
Supplementary information

Spinal neuromotor rehabilitation using a portable isokinetic training robot

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Supplementary Information for

Spinal neuromotor rehabilitation using a portable isokinetic training robot

Author

Yuebing Li^{1#}, Jiabin Ren^{1#}, Tony Shu^{2#}, Fuzhen Yuan^{3#}, Yanggang Feng^{1#*}

1. School of Mechanical Engineering and Automation, Beihang University, Beijing, China.

2. Program in Media Arts and Sciences, MIT Media Lab, MIT, Cambridge, MA, USA.

3. Peking University Third Hospital, Beijing, China.

[#] These authors contributed equally.

^{*} Corresponding author. Email: yanggangfeng@buaa.edu.cn

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147 **Supplementary Methods**

148 **Supplementary Methods 1 | Therapeutic approaches for SMA**

149 SMA primarily results from the deletion or mutation of the survival motor neuron gene 1 (SMN1),
150 leading to a deficiency in the survival motor neuron (SMN) protein, which is crucial for the
151 maintenance of motor neurons. This protein deficiency precipitates atrophy of motor neurons,
152 resulting in muscle weakness and complications related to feeding and respiration¹²⁻¹⁵. Currently,
153 three approved SMN-targeted therapies are available for SMA: nusinersen (Spinraza; Biogen),
154 onasemnogene abeparvovec (Zolgensma; Novartis), and risdiplam (Evrysdi; Roche). These
155 treatments, along with other genetic manipulations, have given hope to families and patients by
156 compensating for the deficiency of SMN protein. In this study, the medication status of the subjects
157 reflects the clinical diversity of these treatments: subjects 1, 3, 4, and 5 received nusinersen every
158 four months, while subject 6 was treated with daily oral risdiplam. Notably, subject 3 also received a
159 one-time administration of GC101, and subject 2 utilized a combination therapy of both nusinersen
160 and risdiplam.

161 **References [12-15] consistent with main text**

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172 **Supplementary Methods 2 | Sample size estimation**

173 We performed a sample size calculation, with the following steps,

174
$$N = 2 * \left[\left(t_{\frac{\alpha}{2}} + t_{\beta} \right) * \frac{S}{\delta} \right]^2 \quad (S1)$$

175 Given that $\alpha = 0.05$ and $\beta = 0.1$, the critical values $t_{\frac{\alpha}{2}}$ and t_{β} are calculated as:

176
$$t_{\frac{\alpha}{2}} = 1.96, \quad t_{\beta} = 1.28 \quad (S2)$$

177 From the Ref. [1], $S = 16.1$, $\delta = 32.3$. After calculation, we obtained

178
$$N > 5.21 \quad (S3)$$

179 Therefore, the minimum sample size $N_{min} = 6$. In this study, we recruited 6 juveniles with SMA
180 type II.

181 **Supplementary Methods 3 | Detailed design of the robot**

182 The robot is equipped with an angular encoder (TLE5012B, Infineon, Germany) and a torque load
183 cell (LZ-NJY40, Lizhi, China) for real-time monitoring of joint state and control feedback. The
184 angular encoder, positioned at the distal end of the large gear and rigidly attached to the frame, is
185 employed to measure the gear's rotational angle, which is mechanically coupled to and thus
186 representative of the knee joint's angular motion. The torque load cell is affixed to the large gear of
187 the reduction mechanism and is connected in series with the variable stiffness mechanism. It
188 continuously measures the torque exerted by the participant against the impedance of the device using

an operational amplifier (AD8221, Analog Devices, USA) with subsequent sampling by an on-board analog-to-digital converter (ADC). Stiffness is controlled through a flexure modulated by a continuously variable pivot point with the position of the pivot slider controlled by a dedicated secondary motor (N20, Bihui Digital, China) (**Supplementary Fig. 24**). A sliding potentiometer (RDC10320RB, ALPS ALPINE, Japan) is affixed to the pivot slider to provide feedback on the slider's position (0-25 mm). Stiffness is mapped to position using empirical models developed through benchtop testing and sampling throughout the slider's range of motion.

The detailed structure of the variable stiffness mechanism is illustrated in **Supplementary Fig. 24(a)**. It primarily consists of a swing arm with a groove, a sliding rail with a pivot and a transmission gear, two symmetrical spring gears and two frames. The swing arm is connected to one frame via a hinge, allowing it to rotate around the frame. On the other frame, a sliding rail with a pivot and a transmission gear is mounted for load transmission. Two symmetrical spring gears are fixed on the frame 1 to ensure symmetrical stiffness for swinging in different directions. The rail's transmission gear (40 teeth, module 0.5 mm) meshes with the two spring gears (80 teeth). The pivot position can be adjusted by rotating a screw (M3) using a brush direct-current motor, with the help of a plain shaft ($\Phi 3$ mm) and the screw.

The two spring gears are 3D-printed using 6061 aluminum alloy, providing elasticity through two hollow Archimedes spiral grooves (1.2 cycles, width 2 mm). Aside from the spring gear and standard components, the other parts are 3D-printed using PLA-CF material (polylactic acid with carbon fibers). To prevent distortion of the spring gear during deformation, a small pinion gear (20 teeth) is mounted to mesh with the spring gear, as shown in **Supplementary Fig. 24**.

Supplementary Methods 4 | Working principle of the variable stiffness mechanism

The variable stiffness mechanism is based on the principle of a movable pivot and employs two symmetrically arranged spring gears as elastic elements. The torque generated by the human body driving the swing arm is first transmitted to the pivot, which then drives the sliding rail. The sliding rail applies the load to the spring gears via the transmission gears, and the load is ultimately transferred from the spring gears to the mechanism's frame and finally to the backdrivable motor. The rotation centers of the transmission gear, the geometric center of the pivot, and the rotation center of the swing arm are denoted as Points A, B, and C, respectively (**Supplementary Fig. 24**).

The distance between Points A and B is defined as l_1 ($l_1 = 25 - l$). By adjusting l , the position of the lever system's pivot can be changed, thereby effectively regulating the output stiffness characteristics of the entire mechanism. The pivot (Point B) slides along a groove in the swing arm. When l is set to its minimum value (0 mm), the joint exhibits high compliance. In contrast, when l is set to its maximum value (25 mm), such that Points A and B coincide, the swing arm is locked (degree of freedom = 0), and the theoretical joint stiffness approaches infinity.

Assuming that all components except for the spring gears are rigid bodies, when the swing arm is subjected to an external load, Points A, B, and C form a triangle as shown on the right side of (**Supplementary Fig. 24**). Let $AC = l_0$, $AB = l_1$, $BC = l_2$, and denote the angular displacements of the sliding rail ($\angle BAC$) and the swing arm ($\angle ACB$) as θ_A and θ_C , respectively. The angular deformation of the spring gear is denoted as θ_g . By applying the law of sines, the following relationship can be derived:

$$\frac{l_0}{\sin(\pi - \theta_A - \theta_C)} = \frac{l_0}{\sin(\theta_A + \theta_C)} = \frac{l_1}{\sin \theta_C} \quad (S4)$$

$$\theta_A + \theta_C = \arcsin\left(\frac{l_0}{l_1} \sin \theta_C\right) \quad (S5)$$

232 θ_A can be represented by θ_C as:

$$233 \quad \theta_A = \arcsin\left(\frac{l_0}{l_1} \sin \theta_C\right) - \theta_C \quad (S6)$$

234 Denote the number of gear's teeth on the sliding rail as z_1 and that on the spring gear as z_2 . θ_g can
235 be represented by θ_C as:

$$236 \quad \theta_g = \frac{z_1}{z_2} \theta_A \quad (S7)$$

237 Subsequently, the torque M acting on the swing arm can be calculated based on the angular
238 deformation θ_g of the spring gear and its inherent stiffness k , as given by the following relationship:

$$239 \quad M = k\theta_g = k \frac{z_1}{z_2} \theta_A = k \frac{z_1}{z_2} \left(\arcsin\left(\frac{l_0}{l_1} \sin \theta_C\right) - \theta_C \right) \quad (S8)$$

240 By differentiating with respect to the angular displacement θ_C , the final instantaneous joint stiffness
241 K_{the} is obtained as:

$$242 \quad K_{the} = \frac{dM}{d\theta_C} = k \frac{z_1}{z_2} \cdot \frac{d\theta_A}{d\theta_C} = k \frac{z_1}{z_2} \cdot \left(\frac{l_0 \cos \theta_C}{\sqrt{l_1^2 - l_0^2 \sin^2 \theta_C}} - 1 \right) \quad (S9)$$

243 **Supplementary Methods 5 | Determining optimal stiffness to improve rehabilitation efficacy**

244 Throughout the study, optimal stiffness was assessed before (Pre) and after (Post) the high-intensity
245 isokinetic training phase (**Supplementary Table 11**). The pre-assessed optimal stiffness was used
246 during the high-intensity isokinetic training phase, while the post-assessed stiffness was applied in
247 Follow-up 1 to maximize rehabilitation outcomes.

248 Based upon data generated by the six intervention subjects, the joint stiffness of the isokinetic training
249 robot significantly affects the peak torque output during isokinetic knee extension. Each participant
250 exhibited an individual optimal stiffness prior to training, and our isokinetic robot was engineered to
251 provide variable stiffness from 0.03 to 28.16 N·m/rad. Most subjects demonstrated increased
252 isokinetic training peak torque at the optimal stiffness configuration compared to the maximum
253 stiffness setting, with the remaining cases having an optimal stiffness coinciding with the maximum
254 (**Supplementary Fig. 2**). In detail, participants exhibited 7% (Pre) and 0.5% (Post) higher peak
255 torque compared with the maximum stiffness setting (28.16 N·m/rad, two-sided paired-sample t -test).
256 Additionally, the optimal stiffness increased significantly ($p < 0.01$, two-sided paired-sample t -test)
257 after the 6-week high-intensity isokinetic training phase, and the group mean increased from 21.42 to
258 27.57 N·m/rad. All participants exhibited a similar trend of increased optimal stiffness. These
259 findings suggest that a variable stiffness joint can better facilitate human-robot coupling through
260 impedance matching and maximized power transfer to the robot, manifesting as maximized force
261 exertion under isokinetic constraints.

262 **Supplementary Methods 6 | Personalized robot configuration**

263 Our isokinetic robot incorporated a gear reduction stage between the variable stiffness mechanism
264 and the backdrivable motor. Different gear combinations affect the robot's resistance range
265 (**Supplementary Table 12**). Gear sets with different transmission ratios were selected based on each
266 participant's strength profile. It is important to note that an excessively high gear reduction ratio can
267 introduce considerable friction resistance, potentially impairing the system's ability to finely
268 modulate compliant resistance during isokinetic training. To accommodate the varying strength levels
269 of individual participants, we implemented two configurations: the GIM4310 motor with gear ratios
270 ranging from 3 to 4.5, and the RobStride01 motor with a fixed ratio of 3. As participants exhibited

gains in knee extension torque during the training program, the gears were upgraded to higher transmission ratios to provide sufficient resistance and ensure optimal training effectiveness (**Supplementary Table 13**). In the case of Participant 6, the considerable gains in strength after the high-intensity isokinetic training phase exceeded the braking capacity of the GIM4310 motor. Consequently, the robot was re-engineered with an upgraded motor (Motor RobStride01, transmission ratio of 3) capable of delivering greater braking torque, along with necessary modifications to the mechanical frame (**Supplementary Table 14**).

Supplementary Methods 7 | Ultrasound-based assessment of muscle pennation angles

Measurement of pennation angle using ultrasound was performed to support the calculation of physiological cross-sectional area (PCSA). During the measurements, participants were positioned in a supine posture. A coupling agent was applied to the participant's thigh, and ultrasound imaging (Apogee 2300, SIUI, China) was used to measure the pennation angles of the rectus femoris, vastus medialis, and vastus lateralis. For the vastus intermedius, the pennation angle could not be directly obtained due to its deep anatomical location and increased echogenicity changes observed in SMA patients. In patients with SMA, severe fatty infiltration and structural alterations make accurate ultrasound-based measurement of the vastus intermedius pennation angle challenging^{2,49}. Based on prior studies indicating that the pennation angle of the vastus intermedius is small and roughly aligned with its line of action, it was assumed to be 0° in this study^{3,4}. To ensure the clarity and accuracy of pennation angle measurements, different regions of each muscle were selected: for the rectus femoris, measurements were taken at the muscle belly; for the vastus medialis and vastus lateralis, measurements were obtained at their distal regions. During imaging, a linear-array probe was first used to acquire transverse images of the target muscle, after which the probe was rotated 90° to obtain longitudinal images. The probe was carefully adjusted and slightly repositioned until the pennation angle was visualized.

Reference [49] consistent with main text

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Supplementary Methods 8 | Isotonic and isometric training

To compare differences in muscle activation during isotonic, isometric, and isokinetic knee joint exercises, sEMG signals were recorded from six participants with SMA and six juveniles with normal neuromuscular development. The isokinetic exercises were performed using our robot. Isotonic and isometric exercises were implemented by attaching sandbags to the participants' ankles to provide resistance (**Supplementary Table 15**). The mass of the sandbag (m_s) for each participant was determined using the following formula:

$$m_s = \frac{\tau_a}{l_c \cdot g} \quad (\text{S10})$$

Where τ_a denotes the mean torque generated during isokinetic knee extension, l_c refers to the lower leg length, and g is the standard gravitational acceleration.

In the isotonic condition, participants performed repeated knee extension movements against the sandbag resistance. In the isometric condition, participants were instructed to extend the knee to their maximum attainable position while wearing sandbags and hold the posture for 15 seconds. For SMA patients unable to sustain the position for 15 seconds, the duration was adjusted to the maximum time they could maintain the posture.

313 **Supplementary Methods 9 | Protocol of the follow-up assessment**

314 The assessments were conducted at four time points: before the high-intensity isokinetic training
315 phase (Pre), before the low-intensity isokinetic training phase (Post), before no isokinetic training
316 phase (FU 1) and after no isokinetic training phase (FU 2).

317 The assessment protocol included magnetic resonance imaging, femoral nerve conduction studies,
318 sit-to-stand tests, and assessments of knee extension under isokinetic, isotonic, and isometric
319 conditions. Additionally, optimal stiffness measurements were performed before the onset of both
320 high-intensity and low-intensity isokinetic training. The specific procedures are detailed as follows:

321 First, magnetic resonance imaging was performed at the Department of Radiology, Peking University
322 Third Hospital. A professional radiologist used a uMR 880 scanner to acquire axial scans of both
323 thighs. Subsequently, femoral nerve conduction studies were conducted in the Department of
324 Neurology by an experienced neurologist. The participants then proceeded to the laboratory, where
325 sEMG modules were affixed to the quadriceps of both legs. Sit-to-stand tests were performed to
326 determine the lowest angle at which each participant could successfully stand, during which sEMG
327 data were recorded.

328 Following this, participants donned the rehabilitation robot to perform isokinetic knee extension tests.
329 Each leg completed two sets of 10 repetitions of isokinetic knee extension, with joint torque and
330 angular position data recorded via the laptop. Subsequently, participants wore ankle weights and
331 performed isotonic knee extension training, also in two sets of 10 repetitions per leg. After a 5-minute
332 rest, isometric knee extension tests were conducted, with each leg performing two 15-second trials.
333 sEMG data were continuously recorded during all knee extension tasks. Finally, the sEMG modules
334 were removed, and participants donned the isokinetic robotic device to perform knee extensions under
335 different stiffness settings. Joint torque data were recorded to evaluate and determine the optimal
336 stiffness for each leg.

337 **Supplementary Methods 10 | The principle of generating braking torque**

338 The braking torque was generated through the dynamic braking of the brushless DC motor. As shown
339 in **Supplementary Fig. 25(a)**, the three-phase circuit (phases a , b , c) consists of the equivalent
340 resistors (R_a , R_b , R_c), the equivalent inductances (L_a , L_b , L_c) and the back electromotive forces
341 (E_a , E_b , E_c). The switching of MOSFETs S2, S4, and S6 is driven by a PWM signal with period T
342 and duty cycle D .

343 When the PWM signal is active, the MOSFETs S2, S4, and S6 are turned ON, forming a closed circuit
344 across the two motor windings. Let i denote the instantaneous phase current flowing through the
345 equivalent inductors L_a and L_b during the PWM-ON period. Applying Kirchhoff's Voltage Law
346 and assuming symmetrical parameters ($R_a = R_b = R_c = R$, $L_a = L_b = L_c = L$), the differential
347 equation during the ON period is (**Supplementary Fig. 25(b)**):

$$348 \quad E_a - E_b = iR_a + iR_b + L_a \frac{di}{dt} + L_b \frac{di}{dt} = 2Ri + 2L \frac{di}{dt} \quad (S11)$$

349 Neglecting the resistive term (*i.e.*, $R \approx 0$), we obtain:

$$350 \quad \frac{di}{dt} = \frac{E_a - E_b}{2L} \quad (S12)$$

351 Integrating over the ON duration DT , the current increment during the PWM-ON phase is:

$$352 \quad \Delta i_{on} = \frac{E_a - E_b}{2L} \cdot DT \quad (S13)$$

353 When the PWM signal is low, the MOSFETs are turned OFF, and there is no conductive path for the
354 winding current. Due to the open-circuit condition, the inductor current cannot freewheel smoothly
355 and is instead rapidly forced to zero. The stored magnetic energy is dissipated as heat by the energy-
356 dissipating components within the motor drive circuit. Therefore, the current waveform over a

complete cycle can be approximated as a linear rise during the ON interval $[0, DT]$, followed by an immediate drop to zero. The average phase current i_{avg} over the entire cycle is calculated as:

$$i_{avg} = \frac{1}{T} \int_0^{DT} i(t) dt = \frac{1}{T} \int_0^{DT} \left(\frac{E_a - E_b}{2L} t \right) dt = \frac{(E_a - E_b) D^2 T}{4L} \quad (S14)$$

The average electromagnetic braking torque T_b is proportional to the average current and the motor's torque constant K_t :

$$T_b = K_t \cdot i_{avg} = \frac{K_t (E_a - E_b) D^2 T}{4L} \quad (S15)$$

The motor damping is controlled by adjusting the duty cycle of PWM. A large duty cycle gives large damping, resulting in a low motor speed, and conversely, a short duty cycle results in small damping and a high motor speed. Consequently, by adjusting the duty cycle of PWM, the isokinetic (constant speed) training was realized. While the aforementioned approach represents an ideal scenario, in practice, the current cannot change instantaneously. As a result, when the MOSFETs are turned off, the current is typically non-zero. Moreover, energy can be regenerated and fed back to a capacitor or battery during this phase. Accordingly, the governing equations should be modified to account for these non-ideal effects.

Supplementary Methods 11 | Properties of energy regeneration

Our robot is capable of implementing complementary energy regeneration during isokinetic training. To evaluate the system's regeneration performance, we conducted technical bench tests using a custom-built test rig to validate the energy recovery capabilities of the robot hardware without subjects. In this configuration, the robot employed a GIM4310 motor (SteadyWin, China) with an adjustable gear ratio ranging from 3.0 to 4.5 to encompass the robot's range of possible operating resistances. Tests were performed at all combinations of the gear ratio limits and three angular velocities: 45°, 60°, and 90°/s. For each condition, three repeated experiments were performed, each consisting of 10 extension–flexion cycles.

The voltage elevation profiles of the supercapacitor across all velocity settings indicated a velocity-dependent improvement in cumulative energy harvesting efficiency (**Supplementary Fig. 26**). The robot exhibited progressively enhanced energy regeneration characteristics with increasing angular velocity. Using the RobStride01 motor with a gear ratio of 3, the system achieved energy regeneration levels of 0.25W at 45°/s, 0.72 W at 60°/s, and 1.44 W at 90°/s. When using the GIM4310 motor with the same gear ratio of 3, the corresponding values were 0.05 W, 0.23 W, and 0.46 W at the same angular velocities. With the GIM4310 configured at its maximum gear ratio of 4.5, the energy regeneration values increased: 0.17 W, 0.33 W, and 0.66 W at 45°/s, 60°/s, and 90°/s, respectively. The proportion of regenerated power to the robot's power consumption (%) was also evaluated. With the GIM4310 motor at a gear ratio of 4.5, this proportion reached 100% at an angular velocity of 90°/s. Using the RobStride01 motor with a gear ratio of 3, the ratio reached 109% at 60°/s and 218% at 90°/s. In these scenarios, the proportion exceeded 100%, indicating that self-sustained operation could be achieved.

Powered by a 3.7 V, 3800 mAh lithium battery, the robot had a baseline endurance of 36.5 days without energy regeneration at 60°/s (**Supplementary Table 16**). With a gear ratio of 3 (GIM4310), the proportion of regenerated power relative to total power consumption reached 8%, 36%, and 70% at angular velocities of 45°/s, 60°/s, and 90°/s, respectively. Correspondingly, the system's endurance was extended to 39.8, 56.8, and 120.8 days. Further improvements were observed with a gear ratio of 4.5, where the proportion of regenerated power relative to total power consumption reached 26% at 45°/s and 51% at 60°/s, resulting in endurance extensions to 49.2 and 74.3 days, respectively. Notably, for subject 6, the system achieved self-sustained operation at angular velocities of $\geq 60^\circ/\text{s}$

when equipped with the RobStride01 motor (gear ratio 3), and at $\geq 90^\circ/\text{s}$ with the GIM4310 motor (gear ratio 4.5).

Supplementary Methods 12 | Sensor calibration

Torque was measured using an LZ-NJY40 sensor ($\pm 10\sim 20\text{ N}\cdot\text{m}$). The sensor generated a differential signal proportional to the applied torque and was powered at 5 V. This signal was amplified with a gain of approximately 200 using an operational amplifier and subsequently acquired via an ADC channel of the STM32F405RGT6 microcontroller.

To calibrate the torque sensor, a custom-designed connecting rod and flange were developed to interface with the sensor's output and input shafts, respectively, and secured using screws (Supplementary Fig. 27). The connecting rod was fixed to the sensor's output shaft, and a digital torque wrench (0-20 $\text{N}\cdot\text{m}$ range) was coupled to the flange on the input shaft. The torque wrench was rotated incrementally, and its displayed torque values were recorded while simultaneously acquiring the torque sensor's output voltage via a microcontroller connected to a host computer. Target torque levels were set at 1, 2, 3, 4, 5, and 6 $\text{N}\cdot\text{m}$ and the wrench emitted an audible signal upon reaching each target torque. At these points, the corresponding output voltages from the torque sensor were logged. A linear regression analysis was then conducted to determine the relationship between the torque sensor's output voltage and the actual torque applied, providing a calibration curve for subsequent measurements.

