

## Effects of somatosensory-stimulating foot orthoses on postural balance in older adults: A computerized dynamic posturography analysis

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### ARTICLE INFO

**Keywords:**

Stimulating insoles  
Tactile sensitivity  
Balance and stability

Feedback  
Elderly

### ABSTRACT

**Background:** Foot orthoses (FO) with protruding knobs designed to stimulate the mechanoreceptors on the glabrous skin of the foot have been proposed to enhance proprioception, thereby improving postural balance and stability. This study aimed to investigate the effects of these FO with stimulating knobs on the postural balance in the elderly using computerized dynamic posturography (CDP).

**Research question:** Do FO with stimulating knobs enhance postural balance in the elderly by improving scores related to sensory organization, motor control, and adaptation in response to different static and dynamic perturbation conditions?

**Methods:** Twenty-three healthy elderly participants performed the CDP, which includes Sensory Organization Test, Motor Control Test, and Adaptation Test in both flat FO and stimulating FO. The Bertec Balance Advantage System with force plates was employed to collect comprehensive CDP data.

**Results:** Our results indicated a significant improvement in the composite equilibrium score ( $MD=1.44$ ,  $p = 0.048$ ) and weight symmetry ( $MD=-1.85$ ,  $p = 0.024$ ) between the two limbs when using the stimulating FO compared to the flat FO condition. The latency and amplitude scaling during backward translation as well as sway energy during toes down perturbations were lower in females than males with stimulating FO (Latency:  $MD=-6.62$ ,  $p = 0.044$ ; Amplitude scaling:  $MD=-1.75$ ,  $p = 0.011$ ; Sway energy:  $MD=-40.08$ ,  $p = 0.007$ ).

**Significance:** These findings highlight the potential of stimulating FO to provide enhanced somatosensory feedback for better postural control and coordination, underscoring their potential clinical application in improving balance and sensory integration.

### 1. Introduction

Balance and stability are crucial for reducing the risk of falls and promoting healthy aging in older adults. Age-related changes in the musculoskeletal and nervous systems can lead to decrease sensory inputs and motor control, impairing postural balance. Given the complexity of the balance system, integrating visual, vestibular, and proprioceptive inputs, even minor disruptions can significantly impact an individual's ability to maintain or regain balance [1]. Older adults with balance impairment are at greater risk of falls and injuries, which

can significantly affect their independence and quality of life [2–4]. Various interventions including physical therapy, exercise programs, and assistive devices have been employed to address balance problems in older adults [5,6]. Among these, foot orthoses (FO) including insoles and shoe inserts have been recommended as a practical intervention to improve gait, balance, and stability [7,8].

Though traditional FO incorporating wedges, posts, raised heel cups, and/or arch-support structures have shown benefits in correcting biomechanical alignments, they have not adequately addressed the sensory deficits contributing to balance impairments in the elderly [9],

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[10]. More recently, FO with textured surfaces or protruding knobs that provide somatosensory stimulation to the mechanoreceptors on the glabrous foot skin have been suggested to enhance proprioception, potentially improving postural balance and stability [9,10]. Although these FO offer a passive intervention by stimulating tactile mechanoreceptors and enhancing somatosensory responses, the effectiveness and underlying mechanisms that influence balance are not fully understood. Comprehensive assessments are needed to evaluate the effects of FO with protruding knobs on postural balance in older adults. Previous studies have often used force plates and motion capture systems to measure the center of pressure (COP) data to investigate the sway variability or employed functional clinical tools to assess balance and stability [9].

Computerized dynamic posturography (CDP) quantitatively measures balance performance under various sensory conditions, including visual, vestibular, and somatosensory inputs [11–13]. It is a comprehensive method to assess how the balance system uses sensory and motor components to maintain balance. The CDP can track the center of gravity (COG) within the limits of stability to determine postural sway. The postural sway assessment can determine the use of ankle or hip postural strategies during static and dynamic perturbations, symmetry of weight-bearing between limbs, and motor adaptations during perturbations [14–16]. This study aimed to investigate the immediate effects of FO with stimulating knobs on the postural balance in older adults using the CDP method. We hypothesized that FO with stimulating knobs would enhance postural balance in the elderly by improving scores related to equilibrium in postural strategies, sensory inputs, postural latencies, gait symmetry, and sway energy for adaptation under various static and dynamic perturbation conditions.

