based training demonstrated significant improvements in the whole field and defective hemifield.

(continued)

Key Points

Question Does a personalized digital therapeutic based on visual perceptual learning effectively and safely improve poststroke visual field defects?

Findings In this multicenter randomized clinical trial of 82 outpatients with poststroke visual field defects, the training group, who completed personalized visual discrimination tasks for 12 weeks, showed significantly greater improvements in visual fields (sensitivity increased by ≥ 6 dB) compared with the control group.

Meaning The 12-week training session, which used visual perceptual learning, effectively enhanced visual field defect recovery in poststroke patients, highlighting its potential as a safe and effective digital therapeutic.

+ [Visual Abstract](#)

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Abstract (continued)

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Introduction

Visual field defects (VFDs) from brain damage, including stroke, limit vision and typically manifest as unilateral homonymous defects, affecting one-quarter (quadrantanopia) or half (hemianopia) of the visual field depending on the lesion location.^{1,2} Spontaneous recovery of VFDs beyond 3 months is rare without treating the underlying brain disorder.^{3,4} Untreated VFDs can impair daily and social activities, reducing the quality of life and the need for effective therapies.⁵⁻⁷

Treatment strategies for VFDs resulting from brain damage encompass compensation, substitution, and restitution.^{1,8} Compensatory and substitutive interventions enhance daily functioning without restoring the visual field by redirecting visual information or guiding attention to the impaired area (Class of Recommendation IIb, Level of Evidence B).^{6,7,9,10} Restitutive interventions, aiming to improve perception within the blind field through training, are less substantiated owing to inconsistent results, nonrandomized designs, and small sample sizes (Class of Recommendation IIb, Level of Evidence C).¹¹⁻¹³

No treatments have been proven through randomized clinical trials to effectively restore VFDs after stroke.¹ However, visual perceptual learning (VPL) shows promise in improving blind visual fields by leveraging experience-dependent repetitive training to enhance adult visual plasticity.^{7,14,15} VPL-driven VFD recovery is facilitated by neuroplasticity, functional reorganization, and enhanced connectivity within the visual processing network. This includes retinotopic reorganization within the primary visual cortex (V1), cross-hemispheric interactions, and altered connectivity between V1 and higher-order cortical regions involved in reward-based learning and perceptual decision-making.^{7,14,16-18} Individual variability in VPL response and the need for personalized protocols remain key challenges.^{2,7,19} As a rehabilitation approach, VPL using Gabor patches for orientation-rotation discrimination has been effective in cortical blindness by refining tuning specificity in the lesioned V1 and engaging higher-order cortical regions involved in visual discrimination.^{15,20-22}

Building on previous studies,²¹⁻²³ we developed a virtual reality (VR)-based digital therapeutic for VFDs using personalized VPL training, which optimizes training locations and Gabor patch sizes for orientation-rotation discrimination. This trial compared VPL training with a no-training condition, reflecting clinical applicability given the current lack of validated VFD treatments in patients with chronic stroke. Expanding on a previous trial, which applied VPL to the defective field (training) vs the central field (control) at the same location across participants,²² this prospective, multicenter randomized clinical trial evaluates whether 12 weeks of personalized training improves VFDs in patients with chronic stroke.

Methods

Study Design and Participants

This prospective, multicenter, intention-to-treat (ITT) randomized clinical trial was conducted in South Korea from October 19, 2022, to November 8, 2023, after approval from the Ministry of Food and Drug Safety and the institutional review boards of the 12 participating hospitals. The trial adhered to the Declaration of Helsinki²⁴ and Consolidated Standards of Reporting Trials (CONSORT) guidelines. The trial protocol and statistical plan are available in [Supplement 1](#).

Inclusion criteria were age of 19 years or older, stroke-induced VFDs lasting more than 3 months, and confirmed visual pathway damage via brain imaging. A board-certified ophthalmologist (B.J.L.)

defined the side and type of VFDs based on the total deviation probability of less than 5% assessed using the Humphrey visual field (HVF) test (30-2, SITA Fast).^{25,26} Participants who consented and could use smartphone-based VR devices were enrolled, with written informed consent obtained from them or their legal representatives. The detailed study procedure and exclusion criteria are described in eTable 1 in [Supplement 2](#).

