Journal of Translational Medicine

RESEARCH

Open Access

# Galvanic vestibular stimulation promotes visuospatial cognitive recovery in acute unilateral vestibulopathy via targeted neural modulation: a randomized controlled trial

Sun-Young Oh[1,2*], Thanh Tin Nguyen[3], Jin-Ju Kang[1,2], Juhee Chae[1,2] and Marianne Dieterich[4,5,6]

## Abstract

**Background** The vestibular system plays a crucial role in spatial orientation and hippocampal-dependent memory. While bilateral vestibular loss is known to impair spatial cognition, recent evidence highlights that even unilateral vestibular deficits—commonly seen in vestibular neuritis—can disrupt visuospatial memory. Galvanic vestibular stimulation (GVS), a non-invasive neuromodulatory technique, has shown promise in enhancing neural plasticity and spatial cognition in preclinical models.

**Objective** To evaluate the therapeutic effects of near-threshold GVS on visuospatial cognition in patients with acute unilateral peripheral vestibulopathy (AUPV) and to investigate its neuromodulatory potential beyond natural recovery.

**Methods** In a single-blind, randomized, sham-controlled trial, 83 AUPV patients were assigned to receive either 10 daily sessions of GVS (cathode on lesion side) or sham stimulation in the acute phase. Cognitive assessments included the Visual Object and Space Perception (VOSP) battery, Corsi Block-Tapping Test (CBTT), Block Design Test (BDT), and a virtual Morris Water Maze (vMWM). Intervention and time-dependent effects were analyzed using generalized estimating equations.

**Results** GVS significantly improved visuospatial memory performance, with enhanced CBTT block span and total scores and superior spatial retention in the vMWM trial. Significant interaction effects between intervention and time suggested that GVS accelerated cognitive recovery beyond spontaneous compensation. No adverse effects were reported.

**Conclusion** These findings support GVS as a neuromodulatory intervention to enhance spatial memory and facilitate cognitive recovery in AUPV. By modulating vestibulo-hippocampal circuits, GVS may offer a promising therapeutic avenue for cognitive rehabilitation in unilateral vestibular dysfunction.

**Trial registration** This study was registered with the Clinical Research Information Service (CRIS), Republic of Korea, under the identifier KCT0007058, registered on May 25, 2022.

*Correspondence:
Sun-Young Oh
ohsun@jbnu.ac.kr

Full list of author information is available at the end of the article

**Keywords** Galvanic vestibular stimulation (GVS), Visuospatial cognition, Unilateral vestibulopathy, Neuromodulation, Hippocampal plasticity, Vestibular neuritis

## Introduction

The vestibular system, beyond its established roles in balance and gaze stabilization, is increasingly recognized as a key modulator of spatial cognition and memory [1, 2]. Neural pathways linking vestibular afferents to the hippocampus, retrosplenial cortex, and entorhinal regions support the integration of self-motion cues essential for navigation and memory encoding [3, 4]. Disruption of these pathways, such as through bilateral vestibular loss, has been shown to impair hippocampal-dependent spatial memory and even induce hippocampal atrophy in both animals and humans. However, unilateral peripheral vestibulopathy (UVP)—a more prevalent and clinically manageable condition—can also lead to measurable deficits in spatial orientation and visuospatial memory [5]. Emerging evidence suggests that asymmetrical vestibular input in UVP disrupts interhemispheric integration within spatial networks, with lesion side and degree of deafferentation influencing the extent of cognitive dysfunction. [6–11]

Galvanic vestibular stimulation (GVS), a non-invasive neuromodulation technique, delivers direct current across the mastoids to stimulate vestibular afferents and downstream neural circuits [12–14]. Preclinical studies have demonstrated that GVS modulates hippocampal theta rhythms, activates place cells, and enhances neuroplasticity, particularly when applied asymmetrically to restore lateralized vestibular tone [9, 15]. Clinical studies have begun to explore GVS as a means to improve postural control and cognitive function in vestibular and neurodegenerative disorders.

In this randomized controlled trial, we investigated whether individualized near-threshold GVS, applied during the acute phase of UVP, could enhance visuospatial cognitive recovery. We hypothesized that GVS would improve spatial memory and navigation by modulating vestibulo-hippocampal pathways and accelerating neural compensation processes beyond natural recovery.

## Method

### Participants and study design

This parallel-group, randomized controlled trial included 83 patients (aged 34–80 years; 51.8% male) with acute UVP (vestibular neuritis) at Jeonbuk National University Hospital from March 2022 to August 2024. The sample size was determined using a medium effect size ($d = 0.6$), a significance level of 0.05, and a power of 80%. Using these parameters, the required sample size was calculated to be 40 participants per group (80 total participants) for a two-sample t-test. Patients were randomly assigned in a 1:1 ratio to either the GVS intervention group or the sham control group. A computer-based randomization program was used to generate the allocation sequence, ensuring unbiased group assignment. The randomization list was securely stored and was accessible only to the investigator responsible for patient enrollment. This study was single-blinded, with patients unaware of their group allocation. Patients diagnosed with acute UVP (vestibular neuritis) during the acute phase (within seven days of symptom onset) were eligible for recruitment. Exclusion criteria included patients presenting beyond the acute phase (more than seven days after symptom onset), those with significant visual or hearing impairments (pure tone audiometry > 30 dB), central neurological signs (e.g., bilateral gaze-evoked nystagmus or skew deviation), abnormal MRI findings, or a diagnosis of dementia. Cognitive status was evaluated using the Mini-Mental State Examination (MMSE), and handedness was assessed with the Edinburgh Handedness Inventory (Table 1). Vestibular and spatial cognitive functions were assessed during the acute phase and at a follow-up four weeks later in the post-recovery phase (Fig. 1).

### Vestibular function tests

Patients underwent neurological and comprehensive neurotological evaluations, including video-oculography, vHIT, caloric testing, ocular and cervical vestibular-evoked myogenic potentials (VEMPs), and pure-tone audiometry. Assessments were performed during the acute phase between day 1 and day 7 (mean day 6), with vHIT repeated during the recovery phase. The vHIT was conducted more than 20 times, utilizing head rotations of 15° to 20°, duration of 150 to 200 ms, and peak velocities exceeding 150°/sec across all planes bilaterally (SLMED, Seoul, Korea). Caloric response was measured by induced nystagmus, with analysis of slow-phase velocity to assess unilateral deficits using the Jongkees formula. Cervical and ocular VEMP results were evaluated based on the asymmetry ratio (AR) of the amplitude, calculated as the difference in amplitudes between the ears divided by the sum of the amplitudes in both ears.

