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Title: The effect of CSF drainage on ambulatory center of mass movement in idiopathic normal pressure hydrocephalus

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Authors' contributions

Study concept and design: YN, TA, Y Kawami, TI, HO, and RS.

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Highlights

• Idiopathic normal pressure hydrocephalus involves abnormal center of mass movements.

- This includes heightened lateral amplitudes and diminished vertical amplitudes.
- The patients' center of mass movements are highly variable.
- Cerebrospinal fluid drainage normalizes the patients' center of mass movements.

Abstract

Background: Although gait and balance disturbances are core symptoms of idiopathic normal pressure hydrocephalus (iNPH), the ambulatory center of mass (COM) movements in patients with iNPH remain unclear. We aimed to clarify the ambulatory COM movements using an accelerometer on the patients' lower torsos and to investigate the changes in COM movement after cerebrospinal fluid tap tests (TT) and shunt surgeries (SS).

Methods: Twenty-three patients with iNPH and 18 age-matched healthy controls (HCs) were recruited. A triaxial accelerometer was fixed with a belt onto each participant's torso at the L3 vertebra level. We assessed each patient's 10-m gait before TT, 3 days after TT, and 1 week after SS.

Results: Compared to the HCs, the patients exhibited decreased gait velocities, increased step numbers, and increased step times. Their movement trajectory amplitudes (i.e., the COM movements) were increased in the medial/lateral direction and decreased in the vertical direction. They also exhibited greater variability (measured as coefficients of variation) in step time and movement trajectory amplitude in both the medial/lateral and vertical directions. The patients' gait parameters were significantly improved after TT and SS.

Significance: Our results suggest that iNPH-associated gait disturbances could cause abnormal ambulatory COM movements and that these disturbances are mitigated by TT and SS.

Key words

Idiopathic normal pressure hydrocephalus; Accelerometer; Center of mass; Gait variability; Gait analysis

1. Introduction

Idiopathic normal pressure hydrocephalus (iNPH) is a condition of enlarged brain ventricles under a normal cerebrospinal fluid (CSF) pressure, and it is characterized by a clinical triad including gait disturbance, cognitive impairment, and urinary incontinence [1]. Gait disturbances are the most common triad symptom, affecting 94–100% of patients [2,3]. The patients characteristically present with slowness; small-stepped, decreased foot-to-floor clearance; and wide-based gaits [4–6]. Additionally, iNPH-associated balance disturbances with disequilibrium [6,7] occur as a result of central and/or peripheral vestibular dysfunctions [8–10] and proprioceptive dysfunction [8]. iNPH-associated gait and balance disturbances are likely to increase the risk of falling [6–9].

Center of mass (COM) movement is the main element of gait because it reflects the whole body's movement [11,12]. COM stabilization during gait is explained by a simple rule called the inverted pendulum model [13,14]. Under this model [13,14], reduced foot placement precision results in wider strides, but this effect can be mitigated by walking with a faster cadence. This model illuminates how slowness, short strides, and disequilibrium may influence ambulatory COM movements in the case of iNPH-associated gait and balance dysfunctions. However, greater motor variability also implies that slowness, short strides, and disequilibrium may constitute a compensation strategy for prolonging motor independence [15]. In any case, clarifying the features of ambulatory COM movement in iNPH may help explain the patients' gait and balance disorders and elucidate the appropriate diagnostic and treatment strategies, which may include exercise therapy. Objective gait assessments in patients with iNPH have examined various gait parameters such as temporal and spatial parameters [4– 6,8,10,16–19], but the ambulatory COM movements in iNPH remain unclear.

Several studies have reported that a waist-mounted wearable accelerometer can easily record ambulatory COM movements [20,21]. We therefore aimed to clarify the characteristics of iNPH-associated ambulatory COM movement using waist-mounted accelerometers on patients and healthy controls (HCs) and to investigate the changes in patients' gait variabilities and COM movements after CSF tap tests (TT) and shunt surgeries (SS). We hypothesized that ambulatory COM movements in patients with iNPH would be larger and more variable than those in HCs and that CSF drainage would reduce COM movement abnormalities in patients with iNPH.

