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# Soft robotic apparel to avert freezing of gait in Parkinson's disease

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Freezing of gait (FoG) is a profoundly disruptive gait disturbance in Parkinson's disease, causing unintended stops while walking. Therapies for FoG reveal modest and transient effects, resulting in a lack of effective treatments. Here we show proof of concept that FoG can be averted using soft robotic apparel that augments hip flexion. The wearable garment uses cable-driven actuators and sensors, generating assistive moments in concert with biological muscles. In this n-of-1 trial with five repeated measurements spanning 6 months, a 73-year-old male with Parkinson's disease and substantial FoG demonstrated a robust response to robotic apparel. With assistance, FoG was instantaneously eliminated during indoor walking (0% versus  $39 \pm 16\%$  time spent freezing when unassisted), accompanied by  $49 \pm 11 \text{ m} (+55\%)$  farther walking compared to unassisted walking, faster speeds (+0.18 m s<sup>-1</sup>) and improved gait quality (-25% in gait variability). FoG-targeting effects were repeatable across multiple days, provoking conditions and environment contexts, demonstrating potential for community use. This study demonstrated that FoG was averted using soft robotic apparel in an individual with Parkinson's disease, serving as an impetus for technological advancements in response to this serious yet unmet need.

Parkinson's disease (PD) is one of the leading causes of disability in the world<sup>1,2</sup>. Over 9.4 million people live with PD globally, and its prevalence is projected to double by 2040 (refs. 3,4). PD is characterized by a loss of dopamine-producing neurons in the basal ganglia, leading to reduced automaticity of movement<sup>5</sup>. The deficits in automaticity lead to gait dysfunction, where walking is bradykinetic, hypokinetic, variable and effortful. With progression of the disease, a substantial proportion of patients (up to 80%) experience freezing of gait (FoG)<sup>6</sup>, which is a profound gait disturbance that is characterized by an episodic absence or marked reduction of forward movement of feet despite the intent to walk<sup>7</sup>. Persons with FoG describe this phenomenon as a feeling that their feet are glued or stuck to the floor<sup>8</sup>. Serious negative consequences of FoG include an overall loss of mobility and independence, an increase in falls<sup>8</sup>, worsening disability and poorer quality of

life<sup>9</sup>. The large number of people with PD experiencing FoG and the substantial burden and impact on their quality of life underscore the importance of developing innovative technologies to address FoG<sup>10</sup>.

Various interventions are available to manage FoG, but they provide only modest and transient benefits<sup>11</sup>. For instance, dopaminergic replacement therapy has been shown to minimize the effects of FoG; however, its effectiveness is refractory with disease progression<sup>12</sup>. Furthermore, freezing episodes persist despite being in the medication 'on-phase<sup>49,13</sup>, which refers to the period when dopaminergic medication is in effect to relieve Parkinson's symptoms. The most common surgical intervention—deep brain stimulation of the subthalamic nucleus—has varying degrees of effectiveness<sup>14,15</sup>, with efficacy that declines over time<sup>16</sup>. Behavioral interventions, such as cueing strategies using auditory, visual or vibrotactile stimuli<sup>17</sup>, can lead to long-term training

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**Fig. 1** | **Soft robotic apparel. a**, Components of the robotic apparel for hip flexion assistance. Hardware components were secured around the waist, with batteries and electronics on the lower back and two hip flexion actuators on each hip positioned around the lower abdomen. **b**, Hip flexion robotic apparel. Bilateral thigh IMUs and load cells on textile attachment points enabled gait detection and

tracking of forces delivered by the device, respectively. Additionally, IMUs on bilateral shank and foot were used for data collection (for example, stride length estimation and FoG assessment). **c**, Hip flexion assistance profile. Forces were delivered around the toe-off subphase of the gait cycle, as marked by the dashed line. The gait cycle was segmented based on heel strike (0% gait cycle).

effects<sup>18</sup>. However, their utility remains largely limited, as cueing fails to elicit consistent immediate effects to alleviate freezing<sup>18</sup> and also requires considerable time for consolidation for transfer effects<sup>19</sup>. Furthermore, the high dependence on cognitive processing makes cueing an impractical compensatory strategy as it can interfere with daily activities<sup>18</sup>. The limitations of current pharmacologic, surgical and behavioral interventions highlight the unmet need for effective interventions for FoG in PD.

The origins of FoG are complex, multi-factorial and poorly understood<sup>20-22</sup>. In general, disruption of the locomotor circuitry in the basal ganglia and brainstem is thought to be responsible for FoG<sup>7</sup>. From a biomechanical perspective, FoG is clearly manifested by an overt breakdown in spatial and temporal mechanics of walking<sup>23-25</sup>. Preceding a freezing episode, there is a marked reduction in movement excursions of the lower limbs<sup>24</sup>. Specifically, there is reduced stride length<sup>23</sup> accompanied by an exponential increase in cadence that leads to reduced gait velocity<sup>25</sup>. This is accompanied by incoordination of muscle activation of agonist/antagonists of the lower limb<sup>26</sup>, along with a reduction in ioint excursions in the sagittal plane involving the hip and ankle<sup>24,27</sup>. Additionally, during regular walking independent of freezing episodes, individuals with PD who are considered freezers have impaired limb coordination during limb advancement during the swing phase of the gait cycle<sup>27</sup> and have greater impairment of hip motion in the sagittal plane compared to non-freezers<sup>28</sup>. Furthermore, freezers demonstrate greater impairment in gait rhythmicity and stride-to-stride variability compared to non-freezers, which is suggestive that FoG is an ongoing gait disturbance<sup>29</sup>. Together, the ongoing accumulation of spatial and temporal motor disturbances during walking are posited to reach a critical threshold of instability, which ultimately leads to a freezing episode<sup>21,30</sup>.

Wearable robots have been shown to be useful in augmenting kinematics in other neurological disorders, such as stroke, cerebral palsy and spinal cord injury<sup>31-34</sup>. In relation to FoG, we posit that the mechanical assistance of wearable robots has the potential to mitigate gait decline preceding a freezing episode by improving spatial and temporal features of walking and may also provide ongoing gait-preserving effects that essentially minimize the accumulation of motor errors that lead to FoG. To date, there are no robotic devices specifically designed to avert or prevent FoG in PD.

Due to the episodic nature of FoG<sup>35,36</sup>, rigorous validation is known to be crucial for any new intervention. Specifically, FoG has

multi-attribute triggers that vary the likelihood of provoking a freezing episode, including the timing of dopaminergic medication<sup>6,13</sup>, the context (for example, start hesitation, turning and passing through doorways) and cognitive loading as in dual-tasking relative to single-tasking. Furthermore, FoG is more commonly triggered in natural home or community environments and often is suppressed in controlled clinic-based or laboratory-based environments, thus making its assessment more challenging<sup>35</sup>. In particular, the environment has been shown to influence gait quality in individuals with PD who are freezers, where rhythm and variability are worsened when walking outside of laboratory environments due to elements that can induce FoG<sup>37</sup>. Altogether, the high variability resulting from these factors, in addition to the natural day-to-day variability, influences the reproducibility of this motor disturbance. Thus, the examination of a new intervention and the confluence of challenges in eliciting FoG reliably warrant detailed and judiciously performed studies.

