Effects of Noisy Galvanic Vestibular Stimulation Combined with Virtual Reality-Based Vestibular Rehabilitation on Depressive Symptoms and Vestibular Function in Women with Moderate Major Depressive Disorder: A Controlled Quasi-Experimental Study

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Highlight:
Between-group beck depression inventory changes were not statistically significant
nGVS+VR produced greater BDI-II reduction than pharmacotherapy alone
Combined nGVS+VR increased right lateral vestibulo-ocular reflex gain versus control

ABSTRACT
Background and Aim: Major depressive disorder (MDD) is associated with dizziness, balance complaints, and abnormalities in vestibular processing. This study examined whether noisy galvanic vestibular stimulation (nGVS), virtual reality (VR)-based vestibular rehabilitation, or their combination, when added to stable pharmacotherapy, could influence depressive symptoms, dizziness-related disability, and vestibular function in women with moderate MDD. We hypothesized that the combined intervention would be associated with greater improvement than vestibular intervention or pharmacotherapy alone.
Methods: This controlled quasi-experimental study included 52 women with moderate MDD. A separately recruited non-randomized control group (n=13) received pharmacotherapy alone. The 39 participants were randomly allocated to nGVS, VR, or nGVS+VR groups (n=13 each). nGVS consisted of three 20-minute sessions once weekly for three weeks. VR-based vestibular rehabilitation comprised eight 45-minute sessions twice weekly over four weeks. Pharmacotherapy remained unchanged during the intervention and follow-up periods. Assessments were performed at baseline, post-intervention, and one-month follow-up.
Results: Depressive symptoms decreased more in the nGVS+VR and VR groups than in the control group post-intervention and in all vestibular intervention groups at follow-up. Between-group changes in dizziness-related disability were not statistically significant. Right lateral canal vestibulo-ocular reflex (VOR) gain showed greater improvement in the combined group compared with the control group.
Conclusion: Vestibular-targeted interventions added to stable pharmacotherapy were associated with greater improvement in depressive symptoms. The combined intervention produced a selective improvement in right lateral VOR gain. These preliminary findings warrant further investigation but do not establish generalized vestibular recovery or superiority of the combined approach across all outcomes.
Keywords: Major depressive disorder, vestibular rehabilitation, galvanic vestibular stimulation, virtual reality, vestibulo-ocular reflex, video head impulse test.

Introduction

Major Depressive Disorder (MDD) is a common and disabling psychiatric disorder characterized by persistent depressed mood, loss of interest or pleasure, and cognitive and somatic symptoms that can substantially interfere with daily functioning [1]. Although vestibular symptoms are not core features of MDD, dizziness and vestibular disorders frequently coexist with anxiety and depressive symptoms [2–4]. This overlap has raised interest in whether vestibular function may contribute to some sensory, autonomic, and functional difficulties experienced by people with depression.

Objective evidence remains limited. Soza Ried and Aviles examined unmedicated patients with major depression using caloric stimulation and reported reduced bilateral vestibular responses, with a greater reduction on the right [5]. Using rotational stimulation, Soza et al. also found right-left asymmetry in MDD, with a lower right-to-left vestibular activity ratio than in healthy controls [6]. The similar direction of these findings across two vestibular stimulation methods is noteworthy. However, both studies were small and do not establish a fixed right-sided peripheral lesion in all patients. A cautious interpretation is that altered vestibular lateralization may occur in a subgroup of patients with depression.

There is also an anatomical basis for vestibular-affective interaction. Vestibular processing extends beyond brainstem pathways for gaze stabilization and postural control. Ascending vestibular signals reach networks involved in spatial cognition, body representation, and higher-order functions [7, 8]. Vestibular nuclei also connect with autonomic and affective circuitry through the parabrachial nucleus and dorsal raphe-amygdala pathways [9, 10]. These connections make interaction with mood-related systems biologically plausible, although experimental anatomy alone does not establish causality in human depression.

Galvanic vestibular stimulation (GVS) is a non-invasive method for modifying vestibular afferent activity [11]. When low-amplitude electrical noise is delivered below the perceptual threshold, noisy GVS (nGVS) may facilitate weak vestibular signals through stochastic-resonance-related mechanisms. GVS has also been associated with reduced anxiety in healthy adults [12]. A systematic review has documented GVS applications across vestibular, balance, cognitive, and clinical domains [13]. These observations support the physiological relevance of GVS but should not be interpreted as established evidence that nGVS is an antidepressant treatment.