Randomization and Intervention

Within 1 month of providing informed consent, patients were randomized in a 1:1 ratio to the training (n = 48) or control (n = 45) group using computer-based permuted block randomization by an independent contract research organization at each clinical center. In the training group, participants underwent a home-based intervention (360 trials per day for 5 days a week for 12 weeks) (eFigure 1A in [Supplement 2](#)) using vividbrain software, version 1.02.00 (Nunaps Inc) through a VR head-mounted display (Oculus Go, Meta Inc).

Patients in the training group underwent 3 phases—tutorial, evaluation, and training—for orientation and rotation discrimination tasks. At the start of the training, participants completed a mandatory tutorial. The evaluation phases determined the optimal training locations and sizes of the Gabor patch both before training and after 3600 trials (eFigure 1C in [Supplement 2](#)). On the basis of this information, the software targeted 2 locations in the defective hemifield and another 2 locations in the contralateral normal hemifield at an 8:2 ratio to ensure central fixation. In each task, patients fixated on a central middle-gray screen with a beep (1800 milliseconds), followed by simultaneous presentation of central and personalized peripheral Gabor patches (180 milliseconds) and a response interval (3500 milliseconds). They pressed the thumb button if both stimuli shared the same orientation (horizontal and vertical) and rotation (left and right) or the index finger button if not (eFigure 1D in [Supplement 2](#)), with feedback provided via colored borders and training results. The details of each phase are included in the [Video](#) and the eMethods in [Supplement 2](#).

Outcome Measures

At baseline and 12-week follow-up, HVF tests (30-2 SITA Fast) were conducted. Luminance detection sensitivity and deviation were measured for each HVF point (eFigure 1B in [Supplement 2](#)). Participants with unreliable HVF test results (fixation loss, false positive, or false negative $\geq 20\%$) were excluded from the final analysis.^{27,28}

The primary outcome measure was the difference in the whole field, where sensitivity increased by 6 dB or more during 12 weeks between the training and control groups. A threshold of 6 dB (1 HVF point) was selected because it represents a meaningful change in visual sensitivity beyond chance, accounting for a doubling of the HVF test-retest variability.^{15,29,30} The secondary outcome measures included the difference in the improved area of the defective hemifield (sensitivity increased by ≥ 6 dB during 12 weeks) between the training and control groups. Perimetric mean deviation (PMD) and mean total deviation (MTD) scores, indicating light detection performance relative to expected age-normative values, were averaged for both eyes.¹⁵ The 12-week changes in the PMD scores of the whole field and MTD scores of the defective hemifield were compared between both groups. Additionally, PMD scores for the whole field and MTD scores for the defective hemifield were compared between baseline and 12-week follow-up within each group.

Statistical Analysis

Statistical analyses were conducted using SAS, version 9.4 (SAS Institute Inc) as specified in the study protocol. Analyses of the primary and secondary outcome measures were performed using both the full analysis set (FAS) (training, n = 41; control, n = 41) and the ITT set (training, n = 41; control, n = 42). All tests were 2-sided, with a significance threshold set of $P < .05$ for all analyses. The eMethods in [Supplement 2](#) provide a full explanation of the statistical analysis and adherence and safety measures.