## 2. Methods

### 2.1. Participants

Healthy older adults were recruited through convenience sampling from the nearby elderly centres. Eligible participants were aged 65 or older, capable of walking for 30 minutes continuously without any breaks or external assistance, and engaged in at least 150 minutes of walking per week. Exclusion criteria included being overweight with a BMI over 40, having high foot arches (pes cavus) or flat feet (pes planus), suffering from neuromuscular or central nervous system disorders, experiencing vestibular disorders, or having major foot deformations

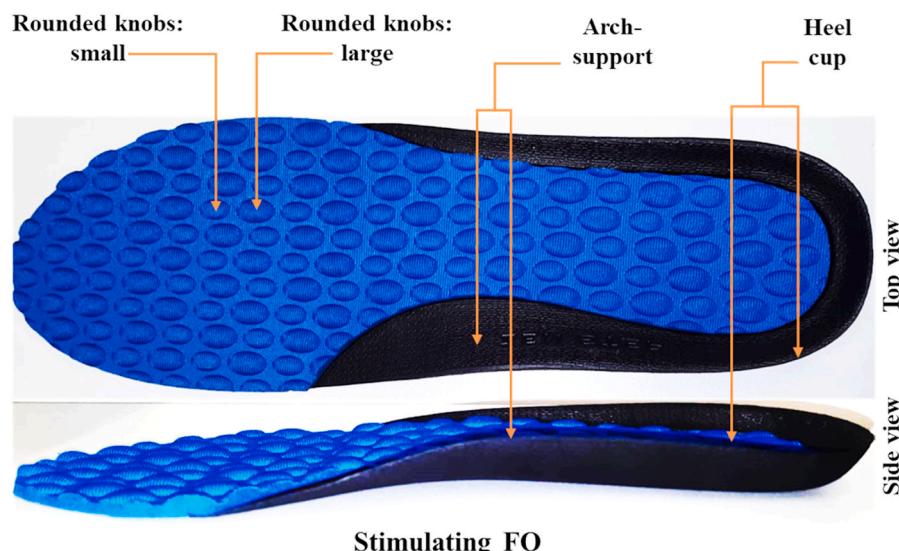
such as peripheral neuropathy/ulcers, or pain. A Semmes Weinstein Monofilament (SWM) test was conducted with a 10 g load at 10 different plantar foot locations, as described in the previous study, to ensure that participants were free from loss of protective tactile sensitivity [17]. Participants who were unable to distinguish monofilament at 4 or more of the tested foot locations were excluded. Participants were informed about the details of the study and provided consent before participating. The study protocol, approved by the Human Subject Ethics Sub-Committee of The Hong Kong Polytechnic University, adhered to the guidelines outlined by the Declaration of Helsinki.

