Once-Daily Incremental Vestibular-Ocular Reflex Adaptation Training in Patients With Chronic Peripheral Vestibular Hypofunction: A 1-Week Randomized Controlled Study

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Background and Purpose: This was a double-blinded randomized controlled study to investigate the effects of once-daily incremental vestibulo-ocular reflex (VOR) training over 1 week in people with chronic peripheral vestibular hypofunction.

Methods: A total of 24 patients with peripheral vestibular hypofunction were randomly assigned to intervention (n = 13) or control (n = 11) groups. Training consisted of either x1 (control) or incremental VOR adaptation exercises, delivered once daily for 15 minutes over 4 days in 1 week. *Primary outcome*: VOR gain with video-oculography. *Secondary outcomes*: Compensatory saccades measured using scleral search coils, dynamic visual acuity, static balance, gait, and subjective symptoms. Between-group differences were analyzed with a linear mixed-model with repeated measures.

Results: There was a difference in the VOR gain increase between groups ($P < 0.05$). The incremental training group gain increased during active (13.4% ± 16.3%) and passive (12.1% ± 19.9%) head impulse testing ($P < 0.02$), whereas it did not for the control group ($P = 0.59$). The control group had reduced compensatory saccade latency ($P < 0.02$). Both groups had similarly improved dynamic visual acuity scores ($P < 0.05$). Both groups had improved dynamic gait index scores ($P < 0.002$); however, only the incremental group had improved scores for the 2 walks involving head oscillations at approximately 2 Hz (horizontal: $P < 0.05$; vertical: $P < 0.02$), increased gait speed ($P < 0.02$), and step length ($P < 0.01$) during normal gait, and improved total Dizziness Handicap Inventory ($P < 0.05$).

Conclusions: Our results suggest incremental VOR adaptation significantly improves gain, gait with head rotation, balance during gait, and symptoms in patients with chronic peripheral vestibular hypofunction more so than conventional x1 gaze-stabilizing exercises.

Video Abstract available for more insights from the authors (see the Video, Supplemental Digital Content 1, available at: http://links.lww.com/JNPT/A336).

Key words: *gaze stability, vestibular hypofunction, vestibular rehabilitation, vestibulo-ocular reflex*

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INTRODUCTION

Causes of unilateral vestibular hypofunction (UVH) include vestibular neuritis, labyrinthitis, and postsurgical interventions such as labyrinthectomy or neurectomy (ie, vestibular schwannoma). UVH is estimated to occur in over 9% of dizziness-related clinic visits.[1-3] The dynamic manifestations remain, and for many (∼40%) chronic functional impairments of dizziness, imbalance, oscillopsia, and fear of movement persist.[4-6]

The dominant clinical sign of having UVH is a weakened vestibulo-ocular reflex (VOR), thereby affecting the main vision stabilizing mechanism during rapid head movements. Compensatory saccades (CSs) are a hallmark feature of VOR hypofunction, which act to improve visual stability during head motion.[7] When the VOR is weak, retinal slip occurs, defined as motion of the visual world on the retina, resulting in blurred and unstable vision that is particularly distressing during high-frequency head motion.[8,9] Most patients with vestibular hypofunction report symptoms are most severe when they move their head quickly. Appropriately, the diagnosis of

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A.A.M. and M.C.S. hold US and Australian patents on the StableEyes device through their respective employers (NeuRA and Johns Hopkins).

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high-frequency VOR function is quantified with high-speed oculography using the high-frequency head impulse test.[10,11]

Patients with chronic vestibular symptoms can benefit from vestibular rehabilitation therapy (VRT).[12,13] Despite VRT's aim to improve the VOR via gaze stability exercises, typically known as x1 training,[14,15] very few studies have objectively demonstrated improvements in the VOR.[16-18] Most studies do not objectively measure the VOR with eye-tracking systems, but rather consider balance, subjective inventories, and other nonquantitative outcomes.[19-21] In a recent study, we showed that VOR adaptation is frequency selective and that in order to adapt/modify the physiologically relevant high-frequency VOR, adaptation training must involve high-frequency head rotations.[22]

Incremental VOR adaptation (IVA) training is a technique that can increase the VOR gain to one or both sides via controlling visual target motion with respect to the head, so that the gain demand required to stabilize the target (and minimize the retinal image error) increases in small increments, thereby demanding a gradual increase in the subject's actual VOR gain (eye/head velocity).[23,24] The IVA technique used for the intervention training has been used in 11 studies involving healthy subjects and 6 studies involving small numbers of patients with vestibular hypofunction.[22,24-32] These early studies in humans demonstrated significant increases of approximately 15% in VOR gain with just 15 minutes of training.

The aim of this double-blinded, randomized-controlled study was to investigate the outcomes of 2 gaze-stabilizing therapies (x1 and IVA training) applied over 4 days in 1 week in 24 subjects with chronic and stable peripheral vestibular hypofunction. The main outcomes were quantitative measures of VOR response, including gain and CS profiles, with secondary outcomes including dynamic visual acuity (DVA), gait, balance, and quality-of-life measures.

METHODS

Design

This was a double-blinded placebo-controlled study. Subjects were pseudorandomly allocated to either the control or intervention group. Figure 1 shows the study flow diagram. All data were collected at 1 site (Neuroscience Research Australia [NeuRA], Australia).

Participants

Patients attending the neurologist (P.D.C.) for diagnosis and treatment of vestibular hypofunction were provided an information leaflet that included the contact details of the research team at NeuRA. Twenty-four participants made contact between September 2016 and July 2018 and were offered the opportunity to participate in the study. Written consent was obtained prior to commencement and participants were free to withdraw from the study at any time in accordance with the University of New South Wales Human Ethics Committee.

Inclusion criteria were: (1) adults aged between 18 and 85 years, with the capacity to understand English and provide consent, (2) greater than 6 months of stable and isolated peripheral vestibular hypofunction as verified by the neurologist with a minimum of 2 assessments with the video head impulse test. Exclusion criteria were: (1) fluctuating peripheral vestibular condition including active benign paroxysmal positional vertigo (BPPV) and Meniere's disease, (2) central vestibular condition including vestibular migraine, (3) history of seizures, (4) recent motion sickness with vomiting, (5) blood pressure below 90 mm Hg systolic and 60 mm Hg diastolic, (6) heart rate below 60 beats per minute, and (7) cervical spine pain and range of motion less than 45° rotation in either direction (ie, leftwards or rightwards). Table 1 shows the baseline patient demographics for all participants according to their allocation. There were no statistically significant differences between groups with age, sex, and length of illness prior to commencing the study.

Randomization

A custom LabVIEW allocation program was written using *minimization* to place a (roughly) equal number of subjects into the 2 study groups (control and intervention), while maintaining an equal distribution across age (2 groups: <65 and ≥65) and gender (2 groups: male and female).[33] The allocation was concealed from everyone in the research team except for the operator of the allocation program. Allocation could not be guessed ahead of time.