In this study, we conducted single-subject research with repeated measurements, which is a foremost and distinct step in our evidence-generating research pathway<sup>38,39</sup>. The objective of the study was to examine the effects of robotic apparel on averting FoG in individuals with PD. We developed soft robotic apparel that provides bilateral assistive hip flexion torgues to aid with limb advancement during the swing phase of walking (Fig. 1a). Functional apparel was worn around the waist and thighs (Fig. 1b), which served as anchor points on the body and an interface for attachment points for flexible cable-driven actuators and sensors (load cells to measure applied force and inertial measurements units (IMUs) to measure wearer movement). Algorithms using data from IMUs estimate the phase of the walking cycle and trigger the actuators to generate an external, assistive moment in concert with the biological moment generated during hip flexion<sup>40</sup> (Fig. 1c and Methods). Through minimal mass on the limbs and the flexible nature, the robotic apparel was designed not to impede limb motion during the unassisted portions of the gait cycle.

#### Results

#### **Patient characteristics**

To address the above-mentioned challenges on the reproducibility of FoG, we studied the effects of the robotic apparel through repeated examination and systematic manipulation of designated triggers of FoG in a single individual. The study participant was a 73-year-old male

#### Table 1 | Baseline characteristics of the study participant

Demographic and clinical information	
Age (years)	73
Height (cm)	173
Weight (kg)	93.5
Sex	Male
Disease duration (years)	10
H&Y stage	2
MMSE (out of 30)	29
ABC Scale (%)	89
MDS-UPDRS (score):	
Part I (out of 52)	7
Part II (out of 52)	11
Part III (out of 132)	33
Part IV (out of 24)	7
NFoG_Q (score):	
Part II (out of 19)	15
Part III (out of 9)	4

H&Y stage<sup>63</sup>, modified Hoehn & Yahr scale stage; MMSE<sup>64</sup>, Mini-Mental State Examination; ABC Scale<sup>65</sup>, Activities-specific Balance Confidence Scale; MDS-UPDRS<sup>66</sup>, Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale; NFoG-Q<sup>67</sup>, New Freezing of Gait Questionnaire.

(Table 1) with idiopathic PD of 10 years. He underwent deep brain stimulation surgery to the globus pallidus internus 5 years after diagnosis, and the stimulator is constantly turned on throughout the day, including during the study visits. Pharmacologic management included 1.5 tablets of 25-100-mg carbidopa/levodopa taken four times per day, one tablet of 100-mg amantadine twice per day and one tablet of 200-mg entacapone taken four times per day. Despite surgical and pharmacologic management in addition to implementing behavioral strategies, the participant endured substantial, incapacitating FoG, where he experienced numerous freezing episodes (>10 per day) with associated daily falls. Due to the disruptive nature of FoG, the participant compensates by holding on to walls when walking indoors. Furthermore, the participant reported that he was unable to walk in the community and had learned to depend on a kick scooter for any mobility outside the home. At study entry, the physical therapist verified the presence of FoG based on overt freezing episodes that were repeatedly triggered during regular walking in open space, without the aid of any assistive device or support surfaces (walls and furniture). Specifically, freezing episodes were primarily observed during walking in open hallways, dual-tasking (that is, walking and talking simultaneously), turning and walking outdoors but not during gait initiation. Because the task of unassisted walking in open space reliably provoked FoG for this individual, we regarded this task as the basis for our examination on the effects of the robotic apparel on FoG.

To assess the reproducibility of the impact of robotic apparel on FoG and to determine whether it was sustainable in the presence of designated triggers, we performed repeated measurements during timed walking trials across a total of five study sessions over the course of 6 months (Extended Data Fig. 1). Specifically, we administered four study sessions in the laboratory (study visits 1–4; 2-minute walk test (2MWT)) to assess the repeatability of effects that account for day-to-day variability and one study session in real-world outdoor community settings (study visit 5; 6-minute walk test (6MWT))–all tested during medication on-phase and under single-task conditions. Furthermore, within these study visits, we administered testing conditions with greater levels of provocation, which included attention-demanding contexts through dual-tasking during medication on-phase (study visit 3) and single-task walking during suboptimal timing of medication cycle when dopaminergic effects wore off (study visit 2). To assess the immediacy of effects of the robotic apparel (study visits 2 and 4), we altered the schedule of assistance of the robotic apparel by serially toggling the power on and off during uninterrupted walking (coined here as intermittent assistance) during medication on-phase under single-task conditions. Finally, a biomechanical analysis of walking was performed (study visit 1) using three-dimensional motion capture during short-distance walking (10-m walk test) under single-task conditions during medication on-phase. For each instance, we compared the effects when the assistance of the robotic apparel was on (ASSIST ON) against no device (NO SUIT) or simply turned off (ASSIST OFF). We measured the percent time spent freezing $^{41}$ -a recommended performance metric for FoG<sup>42</sup>-and the total distance traveled as a measure of walking function. FoG episodes were initially identified through a review of recorded videos<sup>41,43,44</sup> by two neurologic physical therapists trained in PD management (N.W. and T.B.). Video annotation was mapped against time events of wearable sensors to precisely determine the onset and termination timings of the identified FoG episodes (Methods), which were subsequently reconfirmed by the physical therapists. This combined approach involved detecting the absence of movement and rapid limb movements<sup>7</sup> (for example, trembling in place or shuffling forward) within the frequency range of 3-8 Hz (refs. 7,45-48).

#### Multiple-day evaluation with varying levels of provocation

The fundamental effect of the robotic apparel was examined under the least challenging conditions based on single-task, medication on-phase and in-laboratory settings tested across four separate study visits (study visits 1-4). Based on these repeated assessments of walking with the assistance of the robotic apparel during the 2-min walking bout, we found an overwhelming elimination of FoG where 0% time spent freezing was observed in every testing instance (Fig. 2a and Supplementary Video 1). In contrast, walking without the assistance of the robotic apparel (either walking without wearing the robotic apparel or walking with robotic apparel unpowered) resulted in freezing episodes that averaged  $30 \pm 5\%$  time spent freezing. Furthermore, the robotic apparel had positive functional benefits where an improvement of 50% in total distance walked was observed relative to walking without the assistance of robotic apparel (143 m versus 96 m). Next, we examined the effects of the robotic apparel under more challenging conditions by altering cognitive loading (study visit 3) and medication timing (study visit 2)factors that sought to provoke FoG. Based on the dual-task condition during medication on-phase, walking with the robotic apparel averted FoG with 0% time spent freezing and enabled the participant to walk 115 m, which contrasted walking without the assistance of the robotic apparel with 44% time spent freezing and 75 m. Based on medication timing where we tested single-task conditions when dopaminergic medication wore off (known as relative off-phase), walking with the robotic apparel averted FoG with 0% time spent freezing and enabled the participant to walk 137 m, which contrasted walking without the assistance of the robotic apparel with 69% time spent freezing and 73 m (Supplementary Video 2). In summary, regardless of the condition, the assistance of the robotic apparel consistently and completely eliminated FoG (0%), whereas walking without the robotic apparel resulted in FoG that was present  $39 \pm 16\%$  of the time during the 2-min walking bout (Fig. 2a) (P = 0.03). Consequently, the robotic apparel enabled the study participant to walk substantially farther across all timed trials with an average improvement of 49 m (+55%) compared to walking without assistance (Fig. 2b) (P = 0.03) – a change that is considered to be clinically meaningful based on thresholds established for older adults<sup>49</sup> (12.2 m) and other neurological populations<sup>50</sup> (19.2 m). Altogether, these effects observed across all conditions were immediate without any prior training, in contrast to what is often observed with behavioral approaches<sup>18,19</sup>. Finally, as an exploratory procedure,



2-minute walk tests (2MWT) over multiple study visits

**Fig. 2** | **Effects of the robotic apparel based on repeated measurements.** Each study visit was conducted on a separate day. Summary bar plots are presented as mean  $\pm$  s.d., with asterisks indicating statistically significant differences (two-sided Wilcoxon signed-rank test; \**P* < 0.05). Baseline includes both NO SUIT and ASSIST OFF conditions. **a**, Comparison of walking with and without the assistance of the robotic apparel during the 2MWT based on the occurrence of freezing (*n* = 6 independent walking bouts for BASELINE and *n* = 6 independent walking bouts for ASSIST ON; P = 0.031), expressed as absolute duration (left y axis) and percent time spent freezing (right y axis). The stacked bar graph denotes segments of each freezing episode, as marked by horizontal lines. **b**, Corresponding effects on the walking distance covered during timed 2-min walking trials (n = 6 independent walking bouts for BASELINE and n = 6 independent walking bouts for ASSIST ON; P = 0.031).

instead of standard assistance (80 N of peak force), low assistance (20 N) was provided during walking. The participant was aware that the assistance was turned on, but the low assistance was unsuccessful in averting FoG, suggesting that the magnitude of assistance was crucial (Extended Data Fig. 2).