### 2.2. Foot orthoses

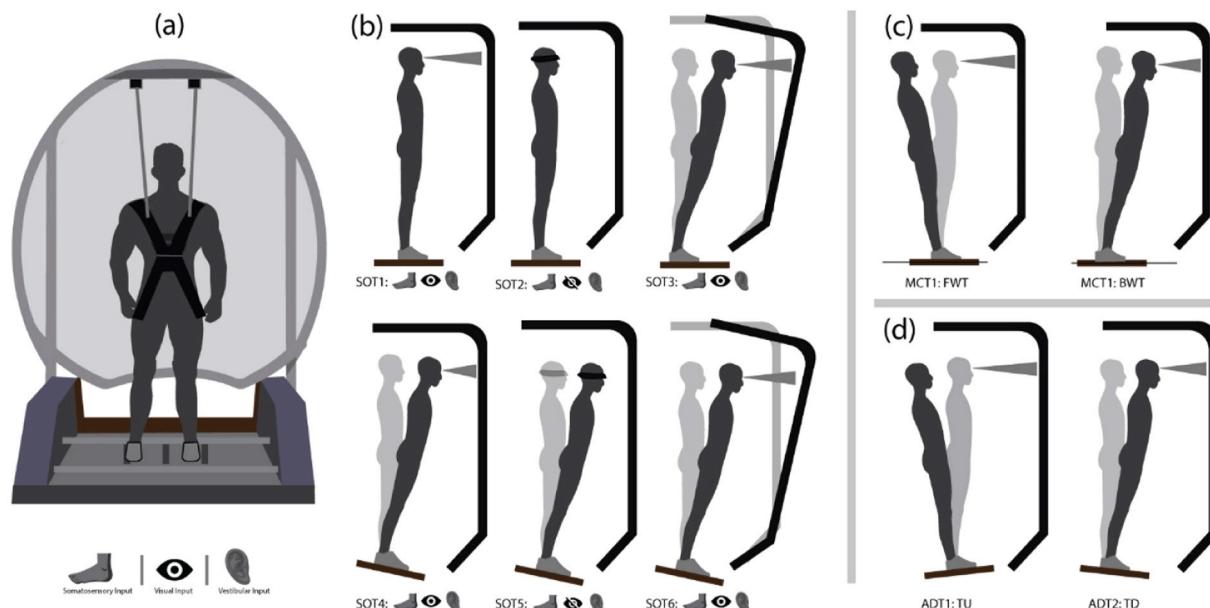
The participants' postural balance was examined under two FO conditions: (i) flat FO and (ii) prefabricated stimulating FO. The surface of the stimulating FO (Copper Fit Zen Step Comfort, China) was entirely covered with protruding rounded knobs (larger knobs: length=15 mm, width=10 mm, height=3 mm; smaller knobs: length=12 mm, width=8 mm, height=2 mm; hardness: Shore A 30) that were distributed evenly across the entire bottom surface. A raised heel-cup with medial and lateral arch-supports (hardness: Shore A 40) was integrated into the full-length stimulating FO (Fig. 1). During the balance trials, FO were inserted into the standardized elderly shoe (Shiying 520 A, Shiying Trading Co. Ltd., China). To minimize the influence of confounding factors (e.g., sock material and thickness), standard socks made of 75 % cotton and 1 mm thickness (Zhuji Dongling Needle Textile Co., Ltd., China) were provided to all participants throughout the entire study.

### 2.3. Experimental procedures

The Bertec Balance Advantage System (Bertec Corporation, Columbus, OH, USA), was employed to collect comprehensive CDP data [11, 18,19]. The system is equipped with built-in dynamic force plates that record the displacement of the participant's weight on the foot in response to body movement. Additionally, a visual background displayed anterior/posterior displacement to alter visual information with the built-in software (Fig. 2a). Prior to data collection, participants were given full demonstrations of each experimental component. To ensure safety and alleviate fears of falling, participants were secured with a harness, ensuring both safety and comfort throughout the trials. The order of the FO conditions was random across participants to minimize potential confounding effects e.g. learning effects. A rest period of



**Fig. 1.** Illustration of prefabricated foot orthoses (FO) featuring protruding knobs (blue) across the entire bottom surface and a raised heel-cup with arch-supports (black).



**Fig. 2.** Illustration of experimental set-up: (a) Force plates integrated Bertec Balance Advantage System; (b) Six different conditions of the Sensory Organization Test (SOT); SOT1–SOT3 involve a fixed platform for the three visual conditions (eyes open, eyes closed, sway referenced), SOT4–SOT6 involve a sway referenced platform for the same three visual conditions (c) Two different conditions of the Motor Control Test (MCT); forward translation (MCT1:FWT) and backward translation (MCT2: BWT) of the platform, and (d) Two different conditions of the Adaptation Test (ADT); toes up (ADT1:TU) and toes down (ADT2:TD) of the platform.

7–10 minutes was provided between testing conditions to mitigate the potential fatigue effects [20,21].

#### 2.4. Data collection and analysis

The CDP measurement consisted of three basic tests including the Sensory Organization Test (SOT), Motor Control Test (MCT), and Adaptation Test (ADT). The SOT included six experimental conditions, each with three trials, and each trial lasted for 20 seconds (Fig. 2b). During the first three conditions, the support surface under the foot was stationary while the visual surroundings varied: SOT1—eyes open, fixed support; SOT2—eyes closed, fixed support; SOT3—vision sway referenced, fixed support. The next three conditions were performed with a dynamic support surface while visual surroundings varied similarly to the first three conditions: SOT4—eyes open, support sway referenced; SOT5—eyes closed, support sway referenced; SOT6—both vision and support surface sway-referenced. In SOT, the composite equilibrium score—a weighted average of scores from six conditions and sensory scores—somatosensory (SOT2 vs. SOT1), visual (SOT4 vs. SOT1), vestibular (SOT5 vs. SOT1), and vision preference (sum of SOT3 and SOT6 vs. the sum of SOT2 and SOT5) were calculated. The composite equilibrium score quantified the COG sway or postural stability in the anteroposterior direction. The somatosensory score quantified the ability to utilize the tactile sensory input to maintain balance. In addition, the degree to which the participant is overly reliant on visual input was assessed as vision preference.

