NEUROREHABILITATION

A multidirectional gravity-assist algorithm that enhances locomotor control in patients with stroke or spinal cord injury

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Gait recovery after neurological disorders requires remastering the interplay between body mechanics and gravitational forces. Despite the importance of gravity-dependent gait interactions and active participation for promoting this learning, these essential components of gait rehabilitation have received comparatively little attention. To address these issues, we developed an adaptive algorithm that personalizes multidirectional forces applied to the trunk based on patient-specific motor deficits. Implementation of this algorithm in a robotic interface reestablished gait dynamics during highly participative locomotion within a large and safe environment. This multidirectional gravity-assist enabled natural walking in nonambulatory individuals with spinal cord injury or stroke and enhanced skilled locomotor control in the less-impaired subjects. A 1-hour training session with multidirectional gravity-assist improved locomotor performance tested without robotic assistance immediately after training, whereas walking the same distance on a treadmill did not ameliorate gait. These results highlight the importance of precise trunk support to deliver gait rehabilitation protocols and establish a practical framework to apply these concepts in clinical routine.

INTRODUCTION

Terrestrial locomotion is inherently contingent on gravity (*1*). Although gravity challenges equilibrium at each step, the gravitational forces acting upon body mechanics enable the generation of ground reaction forces (GRFs) that propel the body forward (*2*, *3*). The bipedal posture of humans exacerbates the beneficial impact of gravity on gait dynamics (*3*–*7*). The elevated center of mass (CoM) allows the human body to vault up and over the stance leg analogous to an inverted pendulum (*6*), whereas the contralateral leg performs a near-ballistic oscillation (*8*).

The apparent simplicity of the inverted pendulum-like gait behavior conceals sophisticated neurological control mechanisms (*9*, *10*), which require several years of neural development to become mature (*11*). However, locomotor impairments resulting from neurological insults such as spinal cord injury (SCI) and stroke remind us of the instability of human gait and the complexity of its neural control. Neurologically impaired individuals must exploit residual neural circuits to regain strength, precision, and balance to remaster the delicate interplay between body mechanics and gravitational forces.

Partial body weight–supported gait therapy is the most common medical practice to facilitate this process (*12*, *13*). Robotic engineering has developed various types of body weight support systems. The most common solutions include passive springs, counterweight mechanisms, or force-controlled apparatus that deliver upward trunk support during stepping on a treadmill. These approaches suffer from several drawbacks. First, treadmill belt motion dictates the locomotor pace, imposing challenging conditions for neurologically impaired individuals who exhibit variable gait patterns (*14*). Second, treadmill-restricted environments markedly differ from the rich repertoire of natural locomotor activities underlying daily living. Task-specific rehabilitation is essential to maximize gait recovery (*15*, *16*). Third, vertically restricted trunk support creates undesired forces that impede gait execution (*17*–*19*). Fourth, overground rehabilitation triggers more active participation than treadmill-restricted training, which is critical for steering neural circuit reorganization after neurological disorders (*20*).

We previously developed robotic systems for mice (*21*) and rats (*22*) that addressed these issues. These suspension devices integrate soft actuation mechanisms that allow the application of multidirectional forces to the trunk while the rodents are progressing freely within a large workspace. These robot systems enabled skilled locomotion in rodents with SCI or stroke (*22*–*24*) and maximized activity-dependent neural circuit reorganization during rehabilitation (*20*, *23*). To establish a similar gait rehabilitation platform for humans, we used a robotic system that allows fine adjustment of forces applied to the trunk along the three Cartesian directions (*25*). The quadrupedal posture of rodents minimizes the mechanical impact of trunk support on dynamic balance. However, the application of forces to the trunk in the bipedal posture of humans is likely to exert additional and specific constraints. We found that a vertically restricted trunk support profoundly alters gait dynamics. The addition of well-calibrated forward forces alleviated these effects. Therefore, we developed an adaptive multidirectional gravity-assist (MGA) algorithm that determines upward and forward forces applied to the trunk to reestablish gravity-dependent gait interactions while providing a support tailored to patient-specific needs.

This MGA enabled natural walking in nonambulatory individuals with SCI or stroke and enhanced skilled locomotion in less-impaired subjects. After a 1-hour gait training session with MGA, individuals

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with SCI exhibited improved locomotor performance without robotic assistance. These combined results stress the importance of applying precise assistive trunk support during gait rehabilitation.

RESULTS

Properties of the neurorobotic platform

We used a cable robot (*25*) that provides a safe environment, preventing falls while allowing control of forces applied to the trunk through a dedicated harness (fig. S1) along the three Cartesian directions during locomotion in a large workspace (Fig. 1A). We integrated the robotic interface within a platform (*21*), allowing real-time acquisition of forces applied to the trunk, whole-body kinematics, GRFs, and muscle activity (Fig. 1B).

To evaluate the absence of detrimental interactions between the robotic system and locomotor performance, we recorded leg kinematics, muscle activity, and kinetics during walking without and with robot in eight healthy individuals. The robot delivered a 40-N upward force, which corresponds to the minimal upward force necessary to maintain tension in the cables (transparent mode). Most of the computed gait parameters did not differ between both conditions (fig. S2A). However, the upward force (40 N) did lead to a small decrease in the amplitude of the vertical and anteroposterior components of GRFs (fig. S2B). These kinetic alterations were associated with a decrease in speed (fig. S2A) and an increase in the activity of ankle extensor muscles (medial gastrocnemius; fig. S2C).

When applying forces with the robot, the resulting interaction force components displayed variabilities due to imprecision in the force controller, dynamic friction, and inertia (*25*). However, the variability remained confined within 4.2 ± 1.7 N for forward forces, 3.5 ± 1.8 N for lateral forces, and 6.2 ± 1.2 N for upward forces (net force, 6.4 ± 1.3N). As expected, inaccuracies increased during locomotion along a sinusoidal path (n = 6 subjects), but even in these challenging conditions, the alterations of gait patterns remained minimal (fig. S2D). These combined results indicate that the robotic attachment exerted minimal interference with the production of gait.

Impact of upward and forward forces on posture and gait

We next evaluated the effects of forces applied to the trunk during standing and walking in healthy individuals. We first studied the impact of upward forces during standing. The upright human body can be modeled as an inverted pendulum (Fig. 2A). Because of the natural forward tilt of the body (β), the CoM projects in front of the rotational axis (ankle) of the pendulum. Consequently, the mean anteroposterior position of the center of plantar pressure (CoP) was located at 25 ± 1% of the base of support length (n = 5 subjects). This biomechanical configuration allowed the maintenance of balance through the tonic activation of antigravity muscles acting at the ankle (Fig. 2A) (*26*).

The application of upward forces (40 to 500 N) induced a backward tilt, which shifted the CoP position toward the heels (Fig. 2B). Subjects displayed increased postural sways, paralleled by considerable changes in ankle muscle activity patterns (Fig. 2A). We found that a forward force compensated for the detrimental impacts of upward force. Forward forces restored the position and dynamics of the CoP, which reestablished appropriate ankle muscle activity (Fig. 2, A and B).

We then evaluated the occurrence of similar interactions between upward and forward forces during locomotion. To capture the effects of force interactions, we calculated a comprehensive number of parameters (n = 120; table S1) that we subjected to a principal components analysis (PCA) (fig. S3) (*22*, *27*). Upward forces alone led to a gradual alteration of gait features and muscle activity (Fig. 2, B to D, and fig. S4, A and B). We detected negative correlations between upward forces and the alteration of key gait features, such as the stride length (R^2 = 0.78), speed (R^2 = 0.91), and antigravity muscle activity (fig. S4, C and D). Large upward forces required an abnormal activation of knee flexor muscles during stance to pull the body forward, concomitant to a threefold drop in the activation of antigravity muscles (Fig. 2C and fig. S4, A and C).

The application of increasing forward forces mediated a gradual recovery of the stride length, speed, double stance duration, and antigravity muscle activity (Fig. 2, B to D, fig. S4, E to H, and movie S1). Forward forces improved the oscillations of the CoM and the profile of GRFs (Fig. 2C). Analysis of the interactions between upward and forward forces during walking on a treadmill confirmed these observations (fig. S5A and movie S1). These results highlight critical interactions between upward and forward forces on posture and gait with body weight support, stressing the importance of developing evidence-based procedures to configure these forces based on patient-specific needs.