Results

Participant Characteristics

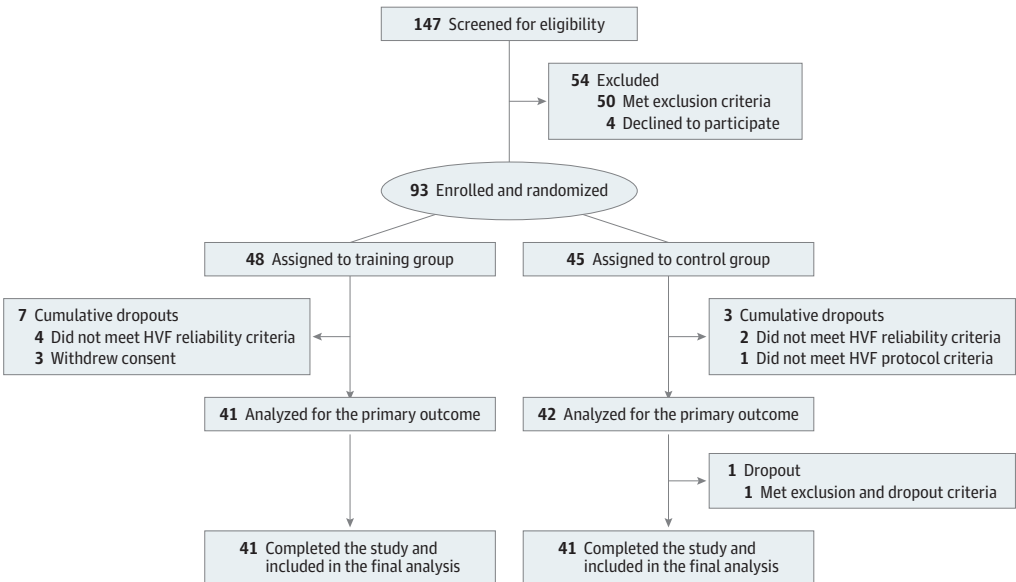
Figure 1 shows the flow diagram of study participants. A total of 147 patients were screened, and 54 of those were excluded due to ineligibility or withdrawal. The remaining 93 patients in the safety population were randomized into the training (n = 48) or control (n = 45) group. Ten patients dropped out (7 from the training group and 3 from the control group) due to unreliable HVF test results, use of an incorrect HVF protocol, or consent withdrawal. The ITT group included all randomized participants with reliable postbaseline HVF assessment (41 in the training group and 42 in the control group). For the FAS, which was specified as the primary analysis group in the statistical analysis plan, 1 participant in the control group was excluded due to serious violation of the eligibility criteria. The final analysis comprised the FAS (participants with reliable postbaseline HVF assessment and no serious violations of the eligibility criteria; 41 in the training group and 41 in the control group). These 82 patients had a median (IQR) age of 52 (42-65) years; 57 (69.5%) were male and 25 (30.5%) were female. The per-protocol set was identical to the FAS because all participants strictly adhered to the study protocol. Baseline characteristics, including VFD severity, showed no significant between-group differences (**Table 1**; eTable 2 in [Supplement 2](#)).

Improved Areas

In the FAS, the training group showed a significantly greater improvement (sensitivity ≥ 6 dB during 12 weeks) across the whole field. This finding corresponded to a clinically significant increase of 5.4 HVF points (mean [SD], 194.1 [197.3] degrees squared), exceeding the 2.3 HVF points (82.5 [95.0] degrees squared) in the control group (median difference, 72 degrees squared; 95% CI, 36-108 degrees squared; $P = .003$) (**Figure 2A**). This significance remained unchanged in the ITT set (5.4 vs 2.8 HVF points; median difference, 72 degrees squared; 95% CI, 36-108 degrees squared; $P = .006$) (eResults in [Supplement 2](#)).

In the FAS, the improved area in the defective hemifield (sensitivity ≥ 6 dB) was clinically meaningful and significantly larger in the training group (mean [SD], 158.9 [159.0] degrees squared;

Figure 1. Flow Diagram of Study Participants



The final analysis included 82 patients (41 in the training group and 41 in the control group) who completed the trial. The dropout rates due to unreliable Humphrey visual field (HVF) test results, inconsistent HVF protocol, meeting dropout criteria, and consent withdrawal did not differ significantly between the training and control groups (7 [14.6%] in the training group and 4 [8.9%] in the control group; $P = .52$).

4.4 HVF points) than in the control group (mean [SD], 72.0 [91.4] degrees squared; 2 HVF points; median difference, 72 degrees squared; 95% CI, 36-108 degrees squared; $P = .002$) (Figure 2B). This significance remained unchanged in the ITT set (4.4 vs 2.3 HVF points; median difference, 54 degrees squared; 95% CI, 0-108 degrees squared; $P = .003$) (eResults in Supplement 2).