The MCT also consisted of two conditions, including three backward and three forward translations of the support surface (Fig. 2c). Each condition was comprised of three trials with a random delay of 1.5–2.5 seconds between trials, and each trial lasted less than a second [15]. The MCT evaluated latency score—time lapse in milliseconds between the start of translation and the participant's active force response, amplitude scaling—degree of recovery per second from the support surface disturbances to indicate inappropriate or asymmetrical force exertion, and weight symmetry score—a distribution of weight bearing between left and right limbs. The weight symmetry score ranges from −100 to 100, with 0 indicating perfect symmetry (equal weight distribution between the two limbs) and −100 or 100 indicating complete asymmetry (all weight borne by the left limb or right limb, respectively).

The ADT consisted of two conditions: rotations with toes up and toes down, with the axis of motion in the ankles (Fig. 2d). Each condition consisted of five trials of rotational perturbations with randomized intervals to prevent participants from predicting the timing of the next rotation. The sway energy required to restore the body balance after each platform perturbation was evaluated. The psychometric properties i.e., the test-retest reliability of the SOT and MCT scores were demonstrated excellent ( $ICC=0.90$  and 0.85, respectively), for assessing balance in older adults [22].

#### 2.5. Statistical analysis

All data were checked for normality using the Shapiro-Wilk test. Independent t-tests as well as one-way ANOVA with Bonferroni post-hoc corrections were used to examine the potential interaction between gender and age variations on sensory inputs in the balance system. After combining male and female participants, paired samples t-tests were used for each outcome measure to investigate the significant differences between the FO conditions. All statistical analyses were performed using the IBM SPSS software (version 22, SPSS Inc., Chicago, IL). The threshold for statistical significance was set at  $p < 0.05$  for each test conducted.

### 3. Results

#### 3.1. Participants characteristics

Twenty-three elderly individuals (Female: 16; age=72 ± 3 yrs; height=154 ± 6 cm; BMI=22.5 ± 3.4; foot length: 236 ± 9 mm; US shoe size: 5.5–8.5; SWM: 9.9 ± 0.2; Male: 7; age=72 ± 4 yrs; height=165 ± 7 cm; BMI=22.8 ± 2.0; foot length: 251 ± 7 mm; US shoe size: 5.5–7.5; SWM: 9.5 ± 0.9) who meet the eligibility criteria were included in the balance assessment. The sample size can be justified based on a recent study involving protruding FO for older adults, which demonstrated 80 % power with 20 participants at a 95 % confidence level [23]. A summary of demographic characteristics is provided in the Table 1. There was no significant interaction between age variations and balance performance in the CDP assessment. However, a

**Table 1**

A summary description of the demographic variables.

PN	Age, year	Gender	Body weight (Kg)	Body height (cm)	BMI (Kg/m <sup>2</sup> )	Foot length (mm)	Shoe size (USA)	SWM (10 g)
01	77	Female	46.0	155	19.2	233	5.5	9.5
02	68	Male	68.7	172	23.7	258	7.5	8.5
03	76	Male	72.0	171	25.6	254	7	8.0
04	72	Female	49.3	167	17.8	241	6.5	10
05	74	Female	49.5	152	21.4	228	5	10
06	70	Male	64.2	164	24.3	258	7.5	10
07	67	Female	62.0	154	26.1	241	6	10
08	76	Female	56.0	150	24.9	233	5.5	10
09	73	Female	58.0	154	24.4	237	6.5	10
10	69	Female	48.0	150	21.3	229	4.5	10
11	65	Female	71.7	157	29.0	250	7.5	10
12	73	Female	51.2	153	21.9	228	5	10
13	72	Female	60.7	153	25.9	233	5	10
14	67	Female	40.4	154	17.0	237	5.5	10
15	71	Female	55.5	145	26.3	224	4.5	10
16	76	Female	46.0	150	20.4	233	5.5	10
17	67	Female	49.5	160	19.3	228	5	9.5
18	74	Female	55.1	162	20.9	258	8.5	10
19	76	Male	55.0	170	19.0	258	7.5	10
20	72	Male	68.3	166	24.8	245	5.5	10
21	72	Female	57.5	152	24.9	237	6	10
22	69	Male	54.5	154	22.9	241	5.5	10
23	78	Male	54.5	160	21.3	245	6	10
<b>Mean±SD</b>								
Female	72 ± 3	—	71.6 ± 3.6	154 ± 6	22.5 ± 3.4	236 ± 9	—	9.9 ± 0.2
Male	72 ± 4	—	72.9 ± 3.8	165 ± 7	22.8 ± 2.0	251 ± 7	—	9.5 ± 0.9