### Visuospatial perception testing

The Visual Object and Space Perception (VOSP) battery was used to assess visual and spatial processing abilities. Participants first completed the Shape Detection Screening Test to confirm adequate visual capacity. Subtests included Position Discrimination, Number Location, and Cube Analysis. In Position Discrimination, participants identified the cen-

**Table 1** Demographic characteristics and vestibular function tests in AUVP patients with and without GVS intervention

| | GVS (n = 41) | Sham (n = 42) | *p*-value |
|---|---|---|---|
| *Demographics* | | | |
| Sex, male, n (%) | 20 (47.62) | 23 (54.76) | 0.154 |
| Age, years, median (IQR) | 58 (53–65.25) | 61.5 (57.25–66.75) | 0.479 |
| Education, years, median (IQR) | 12 (9–16) | 12 (9–16) | 0.732 |
| MMSE (30 points), median (IQR) | 28.5 (27.25–30) | 28.0 (26.8–30) | 0.289 |
| Lesion side, right, n (%) | 23 (61.9) | 18 (42.86) | 0.593 |
| Handedness, right, n (%) | 41 (100) | 42 (100) | |
| Application initiation day from symptom onset (mean ± SD, days) | 5.1 ± 2.3 | 3.9 ± 1.9 | 0.510 |
| *Audio-vestibular function tests* | | | |
| *Acute phase* | | | |
| Spontaneous nystagmus, mean (º/sec) | 6.2 ± 5.2 | 6.5 ± 5.7 | 0.868 |
| vHIT | | | |
| hVOR gain, ipsilesional, median (IQR) | 0.52 (0.38–0.74) | 0.73 (0.54–0.84) | 0.113 |
| hVOR gain, contralesional, median (IQR) | 0.95 (0.87–1.03) | 0.96 (0.92–1.03) | 0.498 |
| Presence of corrective saccades, n (%) | 19 (90.48) | 34 (80.95) | 0.329 |
| Caloric paresis, %, median (IQR) | 98.01 (36.37–196.25) | 74.71 (34.93–125.55) | 0.475 |
| Caloric paresis ≥ 35%, n (%) | 15 (71.43) | 30 (71.43) | 0.739 |
| Cervical and ocular VEMP | | | |
| cVEMP p13 latency | | | |
| Ipsilateral (ms), median (IQR) | 13.9 (13.25–16.8) | 13.9 (13.2–15.1) | 0.614 |
| Contralateral (ms), median (IQR) | 13.2 (12.9–14.9) | 14 (13.2–14.4) | 0.364 |
| cVEMP amplitude AR, %, median (IQR) | 18 (10–28) | 24 (9.75–40.5) | 0.371 |
| cVEMP amplitude AR ≥ 40%, n (%) | 1 (4.8) | 9 (21.43) | 0.064 |
| oVEMP n10 latency | | | |
| Ipsilateral (ms), median (IQR) | 11.1 (10.9–12.6) | 11 (10.7–12.25) | 0.581 |
| Contralateral (ms), median (IQR) | 10.7 (10.08–11) | 10.6 (10.18–11) | 0.915 |
| oVEMP amplitude AR, %, median (IQR) | 17 (6.5–43.2) | 30.5 (17–46) | 0.086 |
| oVEMP amplitude AR ≥ 40%, n (%) | 5 (23.81) | 14 (33.33) | 0.264 |
| PTA, dB, median (IQR) | 18 (15.1–24.5) | 19.5 (12–30.5) | 0.81 |
| Completion day of audio-vestibular function tests (mean ± SD, days) | 6.1 ± 3.8 | 8.9 ± 2.2 | 0.222 |
| Mean cutaneous threshold of GVS (mean ± SD, mA) | 0.9 ± 0.05 | 0.9 ± 0.05 | |
| *Recovery phase* | | | |
| vHIT | | | |
| hVOR gain, ipsilesional, median (IQR) | 0.87 (0.55–1.07) | 0.66 (0.35–1.01) | 0.194 |
| hVOR gain, contralesional, median (IQR) | 1 (0.92–1.06) | 0.94 (0.91–1.03) | 0.456 |
| Presence of corrective saccades, n (%) | 9 (42.86) | 12 (28.57) | 0.535 |
| *Visuospatial cognitive performances during the acute phase* | | | |
| Position Discrimination (mean ± SD) | 19.57 ± 0.81 | 19.17 ± 2.13 | 0.405* |
| Number Location (mean ± SD) | 8.05 ± 2.54 | 8.43 ± 2.43 | 0.566* |
| Cube Analysis (mean ± SD) | 8.57 ± 1.47 | 8.74 ± 1.75 | 0.709* |
| Block Design Test (BDT) (mean ± SD) | 32.95 ± 7.26 | 32 ± 7.39 | 0.639* |
| BDT Plus (mean ± SD) | 36 ± 10.44 | 34.24 ± 9.63 | 0.508* |
| Corsi Block-Tapping Test (CBTT) Block Span (mean ± SD) | 6.3 ± 1.42 | 5.29 ± 3.2 | 0.182* |
| CBTT Total Score (mean ± SD) | 35.2 ± 13.2 | 32.98 ± 11.64 | 0.101* |

Data are presented as median [IQR, 25th–75th percentile] or n (%), unless otherwise indicated. P-values were calculated with the Mann–Whitney U test; values marked with an asterisk were analysed with an independent-samples t-test.*

*vHIT-ipsi* video head-impulse test (ipsilesional gain), *UW* unilateral weakness (caloric paresis), *VEMP* vestibular-evoked myogenic potential, *AR* asymmetry ratio, *MMSE* Mini-Mental State Examination, *PTA* pure-tone audiometry, *dB* decibel, *ms* millisecond

tered dot on 20 boards (normal: ≥ 18). In Number Location, participants matched a number to its-corresponding dot position on 10 boards (normal: ≥ 7). In Cube Analysis, participants counted visible and hidden cubes on 10 boards (normal: ≥ 6).

### Visuospatial memory testing

Visuospatial memory was evaluated using the Block Design Test (BDT), the Corsi Block-Tapping Test (CBTT) and the virtual Morris Water Maze test (vMWM). In the BDT, participants used nine colored blocks to reconstruct

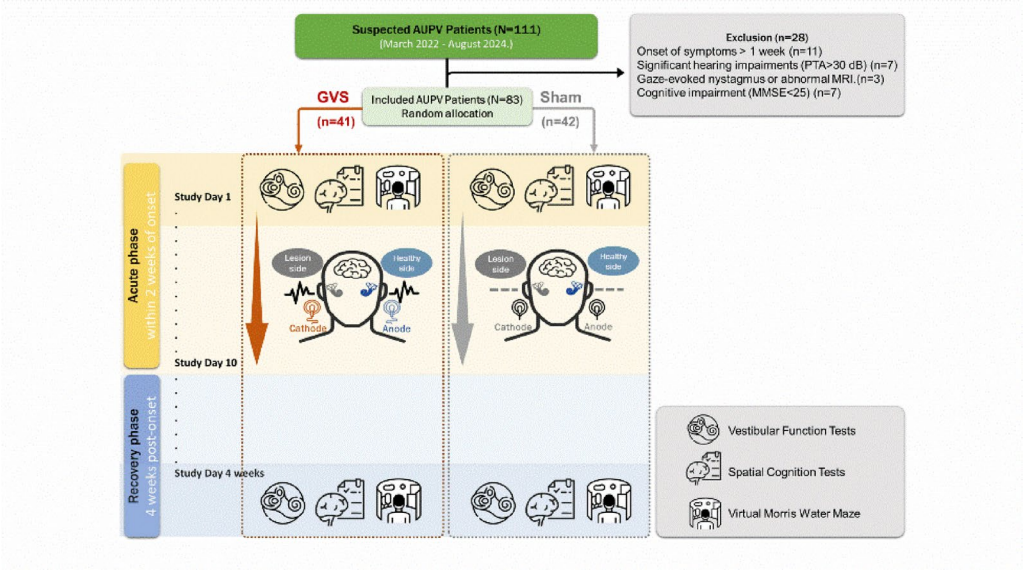


**Fig. 1** CONSORT diagram for study flow. Flowchart depicting the enrollment, randomization, and follow-up of acute unilateral peripheral vestibulopathy (AUPV) patients (N = 83). Patients were assessed in the acute phase (within 1 week of symptom onset) and the recovery phase (4 weeks post-onset). Following random allocation to either the galvanic vestibular stimulation (GVS, n = 41) or sham stimulation group (n = 42), participants underwent a series of tests including vestibular function tests, spatial cognition tests including the virtual Morris Water Maze. Testing was conducted over 10 consecutive days in both phases to evaluate the impact of interventions on vestibular and cognitive recovery

