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Case Report

Neurovisual Training With Acoustic Feedback: An Innovative Approach for Nystagmus Rehabilitation

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KEYWORDS
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Case report

Abstract Nystagmus has various clinical manifestations, including downbeat, upbeat, and torsional types, each associated with distinct neurologic features. Current rehabilitative interventions focusing on fixation training and optical correction often fail to achieve complete resolution. When nystagmus coexists with fragile X-associated tremor/ataxia syndrome (FXTAS), functional impairments worsen, particularly affecting balance. Recognizing these limitations, the authors propose an innovative approach using audiovisual stimulation to complement visual pursuit training and optical compensation, potentially improving rehabilitation outcomes. This study describes the case of a 60-year-old woman with worsening nystagmus and cerebellar ataxia suggestive of FXTAS who underwent a customized rehabilitation program. The program included 30 sessions involving audiovisual training and physical exercises. Visual performance assessments were conducted using AV-Desk and Nidek MP-1 microperimeters, with functional assessments including the Barthel Modified Index, 10-meter walking test, timed Up and Go, and Berg Balance Scale. After treatment, visual performance improved with reduced response times and higher success rates, especially without drugs. Fixation stability improved consistently using the bivariate contour ellipse area method. Functional assessments showed enhanced mobility and balance, with benefits sustained at the 6-month follow-up. The combined approach of audiovisual training, proprioceptive training, and targeted muscle strengthening has proven effective. Notable improvements in overall physical performance, especially in balance and gait, and a reduction in nystagmus severity were observed. Integrating audiovisual stimulation into rehabilitation protocols shows promising results in managing nystagmus and ataxia, significantly enhancing

List of abbreviations: 10mWT, 10-meter walking test; BBS, Berg Balance Scale; BCEA, bivariate contour ellipse area; BMI, Barthel Modified Index; FXTAS, fragile X-associated tremor/ataxia syndrome; SD, standard deviation.

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patients' quality of life. Further studies are needed to validate these findings and expand upon this approach.

Nystagmus is characterized by involuntary eye movements and varies in form. Downbeat nystagmus is linked to vestibulocerebellar and medullary bulb lesions; upbeat nystagmus to bulb, ventral tegmentum, and anterior vermis lesions; torsional nystagmus to brainstem lesions.[1] Periodic alternating, saw-saw, and gaze-evoked nystagmus have distinct traits.[1] Diagnosis relies on clinical evaluation and neuroimaging. Recently, microperimetry and biofeedback fixation training[2] have improved assessments. Treatments include pharmacologic therapy, surgery, and rehabilitation training that focuses on fixation and optical correction with specialized aids. Customization is crucial for optimal outcomes, requiring comprehensive severity assessment and patient compliance.[3-10]

Fragile X-associated tremor/ataxia syndrome (FXTAS) is a neurodegenerative disorder characterized by tremors progressing to cerebellar ataxia. This condition affects balance, coordination, and cognitive function, and includes symptoms such as visual dysfunctions, dysphagia, and dysarthria. FXTAS is a progressive genetic condition that is associated with specific brain abnormalities. Therapeutic approaches target symptoms because of its progressive nature and genetic basis.[11-15] Rehabilitation involves physical therapy for mobility and fall prevention, occupational therapy for daily activity independence, and exercises for coordination and balance to enhance safety.

When these 2 conditions are associated, they could result in significant functional deficits and loss of autonomy, with the potential for a synergistic effect exacerbating the impairment, persisting despite conventional rehabilitative interventions. Therefore, innovative rehabilitative interventions are necessary to address these challenges effectively.

The use of audiovisual stimulation has recently been explored to enhance the management of visual field disorders such as hemianopsia or attentional disorders such as neglect.[16,17] We attempted to combine visual training with acoustic feedback to improve the severity of nystagmus by leveraging brain plasticity mechanisms.[16,17] Simultaneously, we incorporated motor performance training to treat ataxia syndrome. Our goal was to investigate whether the combination of these 2 treatments would have a synergistic effect on patients' rehabilitation outcomes.

Case report

The patient was a 60-year-old woman with worsening nystagmus.

The reporting of this study conforms to the CARE guidelines (for CAse REports).[18] The patient provided signed informed consent for treatment and publication.

Genetic investigations revealed mutations in the MTHFR gene, a permutation in the fragile X gene (55 repetitions), and a heterozygous variant in the SYNE1 gene, indicating potential tremor ataxia syndrome.

A magnetic resonance imaging investigation revealed no major pathologic signs, but a positron emission tomography scan revealed a widespread decrease in metabolic activity in the cerebellum and midbrain (fig 1).

An ophthalmologic assessment revealed optic disc atrophy with temporal pallor in the left optic papilla. Additional tests indicated an altitudinal scotoma, a condition where vision loss occurs in either the upper or lower visual fields.