PN: participants number; BMI: body mass index; SWM: semmes weinstein monofilament

significant gender interaction was observed. Female participants exhibited lower amplitude scaling than male participants during forward translation with both flat FO (medium: MD=−1.83, 95 %CI: −2.807 to −0.870,  $p = 0.001$ ; large: MD=−2.62, 95 %CI: −3.842 to −1.416,  $p < 0.001$ ) and stimulating FO (medium: MD=−2.55, 95 %CI: −4.030 to −1.085,  $p = 0.002$ ; large: MD=−2.70, 95 %CI: −4.089 to −1.321,  $p = 0.001$ ). The latency and amplitude scaling during backward translation as well as sway energy during motor adaptation in response to

downward perturbations were lower in females than males with stimulating FO (Latency: MD=−6.62, 95 %CI: −13.042 to −0.208,  $p = 0.044$ ; Amplitude scaling: MD=−1.75, 95 %CI: −3.050 to −0.449,  $p = 0.011$ ; Sway Energy: MD=−40.08, 95 %CI: −68.149 to −12.029,  $p = 0.007$ ).

### 3.2. Sensory organization test

The descriptive data of CDP assessments including the SOT, MCT,

**Table 2**

Data for computerized dynamic posturography assessments.

Tests	Parameters	Magnitudes of CDP assessment				P values	
		Flat FO		Stimulating FO			
		Mean	±SD	Mean	±SD		
SOT	Composite equilibrium (score)	68.17	3.54	69.61	3.92	0.048 *	
	Somatosensory (score)	99.04	1.71	100.13	1.20	0.188	
	Visual (score)	67.26	5.94	69.13	7.31	0.337	
	Vestibular (score)	65.57	5.74	67.00	6.02	0.401	
	Preference (score)	96.09	2.61	97.04	1.98	0.481	
	Latency_BWT (msec)	137.26	4.11	136.39	3.67	0.558	
MCT	Latency_FWT (msec)	137.13	4.96	135.17	5.42	0.173	
	Weight asymmetry_BWT (%)	9.45	3.65	7.60	3.01	0.024 *	
	Weight asymmetry_FWT (%)	8.70	3.13	8.09	2.99	0.323	
	Amplitude Sc_BWT_Small (degrees/sec)	2.91	0.62	2.93	0.64	0.901	
	Amplitude scaling_BWT_Medium (degrees/sec)	4.21	0.78	4.28	0.79	0.678	
	Amplitude scaling_BWT_Large (degrees/sec)	4.60	0.80	4.70	0.87	0.628	
	Amplitude scaling_FWT_Small (degrees/sec)	3.50	0.75	3.83	0.65	0.189	
	Amplitude scaling_FWT_Medium (degrees/sec)	4.43	0.66	4.93	0.97	0.065	
	Amplitude scaling_FWT_Large (degrees/sec)	4.95	0.88	5.26	0.96	0.157	
ADT_Toes Up	Sway energy_Toes up1	97.74	10.11	99.04	15.86	0.788	
	Sway energy_Toes up1	98.96	16.87	102.22	16.01	0.657	
	Sway energy_Toes up1	100.57	13.97	102.00	13.27	0.813	
	Sway energy_Toes up1	94.74	12.9	91.78	12.69	0.641	
	Sway energy_Toes up1	92.83	16.22	92.74	12.35	0.991	
ADT_Toes Down	Sway energy_Toes down1	92.87	13.05	101.30	15.91	0.061	
	Sway energy_Toes down1	94.83	15.05	95.17	14.89	0.940	
	Sway energy_Toes down1	83.04	13.61	86.91	16.09	0.475	
	Sway energy_Toes down1	83.22	15.39	80.83	17.33	0.677	
	Sway energy_Toes down1	81.00	14.78	80.00	16.10	0.853	