Supplementary Methods 13 | Stiffness adjustment

A 12 V brushed DC motor (200 rpm) is employed to adjust the stiffness of the mechanism, driven by an RZ7899 (Wuxi Smart Microelectronics, China) bidirectional DC motor driver chip. The motor rotates a lead screw, which in turn moves the pivot along the plain shaft. The pivot position is monitored via a sliding potentiometer, whose wiper is mechanically coupled to the pivot. Two GPIO pins of an STM32 microcontroller are used to output high/low signals, enabling forward/reverse motor rotation and a locking function. In manual mode, the motor can be directly controlled using two buttons on the driver board to drive it forward or reverse. In automatic mode, the STM32 continuously reads the pivot position from the potentiometer, compares it with a preset target value, and drives the motor to align the pivot near the target. Once the positional error falls below a specified threshold, the motor halts, thereby achieving closed-loop control.

Supplementary Methods 14 | Stiffness calibration

Stiffness is a fundamental mechanical parameter describing an object's capacity to resist deformation under applied external forces. It provides an indication of the material's rigidity and its resistance to both compressive and tensile stresses. In particular, torsional stiffness refers to the resistance of a structure to angular deformation under applied torque and is commonly defined as the torque required per unit angular displacement, expressed as:

$$K_{the} = \frac{dM}{d\theta_c} \quad (\text{S16})$$

where K_{the} is the torsional stiffness and is typically measured in newton-meters per radian ($\text{N}\cdot\text{m}/\text{rad}$) or newton-meters per degree ($\text{N}\cdot\text{m}/\text{deg}$), M is the applied torque, measured in newton-meters ($\text{N}\cdot\text{m}$). θ_c is the resulting angular displacement, expressed in radians (rad) or degrees (deg).

To ensure system stability during the calibration process, the motor shaft and motor bracket were first securely fixed. The variable stiffness slider was then adjusted to multiple predefined positions, and the shank support (the swing arm of the variable stiffness mechanism) was rotated within a specified angular range. Torque and angle data were synchronously recorded using a torque sensor and an

angular position sensor. The angle sensor was mounted on the opposite side of the swing arm to directly measure its angular displacement. All collected data were transmitted to the host computer for storage and subsequently processed in MATLAB to generate torque-angle curve. The detailed process is outlined below:

The motor rotor was fixed in place to prevent any rotation during the calibration process, while the motor bracket was securely fastened to the table to ensure overall system stability. Subsequently, the swing arm was gently rotated to eliminate any backlash in the transmission mechanism. Prior to calibration, the torque sensor was zeroed to ensure accurate measurements.

The pivot point of the variable stiffness mechanism was sequentially fixed at 13 positions: 0, 5, 10, 13, 15, 16.25, 17.50, 18.75, 20.00, 21.25, 22.50, 23.75 and 25.00 mm. At each stiffness setting, the swing arm of the mechanism was subjected to 10 cycles of bidirectional alternating deformation applied manually in a controlled manner, while experimental data were recorded using the host computer software. It is important to note that as the stiffness increased, the deformation was reduced. After decoding the recorded data using MATLAB, plots of angle and torque as functions of time were generated. During analysis, the initial and terminal data segments reflecting backlash were excluded. A segment with consistent variation was selected to construct the torque-angle curves (**Supplementary Fig. 28**). Each curve was then fitted linearly, and the slope of the fitted region was calculated to obtain the stiffness at that position, expressed in N·m/rad. A scatter plot of stiffness versus pivot position was subsequently generated, and a cubic polynomial fitting was applied to establish the relationship between stiffness and pivot position.

Supplementary Methods 15 | Biomechanical knee extension model

The knee joint can be modeled as a bio-mechanical system composed of two skeleton bones: femur and tibia, and two antagonistic muscle groups: the quadriceps femoris, which primarily facilitates knee extension, and the hamstring muscles, which primarily drive knee flexion, as illustrated in **Supplementary Fig. 29**. The angle formed between the femur and tibia is defined as the knee angle θ , with its time derivative $\dot{\theta}$ representing the angular velocity of knee movement. The quadriceps generate a contractile force denoted as F_Q , while the hamstrings produce a force F_H . Additionally, G represents the gravitational force acting on the calf segment. Each of these forces acts through a specific moment arm: l_Q for the quadriceps, l_H for the hamstrings, and l_G for gravity.

The net torque T applied to the isokinetic training robot reflects the resultant moment from these three contributors:

- Torque from the quadriceps: $T_Q = F_Q \cdot l_Q$
- Torque from the hamstrings: $T_H = F_H \cdot l_H$
- Torque due to the calf weight: $T_G = G \cdot l_G$

According to the principle of moment equilibrium, the total torque at the knee joint is given by:

$$T = T_H + T_Q + T_G \quad (S17)$$

According to Hill's three-element muscle model⁵, the quadriceps femoris can be represented by a serial element (SE), contractile element (CE), and a parallel element (PE) as illustrated in **Supplementary Fig. 29**. The total force generated by the muscle is equal to the force in the serial element, denoted as F_{SE} , which consists of the active contractile force from the CE (F_{CE}) and the passive force from the PE (F_{PE}), *i.e.*, $F = F_{CE} + F_{PE}$. The active force F_{CE} is modeled as a product of four components⁶: the maximum voluntary contractile force (MVC, denoted by F_m), the muscle activation level (α), the force-length factor (w_l), and the force-velocity factor (w_v). The passive

487 component F_{pE} contributes minimally throughout most of the movement range, with its peak value
 488 typically below 10% of F_m at full extension⁷. Therefore, F_{pE} is considered negligible, and the total
 489 force from the quadriceps F_Q is approximated as:

$$490 \quad F_Q \approx F_{CE} = F_m \cdot \alpha \cdot w_l \cdot w_v \quad (S18)$$

491 The focus of the current study is on isokinetic knee extension training. During maximal knee
 492 extension, the contribution of the hamstring muscles is assumed negligible, *i.e.*, $T_H = 0$. In addition,
 493 the isokinetic robot compensates for the gravitational torque from the calf ($T_G = 0$) through a self-
 494 weight calibration procedure. As a result, the net joint torque T is mainly due to the quadriceps:

$$495 \quad T \approx T_Q = F_Q \cdot l_Q \approx F_{CE} \cdot l_Q \quad (S19)$$

496 When the quadriceps femoris generates the maximum torque T_m , the corresponding muscle force is
 497 F_{op} and the associated moment arm is l_{op} : $T_m = F_{op} \cdot l_{op}$. Given the structural and functional
 498 similarities between the elbow and knee joints, it is reasonable to adapt muscle-joint torque models
 499 developed for the elbow to the knee. In this context, the torque generated during knee extensions
 500 depends on activation level α , joint angle θ , and angular velocity $\dot{\theta}$:

$$501 \quad T \approx T_m \cdot \alpha \cdot \widetilde{w}_l(\theta) \cdot w_v(\dot{\theta}) \quad (S20)$$

502 The function $\widetilde{w}_l(\theta)$ can be rewritten as:

$$503 \quad \widetilde{w}_l(\theta) = \frac{F_m}{F_{op}} \cdot \frac{l_Q(\theta)}{l_{op}} \cdot w_l(\theta) \quad (S21)$$

504 The muscle activation level α is further modeled as a function of the circumferential muscle strain s
 505 during isokinetic contractions, based on prior studies⁸. A linear simplified approximation is used:

$$506 \quad \alpha = \alpha(s) \approx ks + b \quad (S22)$$

507 Where:

$$508 \quad k = k_1(\theta) \cdot k_2(\dot{\theta}) \quad (S23)$$

509 If $b = 0$, substituting Eq. S22 and Eq. S23 to Eq. S20 gives:

$$510 \quad T \approx T_m \cdot s \cdot W_l(\theta) \cdot W_v(\dot{\theta}) \quad (S24)$$

511 Where:

$$512 \quad W_l = k_1(\theta) \cdot \widetilde{w}_l(\theta) \quad (S25)$$

$$513 \quad W_v = k_2(\dot{\theta}) \cdot w_v(\dot{\theta}) \quad (S26)$$

514 To account for subject variability, the strain s is normalized by the maximum strain $s_{max}(\theta)$ at a
 515 given joint angle, yielding the normalized strain β ($0 \leq \beta \leq 1$): $\beta = s/s_{max}(\theta)$ ⁸. The final expression
 516 for knee joint torque becomes:

$$517 \quad T \approx T_m \cdot \beta \cdot \widetilde{W}_l(\theta) \cdot \widetilde{W}_v(\dot{\theta}) \quad (S27)$$

518 with

$$519 \quad \widetilde{W}_l = k_1(\theta) \cdot s_{max}(\theta) \cdot \frac{F_m}{F_{op}} \cdot \frac{l_Q(\theta)}{l_{op}} \cdot w_l(\theta) \quad (S28)$$

$$\widetilde{W}_v = k_2(\dot{\theta}) \cdot w_v(\theta) \quad (S29)$$

The net torque T applied to the isokinetic training robot is determined by these factors, and the modeling framework is detailed in Eq. S17-S29.

Supplementary Methods 16 | Gamified human-machine interface enhances participant engagement and compliance

Several studies have demonstrated that the integration of gamification elements, such as goal setting, real-time feedback, and reward systems, into human-computer interaction (HCI) designs can significantly improve user motivation, participation, and long-term adherence. For instance, a study published in *Journal of Technology in Behavioral Science* reported that gamified interventions led to higher usage frequency and improved retention in 2025⁽⁹⁾. Likewise, a systematic review of 86 brain-computer interface (BCI) studies concluded that gamification strategies consistently enhanced user experience and engagement in 2024⁽¹⁰⁾. Additional evidence from *Technology in Society and Multimodal Technologies*^{11,12} further confirms the positive impact of gamified features in maintaining user compliance across various domains.

Supplementary Methods 17 | Inverse dynamic analysis during sit-to-stand

As shown in **Supplementary Fig. 30**, the participant's arms, thighs, and body (trunk) were modeled as rigid rods, while the head was considered as a point mass. During the sit-to-stand transition, the part segments above the knee were assumed to maintain fixed relative positions. The part movement above the knee during sit-to-stand can be described by the following equation¹³:

$$\tau - mgl\cos\gamma = I \cdot \ddot{\gamma} \quad (S30)$$

where τ denotes the torque generated by the knee joint, m represents the mass of the part segments above the knee (including the arms, thighs, body, and head), l is the distance from the center of mass of the part above the knee to the knee joint, γ is the angle between the line connecting the knee joint to the center of mass and the horizontal plane, and I is the moment of inertia of the part segments above the knee about the knee joint.

$\ddot{\gamma}$ is obtained by processing data from the IMU, which is attached directly above the subject's thigh; l is obtained by first determining the position of the center of mass of the part above the knee¹³, and I is calculated by the following equation:

$$I = I_a + I_t + I_b + I_h \quad (S31)$$

Where the moments of inertia of the participant's arms, thighs, body, and head about the knee joint are denoted as I_a , I_t , I_b and I_h , respectively, as described below:

$$I_a = \frac{1}{3} m_a l_a^2 \quad (S32)$$

$$I_t = \frac{1}{3} m_t l_t^2 \quad (S33)$$

$$I_b = \frac{1}{12} m_b l_b^2 + m_b r_b^2 \quad (S34)$$

$$I_h = m_h l_h^2 \quad (S35)$$

Where m_a , m_t , m_b , and m_h represent the masses of the arms, thighs, body, and head, respectively^{14,15}. Likewise, l_a , l_t , l_b and l_h denote the lengths of these segments, respectively. To simplify the modeling, the head was regarded as a point mass, and $l_h = l_a$. The r_b denotes the distance from the center of mass of the body to the knee joint. Peak knee extension torque using inverse dynamic analysis during sit-to-stand (end of Follow-up 2) is shown in **Supplementary Table 17**.

561 **Supplementary Notes**

562 **Supplementary Notes 1 | Isokinetic training is a more effective resistance training method**
563 **compared to isometric and isotonic training**

564 Resistance rehabilitation exercises can be broadly categorized into isotonic, isometric, and isokinetic
565 training based on the type of muscle contraction¹⁶⁻¹⁸. Isotonic training involves dynamic muscle
566 contractions with constant load but varying speed, commonly used in resistance exercises such as
567 weight lifting. Isometric training refers to static contractions where the muscle generates force
568 without joint movement, often applied to maintain strength or stabilize joints. In contrast, isokinetic
569 training involves dynamic contractions performed at a constant angular velocity, allowing maximal
570 muscle tension throughout the full range of motion¹⁶⁻²⁰. This constant-speed characteristic naturally
571 integrates a safety mechanism that reduces resistance if the patient experiences pain or discomfort²¹,
572 while also enabling continuous monitoring of rehabilitation progress through objective assessments
573 of muscle strength^{22,23}. Recent studies have demonstrated the effectiveness of isokinetic training for
574 knee rehabilitation²⁴⁻²⁶, such as enhancing muscle strength, improving stability, increasing
575 postoperative walking speed, and reducing knee pain, in various knee conditions, including anterior
576 cruciate ligament (*ACL*²⁴), posterior cruciate ligament (*PCL*²⁵) and osteoarthritis (*OA*²⁶).

577 **Supplementary Notes 2 | A lack of rehabilitation strategies for juveniles with SMA**

578 To date, rehabilitation interventions targeting juveniles with spinal muscular atrophy (SMA) remain
579 poorly studied, and there is a notable lack of high-quality evidence systematically evaluating their
580 efficacy. While physical therapy and exercise programs are routinely recommended as part of
581 standard care to maintain muscle strength and function, most existing studies are limited by small
582 sample sizes, heterogeneous protocols, and a predominant focus on adult populations or animal
583 models. For example, a recent narrative review by Ref. [34] highlighted the scarcity of rigorous
584 clinical trials specifically addressing rehabilitative exercise outcomes in pediatric SMA, emphasizing
585 that most protocols rely on passive or low-intensity modalities with unclear functional benefits.
586 Similarly, Ref. [27] concluded that although strength and mobility exercises are widely prescribed,
587 their impact on long-term motor function and quality of life in juveniles with SMA remains largely
588 anecdotal and under-researched. Supporting this, Ref. [33] conducted a scoping review and found a
589 disproportionate research focus on adult populations, while pediatric rehabilitation remains
590 underrepresented. This gap underscores an urgent need for well-designed clinical trials to establish
591 evidence-based rehabilitation strategies tailored for this vulnerable population.

592 **References [33] and [34] consistent with main text**

- 593 33. Wan, H. W. *et al.* Health, wellbeing and lived experiences of adults with SMA: a scoping
594 systematic review. *Orphanet J. Rare Dis.* **15**, 70 (2020).
595 34. Mortenson, P., Cielecka, J., Harrison, E. *et al.* Rehabilitation practices for childhood spinal
596 muscular atrophy. *Disabil. Rehabil.* **47**, 1–10 (2025).

597 **Supplementary Notes 3 | Resistive training is superior compared to assistive training**

598 We have carefully considered the distinction between resistive and assistive training approaches
599 (**Supplementary Table 18**). Accumulating evidence supports the superiority of resistive training in
600 promoting neuromuscular engagement, strength gains, and functional performance. For example, Ref.
601 [29] demonstrated that resistive robotic training led to significantly greater improvements in upper-
602 limb motor function post-stroke compared to active-assisted modalities. Similarly, Ref. [30] found
603 that strength-based training outperformed robot-assisted gait training in enhancing walking speed in
604 individuals with incomplete spinal cord injury. In the context of athletic performance, both Ref. [31]
605 and Ref. [28] reported that resisted sprint or plyometric training yielded superior improvements in
606 acceleration and jump height compared to assisted training, likely due to greater muscular loading

607 and motor unit recruitment. These findings collectively support the rationale for prioritizing resistive
608 training in our study design, particularly for individuals who retain partial voluntary control.

609 **Supplementary Notes 4 | Conventional rehabilitation programs for juveniles with SMA**

610 Conventional rehabilitation programs for juveniles with neuromuscular disorders have primarily
611 relied on isometric or isotonic training (physical exercises)^{32,33}, and these programs are typically
612 delivered in passive or low-engagement formats. While such approaches may be valuable for
613 maintaining basic muscle strength or in the early stages of recovery, they offer limited neuromuscular
614 stimulation and lack dynamic loading across the full range of joint motion.

615 **Supplementary Notes 5 | Achieving a full upright standing posture requires multi-muscle** 616 **synergy**

617 Regarding the concern that participants were still unable to stand fully upright, it is important to
618 clarify that our study specifically targets the quadriceps femoris, the primary muscle responsible for
619 knee extension during the transition from sitting to standing. Achieving full upright posture is a
620 complex movement that requires the coordinated engagement of the lumbar, abdominal, and hip
621 muscles³⁴⁻³⁶. Our training device is designed to effectively strengthen the quadriceps femoris,
622 addressing the primary weakness experienced by subjects with SMA in the process of rising from a
623 seated position. However, attaining complete upright standing would require additional training
624 focused on the associated muscle groups.

625 **Supplementary Notes 6 | Peak extension torque measured by the dynamometer is comparable** 626 **to values observed in previous study on SMA adults (*Nature medicine* - Ref. [36]) and healthy** 627 **juveniles from our study**

628 We analyzed data from participant SMA01 reported in Ref. [36], who consistently maintained
629 standing and walking abilities. Following the intervention, SMA01 demonstrated a normalized
630 maximum knee extension torque of 0.26 N·m/(kg·m) (Torques were normalized to body-mass times
631 height.) (**Supplementary Fig. 31**). By comparison, the average normalized peak knee extension
632 torque among participants in our study was 0.16 N·m/(kg·m). SMA01 is a 22-year-old adult
633 diagnosed with SMA type III. He presented with mild motor impairments and was able to stand and
634 walk independently prior to study enrolment. However, all six of our participants are juveniles
635 diagnosed with SMA type II and were non-ambulatory. SMA classification is based on motor function
636 and age of onset, with individuals with SMA type II exhibiting more severe motor impairment than
637 those with type III. Given these considerations, the lower torque output observed in our participants
638 compared to SMA01 is consistent with their clinical classification and motor functional status.

639 An age-matched group of six healthy juveniles was recruited to provide reference data. These
640 participants were free of neuromuscular or orthopedic conditions and exhibited normal motor
641 development. They completed muscle strength assessments using our robot. The group's average
642 normalized peak knee extension torque was 0.33 N·m/(kg·m), which was more than twice the value
643 observed in the SMA group. However, it remained lower than the 1.17 N·m/(kg·m) reported for
644 healthy individuals in Ref. [37], highlighting that peak knee extension torque using our isokinetic
645 robot and that using the inverse dynamic analysis during sit-to-stand movement are not directly
646 comparable.

647 However, we also analyzed the peak knee extension torque using the inverse dynamic analysis during
648 sit-to-stand movement. And the average normalized peak knee extension torque across the 6
649 participants was 0.98 Nm/(kg·m), which, although lower than the value of 1.17 Nm/(kg·m) reported
650 for healthy individuals in Ref. [37], remains comparable and within the same order of magnitude
651 (**Supplementary Table 17**).

652 **Reference [36] consistent with main text**

653 36. Prat-Ortega, G. *et al.* First-in-human study of epidural spinal cord stimulation in individuals with
654 spinal muscular atrophy. *Nat. Med.* **31**, 1246–1256 (2025).

655 **Supplementary Notes 7 | Comparison with results of Ref. [38]**

656 The system in Ref. [38] applies resistance during the swing phase of walking, implying that the user
657 must be able to walk to benefit from the intervention, thus excluding lower-functioning patients such
658 as those with Type II SMA. Moreover, there is no clear evidence that the resistance applied in these
659 systems follows an isokinetic pattern, which may limit their suitability for precise, controlled
660 rehabilitation. In contrast, our isokinetic platform enables high-repetition, targeted training in a seated
661 position, offering a safe and effective rehabilitation option for this population. Our robot operates in
662 a fully passive mode, driven by participants. The robot can provide real-time monitoring of key
663 biomechanical parameters such as joint angular velocity, ROM, and torque. This enables clinicians
664 to develop individualized training protocols based on objective data. The passive feature of our
665 system ensures safety, especially for users with severe motor impairment, and allows for accurate
666 quantification of neuromuscular improvements, something that is often difficult to achieve during
667 dynamic, gait-based resistive training. Moreover, due to the inherent efficiency of isokinetic
668 resistance in activating target muscle groups, our robot facilitates more effective strengthening of the
669 knee joint. For instance, we observed significantly greater gains in knee extension ROM compared
670 to the resistive robot study³⁸. In our SMA type II participants, who are non-ambulant, we achieved
671 improvements of 24.5° (right leg) and 18.1° (left leg), whereas their study, conducted on ambulatory
672 juveniles with cerebral palsy, reported only 15.2° (right leg) and 7.9° (left leg) (**Supplementary**
673 **Table 19**).

674 **Supplementary Notes 8 | A variable-stiffness joint enhances the robot's compatibility with the**
675 **human knee joint**

676 Several studies have shown that human muscles and joint stiffness are not fixed but can be modulated
677 to accommodate different motor tasks and environmental demands (**Supplementary Table 20**)³⁹⁻⁴³.
678 Ref. [39] highlights stiffness as one of the most critically regulated properties of muscle. Ref. [40-42]
679 further demonstrate that muscle co-contraction modulates muscle or limb stiffness. Ref. [43]
680 demonstrated that the central nervous system gradually reduced the balance strategy of using muscle
681 co-contraction to increase joint stiffness and damping. Collectively, these findings indicate that
682 human muscle and joint stiffness are not static but are dynamically tuned to optimize motor
683 performance and maintain stability under varying biomechanical and environmental conditions.