Virtual reality (VR) has also been increasingly studied in depression, including VR-based cognitive behavioral therapy and Avatar Therapy [14–16]. These studies are relevant to psychiatric uses of VR but differ substantially from the present intervention: their main purpose was psychotherapeutic rather than vestibular rehabilitation, and objective vestibular outcomes were not primary targets.

VR can also serve as an active rehabilitation environment that permits repeated, interactive, task-oriented sensorimotor practice [17]. VR-enhanced exercises have been evaluated in peripheral vestibular dysfunction and unilateral vestibular hypofunction [18, 19]. Vestibular rehabilitation promotes adaptation, habituation, substitution, and compensation through repeated sensory and motor exposure [20]. In this context, VR provides a structured way to challenge visual, vestibular, proprioceptive, and motor systems simultaneously.

A previous randomized study in unilateral vestibulopathy combined vestibular rehabilitation with three sessions of nGVS and reported greater improvement in selected postural, VOR, and dizziness-related outcomes [21]. This provides a rationale for combining the two approaches, but that population had a primary peripheral vestibular disorder rather than MDD. Conversely, depression-focused VR studies have generally not used vestibular-targeted balance rehabilitation [14–16]. It therefore remains uncertain whether combining vestibular-afferent modulation with active VR-based vestibular training can influence affective symptoms and objective vestibular function in MDD.

Only women were included to reduce between-participant variability in this relatively small initial study; MDD is also more prevalent among women [1]. This restriction limits generalizability and does not imply similar effects in men.

Accordingly, this study examined nGVS, VR-based vestibular rehabilitation, and their combination as adjuncts to stable pharmacotherapy in women with moderate MDD. Outcomes included depressive symptoms, dizziness-related disability, and objective vestibular function. We hypothesized that the combined intervention would be associated with greater improvement than either vestibular intervention alone or pharmacotherapy alone.

Methods

Study design

This controlled quasi-experimental study with randomized intervention arms was conducted between September 1, 2022, and May 1, 2024. It included one separately recruited, non-randomized pharmacotherapy-only control group and three randomized vestibular intervention groups. The non-randomized nature of the control group was predefined and considered when interpreting the findings.

After eligibility confirmation and informed consent, participants completed baseline assessments using the Beck Depression Inventory-II (BDI-II), Dizziness Handicap Inventory (DHI), and video Head Impulse Test (vHIT). Outcomes were reassessed within one week after intervention completion and again one month later. All 52 participants completed baseline, post-intervention, and follow-up assessments.

Participants

Women aged 20–45 years with moderate MDD were enrolled. MDD was diagnosed by a psychiatrist through clinical interview according to DSM-5 criteria, and moderate severity was defined as a BDI-II score of 20–28.

All participants were receiving pharmacological treatment. Medication type and dosage were required to remain unchanged from at least one month before vestibular intervention until completion of the one-month follow-up. Participants whose medication changed during this period were excluded. Pharmacological regimens were individualized and were not necessarily identical across participants. None was receiving ototoxic medication.

Exclusion criteria were chronic depression, more than two previous depressive episodes, previous vestibular rehabilitation, neurological or diagnosed vestibular disorders, musculoskeletal or systemic disorders affecting balance or vestibular function, and psychiatric comorbidity other than MDD. The same eligibility criteria applied to all groups.

A total of 52 participants were included, with 13 in each group. The pharmacotherapy-only control group (n=13) was recruited separately and was not randomized. These participants continued prescribed pharmacotherapy without vestibular or sham procedures.

The remaining 39 participants were randomly allocated in a 1:1:1 ratio using block randomization with a block size of six. The allocation sequence was generated by an independent researcher not involved in recruitment or outcome assessment. Allocation concealment used sequentially numbered, sealed, opaque envelopes opened after baseline assessment.

The nGVS group (n=13) received stable pharmacotherapy, active nGVS, and sham VR; the VR group (n=13) received stable pharmacotherapy, active VR-based vestibular rehabilitation, and sham nGVS; and the combined group (n=13) received stable pharmacotherapy, active nGVS, and active VR-based vestibular rehabilitation.