FO: foot orthoses; CDP: computerized dynamic posturography; SOT: sensory organization test; MCT: motor control test; ADT: adaptation test; BWT: backward translation; FWT: forward translation;

and ADT are demonstrated as mean $\pm$ standard with p values in Table 2. A statistically significant difference was found, with a higher composite equilibrium score for the stimulating FO ( $MD=1.44$ , 95 %CI:  $-2.856$  to  $-0.014$ ,  $p = 0.048$ ) (Fig. 3a). However, there were no statistically significant differences in the balance scores related to sensory inputs, although increasing trends in the somatosensory, visual, and vestibular scores were observed with stimulating FO (Fig. 3b).

### 3.3. Motor control test

There were statistically significant differences in weight symmetry during backward translation, with lower asymmetry values for the stimulating FO ( $MD=-1.85$ , 95 %CI:  $0.270$ – $3.438$ ,  $p = 0.024$ ) (Fig. 3c). Additionally, there were trends towards lower postural latencies and higher amplitude scaling during both backward and forward translations for the stimulating FO (Fig. 3d-e).

### 3.4. Adaptation test

There were no statistically significant differences in sway energy for motor adaptation in response to perturbations. The findings were consistent regardless of whether the rotations were directed toes-up or toes-down when comparing the stimulating FO to the flat FO conditions (Fig. 3f).

## 4. Discussion

By employing the computerized dynamic posturography (CDP), this study is the first to explore the comprehensive effect of plantar tactile stimulation using FO with protruding knobs on postural control and balance in older adults. Consistent with our original hypothesis, the stimulating FO improved overall equilibrium in postural strategies and weight symmetry, indicating better weight distribution between the two limbs during backward translation compared to the flat FO.

The increased composite equilibrium score indicates improved balance by reducing anteroposterior center of gravity (COG) sway, enhancing motor strategies and postural effectiveness in response to perturbations, by maintaining COG alignment within the normal maximum limit [15]. A composite equilibrium score near 100 indicates perfect stability achieved through the ankle strategy, while a score near 0 indicates a loss of balance, typically managed by the hip strategy [15]. The stimulating FO appear to enhance overall equilibrium by better integrating sensory inputs from the somatosensory, visual, and vestibular functions, as indicated by the improved trend in sensory scores. This integration with the support of tactile stimulation could facilitate more prompt information transmission to the cognitive system, and enable the musculoskeletal system to execute the ankle strategy more effectively for improved balance control [24].