684 A variable-stiffness joint offers distinct advantages over rigid joints in human-robot coupling by
685 providing adaptive compliance, which enhances comfort and better accommodates natural movement
686 patterns. Specifically, variable stiffness mechanisms have been shown to absorb perturbations
687 efficiently, thereby improving joint control during spasticity and involuntary movements common
688 among users with motor impairments⁴⁴. Such joints significantly reduce misalignment issues, thus
689 decreasing undesired interaction forces and internal joint loading⁴⁵. Furthermore, variable stiffness
690 interfaces demonstrate superior backdrivability, improving mechanical transparency, and increasing
691 voluntary effort by facilitating smoother force transfer. Collectively, these features contribute to
692 increased user comfort, safer interactions, and improved biomechanical performance compared to
693 traditional rigid joints, highlighting their potential for broader adoption⁴⁴⁻⁴⁷.

694 In this study, we hypothesized that the stiffness of the robot would influence the participants' ability
695 to generate maximum muscular force. Based on this hypothesis, we conducted an experiment to
696 determine the optimal stiffness that elicits the maximum peak torque during isokinetic knee extension
697 movements (**Supplementary Methods**). We determined that an optimal stiffness existed for each
698 participant and observed that its magnitude increased throughout isokinetic training (**Extended Data**
699 **Fig. 1**). Considering optimal stiffness' positive correlations to other neuromuscular outcomes of our

study (**Figs. 4 and 5**), we further hypothesized that the continuous relationships between optimal stiffness, muscle hypertrophy, and increased CMAPs can be determined with more frequent measurements of each throughout a phase of isokinetic training. This may enable estimation of physiological improvements of clinical relevance without invasive measurements using optimal stiffness as a proxy. Because optimal stiffness is the series compliance setting of a robotic joint operating with variable damping to provide isokinetic training, it can feasibly be applied as a singular metric to determine the set of devices that is available to a specific patient, *i.e.*, in a future where multiple isokinetic training devices are available, they may be procedurally determined as suitable for a patient if the range of possible series compliance settings includes the patient's optimal stiffness setting.

Supplementary Notes 9 | Revised hammersmith scale

The Revised Hammersmith Scale (RHS) is a clinically validated, performance-based motor function assessment specifically developed for ambulant and non-ambulant individuals with SMA types II and III. It was introduced to improve upon the sensitivity and functional coverage of earlier scales, such as the original Hammersmith Functional Motor Scale and its expanded version, by incorporating refined scoring criteria, broader item coverage, and an improved testing protocol. The RHS comprises 36 items arranged hierarchically, assessing motor functions across domains such as axial control, upper and lower limb function, transitional movements, standing, and gait. Each item is scored on a 0-2 or 0-1 ordinal scale depending on complexity, resulting in a maximum total score of 69. The scale has demonstrated high inter-rater reliability, strong construct validity, and good responsiveness to clinical change in natural history studies and therapeutic trials⁴⁸.

In the present study, all 6 participants completed RHS assessments conducted by trained physiotherapists. Individual scores were 35, 29, 42, 35, 34, and 40, respectively (**Supplementary Fig. 32 and Supplementary Table 7**). The mean RHS score was 35.83 with a standard deviation of 4.62, indicating a moderate range of functional heterogeneity within the cohort.

One item evaluates a participant's ability to rise from a seated 90°/90° position (hips and knees at 90 degrees) using a plinth, bench, or chair (**Supplementary Table 21**). The assessment allows for external support, and scores range from 0 to 2:

- Score 2: Able to stand up without using arms (arms folded, feet do not move)
- Score 1: Able to stand using compensatory strategies (e.g., hands on legs/chair, turning prone, widening base)
- Score 0: Unable to stand up

In our study, 3 out of 6 participants improved from a score of 0 to 1, indicating newly acquired ability to stand with minimal support strategies. The other three participants reported that, while they remained at score 1, they now found it noticeably easier to stand up, requiring only light assistance.

Supplementary Notes 10 | Juvenile with Type II SMA failed to use commercial stationary isokinetic device due to high friction (> 5 N·m from our experiment)

In our preliminary experiments, we observed that pediatric participants with SMA had muscle strength that was far too weak to effectively use the commercial isokinetic training device. For instance, when one participant's knee joint torque improved to approximately 5 N·m, we arranged a trial session using a standard isokinetic dynamometer. However, the juvenile was still unable to complete the movement cycle properly, indicating that even moderate gains in torque were insufficient to meet the mechanical demands of commercial devices. Notably, all participants in our

study had initial peak torque values below 3.66 N·m, rendering them uniformly incapable of engaging with such traditional systems for meaningful training (**Supplementary Table 22**). Furthermore, conventional isokinetic machines are large, heavy, and prohibitively expensive, typically requiring installation and operation in specialized clinical or hospital settings. This limits their accessibility for juveniles with SMA, who often require frequent, flexible, and ideally home-based rehabilitation sessions. These limitations, both biomechanical and logistical, highlighted the urgent need for an alternative solution. In response, we developed a lightweight (0.96 kg), low-cost (**Supplementary Table 23**), wearable isokinetic resistance training device specifically designed to accommodate the unique physical limitations and practical needs of juveniles with SMA. The system's portability, low friction resistance ($\leq 0.7\sim 1.5$ N·m) (**Supplementary Table 12**), and task-specific design make it well suited for early-stage neuromuscular intervention, particularly in low-strength populations that cannot benefit from traditional stationary devices. In our closed-loop isokinetic control system, velocity feedback is utilized to provide an adaptive and accommodating resistance. The resistance level is not fixed, but instead, it varies based on the exerted force of the subject during training. For example, both subject 2 and subject 6 underwent isokinetic training at a speed of 60°/s (**Supplementary Fig. 33**). Their isokinetic torque curves reflect the differences in knee extension torque, *i.e.*, the varying levels of resistance applied by the robot, which is dynamically adjusted according to the force generated by the subject. Therefore, the resistance is tailored to each subject's abilities.

Supplementary Notes 11 | Isokinetic torque comparison (at 60°/s): SMA type II (pre/post intervention) vs. healthy

During isokinetic training at a standardized angular velocity of 60°/s, the healthy subject H5 demonstrated clear advantages in both the duration of sustained movement and peak torque generation. Specifically, she was able to maintain isokinetic knee extension for a longer period and produced substantially higher peak torque compared to the SMA participant. Prior to intervention, the SMA subject 2 exhibited limited functional capacity, producing peak torques of only 1.44 N·m (right) and 1.59 N·m (left). However, following 6 weeks of high-intensity isokinetic training, notable improvements were observed. Peak torques increased to 2.12 N·m and 2.31 N·m, respectively. Crucially, these gains were accompanied by extended durations of sustained isokinetic contraction and elevated sEMG amplitudes. While still below the torque levels observed in the healthy juvenile, these gains indicate adaptive neuromuscular improvements and enhanced motor output capacity as a result of the training.

Supplementary Notes 12 | Muscle activation during the sit-to-stand transition: comparison between healthy and SMA type II juvenile

sEMG data recorded during the sit-to-stand transition revealed pronounced differences in muscle activation strategies between the two participants. The healthy juvenile exhibited a brief, high-amplitude burst of quadriceps activation during the transition phase, followed by minimal activity once an upright posture was achieved. This pattern is consistent with the functional role of the quadriceps in initiating knee extension rather than maintaining postural stability (**Supplementary Fig. 34**). In contrast, the SMA participant required more time to complete the sit-to-stand transition and displayed prolonged quadriceps activation even after standing. This sustained activity may reflect compensatory mechanisms due to weakness in other muscle groups, such as the gluteal or trunk extensor muscles, which normally assist in stabilizing posture.

Supplementary Notes 13 | Gravity compensation enhances torque-sEMG alignment

All sEMG data underwent DC offset removal, band-pass filtering (20-450Hz), full wave-rectification, and low-pass filtering with a 1 Hz cut-off to create linear envelopes (**Supplementary Fig. 35**). After applying gravity compensation, we indeed observed that the torque profiles more clearly reflect the

790 extended muscle activation seen in the sEMG (**Supplementary Fig. 36**). Specifically, the
791 compensated torque traces show a longer duration of force output that aligns more closely with the
792 extended period of sEMG activation during knee extension.

793 **Supplementary Notes 14 | Fatigue onset analysis**

794 To explore whether fatigue may have influenced the results, we analyzed the distribution of these top
795 20 peak torque values across the full training session. Because the number of sessions varied between
796 participants, we normalized the session progress for each individual (*i.e.*, 100% representing
797 completion of all sessions within one trial). The resulting distributions did not show a consistent
798 decline in peak torque over time (**Supplementary Fig. 37**). Instead, the top torque efforts appeared
799 relatively randomly distributed throughout the session, suggesting that fatigue did not systematically
800 affect performance. We believe this may be partly attributable to our experimental design:
801 participants were instructed to alternate between left and right legs throughout training, a strategy
802 specifically aimed at minimizing localized fatigue and preserving training quality.

803 **Supplementary Notes 15 | Benchmarks of performance with alternative methodologies**

804 We conducted a benchmarking of the performance with alternative methodologies including assistive
805 robot¹, isotonic & isometric physical training²¹, non-invasive transcutaneous spinal cord stimulation³⁵
806 and epidural spinal cord stimulation³⁶ (**Supplementary Table 24**). Our study demonstrated some
807 improvements in knee joint strength and range of motion (ROM) compared to these four studies.
808 Moreover, we found that given the same training durations, isotonic and isometric training
809 (conventional training therapy) could maintain the improvements achieved through isokinetic training.
810 In addition, by measuring electrophysiological indicators of femoral nerve conduction, we observed
811 that high-activation isokinetic training induced neural improvements, which may offer valuable
812 insights for guiding neuromuscular rehabilitation in individuals with SMA.

813 The comparison was performed from the following perspectives:

814 Our high-activation isokinetic training increased knee extension strength beyond that provided by
815 robot therapeutics, spinal stimulation, and conventional exercise. The effectiveness of physical
816 exercise in individuals with SMA remains controversial. Ref. [21] and Ref. [36] reported that physical
817 training had no significant impact on SMA patients. For example, physical exercise was associated
818 with a 7% decline in torque^{21,36}. In contrast, Ref. [1] demonstrated that physical training with an
819 assistive robot improved knee extension torque. In our study, we employed a more efficient isokinetic
820 resistance training approach and showed that high-activation isokinetic training enhanced muscle
821 strength in juveniles with SMA type II. Following high-activation isokinetic training with our
822 isokinetic robot, participants' average peak torque increased by 130%, surpassing the 90.3%
823 improvement reported with assistive robot rehabilitation¹ and the 44.4% gain observed after epidural
824 spinal cord stimulation³⁶ (**Supplementary Fig. 38a**).

825 Our isokinetic training improved range of motion (ROM). Although assistive robot rehabilitation
826 resulted in notable improvements (90.3%)¹ in knee extension strength, the participants' knee ROM
827 paradoxically decreased by an average of 1.65°⁽¹⁾, indicating an inconsistency between muscle
828 strength and joint mobility (**Supplementary Fig. 38b**). A non-invasive transcutaneous spinal cord
829 stimulation approach increased the average knee ROM by 13° in patients with SMA type II and 2.75°
830 in patients with SMA type III³⁵. However, the study did not report whether this intervention improved
831 knee extension torque³⁵. In our study, high-activation training with the isokinetic robot not only
832 produced substantial gains in knee extension torque but also led to concurrent improvements in ROM,
833 with an average increase of 21.31°, surpassing the ROM enhancement achieved by non-invasive
834 electrical stimulation. This further demonstrates the efficacy of training using our robot.

Given the same training durations, isotonic and isometric training can help maintain the gains from prior isokinetic training (Follow-up 2). In accordance with medical ethics, juveniles required continuous rehabilitative training throughout the study, making a no-exercise control during follow-up unfeasible. To ensure consistency, all training sessions were matched in duration, whether using our isokinetic robot or performing conventional isotonic or isometric exercises. Motor function improvements achieved through our intervention were maintained during both follow-up phases. Notably, knee extension torque slightly increased during the low-intensity isokinetic training maintenance phase and remained stable even during the subsequent no isokinetic training period. In comparison, Ref. [36] using epidural spinal cord stimulation, reported a functional decline during the follow-up phase (**Supplementary Fig. 38c**). These findings suggest that given equal training durations, high-activation isokinetic training can produce greater immediate gains in motor performance, and conventional isotonic & isometric training can retain the gains.

Our experimental protocol proffers a reconciliation of previous conflicting results by emphasizing the relative importance of high-activation isokinetic training in rehabilitative outcomes: low-activation conventional training may merely maintain existing musculature, whereas high-activation isokinetic training can yield significant strength improvements and hypertrophy. If so, the enhanced effectiveness of isokinetic training likely stems from sustaining maximal muscle tension throughout a joint's full range of motion as a consequence of enforcing constant velocity. Additionally, traditional physical training often fails to balance safety with intensity in the context of children with SMA who are highly susceptible to fatigue and muscle damage⁴⁹⁻⁵¹.

Preliminary evidence from our CMAP analysis suggests that high-activation isokinetic training improves and low-activation conventional training preserves femoral nerve conduction in participants with SMA. In addition to measuring conventional muscular outcomes, our study incorporated neural conduction metrics, specifically, femoral nerve conduction as reflected by compound muscle action potential (CMAP), which have not been reported in previous research on resistance training in individuals with SMA (**Supplementary Table 25**). The nerve conduction indicator offers a direct and objective assessment of neuromuscular system integrity and function, complementing conventional measures such as MRI-based muscle cross-sectional area and biomechanical torque output. Due to the severe muscle weakness of our participants (unable to walk or perform sit-to-stand, SMA type II), commonly used motor function tests, such as the 6-minute walk test or the timed up-and-go test, could not be performed. Therefore, the 6-minute walk test or the timed up-and-go test were omitted from our study. In addition, we found that CMAP values improved significantly following high-activation isokinetic training (+19%) and were maintained under low-intensity conditions. Isokinetic resistance training, by enabling safe and consistent delivery of high-activation muscle loading, appears particularly well-suited for this population with limited mobility. By integrating neural conduction metrics into our evaluation framework, we not only offer new insights into the neurophysiological effects of isokinetic resistance training in SMA patients, but also lay the foundation for more comprehensive and multidimensional efficacy assessments in future clinical trials, especially for patients with severely limited motor function.

References [1], [21], [35] and [36] consistent with main text

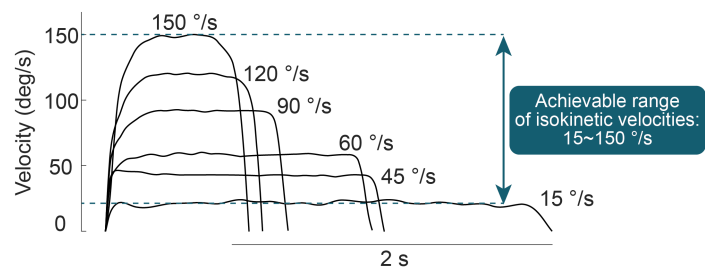
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35. Novikov, A., et al. First use of non-invasive spinal cord stimulation in motor rehabilitation of children with spinal muscular atrophy. *Life* **13**, 449 (2023).
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884 **Supplementary Notes 16 | More information**

885 **Supplementary Table 26** details the knee joint training exercises and their corresponding durations
886 for subjects during conventional training. A comparison between our initial and revised study
887 protocols is provided in **Supplementary Table 27**, while **Supplementary Table 28** contrasts our
888 sample size with those of previous studies. Furthermore, **Supplementary Table 29** presents diverse
889 perspectives on the efficacy of exercise for individuals with spinal muscular atrophy. The current gap
890 in research regarding the long-term effects of exoskeleton use is highlighted in **Supplementary Table**
891 **30**. Finally, **Supplementary Table 31** summarizes the literature on the challenges associated with
892 small sample trials.

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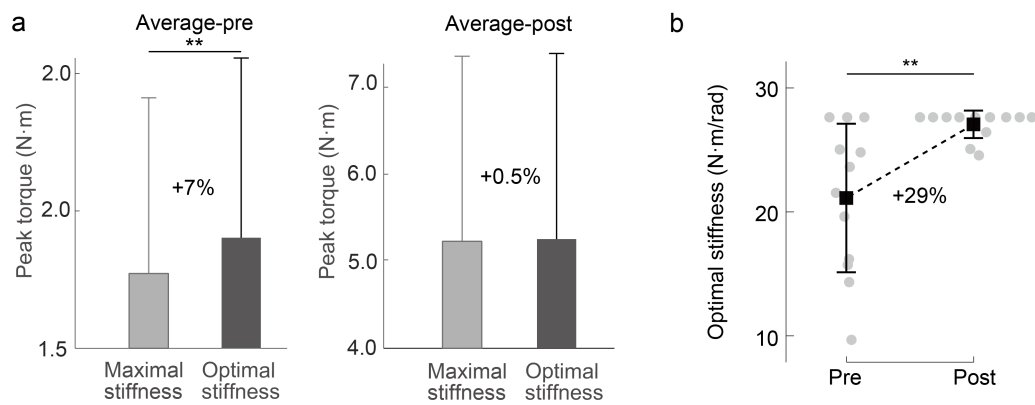
894 **Supplementary Figures**



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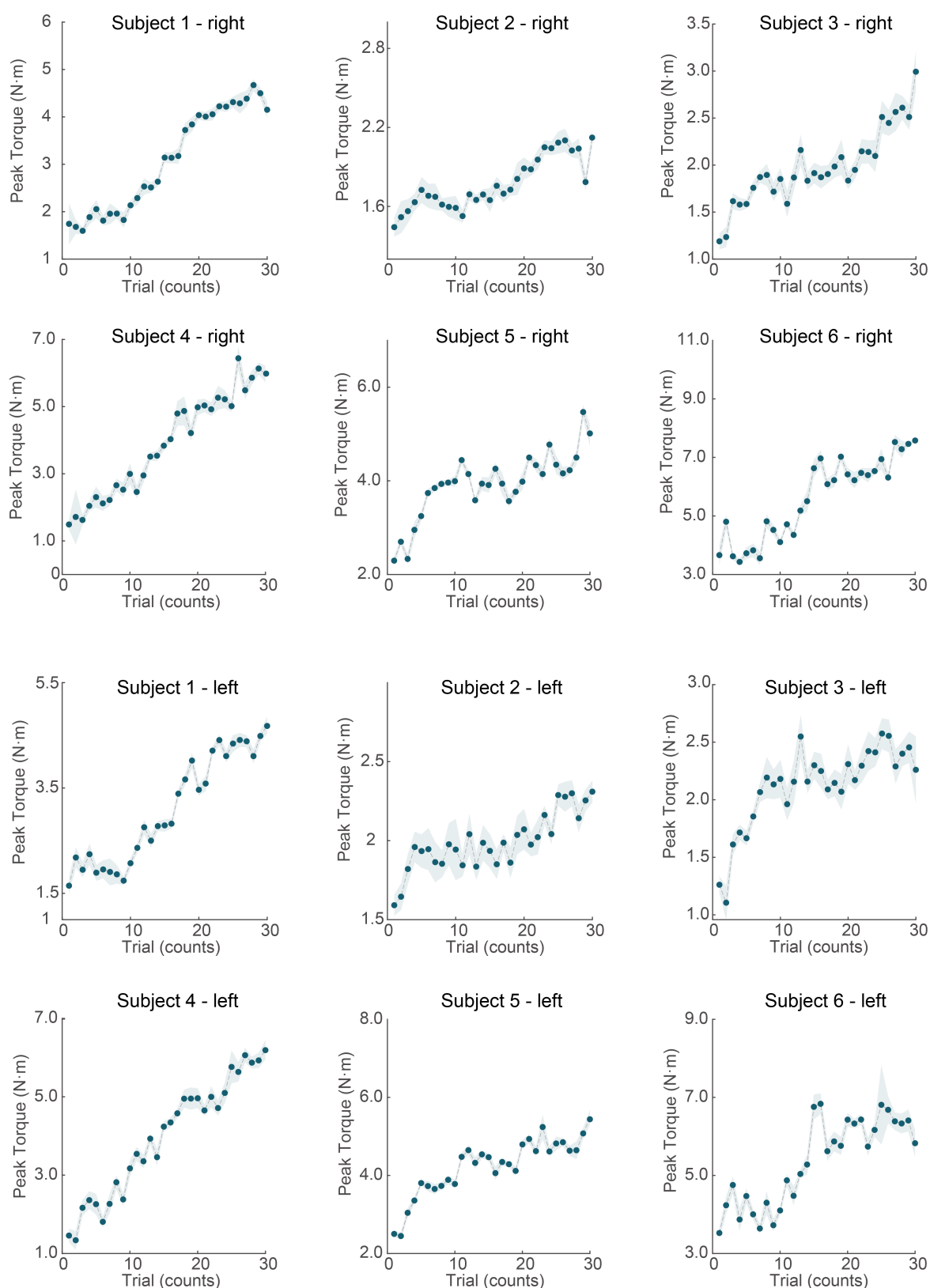
896 **Supplementary Fig. 1 | Range of isokinetic velocities of the robot achieved by closed-loop**
897 **application of resistance.**

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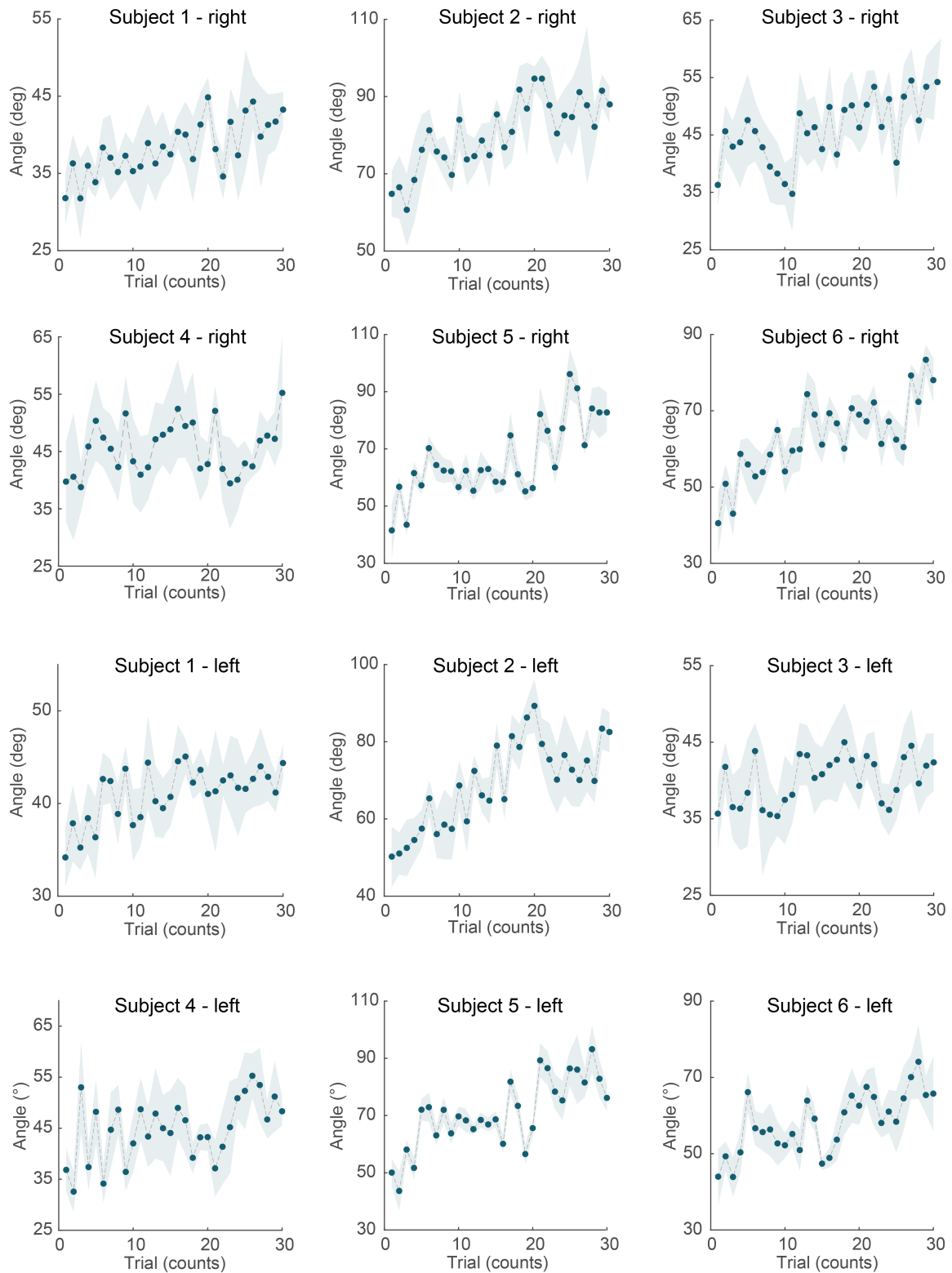


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900 **Supplementary Fig. 2 | Optimal stiffness improves rehabilitation efficacy.** (a) Optimal stiffness
 901 enhances isokinetic training effects as evidenced by increased peak knee torque (bars, mean; error
 902 bars, SD; $n = 12$; average-pre, $**P = 0.0094$, two-sided paired-sample t -test). (b) Optimal stiffness
 903 changes and distributions. Optimal stiffness experienced a significant increase after 6 weeks of high-
 904 intensity isokinetic training (rectangles, mean; error bars, SD; scatters, each leg; $n = 12$; $**P = 0.0040$,
 905 two-sided paired-sample t -test). The 0.5% value is a relatively small increment and is maintained
 906 without rounding to 1% to avoid overestimating the effect.