Outcome Measures

The primary outcome measure of the intervention was VOR gain (eye velocity/head velocity) as measured by the video head impulse test. Active (self-generated) and passive (operator-generated) high-frequency head impulses were performed/delivered, which were rapid, unilateral, transient head rotations with peak amplitude approximately 10°, peak velocity approximately 150°/s, and peak acceleration approximately 2000°/s.[2] VOR gain values were objectively measured using the EyeSeeCam (Interacoustics, Denmark) monocular video-goggle system that measures angular eye and head velocity. EMA (Eye Movement Analyser, Balance and Vision Laboratory, NeuRA, Australia) was used to process all video head impulse data, with prepeak head velocity saccades removed for calculating gain values. The EyeSeeCam system and our techniques have been published elsewhere.[27]

Secondary measures included the oculomotor response (VOR + smooth pursuit + saccades) as assessed by the head thrust DVA test (a computerized system measuring visual acuity during horizontal head impulses[34-36]) and CS during head impulses. Subjects who normally wore glasses or contact lenses for distant viewing were instructed to wear them. The tumbling "E" optotype was displayed on the screen only while head velocity was between 150° and 300°/s for 40 ms, and was otherwise not visible. The DVA LogMAR score was calculated for both active and passive head impulses. CSs of the left eye were recorded in 3 dimensions using a monocular dual-axis scleral search coil system embedded in a silicon annulus. The instrumentation and technique using the same system and setup have been described in detail elsewhere.[24,37]

Other secondary measures included assessment of gait, balance and self-reported symptoms. Thirteen individual gait tasks were performed, which included the 8 used to calculate the dynamic gait index (DGI),[38] manually scored with the

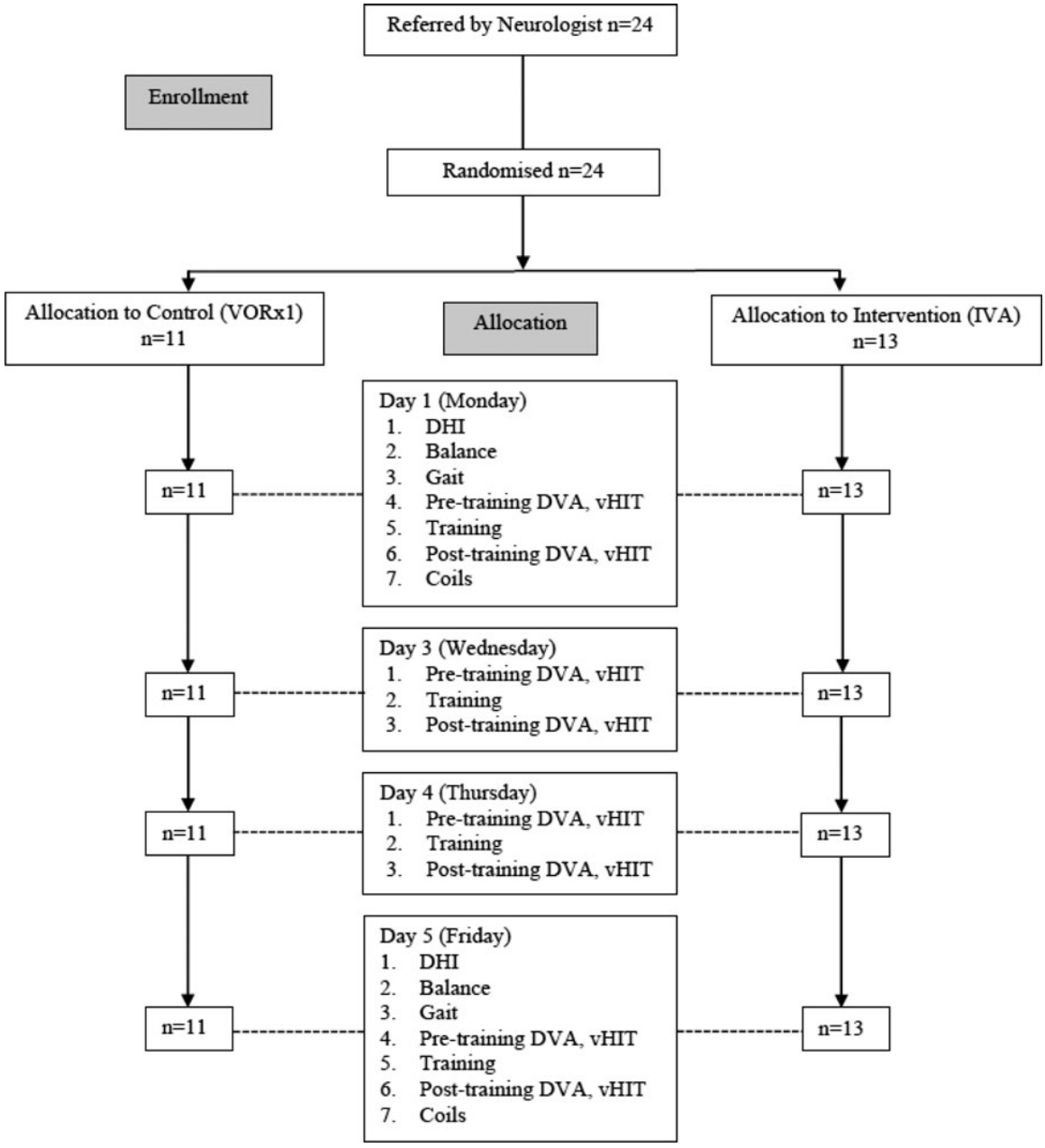

Figure 1. Study flow diagram.

4-point ordinal scale (ranging from 0 to 3) giving a maximum score of 24. Additional gait tasks included: walk while reading (holding a page of 12-font words at arm's length), walk while making rapid horizontal and rapid vertical head oscillation (moving in synchronization to a metronome set at 2 Hz), dual-task walking (serial subtraction by 7s), and walking with eyes closed—all performed at normal gait speed. All walks were performed on the GAITRite walkway (GAITRite, CIR Systems, New Jersey). The gait spatiotemporal outcomes were: self-preferred gait speed (meters/second), cadence (steps/meter), step length (cm), and support base (cm) as reported by the GAITRite software (version 4.8.6). The rhythmicity outcome measures were the coefficient of variation (CV) for stride time, step width, step time, step length, and swing time. Calculations for CV Mean = ([(Left SD/Left Mean) + (Right SD/Right Mean)]/2) × 100, with SD and mean produced by GAITRite.

Standing balance was measured using the modified clinical test of sensory interaction for balance including the 4 test conditions—firm surface eyes open, firm surface eyes closed, foam surface eyes open, and foam surface eyes closed[39]—using a previously described protocol.[40] Center of pressure (COP) area (representative of the 95% confidence ellipse) (mm^2), mean speed (mm/s), root mean square, sway angle,

Table 1. Subject Demographics and Baseline Characteristics

Demographic	Control (n = 11)	Intervention (n = 13)	Significance
Age at start, y	68.39 ± 9.27	60.05 ± 15.22	$P = 0.13$
Sex			
Male	7	7	($\chi^2_{1,24} = 0.24$,
Female	4	6	$P = 0.63$)
Length of illness before start, mo	44.18 ± 50.63	46.23 ± 71.93	$P = 0.94$
Side effected			
Left	4	9	
Right	5	4	
Bilateral	2	0	
Diagnosis			
Neuritis	2	4	
Labyrinthitis	5	7	
Schwannoma	1	0	
UVD following concussion	1	0	
CPA meningioma	1	0	
Radiotherapy (parotid tumor)	0	2	
Unknown	1	0	

Abbreviations: CPA, cerebellopontine angle; UVD, unilateral vestibular deafferentation.

anterior-posterior, mediolateral, and frequency (80% power) were objectively measured with a force platform, Xtran load cell S1 (Applied Measurement, Victoria, Australia), COP accuracy 0.1 mm, precision 0.05 mm, data captured at 100-Hz sample rate.[41] We measured the Dizziness Handicap Inventory (DHI), which is a self-reported scale that quantitates the level of disability and handicap on 3 subscales: physical, emotional, and functional.[42]

Training

Both groups used the StableEyes rehabilitation device.[30,32] StableEyes consists of a lightweight head unit with 9D IMU (3D magnetometer, gyroscope and accelerometer) (Pololu Corporation, USA) and electrostatic MEMS micromirror (Mirrorcle Technologies Inc, USA) that dynamically controls the 2D position of a 1-mW red laser projected on a wall 1 m in front of the subject, which is a programmable function of head motion. StableEyes is controlled via a lightweight control unit (on a necklace) with touchscreen interface tethered by cable to the head unit. StableEyes is currently used for research purposes only and is not commercially available. StableEyes was set to either control or intervention mode based on the subject allocation, and blinded to all other researchers including the operator/assessor. All subjects had their passive and active VOR gain measured prior to training each day. The active VOR gain (rounded up to the nearest 0.05) was entered in the StableEyes system as the starting gain demand value for all subjects (ie, the assessor treated each subject as if they belonged to the intervention group). However, if the device was in control mode, the starting gain value was overwritten (unknown by the operator) and set to a fixed value of 1.0. If the subject had a unilateral lesion, the normal "contralesional" side was set to a gain demand of 1.0. If the subject had bilateral vestibular hypofunction, the starting gain demand was set at the VOR gain as measured for each ear. For example, if the left ear gain was 0.33 and the right ear gain was 0.67, then the starting gains set by the operator were 0.35 for the left and 0.70 for the right. When the device generates a VOR demand equal to the subject's starting gain, they should experience no retinal image slip during head impulses. Training for both groups consisted of self-generated repeated left-right high-acceleration head impulses for 15 minutes wearing "StableEyes."[25,29] For the IVA group, the ipsilesional VOR gain demand incremented automatically by 0.1 every 90 seconds of training, whereas for the control group the gain demand remained fixed at 1. Training was performed in a near-dark room (<1 lux) with the only visible light (laser) emitted by the training device. All training parameters were exactly the same for control and intervention groups, apart from the difference in device modes that were indistinguishable to the subject (ie, in both control and intervention modes patients found it difficult to track the laser target due to their vestibular hypofunction).

