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Original Article

Temporary Unilateral Caloric Vestibular Stimulation Affects Balance and Gait Control During Walking in Healthy Young Adults

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OBJECTIVE: This study aimed to examine the individual differences and factors affecting balance and gait control during walking (i.e., dynamic equilibrium) in healthy young adults subjected to unilateral caloric vestibular stimulation (CVS).

METHODS: Sixty-six participants completed questionnaires related to motion sickness. All participants were subjected to the head-up tilt test (HUT), which assesses orthostatic dysregulation, followed by inner ear stimulation with cold water (20°C) for 60 s. Subsequently, all participants performed a 6 m walking test with their eyes open.

RESULTS: CVS resulted in horizontal nystagmus. The measured distance of sway from the centerline on the goal line ranged from 0 to 600 cm. Both motion sickness and orthostatic dysregulation (OD) were associated with the distance of sway from the centerline.

CONCLUSIONS: Autonomic dysfunction affects the dynamic equilibrium and might cause individual gait differences. Further study is warranted to quantify the autonomic function and clarify individual variations in dynamic equilibrium, after unilateral CVS.

KEYWORDS: Caloric vestibular stimulation, balance, gait control, orthostatic dysfunction

INTRODUCTION

Spatial and bodily representations are multisensory processes that imply the integration of several afferent signals into a coherent internal model of the egocentric space. Crucially, this model also involves vestibular information received from the balance organs in the inner ear.[1] Indeed, vestibular system projections have been proven to overlap with the somatosensory system as well as the brain regions involved in body and space representations.[2] These representations can be altered by brain lesions and can be dramatically restored by physiological manipulations that target specific sensory components, such as caloric vestibular stimulation (CVS).[3] CVS, involving the irrigation of the external auditory canal with ice water, induces a change in temperature that causes convection currents in the semicircular canals and subsequently evokes quick-phase nystagmus [i.e., vestibulo-ocular reflex (VOR)] toward the non-stimulated ear. This effect can elicit sensations of virtual body rotations and vertigo.

Previous studies have demonstrated that CVS can modulate a wide range of cognitive and sensory functions in both brain-damaged patients and healthy participants,[4] and can affect tactile perceptions in patients with either right- or left-brain damage.[5] These observations suggest that CVS strongly affects the vestibular, somatosensory, and motor systems. Moreover, the direct and indirect visual pathways are immediately affected, influencing spatial orientation during locomotion.[6] In addition, Matsuyoshi et al.[7] observed that CVS induced powerful vertigo in healthy participants with autonomic dysfunction tendencies and motion sickness, and demonstrated that these individual somatosensory system-related factors contributed to the diversity and variance of vestibular symptoms among individuals.

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Notably, gait and posture are important aspects of daily living in humans, and vestibular stimulation has been applied clinically for vestibular rehabilitation.[8–12] Individual factors, such as orthostatic dysregulation (OD)[13–19] and motion sickness,[20,21] have been well-studied in patients with vestibular disorders. However, comparative examinations are difficult because of differences in the degree of disequilibrium between individual patients. Indeed, no study has investigated the individual factors affecting balance and gait control during walking (i.e., dynamic equilibrium), after CVS. Accordingly, I hypothesized that autonomic dysfunction affects gait control (dynamic equilibrium) during walking after CVS, and this study examined these factors in healthy young adults.

MATERIALS AND METHODS

Participants

The participants in this study were medical students who were enrolled at Kumamoto University (49 men and 17 women; age [mean ± standard deviation], 24.6 ± 2.32 years; range, 22-29 years), with no history of vestibular disorders. All participants provided informed consent before enrolment. The study was approved by the Institutional Review Board of Kumamoto University (Number 1435) and was conducted in accordance with the guidelines and regulations of the institution.

Study Procedures

The questionnaire surveys and tests were conducted according to Figure 1A. The participants completed the surveys regarding individual factors. Motion sickness was assessed using the Graybiel motion sickness score.[21] The scoring methods for the questionnaires are shown in Table 1.

