Research Article

Combining Vestibular Rehabilitation and Noisy Galvanic Vestibular Stimulation for Treatment of Unilateral Vestibulopathy: A Randomized Controlled Trial

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Highlights

- nGVS can be considered as a powerful vestibular stimulus
- nGVS with VR can be promising for rehabilitating patients with UVP
- nGVS with VR can accelerate static and dynamic vestibular compensation after UVP

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ABSTRACT

Background and Aim: Vestibular Rehabilitation (VR) is a well-accepted treatment for Unilateral Vestibulopathy (UVP). Since noisy Galvanic Vestibular Stimulation (nGVS) improves the processing of vestibular inputs, we assessed the synergistic effects of adding nGVS to vestibular rehabilitation for the treatment of UVP.

Methods: Patients with UVP were randomly assigned into two groups receiving either VR for four weeks (VR group, n=12) or VR for four weeks combined with nGVS for three sessions (VR+nGVS group; n=12). Outcome measurements were postural control parameters measured with eyes open/closed conditions on hard/soft surfaces, Vestibulo-Ocular Reflex (VOR) gain, and Dizziness Handicap Inventory (DHI) scores that were assessed at baseline and after four weeks.

Results: All postural control parameters, mean total and subscale scores of DHI, and mean VOR gain in directions of affected canals significantly improved in both groups after interventions ($p<0.05$) except mean mediolateral displacement in conditions with eyes closed on hard surface and with eyes open on soft surface, mean mediolateral velocity in conditions with eyes closed on hard surface, ability to stance with eye closed condition on soft surface and mean emotional subscale of DHI in VR group. Improvements were significantly higher in postural control outcomes measured in stances with eyes closed on hard surface and with eyes open and closed on soft surface, mean VOR gains in directions of affected horizontal and anterior canals, and mean total, physical, and functional scores of DHI in VR+nGVS group ($p<0.05$).

Conclusion: When combined with VR, nGVS shows additional therapeutic effects in UVP patients.

Study protocol location: https://irct.ir/trial/58375

IRCT Registration Number: IRCT20160131026279N4

Keywords: Unilateral peripheral vestibulopathy; vestibular compensation; galvanic vestibular stimulation; vestibular rehabilitation; postural control

Introduction

Unilateral Vestibulopathy (UVP) is considered the third most common peripheral vestibular disorder after benign paroxysmal positional vertigo and Meniere's disease [1]. In the general population, the lifetime prevalence of UVP is 0.2% [2]. UVP leads to the emergence of complex symptoms and disorders, which usually occur in three areas: eye control, posture control and cognitive abilities [3]. These patients complain of equilibrium and gait impairment, vertigo, dizziness, and oscillopsia [4, 5]. The most common treatment and rehabilitation approach in unilateral vestibular disorders is structured physical exercises in the form of Vestibular Rehabilitation (VR) [6]. Although the effect of vestibular rehabilitation exercises on improving patients' balance and accelerating the recovery process has already been proven in several past studies [6-9], it may not completely compensate for the problems patients with UVP face in their real daily life,especially in situations where their vestibular system is challenged, such as walking up and down stairs, walking on the pavement, sandy beaches, and low light environments recently, Galvanic Vestibular Stimulation (GVS) has been introduced as another stimulation that can affect the vestibular system. GVS is a non-invasive technique that activates different parts of the peripheral vestibular system, vestibular nuclei, and several points in the cortical and subcortical areas through electrodes placed on the mastoid [10]. In normal people, GVS improves dynamic walking [11], postural [12] and locomotor stability [13]. In patients with Parkinson's disease, GVS improves motor and autonomic responsiveness, affects motor performance in manual pursuit behaviors, reduced the total sway with eyes closed and improves balance and movement symptoms [14, 15]. It seems that adding a suitable amount of noise to GVS improves the perception and processing of vestibular inputs [16]. The underlying mechanism, known as stochastic resonance, is the improvement of a nonlinear system's responsiveness to weak input signals in the presence of a little amount of random noise [17, 18]. Noisy GVS (nGVS) is considered a potent and reasonably pure vestibular stimulus, affecting the output motor activities of the vestibular system, such as the vestibulo-ocular and vestibulospinal reflexes [11, 19]. Recent studies showed that nGVS improves vestibulospinal function [20, 21], stabilized static balance [22, 23] and gait performance in bilateral vestibulopathy patients [24, 25]. In an animal study, low - and high-rate GVS caused motor outputs, improving vestibular compensation and motor coordination in unilateral labyrinthectomy rats [26]. As a previous study showed that the combined use of two methods (electrical stimulation and vestibular exercises) induce beneficial synergistic effects on patients' function [27], this study aimed to investigate the synergistic effects of nGVS with vestibular physical rehabilitation exercises in the improvement of vestibulo-ocular and balance disorders in UVP patients.