#### Immediacy of device effects

Furthermore, we conducted an experiment that scrutinized the immediacy of device effects to further establish causation of preventing FoG. We asked the participant to perform single-task walking during the medication on-phase with the robotic apparel that provided intermittent assistance (study visit 2) (Supplementary Video 3). This was achieved by serially toggling the assistance of the robotic apparel on and off through wireless commands at four equal 1-min intervals during a 4-min walk trial (Fig. 3a). The study participant was made aware every time there was a change in assistance. With the assistance turned on, FoG was immediately averted with 0% time spent freezing in all intervals of the walking trial (Fig. 3c). In contrast, with assistance turned off, FoG was present in three out of four intervals of the 4-min walk trial, ranging from 41% to 62% time spent freezing. In addition, the assistance of the robotic apparel was accompanied by significant increases in stride length compared to unassisted walking (Fig. 3b) (all P < 0.001). To rule out the potential influence of motor preparation from verbal prompts, we repeated the same procedure of intermittent assistance without verbal prompts on a different day (study visit 4). We replicated the same results, therefore confirming that the instantaneous elimination of FoG was device based and not due to verbal prompts (Extended Data Fig. 3). This intermittent assistance paradigm further validates our findings in that the onset of FoG was prevented during the 'robotic assistance' periods, in striking contrast to numerous FoG episodes observed when assistance was not applied.

#### Demonstrating its potential to be used in the community

On the bases of successful demonstration of averting FoG across all our laboratory-based experiments, we expanded our examination and explored its utility in outdoor, real-world environments (study visit 5) (Fig. 4a and Supplementary Video 4). We compared walking with and without the robotic apparel during a timed 6-min walking trial where the participant was asked to cover as much distance as possible walking back and forth on a 150-m straight and level sidewalk (Fig. 4b). This was performed in a community setting, where the path is shared with other pedestrians, and was performed in open space without immediate access to walls or railings for balance support. With the assistance of the robotic apparel, FoG was present 6% of the time during the timed walking trial (Fig. 4c and Supplementary Video 4). In contrast, without the assistance of the robotic apparel, we observed substantial FoG that was experienced 63% of the time during the walking trial. There was a corresponding substantial improvement in walking distance during the 6-min walking bout when walking with the assistance of the robotic apparel compared to without assistance (361 m versus 217 m), with a magnitude of change of 144 m in walking distance that is near threefold of minimal clinically important difference (MCID) established for older



**Fig. 3** | **Intermittent assistance test as direct validation on the immediate effects of the robotic apparel. a**, Time series data of applied hip flexion force (top) and participant's stride length (bottom). Sequential intervals of 30-s bouts without and with assistance were implemented across four intervals amounting to a total of 4 min of walking. Data during ASSIST OFF and ASSIST ON are plotted in gray and red, respectively, and the gray shaded regions indicate FoG episodes during ASSIST OFF. There was no FoG episode during ASSIST ON. **b**, Stride length per interval. Stride lengths in all intervals are presented in box plots (center line: median; box limits: upper and lower quartiles; whiskers: 1.5× interquartile range; points: outliers), and asterisks indicate statistically

significant differences (two-sided randomization test with a stride-level median as a test statistic; \*\*\*P < 0.001). Interval 1 (n = 33 independent strides for ASSIST OFF and n = 29 independent strides for ASSIST ON; P < 0.001); interval 2 (n = 33independent strides for ASSIST OFF and n = 29 independent strides for ASSIST ON; P < 0.001); interval 3 (n = 29 independent strides for ASSIST OFF and n = 27independent strides for ASSIST ON; P < 0.001); and interval 4 (n = 26 independent strides for ASSIST ON; P < 0.001); and interval 4 (n = 26 independent strides for ASSIST OFF and n = 29 independent strides for ASSIST ON; P < 0.001). **c**, Occurrence of freezing per interval based on duration (left y axis) and percent time spent freezing (right y axis).

adults<sup>\$1</sup> (50 m) (Fig. 4d). Although FoG was not completely eliminated during outdoor walking, as was demonstrated during indoor walking, the task complexity of outdoor walking based on longer walking duration (6 min in outdoor versus 2 min in indoor) and the presence of potential triggers that can induce FoG in an uncontrolled outdoor environment may account for the FoG. Nonetheless, the robotic apparel was capable of substantially averting FoG despite these provoking factors. Benefits can be optimized further by addressing other potential contributing factors, such as task novelty (that is, walking outdoors without an assistive device is not customary for the participant), by offering context-specific exposure with the device and accounting for change in ground surface by prescribing force magnitudes that are suitable for less smooth outdoor surfaces to enhance the swing phase and prevent FoG. Altogether, these results provide early demonstration of the versatility of robotic apparel that can be used across a range of environments.



**Fig. 4** | **Utility of robotic apparel in outdoor, community-based environments. a**, Experimental setup on the evaluation of the utility of the robotic apparel in community settings. **b**, Schematic map of walking course of 150-m straight, level sidewalk (marked in red). **c**, Occurrence of freezing during timed 6-min walking trials. **d**, Walking distance during timed 6-min walking trials.

#### Underlying biomechanical mechanisms of robotic apparel

To identify potential mechanisms underpinning the effects of robotic apparel, we examined biomechanics of walking. We obtained kinematic measurements of walking during a 10-m walk test at self-selected comfortable walking speed using a three-dimensional motion capture system and wearable sensors (study visit 1). With the assistance of the robotic apparel, we observed a direct effect on increasing hip range of motion (+21°) that is twice the range compared to unassisted walking, thus serving as direct validation that the device has a joint-targeting effect (Fig. 5a) (P < 0.001). Associated improvements were observed in step length (+29 cm), where increases were twofold relative to unassisted walking (Fig. 5b) (P < 0.001). Median cadences during assisted walking were better regulated at 100 steps per minute compared to an unusually high cadence of a median of 162 steps per minute during unassisted walking (Fig. 5c) (P < 0.001). Finally, there were complementary improvements in foot orientation based on substantial increases in foot-to-floor angle at heel strike (1.2° versus 21.1°) (Fig. 5d) and foot clearance during the swing phase of gait (19.3 cm versus 23.1 cm) (Fig. 5e) (all P < 0.001), with magnitudes similar to those observed in healthy individuals (foot-to-floor angle<sup>52</sup>:  $18.7 \pm 2.8^{\circ}$ ; maximal foot height<sup>53</sup>:  $24 \pm 2$  cm). Complementary video observations demonstrate sufficient toe and heel clearance without shuffling with the assistance of robotic apparel, which contrasts near toe dragging without assistance (Supplementary Video 5). Foot trajectory was improved in the vertical and fore-aft directions, allowing for enhanced foot clearance and longer steps (Fig. 5f). These improvements in gait quality translated to improvements in gait function based on increased walking speeds by an average improvement of 0.22 m s<sup>-1</sup>, which is a change that well exceeds the minimum clinical difference<sup>54</sup> of  $0.18 \text{ m s}^{-1}$  (Fig. 5g). Altogether, these findings demonstrate a fundamental change in gait quality independent of onset of a freezing episode.