2. Methods

2.1. Participants

Twenty-three patients with iNPH (age [mean \pm standard deviation]: 76.9 \pm 5.7 years; 19 men and 4 women) and 18 HCs (age: 74.3 ± 3.4 years; 12 men and 6 women) participated in this study. The Osaka Medical College's ethics committee approved this study protocol (No. 1555), and all participants provided written informed consent. The study was performed in accordance with the Declaration of Helsinki. The patients had probable diagnoses with positive TT results according to the iNPH diagnostic criteria [22]. They underwent lumboperitoneal or ventriculoperitoneal SS 1 month after TT. A Codman-Hakim programmable valve with a siphon-guard (Codman and Shurtleff, Raynham, MA) was implanted in each patient, and the initial pressure settings were decided according to the patient's height and weight using Miyake's quick reference table [23]. The HCs were recruited from senior community service clubs. Table 1 shows the participants' demographics. Patients were excluded for (1) additional neurological or orthopedic disorders interfering with gait or (2) an inability to walk unassisted for at least 15 m. Each patient's cognitive function was examined using the Mini-Mental State Examination (MMSE) before TT, and the history of falling within the past 6 months was recorded.

2.2. Gait assessment procedure

Each participant had a triaxial accelerometer (MG-M1100-HW, LSI Medience, Tokyo, Japan; size: $7.5 \times 5 \times 2 \text{ cm}^3$; weight: 120 g) attached to the lower torso at the L3 vertebra level with a belt. This device can measure ambulatory COM movement [20]. Acceleration data were recorded at a sampling rate of 100 Hz.

The walkway was a 15-m straight path with 3-m acceleration and 2-m deceleration sections at the beginning and end, respectively. The participants walked twice at their normal, comfortable speed without assistance. We assessed the patients' movements before TT, 3 days after TT [17], and 1 week after SS.

2.3. Data analysis

The acceleration data were imported into dedicated software (MG1100-PC, Gait View, Tokyo, Japan). The data from the 10-m section between the acceleration and deceleration zones were analyzed to calculate velocity, number of steps, and step time [20]. Step time was defined as the interval between acceleration minima. To calculate movement trajectory amplitudes that reflect COM movements, the acceleration signals in the medial/lateral (ML) and vertical (VT) directions were integrated twice in the time

domain and high-pass filtered with a moving-window average [20]. Relative displacement in the anterior/posterior direction was not calculated this way because it can easily be calculated for participants walking forward at a constant speed. The ambulatory movement trajectory amplitudes for 1 participant are shown in Figure 1. Gait variability was assessed as the percent coefficient of variation (CV = standard deviation/mean×100) [24] of step time and movement trajectory amplitudes. Each participant's CVs were calculated based on acceleration data from the 10-m section between the acceleration and deceleration sections. All gait parameter variables are presented as an average of 2 trials.

2.4. Statistical analysis

Data are expressed as means ± standard deviations. Statistical analyses were conducted using JMP Pro v. 12.0 (SAS Institute, Cary, NC). To compare the characteristics and gait parameters (pre-TT for the patients) of the patients and HCs, significant intergroup differences were tested for using independent t-tests. The patients' gait parameters at different timepoints (i.e., pre-TT, post-TT, and post-SS) were compared using 1-way repeated-measures ANOVA. When significant differences were observed, multiple comparisons corrections were performed with the Bonferroni method to confirm significance. Furthermore, to quantify effect sizes, we calculated Cohen's d–based standardized mean differences (SMDs) [25] and confidence intervals (CIs) [25] for gait comparisons data. We defined statistical significance as p < 0.05.