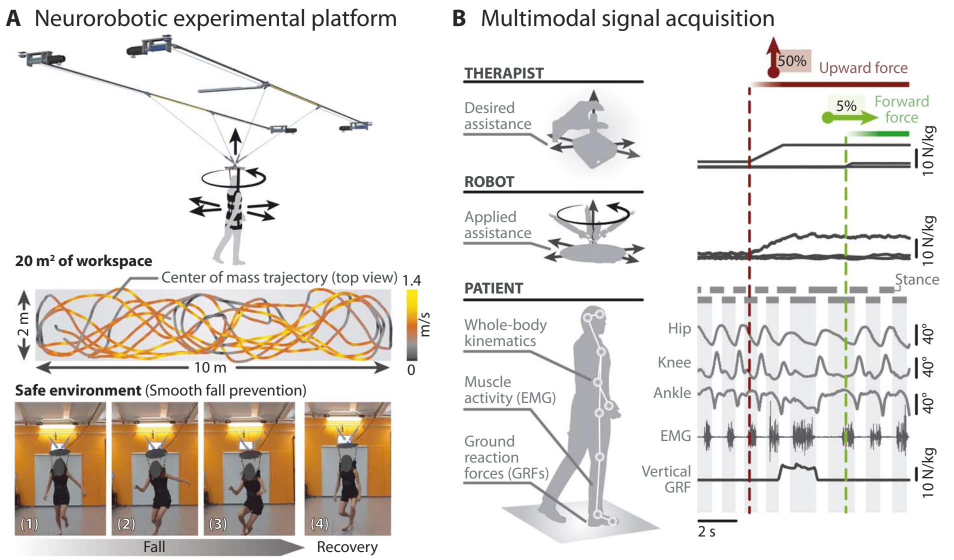

Fig. 1. Technological framework of the multidirectional gravity-assist. (**A**) Schematic and image of the robotic support system, including the directions of the actuated and passive (rotation) degrees of freedom. The spatial trajectory and instantaneous speed of the CoM are shown during locomotion within the entire workspace. Images (1 to 4) illustrating the recovery from a fall. (**B**) Kinematics, electromyogram (EMG) activity, and GRFs are recorded concomitantly. A gait sequence is shown, during which an upward force followed by an increasing forward force are applied to a healthy subject during walking. From top to bottom: Desired forces, measured forces, left and right stance durations, leg joint angles, EMG activity, vertical GRFs, and timing of applied forces.

Gravity-assist: Personalization of upward force

Individuals with motor deficits require personalized upward forces to compensate for their specific impairments. Currently, therapists select this support from empirical observations. Here, we aimed at developing an algorithm that configures upward forces based on objective measurements.

Nine subjects with SCI or stroke were asked to stand with robotic assistance (table S2). To determine the optimal upward force, we recorded kinematics, kinetics, and muscle activity over a range of upward forces (from 15 to 70% of body weight, depending on the capacity of each subject; Fig. 3A). We applied a PCA on the computed parameters (n = 15, table S1) recorded in each subject and healthy

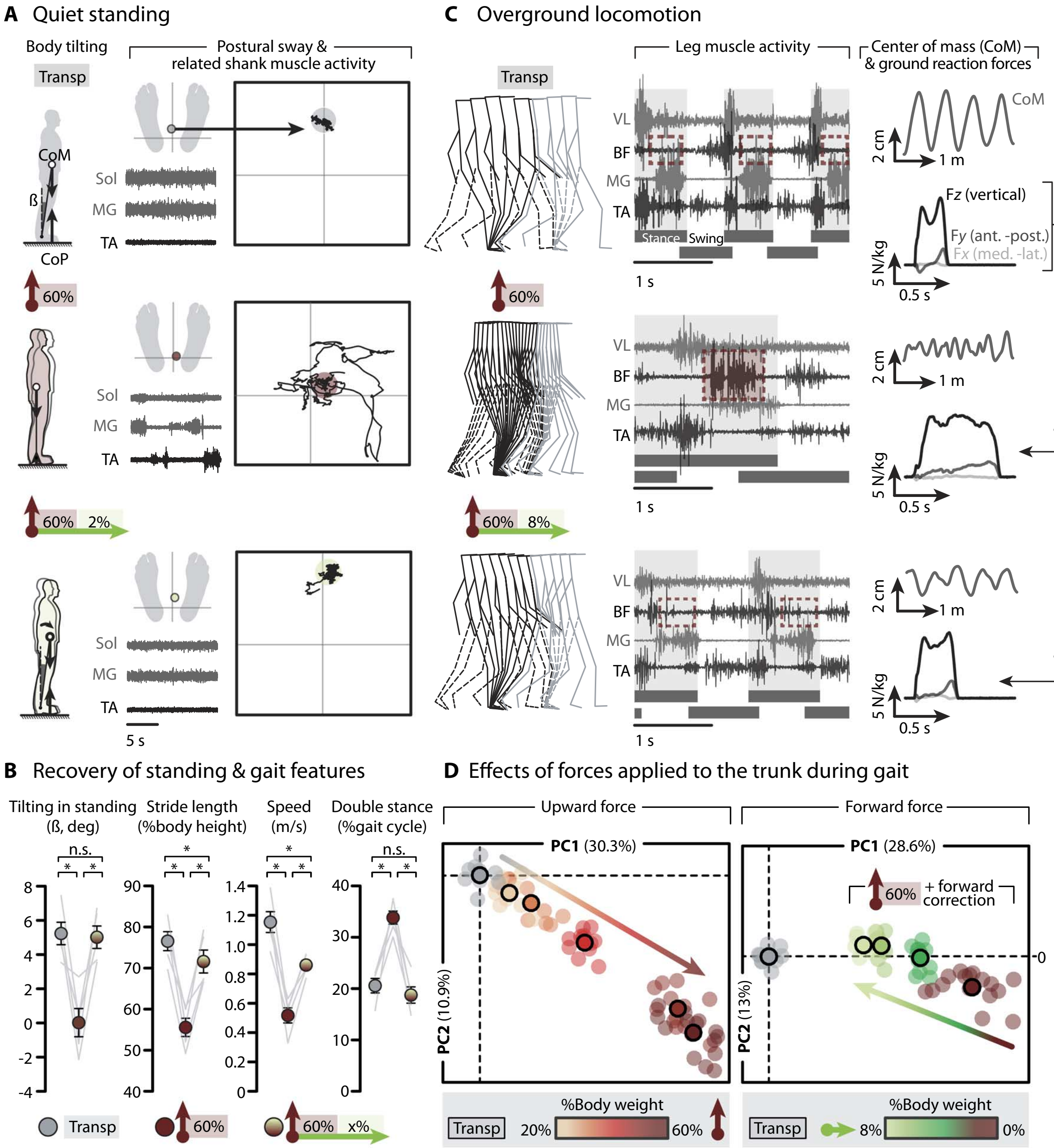

Fig. 2. Interaction between upward and forward forces during standing and walking. (**A**) Schematic of the body, including the CoM, the postural orientation (β), and CoP. The mean position of the CoP with respect to the feet is shown during standing with transparent (Transp) support, upward force only, and both upward and forward forces. A concomitant sequence of EMG activity from ankle extensor (Sol, soleus; MG, medial gastrocnemius) and ankle flexor muscles (TA, tibialis anterior) is displayed. The plot represents the continuous and mean (colored circle) positions of the CoP for each condition. The x axis refers to the axis passing through the malleoli, whereas the y axis corresponds to the midline between the feet. (**B**) Plots reporting the means ± SEM of β during standing and gait parameters under the conditions shown in (A) and (C). *P < 0.05, Wilcoxon signed-rank tests, n = 5 healthy subjects. n.s., not significant. (**C**) Stick diagram decomposition (rate, 120 ms) of head, trunk, and leg movements during stance (dark, shading) and swing (light, unshaded). The stick diagram decomposition of trunk and leg movements is shown for sides. The filled and dashed lines differentiate the right and left legs, respectively. The EMG activity of extensor and flexor muscles acting at the ankle and knee (VL, vastus lateralis; BF, biceps femoris) is displayed, together with the CoM trajectory in the sagittal plane and GRFs. (**D**) Gait kinematics of one subject shown in the space created by PC1 and PC2 (%, explained variance). Each color-coded dot corresponds to a single gait cycle, whereas the black circles indicate the average value for each condition.

individual (n = 5). The optimal upward force was defined as the condition minimizing the distance to healthy individuals (Fig. 3B).