To further examine the mediating role of gait quality on FoG. we tracked stride length and its variability over the course of a 2-min walking trial with and without the robotic apparel (study visits 1-4). Stride length was measured in real time using a gait metric estimation algorithm with foot IMUs<sup>55</sup>, and variability of stride length was calculated at post-processing. Extended Data Fig. 4 provides representative time series data of single-task walking during the medication on-phase, and Extended Data Fig. 5 shows the average stride length variability. Previous studies noted a step-to-step reduction in stride length that precedes the occurrence of  $FoG^{23,56}$ . Therefore, the current study examined the regression slope of stride length leading to the onset of FoG with and without the assistance of robotic apparel. Without assistance, stride length significantly deteriorated over time leading to FoG (P < 0.001). In contrast, with the assistance of the robotic apparel, stride length was held steady throughout the course, and no FoG was observed. Moreover, stride length was kept at a substantially higher magnitude compared to unassisted walking. Finally, there is marked reduction in variability of stride length on a stride-by-stride basis with the assistance of the robotic apparel across all conditions to an average of 6% in comparison to 31% when walking unassisted (P = 0.03), which suggests improved regularity in steps. Altogether, these findings on stride length and its variability demonstrate both gait-enhancing and gait-preserving effects of the robotic apparel that deter the onset of FoG. These results lend support to the perspective that FoG is a continuous gait disturbance<sup>29</sup> and that, by correcting fundamental issues with



**Fig. 5** | **Effects of hip flexion robotic apparel on gait biomechanics.** Gait quality (kinematics and spatiotemporal metrics) was examined during 10-m walk tests at a self-selected comfortable walking speed using a motion capture system and IMUs. All metrics, except walking speed, were measured on the more affected leg as a reference.  $\mathbf{a}$ - $\mathbf{e}$ , All metrics are presented in box plots (center line: median; box limits: upper and lower quartiles; whiskers:  $1.5 \times$  interquartile range; points: outliers), and asterisks indicate statistically significant differences (two-sided randomization test with a stride-level median as a test statistic; \*\*\*P < 0.001). **a**, Hip range of motion (n = 91 independent strides for ASSIST OFF and n = 46 independent strides for ASSIST OFF and n = 18 independent strides for ASSIST ON; P < 0.001). **c**, Cadence (n = 91 independent strides for ASSIST OFF and n = 46 independent

strides for ASSIST ON; P < 0.001). **d**, Foot-to-floor angle at initial ground contact (n = 35 independent strides for ASSIST OFF and n = 18 independent strides for ASSIST ON; P < 0.001). Positive values indicate heel strike, whereas negative values indicate forefoot landing. **e**, Foot clearance (n = 35 independent strides for ASSIST OFF and n = 18 independent strides for ASSIST OFF and n = 18 independent strides for ASSIST OFF and n = 18 independent strides for ASSIST OFF and n = 18 independent strides for ASSIST ON; P < 0.001). The foot clearance is defined as the maximal foot height during the swing phase relative to the height at foot-flat. **f**, Foot trajectory during the swing. Green dots indicate motion capture markers positioned at the toe and heel. The solid lines are the mean trajectories, and the shaded regions are standard deviations. **g**, Walking speed. Data are presented as mean  $\pm$  s.d. (n = 3 independent walking bouts for ASSIST ON). deg, degrees. MDC, minimal detectable change.

walking mechanics and rhythmicity, FoG can be averted. Finally, our results offer new data on the potential of biomechanical approaches in the form of external mechanical assistance in disrupting the onset of FoG, which sharply contrasts existing pharmacological, surgical and behavioral approaches (for example, cueing).

#### User experience

All procedures were completed without adverse events. The participant reported that the robotic apparel allowed him to lengthen his strides and reduce foot dragging, made his walking less effortful and ultimately prevented FoG. The participant expressed that the robotic apparel will be helpful in expanding his walking activities to different places outside of his house, and he would be interested in wearing it.

#### Discussion

This initial work prioritized rigorous testing with repeated measurements on a single participant to assemble potential evidence on the durability of device-related effects on FoG. Detailed and systematically conducted single-subject observations or *n*-of-1 trials, along the lines of the current study, have served as an important stage in the discovery of mechanisms of pathology and intervention in PD, as opined by Bloem et al.<sup>38</sup>. The relevance of this consideration becomes more meaningful in developing new interventions for FoG, in light of the clinical and methodological challenges in examining FoG<sup>57</sup>. In this study, we leveraged the use of wearable sensors to objectively demonstrate the timely coupling of device-related therapeutic effects with FoG across a range of conditions and environments. The use of wearable sensors not only allowed for quantifying the severity of FoG episodes based on time and occurrence but also offered spatiotemporal measurements of walking that can be used to understand the underlying motor control mechanisms of FoG.

The promising findings prompt further investigation to validate the effects of the robotic apparel on a broader range of individuals with PD experiencing FoG and across various FoG phenotypes, environment contexts and task contexts, complemented with FoG metrics that include quantification of severity of freezing episodes (for example, FoG ratio<sup>47,48,57</sup>). Although hip flexion assistance was effective for the participant in this study, tuning assistance across joints may better accommodate the specific gait features of different patients with PD. Additionally, we designed the controller for the robotic apparel to deliver assistance during straight-ahead walking. Because FoG can occur during other subtasks of gait, such as gait initiation and turning, advancements to the technology (for example, manually triggered or sensor-based assistance) are necessary to encompass a full range of walking contexts to accommodate typical everyday mobility. Furthermore, the assistance was continuously on in this study, but, in the future, it would be interesting to investigate assistance that is only turned on, or increased, in response to a downward cascade of step length or real-time prediction of FoG<sup>58,59</sup>. This approach may need to be tuned on an individual basis (and some individuals may need continuous assistance), but there could be benefits to comfort and battery life. Finally, it is also possible that training with the robotic apparel may be beneficial, as examined by technology-augmented interventions in PD<sup>60-62</sup>. Exploration of this can occur through the successive stages of strategic piloting of robotic clinical trials<sup>39</sup>.

In this work, we demonstrated an early proof of concept of the potential of soft robotic apparel in averting freezing through a robust response of a participant with PD with substantial FoG. By providing a relatively moderate level of hip flexion assistance during the swing phase of walking, the robotic apparel delivered instantaneous effects of averting FoG and provided enhancements in walking quality and function that are durable across a range of conditions. The robustness of these early findings based on immediate, repeatable and clinically meaningful outcomes that improve gait quality, improve walking function and ultimately avert FoG offers new directions for innovation in FoG interventions. Given that there are no clear solutions capable of averting FoG, this study marks an important juncture in advancing technology-based solutions for FoG.

#### **Online content**

Any methods, additional references, Nature Portfolio reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41591-023-02731-8.

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#### Methods

All experiments and study protocol were approved by the Harvard Longwood Campus Institutional Review Board. The participant provided written informed consent before study procedures, including consent to photo/video recording with blurred face for publication. Study recruitment was based on convenience sampling. Sex or gender was not considered in the design due to the *n*-of-1 nature of the study and the absence of known sex-specific differences in FoG prevalence<sup>68</sup>. Modest participant remuneration was provided per visit to cover for transportation and other related expenses. Additionally, all researchers included in the figures and videos provided consent to have their faces unblurred in the paper.