To determine whether the IVA or x1 training paradigm influenced training performance over the 4 training sessions, we measured 3 training parameters: the total number of head impulses, the number of head impulses above 150°/s (velocity required for predominantly vestibular-mediated gaze stabilization) termed "ideal head," and the number of head impulses that were above 150°/s with no saccades prior to peak head velocity (number of head impulses that provided smooth retinal image slip feedback) termed "ideal eye and head."

Data Analysis

Data were analyzed using SPSS version 23 (IBM, USA) and Excel 2013 (Microsoft, USA) software. Sample size was calculated using G*Power 3.1.9.4 (Universitat Kiel, Germany). A *P* value below 0.05 was considered statistically significant. Data were compared using a linear mixed model (LMM) with repeated measures when data were obtained over multiple time points. Independent variables included (when appropriate): subject *ID*, subject *group* (control, intervention), *day* (1, 3, 4, 5), head rotation *type* (active, passive), head rotation *side* (ipsilesional and contralesional), *time* (pretraining, posttraining), *DGI* test (1, 2, 3, 4, 5, 6, 7, 8), *gait* test (normal, reading, horizontal, vertical), and standing *balance* test ("eyes open firm surface," "eyes closed firm

surface," "eyes open foam surface," "eyes closed foam surface"). Dependent variables for VOR analysis were analyzed separately and included: gain, total number of head impulses, number of "ideal head" impulses, number of "ideal eye and head" impulses, gain change (difference between same-day pre- and posttraining gains); first CS onset (latency) and first CS peak velocity; DVA score, DVA score change (difference between same-day pre- and posttraining DVA scores); DHI total, DHI total change (difference in score between days 1 and 4) and the corresponding variables for the subdomain scores (functional, emotional, and physical); DGI total, DGI total change (difference in total between days 1 and 4) and the score for each of the 8 DGI walks; gait rhythmicity parameters (step time CV, step length CV, step width CV, swing time CV, stride time CV, gait speed, cadence, step length, support base) and standing balance parameters (time to fall, COP area, COP speed). Between-group and within-group (repeated-measures) independent variables were treated as follows. Independent variables with 3 or more levels that significantly affected the dependent variable (ie, the outcome) were further analyzed using pairwise comparison with Bonferroni correction. When an independent variable did not significantly affect an outcome, those data were pooled (ie, the variable was removed from the model). The 1-sample *t* test was used when comparing a mean to zero. Eleven subjects per group with 4 repeated measures detects a change of 0.014 in primary outcome (or 2.8% change in VOR gain in someone with 50% of normal starting function) with 80% power. The statistical interaction of group and day (group × day) was reported as an indicator of training effect between groups. Ipsilesional data were used, unless specified. Linear regressions were performed to examine the relationship between subject age or length of illness with ipsilesional gain change, for both the active and passive VOR and for both groups (ie, a total of 8 linear regressions were performed). A slope coefficient that significantly differed from zero indicated a significant relationship. Differences in proportions between groups were analyzed using the χ^2 test. Pooled data are described as mean ± 1 SD.

RESULTS

There were no reported adverse effects including no additional dizziness or nausea, apart from intermittent cervical muscle soreness, which lasted no more than 1 day. There was no difference in ipsilesional and contralesional active head impulses during training in terms of: the total number of head impulses ($F_{1,44} = 0.01$, $P = 0.93$), the subset of those head impulses with peak velocity above 150°/s ("ideal head"; $F_{1,45} = 0.05$, $P = 0.83$), and the subset of those head impulses with no saccades ("ideal eye and head"; $F_{1,43} = 1.33$, $P = 0.72$). Table 2 shows these 3 parameters for each day, with pooled ipsilesional and contralesional head motion data, for control and intervention groups. The total number of head impulses was not different between groups ($F_{1,44} = 0.07$, $P = 0.79$) or days ($F_{3,83} = 2.07$, $P = 0.11$), nor was there an interaction between group and days ($F_{3,83} = 1.63$, $P = 0.19$), suggesting that the number of head impulses did not change with days more so for 1 group. Similarly, the number of "ideal head" impulses was not different between groups ($F_{1,45} = 1.34$, $P = 0.25$), nor was there an interaction between group and days ($F_{3,80} = 0.95$, $P = 0.42$), but day was significant ($F_{3,76} = 5.46$, $P < 0.005$), with (only) day 1 significantly lower than days 3, 4, and 5 (pairwise comparisons with day 1, $P < 0.05$). The intervention group had 25% to 42% (range across days) more "ideal eye and head" impulses compared to the control group ($F_{1,43} = 4.92$, $P < 0.02$). However, there was no significant interaction between group and days ($F_{3,100} = 0.24$, $P = 0.87$). Day was significant ($F_{3,100} = 5.46$, $P < 0.005$) with (only) day 1 significantly lower than days 3, 4, and 5 (pairwise comparisons with day 1, $P < 0.05$).

Pretraining VOR Gain Across Days

The active and passive ipsilesional starting VOR gains (pretraining day 1) were significantly higher in the control (passive: 0.49 ± 0.20, active: 0.68 ± 0.18), compared to the intervention group (passive: 0.41 ± 0.15, active: 0.57 ± 0.12) (group: $F_{1,49} = 4.33$, $P < 0.05$, type: $F_{1,49} = 15.8$, $P < 0.0001$). In contrast, the contralesional starting VOR gains were not different between control (active and passive gains pooled: 0.91 ± 0.10) and intervention groups (0.95 ± 0.06) (group: $F_{1,41} = 2.2$, $P = 0.15$), nor were they affected by whether the head impulse was active or passive (type: $F_{1,41} = 0.45$, $P = 0.51$). Figure 2 shows a representative subject from the control and intervention groups.

Table 3 shows the daily ipsilesional pre- and posttraining active and passive VOR gains for the control and intervention groups. There were significant differences in ipsilesional pretraining active and passive VOR gains irrespective of the group (type: $F_{1,48} = 16.6$, $P < 0.0001$). There was not a significant difference between groups ($F_{1,48} = 0.55$, $P = 0.46$); however, there was a significant interaction between group and day ($F_{3,109} = 2.8$, $P < 0.05$), suggesting training most affected the intervention group. For the intervention group, there were

Table 2. Training Parameters

Group	Day	Total Head Impulses Mean ± SD	Ideal Head Impulses Mean ± SD	Ideal Head and Eye Impulses Mean ± SD
Control	1	111.42 ± 52.16	57.42 ± 32.20	30.25 ± 29.60
(VORx1)	3	117.17 ± 30.50	71.75 ± 23.23	49.83 ± 25.90
	4	123.46 ± 53.21	78.31 ± 39.29	51.00 ± 40.34
	5	132.46 ± 46.06	78.23 ± 27.05	49.38 ± 35.96
Intervention	1	110.54 ± 37.76	65.15 ± 27.36	43.08 ± 20.16
(IVA)	3	136.46 ± 46.41	80.62 ± 40.70	62.46 ± 43.94
	4	134.42 ± 56.92	90.67 ± 35.88	68.08 ± 37.43
	5	132.83 ± 42.16	92.75 ± 36.07	70.17 ± 44.30