Head-up Tilt Test Before CVS

The head-up tilt (HUT) test was administered to assess OD, which is closely related to autonomic dysfunction.[23] The HUT test was performed according to the method established by the Japan Society of Neurovegetative Research in 2015.[24] Non-invasive oscillatory measurements of blood pressure (BP) and pulse rate were performed 4 times using an automated sphygmomanometer (ES-H55P; Terumo, Tokyo, Japan) at the following time points: (1) after 10 minutes in a horizontal position, (2) after 10 seconds of standing, (3) after 1 minute of standing, and (4) after 10 minutes of standing.[24] The cuff of the BP-recording device was attached to the left arm, which was supported at the heart level throughout the study. The testing was conducted during daytime hours in a quiet environment at a constant room temperature of 22-25°C to exclude the effects of chronobiologic factors on the test outcomes. The participants maintained a regular meal schedule but were asked to abstain from smoking and caffeine ingestion for 6 hours before the examination. The intake of foods and medications with sympathomimetic activity was also prohibited before the study. The participants were determined as positive or negative according to the outcome of the HUT test and the international scientific definition of OD (Table 1).[15]

Free Gait Before CVS

In an outpatient treatment room (100 m^2) with no other patients present, each participant performed 6 m of free walking with bare feet, with their eyes open. A straight centerline from the start point to the goal point was determined and marked at both points before the free-gait exercise. Each participant was instructed to walk for 10 seconds while looking straight ahead at the whiteboard on the goal line, to avoid visual suppression, and walking in as straight a line as possible, without zigzagging. After 6 m of free walking, each participant stopped and maintained his/her position, and the distance of sway from the goal point was then measured analogically (Figure 1B). The result obtained from this task was used as a control.

CVS and Maximum Slow-Phase Velocity Measurement

Vestibular stimulation via the left external auditory canal was performed using cold water (20°C) for 60 seconds.[24] The maximum slow-phase velocity (MVS) on the horizontal plane was measured

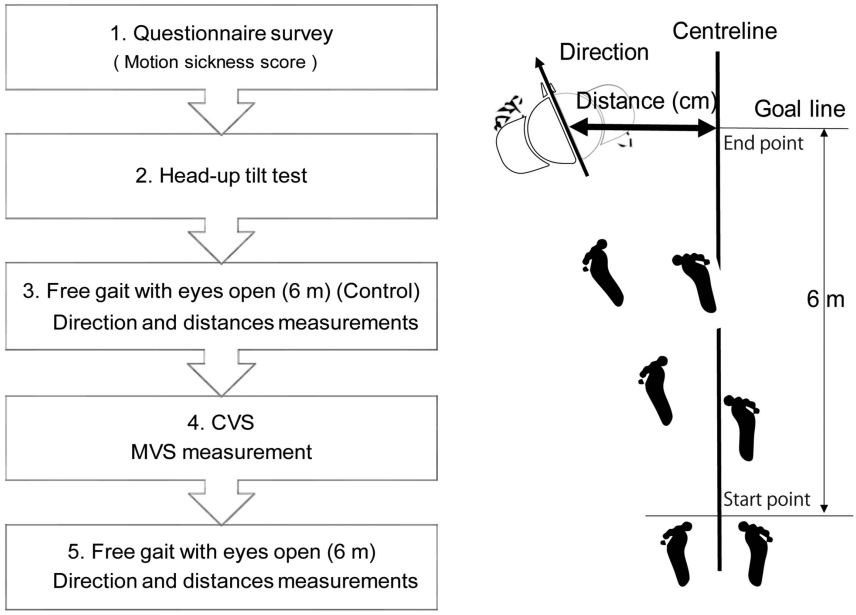

Figure 1. Inspection procedure. (A) Flowchart of the study procedures. CVS, caloric vestibular stimulation; MVS, maximum slow-phase velocity. (B) Direction and distance measurements during free gait.

Table 1. Questionnaires and Tests: Diagnostic Criteria and Results

Aim	Tests	Methods of Scoring or Measure and Criteria	Results
Questionnaires			
Motion sickness	Motion sickness score[2]	Scoring using a 56-point scale with 6 questions	Score: 12–32 (18.8 ± 6.34)
Tests			
OD	HUT test[23,26]	Positive, meeting one of the following criteria: • BP decrease ≥ 20/10 mmHg after 10 seconds of standing • BP decrease ≥ 20/10 mmHg after 1 minute of standing • BP decrease ≥ 20/10 mmHg after 10 minutes of standing • HR increase ≥ 120/min or 30/min above the supine level after 10 seconds, 1 minute, or 10 minutes of standing	Positive: n = 46; Negative: n = 20
VOR	CVS[5]	MVS was measured before free gait	MVS: 12–99 (60.8 ± 21.7)°/s
Gait	Free gait (6 m) with eyes open and bare feet	Before and after cold water stimulation: Direction and distance of sway from the centerline of the goal point were measured after 6 m of free gait	Before
			Direction: all median
			Distance: 0 cm
			After
			Direction: all left
			Distance: 0–600 (189 ± 212) cm

OD, orthostatic dysregulation; HUT, head-up tilt; BP, blood pressure; HR, heart rate; VOR, vestibulo-ocular reflex; CVS, caloric vestibular stimulation; MVS, maximum slow-phase velocity. Scores are shown as the range (mean ± standard deviation) unless otherwise specified.

based on videonystamography recordings (VOG Meditester CD2001, Panasonic, Tokyo, Japan) after CVS, until free gait was assessed.