Masking

Complete masking was not feasible. Sham procedures were used for the inactive modality in the single-modality groups to reduce procedural differences. However, active VR could be distinguished from sham VR, and the therapist knew treatment allocation.

Control participants were aware that they were not receiving vestibular intervention, and outcome assessment, including questionnaires and vHIT, was not blinded. These features may introduce expectancy, performance, and assessment bias, particularly for self-reported outcomes.

Outcome measures

Beck Depression Inventory-II

Depressive symptoms were assessed using the 21-item BDI-II, which evaluates symptoms over the preceding two weeks. Items are scored from 0 to 3, producing a total score of 0–63, with higher scores indicating greater severity. The validated Persian version was used [22].

Dizziness Handicap Inventory

The DHI assessed self-perceived dizziness-related disability. Its 25 items are scored as Yes=4, Sometimes=2, or No=0, producing a total score of 0–100, with higher scores indicating greater disability. Functional, p hysical, and emotional domains can also be evaluated. The validated Persian version was used [23].

Video head impulse test

Semicircular canal vestibulo-ocular reflex function was assessed using a vHIT system (GN Otometrics, Denmark). Participants fixated on a stationary target while approximately 10 brief, rapid, unpredictable head impulses were delivered for each canal at peak velocities of approximately 150–250°/s. Horizontal canals were examined in the yaw plane and vertical canals in the LARP and RALP planes.

Only artifact-free impulses meeting device quality criteria were included. Impulses affected by excessive blinking, inadequate pupil tracking, or goggle slippage were excluded. VOR gain was calculated separately for each canal. Values below 0.8 for horizontal canals and below 0.7 for vertical canals were considered abnormal [24, 25]. Corrective saccades were classified descriptively as covert or overt and recorded as supplementary observations rather than an independent inferential between-group outcome.

Intervention procedures

Active noisy galvanic vestibular stimulation

Active nGVS was delivered using a direct-current stimulator (Neurostim2, Medina Teb, Iran) in one 20-minute session per week for three consecutive weeks. The hairless skin behind each ear was cleaned with Nuprep gel, and adhesive electrodes were positioned bilaterally over the mastoid processes with impedance below 1 kΩ.

At each session, the cutaneous sensory threshold was determined by increasing current in 0.1-mA increments until mild itching or tingling was perceived. Intensity was then set 0.1 mA below this threshold. Participants remained seated with the head facing forward and eyes closed while binaural-bipolar zero-mean Gaussian white noise at 0–30 Hz was delivered [21].

Sham noisy galvanic vestibular stimulation

The sham procedure used the same electrode placement, preparation, position, and session duration. Current was increased until mild cutaneous sensation was reported and then reduced to 0 mA for the remainder of the session, producing an initial sensation without ongoing effective stimulation.

Active virtual reality-based vestibular rehabilitation

Active VR-based vestibular rehabilitation was delivered using Nintendo Wii Fit with the Wii Balance Board. Participants completed eight 45-minute sessions twice weekly for four weeks [21].

The program comprised six activities in a predetermined sequence: Table Tilt, Ski Slalom, Soccer Heading, Tightrope Walk, Ski Jump, and Balance Bubble, each performed for approximately 7–8 minutes. Exercises challenged weight shifting, postural control, visuomotor coordination, and coordinated head and eye movements. Progression was performance-based.

Activity selection was informed by published literature on VR-based balance training and vestibular rehabilitation [17–21]. However, the specific selection and sequence were predefined for this study and should not be considered a universally standardized Wii Fit vestibular rehabilitation protocol.

Sham virtual reality-based vestibular rehabilitation

Participants receiving sham VR attended the same treatment environment with comparable therapist and equipment contact. They remained seated with the back supported and both feet on the inactive or disconnected Wii Balance Board while viewing neutral visual content. No therapeutic weight shifting, balance tasks, or guided head movements were performed.

Combined noisy galvanic vestibular stimulation and virtual reality intervention

The combined group received both active nGVS and active VR rehabilitation. During the first three weeks, the 20-minute nGVS session was administered immediately before VR rehabilitation. VR continued twice weekly for four weeks; therefore, week-four sessions were performed without nGVS.

The sequence was selected so that vestibular afferent stimulation preceded multisensory and sensorimotor training. A priming effect is physiologically plausible but was not directly measured and remains a hypothesis.