Table 1. Baseline Demographic and Clinical Characteristics of Patients

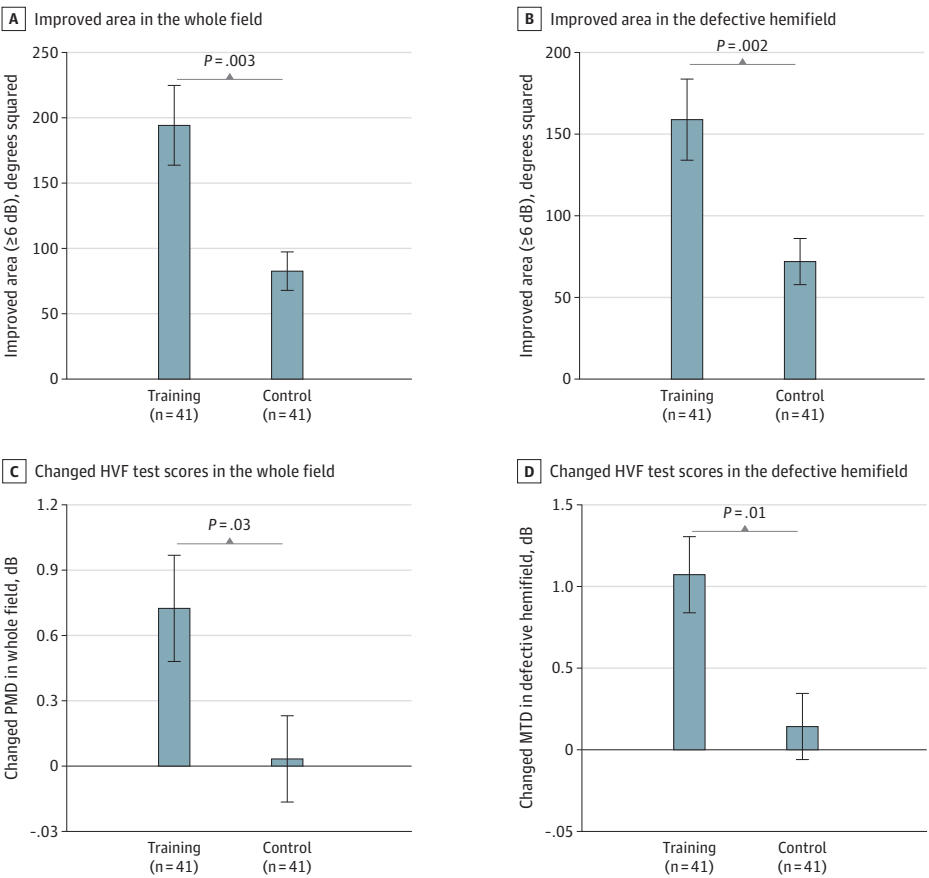
Characteristic	Full analysis set, No. (%) ^a			Intent-to-treat analysis set, No. (%) ^a		
	Training (n = 41)	Control (n = 41)	Total (N = 82)	Training (n = 41)	Control (n = 42)	Total (N = 83)
Sex						
Male	30 (73.2)	27 (65.9)	57 (69.5)	30 (73.2)	28 (66.7)	58 (69.9)
Female	11 (26.8)	14 (34.1)	25 (30.5)	11 (26.8)	14 (33.3)	25 (30.1)
Age, median (IQR), y	50 (43-67)	53 (42-61)	52 (42-65)	50 (43-67)	53 (42-62)	52 (42-65)
Time since stroke, median (IQR), y	2.7 (1.0-7.4)	2.8 (0.6-6.0)	2.8 (0.8-7.0)	2.7 (1.0-7.4)	2.9 (0.6-6.0)	2.8 (0.8-7.0)
Severity of VFD, mean (SD), dB ^b	-10.5 (3.9)	-10.9 (4.6)	-10.7 (4.2)	-10.5 (3.9)	-11.1 (4.7)	-10.8 (4.3)
Type of stroke						
Ischemic stroke	39 (95.1)	39 (95.1)	78 (95.1)	39 (95.1)	40 (95.2)	79 (95.2)
Hemorrhagic stroke	2 (4.9)	2 (4.9)	4 (4.9)	2 (4.9)	2 (4.8)	4 (4.8)
Hemifield of VFD						
Left hemifield	21 (51.2)	20 (48.8)	41 (50)	21 (51.2)	21 (50)	42 (50.6)
Right hemifield	20 (48.8)	21 (51.2)	41 (50)	20 (48.8)	21 (50)	41 (49.4)

Abbreviations: dB, decibel; VFD, visual field defect.