This method requires extensive recordings that are unpractical in clinical practice. To automate this procedure, we applied a supervised machine learning using an artificial neural network that predicted optimal upward forces for each subject based on easily collected kinematic and kinetic variables (n = 12; table S1). The artificial neural network aimed at minimizing errors in the predicted corrections of upward forces (Δ, percentage of body weight). Performances were tested on independent data sets (32 trials, n = 3 subjects). The errors in the predicted corrections never exceeded 5% of the experimentally measured optimal upward force (Fig. 3C).

Gravity-assist: Personalization of forward force

We next sought to calibrate the forward force during walking for each upward force and patient-specific needs. To guide this process, we performed simulations using a damped, spring-loaded inverted pendulum model. This simulation captures the main features of human locomotion (see Supplementary Materials and Methods). As observed experimentally, upward forces reduced the walking speed, stride length, and CoM oscillations. Simulations searched the optimal configuration to normalize the speed, stride length, and CoM oscillations toward values obtained without any external force. We obtained an inverted, U-shaped curve defining the forward force correction at a given speed (Fig. 3D).

We exploited these results to guide the experimental identification of forward force corrections. Individuals with neurological deficits exhibit optimal performance at a preferred speed. Because forward force corrections were linked to the speed, we created a map integrating the preferred speed in the configuration of the MGA. Twenty-two subjects with SCI or stroke walked with optimal upward force and a narrow range of forward forces centered around the values derived from simulations. Optimal locomotor performances were calculated from the PCA (fig. S3). To calculate optimal upward and forward forces for each speed, we fitted an optimal polynomial function to the data. We obtained an inverted, U-shaped map (Fig. 3D). We used this decision map to configure the MGA in the subsequent experiments.

Gravity-assist: Validation

We next evaluated the performance of the MGA algorithm to establish optimal upward and forward forces during locomotion. We tested the algorithm in six individuals with SCI or stroke (table S2) using a framework that can easily be implemented in clinical routine (Fig. 4A). Subjects were first recorded during standing with optimal upward force and with the addition or subtraction of an upward force corresponding to 10% of their body weight. The optimal force was determined with PCA. For each condition of upward forces, kinematic and kinetic recordings were independently provided to the artificial neural network, which calculated upward force corrections to establish the optimal condition for each subject. For example, Fig. 4B shows kinematic and kinetic recordings during walking for one of the subjects included in the testing data set of the artificial neural network. This subject was not capable of standing or walking independently [SCI_BME, American Spinal Injury Association (ASIA) Impairment Scale (AIS) C; table S2]. The artificial neural network yielded the same predictions of optimal upward force, regardless of the initial upward force (among the three tested force values). We used this correction and the preferred walking speed to configure the forward force using the decision map (Fig. 3D).

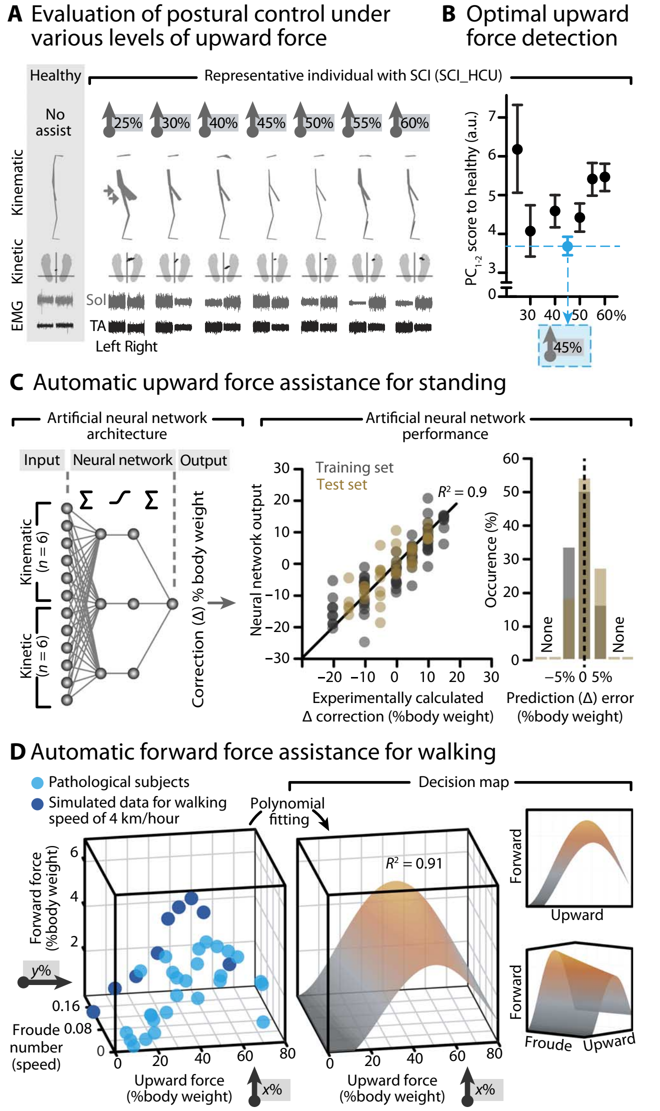

Fig. 3. Design of the MGA algorithm. (**A**) Stick diagram decomposition of whole-body movements, continuous CoP trajectory, and EMG activity of ankle muscles during standing with upward forces ranging from 25 to 60% of body weight support (5% increments) for a nonambulatory individual with a SCI. (**B**) Plot showing the relationship between the upward force and the Euclidian distance between the data of the participant shown in (A) and healthy subjects in the space defined by PC1 and PC2 (PCA performed on 15 parameters). The minimal distance (blue dot) was defined as the optimal upward force. (**C**) The measured variables were fed into an artificial neural network that calculated the correction of body weight support (Δ, upward force in percentage of body weight) to facilitate gait. The plot shows the relationship between the experimentally determined correction and the prediction of the neural network. Each dot corresponds to a given condition of upward force for a subject with SCI or stroke who contributed to the training or test data set. The histogram plot reports the occurrence rate of errors in the prediction of the corrections calculated by the artificial neural network. (**D**) Three-dimensional plots reporting the relationships between the upward force, the optimal forward force, and the speed. Each data point corresponds to values measured in the simulations and in subjects with SCI or stroke. To include data from subjects with varying biometry, the speed is represented as the Froude number, which takes into account the length of the leg to normalize the speed. A polynomial function was fitted through both simulated and experimental data points.

The MGA enabled this subject to progress overground with coordinated, weight-bearing locomotor movements (Fig. 4B). Improved dynamics of the CoM revealed the partial restoration of gravity-dependent gait interactions (Fig. 4C). A 10% increase or decrease in the amount of upward force drastically altered gait features, almost preventing this subject from progressing forward (Fig. 4B and movie S2).

We measure the performance of the MGA algorithm using a PCA applied on all the kinematic parameters (n = 120; table S1 and fig. S3, A and B). Locomotor performance was quantified as the distance between each subject and healthy individuals in the space defined by PC1 and PC2 (fig. S3C). This analysis showed that the MGA algorithm yielded appropriate configurations of upward and forward forces in all of the tested subjects [$P < 0.001$, repeated-measures two-way analysis of variance (ANOVA); Fig. 4C and movie S2]. The importance of the precision in the MGA configuration increased with the severity of gait deficits, as quantified with PCA scores ($R^2 = 0.88$ and $P < 0.01$; Fig. 4D). The pronounced modulation of individual gait parameters confirmed the importance of the MGA configuration to facilitate locomotion (Fig. 4E). These results illustrate the critical importance of personalizing upward and forward forces to enable locomotion in neurologically impaired subjects and validate the capacity of the MGA algorithm to configure these forces based on patient-specific needs.