#### Study flow

At study entry, we verified eligibility through a cognitive screen using the Mini-Mental State Exam<sup>64</sup> (exclude <23 out of 30 points), functional mobility (exclude if requires physical assistance during walking) and a review of medical history and PD diagnosis (exclude if no diagnosis of idiopathic PD). We obtained demographic information (age and sex) based on self-reports; baseline characteristics, including PD-specific motor and non-motor features, using the Unified Parkinson's Disease Rating Scale<sup>66</sup> (UPDRS) Parts I–IV; self-reported FoG based on the New Freezing of Gait Questionnaire<sup>67</sup> (NFoG); and perceived balance self-efficacy using the Activities-specific Balance Confidence (ABC) Scale<sup>65</sup>. Once enrolled, the participant underwent a protocol comprising five study visits from November 2021 to May 2022.

#### Main protocol

2MWT during medication on-phase under single-task conditions (study visits 1-4). We performed repeated examinations across four separate occasions (study visits 1-4) using the 2MWT as the basis to examine the effects of the robotic apparel on averting FoG. These examinations were performed during medication on-phase and under single-task conditions. The 2MWT was administered by having the participant walk at a fast speed on a straight indoor walkway, safely, without physical assistance for 2 min, with the following instructions: 'Cover as much distance as possible over 2 minutes'. The 90-m walkway was marked by two cones on opposite ends, where wide U-turns were performed as the participant walked back and forth. The total distance traveled was measured by a handheld measuring wheel. For every study visit, the 2MWT was performed with the robotic apparel (ASSIST ON) and without the robotic apparel (ASSIST OFF or NO SUIT) administered in random order. During NO SUIT trials, the participant wore IMUs and a small data logger (910 g) for data collection. Standardized rest periods of 2-10 min were provided between trials to account for fatigue (Extended Data Fig. 1).

#### Additional protocols on designated FoG triggers Dual-tasking performed during 2MWT during medication on-phase

(study visit 3). To determine the effect of the robotic apparel under increased cognitive challenge, we administered the 2MWT under dual-task conditions. Dual-tasking refers to the simultaneous performance of primary and secondary tasks, designed to introduce task interference; it can, thus, increase the likelihood of eliciting FoG. This test was performed on study visit 3 during the medication on-phase under ASSIST ON and NO SUIT. The primary motor task was walking, and the secondary cognitive task involved the Oral Trail Making Test B (ref. 69), accomplished by reciting alternate numbers and letters in ascending order. We instructed the participant to: 'Cover as much distance as you can, and simultaneously recite as many numbers and letters as you can for 2 minutes in forward order'. For each dual-task trial, we asked the participant to start counting from 1-A (instead of a different combination of numbers and letters). If the participant reached 26-Z during the 2-min duration, he was asked to restart from 1-A. In the event of errors, the examiner provided the correct number or letter to reorient the participant. We recorded the total number of counts for each dual-task trial.

Medication off performed during 2MWT under single-task conditions (study visit 2). The 2MWT was performed during a relative medication off-phase, operationalized in this study as the period when medication was wearing off in the last 15 min before the next scheduled medication dose. All procedures were performed within a single session (study visit 2) and performed under single-task conditions. We examined the effects of robotic apparel by testing without the assistance of the robotic apparel (ASSIST OFF) followed by the assistance of the robotic apparel (ASSIST ON) (Extended Data Fig. 1). A true medication off-phase (that is, no medication for at least 12 h) was not implemented to minimize alteration in medication schedule, which may impact safe transport to and from our laboratory.

**Outdoor walking performed during 6MWT during medication on-phase under single-task conditions (study visit 5).** To examine the effects of robotic apparel in outdoor, real-world environments, we administered a 6MWT in outdoor community settings during the medication on-phase and under single-task conditions. The participant performed the 6MWT under NO SUIT condition followed by ASSIST ON (Extended Data Fig. 1), separated by a 15-min seated break. The testing site was on a public, paved sidewalk around the Harvard campus, where the path was shared with other pedestrians. No immediate access to walls or rails for balance support was available. The participant was asked to cover as much distance as possible along a 150-m straight and level sidewalk marked by two cones at opposite ends. Wide U-turns around each cone were performed as the participant walked back and forth in the walkway. The total distance walked was measured using a handheld measuring wheel.

## Additional protocols to identify the immediacy and biomechanical analysis of device effects

Intermittent assistance test during medication on-phase under single-task conditions (study visits 2 and 4). We evaluated the immediacy of device effects by providing intermittent assistance of the robotic apparel during a timed 4-min walking trial, administered similarly to a 2MWT, as described previously. This test was performed during the medication on-phase and under single-task conditions during study visit 2 (Extended Data Fig. 1). The following instructions were provided: 'Cover as much distance as you can for 4 minutes. The assistance will be on and off periodically. Walk continuously without pauses or breaks as much as you can'. Walking back and forth on a 90-m clear walkway, the assistance of the robotic apparel alternated between ASSIST ON and ASSIST OFF every 30 s, implemented wirelessly through Bluetooth commands from a host laptop. Verbal prompts were provided 5 s before the assistance mode change.

To minimize possible confounding effects of motor preparation related to verbal prompts during transitions, we repeated the intermittent assistance test as performed in study visit 2 on another testing day on study visit 4 (Extended Data Fig. 1) without verbal prompts. All procedures were identical between study visits, except that study visit 4 implemented a timed 3-min walking trial (versus 4-minute walk test (4MWT)) and that the starting condition was ASSIST ON (versus ASSIST OFF).

Gait biomechanics assessment during 10-m walk test during medication on-phase under single-task conditions (study visit 1). To examine biomechanical changes related to the assistance of the robotic apparel, we administered the 10-m walk test using a 29-camera Qualisys Oqus motion capture system, Qualisys Track Manager software (version 2021) and wearable sensors (MTi-3 AHRS, Xsens). The participant was tested during ASSIST ON and ASSIST OFF conditions, administered three times per condition in random order (Extended Data Fig. 1). These tests were performed during the medication on-phase and under single-task conditions. The 10-m walk test was administered by having the participant walk on a 14-m straight walkway at a comfortable walking speed. The middle 10 m was used for biomechanical analysis (that is, without gait initiation and termination). Walking kinematics were obtained through the three-dimensional position of reflective markers on bilateral heels, toes and sacrum. We calculated step length, cadence and foot trajectory (including foot-to-floor angle and foot clearance) from motion capture data and hip joint excursions in the sagittal plane from thigh IMUs.

#### Exploratory procedure to examine the effects of force levels

Low assistance trial during 2MWT during medication on-phase under single-task conditions (study visit 3). To explore the effects of force levels, the robotic apparel delivered substantially lower amounts of force (Low ASSIST), defined as the lowest force magnitude that is perceivable to the user. Set at 20 N (instead of 80 N as with the rest of the testing), the 2MWT was performed. The onset, peak and offset timings of the low assistance were kept consistent with those of the standard assistance. This test on low assistance served as an add-on during study visit 3, thus allowing for direct comparisons with ASSIST OFF and ASSIST ON that occurred on the same day. The conditions were administered in the following order: ASSIST OFF, Low ASSIST and ASSIST ON.

#### Data collection during timed walking trials

During study visits, a physical therapist walked next to the participant for general safety and to monitor elapsed time using a stopwatch. Other researchers were involved in video recording, measuring walking distance with a measuring wheel and managing controls of the robotic apparel and associated data collection. We measured stride length, stride time and stride speed using a real-time gait metrics estimation algorithm with foot IMUs<sup>55</sup>. This stride time was further verified by measuring the elapsed time between consecutive maximum hip extensions (MHE)<sup>70</sup>. We also measured shank and foot angular velocities in the sagittal plane for FoG assessment.