Clinically, downbeat nystagmus and visual impairment in the left eye were observed. Muscle tone and sensation were normal, with slight weakness on the left side. The patient, while in the Romberg position, would have fallen if she had not been promptly supported by the physician during the examination. The patient exhibited an unsteady gait and wider stance, using a cane indoors and a rollator walker outdoors.

The patient was undergoing pharmacologic treatment with fampridine and reported mild attenuation of nystagmus, especially shortly after administration.

An innovative and personalized rehabilitation program was developed to enhance visual-kinesthetic and visuospatial skills, as well as to improve both static and dynamic balance and walking independence. This cutting-edge program comprised 30 rehabilitation sessions, each lasting approximately 2 hours and conducted 5 times a week.

The treatment regimen integrated 1 hour of advanced audiovisual training with 1 hour of specialized exercises designed to improve balance and gait, offering a comprehensive approach to rehabilitation.

Assessment

All evaluations were conducted before treatment, after treatment, and at the 6-month follow-up. The patient was evaluated at each stage twice: once during drug (fampridine) intake and once without medication.

The audiovisual training and visual performance assessment were conducted by a multisensory stimulation device called AV-Desk.[a]

The AV-Desk is a semicircular panel that provides visual and acoustic stimuli, covering a 180° field of view. These devices include Light Emitting Diod (LED)s with piezoelectric crystals capable of emitting various colors and frequencies (fig 2).

The device has 3 evaluation test modes: bimodal, unimodal, and pursuit. The bimodal test assesses multisensory integration by presenting visual and auditory stimuli, with the patient detecting "true" stimuli. The unimodal test evaluates visual exploration and discrimination abilities with only visual stimuli. Pursuit involves tracking bimodal stimuli with triangular and quadrangular oscillatory movements.