progressively complex 2D patterns, with scores ranging from 0 to 66 based on accuracy and speed. The CBTT involved replicating sequences of tapped blocks, measuring block span (the length of the last correctly repeated sequence) and total score (span × correct sequences) to evaluate visuospatial working memory and attention. The total score provided a more accurate assessment of visuospatial working memory and spatial attention. The vMWM assessed spatial learning by recording latency to find a hidden platform in five trials, followed by a probe trial to measure memory retention. Time spent in the target quadrant was the primary metric, and movement velocity was tracked to ensure results weren't influenced by differences in activity level.

### GVS and sham stimulation

Patients were randomized into two groups: a GVS group and a sham group (Fig. 1). A CE-certified battery-driven constant current stimulator (neuroConn DC-Stimulator Plus; neuroConn, Ilmenau, Germany) was used for both GVS and sham stimulation sessions. Each session was conducted in a quiet, dedicated room within our outpatient clinic, minimizing external stimuli and potential distractions. A trained clinician, experienced in vestibular therapies, supervised all sessions to monitor patient responses and manage any adverse effects promptly. Participants were seated upright in a chair, and stimulation was delivered through a pair of 35 cm [2] (5 × 7 cm) rectangular conductive rubber electrodes coated with electrode gel. These electrodes were placed binaurally over both mastoids and secured with a rubber head strap to ensure stability. To optimize conductivity and minimize skin impedance, a conductive gel was applied to the electrode sites before testing.

In the GVS group, direct current (DC) stimulation was individualized, with the cathode on the lesion side and the anode on the healthy side. Sensory threshold amplitudes ranged from 0.8 to 1.0 mA, determined using established protocols, to activate the vestibular pathways while minimizing discomfort. Each session lasted 30 min and was administered daily for 10 consecutive days during the acute phase of vestibular neuritis. The sham group used the same setup and equipment, but the stimulator delivered only a brief initial current to mimic stimulation, with no ongoing current for the remainder of the session. This approach maintained participant blinding and preserved study integrity by controlling for placebo effects. The primary outcome was the differential improvement in visuospatial perception and memory function, assessed using the VOSP battery, CBTT, and vMWM tests after the interventions.

### Standard protocol approvals, registrations, and patient consents

The study design, illustrated in Fig. 1, followed the Declaration of Helsinki and received approval from the Institutional Review Boards of Jeonbuk National University Hospital (IRB no. 20220404500), and from the Clinical Research Information Service (CRIS) (KCT0007058). All participants provided written informed consent.

### Data sharing statement

All individual participant data that support the results in this study will be shared after de-identification (manuscript, tables, and figures).

### Statistical analysis

All analyses were performed with SPSS Statistics v 23.0 (IBM Corp., Armonk, NY) under a prespecified plan (eSAP 1–2). Continuous variables were inspected for normality with the Shapiro-Wilk test. Non-Gaussian variables are reported as median (IQR), whereas Gaussian variables appear as mean ± SD (baseline) or mean ± SE (model-adjusted end-points). Group differences in baseline demographics and vestibular test results were evaluated with the Mann-Whitney U test (continuous data) or $\chi^2$/Fisher's exact test (categorical data).

Longitudinal outcomes—visuospatial test scores and vMWM latencies—were modelled with generalised estimating equations (GEE) to accommodate repeated measures. The working correlation structure was set to exchangeable after comparison of quasi-likelihood under the independence model criterion (QIC). Fixed factors were intervention (GVS vs sham), temporal phase (acute vs 4-week recovery) and, where appropriate, trial number (vMWM Trials 1–5 + probe); gender and lesion side were retained as covariates, whereas age and education were excluded because their inclusion did not improve QIC or alter any parameter estimate by > 5%. A linear distribution with identity link was used for all continuous outcomes, and robust (sandwich) standard errors were requested. Significance of main and interaction effects was determined with Wald $\chi^2$ statistics.

To control for multiple testing across GEE contrasts, a Bonferroni correction was applied within each family of related hypotheses; two-sided, adjusted $p < 0.05$ was considered statistically significant. Effect sizes are reported as β ± SE for GEE coefficients and Cramer's V or rank-biserial r for $\chi^2$ and Mann-Whitney tests, respectively. No imputation was required because the data set was complete.

## Results

### Clinical characteristics

A total of 83 AUVP patients were randomized into the GVS group (n = 41) or the sham group (n = 42) using a computer-generated sequence with equal allocation (Fig. 1). Table 1 summarizes the demographics and vestibular function test results of patients with AUVP who underwent either GVS or a sham intervention. Baseline demographics, cognitive status and audio-vestibular metrics were closely matched between groups: sex distribution (48% vs 55% male), age (median 58 vs 61.5 y), years of education (median 12 in both arms), MMSE (median 28.5 vs 28.0) and lesion laterality (62% vs 43% right-sided) all yielded non-significant Mann-Whitney/$\chi^2$ tests ($p \geq 0.15$). Stimulation commenced a median 5 days (GVS) and 4 days (sham) after symptom onset, again without statistical difference, and the near-threshold current (0.9 ± 0.05 mA) was well tolerated—no adverse events or withdrawals occurred. Measures of spontaneous nystagmus, video head-impulse test gains, caloric paresis, cervical/ocular VEMP asymmetry and pure-tone thresholds were likewise comparable, confirming equivalent vestibular deficits at enrolment (Table 1).

### Visuospatial cognitive performance

Generalised estimating equations (GEE) were fitted with intervention (GVS vs sham), temporal phase (acute vs 4-week), sex and lesion side as fixed factors (Table 2 and Fig. 2). Age and education were explored as covariates but were excluded from the final model because they did not improve model fit (QIC) or alter any point estimates by > 5%.

- Intervention effect: Across acute and four-week assessments the GVS cohort achieved larger gains on the CBTT than sham (adjusted + 1.2 blocks in span; + 8.8 points in total score; both $p < 0.001$).
- Lesion-side effect: Participants with left-sided vestibular neuritis out-performed those with right-sided lesions on CBTT span (p = 0.008) and total score ($p = 0.014$).
- Temporal effect: Irrespective of treatment, position discrimination, cube analysis and BDT scores increased significantly from the acute to the four-week recovery phase (all $p \leq 0.014$).
- Intervention × time interaction: Crucially, intervention-by-time interactions reached significance for position discrimination, cube analysis, BDT and both CBTT metrics (interaction $p = 0.029$– < 0.001), indicating that GVS accelerated the trajectory of cognitive recovery rather than merely shifting group means.