#### Soft robotic apparel

**Textiles.** We designed the soft robotic apparel to assist hip flexion by slightly modifying a previous, portable hip exosuit<sup>40,70</sup>. The textile components of the robotic apparel consist of a waist belt, two thigh wraps and suspension shoulder straps. Two Fabrifoam calf wraps were additionally needed to attach shank IMUs for FoG assessment at post-processing, but they were not necessary parts of the system. We constructed the waist belt and thigh wraps using layers of inextensible, abrasion-resistant plain-weave textile and lightweight custom sailcloth material. We mounted the actuators onto the front of the waist belt using 3D-printed plastic parts and fastened electronics onto the back of waist belt using Velcro straps. Fit of waist belt and thigh wraps was adjusted using Velcro fastener, laces and a tensioning dial (L4, Boa Technology). The suspension shoulder straps additionally prevented the waist belt with actuators and electronics from sliding down, especially for the wearer with a large abdomen. Both ends of the suspension shoulder straps were connected to the back of the waist belt and the actuator housing to minimize the actuator's rocking motion in the sagittal plane when applying a high magnitude of assistance. This robotic apparel is designed to be user-friendly, featuring only one on/ off switch, and the donning/doffing process takes only about 5-10 min.

Actuator and sensors. We used a miniature rope winch design to generate the hip flexion moment<sup>40</sup>. Two winches were mounted onto the front of the waist, and each of them contained a motor (U5, T-MOTOR), an encoder (AS5145B, AMS; 4,096 counts per revolution) and a Dyneema rope (P/N KL0200, Marlow; 1.8-mm diameter) spanning the length of the thigh. One end of the Dyneema rope was attached to the motor, and the other end was attached to the thigh wrap via a metal buckle (COBRA FM. AustriAlpin). We used a fabric rope cover as protective sheath to cover the entire Dyneema rope. The actuator transmitted torque to a cylindrical drum (4.5-mm diameter) to spool in Dyneema rope and generate an external flexion moment around the hip joint. The hip flexion profile in Fig. 1c delivered approximately 10 W of mechanical power to the user  $^{\!\!\!\!\!\!\!\!\!\!\!\!\!^{40}}$  . Taking into account the energy loss caused by joule heating and friction, the device allowed for 3 h of continuous walking with assistance. The electronics contained a custom-made electronics board using a microprocessor (ATSAME70N21, Atmel), a motor driver (Gold Twitter, Elmo Motion Control) and two lithium-ion batteries (RRC2054, RRC Power Solutions). Two load cells (LSB200, FUTEK) were integrated into the thigh wrap to measure the tensile force on the rope, and two IMUs (MTi-3 AHRS, Xsens) were attached to the anterior part of the thigh wrap to measure thigh segment angle. Additionally, four IMUs were placed at the foot and shank on each leg for stride length measurement and FoG assessment, but they were not necessary parts of the system. The entire robotic apparel is lightweight (2.31 kg), and most of its weight concentrates on the waist (1.87 kg on the waist and 0.22 kg on each thigh). The low torque and small power requirements, along with the lightweight nature of the soft robotic apparel, highlight its practicality for use in a real-world, community setting.

During the NO SUIT trial, the participant wore only IMUs, data logger and its associated textile components for attachment. The data logger consists of a custom-made electronics board using a microprocessor and a small power bank without any actuator components.

Controls. We designed the controller to deliver a consistent hip flexion force profile on each leg during the gait cycle. The high-level controller uses an IMU-based iterative algorithm that detects the MHE in every stride by identifying the sign change in thigh angular velocity and estimates the gait cycle based on the most recent three stride times. This gait cycle is further divided into assisted and non-assisted phases. During the assisted phase, a force controller applies a hip flexion force profile with desired onset, peak, offset timings and peak force magnitude. The assistance began at MHE, just before toe-off, and was then held throughout the swing phase of the gait cycle (Fig. 1c). It reached 80-N peak force magnitude (approximately 9.7-Nm peak hip flexion torque) at 17.9% after the MHE and ended at 38.6% after the MHE. We used prior pre-clinical work on human-in-the-loop optimization of hip flexion assistance<sup>40</sup> as the basis for the assistance profile, and a peak force of 80 N is within range of forces capable of inducing benefits on mobility. User comfort on force levels was verified through participant input within the initial 20 min of study visit 1 and confirmed that force levels were not excessive or destabilizing. We kept this assistance profile for all study visits. During the non-assisted phase, a position controller pushes the rope out in order not to disturb the wearer's limb motion and updates the rope position on a step-by-step basis to reach the desired pretension force just before switching back to the force controller. While the high-level control switches between force and position controllers, a low-level proportional-integral control is continuously used in a servo motor driver operating in a torque control mode. The high-level and low-level controllers were implemented in the standard Clanguage (Visual Studio Code version 1.62, Microsoft), and the graphical user interface and real-time data visualization were developed using Python (version 2.7) and KST Plot (version 2.0.8). The control of the robotic apparel presented here relies on the motion of each leg independently, enabling future extensions to update and adjust the assistance profile as needed. This includes improving symmetry for walkers with irregular or asymmetrical gait patterns commonly seen in PD.

It is important to note that, once FoG occurred, the actuation cable remained slack, and the robotic apparel did not take any action to overcome FoG. The assistance was reactivated when the participant initiated an initial, regular step on his own.

#### Biomechanical data post-processing

We detected foot strike and its lift-off from peak anterior and posterior excursions of heel marker, respectively<sup>71</sup>. We calculated the step length as a horizontal distance between heel markers at each foot strike. We calculated the step time as the time between successive foot strikes. Cadence was derived as an inverse of step time. Walking speed was calculated using the traveled distance of the sacrum marker divided by the time spent in the walking bout. Motion capture-derived spatiotemporal measurements are more accurate than those from the gait metrics estimation algorithm<sup>55</sup>, as they are free from the integration drift error. To examine foot strike angle, we calculated the foot-to-floor angle as an inverse sine of the ratio of altitude difference between the toe and heel markers to the distance between the two markers at the foot strike. We calculated the foot clearance as the maximal vertical position of the heel marker during the swing phase relative to its height at the foot flat. Additionally, we used IMUs to measure the hip range of motion. The IMU-based iterative algorithm detected the maximum hip flexion (MHF) and MHE by identifying the sign change of thigh angular velocity in the sagittal plane<sup>70</sup>. Hip range of motion was calculated using thigh angle difference between MHF and MHE.

#### **FoG identification**

To quantify FoG, we employed a multi-step approach. Initially, two licensed physical therapists trained in Parkinson rehabilitation reviewed videos to identify FoG episodes. Video confirmation served as ground truth, aligning with the perspectives presented by researchers in the field<sup>41,43,44</sup>. Subsequently, time-synchronized wearable sensor data were used to precisely determine the onset and offset timings of the identified FoG episodes. These timings were then verified and confirmed by the physical therapists. Therefore, IMU-based measurements were used to complement the clinician's video-based assessments rather than solely identifying FoG episodes from scratch. Finally, we reported the percentage of time spent in freezing<sup>41</sup> for each walking bout, calculated by dividing the cumulative duration of freezing episodes by the total duration of the walking task. The following section provides further description of the IMU-based algorithm to quantify FoG episodes.