Methods

This study is a randomized controlled trial (RCT). The researchers informed the participants of this study's aim and obtained written consent. The study was registered in the Iranian Registry of Clinical Trials (IRCT20160131026279N4).

Participants

Patients were referred from Amir A'lam Hospital, Tehran University of Medical Sciences, by their otolaryngologist-head and neck surgeons. All assessments and interventions were performed by an audiologist. Age requirements ranged from 20 to 50, and inclusion criteria included having one or more of the following subjective complaints for longer than 6 weeks: disequilibrium, gait instability, vertigo/dizziness, oscillopsia, or motion sensitivity, as well as a clinical diagnosis of uncompensated, non-progressive unilateral peripheral vestibulopathy confirmed with bithermal caloric irrigation and a canal paresis >25%. It also excluded the use of drugs that suppress the vestibular system. If a participant had previously undergone vestibular rehabilitation, had central nervous system involvement, fluctuating peripheral diseases like Meniere's disease, vestibular migraine, active benign paroxysmal positional vertigo, or had any other acute medical conditions that would have limited assessments and treatment options, they were excluded from the study. 40 participants met the requirements for participation and provided their informed permission. Finally, the training programs and the post-treatment assessment were successfully

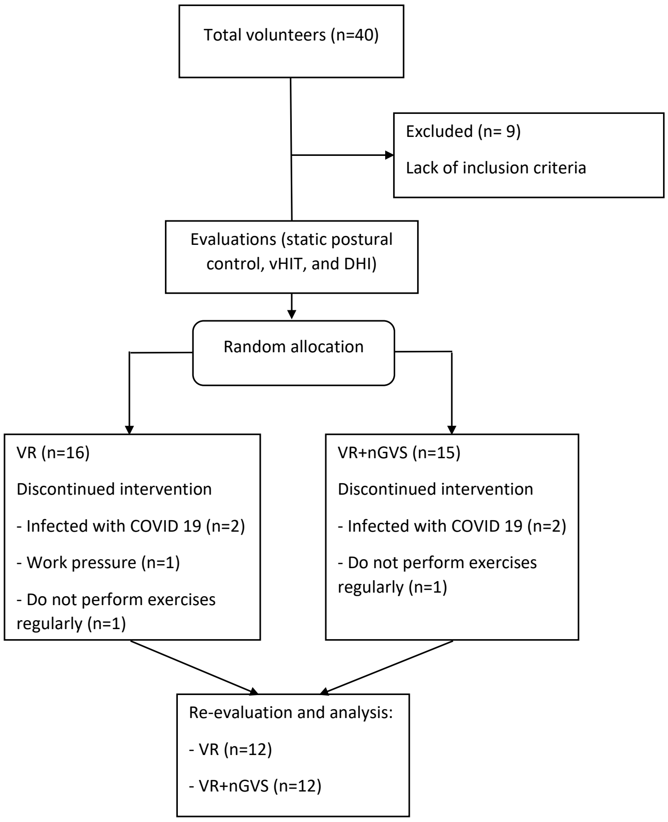

Figure 1. Flowchart of the study. vHIT; video head impulse test, DHI; dizziness handicap inventory, VR; vestibular rehabilitation, nGVS; noisy galvanic vestibular stimulation

completed by 24 individuals (14 females and 10 males, mean age 41.45±7.8 years) (Figure 1). It is necessary to mention that to homogenize the sample, all patients with vestibular neuritis were included in the study (which are common causes of UVP).

Procedures

Patients were randomly allocated into two intervention groups: 1) VR receiving for four weeks of vestibular rehabilitation 2) VR+nGVS receiving for four weeks of vestibular rehabilitation and three 20-minute sessions of noisy galvanic vestibular stimulation [27, 28].

Randomization and blinding

We used a simple random sampling method. The two treatment groups (VR, VR+nGVS) were randomly assigned to 24 individuals using a 1:1 allocation ratio and a randomization sequence created by the Random Allocation Software with a block size of 4. The statistics consultant and patients were blinded to the groups.