3. Results

3.1. Participants

Table 1 shows the participants' demographics. The patients and HCs were comparable in age, sex, height, and weight. The patients had normal cognitive function as measured with MMSE scores (25.0 ± 3.6). Eighteen patients (78.3%) had a history of falling.

3.2. Gait analysis

Compared to measurements in the HCs, pre-TT measurements in the patients revealed significantly slower velocities (SMD: 1.98, 95% CI: -0.66 to -0.36 m/s, p < 0.001; Fig. 2a), significantly more steps (SMD: 1.18, 95% CI: 8.85 to 24.71 steps, p < 0.001; Fig. 2b), significantly longer step times (SMD: 1.01, 95% CI: 0.02 to 0.07 s, p < 0.001; Fig. 2c), and significantly larger step time CVs (SMD: 1.38, 95% CI: 4.7% to 11.11%, p < 0.001; Fig. 2d).

Compared to the movement trajectory amplitude measurements in the HCs, pre-TT measurements in the patients revealed significantly larger ML amplitudes (SMD: 2.03, 95% CI: 2.01 to 3.64 cm, p < 0.001; Fig. 2e) but significantly smaller VT amplitudes (SMD: 2.45, 95% CI: -2.17 to -1.31 cm, p < 0.001; Fig. 2f). The patients' CVs of movement trajectory amplitudes were significantly larger in both the ML (SMD: 0.79, 95% CI: 0.43% to 3.28%, p = 0.011; Fig. 2g) and VT directions (SMD: 1.58, 95% CI: 11.28% to 23.61%, p < 0.001; Fig. 2h).

3.3. Gait analysis in patients with iNPH

The patients' pre-TT, post-TT, and post-SS gait measurements revealed the longitudinal development of significantly faster velocities (post-TT vs. pre-TT, SMD: 0.46, 95% CI: -0.21 to -0.07 m/s, p = 0.004; post-SS vs. pre-TT, SMD: 0.58, 95% CI: -0.24 to -0.09 m/s, p = 0.004; Fig. 3a), significantly smaller step counts (post-TT vs. pre-TT, SMD: 0.42, 95% CI: 2.65 to 10.80 steps, p = 0.023; post-SS vs. pre-TT, SMD: 0.51, 95% CI: 3.77 to 12.34, p = 0.010; Fig. 3b), significantly shorter step times (post-TT vs. pre-TT, SMD: 0.63, 95% CI: 0.01 to 0.05 s, p = 0.007; post-SS vs. pre-TT, SMD: 0.66, 95% CI: 0.01 to 0.05 s, p = 0.008; Fig. 3c), and significantly reduced step time CVs (post-TT vs. pre-TT, SMD: 0.79, 95% CI: 2.23% to 6.85%, p = 0.004;

post-SS vs. pre-TT, SMD: 0.88, 95% CI: 2.59% to 7.60%, p < 0.001; Fig. 3d). There were no significant differences between the post-SS and post-TT measurements in velocity (SMD: 0.11, 95% CI: -0.08 to 0.02 m/s, p = 1.000; Fig. 3a), step number (SMD: 0.11, 95% CI: -1.15 to 3.82 steps, p = 0.957; Fig. 3b), step time (SMD: 0.01, 95% CI: -0.01 to 0.01 s, p = 1.000; Fig. 3c), or step time CV (SMD: 0.18, 95% CI -0.28% to 1.34%, p = 0.673; Fig. 3d).

Compared to the patients' movement trajectory amplitudes at the pre-TT timepoint, those at the post-TT and post-SS timepoints were significantly lower in the ML direction (post-TT vs. pre-TT, SMD: 0.54, 95% CI: 0.50 to 1.18 cm, p < 0.001; post-SS vs. pre-TT, SMD: 0.56, 95% CI: 0.45 to 1.25 cm, p < 0.001; Fig. 3e) but significantly greater in the VT direction (post-TT vs. pre-TT, SMD: 0.43, 95% CI: -0.51 to -0.15 cm, p < 0.001; post-SS vs. pre-TT, SMD: 0.60, 95% CI: -0.66 to -0.27 cm, p < 0.001; Fig. 3f). There were no significant differences between post-SS and post-TT amplitudes in the ML (SMD: 0.01, 95% CI: -0.19 to 0.20 cm, p = 1.000; Fig. 3e) or VT directions (SMD: 0.17, 95% CI: -0.41 to 0.68 cm, p = 0.346; Fig. 3f).