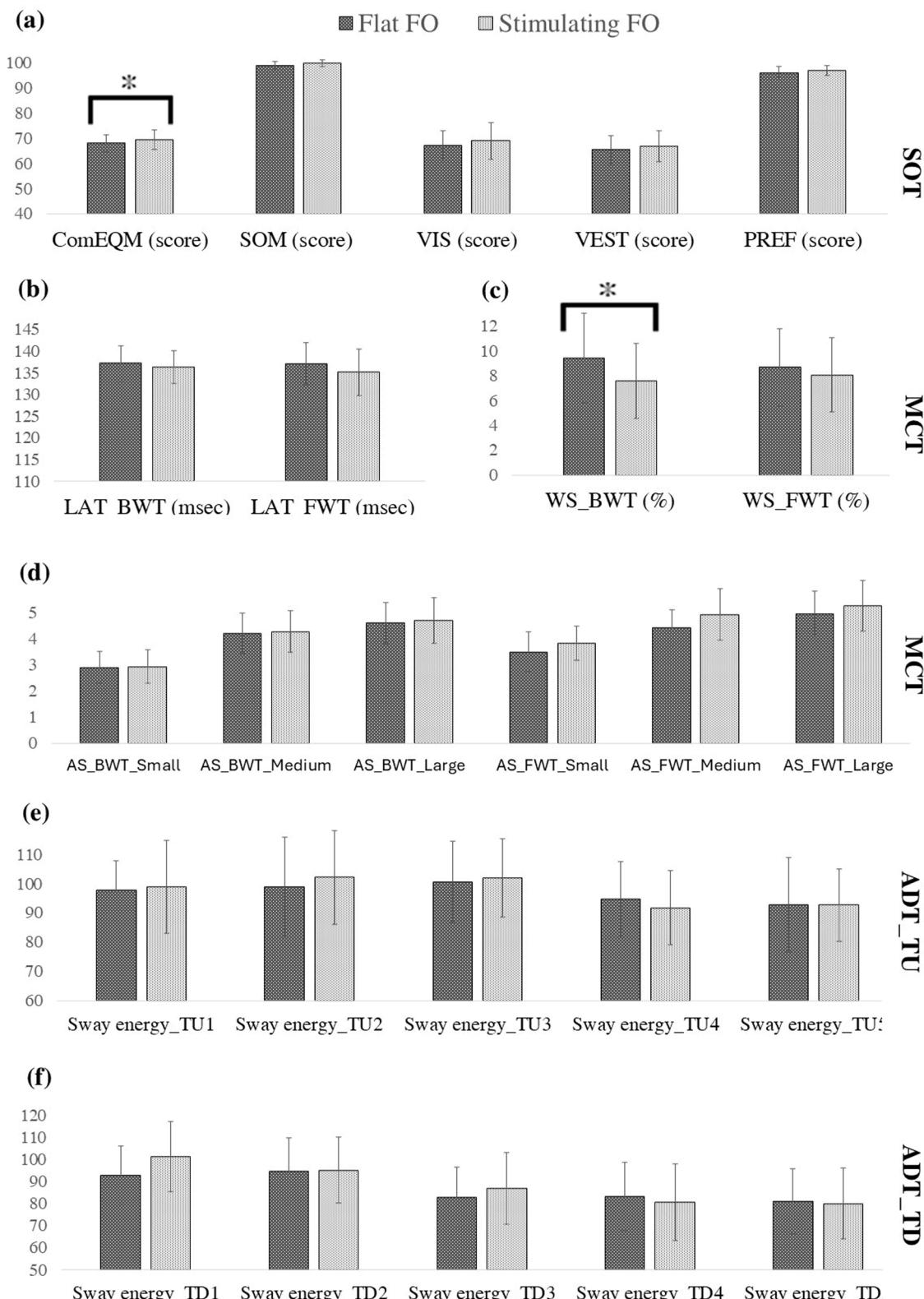
The findings of symmetrical weight distribution between the two limbs further support the improvement in balance performance with the stimulating FO. Since the ankle strategy is a more energy-efficient strategy for maintaining balance to counteract mild perturbation than other strategies [25], enhancing balance posture through this strategy could be beneficial. This could help maintain uniform weight distribution between the two limbs before and after the translations, particularly in the backward direction. During backward translation, a participant's full weight shifts to the foot plantar surface, while attempting to maintain balance by applying plantar force on the base of support [26]. The transfer of body weight to the feet provides an opportunity to utilize information from the support surface specifically, the FO with protruded knobs to maintain appropriate posture. In this context, the protruding knobs on the FO may better stimulate mechanoreceptors in the glabrous foot skin, promptly sending information to the brain to activate and coordinate muscle contractions around the ankle to counteract disturbances and correct posture.

The improvements in balance performance with the stimulating FO in

response to perturbations align with findings from previous investigations during static and dynamic gait analyses [9,10]. Previous studies have primarily explored the effects of tactile stimulating FO on postural balance through centre of pressure (COP) distribution [27,28] and clinical functional outcomes [23]. These studies employed FO with protruding knobs of various sizes and shapes to improve static and dynamic balance. Notably, studies employing flat FO with smaller granulations have reported non-significant changes in static balance [27,29,30]. A plausible explanation could be the insufficient stimulation of mechanoreceptors distributed across the plantar glabrous skin of the foot. Tactile stimulation of these mechanoreceptors is crucial for maintaining the COG within its maximum sway in the anteroposterior direction. [31,32]. The limited contact surfaces between the foot's plantar skin and the flat FO may restrict tactile stimulation, thereby reducing mechanoreceptor activation. In contrast, the stimulating FO with a 3 mm ridge around the perimeter effectively engages the lateral perimeter areas of the foot, counteracting sway movements and enhancing lateral stability during walking [33]. Additionally, incorporating arch-support into the stimulating FO has been shown to improve dynamic stability [34]. The FO configuration with larger knobs placed in high plantar pressure regions such as the heel and metatarsal head areas may provide enhanced tactile stimulation, resulting in improved dynamic stability. Protruding knobs with sufficient tactile input may boost afferent axon recruitment in mechanoreceptors through sensory stimulation [35]. This additional sensory feedback to the nervous system may aid in filtering receptor information and contribute to enhanced posture and joint positioning for better balance performance. The current stimulating FO, featuring protruding knobs across the entire surface along with arch-support and a heel-cup, presents a promising approach for maximizing tactile stimulation of the glabrous skin to improve balance performance. By providing greater sensory feedback to the nervous system, it can ultimately support better equilibrium and weight distribution, although significant improvements were observed in only a few variables. These variables may be more sensitive to tactile stimulation. Future studies should evaluate the effectiveness of protruding knob sizes and mechanoreceptor thresholds on balance performance before a definitive conclusion can be made.