Outcome measures

Static postural control

A force platform (Bertec Corporation, Columbus, OH, USA) was used to record the Center of Pressure (COP) trajectory data at a sampling frequency of 500 Hz. The X and Y axes of the force platform represented the Mediolateral (ML) and Anteroposterior (AP) displacement of the center of pressure. The participant was asked to stand with bare feet on the faceplate [29]. Each patient was randomly tested in the following four conditions: 1) stance with eyes open on a hard surface, 2) stance with eyes closed on a hard surface, 3) stance with eyes open on a soft surface, and 4) stance with eyes closed on a soft surface. Each condition was repeated three times and every recording lasted 20 seconds with a short break between trials. In each condition (except for 4), displacement and velocity of the COP in directions of the AP and ML and total area of body sway were estimated and averaged three times repeatedly. MATLAB software as well as related mathematical formulas in Excel software were used for extracting outcome measures of postural control. In condition four, due to the fact that most of the patients fell in this condition and we were not able to analyze the data, we examined the results of the patients in terms of their ability to stand or fall in this condition [29, 30].

Video head impulse test

We used a video system (vHIT GN Otometrics, Denmark) and gave the patient's head roughly twenty unexpected, quick, and short impulses (10–20°) while they looked at a fixed target. to measure VOR in every semicircular canal direction. Head impulses were given in the yaw axis to test the left and right horizontal canals. To assess Left Anterior/Right Posterior (LARP) and Right Anterior/Left Posterior (RALP) semicircular canals, the head impulses were delivered at the pitch axis whereas the patient was looking at a fixed target. A VOR deficit was represented for lateral and vertical canals, with a vHIT gain of <0.8 and <0.7, respectively [31].

Dizziness handicap inventory

The Persian version of the Dizziness Handicap Inventory (DHI) has been designed for the measurement of dizziness [32]. There are 25 questions in this questionnaire, and they are divided into three subscales: physical, functional, and emotional impacts of dizziness [33].

All assessments were performed at baseline and after four weeks.

Interventions

Vestibular rehabilitation therapy

The vestibular rehabilitation exercises were mostly based on Cawthorne and Cooksey's protocols. These exercises include repetitive movements of the eyes, head, and trunk in positions of lying down, sitting, standing, and moving with eyes open and closed. After baseline evaluations were completed, instructions were given to the patients on how to perform and gradually increase the exercise speed at home. In order to ensure that the exercises are performed, the patients were contacted twice a week and patients had to fill in the given checklist daily. Participants were asked to perform the usual Cawthorne and Cooksey vestibular rehabilitation exercises for 30 minutes twice a day for a month at home [3].

Noisy galvanic vestibular stimulation

Binaural-bipolar electric currents of the noise were provided by using a direct current stimulator (Neurostim2, Medina Teb, Iran), with characteristics of a zero-mean Gaussian white noise, ranging from zero to 30 Hz frequency and sub-threshold intensity within 20 min [27]. Pairs of disposable adhesive electrodes for delivering the nGVS were attached to the two mastoids in the hairless area. The impedance of the electrodes was continuously kept below 1 KΩ. The skin behind the ear was completely cleansed using Nuprep gel. Afterward, the participant was guided on the chair to sit with a fixed forward head and closed eyes, maintaining the posture until the stimulus ended. Before delivering nGVS, the participant's cutaneous sensory threshold was specified at the beginning of each session. So, the threshold was gradually acquired by boosting the current intensity in 0.1 mA steps to the point where the patient declared itching or tingling. Then, the current intensity was reduced to such an extent that the patient perceives a slight tingling sensation. Because our electrical intervention was below the threshold, nGVS was applied with an amplitude of 0.1 mA below the threshold level [34]. VR+nGVS group received a 20-minute nGVS session once a week for three consecutive weeks.

Statistical analysis

Descriptive statistics were reported as mean and standard deviation. For analysis of data normality and homogeneity of variance, we used Kolmogorov-Smirnov and Levene's tests, respectively. An Independent t-test was used to compare normal baseline characteristics, and Chi-Square was used to compare the sex and side-affected distribution of the two groups. For within-group comparisons, paired t-test was used for normal data and the Wilcoxon test was used for parameters with no normal distribution. Cohen's d (d) (small=0.2, medium=0.5, and large=0.8) was used to measure the effect size for within-group comparisons [35]. In addition, the ANCOVA test was used for between-group comparison of each variable with normal distribution and pre-intervention measures were adjusted as covariances. Partial Eta squared (η 2) (small=0.01, medium=0.06, and large=0.14) was used to measure the effect size for between-group comparisons [36]. Mann-Whiney U test was used to compare changes in outcomes (subtracting the results after from the results before the intervention) without normal distributions between groups and Cohen's d was used to measure the effect size. Mc Nemar and Fisher's exact tests were used to compare patients' stance ability improvement in condition four (stance with eyes closed on a soft surface) static postural control for within-group and between-group comparison, respectively. The statistical analysis of data was performed using SPSS 17 (SPSS Inc., Chicago, IL, the USA), and p<0.05 were considered statistically significant for all tests.