No other main or interaction effects were detected, and the equivalence of intervention initiation times (5.1 ± 2.3 days for GVS versus 3.9 ± 1.9 days for sham, $p = 0.510$) rules out confounding by treatment delay.

### Virtual morris water maze (vMWM) outcomes

The vMWM data were modelled with a three-factor GEE that included intervention (GVS vs sham), study phase (acute vs 4-week recovery) and trial (1-5 + probe) (Table 3). Latency curves were parallel during the acute phase, confirming equivalent baseline navigation, but in the recovery phase they diverged after Trial 3. From Trial 4 onward the GVS group located the hidden platform markedly faster than controls, yielding a significant

**Table 2** Comparative analysis of visuospatial cognitive performance in AUVP patients: Generalized estimating equations (GEE) applied to groups with and without GVS intervention (multi-factorial approach)

| | | Main effects | | | | | | | | Interaction |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Intervention | | Temporal course | | Gender | | Lesion side | | Intervention x Temporal |
| | | GVS | Sham | Acute | Recovery | Male | Female | Right | Left | |
| Position discrimination | Mean ± SE | 19.8 ± 0.08 | 19.85 ± 0.043 | 19.71 ± 0.07 | 19.93 ± 0.047 | 19.87 ± 0.063 | 19.78 ± 0.059 | 19.79 ± 0.065 | 19.86 ± 0.052 | 10.223 |
| | Coefficient | − 0.045 | Ref | − 0.221 | Ref | 0.085 | Ref | -0.068 | Ref | |
| | *p* value | 0.625 | | 0.005 | | 0.302 | | 0.365 | | 0.006 |
| Number location | Mean ± SE | 8.77 ± 0.258 | 9.14 ± 0.134 | 8.88 ± 0.206 | 9.03 ± 0.163 | 8.95 ± 0.205 | 8.96 ± 0.161 | 8.72 ± 0.204 | 9.19 ± 0.173 | 3.098 |
| | Coefficient | − 0.376 | Ref | − 0.147 | Ref | − 0.01 | Ref | -0.471 | Ref | |
| | *p* value | 0.208 | | 0.543 | | 0.966 | | 0.06 | | 0.212 |
| Cube analysis | Mean ± SE | 9.08 ± 0.178 | 9.37 ± 0.095 | 8.99 ± 0.16 | 9.45 ± 0.102 | 9.28 ± 0.136 | 9.16 ± 0.135 | 9.2 ± 0.145 | 9.24 ± 0.124 | 7.097 |
| | Coefficient | − 0.291 | Ref | − 0.46 | Ref | − 0.114 | Ref | -0.04 | Ref | |
| | *p* value | 0.142 | | 0.008 | | 0.52 | | 0.817 | | 0.029 |
| BDT | Mean ± SE | 33.71 ± 0.912 | 33.04 ± 0.818 | 31.86 ± 0.774 | 34.9 ± 0.931 | 33.24 ± 0.963 | 33.51 ± 0.754 | 32.42 ± 0.824 | 34.33 ± 0.93 | 6.154 |
| | Coefficient | 0.666 | Ref | − 3.04 | Ref | − 0.271 | Ref | -1.911 | Ref | |
| | *p* value | 0.598 | | 0.014 | | 0.829 | | 0.14 | | 0.046 |
| BDT Plus | Mean ± SE | 34.04 ± 0.852 | 35.11 ± 1.008 | 32.62 ± 0.899 | 36.54 ± 1.082 | 33.89 ± 1.081 | 35.27 ± 0.915 | 33.74 ± 0.934 | 35.41 ± 1.075 | 6.928 |
| | Coefficient | − 1.072 | Ref | − 3.917 | Ref | − 1.383 | Ref | -1.669 | Ref | |
| | *p* value | 0.417 | | 0.009 | | 0.359 | | 0.276 | | 0.031 |
| CBTT-block span | Mean ± SE | 6.29 ± 0.181 | 5.14 ± 0.143 | 5.5 ± 0.17 | 5.93 ± 0.153 | 5.79 ± 0.163 | 5.64 ± 0.16 | 5.41 ± 0.152 | 6.02 ± 0.173 | 23.21 |
| | Coefficient | 1.157 | Ref | − 0.424 | Ref | 0.144 | Ref | -0.612 | Ref | |
| | *p* value | < 0.001 | | 0.061 | | 0.524 | | 0.008 | | < 0.001 |
| CBTT-total score | Mean ± SE | 33.81 ± 1.928 | 24.97 ± 1.165 | 27.49 ± 1.527 | 31.29 ± 1.47 | 29.92 ± 1.494 | 28.86 ± 1.508 | 26.85 ± 1.24 | 31.93 ± 1.763 | 12.913 |
| | Coefficient | 8.844 | Ref | − 3.8 | Ref | 1.066 | Ref | -5.073 | Ref | |
| | *p* value | < 0.001 | | 0.56 | | 0.593 | | 0.014 | | 0.002 |

Data are presented as mean ± standard error. P-values were derived from Wald $\chi^2$ tests using generalized estimating equations (GEE) with a linear distribution and identity link. Main effects were tested for intervention, temporal phase, gender and lesion side; the intervention × temporal phase interaction was also assessed. Values in **bold** denote statistical significance

intervention × trial × phase interaction (Wald $\chi^2$, $p < 0.01$) (Fig. 3).

During the platform-free probe trial, GVS participants spent more time in the target quadrant ($p = 0.023$) while motor velocity remained identical ($p = 0.704$), indicating superior spatial-memory retention unconfounded by motor speed. These findings show that near-threshold GVS accelerates both the acquisition and the persistence of spatial information beyond spontaneous compensation.

## Discussion

Recent research has expanded our understanding of the vestibular system beyond its traditional roles in gaze stabilization and balance maintenance, revealing its critical involvement in spatial cognitive functions—essential for perceiving, processing, and navigating spatial environments in daily life [16–18]. The hippocampus, entorhinal cortex, and retrosplenial cortex with its highly specialized cell ensembles (place cells, grid cells, and head direction cells), which are pivotal in spatial processing, have emerged as key neural substrates in studies of vestibular hypofunction [19, 20]. While bilateral vestibulopathy (BVP) is well known to cause spatial cognitive deficits and hippocampal atrophy [4], increasing attention has focused on the effects of unilateral vestibulopathy (UVP), a more common and treatable condition, on visuospatial abilities related to orientation and navigation [9]. Previous studies, including those using rodent models with unilateral vestibular loss induced by chemical labyrinthectomy, have demonstrated acute deficits in both short- and long-term visuospatial memory and navigation [6]. These impairments were more pronounced in those with lesions on the vestibular dominant side compared to those with lesions on the non-dominant side, highlighting the influence of lesion location on the