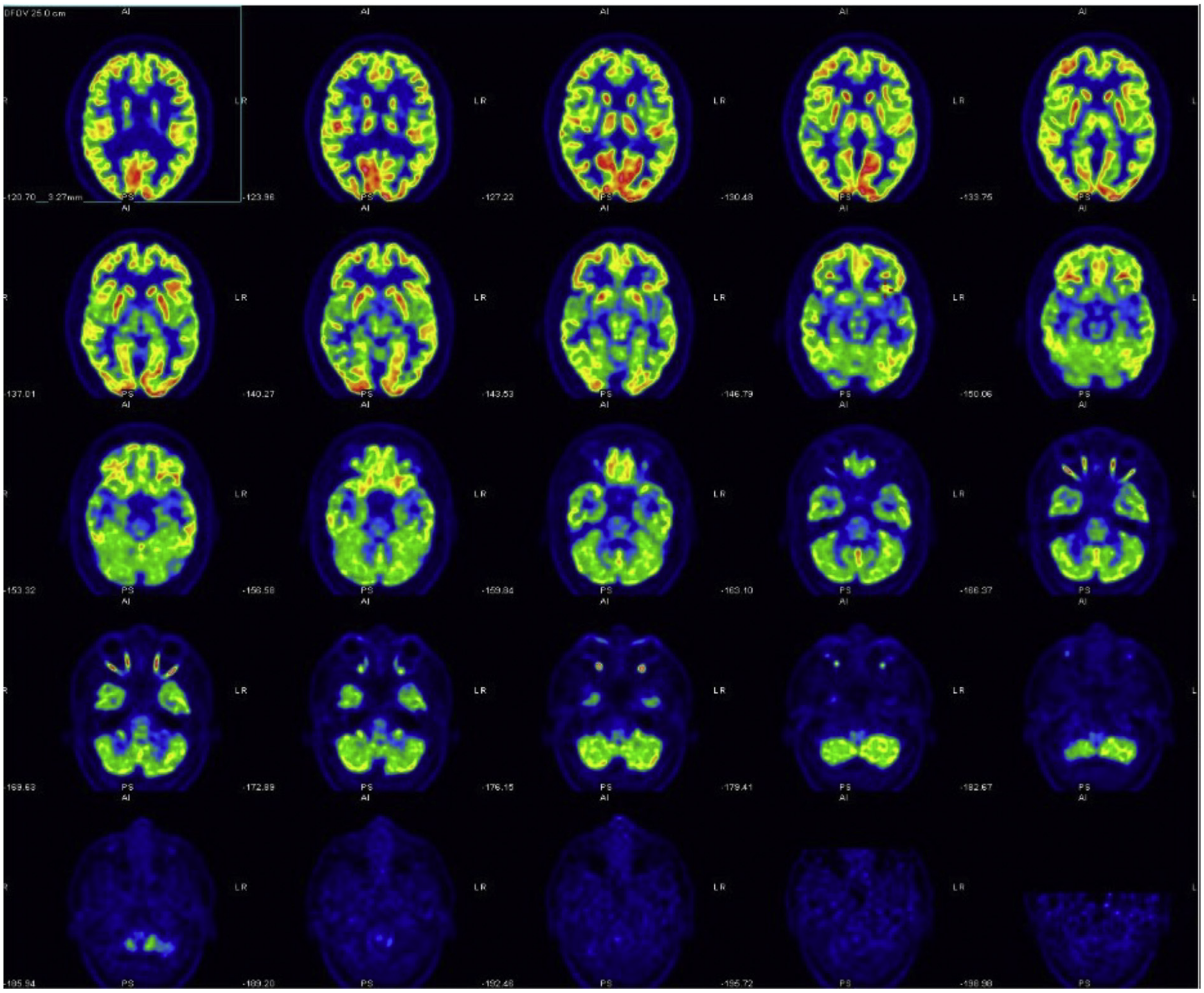

Fig 1 Cerebral positron emission tomography scan with fluorodeoxyglucose.

The data from the tests included response time, success rate for "true" stimuli, success rate for individual LEDs, and error rate for responding to "fake" stimuli.[19]

The fixation tests were conducted with a Nidek MP-1 microperimeter[b] according to the bivariate contour ellipse area (BCEA) and Fujii classification.[20]

Real-time imaging of the retina was possible through an infrared camera for ocular fundus with a liquid crystal display, which showed a single red cross (28 visual angles in width and 18 visual angles in thickness by default, both adjustable if necessary) on a monochromatic white background.

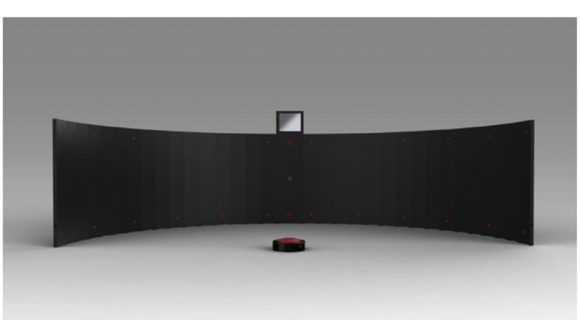

Fig 2 AV-Desk, a multisensory stimulation device.

Fixation stability was quantified by calculating the BCEA, which is the smallest elliptical area encompassing 1, 2, or 3 standard deviations (SDs) of all fixation events and determining their horizontal and vertical dispersion.[21] This provided a precise continuous value for fixation stability, with smaller values indicating more stable fixation.

The monocular test, with the contralateral eye covered, involved the patient fixating on a cross center for 1 minute, using peripheral fixation if needed. After identifying the red target, fixation activity began for approximately 1 minute while Nidek MP-1 captured real-time ocular fundus images at 25 Hz. If tracking failed, the test paused until retracking was possible. Fixation files (MDF format) were exported.[22,23] Additional tests administered included Barthel Modified Index (BMI),[24] 10-meter walking test (10mWT),[25] timed Up and Go,[26] and the Berg Balance Scale (BBS).[27]

Training

In the audiovisual training, the following 7 distinct sensory stimulation modalities were introduced: (1) unimodal visual condition: patients responded to at least 50 red and green light stimuli without auditory cues, focusing only on the red stimuli without head movement; (2) unimodal auditory condition: patients localized at least 50 purely auditory stimuli on a panel while keeping their gaze fixed on a central point; (3) focused cross-modal visual-auditory conditions: patients detected coinciding visual and auditory stimuli, maintaining fixation on a central point through 6 progressively challenging levels; (4) cross-modal visuo-auditory mismatch condition: patients identified spatially mismatched audiovisual stimuli, with the visual stimulus near but not exactly at the auditory stimulus location, across 6 difficulty levels; (5) bimodal tracking with triangular stimulation pattern: patients tracked sequential stimuli using a triangular pattern, pressing a button to indicate detection, with variations in allowed eye or head movements; (6) bimodal tracking with a quadrangular stimulation pattern: similar to the previous task but with a square-shaped tracking pattern; and (7) bimodal tracking with linear stimulation pattern: patients tracked visual stimuli on the upper part of the panel sequentially, reporting their detection with only eye or head movements allowed.

During bimodal focused stimulation training, difficulty increased by reducing the time delay between sound and LED light. In mismatched bimodal stimulation, difficulty involved both time delay and angle displacement. Participants advanced to the next level with at least 75% success in 2 cross-modal tests. This training was combined with treadmill gait training, lower limb strengthening, proprioception, and trunk control and balance exercises.