Free Gait After CVS

Before vestibular stimulation and walking, each participant was provided with the same instructions as described above. One minute after vestibular stimulation, each participant stood up from the chair and immediately stood at the starting point. When signaled, each participant walked freely for 6 m with bare feet, keeping their eyes open. After 6 m of free walking, the direction of the gait and the distance of sway from the goal point were recorded using the same methods described above (Figure 1B).

Statistical Analysis

This study used standard methods to estimate the sample size for a multiple-linear regression and determined that at least 10 outcomes were needed for each included independent variable. Pearson's correlation coefficient was used to examine the relationship between MVS and the distance of sway from the centerline. A multiple-linear regression analysis was used to determine the independent individual-level factors (motion sickness, OD, and MVS) for the distance of sway from the centerline after adjusting for age and sex. I confirmed that the assumptions of the analysis were verified, by inspection of graphs of residuals. There were no missing data or any outliers in our data set. Explanatory variables that appear in the final regression model were chosen by forward techniques. All potential explanatory variables were assessed for collinearity. Explanatory variables were tested for interaction. The adjusted R-squared was 0.87. The regression model was validated by jack-knife procedures. A P value < .05 was considered statistically significant. All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of R Commander, designed to apply statistical functions which are frequently used in biostatistics.

RESULTS

The results are summarized in Table 1. The Graybiel motion sickness scores ranged from 12 to 32 (18.8 ± 6.34) points. Forty-six (69.7%) participants received positive HUT test results. The VOR was assessed in terms of the MVS, and the latter values ranged from 12 to 99 (60.8 ± 21.7)/s. During the 6 m free-walking test before the CVS, the distance of sway from the centerline on the goal line was 0 cm for all participants. Unilateral (left ear) CVS resulted in horizontal nystagmus, and 44 (65.1%) participants felt a whirling sensation, 14 (21.2%) participants felt swept sway, and 8 (12.1%) participants felt unsteadiness. In addition, some participants felt autonomic symptoms, including nausea and cold sweat. Most of the participants walked with a deviation to the left. The distance of sway from the centerline ranged from 0 to 600 (189 ± 212) cms after CVS (Table 1).

Next, we investigated the association of MVS with the distance of sway from the centerline. Pearson's correlation analysis showed no significant correlation between MVS and the distance of sway from the centerline (Figure 2; R^2 = 0.031, P = .56). We then performed multiple-linear regression analyses and evaluated the variables listed in Table 2 for inclusion in the models. The results, adjusted for age and sex, revealed that a higher Graybiel motion sickness score (Table 2; Coefficient = −2.53, 95% confidence interval [CI]: 0.04-10.7, P = .04) and the positive HUT test result (Table 2; Coefficient = 142.1, 95% CI: 59.6-224.6, P = .001) were significantly associated with the distance of sway from the centerline.

DISCUSSION

In this study, we examined the factors affecting dynamic equilibrium after unilateral CVS in a group of healthy young adults with no history of equilibrium disorders. We found that participants with OD and motion sickness were more likely to experience dynamic disequilibrium after CVS.

Previous studies have shown that CVS may input additional modulating information to the sensorimotor system, thus evoking the VOR

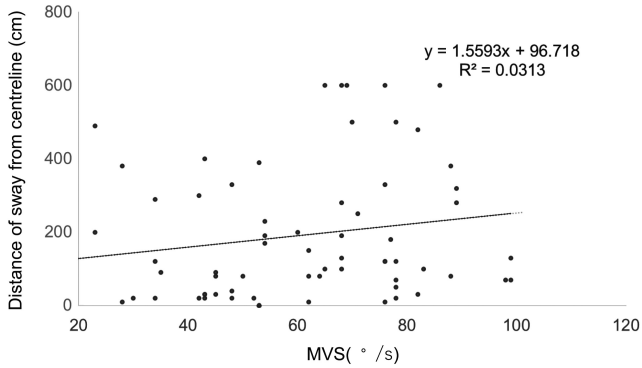

Figure 2. Distance of sway and MVS. No significant correlation was observed between the MVS and the sway distance from the centerline ($R^2 = 0.031$, $P = .56$). MVS, maximum slow-phase velocity.

and vestibulo-spinal reflex, and affecting somatosensory functions including tactile perception.[2,26] Therefore, we compared the VOR with the distance of sway from the centerline after CVS, to exclude the possibility of the effect of the former on dynamic equilibrium. We did not observe a significant correlation between the VOR value (i.e., MVS) and the distance of sway from the centerline, either by Pearson's correlation analysis or by multiple-linear regression analysis. Therefore, dynamic equilibrium following CVS was affected by factors other than the VOR. Taken together, this study demonstrated the effects of individual factors that contribute to the diversity and variances of dynamic equilibrium change after CVS.