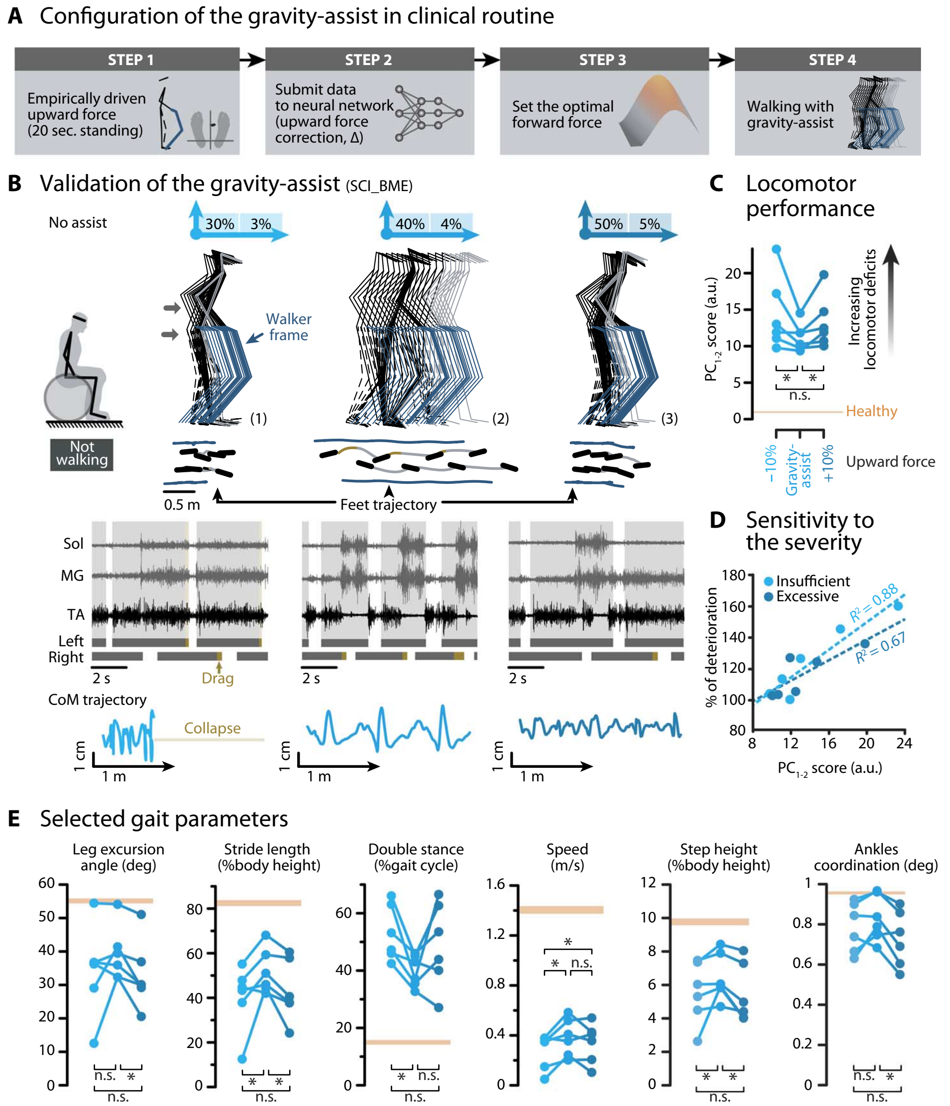

Fig. 4. Validation of MGA algorithm in individuals with SCI or stroke. (**A**) Steps for configuration of the MGA. (**B**) Stick diagram decomposition of whole-body movements (and walker, blue) for a nonambulatory subject with SCI walking with three ranks of upward force and associated forward force. The position of the feet during stance and their trajectories during swing is indicated (gray) together with the trajectory of the wheels of the walker (blue). A representative sequence of EMG activity recorded from ankle muscles is reported for each condition together with the stance duration of each leg (gray bar). Foot dragging is indicated in brown. The CoM trajectory is displayed at the bottom in blue. (**C**) Locomotor performance was quantified as the Euclidian distance between gait cycles of each subject in three different conditions of upward assistance versus healthy individuals in the PCA space (fig. S3). Middle blue refers to the gravity-assist condition. Light blue and dark blue correspond to a 10% decrease and increase in the amount of upward force, respectively. *$P < 0.05$, Friedman test with Tukey-Kramer post hoc tests. (**D**) Impact of suboptimal force configurations based on locomotor performance. (**E**) Plots reporting the means of selected gait parameters under the three conditions of upward force. The mean (horizontal orange bar) ± SEM (thickness) measured during locomotion in healthy subjects is represented. *$P < 0.05$, Wilcoxon signed-rank tests. Data are means per subject, n = 6 pathological subjects.

Gravity-assist: Improvement of locomotor performance after SCI and stroke

We next tested the capacity of the MGA to enable or enhance locomotor performance in two cohorts of individuals with varying severities of SCI (n = 15) and stroke (n = 12). Locomotor performance ranged from nonambulatory individuals who could neither stand nor walk independently to individuals with mild motor impairments who could walk without assistive device (table S2).

With the exception of nonambulatory individuals, all of the subjects were first recorded during locomotion without the robot using the assistive device that they used in their daily life. All the subjects were then evaluated during locomotion with MGA, both with and without assistive device when possible. Kinematic variables (n = 120; table S1) recorded in healthy individuals (n = 13) and in all of the subjects with SCI or stroke were subjected to separate PCA analyses to quantify locomotor performance. These quantifications revealed that the MGA enabled walking in nonambulatory subjects with kinematic features similar to ambulatory subjects, both after SCI (Fig. 5) and stroke (Fig. 6). Each subject showed specific responses, which are documented in database S1 that shows individual gait analyses for the 26 individuals with SCI or stroke.

To identify the specific gait features improved by the MGA, we extracted the parameters that highly correlated with PC1 and PC2 (factor loadings, |value| > 0.5) and regrouped them into functional clusters corresponding to basic gait features. We first conducted this analysis for individuals with SCI (Fig. 5A). We found that PC1 quantified improvements of leg kinematics, whereas PC2 captured changes in postural control. The improvements depended on the initial locomotor performance ($R^2 = 0.64$, $P < 0.005$). For example, the MGA enabled subjects who could not stand independently to walk overground with or without assistive device (three of three subjects; Fig. 5, B and C, top row). Subjects who were only able to locomote with crutches or a walker progressed without assistive device (4 of 10 subjects) and exhibited improved spatiotemporal gait features (Fig. 5, B and C, middle rows). Subjects who were able to walk without assistive device exhibited increased postural stability (Fig. 5, B and C, bottom row, and movie S3).

Individuals with stroke exhibited similar or even superior amelioration of locomotor performance (Fig. 6 and movie S3). The PCA (Fig. 6A) showed that individuals who could only walk with crutches exhibited improved intralimb coordination (Fig. 6, B and C, middle row). Individuals who walked without assistive device showed improvements of basic gait parameters, such as the stride length and walking speed, as well as enhanced arm movements and improved gait symmetry (Fig. 6, B and C, bottom row). Together, these results show that the MGA enabled or enhanced locomotor control in individuals with severe to moderate gait deficits due to SCI or stroke.

Gravity-assist: Improvement of locomotor performance after a 1-hour training session

We then sought to demonstrate the ability of the overground gait training environment with MGA to improve locomotor performance. We enrolled five subjects with a chronic SCI who were capable of walking overground but only with an assistive device (table S2). They participated in two training sessions, separated by 1 week (Fig. 7A). During the first session (60 min), subjects walked overground with MGA. During the second training session (week 2), they were asked to walk the same distance on a treadmill. Immediately before and after each training session, the subjects were recorded during overground locomotion without MGA at their own selected pace using their preferred assistive device.

With the exception of the least-affected subject, the training session with MGA mediated a significant increase ($P < 0.001$ for four of five subjects) in locomotor performance in all the participants. For example, the increase in gait speed and decrease in double stance duration enabled by the MGA throughout the training persisted during overground locomotion without MGA (Fig. 7B, left). However, evaluations conducted 1 week later revealed that these improvements did not persist (Fig. 7B). In contrast, overground locomotor performance remained unchanged or even deteriorated after treadmill-restricted step training (Fig. 7C). Basic gait features, such as the speed and double stance duration, improved during training, but the values returned to baseline when the subjects walked overground with their assistive device after training (Fig. 7B). These results show that a 1-hour gait training session facilitated by the MGA improved locomotor performance immediately after training (movie S4).