Statistical analysis

In the present study, continuous variables were expressed as mean ± standard deviation, and categorical variables as frequency (%). Since the assumptions of analysis of covariance (ANCOVA) were not fully met for continuous outcomes, change score analysis (or gain score analysis) which is one of the best alternative methods for data analysis in baseline, posttest, follow-up design, was used. To examine differences between the four groups, a one-way ANOVA was conducted on the change scores of each variable, followed by Tukey's post hoc test. For all ANOVAs, the assumptions of normality and homogeneity of variance were examined using the Shapiro–Wilk and Levene's tests, respectively. Before performing the one-way ANOVA, we tested the assumptions of normality and homogeneity of variances. Based on the Shapiro-Wilk test, the normality assumption was met for almost all outcomes across study groups at both posttest and follow-up measurements. According to Levene's test, the homogeneity of variances was also met for all outcomes except for DHI (P-values not shown here). On the other hand, one-way ANOVA is robust to mild to moderate departures from the assumption of homogeneity of variances, especially when the sample sizes of the groups are equal. The effect size for one-way ANOVA was reported in eta squared (η2); η2 values of 0.01-0.06, 0.06-0.14, and >0.14 were considered small, medium, and large effect sizes, respectively. Data analysis was performed using SPSS for Windows, version 16.0 (SPSS Inc., Chicago, IL, USA), and error bar graphs were depicted using GraphPad Prism, version 8.0.1 (GraphPad Prism Software Inc., San Diego, CA, USA). A $P<0.05$ was considered statistically significant.

Results

Participants characteristics

A total of 52 patients were screened, and 39 patients underwent randomization. Of these, follow-up data were available for all patients to be included in the intention-to-treat analysis (Figure 1). The distribution of age and disease duration is presented in Table 1. The mean age of the participants was 32.69 (SD = 6.60) years, and the mean disease duration of the participants was 4.85 (SD = 1.33) months.

Beck depression inventory-II

At the posttest measurement, there was a significant difference between the mean BDI-II change scores of the study groups ($F_{(3,48)}=8.94$, $p<0.001$, $\eta^2=0.358$); Tukey's post-hoc test showed that the reduction in BDI-II scores in the VR+ nGVS and VR groups was significantly greater than that in the control group ($p<0.001$ and $p=0.005$, respectively) (Table 2 and Figure 1). A significant difference was also observed at the follow-up measurement between the groups ($F_{(3,48)}=8.90$, $p<0.001$, $\eta^2=0.357$), such that the reduction in BDI-II scores in the VR+ nGVS, VR, and nGVS groups was significantly greater than that in the control group ($p<0.001$, $p=0.003$, and $p=0.040$, respectively).

Dizziness handicap inventory

At the posttest measurement, there was no significant difference between groups on the DHI change scores, although the reduction in the DHI score in the nGVS, VR, and VR+ nGVS groups was greater than that in the control group ($F_{(3,48)}=2.75$, $P=0.053$, $\eta^2=0.147$). The effect size, calculated using eta squared, was 0.147, which is considered to be large. Approximately similar results were also obtained at follow-up measurement ($F_{(3,48)}=1.73$, $p=0.173$, $\eta^2=0.098$).

Vestibulo-ocular reflex gain

At the posttest measurement, there was a significant difference between groups on the change scores of VOR gain in the right lateral side with a large effect size ($F_{(3,48)}=5.96$, $P=0.002$, $\eta^2=0.271$). Pairwise comparisons showed that the increase in VOR gain in the VR+ nGVS groups was significantly greater than that in the control and VR groups ($p<0.001$ and $P=0.043$, respectively). At the follow-up, a significant difference was also observed between the groups ($F_{(3,48)}=5.36$, $p=0.003$, $\eta^2=0.251$), such that the increase in VOR gain in the VR+ nGVS group was significantly greater than in the control group ($p=0.001$). For the left lateral side, at both posttest and follow-up measurement, there were no statistically significant difference in the change scores of VOR gain between the groups ($p=0.502$ and $p=0.464$, respectively). Approximately similar results were found for VOR gain in the left and right anterior side (Table 3). In the left and right posterior side, there were no statistically significant difference in the change scores of VOR gain between the groups (Table 3).