Compared to pre-TT measurements, those at the post-TT and post-SS timepoints also revealed significantly decreased amplitude CVs in both the ML (post-TT vs. pre-TT, SMD: 0.74, 95% CI: 1.02% to 3.10%, p < 0.001; post-SS vs. pre-TT, SMD: 0.65, 95% CI: 0.87% to 2.75%, p = 0.002; Fig. 3g) and VT directions (post-TT vs. pre-TT, SMD: 0.65, 95% CI: 4.08% to 11.39%, p = 0.010; post-SS vs. pre-TT, SMD: 0.85, 95% CI: 5.08% to 14.43%, p < 0.001; Fig. 3h). There were no significant differences between post-TT and post-SS amplitude CVs in the ML (SMD: 0.08, 95% CI: -1.16% to 0.67%, p = 1.000; Fig. 3g) or VT directions (SMD: 0.15, 95% CI: -5.66% to 9.70%, p = 0.156; Fig. 3h).

4. Discussion

We aimed to explore gait abnormalities in patients with iNPH and the potential of CSF drainage procedures to normalize gait abnormalities. The current study revealed abnormalities of ambulatory COM movement in patients with iNPH. Moreover, we found that these abnormalities were mitigated after TT and SS.

Previous studies on COM movement showed that the validity and reliability of waist-mounted accelerometers are equal to those of 3-dimensional gait analysis [20,21]. Three-dimensional gait analysis of Japanese HCs has revealed COM amplitudes of approximately 3.5 cm and 3.2 cm in the ML and VT directions, respectively [11]. Our results for the HCs are consistent with these earlier findings. We therefore believe that the accelerometer-based COM movement analysis in this study is reliable and comparable to 3-dimensional gait analysis.

We found that our patients with iNPH exhibited pre-TT COM movements involving heightened ML amplitudes and diminished VT amplitudes relative to the HCs' movements, but Iida et al. [11] reported that patients with hemiplegia exhibited heightened VT and ML amplitudes. One possible explanation for the different effects of these disorders is that patients with hemiplegia are exhibiting a dynamic gait pattern that compensates for motor dysfunctions, whereas the suppression of VT COM movement in iNPH represents a static gait pattern that is small-stepped and magnetic [4,5].

Patients with iNPH also exhibit a wide-based gait to compensate for disturbances to dynamic equilibrium [4,5]. In fact, previous studies have shown that the patients' orthostatic and ambulatory torso movements were impaired relative to age-matches HCs [18] and that iNPH-associated postural instability may result from disequilibrium with central and/or peripheral vestibular dysfunction [8–10] and involvement of proprioceptive dysfunction [8]. Therefore, the ML movements observed in patients with iNPH may be caused by disequilibrium-induced increases in ML COM movements.

Gait parameters vary minimally in healthy individuals, which allows them to exhibit a repetitive and stable gait [24,26]. Conversely, several studies have reported more variable gaits relating to a risk of falling in elderly persons and in patients with Parkinson's disease, vestibular disorder, or cerebellar ataxia [24,26–28]. A few studies have also reported increased stride length CVs in patients with iNPH [4,5]. In this study, the patients had remarkably larger CVs for step time and movement trajectory amplitude than the HCs did, and 78.3% of the patients had a history of falling. Accordingly, gait parameter variations may reflect an unstable gait and increase the risk of patients falling [24,26–28]. However, the "uncontrolled manifold" hypothesis suggests that highly variable motor control strategies allow greater freedom of movement [29]. Greve et al. [15] reported that movement variability in older adults is a compensation strategy for strength or balance deficits. This suggests that our patients' gait variability might have resulted from a compensation strategy.