Gravity-assist: Training of skilled locomotion and dynamic balance

Task-specific training plays a critical role in determining the outcome of gait rehabilitation (*16*). We thus tested the ability of the MGA to enable tasks underlying activities of daily living. We first tested skilled foot placements along the rungs of a horizontal ladder placed 15 cm above the ground in subjects with SCI or stroke who displayed sufficient locomotor performance for this task ($n = 13$). Without the MGA, these subjects considered this task too challenging or too risky. The MGA allowed all the tested subjects to climb up the staircase and progress with accurate foot placement onto the rungs of the ladder (Fig. 8A and movie S5).

The multidirectional actuation of the MGA also allowed the subjects to practice their steering abilities, dynamic balance, and upper/lower limb coordination during natural walking. For instance, they could walk safely along a curvilinear path projected onto the floor without assistive device (Fig. 8B). Finally, we studied the ability to train dynamic balance. We designed perturbations consisting of laterally oriented forces that were applied to the trunk suddenly or continuously during walking. As expected, the perturbations altered the trajectory, position, and posture of the trunk (Fig. 8C and movie S5). These perturbations thus allow training and evaluation of dynamic balance in a safe environment. Together, these results illustrate the ability of the MGA to enable activities of daily living that require skilled and finely balanced movements, thus providing the opportunity to expand task-specific training in neurologically impaired individuals.

DISCUSSION

We developed an algorithm that configures upward and forward support forces applied to the trunk to restore gait dynamics despite the application of a body weight support during standing and walking. The MGA establishes a safe and natural rehabilitation environment wherein individuals with neurological deficits can perform basic and skilled locomotor activities that would not be possible without robotic assistance. This environment allows task-specific training in optimal conditions. The immediate and short-term ameliorations of gait performance during locomotion with MGA illustrate the potential of this environment to augment motor recovery.

Partial body weight–supported gait therapy is a common medical practice to improve recovery after neurological disorders (*12*, *13*). This condition allows the repetition of locomotor movements that would not be possible without assistance. Currently, therapists configure the amount of support empirically based on visual observations. As observed in rodents (*22*, *23*), we found that the clinical phenotype of each neurologically impaired subject determined the precise amount of upward support required to facilitate gait execution. In most of the affected subjects, even minimal changes in support conditions strongly affected locomotor performance.

Current body weight support systems generally deliver assistance restricted to the upward direction (*18*). Yet, we found that the application of upward forces induced a backward shift in body orientation, which considerably destabilized the control of standing and walking. The addition of well-calibrated forward forces was critical to restore the postural orientation and thus alleviate the undesirable impact of upward forces on gait and balance. The detrimental effects of a vertically restricted body weight support were similar on a treadmill.

These results confirmed previous findings that high amounts of body weight support lead to abnormal patterns of leg muscle activity, which would be detrimental for relearning to walk (*19*). This observation led to the recommendation to limit the amount of body weight support to 30 or 40% (*19*, *28*). This guideline has been consistently

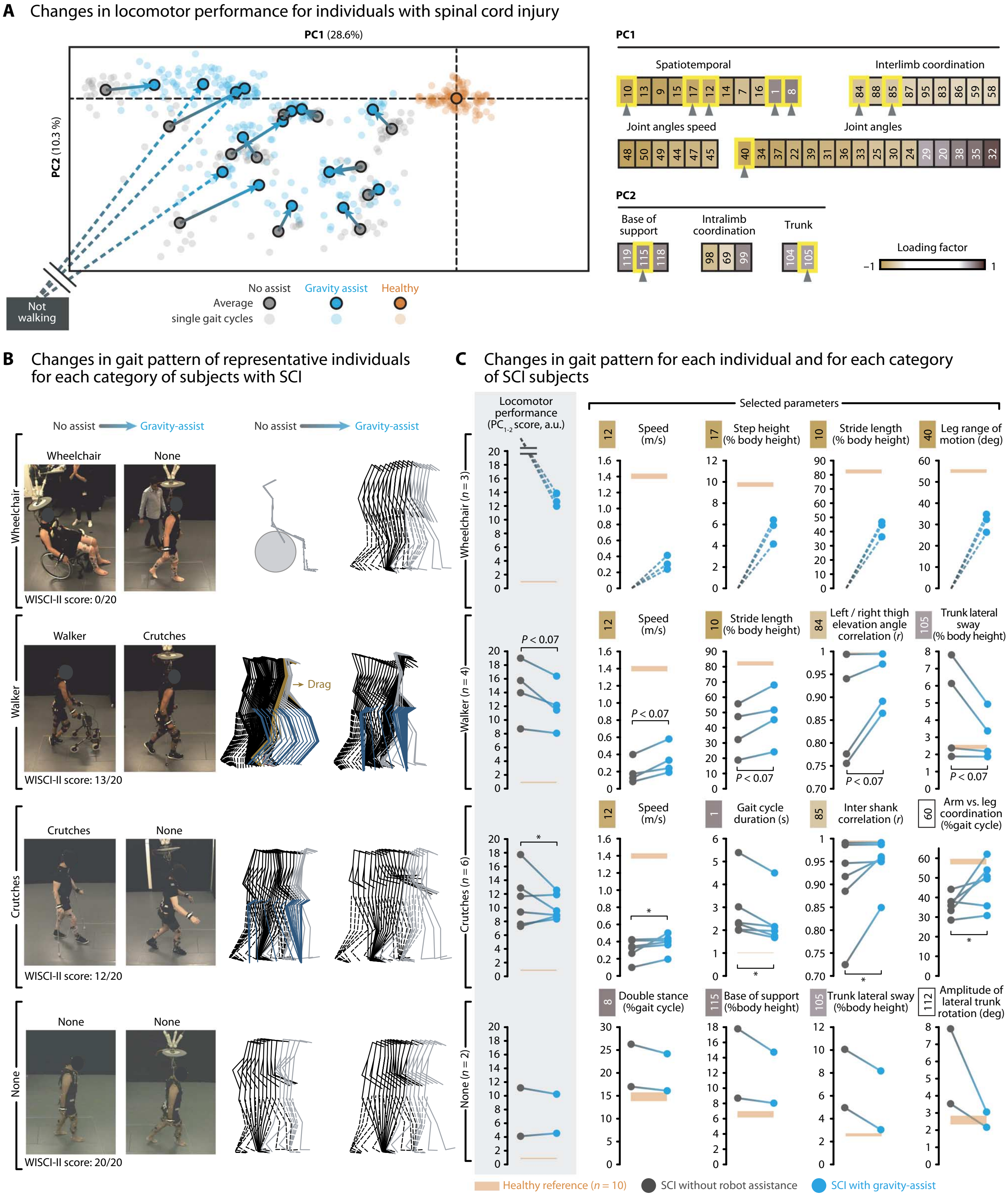

Fig. 5. Performance of the MGA to enable or enhance locomotor control after SCI. (**A**) Subjects with SCI walked overground without and with MGA using the least-assistive device possible. To quantify locomotor performance and identify the most relevant parameters, a PCA-based method has been applied, as described in fig. S3. On the right, the computed parameters that strongly correlated with a given PCA (|loading factors| > 0.5) were regrouped into functional clusters. Numbers refer to table S1. (**B**) Subjects were segregated into four categories: nonambulatory (wheelchair), walker, crutches, and none. Image and stick diagram decomposition of whole-body movements (and assistive device) are shown for each category and condition. (**C**) Plots reporting the mean values of locomotor performance and classic gait parameters for each subject during locomotion without and with MGA. The horizontal orange bars report the means ± SEM (thickness) measured during locomotion in healthy subjects. *$P < 0.05$, Wilcoxon signed-rank tests, n = 15 subjects with SCI.

applied in clinical studies (*29–31*). However, our results indicate that this recommendation arises from an improper configuration of the trunk support. These findings may partly explain why locomotor training on a treadmill with body weight support was not shown to be superior to progressive exercise at home managed by a physical therapist after SCI (*32*) or stroke (*33*). Together, these observations reveal that the prevailing design and utilization of clinical body weight support systems are suboptimal for the rehabilitation of posture and gait.