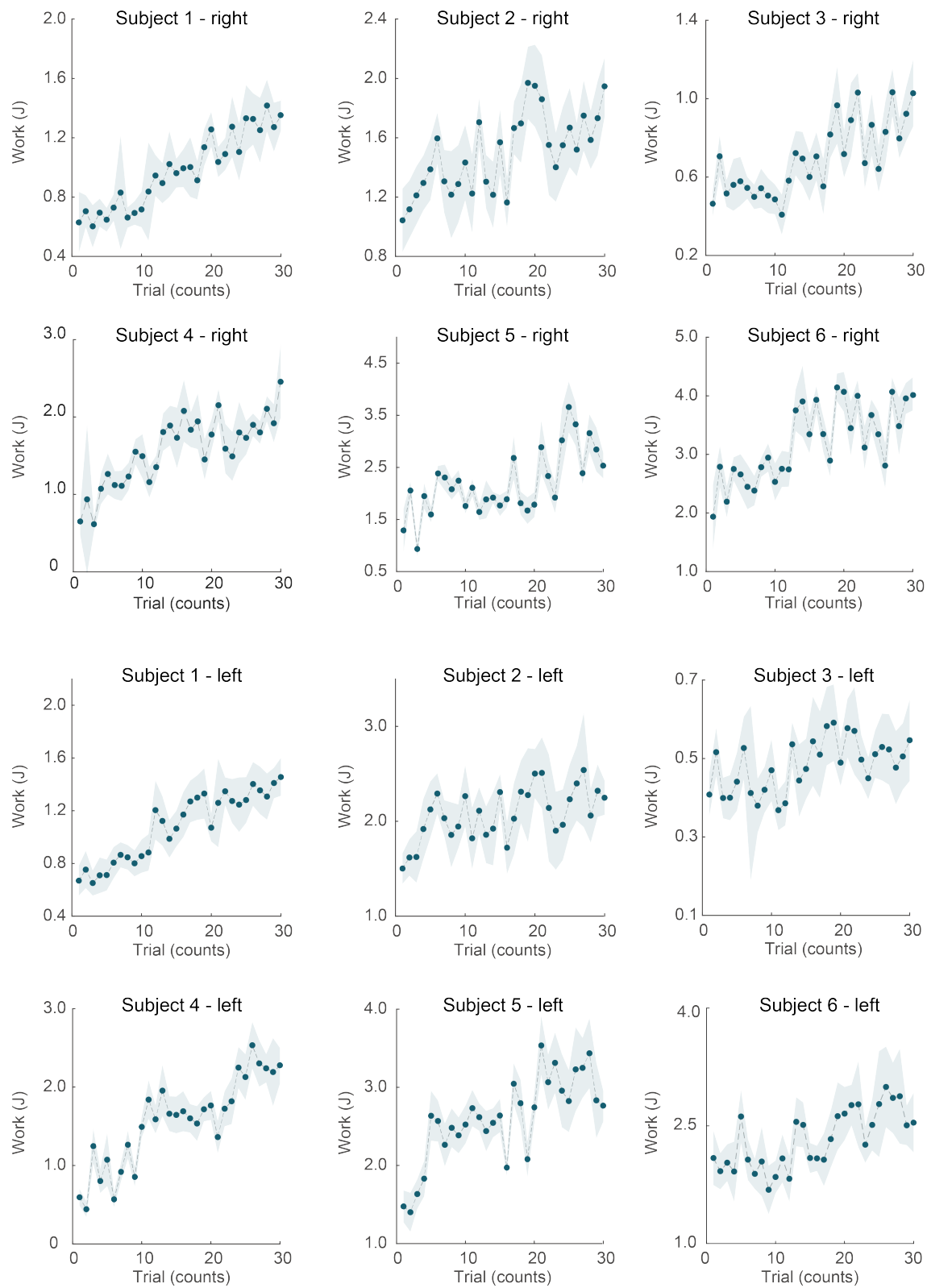


Supplementary Fig. 3 | Peak torque of all subjects during the intervention. The intervention (high-intensity isokinetic training phase) lasted for 6 weeks and included 30 trials (scatters, mean; shaded regions: SD; n = 20). Peak torque of all subjects showed an almost steady increase throughout the training period.

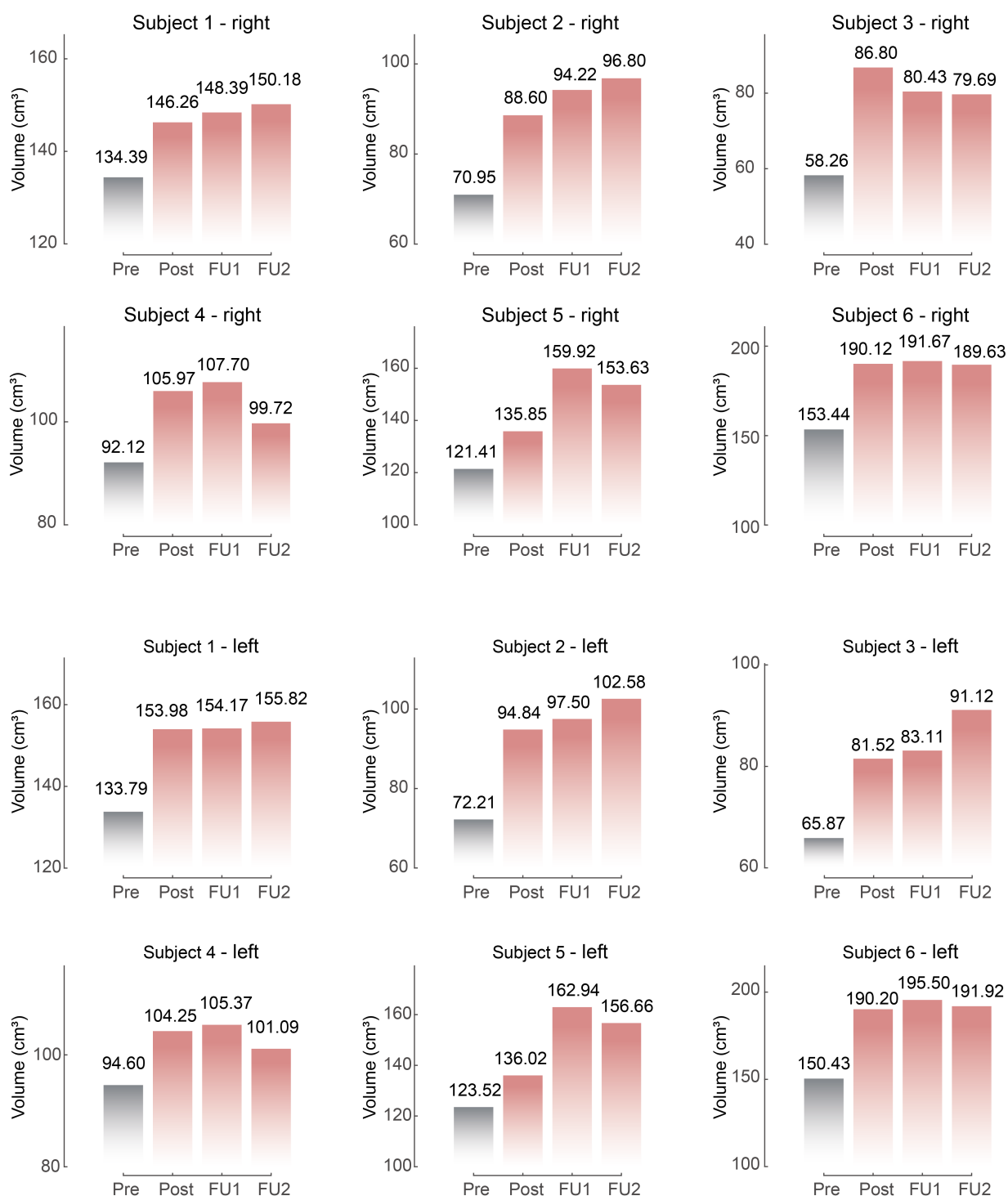


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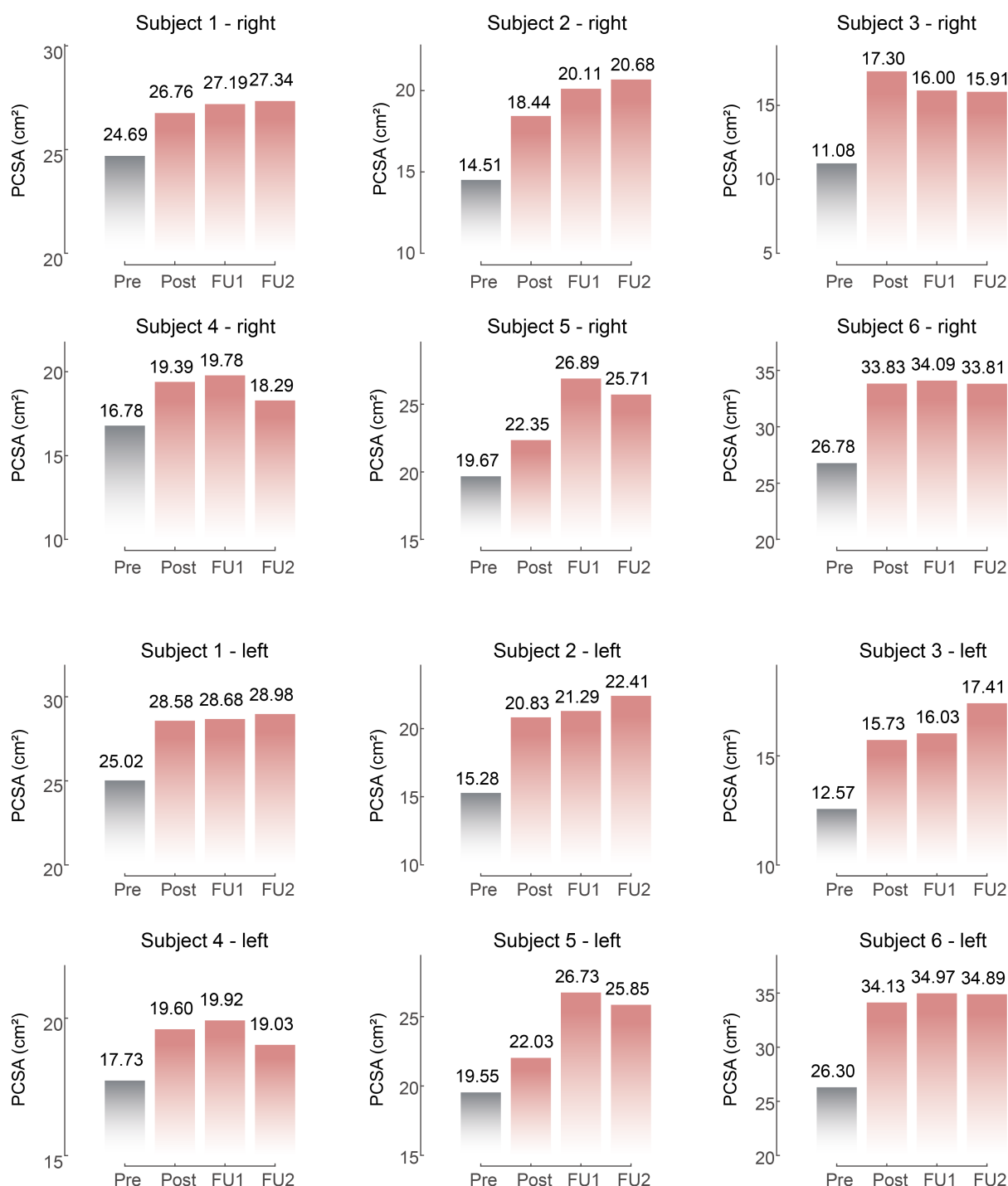
914 **Supplementary Fig. 4 | Range of motion (ROM) of all subjects during the intervention.** The
 915 intervention (high-intensity isokinetic training phase) lasted for 6 weeks and included 30 trials
 916 (scatters, mean; shaded regions, SD; n = 20). Compared to peak torque, the ROM exhibited greater
 917 variability during the progression, but still demonstrated a clear overall upward trend.



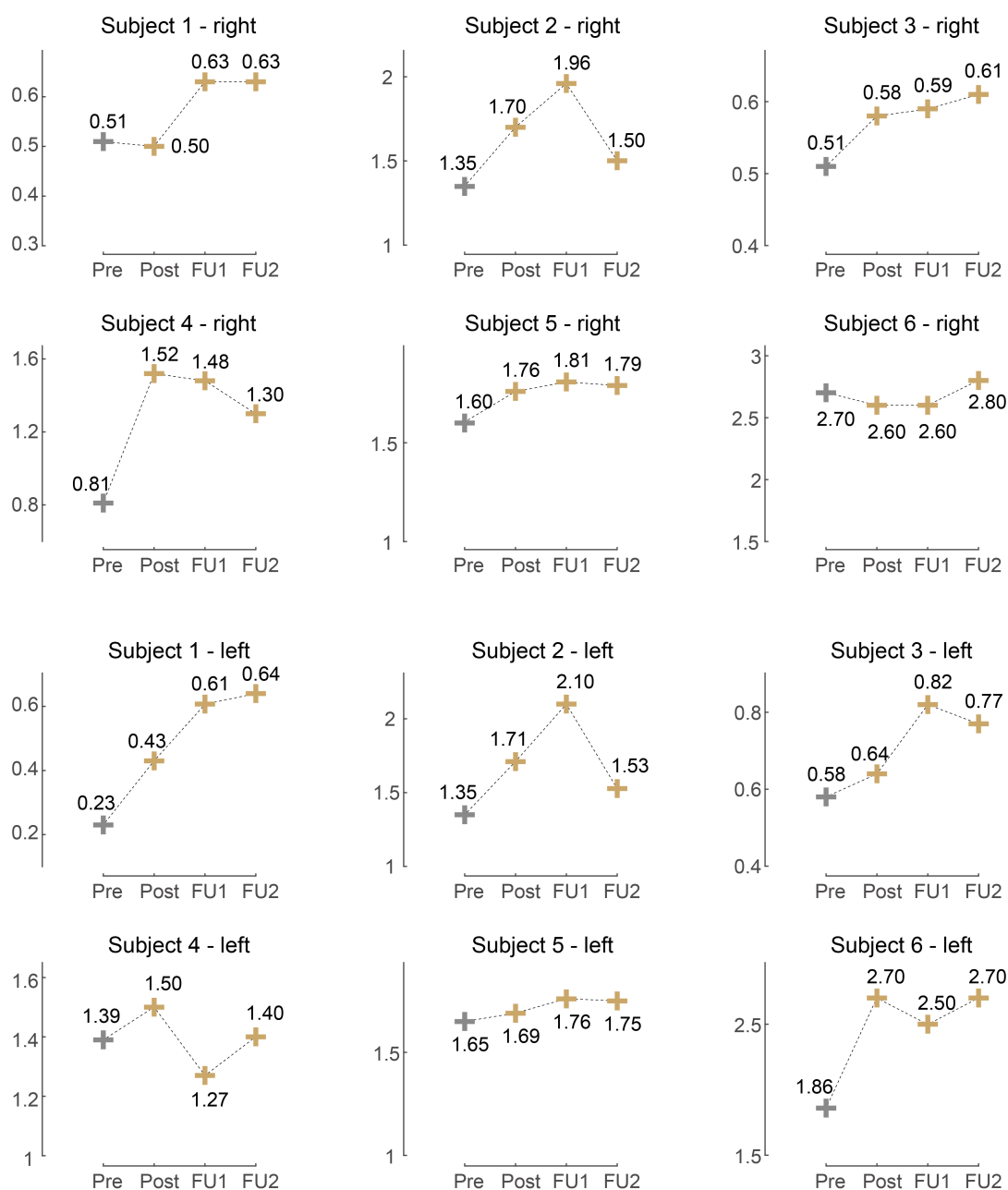
920 **Supplementary Fig. 5 | Work per extension of all subjects during the intervention.** The
921 intervention (high-intensity isokinetic training phase) lasted for 6 weeks and included 30 trials
922 (scatters, mean; shaded regions, SD; n = 20). Work is influenced by both torque and angle during
923 knee extension. Despite some fluctuations, all subjects showed a significant increase in work over the
924 course of the 30 trials.



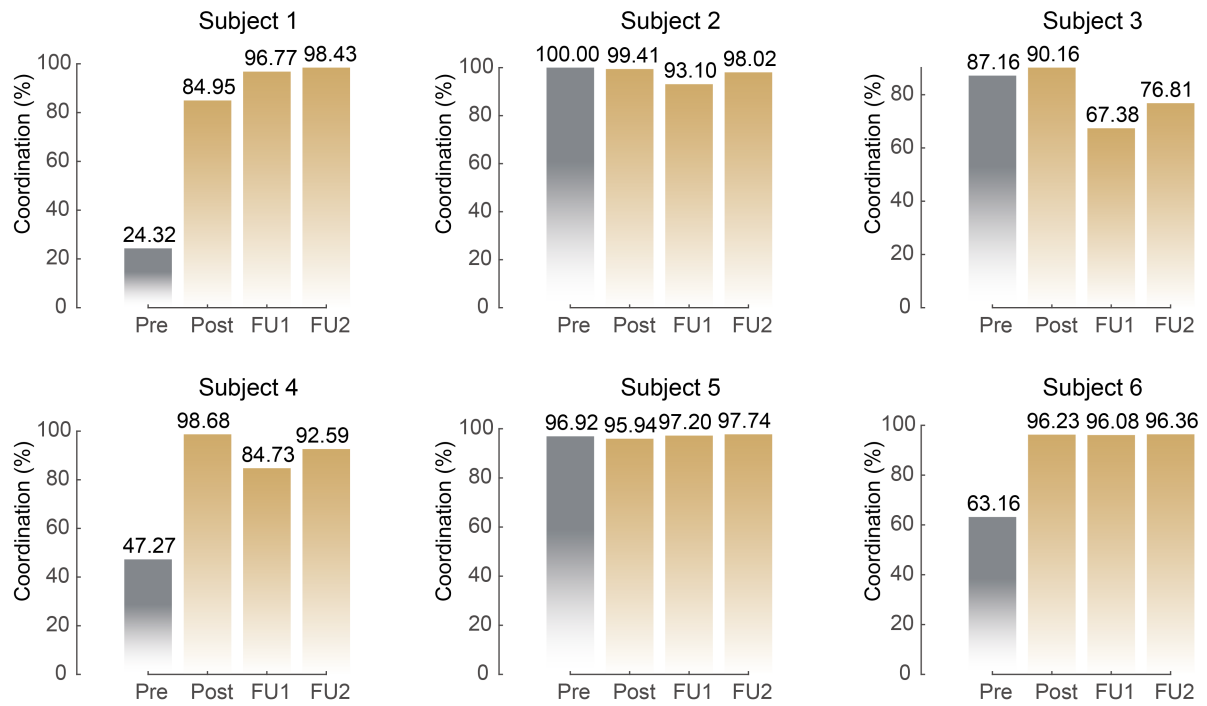
Supplementary Fig. 6 | Quadriceps muscle volume of the left and right legs in all subjects with SMA. Quadriceps muscle volume was measured for both legs at each monitoring time point. Gray indicates pre-intervention values, while red represents post-intervention, follow-up 1, and follow-up 2. All subjects showed increased muscle volume after the intervention compared to pre-intervention. By follow-up 2, all subjects exhibited quadriceps volumes greater than their pre-intervention levels.