We used IMUs to extract the different patterns of FoG<sup>7</sup> during post-processing, which included the absence of limb movement, trembling in place (alternating tremor of the legs) and shuffling forward (very short, shuffling steps). First, we analyzed shank angular velocity in the sagittal plane<sup>72</sup> to identify the absence of limb movement. This involved detecting the start and end of the swing phase (positive and subsequent negative slope zero crossings) and capturing the peak shank angular velocities during swing (first positive peak after the start of the swing phase). Peaks were considered as steps only if they exceeded a minimum threshold of 30 degrees per second. Subsequently, we identified the lack of forward leg movement when the peaks fell below this threshold or when the time between consecutive peaks exceeded 2 s. Second, we analyzed the foot angular velocity in the sagittal plane to identify rapid movements of the limbs (for example, trembling in place or shuffling forward) within the frequency range of 3-8 Hz<sup>7,45-48</sup>. We detected the toe-off of the ipsilateral leg (negative peak) and the subsequent foot-flat instance of the contralateral leg (positive slope zero crossing after the negative peak)<sup>55</sup>. From these measurements, we calculated stride times as the duration between consecutive foot-flats. Strides were marked as rapid limb movements if their corresponding stride times were below 0.67 s (equivalent to three steps per second or 3 Hz). Finally, we merged different patterns of FoG into a single FoG episode if they immediately followed one another. The approach used is unable to differentiate voluntary versus involuntary stops, especially those induced by dual-task challenges. In such events, we relied on clinician input to confirm FoG episodes. These methodological challenges can be extenuated with more expansive FoG metrics<sup>57</sup> for future studies.

In this study, the controller of the robotic apparel was designed to assist straight-ahead walking but was not optimized for turning. Consequently, when the participant made a wide U-turn at the end of the walkway under the ASSIST ON condition, although most steps were assisted, some steps were missed due to the lack of a specific turning algorithm. In such cases, the corresponding turning portion was excluded from the data analysis, which accounted for 2.9% of the total time during all ASSIST ON trials (Extended Data Table 1).

#### **Gait metrics estimation**

The spatiotemporal gait parameters were measured in real time using a gait metric estimation algorithm with foot IMUs<sup>55</sup>. To measure the stride length, the algorithm double-integrated linear accelerations of the foot IMU in the horizontal plane and corrected sensor drift with a zero-velocity update at the contralateral toe-off. In addition, the algorithm measured stride time as the time between consecutive toe-offs from the same leg. Finally, stride speed was calculated as the stride length divided by the stride time.

#### Statistics

Data analysis and visualization were performed using MATLAB (version R2021a, MathWorks). We conducted statistical analyses of single-participant data as has been implemented in single-subject studies in motor control and biomechanical studies, based on the premise of within-subject variability<sup>73,74</sup>. For 2MWT (Fig. 2 and Extended Data Fig. 5), we used descriptive statistics on the percent time spent in freezing, walking distance and the coefficient of variance of the stride length, with central tendencies reported as mean ± s.d. To compare ASSIST ON versus ASSIST OFF/NO SUIT, we ran two-sided Wilcoxon signed-rank tests. To evaluate the step-to-step trajectory slope of stride length leading to the onset of FoG, we used linear regression on the time series data (Extended Data Fig. 4). The normality of data for linear regression was verified using the Kolmogorov-Smirnov test. For the intermittent assistance tests in Fig. 3 and Extended Data Fig. 3, we reported stride length for each condition at each interval using median and interguartile range. To compare differences between conditions (ASSIST ON and ASSIST OFF) at each 1-min interval, we used a two-sided randomization test<sup>75</sup> (with a stride-level median as a test statistic). For the 10-m walk test in Fig. 5, we measured biomechanical parameters at the stride level and merged three walking bouts data for each condition (ASSIST ON and ASSIST OFF) into one box plot. To compare differences between the two conditions, we used a two-sided randomization test (with a stride-level median as a test statistic).

#### **Reporting summary**

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

#### **Data availability**

All study data necessary to interpret, verify and extend this work are available in the Source Data section. This includes data for Figs. 1–5 and Extended Data Figs. 2–5. Source data are provided with this paper.

#### **Code availability**

The controls for robotic apparel were adapted from Kim et al. $^{40,70}$ , and the IMU-based real-time gait metric estimation algorithm was adapted from Arens et al. $^{55}$ .

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#### **Author contributions**

J.K., F.P., T.D.E. and C.J.W. conceived of the study concept and designed the research. J.K. implemented the control and hardware of the robotic apparel. J.K., H.D.Y., N.W., T.B. and A.C. conducted the

experiments. J.K. processed and analyzed the experimental data. J.K., F.P., T.D.E. and C.J.W. prepared and revised the paper. All authors reviewed and approved the final manuscript.

#### **Competing interests**

Patents describing the robotic apparel components documented in this article have been filed with the US Patent Office by Harvard University. C.J.W. is an inventor on the following patents and patent applications: US 9,351,900, US 10,278,883, US 14/660,704, US 15/097,744 and US 14/893,934. Harvard University has entered into a licensing agreement with ReWalk Robotics. C.J.W. was previously a paid consultant for ReWalk Robotics. The other authors declare no competing interests.

#### **Additional information**

**Extended data** is available for this paper at https://doi.org/10.1038/s41591-023-02731-8.

**Supplementary information** The online version contains supplementary material available at https://doi.org/10.1038/s41591-023-02731-8.

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**Extended Data Fig. 1** | **Study flow and protocol overview.** Summary schematic of five study visits. For each study visit, timed walking trials under single-task conditions during medication on-phase were performed (middle column in Study Visits 1-5). Additionally, conditions that further provoked FoG were administered based on medication timing (Study Visit 2), cognitive loading using

dual-task challenge (Study Visit 3), and outdoor walking (Study Visit 5). The study also included conditions examining the immediacy of device effects through intermittent assistance (Study Visit 2 and 4), the underlying biomechanical mechanisms (Study Visit 1), and the effects of force levels when providing low assistance (Study Visit 3).



**Extended Data Fig. 2** | **Effects of force levels. a**, Occurrence of freezing during timed 2-minute walking trials. **b**, Walking distance during timed 2-minute walking trials. All trials were conducted in the laboratory during the medication on-phase

and under single-task conditions (Study Visit 3). A peak force of 80 N was applied during ASSIST ON, while a peak force of 20 N was applied during Low ASSIST. Data for ASSIST OFF and ASSIST ON were previously included in Fig. 2.



Extended Data Fig. 3 | Intermittent assistance without verbal prompts. a, Time series data of applied hip flexion force (top) and participant's stride length (bottom). Sequential intervals of 30-s bouts with and without assistance were implemented across three intervals amounting to a total of 3 min of walking. Different from Fig. 3, the operator did not give any verbal notice of the assistance mode change to the participant. Data during ASSIST ON and ASSIST OFF are plotted in red and gray, respectively, and the gray shaded regions indicate FoG episodes during ASSIST OFF. There was no FoG episode during ASSIST ON. b, Stride length per interval. Stride lengths in all intervals are presented in box plots (center line: median; box limits: upper and lower quartiles; whiskers:

1.5× interquartile range; points: outliers), and asterisks indicate statistically significant differences (two-sided randomization test with a stride-level median as a test statistic; \*\*\*P < 0.001). Interval 1 (n=26 independent strides for ASSIST ON and n=32 independent strides for ASSIST OFF; P < 0.001), interval 2 (n=29 independent strides for ASSIST ON and n=31 independent strides for ASSIST OFF; P < 0.001), and interval 3 (n=26 independent strides for ASSIST ON and n=19 independent strides for ASSIST OFF; P < 0.001). **c**, Occurrence of freezing per interval based on duration (left y axis) and percent time spent freezing (right y axis).