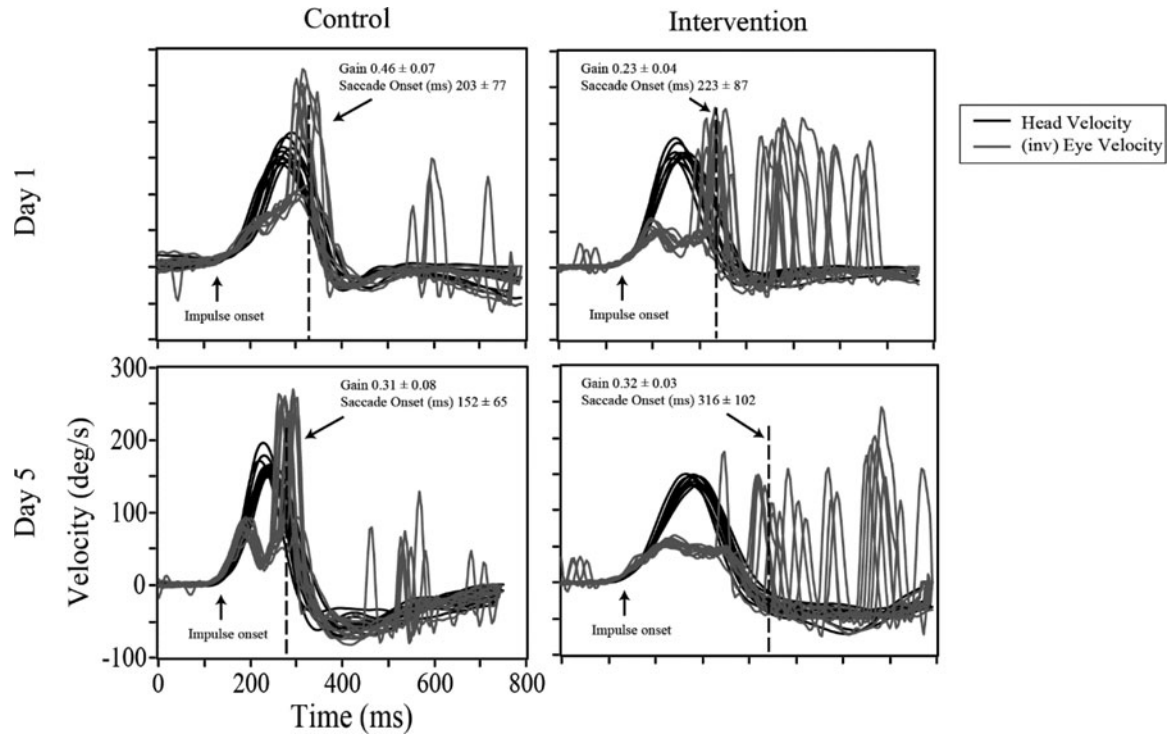

Figure 2. Video head impulse raw pretraining data from a subject in the control group (x1) and a subject in the intervention group (IVA), recorded on day 1 and day 5 (3 days of training). The head impulse eye (gray) and head (black) velocity traces are superimposed. Mean (SD) vestibulo-ocular reflex (VOR) gains and first saccade onsets (latencies) are shown. The dashed line is the mean latency for the compensatory saccades.

significant changes in active and passive ipsilesional pretraining VOR gains between days (day: $F_{3,46} = 3.61$, $P = 0.02$; type: $F_{1,24} = 13.65$, $P < 0.001$), with passive gain increasing from 0.41 ± 0.15 on day 1 to 0.45 ± 0.10 on day 5 (12.1% ± 19.9%; see Figure 3, top right panel) and the active gain increasing from 0.57 ± 0.12 (day 1) to 0.64 ± 0.13 (day 5) (13.4% ± 16.3%; see Figure 3, top left panel). In contrast, the control group pretraining passive gain decreased from 0.49 ± 0.20 (day 1) to 0.46 ± 0.20 (day 5) (−2.8% ± 10.7%) and active gain decreased from 0.68 ± 0.18 (day 1) to 0.64 ± 0.19 (day 5) (−5.4% ± 9.6%); however, these decreases were not significant (day: $F_{3,63} = 0.65$, $P = 0.59$; type: $F_{1,24} = 6.08$, $P < 0.05$).

VOR Adaptation Across Days

There was a significant difference in ipsilesional VOR adaptation (difference between pre- and posttraining gains per session) between control and intervention groups ($F_{1,69} = 15.8$, $P < 0.0001$), but there was no interaction between group and day ($F_{3,87} = 0.79$, $P = 0.50$), suggesting that adaptation did not change with day more so for one group. Adaptation was not different between active and passive testing (type:

Table 3. Daily Ipsilesional Active and Passive VOR Gain Values, Pre- and Posttraining

		Control			Intervention		
Test	Day	Pretraining Mean ± SD	Posttraining Mean ± SD	Gain Change	Pretraining Mean ± SD	Posttraining Mean ± SD	Gain Change
Passive	1	0.487 ± 0.20	0.483 ± 0.20	−0.004 ± 0.05	0.412 ± 0.15	0.448 ± 0.13	0.040 ± 0.06
	3	0.459 ± 0.20	0.436 ± 0.20	−0.026 ± 0.05	0.440 ± 0.14	0.470 ± 0.13	0.034 ± 0.04
	4	0.477 ± 0.21	0.485 ± 0.21	0.009 ± 0.03	0.437 ± 0.14	0.456 ± 0.13	0.021 ± 0.04
	5	0.458 ± 0.20	0.441 ± 0.18	−0.019 ± 0.05	0.445 ± 0.10	0.478 ± 0.11	0.037 ± 0.05
Change	1-5	−2.8% ± 10.7%			12.1% ± 19.9%[a]		
Active	1	0.684 ± 0.18	0.651 ± 0.17	−0.020 ± 0.08	0.572 ± 0.12	0.620 ± 0.11	0.053 ± 0.07
	3	0.664 ± 0.19	0.660 ± 0.19	−0.004 ± 0.05	0.620 ± 0.13	0.632 ± 0.11	0.012 ± 0.03
	4	0.635 ± 0.20	0.664 ± 0.19	0.020 ± 0.05	0.595 ± 0.16	0.614 ± 0.14	0.021 ± 0.06
	5	0.637 ± 0.19	0.637 ± 0.19	0 ± 0.04	0.643 ± 0.13	0.672 ± 0.13	0.032 ± 0.04
Change	1-5	−5.4% ± 9.6%			13.4% ± 16.3%[a]		

Abbreviation: VOR, vestibulo-ocular reflex.
[a]Denotes statistically significant difference ($P < 0.05$).