OD, an autonomic disorder that occurs with postural changes, reflects sympathetic nervous function and is diagnosed using the HUT test.[27,28] Previous studies have shown that OD affects vestibulo-autonomic sympathetic nervous reflex hypersensitivity during CVS in patients with vestibular disorders.[16,18,19] It is generally accepted that sympathetic activation largely supports motor function.[13] Therefore, motor function may be more strongly affected in CVS in individuals who are prone to sympathetic nerve dysfunction than in those who are not. Multiple-linear regression analyses have shown that OD, which indicates sympathetic nervous dysfunction (i.e., autonomic dysfunction), affects dynamic equilibrium, but not VOR (i.e., MVS), after CVS. These findings suggest that individual factors such as OD might contribute to the diversity and variance of dynamic equilibrium after CVS.

Motion sickness is an autonomic disorder triggered by vestibular and visual stimulations and may be caused by a sensory conflict between visual information and vestibular and somatic sensations.[29,30] Patients with vestibular disorders and motion sickness exhibit enhanced vestibulo-autonomic reflexes during CVS.[20] Impaired proprioception via motion sickness may disrupt the control and coordination of movements and can cause sensory conflicts, reduced postural control, and unsteadiness.[31] Our multiple-linear regression analyses showed that individuals susceptible to motion sickness present with an altered dynamic equilibrium, but not an altered VOR (i.e., MVS), after CVS. These findings suggest that an increased sensory conflict in response to CVS contributes to the diversity and variance of dynamic disequilibrium among individuals.

Table 2. Multiple-Linear Regression Analysis of Factors Related to the Distance of Sway From the Centerline

Variables	Coefficient	SE	95% CI	*P*
(Intercept)	−149.3	197.0		
Age	−2.53	8.50	−19.5 to 14.4	.76
Sex	39.8	44.3	−48.7 to 128.5	.37
Motion Sickness	5.38	2.67	0.04 to 10.7	.04*
OD	142.1	41.2	59.6 to 224.6	.001**
MVS	1.86	0.99	−0.13 to 3.86	.06

SE, Standard error; OD, orthostatic dysregulation; MVS, maximum slow-phase velocity

The present study had several limitations. Particularly, CVS has important methodological limitations.[32] During CVS, the participant's ear is irrigated with cold water for a few seconds. This technique does not permit complete control of the parameters of the stimulation, such as the exact volume of water that enters the external ear canal and the precise timing of vestibular organ stimulation. Moreover, non-vestibular contributions to the CVS-induced modulation of somatosensory processing, such as the effects of a cold sensation in the outer ear, cannot be ruled out, because of the absence of a reliable sham stimulation. As the participants performed the 6 m free-walking exercise with their eyes open, we also cannot rule out the possibility that visual factors and retinal slip affected the free-gait assessment.[33] In addition, the cerebellum physiologically tends to suppress the VOR by means of visual fixation, and this might be considered as another uncontrolled factor in this study. When we investigated dynamic equilibrium in the preliminary study, no participant could complete the walk without falling when their eyes were closed. Therefore, we instructed the participants in this study to walk with their eyes open. In future research, visual control (stimulation or suppression) using 3D virtual reality goggles should be demonstrated during free walking. In addition, persistent CVS during free walking should be demonstrated using custom devices that were introduced in previous studies.[34] This approach would reduce the effect of individual-level variability related to temporal CVS.

CONCLUSION

In conclusion, this study demonstrated that autonomic dysfunction seems to affect dynamic equilibrium after unilateral CVS, and might cause individual gait differences among healthy young adults. Further studies are warranted to quantify the autonomic function and further clarify how individual variations affect the dynamic equilibrium after unilateral CVS. Our findings may help to determine the individual factors that affect gait during vestibular rehabilitation, using CVS.

Ethics Committee Approval: All participants provided informed consent before enrolment. This research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki, was approved by the Institutional Review Board of Kumamoto University (Number 1435), and was conducted in accordance with our institution's guidelines and regulations for human studies.

Informed Consent: All participants provided informed consent before enrolment.

Peer Review: Externally peer-reviewed.

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