Results

Demographic characteristics of the participants including age, sex, months since the first onset of symptoms diagnosis, unilateral weakness degree and side affected were not significant between groups before the intervention (Table 1).

Static postural control

In condition one, stance with eyes open on hard surfaces, the mean displacement and velocity of the COP in the AP and ML direction and total body sway area improved in two treatment groups after the intervention compared to before (Table 2). Using the ANCOVA

Table 1. Demographic characteristics of the participants

Characteristics	VR (n=12)	VR+nGVS (n=12)	p
Age (year)	41.83±6.67	41.08±9.12	0.820*
Sex (male/female)	5/7	5/7	0.839**
Months since first onset of symptoms diagnosis (month)	18.33±5.29	17.91±4.94	0.844*
Unilateral weakness degree (percent)	74.51±19.29	75±15.94	0.945*
Side affected (left/right)	8/4	5/7	0.673**

VR; vestibular rehabilitation, nGVS; noisy galvanic vestibular stimulation
Values are mean±SD, * Independent t-test, ** Chi-Square test

Table 2. Within-group comparisons for static postural control outcome measures in different conditions

		Mean stance with eye open on hard surface(SD)				Mean stance with eye closed on hard surface(SD)				Mean stance with eye open on soft surface(SD)			
Test	**Group**	**Before**	**After**	**p**	**d/P**	**Before**	**After**	**p**	**d/P**	**Before**	**After**	**p**	**d/P**
Mean ML displacement (cm)	VR	2.33(0.80)	1.85(0.71)	**<0.001***	1.42	4.71(2.24)	3.99(1.80)	0.061†	0.62	5.66(2.54)	4.72(1.93)	0.073*	0.58
	VR+nGVS	2.29(0.83)	1.67(0.68)	**0.031***	0.72	4.20(1.91)	2.43(1.09)	**0.002***	1.11	5.75(2.25)	3.06(0.91)	**0.002***	1.19
Mean AP displacement (cm)	VR	2.29(0.52)	1.89(0.69)	**0.015***	0.88	5.16(2.00)	4.24(1.43)	**0.044***	0.65	6.09(2.19)	4.85(1.83)	**0.035***	0.69
	VR+nGVS	2.24(0.67)	1.66(0.55)	**0.003***	1.03	4.12(1.95)	2.49(1.07)	**0.006***	0.96	5.63(1.63)	2.98(0.88)	**0.001***	1.26
Mean ML velocity (cm/s)	VR	1.10(0.54)	0.72(0.36)	**0.011***	0.82	2.09(0.75)	1.81(0.60)	0.056*	0.61	2.55(1.20)	1.95(0.62)	0.051*	0.63
	VR+nGVS	1.11(0.53)	0.65(0.24)	**0.023***	0.75	1.79(0.93)	1.03(0.45)	**0.005***	1.04	2.39(0.92)	1.30(0.43)	**0.007***	0.96
Mean AP velocity (cm/s)	VR	1.06(0.58)	0.73(0.56)	**0.034**†	0.62	1.98(0.79)	1.71(0.68)	**0.021***	0.82	2.38(0.87)	1.84(0.44)	0.066*	0.59
	VR+nGVS	1.11(0.55)	0.73(0.35)	**0.026***	0.73	1.58(0.87)	0.89(0.28)	**0.008***	0.93	2.11(0.80)	1.19(0.46)	**0.002***	1.19
Area (cm^2)	VR	4.24(1.73)	3.28(1.28)	**0.007***	0.96	9.87(6.85)	6.91(3.73)	**0.033***	0.70	17.25(4.21)	14.07(4.20)	**0.016***	0.82
	VR+nGVS	4.35(2.64)	3.14(2.07)	**0.017***	0.81	10.63(4.94)	4.18(2.53)	**0.001***	1.23	18.34(7.57)	6.63(3.36)	**0.001***	1.25

d/P; effect size with Cohen's d (small=0.2, medium=0.5, and large=0.8) or power (for p<0.05, effect size was calculated and for p>0.05 power of the test was calculate with Cohen's d), values are presented as mean (standard deviation), ML; mediolateral, VR; vestibular rehabilitation, nGVS; noisy galvanic vestibular stimulation, AP anteroposterior
Bold numbers: p <0.05, † Wilcoxon test, * Paired t-test

test, the difference between VR and VR+nGVS group was not statistically significant for ML and AP mean displacements and mean velocities, and total body sway area (Table 3).