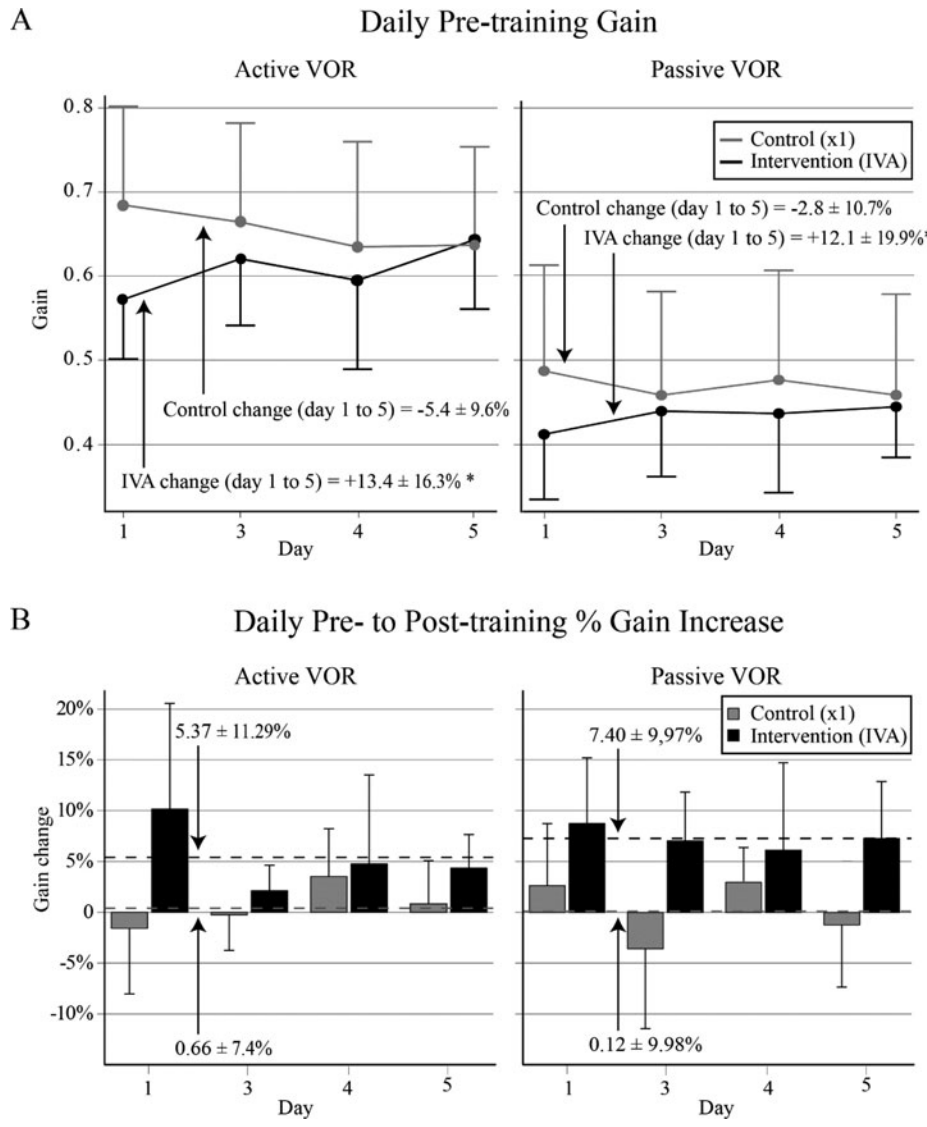

Figure 3. (A) Pretraining vestibulo-ocular reflex (VOR) gains (means and SD) recorded each day with active and passive head impulse testing for both the control (x1) and intervention (IVA) groups. (B) Percentage change (mean and SD) in VOR gain after each training session for active and passive head impulse testing for both groups. The mean change over the week for each group is shown with the dashed line.

$F_{1,69} = 0.28$, $P = 0.60$) or between days ($F_{3,86} = 1.61$, $P = 0.19$). For the intervention group, IVA training resulted in significant VOR adaptation (1-sample t test, $t = 5.74$, $P < 0.0001$), with a mean increase over the 4 days of 6.39% ± 11.29% for the pooled active and passive VOR (see Figure 3). In contrast, for the control group x1 training resulted in no significant adaptation (1-sample t test, $t = 0.44$, $P = 0.66$) with a change of 0.38% ± 8.79%.

Effects of Age and Length of Illness on VOR Adaptation

The effect of subject age on ipsilesional gain change (%) (pretraining day 1 to pretraining day 5) was evaluated. In the intervention group, there was a close to 5% significant trend between increased subject age and higher active VOR adaptation (active VOR: $R^2 = 0.21$, slope coefficient = 0.36, $F_{1,11} = 3.0$, $P = 0.11$; passive VOR: $R^2 = 0.03$, slope coefficient = 0.23, $F_{1,11} = 0.31$, $P = 0.59$). For the control group, subject age did not have a significant effect on VOR gain adaptation over the week (active VOR: $R^2 = 0.11$, slope coefficient = −0.24, $F_{1,9} = 1.0$, $P = 0.35$; passive VOR: $R^2 = 0.01$, slope coefficient = −0.07, $F_{1,9} = 0.05$, $P = 0.83$). The length of illness (prior to the start of the study) did not affect VOR adaptation (% gain change) for both the intervention (passive VOR: $R^2 = 0.03$, slope coefficient = −0.05, $F_{1,11} = 0.31$, $P = 0.59$; active VOR: $R^2 = 0.01$, slope coefficient = −0.01, $F_{1,11} = 0.02$, $P = 0.89$) and control groups (passive VOR: $R^2 = 0.07$, slope coefficient = 0.04, $F_{1,11} = 0.57$, $P = 0.47$; active VOR: $R^2 = 0.03$, slope coefficient = 0.02, $F_{1,11} = 0.2$, $P = 0.66$).

Compensatory Saccades

CSs were measured on days 1 and 5 post-training. For ipsilesional rotations there was a significant difference in first CS onset (latency) between control and intervention groups ($F_{1,30} = 7.8$, $P < 0.01$). There was a significant interaction between day and group, with the latency changing significantly between days only for the control group ($F_{1,30} = 5.6$, $P < 0.03$). There was no difference in CS latency between passive and active head movements, so these data were pooled ($F_{1,30} = 2.9$, $P = 0.10$). For the control group, the ipsilesional first CS latency went from 271 ± 98 ms on day 1 to 193 ± 117 ms on day 5, a significant decrease of approximately 80 ms ($F_{1,13} = 4.7$, $P < 0.05$). In contrast, for the intervention group the latency went from 152 ± 63 ms on day 1 to 184 ± 82 ms on day 5, a nonsignificant increase of approximately 30 ms ($F_{1,16} = 1.3$, $P = 0.28$). There was a significant increase in peak velocity for the first CS from day 1 (137° ± 48°/s) to day 5 (165° ± 60°/s) ($F_{1,27} = 4.7$, $P < 0.04$) (pooled across groups and active and passive) for both groups (group: $F_{1,30} = 2.2$, $P = 0.148$; group interaction with day: $F_{1,30} = 2.2$, $P = 0.148$) and for both active and passive testing ($F_{1,27} = 0.23$, $P = 0.63$). Figure 2 shows a representative subject from the control and intervention groups.

Head Thrust Dynamic Visual Acuity

There was no significant difference in ipsilesional head thrust DVA scores on day 1 (pretraining) between groups (LMM: $F_{1,45} = 0.093$, $P = 0.76$); however, there was a significant difference in scores between active and passive testing (LMM: $F_{1,45} = 5.4$, $P < 0.03$). There was no significant difference in daily pretraining scores between groups ($F_{1,48} = 0.5$, $P = 0.47$), nor was there a significant interaction between group and day ($F_{3,108} = 0.09$, $P = 0.97$) (that would have suggested the score changed significantly more so in one group), so the group data were pooled. Pretraining scores (groups pooled) improved over the 5 days (illustrated in Figure 4) with significant changes in the passive scores ($F_{3,57} = 4.3$, $P < 0.01$), decreasing from 0.50 ± 0.17 on day 1 to 0.37 ± 0.17 on day 5, as well as the active ($F_{3,54} = 3.0$, $P < 0.04$), decreasing from 0.39 ± 0.20 on day 1 to 0.28 ± 0.16 on day 5. Both groups showed the same improvement in head thrust DVA scores following training on each day (pre- to posttraining), and the changes were the same for active and passive testing (day: $F_{3,79} = 2.74$, $P < 0.05$; group: $F_{1,75} = 0.005$, $P = 0.95$; type: $F_{1,75} = 0.39$, $P = 0.54$), with a mean daily decrease (active and passive pooled) in the control group of 0.041 ± 0.16 (1-sample t test, $t = 2.58$, $P < 0.02$), and the intervention group of 0.040 ± 0.12 (1-sample t test, $t = 3.32$, $P < 0.002$).

Dizziness Handicap Inventory

Dizziness Handicap Inventory was measured pretraining on day 1 and day 5. Table 4 shows the change in the DHI (and subdomains) between groups over 3 days of training (days 1, 3, and 4). There was no significant interaction between group and day ($F_{1,22} = 0.10$, $P = 0.75$), suggesting that training had not resulted in a significant difference in total scores between control and intervention groups. However, only for the intervention group was there a significant reduction from baseline for: total score ($F_{1,13} = 12.5$, $P < 0.01$), functional score ($F_{1,13} = 12.1$, $P < 0.01$), and emotional score ($F_{1,13} = 5.4$, $P < 0.04$).