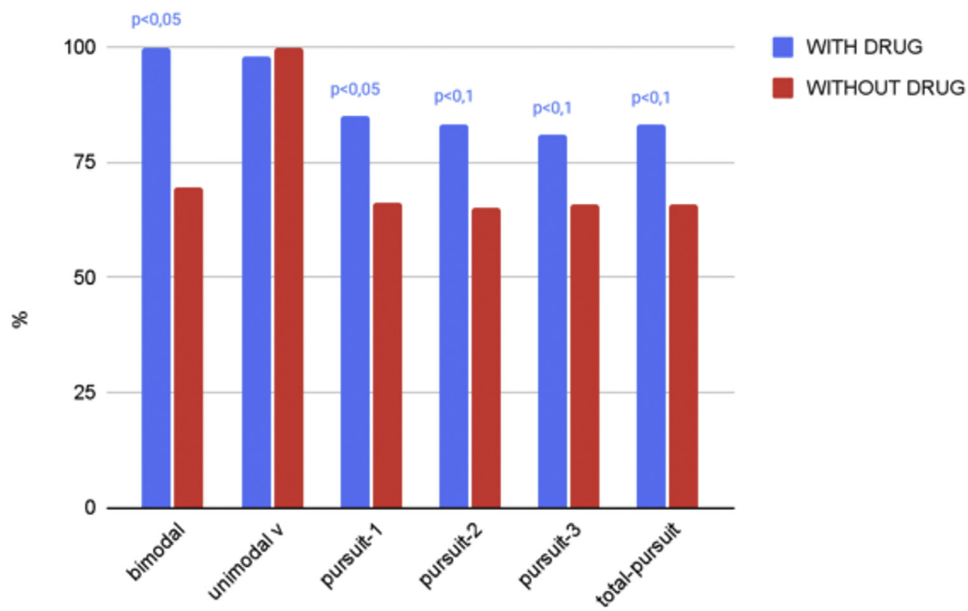

Fig 3 Success rate difference pretreatment.

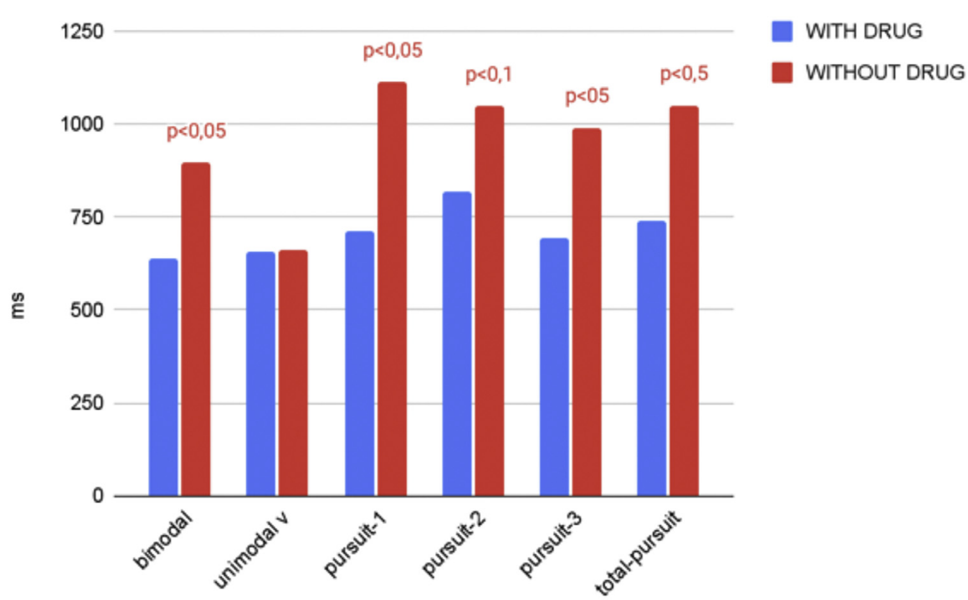

Fig 4 Response time difference pretreatment.

Results

The analysis of visual performance revealed notable differences in test results between sessions conducted with and without drugs (fampridine) (figs 3 and 4). Specifically, the patient showed more significant improvements in response times and success rates during assessments conducted without the administration of the drug; conversely, with the drug, the improvements were less marked.

Tests without drug administration showed more improvements than those with drug administration, including increased success rates for various tests (bimodal, pursuit 1, pursuit 2, pursuit 3, and total pursuit) and faster response times across the board (figs 5 and 6) compared with pretreatment performance results.

The 6-month follow-up indicated the maintenance of improvements in performance detected with the AV-Desk device compared with baseline, particularly in terms of success rates and response times without drug administration (significantly decreased in pursuit 1, pursuit 3, and total pursuit). Improvements from baseline to 6-month follow-up were significantly greater in tests without the drug, with significance levels for pursuit 3 and total pursuit for both parameters (figs 7 and 8).

The results of the fixation tests organized according to the Fuji classification and the BCEA method are reported in tables 1-3 and in figures 9-11.