Discussion

The main finding was that adding vestibular -targeted interventions to stable pharmacotherapy was associated with greater reductions in depressive symptoms across several assessment time points, although the pattern was not consistent across all outcomes. The intervention groups showed greater reductions in depressive symptoms than the pharmacotherapy-only group, whereas between-group differences in DHI were not statistically significant. Objective vestibular change was limited to increased right lateral canal VOR gain in the combined

nGVS+VR group. Thus, the findings do not indicate generalized improvement across clinical and vestibular domains.

Vestibular disorders are frequently associated with anxiety and depressive symptoms [2–4], and vestibular information reaches networks involved in spatial processing, body representation, autonomic regulation, and affective functions [7–10]. These associations do not show that vestibular dysfunction causes MDD but provide anatomical and functional support for investigating vestibular function in depression.

The right lateral canal VOR finding should be considered alongside previous reports of vestibular asymmetry in MDD. Soza Ried and Aviles found reduced bilateral caloric responses, more prominent on the right [5]. Soza et al. similarly reported lower right than left vestibular activity with rotational testing; the right-to-left ratio was 0.77±0.2 in MDD and 1.1±0.3 in controls [6]. The similar direction across methods may indicate functional vestibular asymmetry in a subgroup of patients with depression.

However, these findings do not establish a fixed right-sided peripheral abnormality. Previous studies were small, and the present study showed change only in right lateral VOR gain, without a similar pattern in the left lateral or vertical canals. Increased VOR gain also does not necessarily represent correction of an underlying impairment. Higher baseline left lateral gain may have limited further improvement, but a ceiling effect was not tested. Thus, the result is consistent with altered vestibular lateralization reported in MDD but does not confirm a disease-specific right vestibular deficit.

Future studies should include comprehensive bilateral vestibular assessment rather than assume a specific right-sided abnormality. Examining patients with dizziness, imbalance, or motion sensitivity may help determine whether vestibular alterations are general features of MDD or occur in a subgroup. Whether baseline vestibular status predicts response also remains unknown, and current evidence is insufficient to recommend routine vestibular screening in all patients with MDD.

The VR findings should be interpreted according to the nature of the intervention. Most VR studies in depression have used psychotherapeutic approaches, including cognitive behavioral therapy and Avatar Therapy [14–16], whereas VR here was used as an active balance and vestibular rehabilitation tool. The exercises involved weight transfer, visuomotor coordination, postural regulation, and simultaneous engagement of visual, vestibular, proprioceptive, and motor systems. Therefore, reduced depressive symptoms cannot be attributed solely to a direct psychotherapeutic effect of VR. Physical activity, therapist interaction, feedback, and active participation may also have contributed.

VR-based rehabilitation has improved balance and some vestibular outcomes in populations with peripheral vestibular dysfunction or unilateral vestibular hypofunction [17–21]. These studies involved vestibular disorders rather than mood disorders, so their findings cannot be directly generalized to women with MDD. They nevertheless support using VR as a structured vestibular rehabilitation environment.

nGVS differs from VR in its primary physiological target. Galvanic stimulation can modify vestibular afferent activity and related vestibular signal processing [11, 13]. Subthreshold noisy stimulation has been investigated as a means of facilitating weak vestibular signals, providing a rationale for pairing nGVS with active rehabilitation. These characteristics, however, do not demonstrate a direct antidepressant effect.

The findings are also relevant to the randomized study by Khavarghazalani et al. [21]. In patients with unilateral vestibulopathy, vestibular rehabilitation combined with three nGVS sessions produced greater improvement in selected postural, VOR, and DHI measures. This supports the possibility of complementary effects between vestibular stimulation and rehabilitation, although that population had a primary peripheral vestibular disorder and therefore does not provide direct evidence of efficacy in MDD.

A specific synergistic interaction cannot be concluded from the present design. The nGVS group received 60 minutes of active stimulation, the VR group approximately 360 minutes of active rehabilitation, and the combined group received both. Greater change in the combined group may reflect complementary or additive effects, but

differences in treatment exposure, therapist contact, and therapeutic participation may also have contributed. A priming effect of nGVS before sensorimotor training remains a hypothesis because it was not directly measured. Mean DHI scores decreased numerically in the intervention groups, but between-group differences were not statistically significant. These reductions should therefore not be presented as confirmed treatment effects. Relatively low baseline DHI scores may have limited the observable range of improvement, although a floor effect was not directly tested.