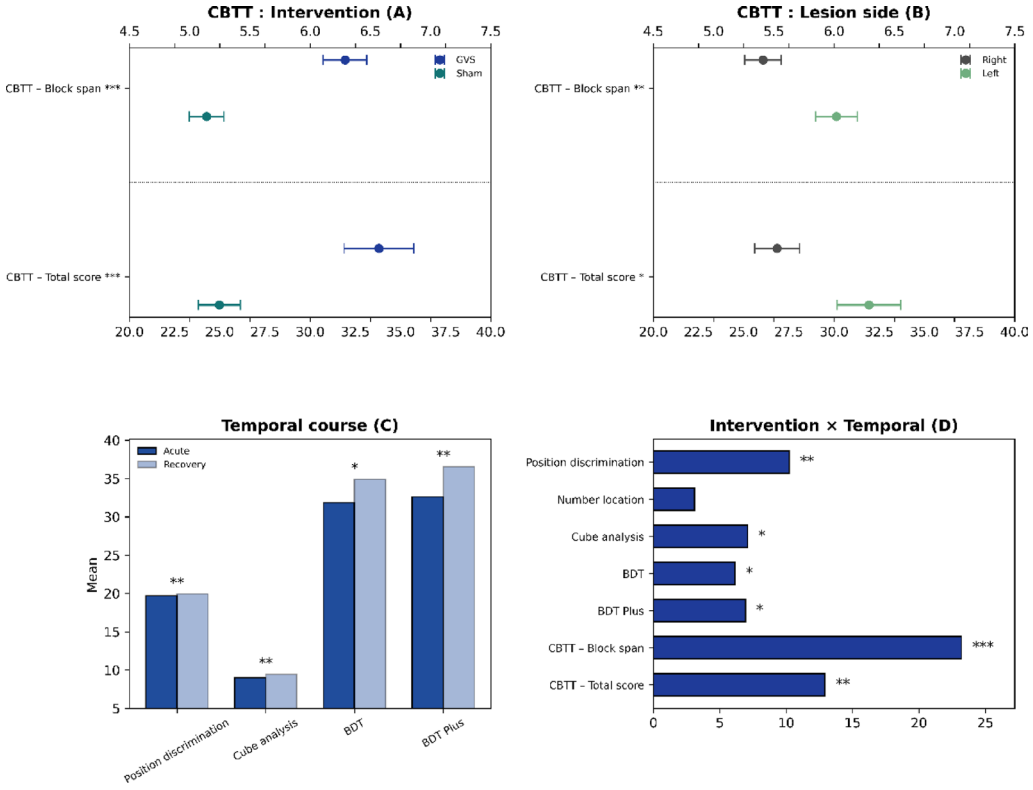


**Fig. 2** Visuospatial cognitive outcomes after near-threshold galvanic vestibular stimulation (GVS) in acute unilateral vestibular paresis (AUVP). **A** Intervention main effect: Adjusted means ± 95% CI for Corsi Block-Tapping Test (CBTT) block span and total score pooled across the acute and 4-week assessments (GVS n = 41; sham n = 42). GVS produced significantly larger gains (***$p < 0.001$, generalised estimating equations [GEE]). **B** Lesion-side main effect: Same CBTT end-points contrasted between left- (n = 39) and right-sided (n = 44) AUVP. Left-sided lesions were associated with better performance (**$p < 0.01$ for span; $p < 0.05$ for total score). **C** Temporal main effect: Mean scores (± SEM) for position discrimination, cube analysis, Block Design Test (BDT) and BDT-Plus during the acute phase and at 4-week recovery, collapsed across interventions. All four tasks improved over time (*$p \leq 0.014$; one-way GEE). (D) Intervention × time interaction: Regression coefficients (β ± SE) from the GEE model depicting the additional 4-week improvement attributable to GVS (relative to sham) for each visuospatial measure. Positive values favour GVS; ***$p < 0.001$, **$p < 0.01$, *$p < 0.05$. Asterisks reflect two-tailed Wald $\chi^2$ tests with Bonferroni adjustment. No adverse events occurred and motor speed did not differ between groups (see Tables 2–3 for full statistics)

**Table 3** Analysis of virtual Morris Water Maze (vMWM) outcomes in patients with AUVP/vestibular neuritis: Generalized estimating equations (GEE) for groups with and without GVS intervention (two-factorial approach)

| | Acute phase | | Recovery phase | | Main effects | | | Interaction |
|---|---|---|---|---|---|---|---|---|
| | GVS (n = 41) | Sham (n = 42) | GVS (n = 41) | Sham (n = 42) | Intervention | Temporal course | Trial | Intervention × Temporal |
| *Latency in Invisible platform task* | | | | | | | | |
| Trial 1 (ms) | 55.51 ± 2.12 | 55.27 ± 4.59 | 54.50 ± 3.29 | 54.26 ± 4.75 | 0.879 | 0.211 | **< 0.001** | 0.445 |
| Trial 2 (ms) | 53.62 ± 3.63 | 52.89 ± 5.29 | 52.23 ± 4.85 | 53.37 ± 3.57 | 0.905 | 0.591 | **< 0.001** | 0.842 |
| Trial 3 (ms) | 48.89 ± 6.68 | 49.53 ± 3.71 | 46.10 ± 5.96 | 49.78 ± 4.81 | 0.19 | 0.24 | **< 0.001** | 0.086 |
| Trial 4 (ms) | 44.84 ± 4.13 | 46.19 ± 3.25 | 37.11 ± 4.19 | 43.67 ± 6.08 | **0.001** | **< 0.001** | **< 0.001** | **< 0.001** |
| Trial 5 (ms) | 40.87 ± 4.1 | 40.70 ± 5.67 | 33.10 ± 6.94 | 39.23 ± 4.62 | **0.041** | **0.004** | Ref | **0.003** |
| *Probe trial* | | | | | | | | |
| Time spent in the target quadrant (%) | 40.45 ± 0.68 | 39.36 ± 7.57 | 49.72 ± 13.40 | 40.26 ± 10.33 | **0.023** | 0.65 | | **0.038** |
| Velocity (m/s) | 0.05 ± 0.017 | 0.05 ± 0.02 | 0.05 ± 0.02 | 0.05 ± 0.02 | 0.704 | 0.721 | | 0.855 |

Data are presented as mean ± standard deviation. *P*-values were obtained from Wald $\chi^2$ tests via generalized estimating equations (GEE) using a linear distribution and identity link. Main effects were assessed for intervention, temporal phase and trial; interaction effects were evaluated for intervention × temporal phase and intervention × trial. Values in **bold** denote statistical significance