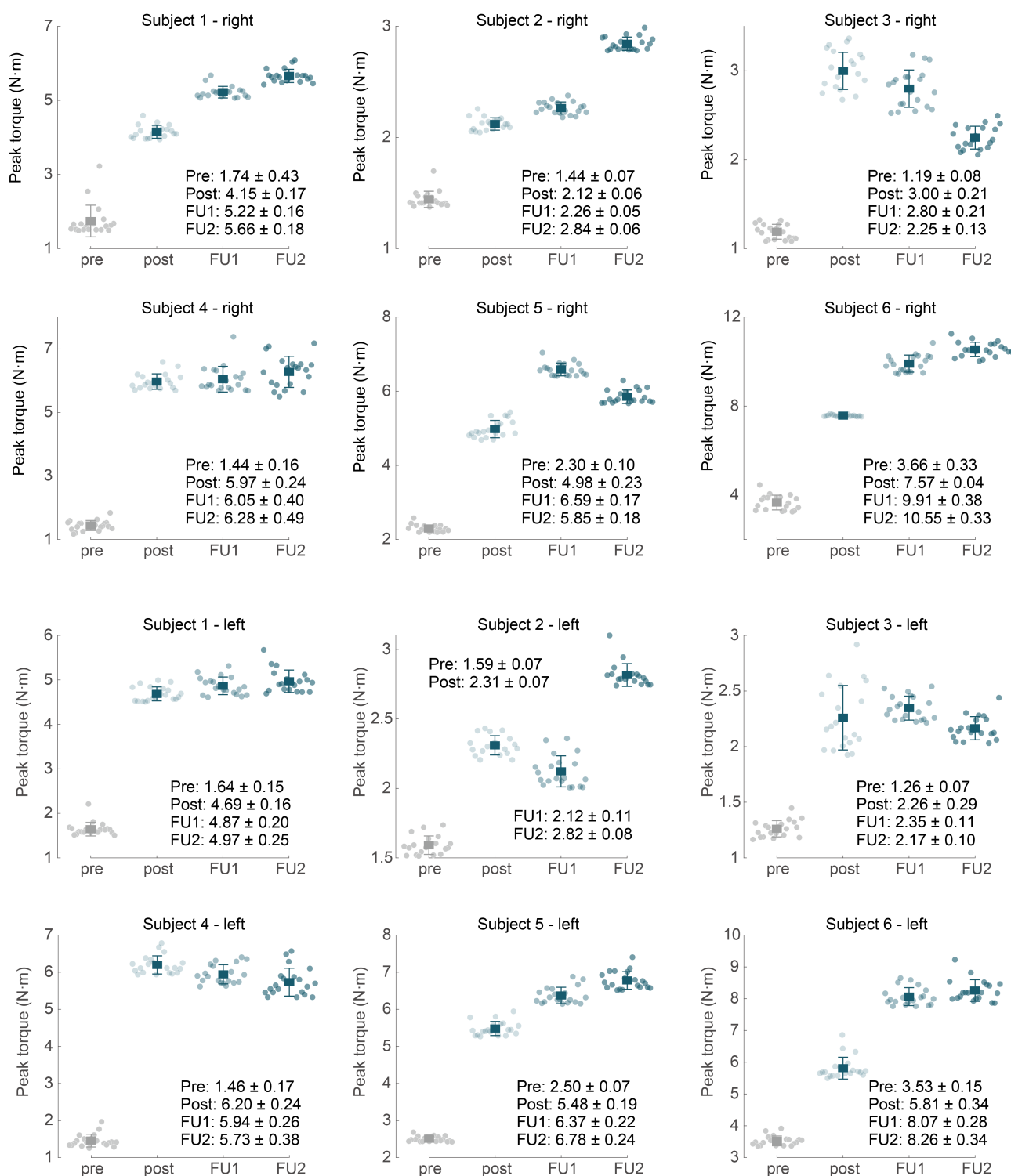
Supplementary Fig. 7 | Physiological cross-sectional area (PCSA) of the quadriceps in the left and right legs of all subjects. The PCSA of the quadriceps was estimated bilaterally at each assessment point. Pre-intervention values are shown in gray, with subsequent measurements at post-intervention, follow-up 1, and follow-up 2 indicated in red. Following the intervention, all subjects demonstrated noticeable increases in PCSA, reflecting muscle architectural adaptations. By follow-up 2, PCSA remained higher than pre-intervention in all subjects.



Supplementary Fig. 8 | Femoral nerve conduction assessed by compound muscle action potential (CMAP) in all SMA subjects. CMAP amplitudes of the quadriceps were recorded bilaterally at each monitoring time point to evaluate femoral nerve conduction. Gray represents pre-intervention values, while yellow indicates post-intervention, follow-up 1, and follow-up 2. Most subjects exhibited clear improvements following the intervention. Although a few subjects showed fluctuations, the overall trend reflected continued neuromuscular enhancement over time.

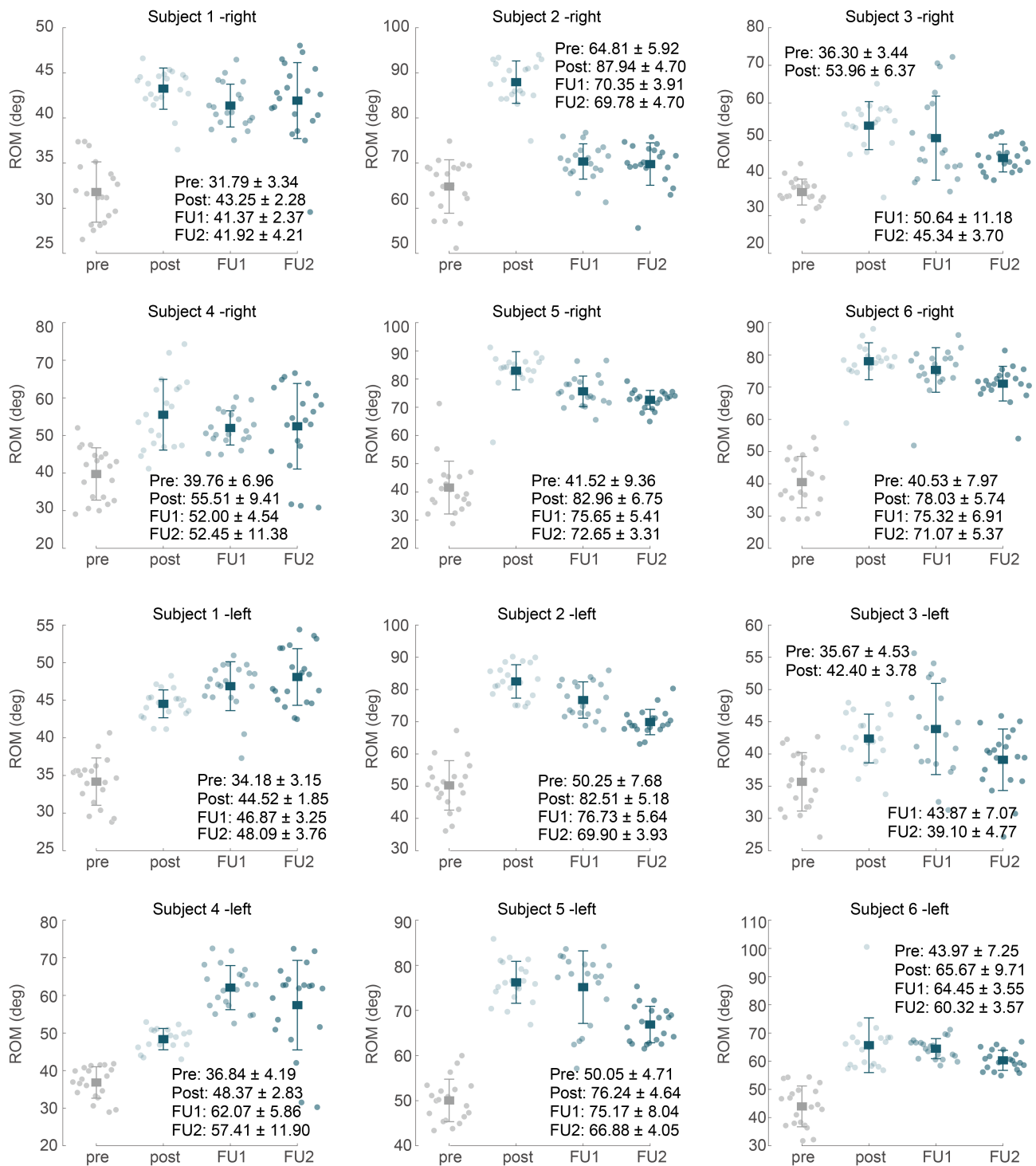


Supplementary Fig. 9 | Inter-limb coordination of the lower limbs in all SMA subjects. Inter-limb coordination was calculated based on the CMAP values of both legs. A significant increase in coordination was observed in three subjects immediately after the intervention (subjects 1, 4 and 6). Coordination levels for all subjects remained relatively stable during the subsequent follow-up periods.

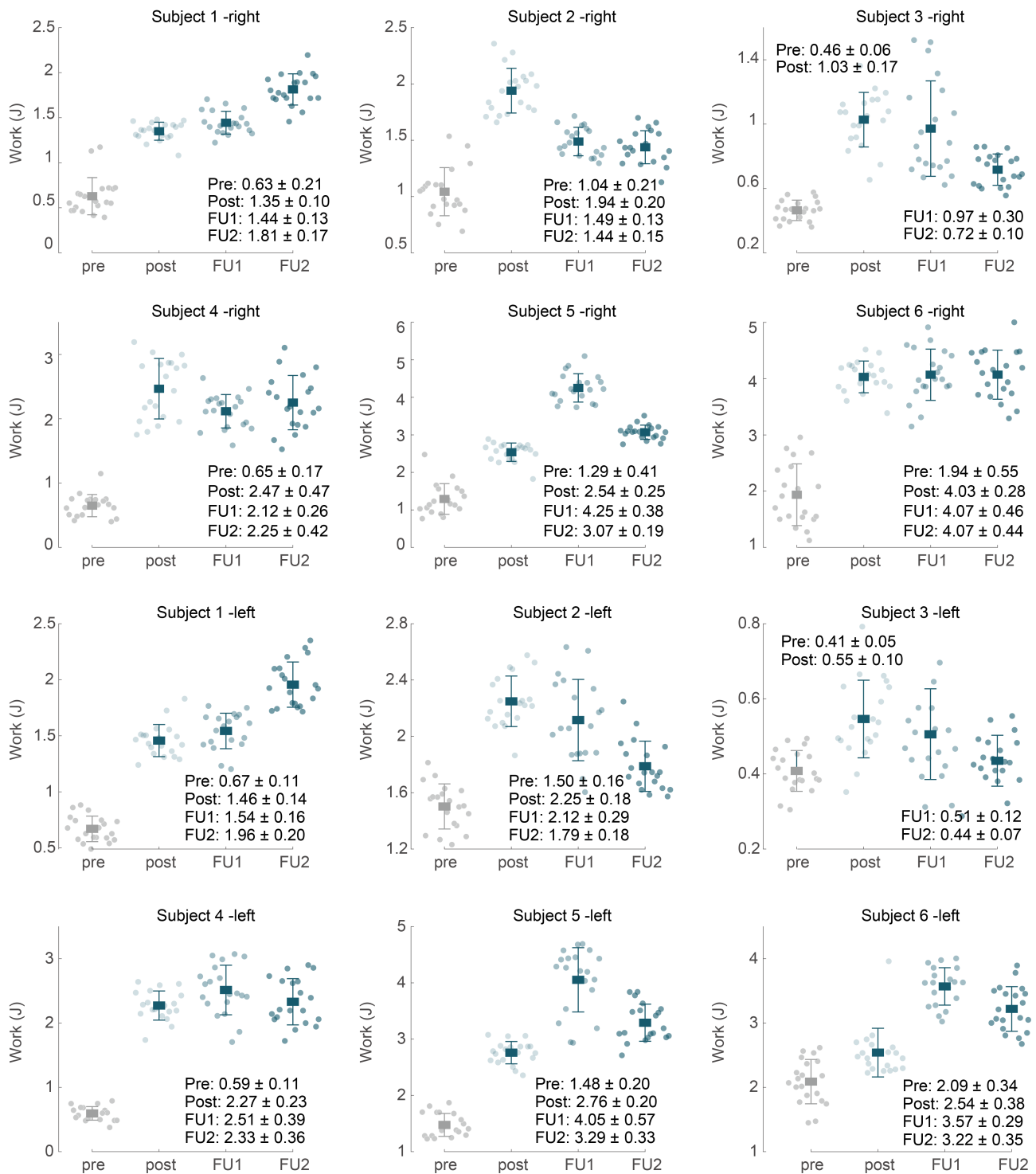


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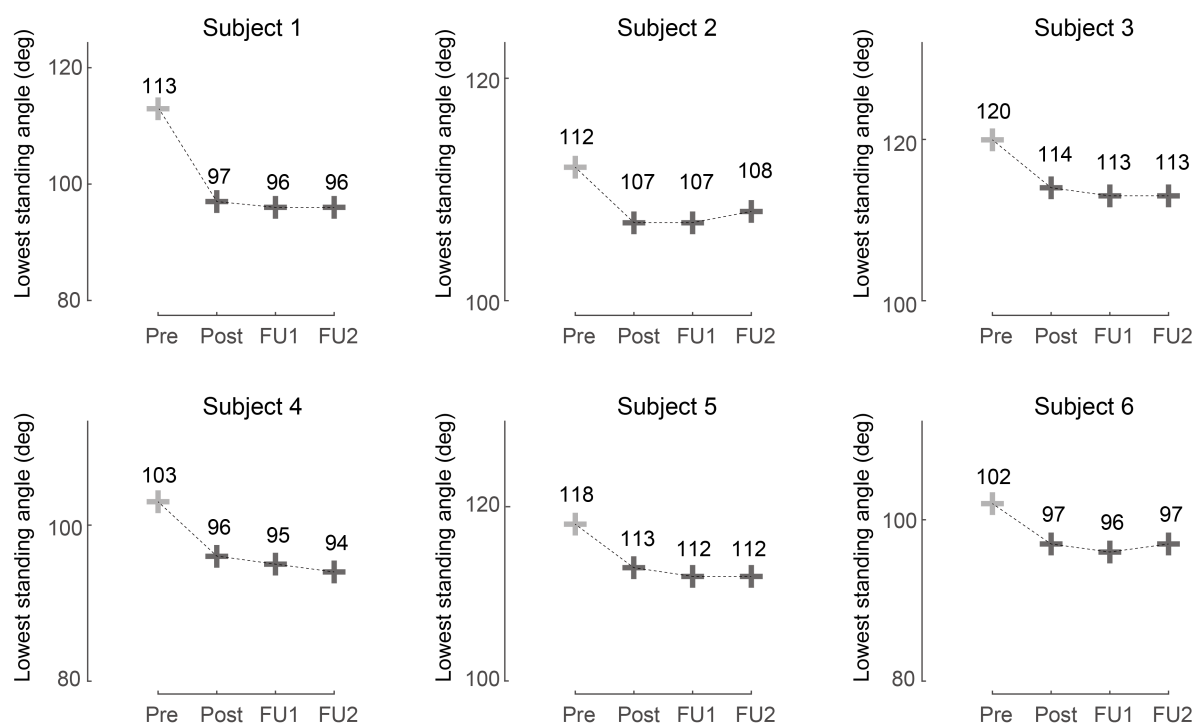
957 **Supplementary Fig. 10 | Peak torque of the left and right legs in all subjects with SMA.** Peak
 958 torque of both legs was recorded at each monitoring time point for every subject (scatters, extension;
 959 rectangles, mean; error bars, SD; n = 20). Gray represents pre-intervention values, while green
 960 indicates post-intervention, follow-up 1, and follow-up 2. All subjects exhibited marked improvement
 961 after the intervention compared to pre-intervention. Some showed continued gains during follow-up,
 962 while others experienced slight declines. Nevertheless, the overall training effect was maintained. By
 963 follow-up 2, all subjects had significantly higher peak torque than at pre-intervention.



Supplementary Fig. 11 | Range of motion (ROM) of the left and right legs in all subjects with SMA. ROM of both legs was recorded at each monitoring time point for every subject (each scatter represents an extension; rectangles, mean; error bars, SD; n = 20). Gray indicates pre-intervention values, while green represents post-intervention, follow-up 1, and follow-up 2. All subjects showed notable improvement in ROM after the intervention compared to pre-intervention. After training intensity was reduced (follow-up 1), most subjects exhibited a decline in ROM. However, the overall effect of training remained. By follow-up 2, ROM remained above pre-intervention levels in all subjects.



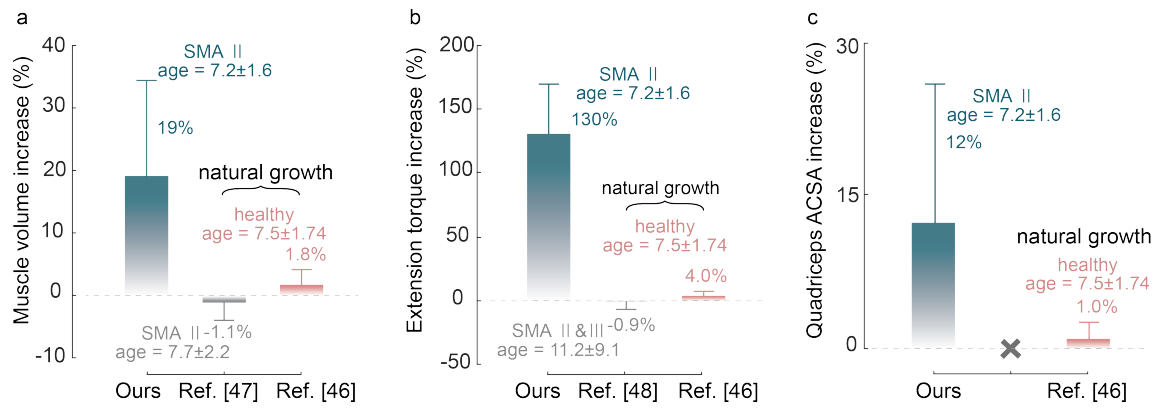
Supplementary Fig. 12 | Work per extension of the left and right legs in all subjects with SMA. Work per extension for both legs was measured at each time point for all subjects (each scatter represents an extension; rectangles, mean; error bars, SD; $n = 20$). Pre-intervention data are shown in gray, with post-intervention, follow-up 1, and follow-up 2 depicted in shades of green. Most subjects experienced significant increases in work per extension immediately following the intervention. When training volume decreased at follow-up 1, a majority showed some reduction, though overall, improvements were largely sustained. By follow-up 2, work per extension values remained elevated above pre-intervention levels for all subjects.



984

985 **Supplementary Fig. 13 | Lowest knee joint angle during sit-to-stand in all SMA subjects.** The
 986 lowest knee joint angle was measured at each monitoring time point. Light gray indicates pre-
 987 intervention values, while dark gray represents post-intervention, follow-up 1, and follow-up 2. All
 988 subjects showed a significant reduction in lowest knee angle after the intervention, indicating
 989 improved knee extension during sit-to-stand. Although some subjects experienced slight increases in
 990 angle during follow-ups, the overall improvement was maintained. By follow-up 2, the lowest knee
 991 angles remained lower than pre-intervention in all subjects.

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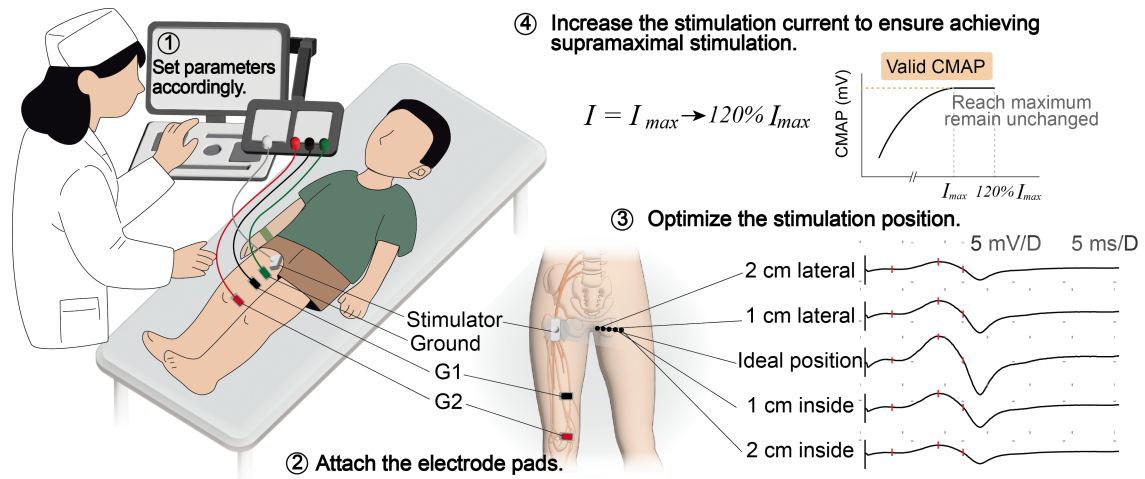
Supplementary Fig. 14 | Comparison of short-term changes in knee extensor muscle physiology between the SMA II study cohort, age-matched subjects progressing according to the natural history of SMA, and age-matched subjects with normal neuromuscular development. (a) Comparison of changes in relative muscle volume over 6 weeks^{46,47}. (b) Comparison of changes in relative knee extension torque over 6 weeks^{46,48}. (c) Comparison of changes in relative quadriceps ACSA over 6 weeks⁴⁶. The 'x' symbol indicates that no longitudinal ACSA data were identified for age-matched SMA natural history cohorts. Additionally, no PCSA data were available for either age-matched SMA natural history cohorts or healthily developing children. Because the study durations in the cited references exceed 6 weeks, the reported percentage changes and SEM values were linearly interpolated to estimate the 6-week changes. All data are presented as mean $\pm$ SEM. To ensure consistency with the values reported in the references, all covariances were assumed to be zero.

Note: All data for comparison are obtained as follows.