After the treatment, there was an increase of 2 points in the BMI score, an increase of 11 points in the BBS score, an 8.3% increase in the speed of the 10mWT, and

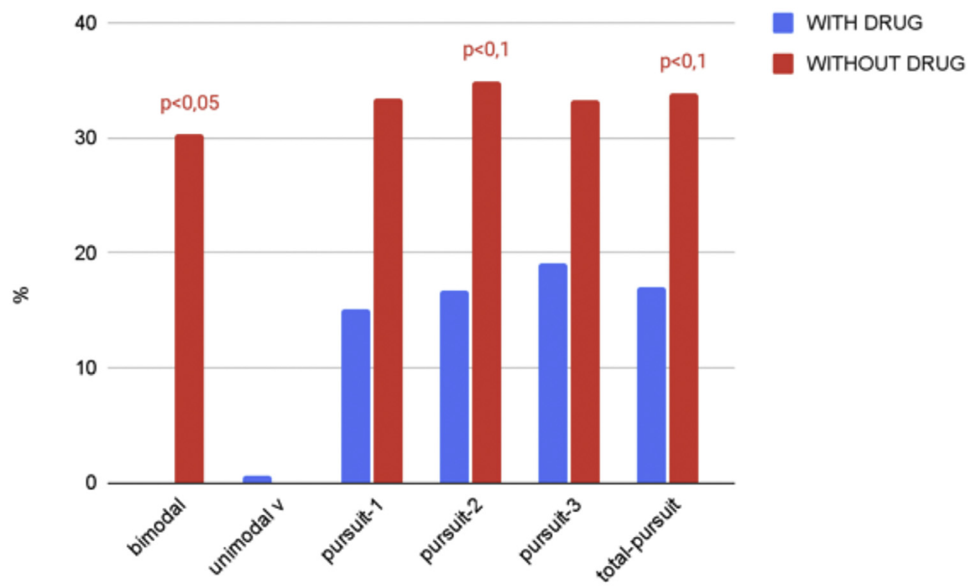

Fig 5 Success rate increment difference (baseline to posttherapy).

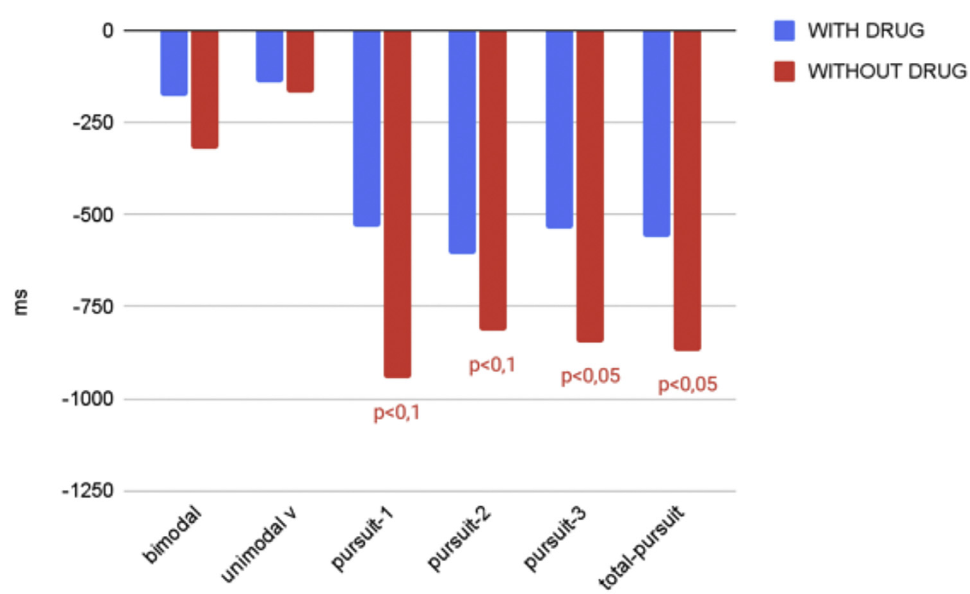

Fig 6 Response time reduction difference (baseline to posttherapy).