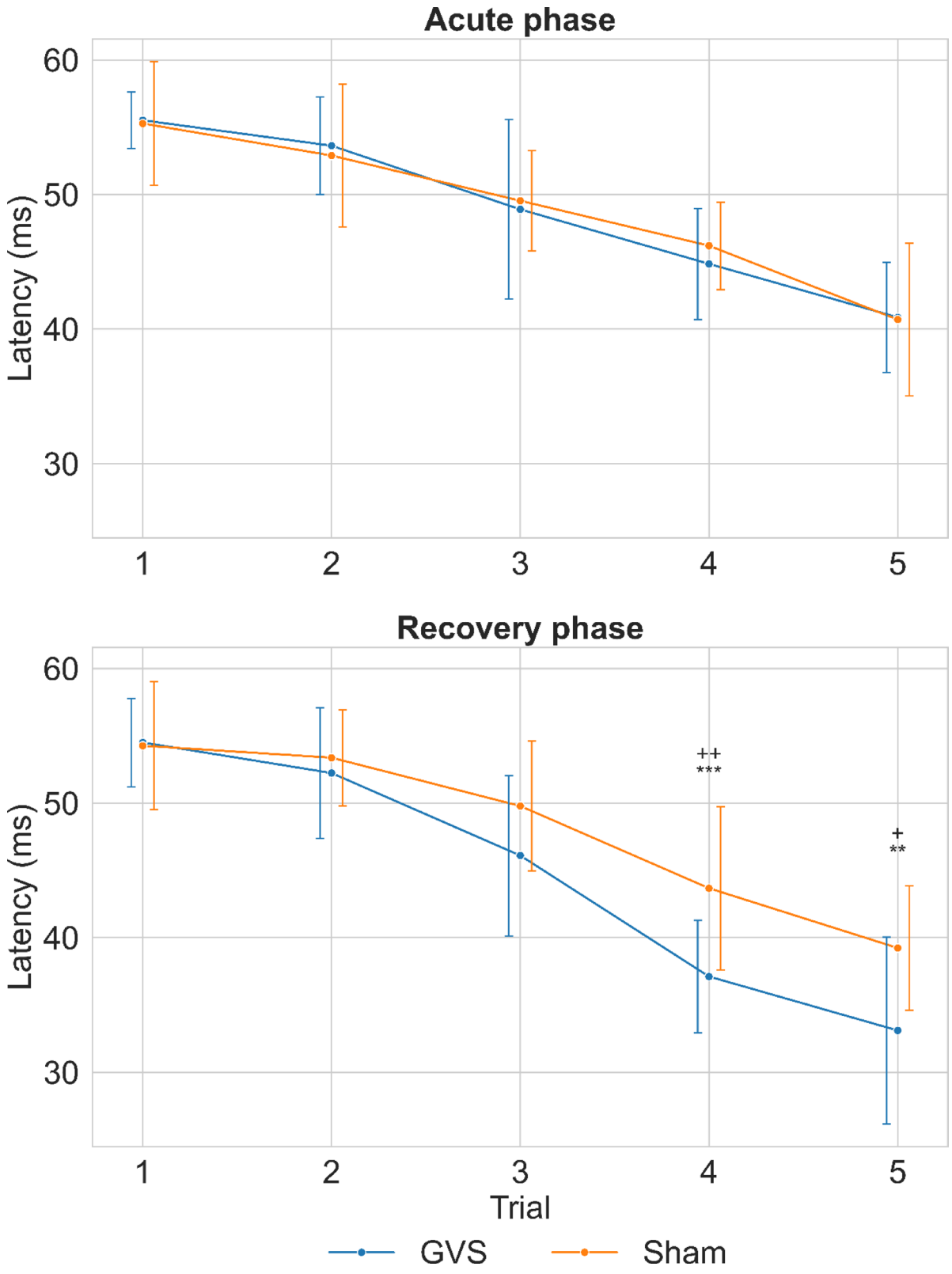


**Fig. 3** Trial-by-trial learning in the virtual Morris Water Maze. Mean escape latencies ± 95% CI are plotted for GVS (blue) and sham (orange) groups during the acute phase (upper panel) and the recovery phase (lower panel). Curves overlap in early trials, diverge from Trial 4 during recovery (***$p < 0.001$; **$p < 0.01$; *$p < 0.05$), and plus signs mark a significant intervention-by-trial interaction. Identical y-axis limits permit direct visual comparison of learning rates

extent of cognitive deficits [21]. Neuronal imaging studies in rodents following unilateral vestibular damage by labyrinthectomy showed decreased glucose metabolism in the ipsilesional hippocampus and entorhinal cortex, alongside increased activity in the contralesional anterior hippocampus and entorhinal cortex [22, 23]. In animal models, such effects are prominent in cases of complete lesions, similar to bilateral vestibulopathy (BVP), where the extent of the lesion influences the severity of the outcomes [8, 24–26]. However, in the current study's patients with incomplete lesions, the effects may be more subtle [9]. Additionally, recent studies indicated that UVP affects multiple domains of spatial memory, including working memory, reference memory, and object-in-place recognition, likely due to disrupted long-term plasticity mechanisms in the ipsilesional hippocampus [10]. The pronounced ipsilateral effects on hippocampal neurobiology suggest a functional lateralization of vestibulo-hippocampal projections, akin to the ipsilateral dominance observed in vestibular projections to the parieto-insular cortex. [27] [28].

Patients with both acute and chronic UVP also experience persistent challenges in spatial memory and navigation, with the severity of deficits often depending on the side of the lesion [19, 29]. Differences in spatial strategies, such as allocentric versus egocentric navigation, and attentional deficits reported across studies may be attributed to variations in assessment methods and patient-specific factors [16]. Structural changes in motion-sensitive areas such as MT/V5 bilaterally and in parietal-temporal regions ipsilateral to the vestibular lesion, have been observed, linking structural and functional deficits [29]. The extent of vestibular damage, whether partial or complete, impacts the processing of spatial information, especially in tasks involving navigation and memory retention [8, 25]. These findings highlight the critical role of symmetrical vestibular input in maintaining spatial memory and underscore the cognitive impairments associated with vestibular hypofunction. While compensatory mechanisms—such as landmark-based strategies, residual head direction system function, or stimulus–response strategies—may help mitigate deficits, patients with incomplete vestibular loss rarely report significant spatial orientation problems in daily life [16, 30, 31]. However, vestibular deafferentation may diminish the functional reserve of hippocampal, insular, and parietal networks with aging, potentially increasing vulnerability to cognitive decline. The same could be true in additional deficits such as, e.g., cardiovascular disease or white matter brain or cerebellar lesions in microangiopathy.

In this study, AUVP patients receiving early GVS outperformed the sham group on the CBTT, showing significant improvements in both block span and total scores (Table 2 and Fig. 2). Patients with right-sided lesions demonstrated greater deficits in visuospatial memory, indicated by lower CBTT block span and total scores, suggesting lateralization effects on cognitive outcomes in vestibular disorders [9, 32]. Additionally, GVS-treated patients had reduced latency in locating the invisible platform and spent more time in the target quadrant during the probe trial of the vMWM task, indicating enhanced spatial learning and memory retention (Table 3 and Fig. 3).