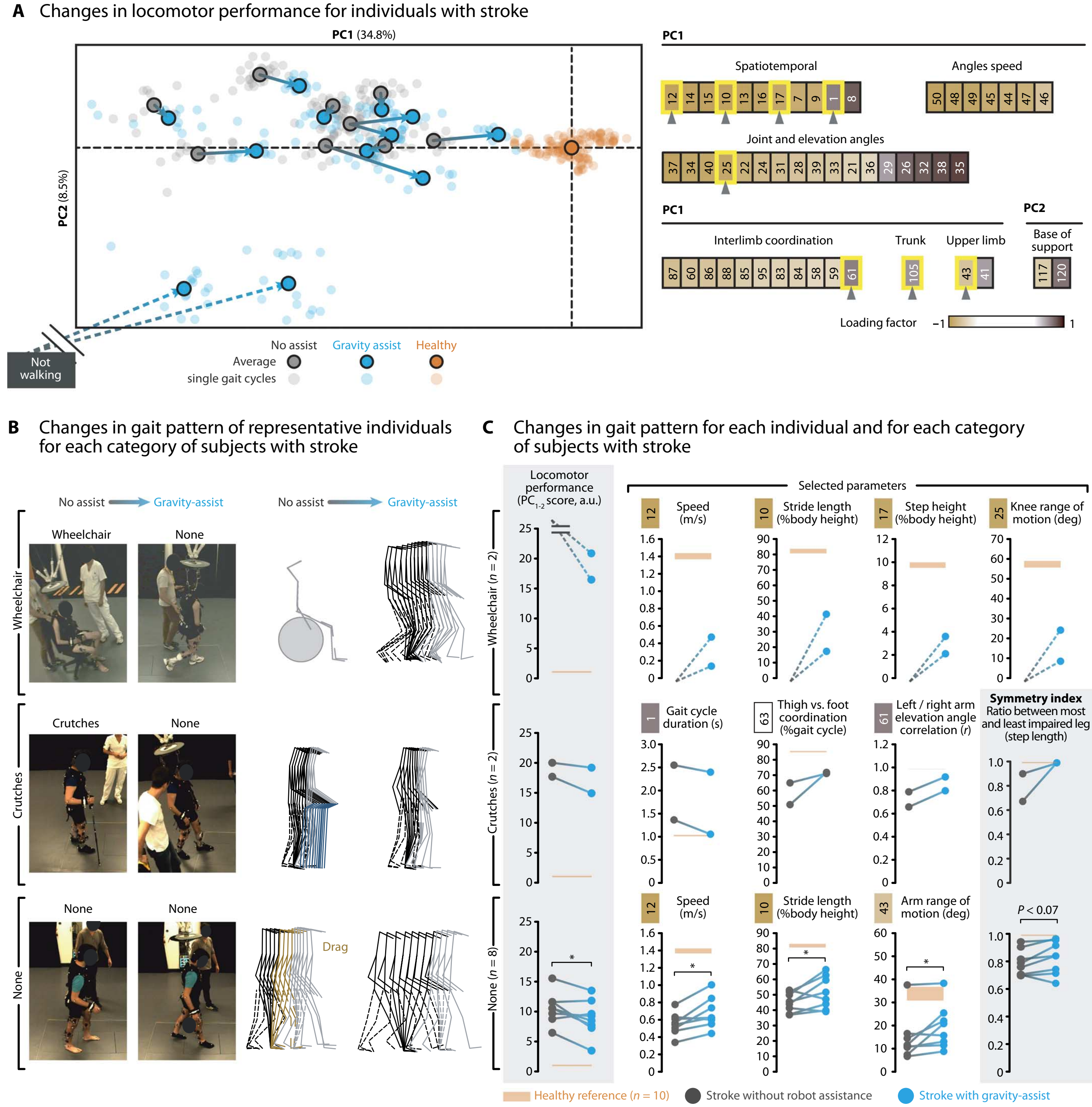

Fig. 6. Performance of the MGA to enable or enhance locomotor control after stroke. (**A**) Subjects with stroke walked overground without and with MGA using the least-assistive device possible. To quantify locomotor performance and identify the most relevant parameters, a PCA-based method has been applied, as described in fig. S3. On the right, the computed parameters that strongly correlated with a given PCA (|loading factors| > 0.5) were regrouped into functional clusters. Numbers refer to table S1. (**B**) Subjects were segregated into three categories: nonambulatory (wheelchair), crutches, and none. Images and stick diagram decomposition of whole-body movements (and assistive device) are shown for each category and condition. (**C**) Plots reporting the mean values of locomotor performance and classic gait parameters for each subject during locomotion without and with MGA. In addition, a symmetry index reports the relative symmetry between left and right step lengths for each subject. The mean (horizontal orange bar) ± SEM (thickness) measured during locomotion in healthy subjects is represented. *$P < 0.05$, Wilcoxon signed-rank tests, $n = 12$ subjects with stroke.

On the contrary, the MGA established a rehabilitation environment that is mechanically and physiologically optimized for patient-specific needs. The external constraints can be adapted to the residual motor control abilities of each patient within each session and throughout a rehabilitation program. The resulting facilitation of gait execution was unexpected. Subjects with SCI or stroke immediately exhibited improved locomotor performance, which translated into the ability to walk overground for nonambulatory individuals who had sufficient residual control over leg movements. For the least-affected individuals, the MGA allowed skilled locomotor activities that were not possible without robotic assistance. This result is important because task-specific training determines the outcome of gait rehabilitation after neurological disorders (*16*).

The MGA restored kinematic and kinetic patterns that resembled natural gait dynamics. Despite the application of upward force, both healthy and neurologically impaired subjects regained the profiles of GRFs that are specific to human walking. We surmise that these gravity-dependent gait interactions are critical for learning and relearning to walk. For example, evidence suggests that gravity-dependent gait interactions during the first unsupported steps in toddlers act as a functional trigger for gait maturation (*34*, *35*).

The short-term improvements of locomotor performance after a 1-hour training session corroborated this hypothesis. The practice of natural walking with the MGA enabled the subjects to become confident in their residual motor abilities and to relearn the interactions between their body mechanics and gravitational forces. Hence, this type of robotic assistance in a safe yet natural environment represents an ecological approach to gait rehabilitation (*36*). Similar learning did not occur on a treadmill. Moreover, the MGA enabled the practice of skilled locomotion, steering, and balance in natural conditions. We suggest that training neurologically impaired individuals in these activities of daily living, which can only be practiced naturally with MGA, may lead to enhanced recovery (*16*). Such task-specific training may facilitate the transition into community ambulation.

These results need to be confirmed in a larger number of subjects and through a long period of rehabilitation. The 1-hour training session was insufficient to mediate lasting locomotor improvements. Here, we provided a clinically relevant framework to implement such rehabilitation programs across multiple activities of daily living for subjects with various types and severities of neurological deficits.

The significant role of gravity-dependent gait interactions in enabling or enhancing motor control after neurological disorders stresses the importance of optimizing the hardware and software underlying the MGA algorithm. In the present scenario, the forces applied to the trunk remained constant throughout gait execution. Moreover, the MGA only targeted upward and forward oscillations. However, the dynamics of human gait require precisely timed trunk movements in multiple directions (*4*, *17*, *34*, *37*). For example, the cyclic mediolateral movements of the trunk play a pivotal function in balance regulation during locomotion. We thus predict that the application of time-varying forces, tailored to specific phases of the gait cycle in each of the relevant Cartesian directions as well as torques, will further improve the interactions between body mechanics and gravitational forces—and thus the facilitation of gait execution. Predicting this dynamic MGA from simulations would require a more advanced biomechanical model to emulate the multidirectional interactions between body dynamics and gravitational forces. This type of assistance also relies on a number of hardware and software innovations to expand the spectrum of locations where forces and moments can be applied and