^a Unless otherwise indicated.

^b The severity of the VFD was evaluated using the perimetric mean deviation scores for the whole field, as measured by the baseline Humphrey visual field test.

Figure 2. Between-Group Differences



The median of visual area improvement (luminance detection sensitivity ≥ 6 decibels [dB] during 12 weeks) in the whole field (A) and defective hemifield (B) was compared between the training and control groups using the Wilcoxon rank sum test. The 12-week mean changes in the perimetric mean deviation (PMD) scores for the whole field (C) and mean total deviation (MTD) scores for the defective hemifield (D) were compared between the training and control groups using independent t tests. Error bars indicate SEs. HVF indicates Humphrey visual field.

The improvement in the normal hemifield was below 3 HVF points and not significant between groups (0.98 vs 0.29 HVF points in the training vs control group, $P = .41$) (eResults in [Supplement 2](#)). The significance of these results also remained unchanged after adjusting for baseline VFD severity scores (eResults in [Supplement 2](#)).

Distribution of Improved Areas

In the FAS, the distribution of the improved areas (sensitivity ≥ 6 dB) significantly differed between the training and control groups for both the whole field (odds ratio [OR], 3.86; 95% CI, 1.63-9.16; $P = .002$) (eFigure 2A in [Supplement 2](#)) and defective hemifield (OR, 4.74; 95% CI, 1.92-11.74; $P < .001$) (eFigure 2B in [Supplement 2](#)). Meaningful improvement (≥ 3 HVF points, ≥ 108 degrees squared) was more frequently observed in the training group than in the control group (whole field: 63.5% vs 34.1%; defective hemifield: 63.5% vs 26.8%) (eFigure 2 in [Supplement 2](#); [Table 2](#)). In the ITT set, this significance remained unchanged for both the whole field (OR, 3.40; 95% CI, 1.46-7.93; $P = .005$) and defective hemifield (OR, 4.10; 95% CI, 1.69-9.91; $P = .002$) ([Table 2](#)).

The significance of these results remained unchanged after adjusting for baseline VFD severity scores (eResults in [Supplement 2](#)). The baseline patient characteristics between the responders (improved area ≥ 108 degrees squared) and nonresponders (improved area < 108 degrees squared) showed nonsignificant differences (eTable 3 in [Supplement 2](#)).

Change in HVF Scores Between Groups

During 12 weeks in the FAS, PMD score changes in the whole field were significantly greater in the training group than in the control group (mean difference, 0.69 dB; 95% CI, 0.07-1.32 dB; $P = .03$) ([Figure 2C](#)). This difference became nonsignificant in the ITT set (mean difference, 0.62 dB; 95% CI, -0.02 to 1.26 dB; $P = .06$) (eResults in [Supplement 2](#)).

For the defective hemifield, MTD score changes were significantly greater in the training group than in the control group of the FAS (mean difference, 1.14 dB; 95% CI, 0.27-2.00 dB; $P = .01$) ([Figure 2D](#)). This significance remained unchanged in the ITT set (mean difference, 1.06 dB; 95% CI, 0.19-1.93 dB; $P = .02$) (eResults in [Supplement 2](#)). The significance of these results remained unchanged after using a linear mixed-effects model for repeated measures and adjusting for baseline VFD severity scores (eResults in [Supplement 2](#)).

Change in HVF Scores Within Groups

In FAS analysis, after 12 weeks, PMD scores of the whole field significantly improved within the training group (mean [SD], 0.72 [1.55] dB; $P = .005$) ([Figure 3A](#)) but not within the control group (mean [SD], 0.03 [1.30] dB; $P = .88$) ([Figure 3B](#)). This significance remained unchanged in the ITT set (training group: mean [SD], 0.72 [1.55] dB; $P = .005$; control group: mean [SD], 0.11 [1.38] dB; $P = .61$) (eResults in [Supplement 2](#)). Similarly, in FAS analysis, MTD scores in the defective hemifield significantly improved within the training group (mean [SD], 1.20 [2.08] dB; $P < .001$) ([Figure 3C](#)), whereas no significant changes occurred in the control group (mean [SD], 0.06 [1.85] dB; $P = .84$).