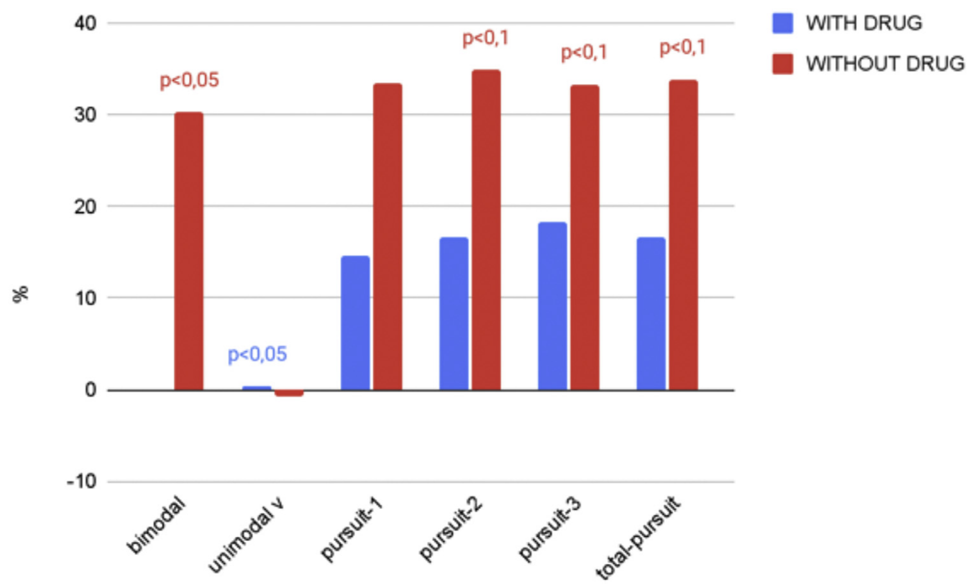

Fig 7 Success rate increment difference (baseline to 6mo follow-up).

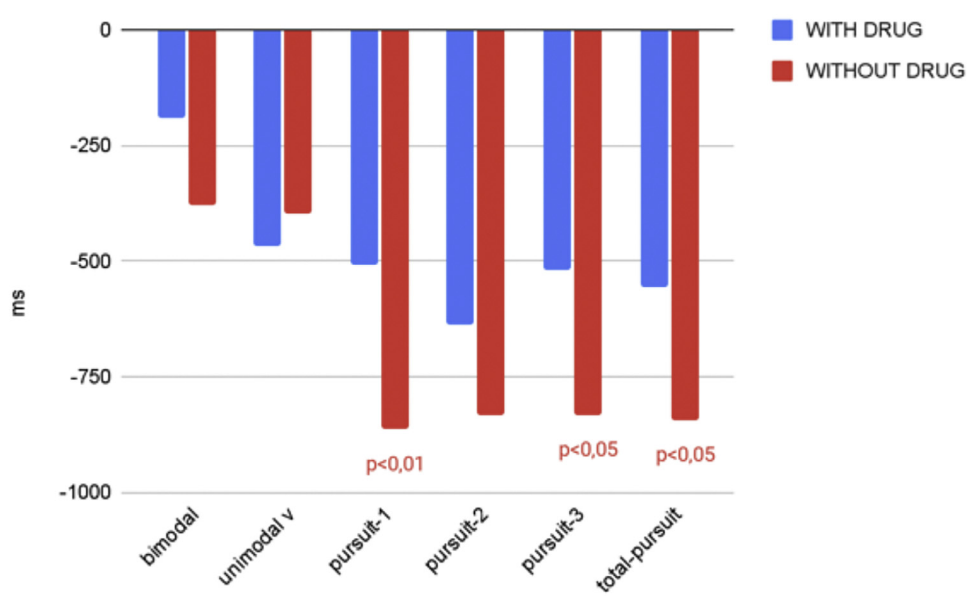

Fig 8 Response time reduction difference (baseline to 6mo follow-up).

a 47.52% reduction in the execution time of the time Up and Go test compared with the previous scores. Although there was a slight decline in the results at 6 months compared with those at posttherapy, they still exceeded those at baseline.

Discussion

Nystagmus and ataxia pose significant challenges in the field of rehabilitation. Without timely implementation of treatments, recovery from these conditions may be limited.[3,4,6]

Table 1 Fuji classification.

Parameters	Before Treatment		After Treatment		6 Mo Follow-Up	
	No Drug	Drug	No Drug	Drug	No Drug	Drug
Instable	0%	0%	0%	0%	0%	0%
Relatively instable	0%	0%	0%	0%	1%	0%
Stable	100%	100%	100%	100%	99%	100%

Table 2 Fixation stability of the BCEA right eye.

BCEA	Before Treatment		After Treatment		6 Mo Follow-Up	
	No Drug	Drug	No Drug	Drug	No Drug	Drug
1 SD area	0.7^2	0.2^2	0.2^2	0.2^2	0.2^2	0.2^2
2 SD area	2.0^2	0.6^2	0.6^2	0.6^2	0.6^2	0.6^2
3 SD area	3.5^2	1.1^2	1.1^2	1.1^2	1.1^2	1.1^2

Abbreviation: BCEA, bivariate contour ellipse area.

Table 3 Fixation stability of the BCEA left eye.

BCEA	Before Treatment		After Treatment		6 Mo Follow-Up	
	No Drug	Drug	No Drug	Drug	No Drug	Drug
1 SD area	1.5^2	1.5^2	1.5^2	1.5^2	1.5^2	1.5^2
2 SD area	4.2^2	4.2^2	4.2^2	4.2^2	4.2^2	4.2^2
3 SD area	7.4^2	7.4^2	7.4^2	7.4^2	7.4^2	7.4^2

Abbreviation: BCEA, bivariate contour ellipse area.