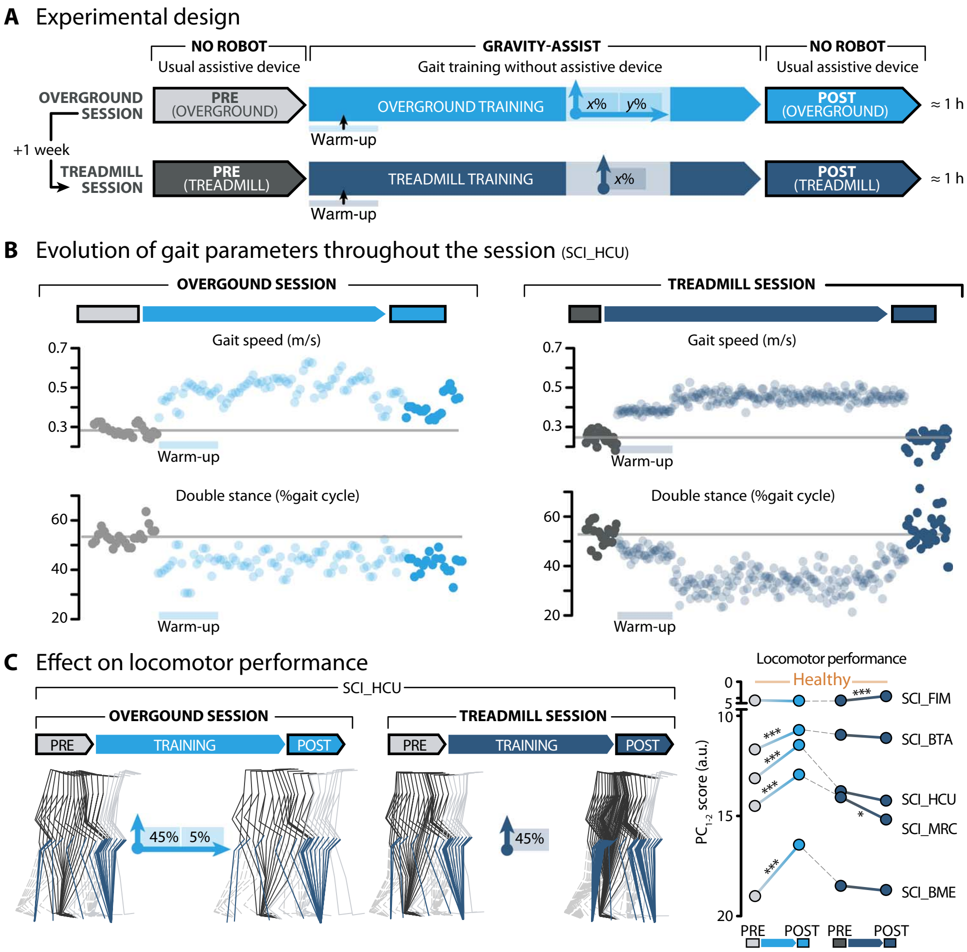

Fig. 7. Gait training session overground with MGA or on a treadmill with upward support. (**A**) Experimental design of the 1-hour training sessions. (**B**) Plots reporting gait speed and double stance duration for each successive gait cycle of subject SCI_HCU over the course of the entire session. The color coding refers to the experimental design detailed in (A). (**C**) Stick diagram decomposition of whole-body movements recorded overground without robotic assistance. The blue stick represents the crutch. The plot reports the locomotor performance of n = 5 subjects with SCI before and after training with MGA (light blue), as well as 1 week later (before and after training restricted to a treadmill, dark blue). Locomotor performance was evaluated using the PCA-based method described in fig. S3. The horizontal orange bars report the means ± SEM (thickness) measured during locomotion in healthy subjects. *P < 0.05, ***P < 0.001, Mann-Whitney U test. Data are means per subject.

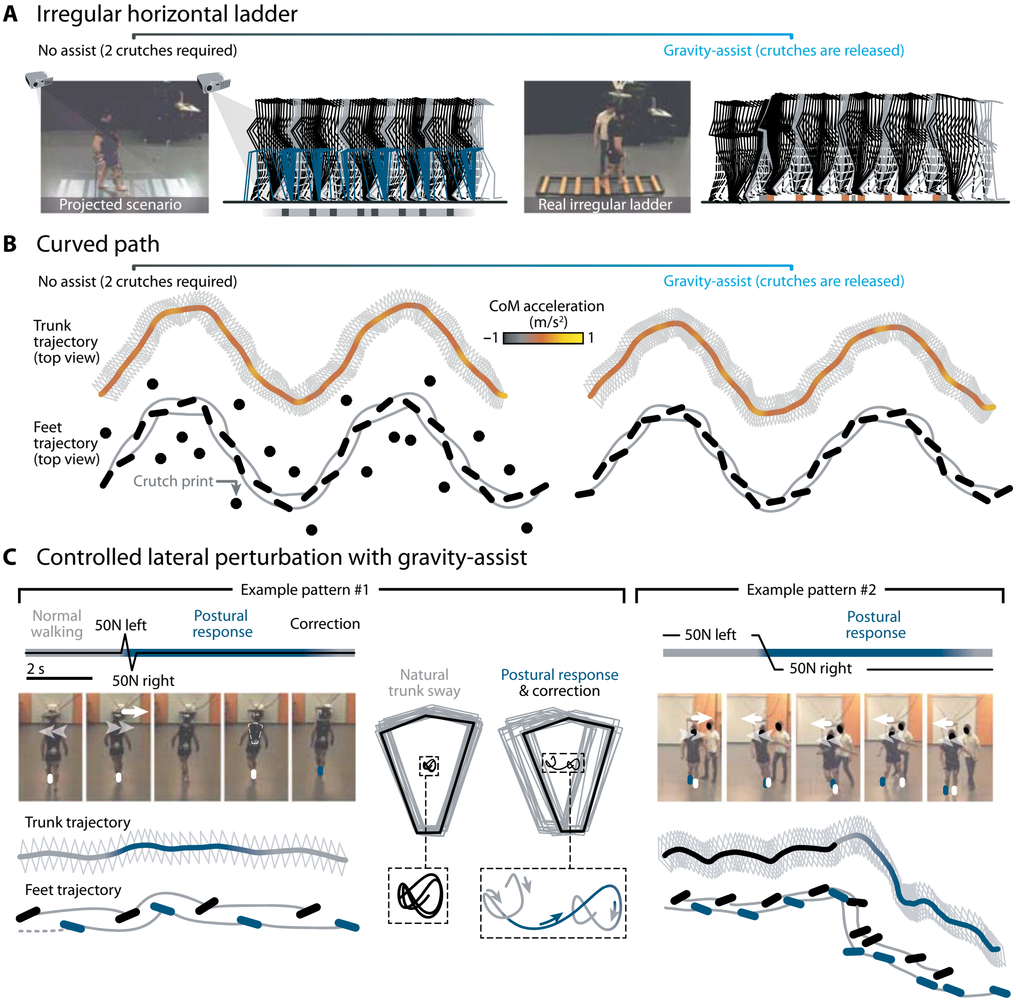

Fig. 8. The MGA allows training of skilled locomotor and postural activities. (**A**) Images and stick diagram decomposition showing a subject with SCI who could position his feet onto the irregularly spaced rungs of a ladder projected onto the floor during locomotion assisted with two crutches. The subject could not walk over the actual ladder in this condition. The MGA enabled the subject to climb up the first staircase and to progress onto the actual ladder without assistive device. (**B**) Successive positions of the trunk in the coronal plane while a subject with SCI was asked to progress along a curvilinear path projected onto the floor, both without and with MGA. The CoM trajectory and acceleration are also displayed, together with the position of the feet (dashes) during stance and their trajectory during swing. The dot indicates the positions of the crutches onto the floor without MGA. (**C**) Image sequences showing the behavior of a subject with SCI during the application of postural perturbations during walking. The perturbation is schematized above each sequence. Left: Sudden leftward and then rightward forces. Right: Sustained leftward and then rightward forces. The impact of these perturbations on the position, posture, and trajectory of the trunk and feet are shown.

to develop control policies for adjusting these loads based on real-time movement feedback. Here, we introduced a neurorobotic platform that combines important features to implement dynamic trunk assistance.

Additional improvements may play an important role in optimizing the performance and usability of the robotic platform, particularly for dynamic assistance. For instance, the force controller introduced variability in the interaction forces that may be optimized with more precise sensors and improved robot mechanics. Furthermore, the smart design of the trunk harness may reduce the displacement of the body CoM by moving the force application to the pelvis (*38*). These hardware and software improvements combined with real-time force adaptation may greatly improve locomotor performance in injured individuals.