**Extended Data Fig. 4** | **Preserved regulation of stride length: A potential reason for the effects of the robotic apparel.** Stride length over time during timed 2-minute walking trials. The linear regression slope of stride length leading to the onset of FoG was examined. **a**, ASSIST OFF vs. ASSIST ON (Study Visit 1). Markers in light gray and red are for ASSIST OFF and ASSIST ON, respectively. The shaded regions in light gray indicate FoG episodes during ASSIST OFF (Linear regression:  $y = -4.65 \cdot 10^{-3} \times time + 1.15$ , n = 48 independent strides; a two-sided,

one-sample *t*-test for the slope,  $P = 3.08 \cdot 10^{-12}$ , t = -9.37, df = 46). There was no FoG episode during ASSIST ON. **b**, NO SUIT vs. ASSIST ON (Study Visit 4). Markers in dark gray and red are for NO SUIT and ASSIST ON, respectively. The shaded regions in dark gray indicate FoG episodes during NO SUIT (Linear regression:  $y = -3.42 \cdot 10^{-3} \times time + 1.09$ , n = 66 independent strides; a two-sided, one-sample *t*-test for the slope,  $P = 2.45 \cdot 10^{-16}$ , t = -10.97, df = 64). There was no FoG episode during ASSIST ON.



2-minute walk tests (2 MWT) over multiple study visits

**Extended Data Fig. 5** | **Variability of stride length: A potential reason for the effects of the robotic apparel.** Stride length arrhythmicity during timed 2-minute walking trials (n = 6 independent walking bouts for BASELINE and n = 6 independent walking bouts for ASSIST ON; P = 0.031). Each study visit was conducted on a separate day. A summary bar plot is presented as mean  $\pm$  s.d., with

an asterisk indicating a statistically significant difference (two-sided Wilcoxon signed-rank test; \*P < 0.05). Baseline includes both NO SUIT and ASSIST OFF conditions. The coefficient of variance (in stride length) was measured as the ratio of the standard deviation to the mean.

#### Extended Data Table 1 | Duration of turns and excluded strides in the timed walking trials

		ASSIST OFF or NO SUIT		ASSIST ON			
		The number of turns	Total duration of turns (s)	Total duration of excluded strides (s)	The number of turns	Total duration of turns (s)	Total duration of excluded strides (s)
	Study Visit 1	0	N/A	N/A	1	4	0
	Study Visit 2 (Med-ON)	1	9	N/A	1	4	0
2-Minute	Study Visit 3 (Single-Task)	0	N/A	N/A	1	29	29*
Walk Test	Study Visit 4	1	11	N/A	1	2	0
	Study Visit 3 (Dual-Task)	0	N/A	N/A	1	3.5	0
	Study Visit 2 (Med-OFF)	0	N/A	N/A	1	5	2
Intermittent	Study Visit 2	1	8	N/A	1	2.5	0
Assistance	Study Visit 3	0	N/A	N/A	1	2.5	0
6-Minute Walk Test	Study Visit 5	1	13	N/A	2	7	6

\*The participant did not take an initial, regular step right after a stop, and, thus, assistance was not reactivated until a later time.

## nature portfolio

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		Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.

#### Software and code

Policy information about availability of computer code

Data collection Data collection was performed using GNU Compiler (GCC) Arm Embedded Toolchain version 5, Visual Studio Code version 1.62 (with C language), CMake version v3.21.1, Python version 2.7, PyKst, Kst Plot Version 2.0.8, Qualisys Track Manager (QTM) version 2021, and IMU-based real-time gait metric estimation (Arens et al., 2021). Controls for robotic apparel were adapted from (Kim et al., 2022; Kim et al., 2019).

#### Data analysis Data was processed and analyzed using Matlab version R2021a.

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All study data necessary to interpret, verify, and extend this work are available in the Source Data section. This includes data for Figures 1-5 and Extended Data Figures 2-5.

#### Research involving human participants, their data, or biological material

Policy information about studies with <u>human participants or human data</u>. See also policy information about <u>sex, gender (identity/presentation)</u>, <u>and sexual orientation</u> and <u>race, ethnicity and racism</u>.

Reporting on sex and gender	This initial work prioritized rigorous testing with repeated measurements on a single participant as a consideration-of- concept study to assemble potential evidence on the durability of device-related effects on freezing of gait. Given the nature of the single-subject study, and that there are no sex-related differences in FOG prevalence, sex was not considered in the study design. We did not make any claims or findings regarding sex.
Reporting on race, ethnicity, or other socially relevant groupings	Due to the nature of single-subject case study, race and ethnicity was not considered in the study design. Therefore, no claims or findings were made regarding race or ethnicity.
Population characteristics	The participant was a 73-year-old male (173cm, 93.5kg) with Parkinson's Disease (PD) of 10 years (Hoehn & Yahr stage: 2, MDS-UPDRS Part III motor examination: 33/132, New Freezing of Gait Questionnaire: 19/28). He underwent deep brain stimulation surgery to the globus pallidus internus 5 years following diagnosis, and the stimulator is constantly turned on throughout the day. Pharmacologic management included 1.5 tablets of 25-100 mg carbidopa/levodopa taken 4 times per day, amantadine twice per day, and entacapone taken 4 times per day. Despite surgical and pharmacologic management in addition to implementing behavioral strategies, the participant endured substantial, incapacitating freezing of gait (FoG), where he experienced numerous freezing episodes (>10/day) with associated daily falls.
Recruitment	General recruitment procedures involved utilization of registries maintained by various institutions in the Greater Boston Area, study flyers, and in-person recruitment efforts. The participant contacted the study team with his interest in participating after hearing about the study from a local Parkinson support group. Our inclusion criteria included individuals with idiopathic Parkinson's disease, with ages of 18-75 years, have trouble walking due to FoG but able to walk at least 20 meters independently. Data from a single participant may limit generalization to other FoG phenotypes, thus warranting future larger studies.
Ethics oversight	All study procedures were approved by Harvard Longwood Campus Institutional Review Board (IRB15-1816) and conducted according to the Declaration of Helsinki.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

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## Life sciences study design

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Sample size	This initial work prioritized rigorous testing with repeated measurements on a single participant (N=1) as a consideration-of-concept study to assemble potential evidence on the durability of device-related effects on FoG. A sample size of a single participant with repeated measurements and varying levels of provocation was sufficient to examine the device's feasibility. The promising findings of this consideration-of-concept trial prompt further investigation to validate the effects of the robotic apparel on a broader range of individuals with PD with FoG and across a range of FoG phenotypes.
Data exclusions	In this study, the controller of the robotic apparel was designed to assist straight-ahead walking but was not optimized for turning. Consequently, when the participant made a wide U-turn at the end of the walkway under ASSIST ON condition, while most steps were assisted, some steps were missed due to the lack of a specific turning algorithm. In such cases, the corresponding turning portion was excluded from the data analysis, which accounted for 2.9% of the total time during all ASSIST ON trials. This exclusion criterion was pre- established.
Replication	The repeated measurements comprising of 5 study visits across 6 months served as replication of the experimental effects. All attempts at replication were successful, notably 0% time spent freezing for all indoor walking trials. We have made the experimental data available and provided all materials and methods used to replicate the results.
Randomization	Randomization related to intervention group does not apply to our study design. Based on study procedures, all experimental conditions (i.e., walking with assistance vs. walking with assistance turned off vs. without wearing the robotic apparel) were in a randomized order.
Blinding	This single-subject study was performed without any group allocation, so the blinding was not relevant to the study. Furthermore, due to the inherent nature of the wearable robotics study, we couldn't blind a study participant to his testing conditions (i.e. walking with assistance vs. walking with assistance turned off vs. without wearing the robotic apparel).

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