What is the mechanism underlying the effects of GVS on spatial cognition? Given the critical role of vestibular input, including gravity-induced linear acceleration, in the development of normal spatial memory, it was hypothesized that enhanced vestibular stimulation may improve or augment spatial memory [33, 34]. Recent evidence suggests that vestibular physical therapy may alleviate disorientation and cognitive decline in patients with cognitive impairment [35, 36], and that bilateral bipolar GVS could serve as a tool to investigate the effects of vestibular input on cognitive function [37]. Animal studies have demonstrated that galvanic current acts at the spike trigger zone of primary vestibular afferents, with cathodal currents depolarizing and causing excitation, and anodal currents hyperpolarizing, leading to inhibition [38]. By positioning the cathode on the lesion side and the anode on the intact side, our approach aims to rebalance firing rates by enhancing reduced activity on the affected side and attenuating the intact side. One of the key effects of GVS is its ability to restore symmetry in vestibular input by facilitating activity on the lesioned side while inhibiting the intact side [39–42]. This rebalancing may enhance the ability of the brain to process spatial information by restoring bilateral vestibular input, which is crucial for accurate spatial perception and memory [15]. Functional imaging studies corroborate these mechanisms, with microPET scans showing that excitatory GVS on the right side activates the left hippocampus, entorhinal cortex, and cingulate cortex [23]. Furthermore, electrical stimulation has been shown to excite the medial vestibular nucleus and increase firing rates in hippocampal CA1 place cells [43], and GVS applied to the ampulla of the semicircular canal has been shown to initiate theta activity in the hippocampal formation [44], a rhythm crucial for spatial information processing and the modulation of self-motion signals [45]. Moreover, increases in c-Fos expression, an indicator of neuronal activation, have been observed in the hippocampus following repeated GVS application [46]. Although the precise mechanisms underlying the effects of GVS on spatial cognition remain unclear, it is hypothesized that in sum GVS modulates vestibular input, activates key brain regions such as the hippocampus, promotes neural plasticity, restores theta rhythms, and thus rebalances vestibular input. In the

acute phase of UVP/vestibular neuritis, visuospatial deficits may result from oscillopsia, nystagmus-induced blurred vision, VOR deficits, or VSR dysfunction. However, improved cognitive performance in the GVS group during recovery suggests that GVS offers benefits beyond natural recovery of VOR or VSR function. The sham-controlled design enabled comparison of natural recovery with intervention effects. Notably, trial-by-trial analysis of the vMWM task showed significant improvements in the GVS group in later trials, indicating enhanced spatial learning (Table 3 and Fig. 3). GEE analysis further revealed significant interaction effects, supporting GVS's role in cognitive recovery.

This study has several limitations. First, the sample size of 83 patients may be insufficient to generalize the findings. Second, the four-week follow-up period limits the evaluation of long-term effects and sustained benefits of GVS on visuospatial cognitive functions. Third, while participant blinding was implemented using a sham intervention, the lack of blinding procedures for researchers may introduce bias. Lastly, the use of standard cognitive tests, such as the VOSP and CBTT, do not fully capture the whole spectrum of cognitive impairments associated with vestibular dysfunction. However, cognitive tests must be feasible for the patients in the acute phase in terms of time in order not to falsify the results. Thus, the long-term impact of GVS still remains uncertain.

In conclusion, these findings suggest that GVS may enhance spatial memory and navigation in acute unilateral vestibular disorders. However, lesion side effects and variability across cognitive tasks underscore the need for further research to optimize GVS parameters and target specific populations. Long-term studies are also necessary to assess sustained effects, optimal timing, and underlying neural mechanisms. These results highlight GVS's potential role in promoting neural plasticity and cognitive function beyond natural recovery what is particularly important for older patients and those with cognitive deficits.

**Acknowledgements**
The authors thank the patients who participated in this study and the clinical staff at Jeonbuk National University Hospital for their support. We also thank Ms. Yeonji Kook for statistical consultation and the Clinical Trial Center for trial registration support.

**Author contributions**
SYO conceptualized and designed the study. TTN and JJK collected and analyzed data. JC contributed to patient recruitment and assessments. SYO and TTN wrote the manuscript. MD supervised the project and provided critical revisions. All authors reviewed and approved the final manuscript.

**Funding**
This work was supported by a National Research Foundation of Korea (NRF) grant funded by the Korean government (Ministry of Science and ICT) (No. RS-2025–00553480) and by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: RS-2025–02223226). This research was also supported by the Biomedical Research Institute Fund, Jeonbuk National University Hospital. MD's work was supported by a grant from the German Foundation for Neurology (Deutsche Stiftung Neurologie, No. 80721017).

**Data availability**
The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request. De-identified individual participant data underlying the results reported in this article (text, tables, figures) will be shared.

## Declarations

**Ethical approval and consent to participate**
The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board of Jeonbuk National University Hospital (IRB No. 20220404500). Written informed consent was obtained from all participants prior to enrollment.

**Consent for publication**
All participants provided written informed consent for the publication of anonymized data.

**Competing interests**
The authors declare the research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

**Author details**
[1]Department of Neurology, Jeonbuk National University Hospital and School of Medicine, Jeonbuk National University, 20 Geonji-Ro, Deokjin-Gu, Jeonju, Jeonbuk 561-712, South Korea
[2]Research Institute of Clinical Medicine of Jeonbuk National University-Jeonbuk National University Hospital, Jeonju 54907, Korea
[3]Department of Pharmacology, Hue University of Medicine and Pharmacy, Hue University, Hue 49120, Vietnam
[4]Department of Neurology, University Hospital, Ludwig-Maximilians-University, Munich, Germany
[5]German Center for Vertigo and Balance Disorders, University Hospital, Ludwig-Maximilians-University, Munich, Germany
[6]Munich Cluster for Systems Neurology (SyNergy), Munich, Germany

Received: 15 May 2025 / Accepted: 18 August 2025
Published online: 24 November 2025

**References**

1. Brandt T, Dieterich M. The dizzy patient: don't forget disorders of the central vestibular system. Nat Rev Neurol. 2017;13:352–62.
2. Smith PF. The vestibular system and cognition. Curr Opin Neurol. 2017;30:84–9.
3. Bird CM, Burgess N. The hippocampus and memory: insights from spatial processing. Nat Rev Neurosci. 2008;9:182–94.
4. Brandt T, Schautzer F, Hamilton DA, et al. Vestibular loss causes hippocampal atrophy and impaired spatial memory in humans. Brain. 2005;128:2732–41.
5. Smith PF, Zheng Y. From ear to uncertainty: vestibular contributions to cognitive function. Front Integr Neurosci. 2013;7:84.
6. El Mahmoudi N, Laurent C, Péricat D, et al. Long-lasting spatial memory deficits and impaired hippocampal plasticity following unilateral vestibular loss. Prog Neurobiol. 2023;223:102403.
7. Nguyen TT, Nam GS, Kang JJ, et al. Galvanic vestibular stimulation improves spatial cognition after unilateral labyrinthectomy in mice. Front Neurol. 2021;12:716795.
8. Zheng Y, Darlington CL, Smith PF. Impairment and recovery on a food foraging task following unilateral vestibular deafferentation in rats. Hippocampus. 2006;16:368–78.
9. Oh SY, Nguyen TT, Kang JJ, et al. Visuospatial cognition in acute unilateral peripheral vestibulopathy. Front Neurol. 2023;14:1230495.