Nonspecific treatment effects may have influenced self-reported outcomes. Placebo and contextual effects are relevant in depression trials [26]. The pharmacotherapy control group received no sham vestibular intervention, active VR was distinguishable from sham conditions, therapists knew group allocation, and outcome assessment was not blinded. These factors may have affected BDI-II and DHI scores. vHIT provided an objective measure but does not remove these methodological limitations.

The right lateral VOR result should be treated as canal-specific because comparable changes were not found consistently in the left lateral or vertical canals. Vertical-canal vHIT can also be influenced by test geometry and recording conditions [27]. Corrective saccades were recorded descriptively and were not an independent inferential outcome.

A possible biological framework involves brainstem serotonergic pathways. Experimental anatomical studies show connections from the vestibular nuclei and nucleus prepositus hypoglossi to the dorsal raphe [28], while dorsal raphe neurons send collateral projections to the vestibular nuclei and amygdala [10]. Serotonergic systems interact with limbic and stress-related networks implicated in depression [29]. Together, these connections provide a plausible anatomical hypothesis for interaction between vestibular input and mood-related networks.

This mechanism was not tested. Dorsal raphe activity, serotonergic function, BDNF, HPA-axis activity, functional brain connectivity, and other neural markers were not assessed. It is also unknown whether VOR changes were associated with or mediated changes in depressive symptoms. Therefore, the simultaneous affective and vestibular findings do not establish a causal relationship.

Overall, vestibular-targeted interventions added to stable pharmacotherapy were associated with greater improvement in depressive symptoms, whereas DHI effects were not statistically significant and the objective vestibular finding was limited to right lateral VOR gain. The results remain preliminary because the sample was small, female-only, and limited to moderate MDD; the control group was separately recruited and non-randomized; complete blinding was not feasible; medication regimens were not standardized across participants; treatment exposure differed among groups; and follow-up was short. Multiple canal analyses, possible vHIT measurement variability, and the absence of objective neurophysiological measures further limit interpretation. Larger, more diverse, fully randomized sham-controlled studies with standardized treatment exposure, long er follow-up, and objective physiological measures are needed.

Conclusion

This controlled quasi-experimental study found that adding vestibular-targeted interventions to stable pharmacotherapy was associated with greater reductions in depressive symptoms in women with moderate MDD than pharmacotherapy alone. The combined nGVS+VR group also showed a greater increase in right lateral VOR gain than the control group. In contrast, between-group differences in DHI change were not statistically significant at posttest or follow-up.

The combined approach therefore warrants further investigation as an adjunctive intervention, but the present results do not demonstrate a specific synergistic mechanism or definitive superiority over both individual vestibular interventions. The right lateral VOR result should be regarded as an exploratory, canal-specific finding rather than evidence of disease-specific right-sided vestibular dysfunction in MDD. Larger, fully randomized studies with stronger control conditions, equal treatment exposure, longer follow-up, and direct assessment of proposed vestibular-serotonergic-limbic mechanisms are required to establish the clinical relevance and mechanisms of these findings.

Ethical Considerations

Compliance with ethical guidelines

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of the University of Social Welfare and Rehabilitation Sciences, Tehran, Iran (Ethics Code: IR.USWR.REC.1400.232). All participants were fully informed about the objectives of the study and the voluntary nature of their participation. Written informed consent was obtained from all participants prior to their enrollment in the study. The study was not prospectively registered in a clinical trial registry.

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Authors' contributions

FH: Conceptualization, study design, data acquisition, data analysis and interpretation, and manuscript drafting. YL: Conceptualization, study supervision, and critical revision of the manuscript for important intellectual content. MKA: Patient referral, study design, and study supervision, EB: Study design, data analysis, and interpretation.

Conflict of interest

The authors declare no conflicts of interest.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Table 1. Baseline demographic and clinical characteristics of study participants by treatment group

characteristic	Total	Group			
		Control mean (SD)	nGVS mean (SD)	VR mean (SD)	VR + nGVS mean (SD)
Age (y)	32.69 (6.60)	31.15 (6.44)	36.31 (7.23)	30.54 (7.03)	32.77 (4.48)
Duration of disease (m)	4.85 (1.33)	4.77 (1.69)	5.15 (1.28)	4.77 (0.60)	4.69 (1.60)

nGVS; noisy galvanic vestibular stimulation, VR;Virtual reality

Table 2. Comparison of mean Beck Depression Inventory-II and Dizziness Handicap Inventory scores between groups in patients with major depressive disorder.