Dynamic Gait Index

Dynamic gait index was measured pre-training on day 1 and day 5. There was no difference in total scores between groups ($F_{1,22} = 1.7$, $P = 0.21$) or interaction between group and day ($F_{1,22} = 0.10$, $P = 0.75$); however, there was a significant difference between days ($F_{1,22} = 16.6$, $P < 0.002$). The total scores significantly increased in both the intervention group from 18.38 ± 4.07 (day 1) to 20.00 ± 4.10 (day 5) ($F_{1,12} = 9.9$, $P < 0.01$) and the control group from 16.36 ± 4.68 to 17.73 ± 3.74 ($F_{1,10} = 5.3$, $P < 0.05$), although only the intervention group had a DGI score on day 5 above 19, which is the threshold below which there is a significantly increased risk of falling.[43] The mean change in total scores for both the intervention (1.62 ± 1.85) and control (1.36 ± 1.96) groups was not statistically significant ($F_{1,22} = 1.7$, $P = 0.21$).

For the intervention group only, walk 3 (horizontal head turn at ~2 Hz) ($F_{1,12} = 4.6$, $P = 0.05$) and walk 4 (vertical head turn at ~2 Hz) ($F_{1,12} = 8.6$, $P < 0.02$) produced significant changes from day 1 to day 5. For walk 4 on day 5, there was a significant difference between groups in the number of

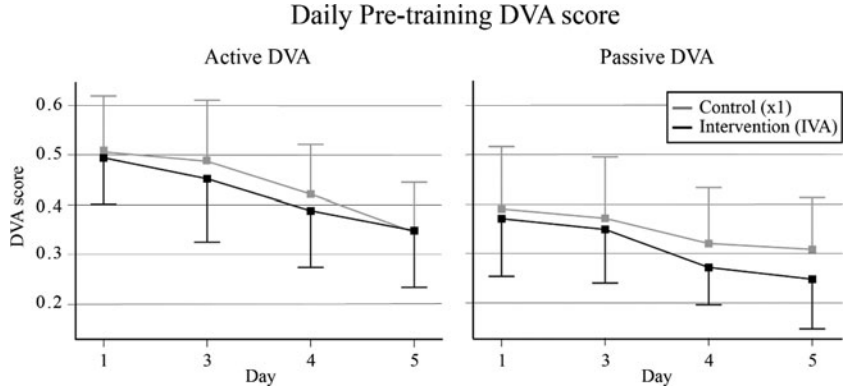

Figure 4. Daily pretraining head thrust dynamic visual acuity LogMAR (mean and SD) during passive and active head impulses for both groups.

Table 4. Dizziness Handicap Inventory[a]

Outcome	Control			IVA			Change Between Groups (*P* Value)
	d 1	d 5	Change (*P* Value)	d 1	d 5	Change (*P* Value)	
Total DHI	30.2 ± 14.8	27.5 ± 14.3	2.7 (0.202)	32.0 ± 14.8	25.7 ± 15.2	*6.3* (*0.004*)[b]	0.197
DHI-f	12.4 ± 6.7	10.9 ± 6.8	1.5 (0.305)	12.1 ± 7.2	9.6 ± 6.7	*2.5* (*0.004*)	0.384
DHI-e	8.5 ± 4.6	8.5 ± 4.7	0.0 (1.0)	9.1 ± 6.5	6.9 ± 5.5	*2.2* (*0.036*)	0.064
DHI-p	9.3 ± 5.8	8.0 ± 5.3	1.3 (0.089)	10.7 ± 3.9	9.3 ± 4.5	1.4 (0.146)	0.823

Abbreviations: DHI, Dizziness Handicap Inventory; IVA, incremental vestibulo-ocular reflex adaptation.
[a]Total score is the addition of the functional (DHI-f), emotional (DHI-e), and physical (DHI-p) subdomains.
[b]*Italicized P* values denote a statistically significant difference ($P < 0.05$).

subjects scoring the maximum of 3 (ceiling) ($\chi^2_{2,24} = 6.21$, $P < 0.05$); that is, of the 8 subjects that scored 3, 2 were from the control group (n = 11, 18.2% within group) and 6 were from the intervention group (n = 13, 46.2% within group).

GAITRite

Gait was measured pre-training on day 1 and day 5. Table 5 shows the values of 8 parameters captured during 4 gait tasks for each group, recorded on day 1 (pretraining) and day 5 (pretraining) following 3 training sessions. Compared to the other 3 tests, the gait task that involved turning the head horizontally at 2 Hz had the most number of rhythmicity parameters (5/9) with change from days 1 to 5 that was significantly different between groups (see group×day *P* values for the parameters of this test in Table 5). Four of the 9 rhythmicity parameters were the same across the 4 gait tasks: step time CV (gait task: $F_{3,86} = 2.22$, $P = 0.09$), support base (gait task: $F_{3,88} = 2.42$, $P = 0.07$), step length (gait task: $F_{3,88} = 1.20$, $P = 0.32$), and gait speed (gait task: $F_{3,88} = 1.66$, $P = 0.18$). With these 4 tests pooled, there was a significant interaction between group and day for gait speed suggesting training affected the gait speed differently depending on group ($F_{1,92} = 10.44$, $P < 0.02$). For the intervention group, there was an increase in gait speed from days 1 to 5 of 0.06 ± 0.39 m/s, whereas for the control group it decreased 0.17 ± 0.32 m/s. There was also a significant interaction between group and day for step length ($F_{1,90} = 1.53$, $P < 0.005$). For the intervention group, step length increased by 5.6 ± 5.9 cm, whereas for the control group it only increased by 2.07 ± 6.65 cm.

When evaluating the change in pre- to posttraining values, only 2 outcomes (gait speed and step length), both in the normal gait test, were greater than the minimal detectable change based on their mean values (denoted by [a] in Table 5) (meaningful detectable change for gait speed is 0.15 m/s and step length is 6.1 cm).[44] For each subject, the minimum detectable change was used to determine whether the outcome had improved (increased value) or whether it had stayed the same or decreased. For gait speed, there was a significant difference between groups in the number of subjects with detectable increase ($\chi^2_{2,24} = 3.96$, $P < 0.05$); that is, of the 7 subjects that had a detectable increase, 1 was from the control group (n = 11, 9.1% within group) and 6 were in the intervention group (n = 13, 46.2% within group). For step length, there was a close to 5% significant difference between groups ($\chi^2_{2,24} = 2.74$, $P = 0.09$); that is, of the 6 subjects that had a detectable increase, 1 was from the control group (n = 11, 9.1% within group) and 5 were in the intervention group (n = 13, 38.5% within group). Figure 5 illustrates the change in step length and support base for a subject in the intervention group from day 1 to day 4.

Standing Balance

Standing balance was measured pre-training on day 1 and day 5. Table 6 shows the mean time to fall for subjects in each group across each modified clinical test for sensory interaction of balance test condition. For condition 2 (firm surface eyes closed) only, there was a significant interaction between group and day, suggesting training affected the time to fall differently depending on group ($F_{1,21} = 4.6$, $P < 0.05$). For the intervention group, there was an increase in time to fall from days 1 to 5 of 0.84 ± 3.02 seconds, whereas for the control group it decreased 3.22 ± 5.92 seconds. Both groups significantly increased their time to fall for condition 4 (foam surface eyes closed) from days 1 to 5 ($F_{1,20} = 4.7$, $P < 0.05$) with the intervention group by 2.10 ± 4.50 seconds and the control group by 2.91 ± 6.34 seconds.