Table 2. Distribution of Improved Areas Between the Training and Control Groups^a

Improved area, degrees squared	Full analysis set, No. (%) (n = 82)						Intent-to-treat set, No. (%) (n = 83)					
	Whole field			Defective hemifield			Whole field			Defective hemifield		
	Training (n = 41)	Control (n = 41)	P value	Training (n = 41)	Control (n = 41)	P value	Training (n = 41)	Control (n = 42)	P value	Training (n = 41)	Control (n = 42)	P value
0-72	15 (36.6)	27 (65.9)		15 (36.6)	30 (73.2)		15 (36.6)	27 (64.3)		15 (36.6)	30 (71.4)	
108-180	11 (26.8)	10 (24.4)		15 (36.6)	8 (19.5)		11 (26.8)	10 (23.8)		15 (36.6)	8 (19.0)	
216-288	7 (17.1)	3 (7.3)	.002	5 (12.2)	2 (4.9)	<.001	7 (17.1)	3 (7.1)	.005	5 (12.2)	2 (4.8)	.002
324-396	4 (9.8)	0		2 (4.9)	0		4 (9.8)	0		2 (4.9)	0	
≥432	4 (9.8)	1 (2.4)		4 (9.8)	1 (2.4)		4 (9.8)	2 (4.8)		4 (9.8)	2 (4.8)	

^a The 5 distributions of improved area (luminance detection sensitivity ≥ 6 decibels during 12 weeks) in the whole field and defective hemifield were compared between the training and control groups using ordinal logistic regression analysis. The analysis was repeated within the full analysis set and the intent-to-treat set.

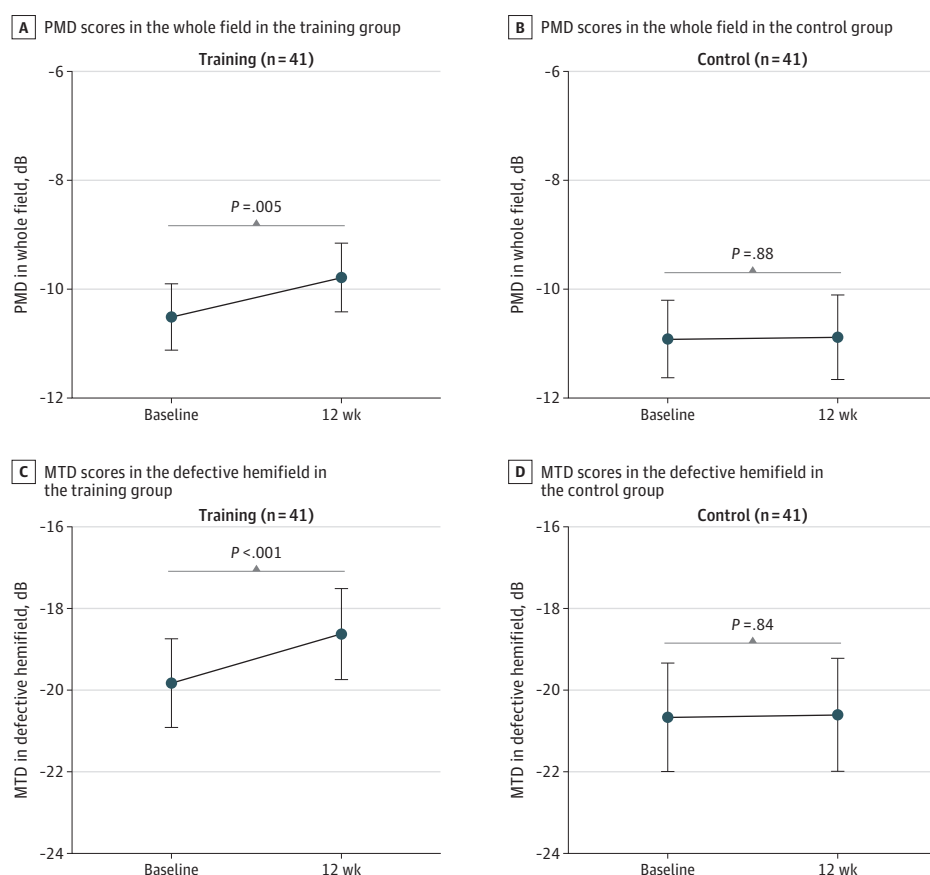
(Figure 3D). This significance remained unchanged in the ITT set (training group: mean [SD], 1.20 [2.08] dB; $P < .001$; control group: mean [SD], 0.14 [1.89] dB; $P = .64$) (eResults in Supplement 2). The significance of these results remained unchanged after adjusting for baseline VFD severity scores (eResults in Supplement 2).