	Group				$F_{(3,48)}$	p	η^{2*}	Pairwise comparison
	Control mean(SD)	nGVS mean(SD)	VR mean (SD)	VR + nGV mean (SD)				
BDI-II								
Baseline	22.00 (1.53)	23.38 (2.22)	23.54 (1.81)	23.23 (2.09)				
Posttest	20.15 (4.04)	18.62 (3.45)	17.48 (3.15)	15.23 (2.31)				
Follow-up	20.31 (3.20)	18.31 (3.71)	17.23 (2.07)	15.46 (3.07				
Change score at posttest	-1.85 (3.05)	-4.77 (3.14)	-6.15(3.13)	-8.00 (3.19)	8.94	<0.001	0.358	VR+ nGVS, VR < control
Change score at follow-up	-1.69 (2.39)	-5.08 (3.28)	-6.31 (3.04)	-7.77(3.68)	8.90	<0.001	0.357	VR+ nGVS, VR, nGVS < control
DHI								
Baseline	10.77 (10.25)	8.46 (9.77)	6.92 (7.29)	10.31 (7.78)				
Posttest	9.08 (9.40)	3.53 (4.77)	1.54 (5.55)	3.23 (3.96)				
Follow-up	8.00 (8.12)	3.38 (4.57)	1.54 (5.55)	3.08 (4.05)				
Change score at posttest	-1.69 (2.43)	-4.92 (5.63)	-5.38 (5.80)	-7.80 (4.94)	2.75	0.053	0.147	-
Change score at follow-up	-2.77 (2.89)	-5.08 (5.75)	-5.38 (5.80)	-7.23 (5.07)	1.73	0.173	0.098	-

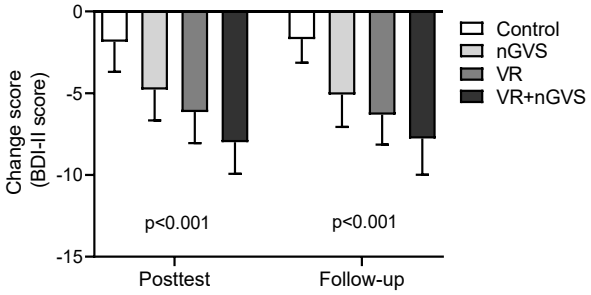
Abbreviations. nGVS; noisy galvanic vestibular stimulation, VR; Virtual reality, BDI-II; Beck Depression Inventory-II, DHI; Dizziness Handicap Inventory.
Between-group differenc es were examined using the one-way ANOVA (followed by Tukey's post-hoc test).
*η^2 values of 0.01-0.06, 0.06-0.14, and >0.14 were considered as small, medium, and large effect size, respectively.

Table 3. Comparison of vestibulo-ocular reflex gain between groups in patients with major depressive disorder.