The findings on amplitude scaling suggest better control of the musculoskeletal system in females than in males, as evidenced by quicker recovery from an unanticipated external disturbance during medium and large translations. This was in line with previous studies, which suggested that females may have better utilization of their motor system due to physiological and morphological characteristics [36–38]. The reduced latency and sway energy observed in females compared to males with stimulating FO are in line with previous studies that females outperformed males in response to sensory perturbations [11,36]. However, the protruding stimulation did not induce substantial sway energy during the Adaptation Test, likely due to the smaller sample size or variations in body mass index and weight, as these factors may influence sway energy [39]. To further explore site-specific and long-term effects, as well as the underlying mechanisms, longitudinal research on afferent axon recruitment and muscle activation is warranted.

There are several limitations to the current study. First, this study included only healthy participants; effects on those with peripheral sensory deficits, balance impairments, or fall risk need investigation. Additionally, this study investigated stimulating FO that featured a single type of protruding knob across the entire surface. Future studies should explore a variety of designs, including different shapes, heights, and placements of the stimulating knobs, to optimize specific knob arrangements for enhancing postural stability. Since the FO were worn only during the assessment period, their effects on performance and physiological changes over the long term remain unclear. Future studies should investigate whether prolonged use of stimulating FO affects somatosensory activity. The assessor was not blinded to the intervention and outcome measurements. In addition, methodological limitations including small sample sizes and a lack of controlled designs, highlight



**Fig. 3.** Prefabricated stimulating FO vs. Flat FO in computerized dynamic posturography assessments: (a) composite equilibrium and sensory scores; (b) postural latencies in msec; (c) weight symmetry in %; (d) amplitude scaling in degrees/sec; (e) adaptation sway energy scores during toes up; (f) adaptation sway energy scores during toes down. The asterisk (\*) refers to a significant difference at  $p < 0.05$ . (Note: SOT: sensory organization test; MCT: motor control test; ADT: adaptation test; BWT: backward translation; FWT: forward translation).

the need for more rigorous randomized controlled trials (RCTs). Future RCTs should focus on isolating design features of stimulating knobs and including larger and more diverse populations to enhance generalizability.

## 5. Conclusion

Although significant improvements were observed in only a few variables, the FO with protruding knobs can enhance postural stability through symmetric weight distribution during backward translation and improve balance in response to both static and dynamic perturbations in healthy older adults. Incorporating protruding knobs into FO has the potential to stimulate mechanoreceptors on the foot's plantar surface. Future studies should carefully interpret the results and consider larger sample sizes and randomized controlled trials to confirm the effects of passive stimulation of plantar tactile mechanoreceptors with protruding knobs.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## CRediT authorship contribution statement

**Khan Mohammad Jobair:** Writing – review & editing, Methodology, Investigation. **He Yufan:** Writing – review & editing, Methodology, Investigation. **Lam Wing-Kai:** Writing – review & editing, Investigation. **Winser Stanley J:** Writing – review & editing, Investigation. **Gao Fan:** Writing – review & editing, Investigation. **Zhang Ming:** Writing – review & editing, Investigation. **Kobayashi Toshiki:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Conceptualization. **Jor Abu:** Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Lai Chun Hei:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation.

## Declaration of Competing Interest

The authors report there are no competing interests to declare.

## Acknowledgments

We gratefully acknowledge the support of Shakawath Hosen Opu, Khulna University of Engineering & Technology for helping with the illustrations of Fig. 2.

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