- (a) Ref. [47], Fig. 2: -1.1% (per 1.5 months) $\approx (6.00\text{mL/cm} - 6.27\text{mL/cm}) \div 6.27\text{mL/cm} \div (6\text{months}/1.5\text{months})$;
 Ref. [46], Tab. 3: 1.8% (per 1.5 months) $\approx (412.0 \text{ cm}^3 - 384.8 \text{ cm}^3) \div 384.8 \text{ cm}^3 \div (6\text{months}/1.5\text{months})$.
 (b) Ref. [48], Tab. 4: -0.9% (per 1.5 months) $\approx -7\%/(12\text{months}/1.5\text{months})$;
 Ref. [46], Tab. 3: 4.0% (per 1.5 months) $\approx (52.9 \text{ N}\cdot\text{m} - 45.6 \text{ N}\cdot\text{m}) \div 45.6 \text{ N}\cdot\text{m} \div (6\text{months}/1.5\text{months})$.
 (c) Ref. [46], Tab. 3: 1.0% (per 1.5 months) $\approx (26.3 \text{ cm}^2 - 25.3 \text{ cm}^2) \div 25.3 \text{ cm}^2 \div (6\text{months}/1.5\text{months})$.

References [46–48] consistent with main text

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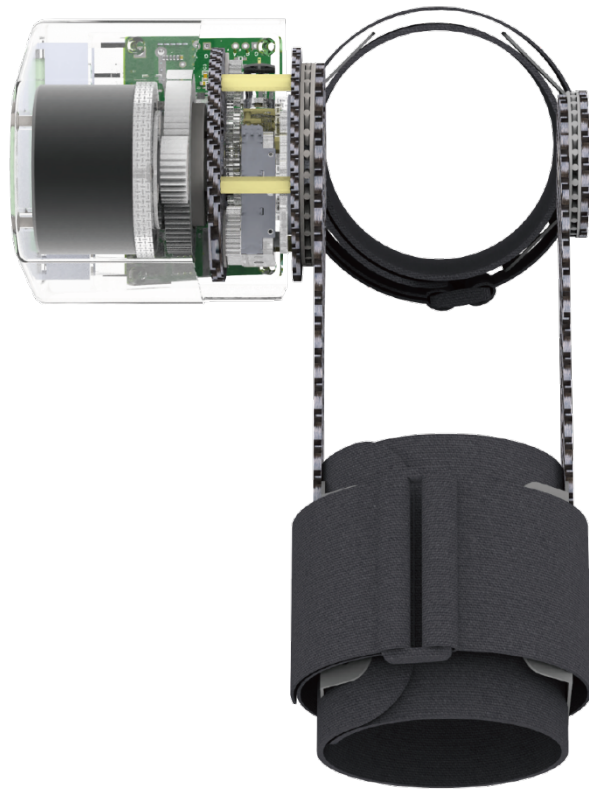


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1024 **Supplementary Fig. 15 | Assessment of femoral nerve conduction.** ① Initialize parameters. The
 1025 clinician first configures the stimulation parameters, including current intensity and duration, to
 1026 ensure effective and safe nerve activation for each patient. ② Attach the electrode pads. The ground
 1027 electrode is attached to either the patient's thigh or wrist. The active recording electrode (G1) is placed
 1028 over the muscle belly of the quadriceps femoris, typically the rectus femoris. The reference electrode
 1029 (G2) is positioned at the quadriceps tendon over the patella. The stimulating electrode (cathode) is
 1030 placed just inferior to the inguinal ligament, over the presumed course of the femoral nerve. ③
 1031 Optimize the stimulation position. After initiating stimulation, the current is gradually increased until
 1032 a small submaximal compound muscle action potential (CMAP) is observed. While maintaining the
 1033 current intensity, the stimulating electrode is carefully shifted slightly medially or laterally from the
 1034 initial site to locate the position that elicits the maximal CMAP amplitude. ④ Confirmation of
 1035 supramaximal stimulation. Once the CMAP amplitude plateaus and no further increase is observed
 1036 with rising current, the intensity is increased by an additional 20% to ensure supramaximal
 1037 stimulation for full recruitment of motor fibers. The positions of the G1 and G2 electrodes were
 1038 adjusted, and the experimental procedure was repeated if necessary to observe the CMAP.

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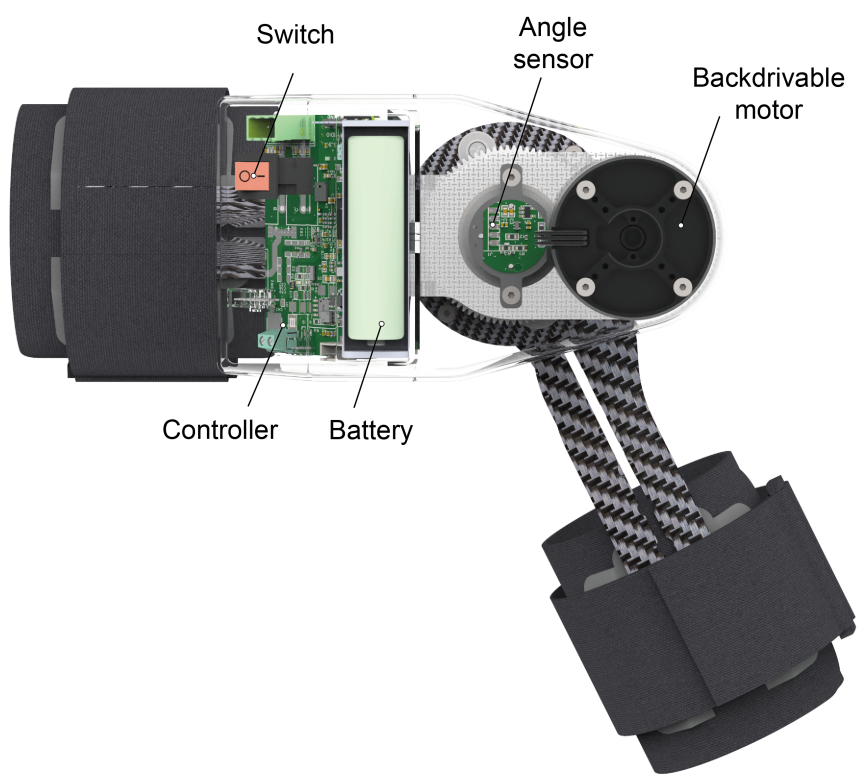


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1042 **Supplementary Fig. 16 | Frontal view of the robot.** Adjustable frame and straps are adapted to suit
1043 lower limbs of different sizes.

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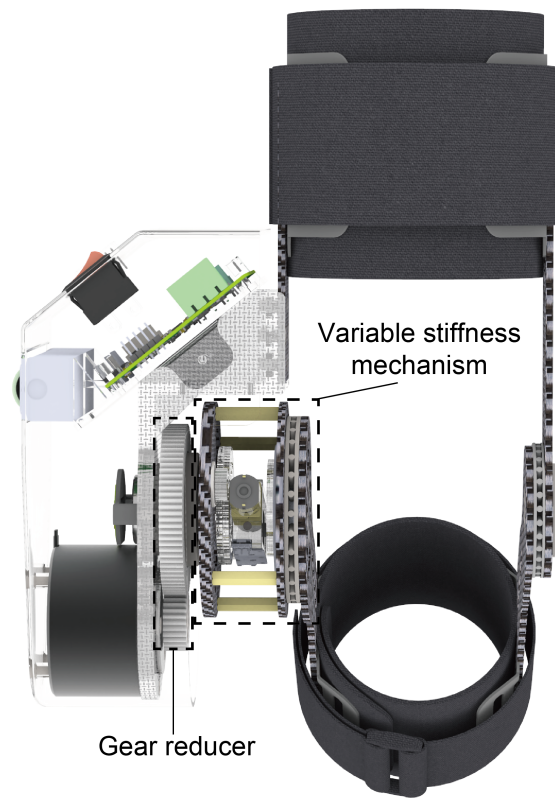
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1047 **Supplementary Fig. 17 | Lateral view of the robot.**

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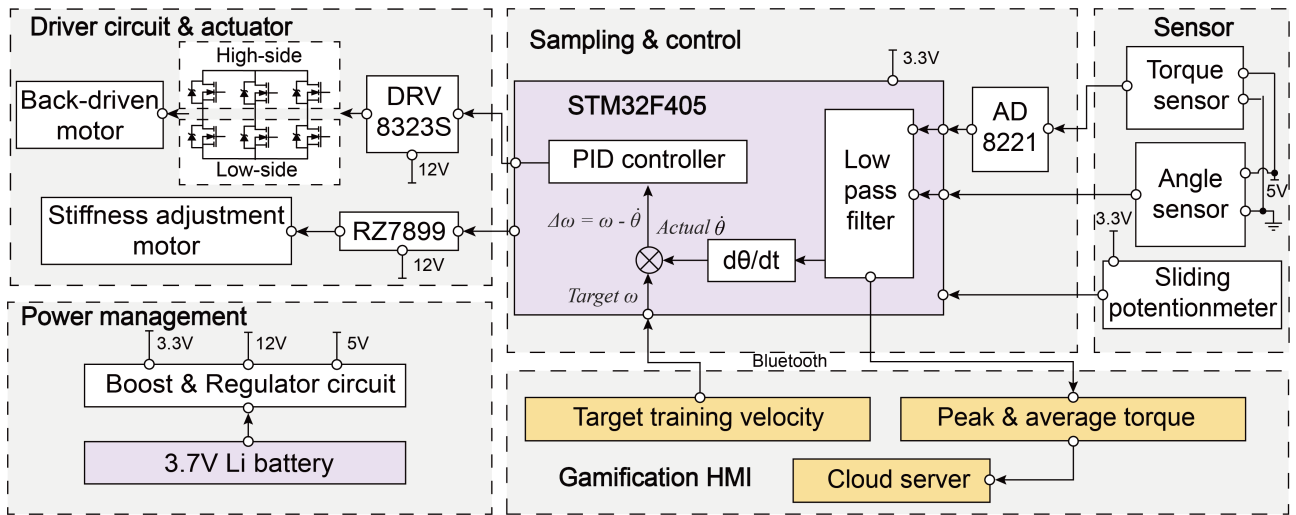


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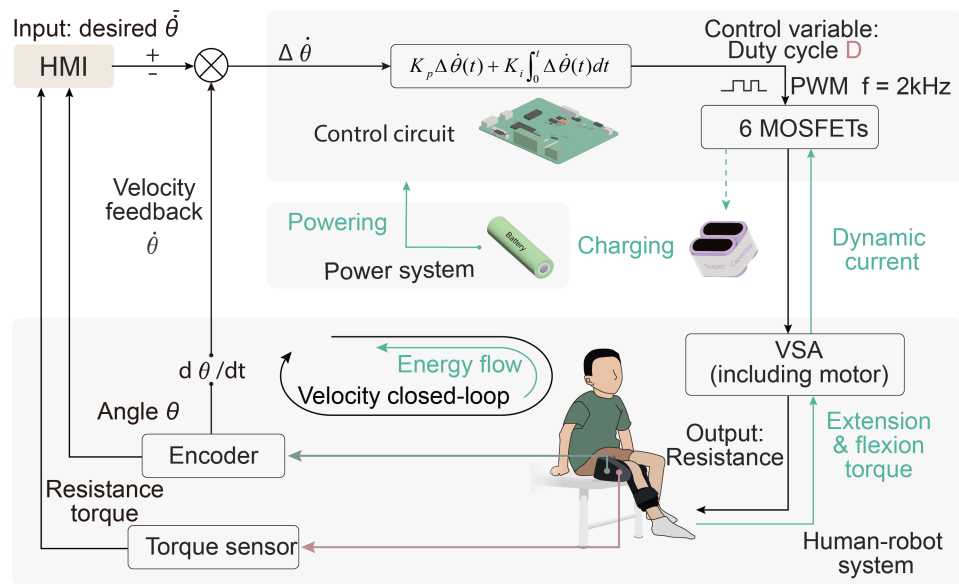
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Supplementary Fig. 18 | Top view of the robot.

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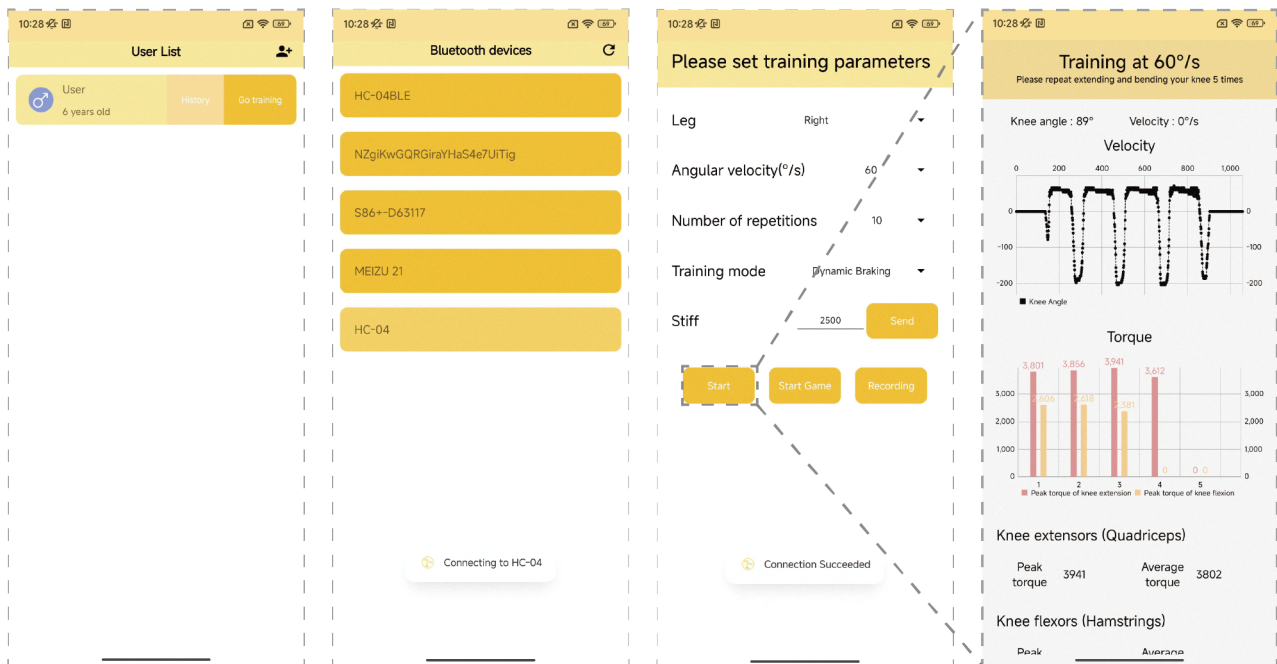
Supplementary Fig. 19 | Detailed block diagram of the robot control circuit.



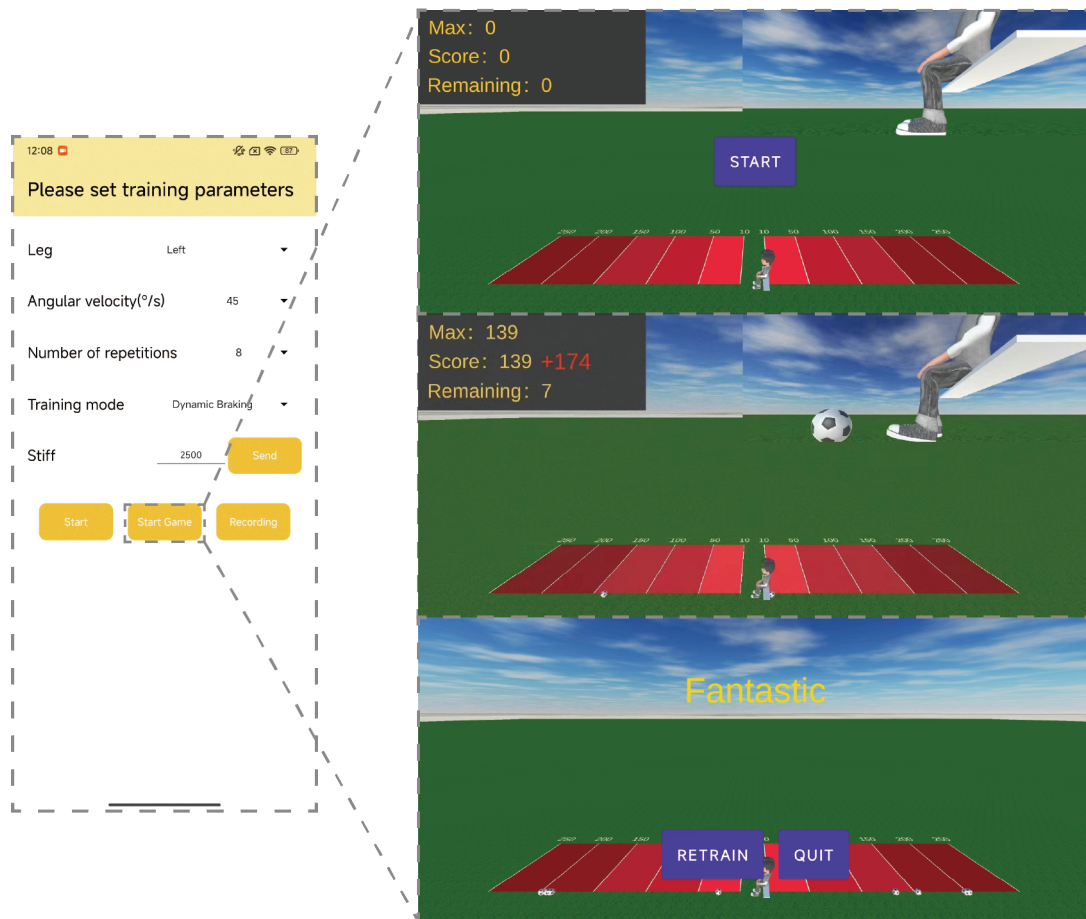
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1056 **Supplementary Fig. 20 | Closed-loop isokinetic control.**

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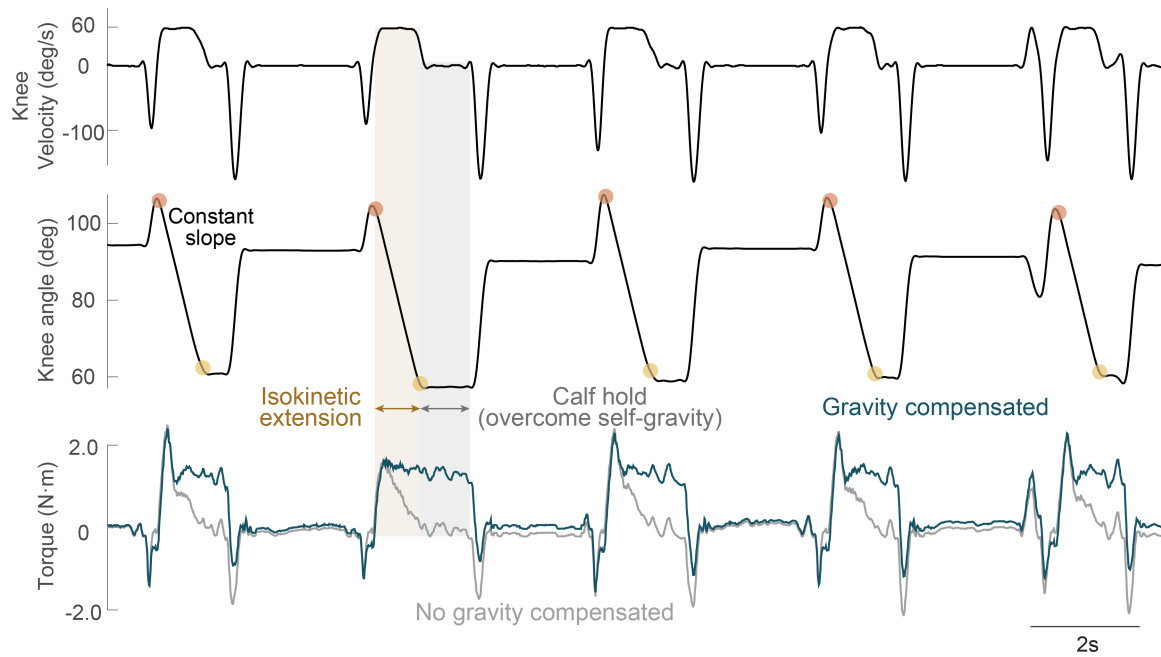
Supplementary Fig. 21 | Mobile app interface for displaying specific training data. When training, the administrator can enter the user interface on the mobile app, connect to the robot via Bluetooth, and set the training parameters.



1063

1064 **Supplementary Fig. 22 | Gamified app interface.** The avatar in the game will kick the ball to a
 1065 corresponding distance according to the magnitude of the peak torque during the extension movement.
 1066 In the upper left corner of the interface, the user will be given points based on their performance, as
 1067 well as the number of reps remaining in a session of training. At the end of each session, the screen
 1068 displays encouraging words and the administrator chooses whether to continue or not.

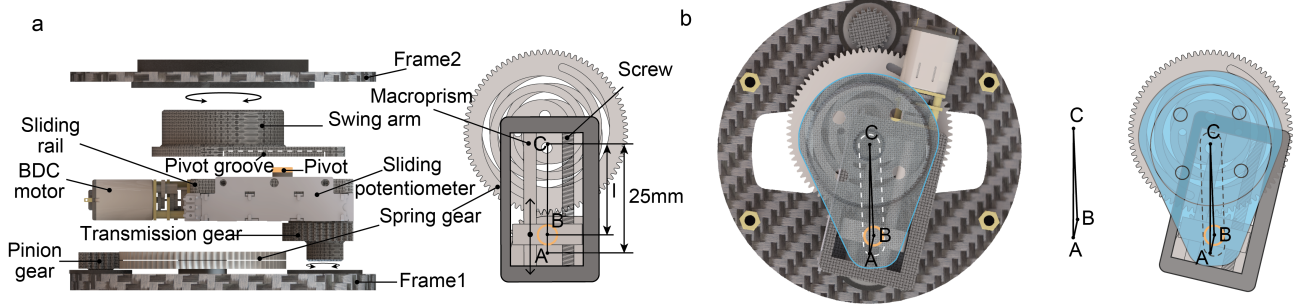
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1071 **Supplementary Fig. 23 | Torque comparison with and without gravity compensation.** For some
 1072 participants, there was a period of posture maintenance after knee extension, during which the robot
 1073 measured zero resistance. However, these participants continued to exert force to counteract gravity
 1074 (calf hold phase). The gravity-compensated torque curve reveals continued muscle output during this
 1075 phase, reflecting the effort required to sustain the extended leg position.