This case report outlines an innovative approach to nystagmus rehabilitation not previously described in the literature. The results obtained are encouraging, indicating a significant effect of rehabilitative treatment, regardless of pharmacologic intervention.

The BCEA method surpasses the Fujii rating scale by offering more comprehensive information and independent variability, enhancing its statistical value. Fixation stability, a new visual function biomarker, was assessed in a patient with vertical nystagmus using the Nidek MP-1 before and after treatment. Increased fixation stability was found to be clinically important and could serve as a secondary outcome measure in future studies.

Before the training, the patient experienced noticeable benefits from taking fampridine. However, after the training, there was a significant enhancement in both the effectiveness and the duration of the drug's action. Additionally, the patient demonstrated remarkable improvements in assessments conducted without the drug. This indicates that the training not only boosted the drug's performance but also enhanced the patient's overall condition, making them less reliant on the medication for managing their symptoms.

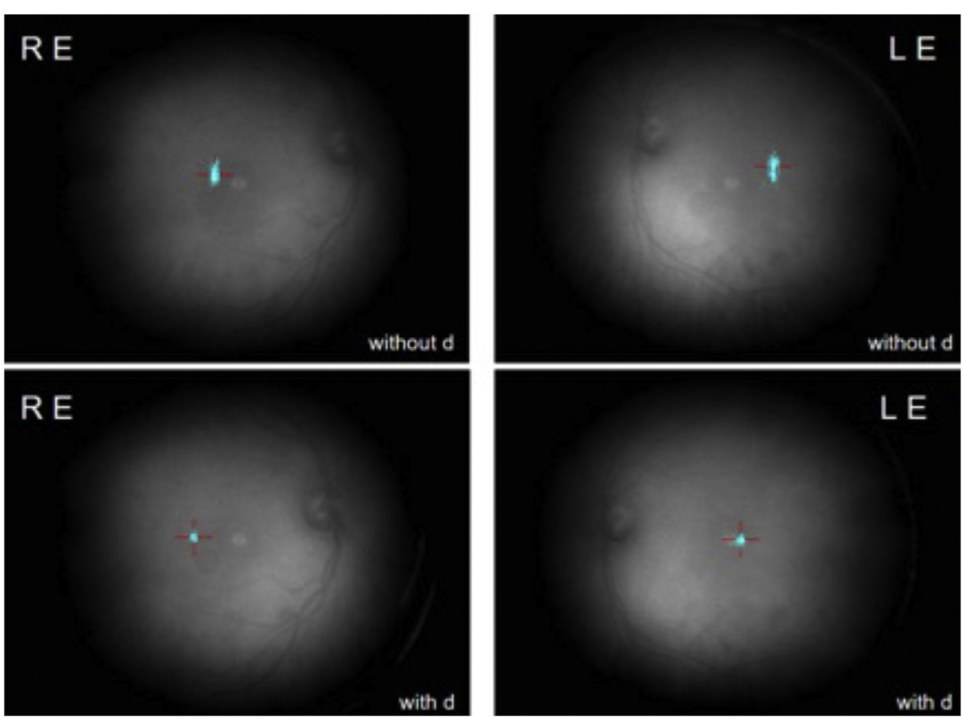

Fig 9 Fixation stability pretreatment in the left eye (LE) and right eye (RE) with and without drugs at baseline.