In condition two, stance with eyes closed on a hard surface, the mean of the displacement and velocity in AP direction and total body sway area improved in two treatment groups after the intervention but the displacement and velocity in ML direction significantly changed only in the VR+nGVS group after the intervention (Table 2). Using the ANCOVA test, mean changes in displacement and velocity of the COP in the AP and ML direction and total body sway area were statistically significant between groups ($p<0.05$; Table 3).

In condition three, stance with eyes open on a soft surface, the mean displacement of the COP in the AP direction and total body sway area improved after the intervention in VR and VR+nGVS groups but the mean velocity of the COP in two directions and the mean displacement of the COP in the ML direction significantly changed only in the VR+nGVS group after the intervention compared to before (Table 2). Using ANCOVA analysis, differences between groups were statistically significant for all assessments ($p<0.05$; Table 3).

Table 3. Between-group comparisons of static postural control and vestibulo-ocular reflex gain measures

		F(df)/z	p	η^2/p**
Stance with eye open on hard surface	Mean ML displacement (cm)	0.52(1,21)	0.476*	0.10
	Mean AP displacement (cm)	0.92(1,21)	0.347*	0.15
	Mean ML velocity (cm/s)	0.39(1,21)	0.538*	0.09
	Mean AP velocity (cm/s)	–0.46	0.645†	0.05
	Area (cm^2)	0.25(1,21)	0.619*	0.07
Stance with eye closed on hard surface	Mean ML displacement (cm)	10.36	**0.004†**	0.33
	Mean AP displacement (cm)	9.69(1,21)	**0.005***	0.31
	Mean ML velocity (cm/s)	13.00(1,21)	**0.002***	0.38
	Mean AP velocity (cm/s)	22.04(1,21)	**0.009***	0.28
	Area (cm^2)	8.25(1,21)	**<0.001***	0.35
Stance with eye open on soft surface	Mean ML displacement (cm)	10.72(1,21)	**0.004***	0.33
	Mean AP displacement (cm)	9.86(1,21)	**0.005***	0.32
	Mean ML velocity (cm/s)	8.59(1,21)	**0.008***	0.29
	Mean AP velocity (cm/s)	10.97(1,21)	**0.003***	0.34
	Area (cm^2)	22.27(1,21)	**<0.001***	0.51
VOR gain	Affected horizontal SCC	26.90(1,21)	**<0.001***	0.56
	Affected anterior SCC	16.29(1,21)	**0.001***	0.43
	Affected posterior SCC	0.98(1,21)	0.333*	0.16
	Unaffected horizontal SCC	0.78(1,21)	0.382*	0.14
	Unaffected anterior SCC	0.28(1,21)	0.603*	0.06
	Unaffected posterior SCC	0.033(1,21)	0.857*	0.05

ML; mediolateral, AP; anteroposterior), VOR; vestibulo-ocular reflex, SCC; semicircular canal

* ANCOVA with pre-treatment measures adjusted as covariances, † with the Mann-Witney test, Bold numbers: $p<0.05$, ** η^2/p: partial eta squared effect size (small=0.01, medium=0.06, and large=0.14) or power (for $p<0.05$, effect size was calculated and for $p>0.05$, power of the test was calculated with partial eta squared)

In condition four, stance with eyes closed on a soft surface, we compared the ability of patients to stand before and after the intervention. According to Mc Nemar’s test results, only the patients in the nGVS+VR group statistically significantly improved in stance ability in this condition (p=0.016, Table 4) after the intervention compared to before. Using Fisher’s exact test, the difference between groups was statistically significant (p=0.037) for improvement of the ability to stand in this condition. So most of the patients in the nGVS+VR group found the ability to stand in this condition after receiving the intervention.

Vestibulo-ocular reflex gain

The mean VOR gain after the intervention statistically significantly improved compared to before in VR and VR+nGVS groups in all affected semicircular canals but there was no statistically significant change in unaffected semicircular canals (Table 5). Using the ANCOVA test, mean changes in VOR gain were statistically significant between groups only in horizontal and anterior affected semicircular canals (p<0.05; Table 3).