Discussion

Our prospective, multicenter randomized clinical trial indicated that a personalized digital therapeutic based on VPL can safely and effectively treat VFDs induced by stroke. After 12 weeks of personalized orientation-rotation direction discrimination tasks, the training group showed clinically significant improvements in VFDs across the whole field and defective hemifield, surpassing those in the control group. The training group maintained high adherence rates, with no serious or unanticipated adverse device effects reported (eTable 4 in Supplement 2).

Considering the chronic nature of poststroke VFDs and the limited 12-week training period, the observed improvement after VPL (5.4 HVF points across the whole field and 4.2 points in the defective hemifield) is noteworthy. A decrease of 3 HVF points (108 degrees squared) is associated with significant visual deterioration in glaucoma,³¹ whereas an increase of 3 HVF points during several months of visual discrimination training represents meaningful improvement in cortical blindness.¹⁵ The mean improved area of 194 degrees squared after VPL training exceeds the clinically significant threshold of 108 degrees squared and aligns with the improved area of previous orientation-rotation discrimination training (101-288 degrees squared).^{15,20,21,23,29}

Figure 3. Within-Group Differences



The mean of perimetric mean deviation (PMD) score for the whole field was compared before and after 12 weeks within the training (A) and control (B) groups using paired *t* tests. The mean of mean total deviation (MTD) score for the defective hemifield was compared before and after 12 weeks within the training (C) and control (D) groups using paired *t* tests. Error bars indicate SEs; dB indicates decibels.

This meaningful improvement after VPL significantly exceeds that of the control group (2.3 HVF points, 82 degrees squared), which falls below the clinical threshold of 3 HVF points and aligns with previously reported no-training outcomes (16-95.1 degrees squared).^{15,21,23} This clinically insignificant change in the control group may reflect confounding factors such as variability in HVF testing (eg, practice effects, environment, and patient status), necessitating further investigation.^{2,32-34} Improvement in the normal hemifield likely resulted from allocating 20% of VPL trials to reinforce central fixation. However, compared with the defective hemifield, improvements in the normal hemifield were minimal and nonsignificant. These findings suggest that VPL, with 80% of trials targeting the defective hemifield, primarily stimulates receptive fields in the lesioned V1 using Gabor stimuli at personalized training locations.³⁵⁻³⁸

VPL responders and nonresponders showed no baseline stroke-related differences, warranting further neuroimaging investigation into the size and location of stroke lesions. Adjusting for baseline VFD severity did not affect statistical significance, reinforcing VPL's effectiveness. The number of completed VPL trials showed no correlation with outcomes, suggesting nonlinear and noncumulative training effects. After prior visual discrimination training, basal functional connectivity of the visual cortex, rather than patient age, lesion volume, or lesion age, was correlated with VPL-induced recovery.^{15,17,23} These findings indicate that VFD improvement results from complex interactions between VPL and patient-specific factors, including brain connectivity as well as lesion size and location.

The noninvasive, VR-based VPL training program used in this study is designed with strong neurobiological principles to enhance neuroplasticity in the lesioned V1.^{16,35,38} Through personalized visual discrimination training and repeated decision-making, it promotes visual restoration beyond substitution and compensation by leveraging adult visual plasticity associated with VPL.^{16,39,40} This process operates through 2 key mechanisms. First, Gabor stimuli, resembling early visual receptive fields, enhance neuronal responsiveness in the lesioned V1, thereby sharpening retinotopic tuning at personalized training locations and improving sensitivity to subtle visual stimuli.³⁵⁻³⁸ Second, VPL strengthens connectivity between the damaged V1 and higher-order regions involved in decision-making as a key mechanism in VFD recovery.^{3,17,18,41,42} Through top-down cognitive modulation, higher cortical regions exert feedback on early visual processing, strengthening connectivity between the lesioned V1 and the intact contralateral V1 or temporal regions.^{3,17,18}