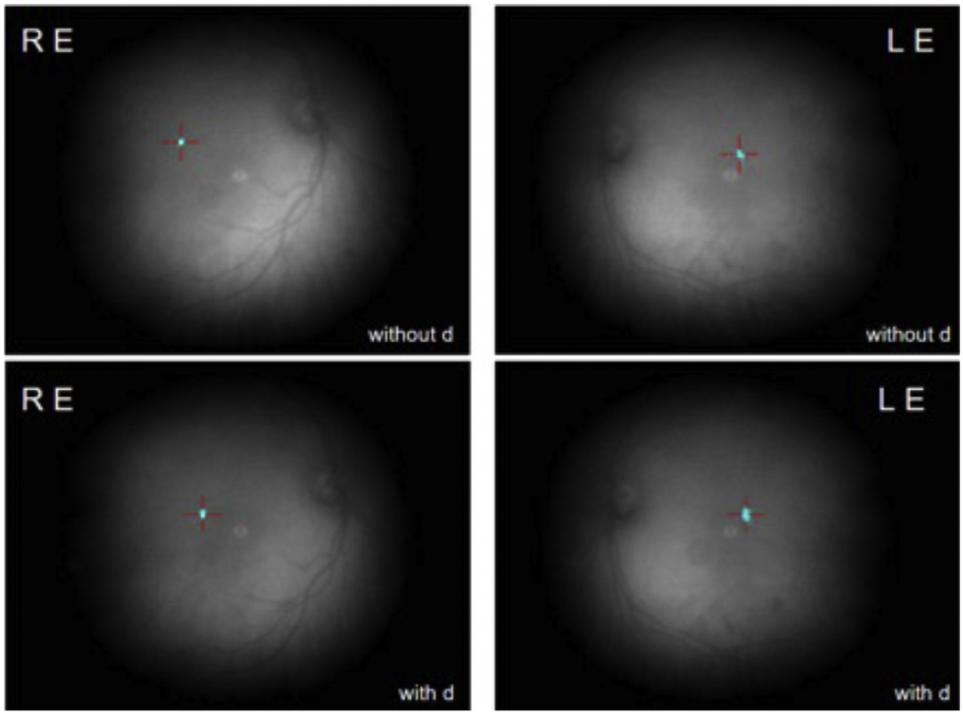

Fig 10 Fixation stability posttreatment in the left eye (LE) and right eye (RE) with and without drugs at post therapy.

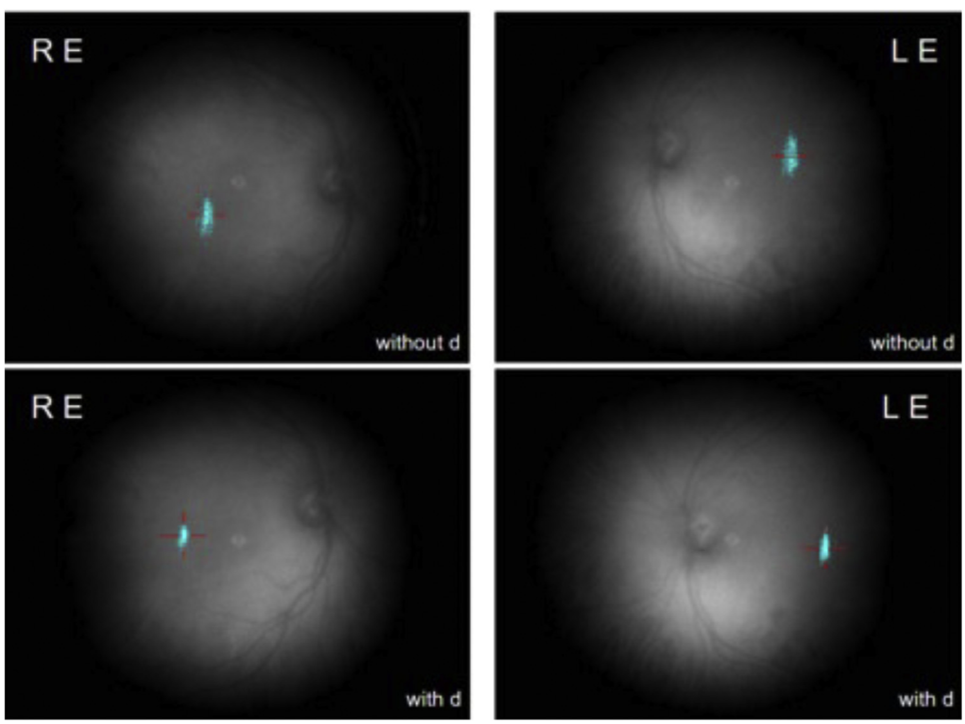

Fig 11 Fixation stability posttreatment in the left eye and right eye at 6-month follow-up.

The enhancements observed in clinical assessment scales suggest a significant treatment effect on the patient's motor improvement, particularly regarding balance (BBS [baseline] 28 vs BBS [posttherapy] 39). The patient reported satisfaction and improvement in daily activities, stopped the use of a rolling walker posttreatment, and relied solely on canes. This improvement is reflected in functional scales and quality-of-life questionnaires (SF12 [baseline] 45 vs SF12 [6mo follow—up] 85), which also indicate increased autonomy in both walking and activities of daily living (Barthel index [baseline] 65 vs Barthel index [6mo follow—up] 90).

Limitations

The case report is limited by its single-patient sample size, lack of a control group, and potential selection bias. More extensive, controlled studies are needed to validate these preliminary results.

Conclusions

The proposed protocol combining audiovisual stimulation with motor training appears to improve nystagmus and ataxia, enhancing patients' quality of life. Its synergistic effect shows promising results, prompting further case studies to confirm these findings.

Suppliers

a. AV-Desk; Linari Medical S.r.l.
b. Navis Software, version 1.7.0; Nidek Technologies Srl

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Disclosure

The investigators have no financial or nonfinancial disclosures to make in relation to this project.

Ethics statement

Ethics committee approval was not required because of the nature of this study (case report). The patient signed her informed consent for treatment and for the publication of this case.

Authorship Contributions/CRediT statements

D. A. conceptualized the study, wrote and reviewed the paper, cured editing. L. M., E. G., and L. A. cured data acquisition and interpretation, reviewed the paper. S. D. and C. C. reviewed the paper. All authors approved the submitted version and agree to be accountable for all aspects of the work.

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