Dizziness handicap inventory

The mean of results for DHI total score after the intervention compared to before statistically significantly improved in the VR group (p=0.002, d=1.1) and VR+nGVS group (p=0.002, d=1.1, Figure 2 A), as well as for physical and functional DHI subscales (Figures 2 B, C). The mean score of the emotional subscale improved after the intervention compared to before only in the VR+nGVS group (p=0.005, d=1.4, Figure 2 D). Using the Mann-Whitney test, the difference between groups was statistically significant for DHI total score (Z=–2.17, p=0.028, d=0.67), physical (Z=–2.03, p=0.045, d=0.59) and functional scores(Z=–2.78, p=0.005, d=1.01)

Discussion

Our main purpose was to investigate the effect of VR with and without nGVS on the improvement of VOR and balance function in UVP patients. We found that the VR+nGVS group showed significant improvements in all outcomes and greater improvements for those several outcome measures for which the VR group showed

Table 4. Within-group comparisons for stance with eyes closed on soft surface condition in static postural control

	Before		After		
Group	**Falling**	**No falling**	**Falling**	**No falling**	**p**
VR	9(75%)	3(25%)	7(58.3%)	5(41.7%)	0.592*
VR+nGVS	10(83.3%)	2(16.7%)	3(25.0%)	9(75.0%)	**0.016***

VR; vestibular rehabilitation, nGVS; noisy galvanic vestibular stimulation
Bold numbers: p <0.05, * Mc Nemar test; values are presented as count (percent)

Table 5. Within-group comparisons for vestibulo-ocular reflex gain in six semicircular canal directions

		Horizontal SCC				Anterior SCC				Posterior SCC			
Side	**Group**	**Before**	**After**	**p**	**d/P**	**Before**	**After**	**p**	**d/P**	**Before**	**After**	**p**	**d/P**
Affected	VR	0.60(0.18)	0.72(0.18)	**0.002***	1.12	0.70(0.16)	0.78(0.13)	**0.032***	0.66	0.74(0.18)	0.86(0.14)	0.045*	0.64
	VR+nGVS	0.54(0.16)	0.94(0.08)	**<0.001***	2.21	0.68(0.21)	0.97(0.08)	**0.003***	0.98	0.75(0.21)	0.91(0.11)	0.011*	0.88
Unaffected	VR	0.85(0.13)	0.84(0.12)	0.663*	0.21	0.84(0.06)	0.88(0.08)	0.071*	0.62	0.86(0.09)	0.92(0.06)	0.137*	0.52
	VR+nGVS	0.86 (0.08)	0.87(0.08)	0.659*	0.23	0.82(0.10)	0.90(0.09)	0.134*	0.48	0.87(0.07)	0.90(0.08)	0.194*	0.41

SCC; semicircular canal, VR; vestibular rehabilitation, nGVS; noisy galvanic vestibular stimulation
Bold numbers: p <0.05, * paired t-test; d/P=Effect size with Cohen's d (small=0.2, medium=0.5, and large=0.8) or power (for p<0.05, effect size was calculated and for p>0.05 power of the test was calculated with Cohen's d), values are presented as mean (standard deviation)

significant enhancement as well. The effect sizes were larger for all outcomes in the VR+nGVS group than in the VR group.

To the extent of our knowledge, the effectiveness of vestibular rehabilitation with nGVS has not been investigated yet. Our results showed that improvement was observed in two groups after rehabilitation and the two groups were not significantly different in static postural control condition one in which patients stand with eyes open on a hard surface. However, in conditions two and three (lack of visual and poor proprioceptive information), which are challenging balance conditions, the patients in the two groups showed different recovery patterns. VR+nGVS group showed statistically significant improvement in all assessment outcomes. In addition, the effect size in the VR+nGVS group was higher than in the VR group. Condition four in which the patient stands with eyes closed on a soft surface is the most challenging condition. Visual inputs are removed and proprioceptive information is degraded, balance is maintained based on vestibular system inputs. Most patients fell in this condition before the intervention. Most of the patients in the VR+nGVS group found the ability to stand in this condition after receiving the intervention compared to the VR group that lost balance and fell again.