Our personalized VPL protocol was designed to compensate for individual variances in VFD types and VPL responsiveness while ensuring central fixation with an 8:2 stimulus allocation to defective and normal hemifields. Recognizing individual variability, prior VPL studies on cortical blindness have provided alternated texture discrimination tasks between normal and defective fields or their boundaries.^{20,43,44} Because VFD recovery occurs during VPL, the Gabor opacity was dynamically adjusted based on 75% accuracy in the latest 20 trials. Initial and posttraining evaluation after 3600 trials also determined tailored Gabor sizes and locations for unique VFDs of each patient.

Strengths and Limitations

This multicenter randomized clinical trial has several strengths. The trial effectively minimized potential biases in sampling and intervention. To reduce the effect of spontaneous VFD recovery mostly occurring within 3 months, only patients 3 months or more after stroke were enrolled.^{3,4} Patient recruitment from 12 medical centers and strict randomization mitigated sampling bias. Real-time monitoring ensured adherence, tracked training progress, and facilitated at-home training by providing immediate feedback through telephone calls, thereby improving adherence. The VR head-mounted display maintained consistent viewing distance, preventing head movement effects and ensuring precise localization of visual stimuli for optimal stimulation of damaged visual fields.⁴⁵

However, some limitations should be considered when interpreting the current results. The absence of eye tracking was partially addressed by briefly presented visual stimuli and excluding participants with more than 20% fixation loss from the analysis. The naturalistic enrollment criteria resulted in uncontrolled clinical characteristics, including comorbidities and medication history.

Although luminance detection was reliably measured using the standard perimetry HVF, additional objective visual measures may improve the generalizability of the findings. Future neuroimaging research may explore the complex interactions among patient-specific characteristics, underlying neural mechanisms, and long-term visual functional outcomes after VPL.

Given the lack of proven treatments for poststroke VFDs beyond compensation and substitution, this study compared VPL training with a no-training condition to enhance clinical applicability in chronic poststroke VFD. However, a passive control may not fully account for nonspecific effects, such as increased attention and arousal, or differentiate VPL from other low-vision therapies, including vision restoration therapy.^{2,32} Future studies incorporating an active control, such as attention-matched training or standard vision restoration therapy, could help reduce these confounding effects, maintain blinding, and better isolate the specific benefits of VPL.

A VPL-based digital therapeutic offers noninvasive treatment with potential long-term visual benefits but demands extensive time and resources.⁴⁵ Alternatives, such as visual prosthetic devices and neuromodulation, provide immediate restoration by targeting damaged neural pathways but are costly and have limited generalization.^{2,7,19} Adjunctive pharmacology and noninvasive neuromodulation lack consensus on safety and efficacy across various recovery stages in chronic poststroke VFDs.^{2,15} Future directions for VPL in cortical blindness include longitudinal studies on visual functions and skill retention, optimizing rehabilitation integration, exploring cross-modal training, and identifying biomarkers for VPL responsiveness.^{2,7,19}

Conclusions

In this randomized clinical trial of a digital therapeutic for chronic poststroke VFDs, the vividbrain platform, which features individualized training locations, real-time difficulty adjustments, and high adherence, demonstrated significant improvements in both whole and defective visual fields. These results underscore the safety and efficacy of this personalized VPL-based digital therapeutic, offering a restorative treatment alternative to traditional compensatory strategies.

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SUPPLEMENT 1.

Trial Protocol

SUPPLEMENT 2.

eMethods. Supplemental Methods

eResults. Supplemental Results

eTable 1. Timeline of the Study Design

eTable 2. Baseline Demographic and Clinical Characteristics of Patients

eTable 3. Baseline Characteristics of the Responder and Non-responder Groups

eTable 4. Adverse Events in Safety Analysis Set

eFigure 1. Study Design

eFigure 2. Distribution of Improved Area

eReferences

SUPPLEMENT 3.

Data Sharing Statement