DISCUSSION

IVA training resulted in significantly increasing the pretraining VOR gain from day 1 to day 5 for both active and passive head-impulse testing by 13.4% and 12.1%, respectively. In contrast, x1 training showed a nonsignificant reduction of both active and passive VOR gains (−5.4% and −2.8%, respectively). To our knowledge very few studies have shown objective changes to the VOR, as measured with an eye-tracking system, following x1 gaze stabilization exercises in subjects with chronic and stable peripheral vestibular hypofunction (head impulse x1 training:[16]; sinusoidal x1 training:[17,18]). x1 training is endorsed by clinical practice guidelines to improve impairment and function[45]; however, it is usually performed using low-frequency sinusoids approximately 0.5 Hz with a low-contrast target. For example, Millar et al[18] showed no change in passive head impulse VOR after 5 weeks of sinusoidal gaze stability training that included x1 training, even though DVA and other functional measures did improve. We previously showed that low-frequency sinusoidal adaptation training results in context-specific low-frequency VOR adaptation.[22] The only study to report the effect of head impulse x1 training demonstrated an increase in VOR gain following 5 days of passive ipsilesional training; however, this was a case study based on a single subject.[16]

Table 5. A Selection of 4 Gait Tasks Performed on the GAITRite Mat

Gait Task and Parameter	Control (n = 11) d 1 Mean ± SD	Control (n = 11) d 5 Mean ± SD	Intervention (n = 13) d 1 Mean ± SD	Intervention (n = 13) d 5 Mean ± SD	Significance (*P* Value) Group × Day
Normal gait					
Step time CV mean	7.28 ± 8.01	3.79 ± 1.32	4.50 ± 2.84	5.17 ± 5.04	0.17
Step length CV mean	5.91 ± 2.08	5.74 ± 3.52	4.33 ± 3.76	4.71 ± 4.99	0.82
Swing time CV mean	7.23 ± 7.32	3.89 ± 2.10	4.83 ± 2.65	5.62 ± 6.62	0.19
Stride time CV mean	2.41 ± 1.56	2.69 ± 0.59	2.51 ± 1.50	3.08 ± 2.86	0.79
Step width CV mean	4.21 ± 1.95	4.15 ± 2.23	2.65 ± 1.15	3.88 ± 4.55	0.38
Gait speed, m/s	1.21 ± 0.33[a]	1.04 ± 0.33[a]	1.01 ± 0.30	1.09 ± 0.21	0.12
Cadence, steps/min	111.3 ± 10.2	108.3 ± 15.2	108.2 ± 14.6	109.9 ± 6.9	0.51
Step length mean, cm	57.93 ± 11.88	55.95 ± 11.18	54.61 ± 17.67[a]	62.38 ± 7.47[a]	0.21
SuppBase mean, cm	10.73 ± 3.19	9.71 ± 4.73	8.66 ± 3.27	9.10 ± 2.29	0.64
Reading gait					
Step time CV mean	5.50 ± 2.83	6.23 ± 5.05	6.63 ± 5.05	3.82 ± 1.63	0.06
Step length CV mean	7.56 ± 5.77	7.11 ± 5.16	8.12 ± 6.53	4.26 ± 2.81	0.10[b]
Swing time CV mean	7.20 ± 5.31	8.27 ± 7.17	8.82 ± 7.01	4.76 ± 2.08	*0.045*[c]
Stride time CV mean	3.82 ± 2.88	4.22 ± 2.75	4.79 ± 4.42	2.78 ± 1.47	0.15
Step width CV mean	5.73 ± 3.97	5.11 ± 2.89	6.91 ± 5.65	3.66 ± 1.98	0.14[b]
Gait speed, m/s	1.08 ± 0.31	0.93 ± 0.41	0.86 ± 0.32	0.95 ± 0.22	0.10
Cadence, steps/min	110.9 ± 11.0	107.6 ± 13.1	106.2 ± 13.7	102.14 ± 13.5	0.93
Step length mean, cm	51.90 ± 15.76	53.77 ± 14.56	53.19 ± 8.12	58.61 ± 7.16	*0.045*[b]
SuppBase mean, cm	11.54 ± 3.72	11.40 ± 4.04	9.45 ± 2.78	9.16 ± 3.97	0.95
Horizontal head gait					
Step time CV mean	5.56 ± 2.24	8.42 ± 7.49	10.25 ± 7.70	5.77 ± 3.50	*0.039*
Step length CV mean	9.11 ± 7.28	10.74 ± 8.26	15.24 ± 10.84	7.18 ± 5.20	*0.028*
Swing time CV mean	7.36 ± 5.35	12.39 ± 15.75	17.92 ± 17.72	8.41 ± 4.86	*0.048*
Stride time CV mean	4.08 ± 1.61	5.85 ± 6.25	8.55 ± 7.59	8.37 ± 3.23	*0.046*
Step width CV mean	6.39 ± 4.81	9.37 ± 9.50	11.81 ± 8.56	6.25 ± 3.72	*0.030*
Gait speed, m/s	1.18 ± 0.32	0.92 ± 0.45	0.95 ± 0.30	0.97 ± 0.23	0.14
Cadence, steps/min	124.9 ± 12.0	109.9 ± 29.4	115.9 ± 17.6	114.7 ± 13.8	0.22
Step length mean, cm	49.64 ± 14.32	54.63 ± 13.00	47.11 ± 11.75	55.25 ± 8.13	0.17[b]
SuppBase mean, cm	12.98 ± 3.17	13.12 ± 3.66	11.45 ± 4.38	9.63 ± 3.46	0.09
Vertical head gait					
Step time CV mean	9.93 ± 12.93	8.30 ± 9.34	9.10 ± 7.52	4.43 ± 2.56	0.56
Step length CV mean	13.00 ± 13.07	9.06 ± 8.89	9.49 ± 8.56	4.74 ± 3.59	0.88
Swing time CV mean	10.04 ± 11.64	9.38 ± 8.12	9.79 ± 8.50	6.38 ± 4.19	0.59
Stride time CV mean	4.14 ± 3.10	6.10 ± 6.89	6.07 ± 5.56	2.83 ± 1.36	0.11
Step width CV mean	10.71 ± 12.33	7.38 ± 7.52	7.29 ± 5.95	4.45 ± 2.73	0.92
Gait speed, m/s	1.21 ± 0.37	1.00 ± 0.46	1.08 ± 0.33	1.14 ± 0.21	0.13
Cadence, steps/min	124.1 ± 10.8	106.4 ± 29.0	119.8 ± 15.5	119.6 ± 12.9	0.14
Step length mean, cm	58.85 ± 12.21	57.02 ± 12.58	52.62 ± 14.67	61.71 ± 9.78	*0.029*
SuppBase mean, cm	12.85 ± 2.52	12.67 ± 1.88	10.51 ± 3.01	9.61 ± 3.85	0.57

Abbreviation: CV, coefficient of variation.
[a]Denotes a possible meaningful detectable change based on the difference in means.
[b]Denotes a statistically significant difference between groups ($P < .05$).
[c]*Italicized P* values denote a statistically significant difference for group-and-day interaction ($P < 0.05$).

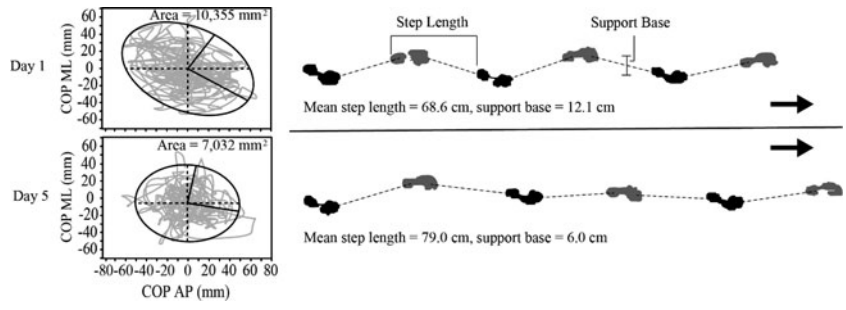

Figure 5. Raw balance and gait data for the same subject in the intervention group for day 1 and day 5. Center of pressure (COP) sway data (left panels) as captured by the force plate with subject eyes closed on foam surface for 30 seconds. Gait data (right panels) as captured by GAITRite illustrate step and stride during horizontal head turns (at 2 Hz) while walking the length of mat. Black footprints represent the right leg; gray footprints represent the left leg. Arrows indicate the walking direction. The dashed lines help illustrate these differences.