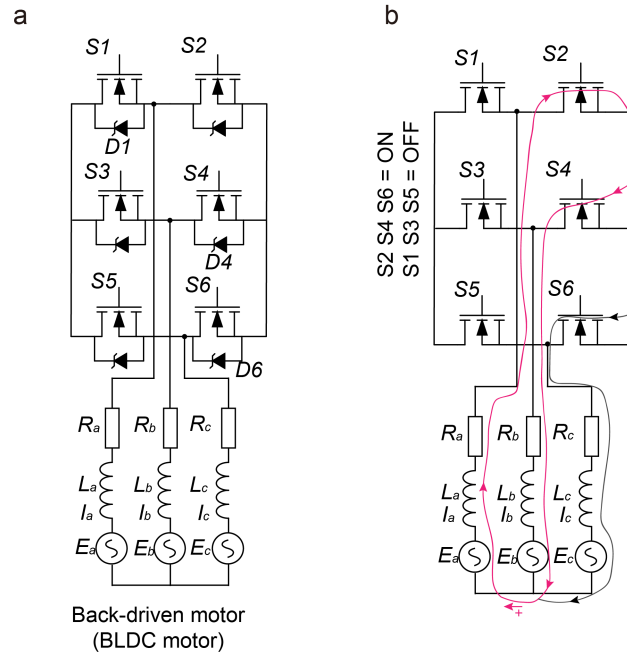
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1078 **Supplementary Fig. 24 | Variable stiffness mechanism.** (a) An exploded view of the variable
 1079 stiffness mechanism. Two mirrored spring gears are used as elastic elements. The torque from the
 1080 swing arm is transmitted to the pivot, which drives sliding rail to swing and transfers the load to the
 1081 spring gear via the transmission gear. Finally, the load is transferred from the spring gear to the frame.
 1082 the rotating center of the transmission gear, the geometric center of the pivot and the rotating center
 1083 of the swing arm are represented by points A, B and C, respectively. The distance from the pivot to
 1084 the joint center is defined as l , and the length of AB is $25 - l$. By adjusting l , the position of the pivot
 1085 in the lever system can be changed, thereby altering the stiffness of the mechanism. (b) The pivot can
 1086 slide along the groove on the swing arm. When the l is close to zero, the joint becomes softer. In the
 1087 limiting case, the main arm can rotate freely and the spring gear does not deform. Conversely, the
 1088 main arm is fixed (degree of freedom is zero) when l is equal to 25 mm or B and A overlap, as a result,
 1089 the theoretical joint stiffness is infinite.

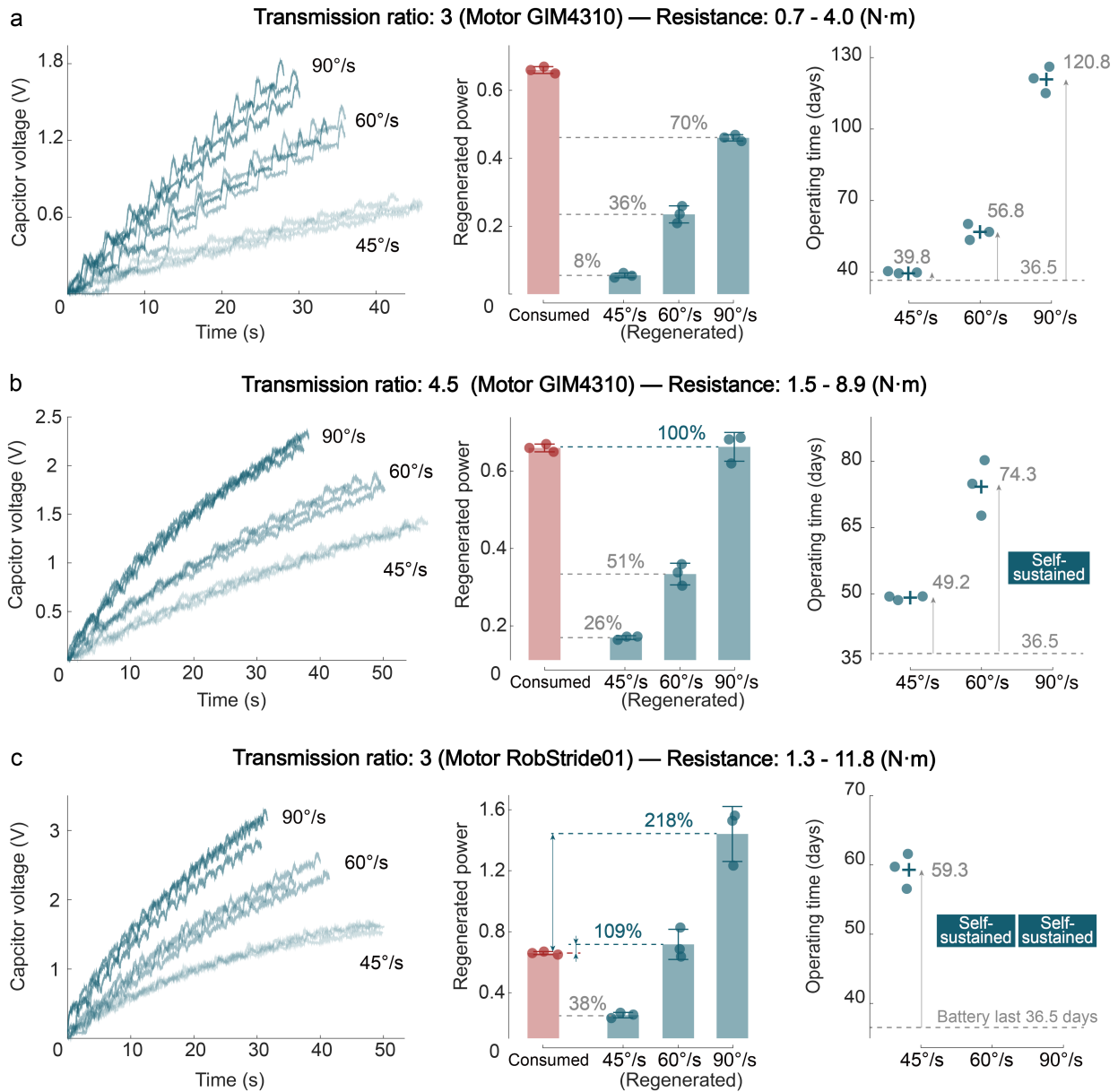
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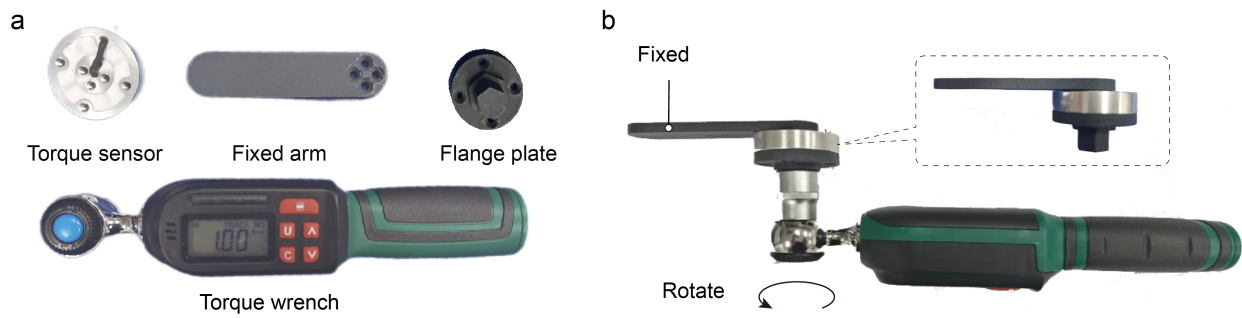
1092 **Supplementary Fig. 25 | Equivalent braking circuit.** (a) The entire braking control circuit. (b) The
 1093 MOSFETs S2, S4, and S6 are ON, showing the flow of the braking current.

1094



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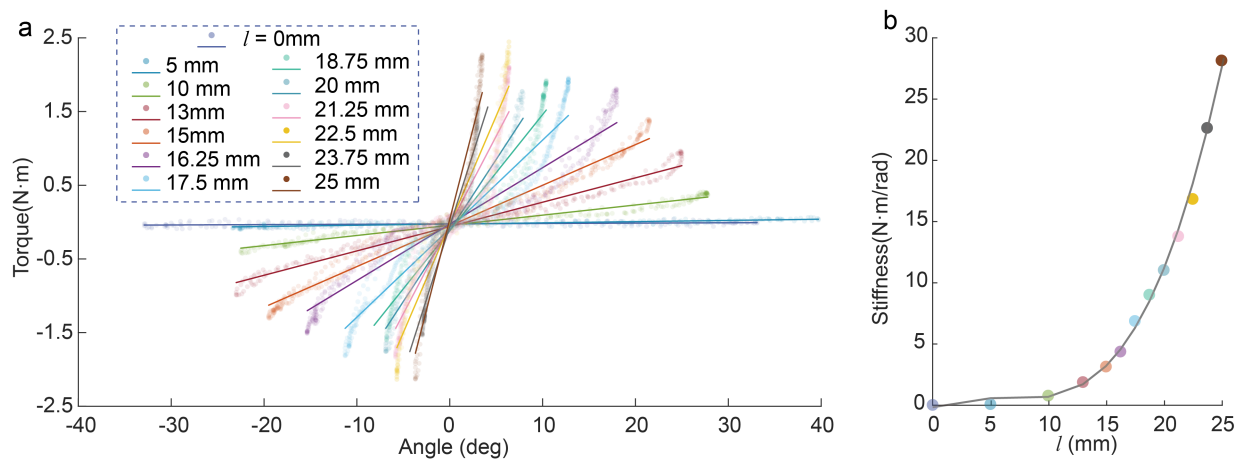
1096 **Supplementary Fig. 26 | Energy regeneration characteristics.** (a) Using the GIM4310 motor with
 1097 a gear ratio of 3, the system was able to regenerate 8%, 36%, and 70% of the consumed energy at
 1098 isokinetic speeds of 45°/s, 60°/s, and 90°/s, respectively. This level of regeneration corresponds to an
 1099 extension in operational lifespan by 39.8 days, 56.8 days, and 120.8 days, respectively. (b) Using the
 1100 GIM4310 motor with a gear ratio of 4.5, the system was able to regenerate 26%, 51%, and 100% of the
 1101 energy consumed at isokinetic speeds of 45°/s, 60°/s, and 90°/s, respectively. These levels of
 1102 energy regeneration translate to an extension of operational lifespan by 49.2 days and 74.3 days at
 1103 45°/s and 60°/s, respectively, and a fully self-sustained operation at 90°/s. (c) Using the RobStride01
 1104 motor with a gear ratio of 3, the system regenerated 38%, 109%, and 218% of the energy consumed
 1105 at isokinetic speeds of 45°/s, 60°/s, and 90°/s, respectively. These levels of energy regeneration
 1106 correspond to a 59.3-day extension in operational lifespan at 45°/s, and fully self-sustained operation
 1107 (infinite) at both 60°/s and 90°/s.



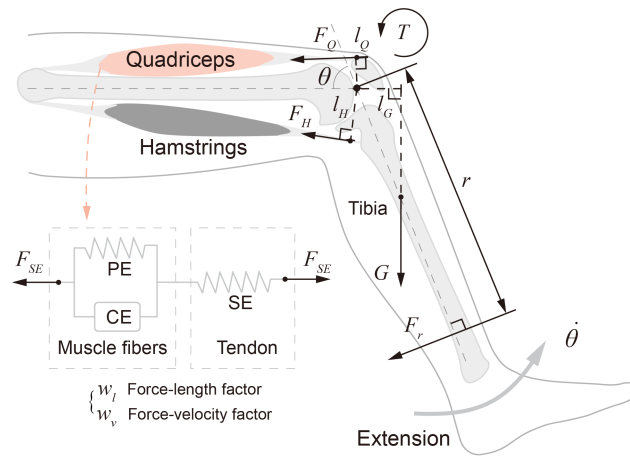
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1109 **Supplementary Fig. 27 | Torque sensor calibration.** (a) A torque wrench, a flange plate and a fixed
 1110 arm were used for calibration of the torque sensor. (b) By comparing the actual torque and the sensor
 1111 signal, the accuracy of the sensor sampling values was verified.

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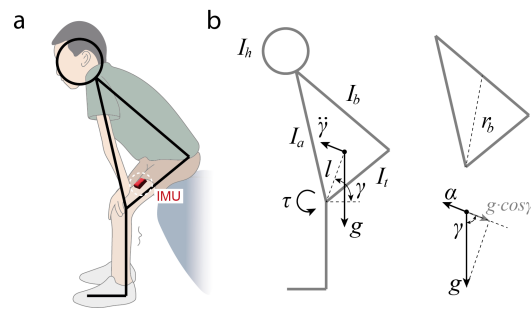
Supplementary Fig. 28 | Stiffness characteristics of the variable stiffness mechanism. (a) Torque-angular displacement at different stiffness. Different colors represent stiffness under different l . (b) Stiffness-position curve.



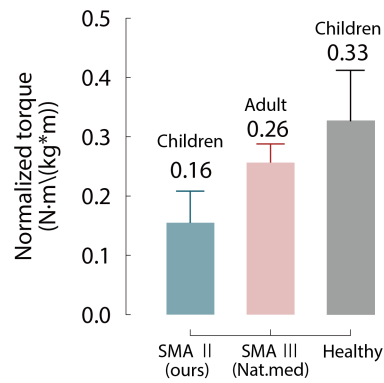
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1119 **Supplementary Fig. 29 | Biomechanical knee extension model.** The contractile forces of the
 1120 quadriceps and hamstrings are denoted by F_Q and F_H , respectively, while G represents the
 1121 gravitational load from the calf. Their corresponding moment arms are l_Q , l_H and l_G . SE: serial
 1122 element, CE: contractile element, PE: parallel element.

1123



Supplementary Fig. 30 | Inverse dynamic analysis during sit-to-stand.



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1128 **Supplementary Fig. 31 | Knee extension torque in our study, a study published in *Nature***
 1129 ***Medicine*, and healthy juveniles measured by ourselves.** The study published in *Nature Medicine*
 1130 ³⁶ did not report the height and weight of their participants. We contacted the authors via email and
 1131 obtained the missing anthropometric data in order to calculate the normalized torque values.

1132 **Reference [36] consistent with main text**

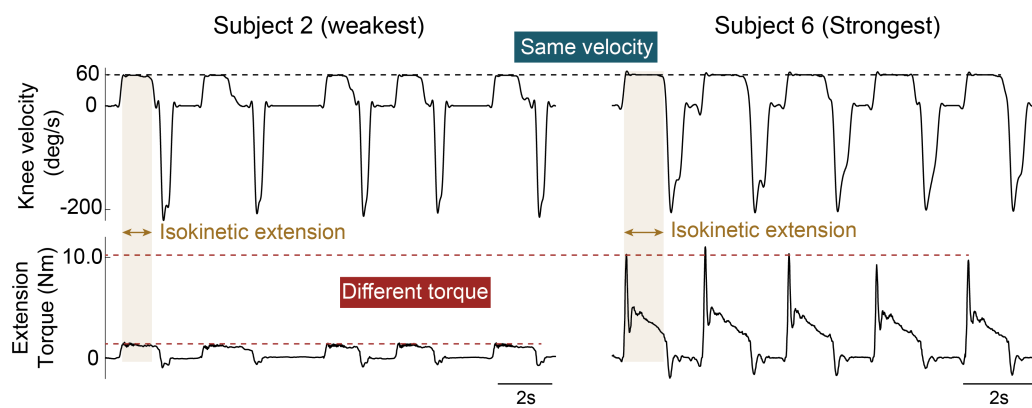
1133 36. Prat-Ortega, G. *et al.* First-in-human study of epidural spinal cord stimulation in individuals with
 1134 spinal muscular atrophy. *Nat. Med.* **31**, 1246–1256 (2025).
 1135

1136



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1138 **Supplementary Fig. 32 | Participant information.** (a) Age and body mass index (BMI) of the 6
 1139 intervention participants. The 6 participants included three 6-year-olds, and one each aged 7, 8, and
 1140 10 years. (b) Distribution of the Revised Hammersmith Scale (RHS) scores wherein 4 participants
 1141 scored ≤ 35 , with one scoring 40 and another 42.

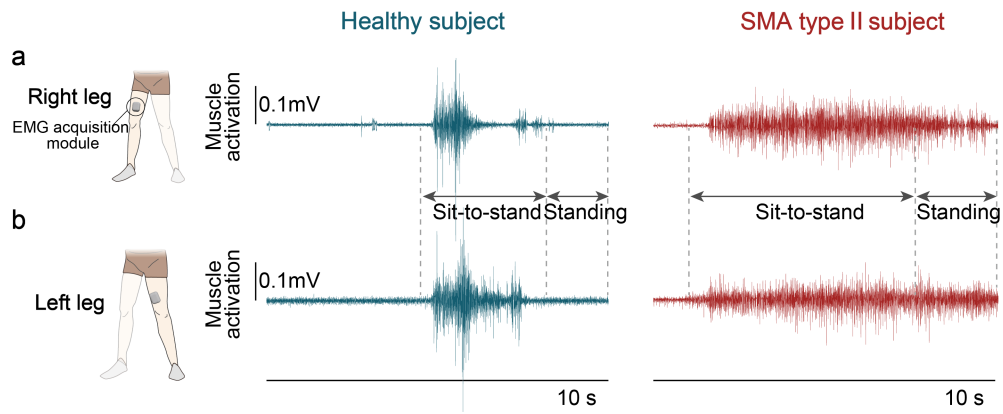


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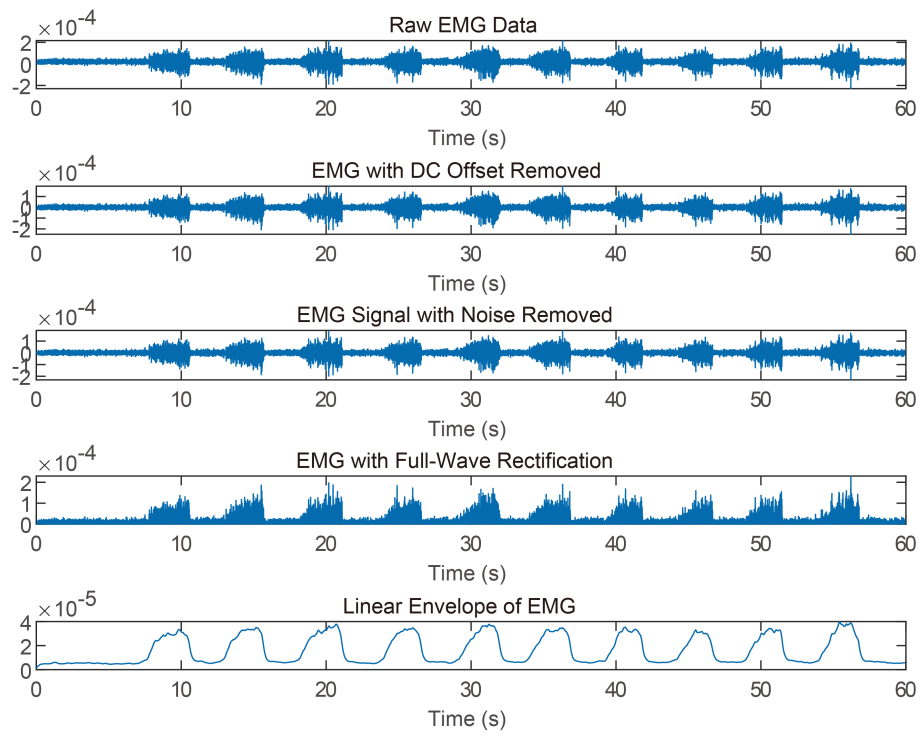
Supplementary Fig. 33 | Isokinetic knee velocity and torque for two representative subjects.



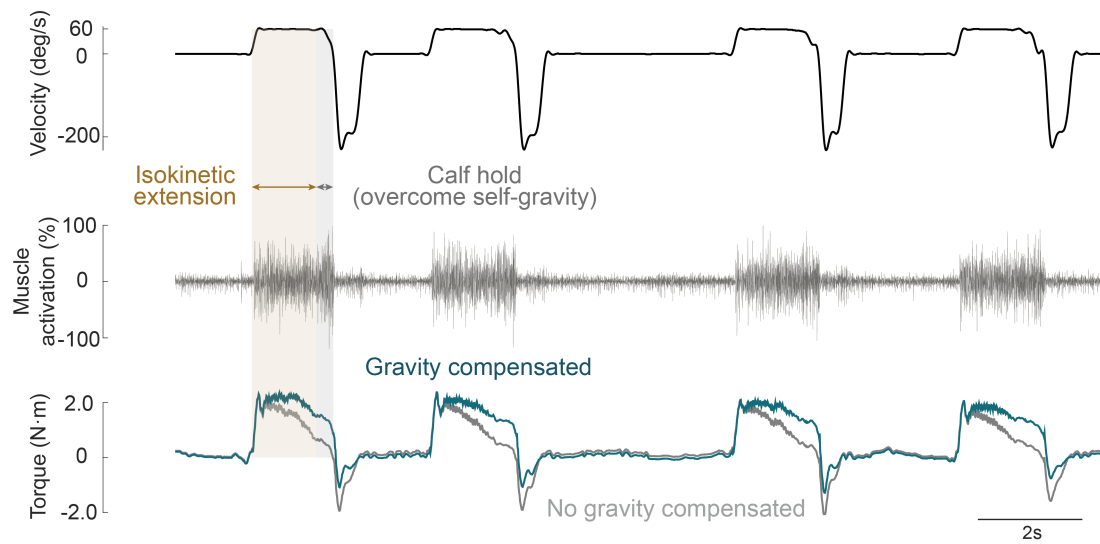
1145

1146 **Supplementary Fig. 34 | Quadriceps activation during sit-to-stand: healthy vs. SMA type II.** In
 1147 healthy juveniles, the quadriceps were briefly activated during the sit-to-stand transition and became
 1148 inactive once standing was achieved. In contrast, juveniles with Type II SMA exhibited continuous
 1149 quadriceps activation both during the transition and while maintaining the standing posture.