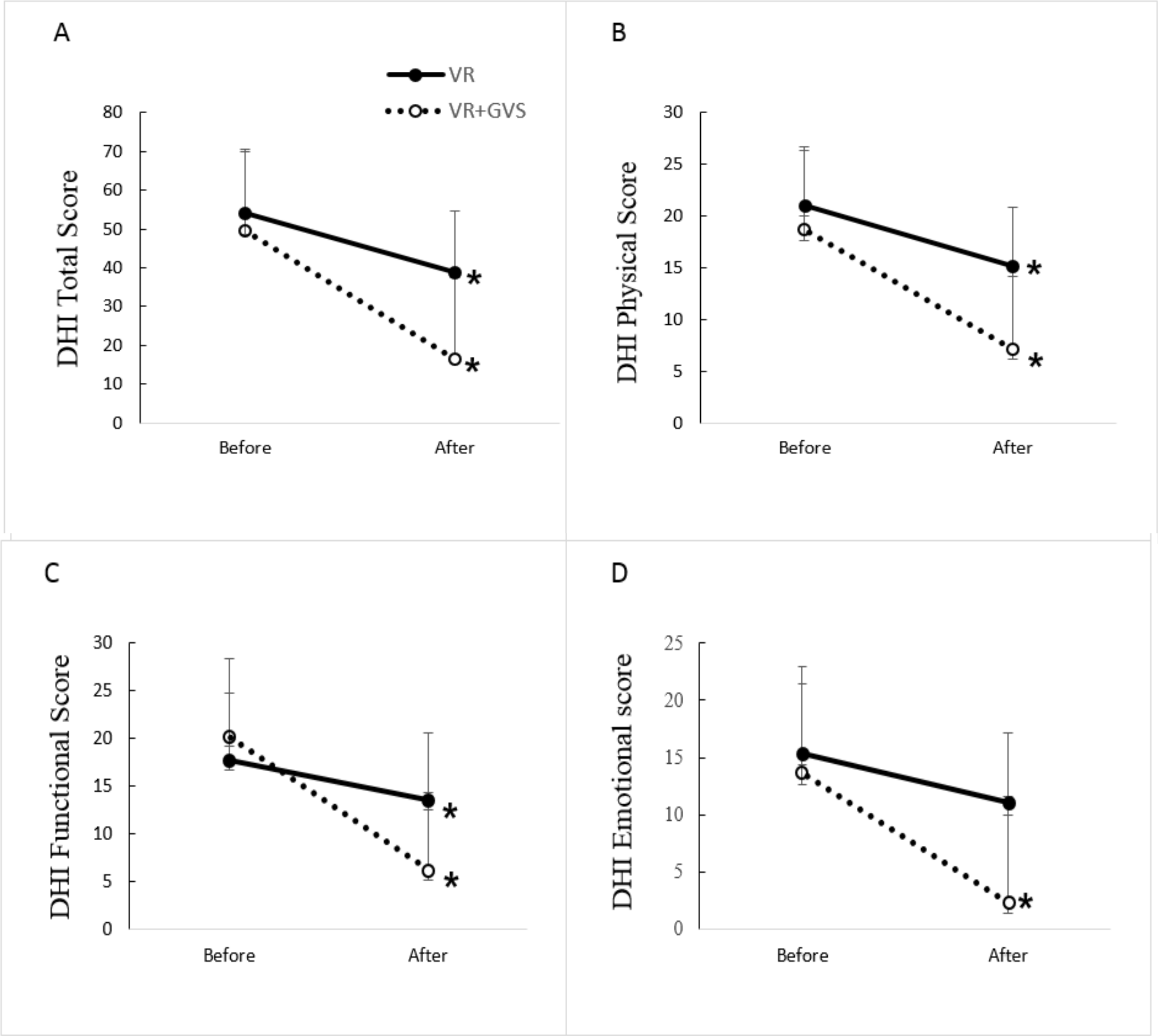

Figure 2. A) Total, B) physical, C) functional, and D) emotional scores of the dizziness handicap inventory before and after intervention in each groups. VR; vestibular rehabilitation, nGVS; noisy galvanic vestibular stimulation, DHI; dizziness handicap inventory questionnaire. Graphs are based on mean±standard deviation