Patients with iNPH commonly exhibit improvements in gait parameters such as velocity and step length after CSF drainage [4,5,8,16]. Following TT and SS, our patients also exhibited improved velocities and step numbers and, notably, mitigated abnormalities of ambulatory COM movement. Some studies have suggested that central and/or peripheral vestibular dysfunction may be the key factor underlying iNPH-associated balance disturbances [8–10], which would account for CSF drainage reducing balance impairments [8,10]. The increased gait variability reflects reduced postural control [26], and postural balance strongly influences velocity [30].

Accordingly, we believe that COM movement improvements after TT and SS may result from the improved posture control accompanying increased velocity and step length.

In this study, we included patients with iNPH who showed post-TT improvements in the typical triad symptoms of iNPH (i.e., gait disturbance, cognitive impairment, and urinary incontinence). We therefore detected no significant differences between post-TT and post-SS ambulatory COM movements. Future studies should explore ambulatory COM movements in patients with iNPH who do not benefit from TT.

This study has several limitations. First, COM movement was not directly measured but rather calculated from the triaxial accelerometer data [20,21], but such calculations are easy and reliably comparable to 3-dimensional analyses [11]. Second, our patient sample was relatively small and was recruited from 1 facility. Third, it should be noted that the methodological reliability was tested on healthy subjects. People with medical conditions may show different motor behaviors and should therefore be viewed with caution. Future studies with larger samples are needed to investigate the relationship between ambulatory COM movement, balance function, risk of falling, and disease severity.

In conclusion, our results suggest that unstable gaits in iNPH may cause abnormal

COM movement. The high variability of ambulatory COM movements may be a compensation strategy for gait and balance disturbances in iNPH. Gait improvements after TT and SS could be explained by the normalization of ambulatory COM movement.

Conflict of interest statement

The authors have no conflicts of interest.

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Figure Captions

Fig. 1. Sample of ambulatory movement trajectory amplitudes in a participant

ML: medial/lateral directions, VT: vertical directions

Fig. 2. Gait analysis in patients before TT vs. HCs

Bars indicate mean values, and error bars show standard deviations. Asterisks indicate

significant differences (p < 0.05). TT: tap test, HCs: healthy controls, ML: medial/lateral directions, VT: vertical directions, CV-ML: coefficient of variation in the medial/lateral direction, CV-VT: coefficient of variation in the vertical direction

Fig. 3. Patients' gait conditions at 3 timepoints

Bars indicate means, and error bars indicate standard deviations. Asterisks indicate significant differences (p < 0.05). TT: tap test, ML: medial/lateral directions, VT: vertical directions, CV-ML: coefficient of variation in the medial/lateral direction, CV-VT: coefficient of variation in the vertical direction

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Table 1Demographic data of the HCs and patients with iNPH.

<u> </u>	1		
	iNPH (n = 23)	HC (n = 18)	<i>p</i> -Value
Age (years)	76.9 (5.7)	74.3 (3.4)	0.079 ^a
Gender (male/female)	19/4	12/6	0.238 ^b
Height (cm)	159.1 (7.9)	160.7 (8.5)	0.548^{a}
Weight (kg)	60.7 (9.7)	58.0 (9.7)	0.516 ^a
MMSE score (preTT)	25.0 (3.6)	_	
History of falls (%)	78.3	0	0.000^{b}
Surgery type (LP/VP)	21/2	—	

Values are mean (SD); ^a p -value of independent-t test; ^b p -value of Chi-Square test MMSE: Mini Mental State Examination;

TT: tap test;

LP: lumbo-peritoneal shunt; VP: ventriculo-peritoneal shunt