Evidence suggests that gait rehabilitation should be conducted overground (*39*) across activities of daily living (*16*, *40*), with optimized support conditions (*39*, *41*, *42*), enabling systems (*41*, *43*–*46*), unconstrained arm movements (*47*, *48*), and active participation (*43*, *49*), but these concepts remain fragmented. Here, we introduced a neurorobotic platform that crystallizes these views into a unified framework to augment gait recovery after neurological disorders.

MATERIALS AND METHODS

Study design

Our goal was to develop an evidenced-based algorithm that configures multidirectional forces applied to the trunk to establish a natural environment enabling each individual with neurological deficits to perform locomotion in natural conditions. For this purpose, we implemented eight experimental protocols that were approved by the local ethical committee of the Canton de Vaud (Switzerland, no. 141/14). The evaluations were conducted at the University Hospital of Vaud (CHUV)

Protocol 1: Evaluation of the neurorobotic platform during locomotion along straight and curvilinear paths in eight healthy individuals.

Protocol 2: Impact of upward and forward forces applied to the trunk on the kinematics, kinetics, and muscle activity during standing and walking. Evaluations in five healthy individuals.

Protocol 3: Development of the algorithm that automatically configures upward forces. Recordings were performed during standing and walking over varying upward forces in nine subjects with SCI or stroke.

Protocol 4: Development of a decision map that automatically adjusts forward force corrections. Computational simulations were completed with recordings of 22 subjects with SCI or stroke during locomotion.

Protocol 5: Validation of the MGA algorithm developed in protocol 3 and 4. Six subjects with SCI or stroke were recorded during walking with MGA and small variations of upward and forward forces.

Protocol 6: Ability of the MGA to improve locomotor performance during walking. Fifteen subjects with SCI and 12 subjects with stroke were recorded during locomotion with MGA. Locomotor performance was compared to 13 healthy individuals.

Protocol 7: Five subjects with SCI performed two 1-hour training sessions: (i) overground with MGA and (ii) on a treadmill with upward support only. Locomotor performance was measured before and after training without robotic assistance.

Protocol 8: Thirteen subjects with SCI or stroke performed skilled locomotion along the irregularly spaced rungs of a horizontal ladder and along a curved path projected on the floor with and without MGA. A virtual ladder was projected on the floor in the condition without robot. The subjects were also tested during walking while receiving a sudden or sustained lateral perturbation.

All measurements were obtained using objective readouts with high-precision equipment. Blinding during data acquisition and analysis was not possible because of obvious differences between conditions with and without robot. All the recorded gait cycles were included in the analyses (excluding gait initiation and termination). No statistical outliners were excluded.

Participants

Twenty-six subjects with SCI or stroke and 13 healthy individuals took part in the study. Written informed consent was obtained for each participant. The protocols conformed to the latest revision of the Declaration of Helsinki. All the subjects were followed by a physician from the neurorehabilitation department (S.C.). Before their enrollment, their medical history was collected together with standard neurological evaluations. For subjects with stroke, motor scores were measured using the Motricity Index (*50*), whereas the severity was evaluated using the Functional Independence Measure (*51*). AIS and WISCI-II (Walking Index for Spinal Cord Injury II) scores were collected in subjects with SCI. The main characteristics of the subjects are summarized in table S2.

Neurorobotic platform

Commercially available technologies were integrated within a neurorobotic platform that combines the following: (i) a physiological recording unit monitoring kinematics (VICON), kinetics (9260AA6, Kistler), and muscle activity signals (myon 320, myon AG); (ii) a robotic body weight support system (The FLOAT, Lutz Engineering) (*22*); and (iii) a control processing unit (see Supplementary Material and Methods). All three units were interconnected via an ethernet network using a real-time EtherCAT bus, as previously described for the system developed in rodents (*21*).

Behavioral tasks

Subjects were recorded during standing or walking without or with robotic assistance across four paradigms: standing on two separate force plates, locomotion along a straight path, locomotion along a sinusoidal path projected onto the floor, and walking along a real or projected horizontal ladder with irregularly positioned rungs (see Supplementary Materials and Methods).

Data acquisition and analysis

Procedures to record kinematics, kinetics, and muscle activity were detailed previously (*27*) (see Supplementary Materials and Methods). For locomotion, 140 parameters were computed automatically from kinematic and muscle activity recordings (table S1) according to published methods (*22*, *27*, *52*, *53*). Clinical reports were generated automatically for each set of trials (database S1). For standing, 15 classic parameters were calculated (table S1). Locomotor performance was evaluated using a PCA (*22*, *52*, *53*), which is summarized in fig. S3 and described in Supplementary Materials and Methods.

Statistical analysis

All data are reported as means ± SEM, unless specified otherwise. The nonparametric Mann-Whitney U test or the Wilcoxon signed-rank test was used to compare two unpaired, respectively paired conditions. Kruskal-Wallis test was used to compare subject's gait cycles in several conditions. Two-way ANOVA or its nonparametric equivalent, Friedman test, was used to compare subjects and conditions (Anderson-Darling test was used to evaluate normal distribution). Post hoc comparisons were performed using the Tukey-Kramer test when appropriate. Statistical tests are specified in the legends of figures.

SUPPLEMENTARY MATERIALS

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Materials and Methods
Fig. S1. Attachment to the robotic support system.
Fig. S2. Transparent mode of the robotic support system.
Fig. S3. Representation and processing of kinematic and muscle activity recordings.
Fig. S4. Impact of upward and forward forces on body kinematics and muscle activity.
Fig. S5. Interaction between upward and forward forces during locomotion on a treadmill.
Table S1. List of parameters computed during walking and standing.
Table S2. Characteristics of the subjects.
Movie S1. Interaction between upward and forward forces during walking.
Movie S2. Accuracy of the algorithm to configure the MGA.
Movie S3. Performance of the MGA to facilitate locomotion after SCI and stroke.
Movie S4. The MGA improved locomotor performance after a 1-hour training session.
Movie S5. The MGA enabled skilled locomotion.
Database S1. Summary of the gait analyses for all the recorded subjects with SCI or stroke, without or with the MGA.
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figures. G.C., S.C., and J.B. supervised the study. G.C. wrote the manuscript with J.-B.M. and C.G.L.G, and all the authors contributed to its editing. **Competing interests:** G.C., J.B., J.v.Z., J.-B.M., A.C., H.V., and C.G.L.G. are inventors on patents submitted by the Swiss Federal Institute of Technology (EPFL), Lausanne, Switzerland, that covers the step-by-step procedure and the use of the multidirectional gravity-assist algorithm described in the present research [apparatus comprising a support system for a user and its operation in a gravity-assist mode (EP16184544.1) and apparatus for unloading a user's body weight during a physical activity of said user, particularly for gait training of said user (EP2811962 A1)]. The present research is currently used by University Hospital of Lausanne, Switzerland, in the framework of a clinical study (STIMO, ClinicalTrials.gov Identifier: NCT02936453) cosponsored by EPFL and G-Therapeutics BV. The present research is also used by G-Therapeutics BV for the development of a commercial version of the gravity-assist. G.C., J.B., and J.v.Z. are founders and shareholders of G-Therapeutics BV, a company developing robotic and neuroprosthetic systems directly related to the present work. G.C. and J.B. receive consulting fees from G-Therapeutics BV for work not in direct relationship with this study. All the other authors declare that they have no competing interests. **Data and materials availability:** Contact G.C. (gregoire.courtine@epfl.ch) for information regarding access to data and algorithms.

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A multidirectional gravity-assist algorithm that enhances locomotor control in patients with stroke or spinal cord injury

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Greater gait with gravity

Often taken for granted, gravity––the force that keeps you on the ground––becomes a notable challenge during rehabilitation from injury. Mignardot *et al.* ''harnessed'' gravity to test whether upward and forward forces, applied to the torso via a robotic body weight supportive device, assist with locomotion. Patients recovering from stroke or spinal cord injury demonstrated improved gait performance with the robotic harness. An important component of the gravity-assistive approach is an algorithm that adjusts the forces provided by the robotic harness according to the patient's needs. Patients unable to walk without assistance (nonambulatory) were able to walk naturally with the harness, whereas ambulatory patients exhibited improved skilled locomotion such as balance, limb coordination, foot placement, and steering. A clinical trial using this robot-assistive rehabilitation approach for patients with spinal cord injury is currently under way.