10. Popp P, Wulff M, Finke K, Ruhl M, Brandt T, Dieterich M. Cognitive deficits in patients with a chronic vestibular failure. J Neurol. 2017;264:554–63.
11. Hufner K, Stephan T, Hamilton DA, et al. Gray-matter atrophy after chronic complete unilateral vestibular deafferentation. Ann N Y Acad Sci. 2009;1164:383–5.
12. Dlugaiczyk J, Gensberger KD, Straka H. Galvanic vestibular stimulation: from basic concepts to clinical applications. J Neurophysiol. 2019;121:2237–55.
13. Shaabani M, Lotfi Y, Karimian SM, Rahgozar M, Hooshmandi M. Short-term galvanic vestibular stimulation promotes functional recovery and neurogenesis in unilaterally labyrinthectomized rats. Brain Res. 2016;1648:152–62.
14. Kwan A, Forbes PA, Mitchell DE, Blouin JS, Cullen KE. Neural substrates, dynamics and thresholds of galvanic vestibular stimulation in the behaving primate. Nat Commun. 2019;10:1904.
15. Nguyen TT, Nam GS, Han GC, Le C, Oh SY. The effect of Galvanic Vestibular Stimulation on visuospatial cognition in an incomplete bilateral vestibular deafferentation mouse model. Front Neurol. 2022;13:857736.
16. Bigelow RT, Agrawal Y. Vestibular involvement in cognition: visuospatial ability, attention, executive function, and memory. J Vestib Res. 2015;25:73–89.
17. Hitier M, Besnard S, Smith PF. Vestibular pathways involved in cognition. Front Integr Neurosci. 2014;8:59.
18. Zwergal A, Grabova D, Schöberl F. Vestibular contribution to spatial orientation and navigation. Curr Opin Neurol. 2024;37:52–8.
19. Hüfner K, Hamilton DA, Kalla R, et al. Spatial memory and hippocampal volume in humans with unilateral vestibular deafferentation. Hippocampus. 2007;17:471–85.
20. Dordevic M, Sulzer S, Barche D, Dieterich M, Arens C, Müller NG. Chronic, mild vestibulopathy leads to deficits in spatial tasks that rely on vestibular input while leaving other cognitive functions and brain volumes intact. Life. 2021;11:1369.
21. Nguyen TT, Nam G-S, Kang J-J, et al. The differential effects of acute right-vs. left-sided vestibular deafferentation on spatial cognition in unilateral labyrinthectomized mice. Front Neurol. 2021;12:789487.
22. Grosch M, Lindner M, Bartenstein P, et al. Dynamic whole-brain metabolic connectivity during vestibular compensation in the rat. Neuroimage. 2021;226:117588.
23. Zwergal A, Lindner M, Grosch M, Dieterich M. In vivo neuroplasticity in vestibular animal models. Mol Cell Neurosci. 2022;120:103721.
24. Smith PF, Darlington CL, Zhen Y. The effects of complete vestibular deafferentation on spatial memory and the hippocampus in the rat: the Dunedin experience. Multisens Res. 2015;28:461–85.
25. Zheng Y, Goddard M, Darlington CL, Smith PF. Long-term deficits on a foraging task after bilateral vestibular deafferentation in rats. Hippocampus. 2009;19:480–6.
26. Baek JH, Zheng Y, Darlington CL, Smith PF. Evidence that spatial memory deficits following bilateral vestibular deafferentation in rats are probably permanent. Neurobiol Learn Mem. 2010;94:402–13.
27. Dieterich M, Bense S, Lutz S, et al. Dominance for vestibular cortical function in the non-dominant hemisphere. Cereb Cortex. 2003;13:994–1007.
28. Conrad J, Baier B, Eberle L, et al. Network architecture of verticality processing in the human thalamus. Ann Neurol. 2023;94:133–45.
29. zu Eulenburg P, Stoeter P, Dieterich M. Voxel-based morphometry depicts central compensation after vestibular neuritis. Ann Neurol. 2010;68:241–9.
30. Gammeri R, Leonard J, Toupet M, et al. Navigation strategies in patients with vestibular loss tested in a virtual reality T-maze. J Neurol. 2022;269:4333–48.
31. Cullen KE, Taube JS. Our sense of direction: progress, controversies and challenges. Nat Neurosci. 2017;20:1465–73.
32. Becker-Bense S, Dieterich M, Buchholz HG, Bartenstein P, Schreckenberger M, Brandt T. The differential effects of acute right- vs. left-sided vestibular failure on brain metabolism. Brain Struct Funct. 2014;219:1355–67.
33. Hilliard D, Passow S, Thurm F, et al. Noisy galvanic vestibular stimulation modulates spatial memory in young healthy adults. Sci Rep. 2019;9:9310.
34. Wuehr M, Eder J, Keywan A, Jahn K. Noisy galvanic vestibular stimulation improves vestibular perception in bilateral vestibulopathy. J Neurol. 2023;270:938–43.
35. Klatt BN, Ries JD, Dunlap PM, Whitney SL, Agrawal Y. Vestibular physical therapy in individuals with cognitive impairment: a theoretical framework. JNPT. 2019;43:S14–9.
36. Goswami A, Sehgal CA, Noohu MM, Parveen S, Azharuddin M. Effect of vestibular therapy as an adjunct to cognitive therapy to improve cognition in elderly with mild cognitive impairment (MCI): a randomized controlled trial. J Gerontol Geriatr. 2024;72:173–84.
37. Fitzpatrick RC, Day BL. Probing the human vestibular system with galvanic stimulation. J Appl Physiol. 2004;96:2301–16.
38. Goldberg JM, Smith CE, Fernández C. Relation between discharge regularity and responses to externally applied galvanic currents in vestibular nerve afferents of the squirrel monkey. J Neurophysiol. 1984;51(6):1236–56.
39. Aw ST, Todd MJ, Lehnen N, et al. Electrical vestibular stimulation after vestibular deafferentation and in vestibular schwannoma. PLoS ONE. 2013;8:e82078.
40. Tohyama T, Kondo K, Otaka Y. Effects of galvanic vestibular stimulation on visual verticality and standing posture differ based on the polarity of the stimulation and hemispheric lesion side in patients with stroke. Front Neurol. 2021;12:768663.
41. Kim J, Curthoys IS. Responses of primary vestibular neurons to galvanic vestibular stimulation (GVS) in the anaesthetised guinea pig. Brain Res Bull. 2004;64:265–71.
42. Forbes PA, Kwan A, Mitchell DE, Blouin JS, Cullen KE. The neural basis for biased behavioral responses evoked by galvanic vestibular stimulation in primates. J Neurosci. 2023;43:1905–19.
43. Horii A, Russell NA, Smith PF, Darlington CL, Bilkey DK. Vestibular influences on CA1 neurons in the rat hippocampus: an electrophysiological study in vivo. Exp Brain Res. 2004;155:245–50.
44. Cuthbert PC, Gilchrist DP, Hicks SL, MacDougall HG, Curthoys IS. Electrophysiological evidence for vestibular activation of the guinea pig hippocampus. NeuroReport. 2000;11:1443–7.
45. Huxter J, Burgess N, O'Keefe J. Independent rate and temporal coding in hippocampal pyramidal cells. Nature. 2003;425:828–32.
46. Holstein GR, Friedrich VL, Martinelli GP, Ogorodnikov D, Yakushin SB, Cohen B. Fos expression in neurons of the rat vestibulo-autonomic pathway activated by sinusoidal galvanic vestibular stimulation. Front Neurol. 2012;3:19151.


## Publisher's note