* $p<0.05$ for within-group comparisons

Our results are in accordance with the results of previous studies. The principle of vestibular rehabilitation is to improve and accelerate the recovery process in the vestibular system. Using central neuroplasticity mechanisms (i.e. adaptation, habituation, and substitution) in this approach enhances dynamic and static postural stability and improves vestibular-ocular interactions in situations with sensory conflict [37]. Sensory substitution is an essential component in vestibular rehabilitation to maintain the postural control of UVP patients while standing and walking. It relies on increasing residual inputs by manipulating visual cues (eyes open, eyes closed, and optokinetic stimulation), by manipulating balance control (on stable surfaces, on foam and on unstable surfaces) and by combining both protocols [38]. GVS preferentially activates otolithic afferents and the reticulo-spinal pathway, which is a stronger input for adjusting standing posture and activates semicircular canal afferents and the vestibulo-spinal pathway [39]. It seems that GVS mainly changes vestibular afferent fibers with irregular discharge that transmit phasic or high-frequency information [40, 41] which are the main input to vestibulospinal projections [42] and postural asymmetries after UVP [43, 44]. This is significantly important for the restoration of the dynamic balance function after UVP [39]. Therefore, it is possible that the simultaneous use of the two methods of interventions causes stimulation of more parts and has higher effects on the performance of balance function in UVP patients. Based on the results of past studies, the use of GVS modulates the activity of calcium and sodium dependent channels and the activity of N-Methyl-D-Aspartate (NMDA) receptors and creates a mechanism similar to Long-Term Potentiation (LTP) and Long-Term Depression (LTD) [27]. Use of GVS resulted in cell proliferation in the ipsilesional Medial Vestibular Nuclei (MVN), fast rebalancing in vestibular nuclei, modulation in motor outputs and speeding up in static and dynamic vestibular compensation in unilaterally labyrinthectomized rats [39] and improved balance and reduced body sway in normal subjects [27]. An fMRI study showed that more functional activation in the central operculum in GVS intervention could be the main factor in standing posture stability [45]. The mean of VOR gain after the intervention significantly improved in the VR and VR+nGVS groups in all affected semicircular canals. VOR gain reached the normal level in the VR+nGVS group after intervention but in the VR group, despite the improvement, it is still below the normal range. Similarly, Nam et al. showed improved VOR and motor coordination and acceleration of vestibular static and dynamic compensation following GVS intervention during the acute phase in the unilateral vestibular deafferentated rats [26]. Hence, nGVS is considered a potent and reasonably pure vestibular stimulus. Noisy GVS may restore the natural stochastic firing patterns that could be important to the vestibular system [46].

Patients in the VR+nGVS group showed fewer problems in DHI total, physical, functional, and emotional scores after the intervention compared to the VR group. This questionnaire characterizes the patients' self-perception of the severity of their dizziness and the degree of disability caused by dizziness and vestibular dysfunction in their daily lives. Therefore, the VR+nGVS intervention leads to a reduction of adverse effects of dizziness in daily life. In contrast to our results, Eder et al. showed that adding GVS stimulation to the VR program in bilateral vestibulopathy patients had no more therapeutic effect than the VR program in different assessments of gait, static body sway in posturography and questionnaires [47]. This disagreement may result from differences in the type and duration of the VR program, patient groups, assessment exams, or the use of GVS at various intensities. Patients with bilateral and unilateral VP have different prognoses with VR. VR has been reported to be the treatment of choice in managing persons with BVP. While VR plays an important role in managing UVP patients and these patients are the best candidate to receive the VR [3], its efficacy has not been fully established in patients with BPV [48, 49]. More than 80% of people with BVP showed poor prognosis with VR [50].

Patients showed poorer performances with increasing challenges from conditions one to four. According to Peterka, healthy individuals who are standing on a hard surface and have access to vision typically rely 70% on somatosensory information, 20% on vestibular information, and 10% on vision for postural orientation. Sensory weighting shifts as surface oscillations rise from 1 to 8 degrees, resulting in individuals relying primarily on vestibular and visual information–only 10% on somatosensory information [51]. Because normal subjects depend primarily on somatosensory information for postural stability, UVP patients have severe balance problems on unstable surfaces [3]. The results of static postural control assessment in condition one, standing with eyes open on a hard surface, showed that the two groups similarly improved in velocity, displacement, and total body sway area.

We could not evaluate the durability of the intervention's effectiveness because the study took place during the Covid-19 pandemic. We suggest an investigation of the long-term effects of this type of intervention in UVP patients in future studies.

Conclusion

Our study supports a synergistic effect of low-amplitude noisy GVS with physical vestibular rehabilitation for accelerating static and dynamic vestibular compensation after UVP and improving VOR and balance functions in these patients. Therefore, GVS may offer hope for individuals with unilateral peripheral vestibulopathy who need rehabilitation.

Ethical Considerations

Compliance with ethical guidelines

The present study followed the ethical protocols of the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of the Tehran University of Medical Sciences (IR.TUMS.FNM.REC.1399.210).

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Authors' contributions

BK: Acquisition of data, drafting the manuscript, analysis, and interpretation of data; MAG: Study concept and design, study supervision, drafting/critical revision of the manuscript for important intellectual content; RH: Study supervision, technical and material support; SJ: Study design, analysis, and interpretation of data; AK and NY: Material support. All authors read and approved the manuscript.

Conflict of interest

There are no competing interests declared by the authors.

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