Table 6. Standing Balance Parameters

Balance Task and Parameter	Control		Intervention		Significance (*P* Value) Group × Day
	d 1 Mean ± SD	d 5 Mean ± SD	d 1 Mean ± SD	d 5 Mean ± SD	
Firm surface eyes open[a]					
COP area (95 ellipse), mm^2	445 ± 178	506 ± 201	524 ± 530	482 ± 292	0.51
COP mean speed, mm/s	17.2 ± 5.6	18.6 ± 7.0	16.4 ± 4.3	16.2 ± 5.1	0.34
Time to fall, s[b]	29.32 ± 2.12	30.00 ± 0.00	30.00 ± 0.00	30.00 ± 0.00	N/A
Firm surface eyes closed[c]					
COP area (95 ellipse), mm^2	1276 ± 798	1096 ± 654	1653 ± 1295	1493 ± 982	0.67
COP mean speed, mm/s	34.4 ± 11.5	30.6 ± 12.8	34.9 ± 12.3	39.4 ± 14.5	0.06
Time to fall, s[b]	27.28 ± 6.08	24.06 ± 9.82	29.16 ± 3.02	30.00 ± 0.00	*0.04*[d]
Foam surface eyes open[e]					
COP area (95 ellipse), mm^2	1150 ± 481	1169 ± 430	1040 ± 497	940 ± 512	0.51
COP mean speed, mm/s	32.5 ± 10.6	33.5 ± 13.5	30.7 ± 9.6	30.3 ± 12.8	0.72
Time to fall, s[b]	30.00 ± 0.00	30.00 ± 0.00	30.00 ± 0.00	30.00 ± 0.00	N/A
Foam surface eyes closed[f]					
COP area (95 ellipse), mm^2	5559 ± 2703	5622 ± 2471	8144 ± 2297	7059 ± 2976	0.14
COP mean speed, mm/s	97.1 ± 26.5	113.1 ± 39.9	128.1 ± 48.5	119.8 ± 26.7	0.29
Time to fall, s[b]	16.49 ± 12.91	19.41 ± 11.42	15.07 ± 10.53	17.17 ± 8.74	0.73

Abbreviations: COP, center of pressure; N/A, not available.
[a]Control n = 10, intervention n = 13.
[b]Control n = 11, intervention n = 13.
[c]Control n = 8, intervention n = 13.
[d]*Italicized P* values denote a statistically significant difference ($P < 0.05$).
[e]Control n = 9, intervention n = 13.
[f]Control n = 4, intervention n = 5.

Compensatory Saccades

The IVA group became less reliant on CS, with latency of the first saccade increasing by approximately 30 ms. In contrast, the control group reduced their latency by approximately 80 ms. At first glance this result may seem to suggest that the control group is benefiting most from the training because their saccade latency is being reduced. However, the presence of CS, along with low gain, is a hallmark feature of peripheral vestibular hypofunction.[10,46,47] When the VOR gain improves, the importance of CS for gaze stability is reduced.[48] In fact, CSs are minimal in persons with VOR gain close to unity.[46,49,50] Conventional x1 therapies can change saccade characteristics including latency.[18,36,48] This extravestibular mechanism is a compensation strategy whose contribution is roughly inversely proportional to the VOR gain.[46] Our data suggest that reduced CS latency as a result of x1 training comes at the cost of reduced VOR gain, which is the opposite of what VRT seeks to achieve (ie, improve vestibular function). In contrast, IVA training results in improved gain and a reduced role for CS.

Dynamic Visual Acuity

Dynamic visual acuity significantly improved by approximately 27% in both groups over the week for both passive and active head movements. Improved DVA scores following IVA training can be attributed to the improved VOR gain, which results in improved visual stability when moving the head.[48] In the control group, DVA scores most likely improved due to the greater role played by CS as previously reported. Herdman et al[51,52] showed via x1 gaze-stabilizing exercises that improved DVA scores were related to the characteristics of the CS (reduced latencies and increased peak velocity). Taken together, these findings suggest that gaze stability during head motion can be improved via 2 mechanisms: improved VOR gain (IVA training) or faster and larger saccades (x1 training).

Gait and Standing Balance

The 2 DGI walks that involved head movement, namely walk 3 (horizontal head turning) and walk 4 (vertical head turning), significantly improved only for the IVA group. This is despite the fact that DVA scores improved for both groups, which suggests that improvement in DVA is not the only explanation for improvement in gait. These 2 walks rely heavily on a peripheral vestibular signal (ie, intact VOR),[38] which projects from vestibular nucleus to the spinocerebellar circuitry important for gait.[53] Our data suggest that both IVA and x1 training improve dynamic visually acuity (ie, both groups had significantly improved total DGI score), but that the boost in peripheral vestibular signal (presumably occurring centrally)[24] due to IVA training results in additional improved gait during walks 3 and 4. IVA training significantly increased gait speed (compared to slowing down within the control group), as well as a greater increase in step length.[19,54,55]

Training

Subjects performing IVA training had significantly more "ideal eye and head" impulses compared with the x1 group, despite having significantly lower pretraining VOR gains on day 1. We hypothesize that the x1 gain demand for controls was a more difficult gaze stability task compared with IVA training given the larger difference between actual VOR gain and target gain demand, especially during the first half of training.

Relevance to Current Gaze Stabilization VRT

This study is the first to show the effect of IVA adaptation training over 1 week in a cohort of subjects with chronic

and stable peripheral vestibular hypofunction, compared with a similar group performing x1 exercises. Most studies have demonstrated a substitution (CS) or habituation mechanism with VRT that improves the function and quality of life, but none have shown substantial improvement in VOR gain in chronic patients.[16-18] Presumably, this is because training that leads to substitution and habituation are counter to VOR adaptation. For example, the earlier introduction of CS reduces the amount and duration of retinal image slip during rapid head movements, which is the main feedback mechanism driving VOR gain change.[56] Similarly, habituation lessens the drive for adaptive change because it desensitizes the response from a repeated stimulus.[57] It may well be that conventional gaze-stabilizing exercises are improving outcomes in patients through nonvestibular mechanisms, but at the cost of improving vestibular function.

Current Clinical Application of Findings

We recently showed that a low-cost easy-to-implement variation to IVA produced significant, albeit small (~2% after 1 session), increases in passive VOR gain in patients with peripheral vestibular loss.[58] In brief, patients trained their VOR by performing active continuous leftward/rightward sinusoidal head rotations while moving their outstretched hand in antiphase with their head. This technique is similar to x2 VOR adaptation training currently performed in some vestibular clinics, but with several major differences. First, the training is incremental in that the patients initially turn their head sinusoidally at 0.5 Hz (where the VOR plays a small role in visual stability) that increments 0.16 Hz every 90 seconds, until 2 Hz (where the VOR plays the predominant role). The correct head rotation frequency was achieved with the aid of a metronome. Second, the training was performed for 15 minutes. Third, the training was performed in darkness while the patient tracked a handheld battery-operated LED so that visual contrast was high. Variability in VOR gain demand due to the inherently poor synchronization between head and target (hand) movement could explain why adaptation was so small after 1 session using this technique. However, it is likely that with continued practice variability will reduce and adaptation will increase. Using the IVA x2 technique in healthy controls resulted in about one-third the adaptation observed when using StableEyes where head and target motion is perfectly synchronized.[22]

Limitations

There were several limitations with this study. One was that many comparisons with measures across many tests and systems were performed, which may have increased the chances of a statistical type 1 error (ie, false positives). Another is that the study was performed over only 1 week, which may have precluded an even greater effect of VOR gain change on improving gait and balance systems. Finally, a larger sample size with greater variety in peripheral loss cause might have led to more statistically significant results.

CONCLUSIONS

This study shows IVA improves VOR gain in patients with vestibular hypofunction, leading to improved balance, gait, and self-reported symptoms. In contrast, VORx1 exercises reduced VOR gain, but improved CS (a nonvestibular mechanism), resulting in only modestly improved gait, balance, and reported symptoms. Therefore, we recommend IVA be incorporated into VRT.

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C.N.R. collected data, analyzed data, made figures, and wrote manuscript. M.C.S. designed study and revised manuscript. P.D.C. diagnosed participants and revised manuscript. W.V.C.F. modified/developed data acquisition and data processing hardware/software, collected data. C.J.T. modified/developed data acquisition and data processing hardware/software, collected data. A.A.M. conceived study, designed study, collected data, analyzed data, modified figures, and wrote and revised manuscript.

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