VOR Gain	Group				$F_{(3,48)}$	p	η^{2*}	Pairwise comparison
	Control mean (SD)	nGVS mean (SD)	VR mean (SD)	VR+nGVS mean (SD)				
Lateral Side- Right								
Baseline	0.67 (0.16)	0.66 (0.17)	0.64 (0.13)	0.62 (0.16)				
Posttest	0.75 (0.19)	0.86 (0.10)	0.79 (0.13)	0.90 (0.10)				
Follow-up	0.74 (0.16)	0.84 (0.10)	0.81 (0.13)	0.88 (0.08)				
Change score at posttest	0.08 (0.10)	0.20 (0.12)	0.15 (0.12)	0.28 (0.14)	5.96	0.002	0.271	VR+ nGVS > Control VR
Change score at follow-up	0.07 (0.08)	0.18 (0.14)	0.17 (0.14)	0.25 (0.11)	5.36	0.003	0.251	VR+ nGVS > Control
Lateral Side- Left								
Baseline	0.84 (0.15)	0.82 (0.11)	0.80 (0.10)	0.81 (0.13)				
Posttest	0.88 (0.15)	0.95 (0.10)	0.89 (0.11)	0.90 (0.10)				
Follow-up	0.87 (0.13)	0.94 (0.08)	0.87 (0.09)	0.89 (0.05)				
Change score at posttest	0.04 (0.20)	0.13 (0.12)	0.09 (0.14)	0.10 (0.14)	0.80	0.502	0.047	-
Change score at follow-up	0.03 (0.14)	0.11 (0.13)	0.07 (0.12)	0.08 (0.14)	0.87	0.464	0.052	-
Anterior Side- Right								
Baseline	0.72 (0.11)	0.68 (0.19)	0.73 (0.15)	0.67 (0.17)				
Posttest	0.78 (0.14)	0.86 (0.14)	0.80 (0.09)	0.92 (0.12)				
Follow-up	0.77 (0.14)	0.82 (0.13)	0.81 (0.09)	0.90 (0.11)				
Change score at posttest	0.07 (0.11)	0.17 (0.17)	0.07 (0.14)	0.25 (0.21)	3.82	0.016	0.193	VR+ nGVS > Control, VR
Change score at follow-up	0.06 (0.11)	0.13 (0.19)	0.08 (0.13)	0.23 (0.20)	3.18	0.032	0.166	VR+ nGVS > Control
Anterior Side- Left								
Baseline	0.84 (0.06)	0.84 (0.09)	0.83 (0.09)	0.87 (0.08)				
Posttest	0.89 (0.10)	0.89 (0.09)	0.86 (0.07)	0.91 (0.09)				
Follow-up	0.86 (0.10)	0.85 (0.06)	0.86 (0.05)	0.90 (0.06)				
Change score at posttest	0.05 (0.08)	0.05 (0.12)	0.03 (0.10)	0.04 (0.10)	0.07	0.975	0.004	-
Change score at follow-up	0.02 (0.09)	0.01 (0.08)	0.03 (0.09)	0.04 (0.08)	0.31	0.819	0.019	-
Posterior Side- Right								
Baseline	0.85 (0.11)	0.85 (0.09)	0.86 (0.09)	0.84 (0.07)				
Posttest	0.89 (0.09)	0.92 (0.08)	0.91 (0.10)	0.92 (0.07)				
Follow-up	0.84 (0.06)	0.91 (0.09)	0.92 (0.07)	0.92 (0.07)				
Change score at posttest	0.04 (0.10)	0.07 (0.13)	0.05 (0.12)	0.08 (0.12)	0.39	0.760	0.024	-
Change score at follow-up	-0.01 (0.08)	0.06 (0.15)	0.05 (0.10)	0.08 (0.10)	1.51	0.224	0.086	-
Posterior Side- Left								
Baseline	0.79 (0.14)	0.76 (0.17)	0.72 (0.18)	0.78 (0.15)				
Posttest	0.84 (0.15)	0.85 (0.14)	0.83 (0.12)	0.95 (0.08)				
Follow-up	0.82 (0.14)	0.82 (0.11)	0.82 (0.09)	0.92 (0.08)				
Change score at posttest	0.05 (0.15)	0.09 (0.10)	0.12 (0.14)	0.17 (0.11)	2.14	0.107	0.118	-
Change score at follow-up	0.03 (0.12)	0.06 (0.10)	0.10 (0.13)	0.14 (0.12)	2.13	0.109	0.117	-

nGVS; noisy galvanic vestibular stimulation, VR; Virtual reality, VOR; vestibulo-ocular reflex.

*η^2 values of 0.01-0.06, 0.06-0.14, and >0.14 were considered as small, medium, and large effect size, respectively.



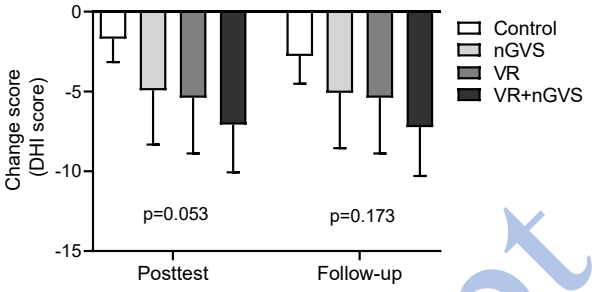


Figure 1. Comparison of mean beck depression inventory-II and dizziness handicap inventory scores between groups in patients with major depressive disorder.
nGVS; noisy Galvanic Vestibular Stimulation, VR; Virtual Reality, BDI-II; Beck Depression Inventory-II; DHI; Dizziness Handicap Inventory.
p-Values are based on the one-way ANOVA.