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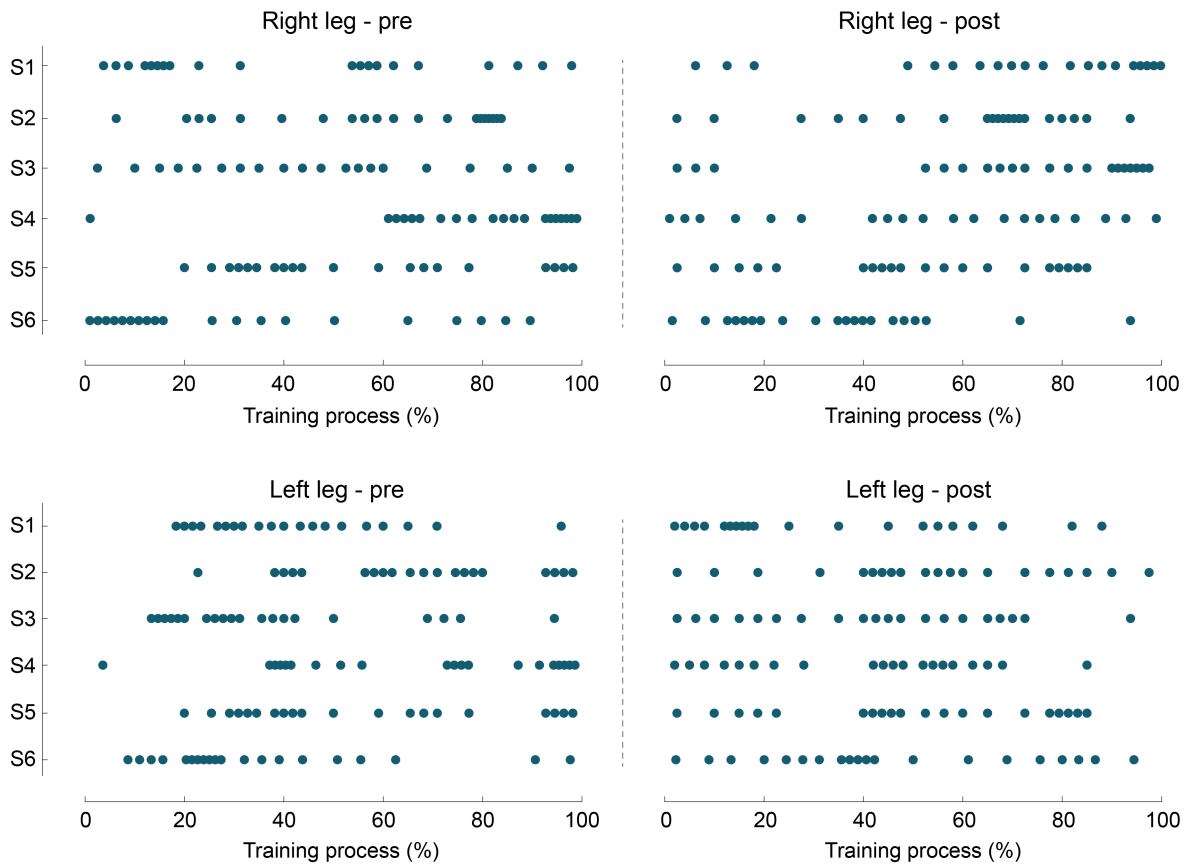
Supplementary Fig. 35 | sEMG data processing demo. The raw sEMG data (a) underwent DC offset removing (b), band-pass filtering (c, 20-450Hz), full-wave rectification (d), low-pass filtering at a 1-Hz cutoff to create linear envelopes (e).



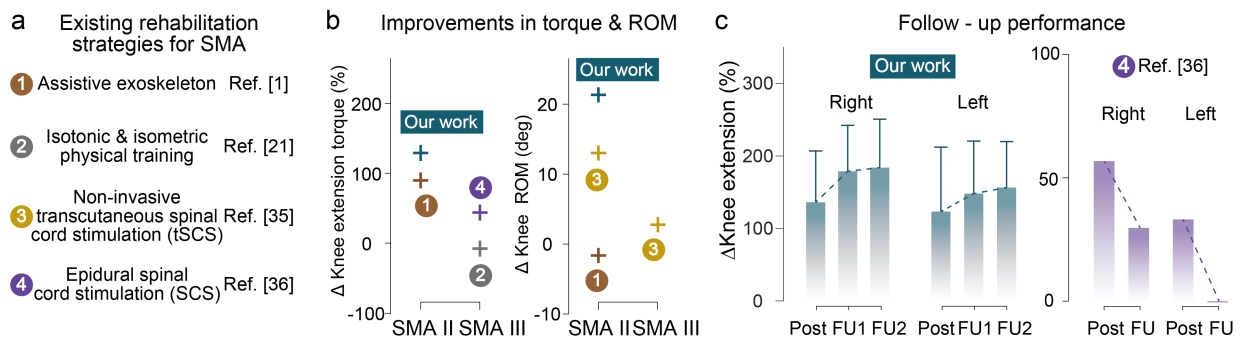
1156

1157 **Supplementary Fig. 36 | Gravity compensation enhances torque-sEMG alignment.** After gravity
 1158 compensation, the torque curve closely matched the muscle activation signals. In contrast, before
 1159 compensation, the measured torque did not reflect the underlying sEMG patterns.

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Supplementary Fig. 37 | Distribution of top 20 peak torque values across the full training session.



Supplementary Fig. 38 | Benchmarks of performance with alternative methodologies. (a) Existing rehabilitation methodologies for SMA: power-assisted, resistance training (isotonic & isometric training), non-invasive transcutaneous spinal cord stimulation (tSCS) and epidural cord stimulation (SCS). (b) Comparison of knee extension torque and range of motion (ROM). The participants in our study and Ref. [1] were diagnosed with SMA type II, whereas those in Ref. [21], [36] were patients with SMA type III. Ref. [35] included 2 juveniles with SMA Type II, and 3 juveniles with SMA type III. (c) Comparison of knee extension torque changes during the follow-up (FU) phases. Two follow-up phases were involved in this study: low intensity isokinetic training and no isokinetic training.

*Note: The torque data of Ref. [21] and Ref. [36] were obtained from the comparative analysis presented in Ref. [36]. Fig. 5i in Ref. [36] adopts the cohort reported in Ref. [21] as the control group, with a mean value of -7.02% based on the provided source data. For Ref. [1], the original raw data was not available in the publication. We contacted the corresponding author via email to request the original data; however, no response was received prior to submission. Therefore, the torque values were extracted by digitizing the graphical data presented in the article. Additionally, follow-up data was only available in Ref. [36].

References [1], [21], [35] and [36] consistent with main text

1. Cumplido-Trasmonte, C. et al. Effects of ATLAS 2030 gait exoskeleton on strength and range of motion in children with spinal muscular atrophy II: a case series. *J. Neuroeng. Rehabil.* **19**, 75 (2022).
21. Montes, J. et al. Single-blind, randomized, controlled clinical trial of exercise in ambulatory spinal muscular atrophy: why are the results negative? *J. Neuromuscul. Dis.* **2**, 463-470 (2015).
35. Novikov, A., et al. First use of non-invasive spinal cord stimulation in motor rehabilitation of children with spinal muscular atrophy. *Life* **13**, 449 (2023).
36. Prat-Ortega, G. et al. First-in-human study of epidural spinal cord stimulation in individuals with spinal muscular atrophy. *Nat. Med.* **31**, 1246-1256 (2025).

1192 **Supplementary Tables**

1193 **Supplementary Table 1 | Lowest sit-to-stand knee angle**

Subject	1	2	3	4	5	6
Pre (°)	113	112	120	103	118	102
Post (°)	97	107	114	96	113	97
Decreased (°)	16	5	6	7	5	5

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Supplementary Table 2 | *P* values and effect sizes for Fig. 3h

Subject	Right leg (Pre-Post)		Left leg (Pre-Post)	
	<i>P</i> values	Effect size (Cohen's d)	<i>P</i> values	Effect size (Cohen's d)
1	< 0.001	8.3315	< 0.001	32.1611
2	< 0.001	21.7067	< 0.001	45.4638
3	< 0.001	14.1179	< 0.001	4.5615
4	< 0.001	41.7504	< 0.001	54.0709
5	< 0.001	18.4727	< 0.001	24.9616
6	< 0.001	13.1347	< 0.001	11.3328

Note: Effect sizes in this table are within-subject values computed from 20 repeated peak-torque measurements per phase. The small within-subject SD inherent to this design yields large Cohen's d values, which reflect response consistency across trials rather than between-subject intervention effects.

Supplementary Table 3 | *P* values and effect sizes for Fig. 4

Metrics	Right leg extensors (Pre-Post)		Left leg extensors (Pre-Post)	
	<i>P</i> values	Effect size (Cohen's d)	<i>P</i> values	Effect size (Cohen's d)
Fig. 4(b) ACSA	< 0.001	2.9579	0.0088	1.7007
Fig. 4(d) Volume	0.0038	2.0720	0.0060	1.8630
Fig. 4(g) PCSA	0.0048	1.9702	0.0065	1.8303

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Supplementary Table 4 | *P* values and effect sizes for Fig. 5

Metrics (Pre-Post)	<i>P</i> values	Effect size (Cohen's d)
Fig. 5(b) Right CMAP	0.0817	0.6667
Fig. 5(b) Left CMAP	0.0413	0.8842
Fig. 5(b) Average CMAP	0.0087	0.8079
Fig. 5(c) Coordination	0.0417	0.8809

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Supplementary Table 5 | *P* values and effect sizes for Fig. 6

	<i>P</i> values			Effect size (Cohen's d)		
	Pre-Post	Pre-FU1	Pre-FU2	Pre-Post	Pre-FU1	Pre-FU2
(a) Right leg normalized peak torque	0.0077	0.0054	0.0062	1.7549	1.9129	1.8491
(a) Left leg normalized peak torque	0.0155	0.0101	0.0043	1.4699	1.6441	2.0174
(b) Right leg ROM increase	0.0045	0.0166	0.0170	1.9980	1.4453	1.4345
(b) Left leg ROM increase	0.0071	0.0014	0.0019	1.7919	2.5960	2.4356
(c) Right leg normalized average work	0.0040	0.0086	0.0099	2.0481	1.7094	1.6497
(c) Left leg normalized average work	0.0248	0.0199	0.0390	1.2945	1.3762	1.1344
(d) Right leg normalized ACSA	0.0009	0.0017	0.0098	2.8775	2.5079	1.6558
(d) Left leg normalized ACSA	0.0066	0.0173	0.0389	1.8223	1.4284	1.1352
(e) Right leg normalized volume	0.0107	0.0049	0.0147	1.6185	1.9596	1.4906
(e) Left leg normalized volume	0.0073	0.0029	0.0139	1.7789	2.2069	1.5129
(f) Right leg normalized PCSA	0.0159	0.0070	0.0199	1.4602	1.7960	1.3750
(f) Left leg normalized PCSA	0.0148	0.0042	0.0151	1.4884	2.0354	1.4822
(g) Right leg CMAP	0.0817	0.0445	0.0130	0.6667	0.8602	1.2767
(g) Left leg CMAP	0.0413	0.0273	0.0330	0.8842	1.0200	0.9574
(g) Coordination	0.0417	0.1128	0.0706	0.8809	0.5642	0.7130
(h) Lowest standing angle	0.0088	0.0064	0.0090	-1.6973	-1.8369	-1.6903

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Supplementary Table 6 | Subjective evaluations from guardians of the participants

Subject ID	Assessment
1	a) Marked increase in active knee extension height and range while seated. b) Improved general mobility (rolling), indicative of better lower limb coordination.
2	a) Improved knee control allowed for slowly climbing onto a bed from a standing position. b) Improved eccentric and concentric knee control during squatting (able to descend, hold, and recover independently). c) Enhanced knee stability while standing, reducing fall risk. d) Increased endurance during static standing.
3	a) Able to perform sit-to-stand transfers in the bathroom using armrests for support. b) Able to independently lift legs to climb onto a bed from a standing position.
4	a) Able to stand from bed using hand-on-thigh support. b) Improved knee stability in a kneeling position (maintained for tens of seconds).
5	a) Increased ROM in active knee extension while seated. b) Increased endurance during static standing.
6	a) Marked increase in force during standing knee extension (kicking). b) Increased leg elevation in 3-point support, demonstrating improved knee control.

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Supplementary Table 7 | Six juveniles with SMA type II

Subject	Sex	Age (years)	Weight (kg)	Height (cm)	RHS (scores)
1	M	7	33	124	35
2	F	6	15	109	29
3	F	6	16	114	42
4	M	6	20	119	35
5	F	8	26	130	34
6	M	10	27	122	40
Mean (SD)	-	7.2 (1.60)	22.83 (7.03)	119.67 (7.45)	35.83 (4.62)

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RHS: Revised Hammersmith Scale

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Before their involvement, participants and their guardians underwent an informed consent process in accordance with the procedure approved by the Medical Science Research Ethics Committee of Peking University Third Hospital and the Biological and Medical Ethics Committee of Beihang University.

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1220 **Supplementary Table 8 | Height and body weight of participants throughout the study period**

Subject	Weight (kg)					Height (cm)				
	Baseline	Pre	Post	FU-1	FU-2	Baseline	Pre	Post	FU-1	FU-2
1	33	33	34	35	35	124	125	125	126	126
2	15	16	16	17	18	109	110	110	112	112
3	16	17	17	16	17	114	115	115	116	116
4	20	20	20	20	21	119	120	120	120	121
5	26	27	27	28	28	130	130	131	131	132
6	27	27	28	28	29	122	123	123	124	125

1221 Before their involvement, participants and their guardians underwent an informed consent process
1222 in accordance with the procedure approved by the Medical Science Research Ethics Committee of
1223 Peking University Third Hospital and the Biological and Medical Ethics Committee of Beihang
1224 University.

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Before their involvement, participants and their guardians underwent an informed consent process in accordance with the procedure approved by the Medical Science Research Ethics Committee of Peking University Third Hospital and the Biological and Medical Ethics Committee of Beihang University.

Subject	Sex	Age (years)	Weight (kg)	Height (cm)
H1	M	7	21	130
H2	M	10	40	147
H3	F	9	30	139
H4	M	6	20	113
H5	F	6	22	115
H6	F	6	23	117
Mean (SD)	-	7.3 (1.75)	26.0 (7.72)	126.8 (14.09)

Before their involvement, participants and their guardians underwent an informed consent process in accordance with the procedure approved by the Medical Science Research Ethics Committee of Peking University Third Hospital and the Biological and Medical Ethics Committee of Beihang University.

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Supplementary Table 10 | Number of training repetitions per trial across all subjects

Subject ID	Mean (SD)
1	112 (16)
2	92 (13)
3	80 (6)
4	98 (16)
5	92 (12)
6	84 (14)
Mean (SD)	93 (11)

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Supplementary Table 11 | Change in optimal stiffness

		S1	S2	S3	S4	S5	S6
Right	Pre	24.02	9.57	28.16	25.23	16.31	28.16
(N·m/rad)	Post	28.16	28.16	28.16	28.16	24.98	28.16
Left	Pre	15.83	28.16	19.87	21.85	25.47	14.39
(N·m/rad)	Post	28.16	28.16	25.51	28.16	28.16	26.91

1234 **Note:** 28.16 (N·m/rad) is the maximum stiffness.

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1236 **Supplementary Table 12 | Resistance range across different motors and gear ratios (60°/s)**

Ratio	GIM4310		Robstride01	
	Min (N·m)	Max (N·m)	Min (N·m)	Max (N·m)
3	0.7(±0.1)	4.0(±0.1)	1.3(±0.1)	11.8(±0.1)
3.5	1.0(±0.1)	6.0(±0.1)	/	/
4	1.2(±0.1)	7.5(±0.1)	/	/
4.5	1.5(±0.1)	8.8(±0.1)	/	/

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Supplementary Table 13 | Change in gear transmission ratio

	S1	S2	S3	S4	S5	S6
Transmission Ratio Change	3.5→4	3	3→4	3→4	3.5→4	4→4.5→3*
Motor	GIM431 0	GIM431 0	GIM431 0	GIM431 0	GIM431 0	GIM4310, RobStride01*
Adjustment Timing	30 th Trial	30 th Trial	30 th Trial	30 th Trial	30 th Trial	20 th Trial, 40 th Trial

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*: In the follow-up 1 phase, the torque generated by subject 6 exceeded the capacity of the GIM4310 to provide sufficient isokinetic resistance. To address this limitation, we replaced it with a higher-torque motor (RobStride01). After the replacement, a gear set with a transmission ratio of 3 was employed.

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Supplementary Table 14 | Comparison of motor parameters

	GIM4310	RobStride01
Voltage Range (V)	12~40	24~48
Rated Torque (N·m)	2.05	6
Power (W)	55	170
Torque Constant (N·m /A)	0.96	1.22
Rated Current (A)	2.3	7
Gear Ratio	10	7.75
Number of Poles	28	28
Weight (g)	217	380
Size (mm)	Ø53*32	Ø78.5*40

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Supplementary Table 15 | Sandbag weight for isometric/isotonic training

Subject	Mean torque (N·m)	lower leg length (m)	Mass of sandbag (kg)
1	2.00	0.26	1.00
2	1.30	0.20	0.75
3	0.90	0.22	0.50
4	2.40	0.25	1.00
5	2.85	0.30	1.00
6	3.00	0.26	1.25

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1251 **Supplementary Table 16 | Power consumption of the isokinetic training robot at 60°/s**

	U (V)	I (A)	P (W)
Expt.1	12.00	0.055	0.66
Expt.2	12.00	0.056	0.67
Expt.3	12.00	0.055	0.66
Expt.4	12.00	0.055	0.66
Expt.5	12.00	0.056	0.67
Mean ± SD	12.00 ± 0.00	0.0554 ± 0.0005	0.66 ± 0.01
Est. Duration (3.7V 3800mAh)	21.3 h (36.5 days)		

1252 * Endurance (in days) was estimated based on a daily usage of 35 minutes (the average training
1253 duration across the 6 participants)
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Supplementary Table 17 Peak knee extension torque using inverse dynamic analysis							
during sit-to-stand (end of Follow-up 2)							
Subject	1	2	3	4	5	6	Mean (SD)
Torque (N·m)/(kg·m)	1.03	1.08	0.92	0.87	0.89	1.10	0.98(0.10)

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Supplementary Table 18 | Resistive training (RT) VS Assistive training (AT)

Year	Subject	Duration	Effect	Indicator
2021(Ref. [28])	47	20 sessions in 8 weeks	RT>AT (Better)	Maximal sprint speed
2024(Ref. [29])	34	20 sessions in 4 weeks	RT>AT (Better)	Smoothness
2014(Ref. [30])	9	16 sessions in 4 weeks	RT>AT (Better)	10 m walk test (max)
2011(Ref. [31])	27	12 sessions in 4 weeks	RT>AT (Better)	Maximal velocity & acceleration (>15 yd)

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Supplementary Table 19 | Comparison of range of motion (ROM)

	Ref. [38]	Our
Right	15.2 deg	24.5 deg
Left	7.9 deg	18.1 deg

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* Since the referenced study did not report torque data, only range of motion (ROM) can be used for comparison.

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Supplementary Table 20 | Variability of muscle and joint Stiffness

Study	Journal	Original Text
Ref. [39]	The Journal of Physiology (1991)	“ We believe that the negative muscle stiffness is a property of decisive functional importance in motor control and that stiffness is one of the most important regulated properties of muscles.”
Ref. [40]	PLOS One (2025)	“Our results suggest that the neural control strategy for limb dynamics compensation involves the modulation of the co-contraction of proximal and distal antagonistic muscles that change limb stiffness .”
Ref. [41]	Frontiers in Neurorobotics (2012)	“Co-contraction alters the biomechanical operating ranges of muscle and tendon by increasing both muscle damping (viscosity) and musculotendon stiffness (elasticity).”
Ref. [42]	Experimental Brain Research (1994)	“Co-contraction results in a larger stiffness of the limb about the joint than that which is obtained by activity of any of the two antagonistic muscle groups separately.”
Ref. [43]	2025 11th International Conference on Mechatronics and Robotics Engineering	“The decrease in passive stiffness and damping suggests that the CNS gradually reduced the balance strategy of using muscle co-contraction to increase joint stiffness and damping.”

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Supplementary Table 21 | “Sit-to-stand” item of the RHS scale

Test	Instruction	2	1	0
Sit-to-stand (Starting in a stand up from 90°/90° position the chair/bench using a keeping your Plinth/Bench/Chair arms folded if) you can?	Can you stand up from the chair/bench keeping your arms folded if you can?	Able to stand up without using arms (keeping arms folded, feet do not move)	Stands by using strategies: (circle relevant) Uses hands on legs / chair Turns Prone / Widens Base	Unable

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1273 **Supplementary Table 22 | Peak torque measured by our robot before intervention study (Pre)**

Subject	1	2	3	4	5	6
Right (N·m)	1.74(±0.43)	1.44(±0.07)	1.19(±0.08)	1.44(±0.16)	2.30(±0.10)	3.66(±0.33)
Left (N·m)	1.64(±0.15)	1.59(±0.07)	1.26(±0.07)	1.46(±0.17)	2.50(±0.07)	3.53(±0.15)

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Supplementary Table 23 | Cost estimation

Items	Cost (\$)
Machine work (batch production)	70
3D-printing	50
Sensors	62
motor	77
Straps	12
Circuits and electronic components	98
Total	369

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Supplementary Table 24 | Comparison of prior studies

Number	Type	Intervention
Ref. [1]	3 Type II	Assistive robot
Ref. [21]	9/14 Type III	Isotonic & isometric physical exercise
Ref. [35]	2 Type II, 3 type III	Non-invasive transcutaneous spinal cord stimulation
Ref. [36]	3 type III	Epidural spinal cord stimulation
Ours	6 type II and 6 healthy	Isokinetic training with robot

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References [1], [21], [35] and [36] consistent with main text

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1. Cumplido-Trasmonte, C. et al. Effects of ATLAS 2030 gait exoskeleton on strength and range of motion in children with spinal muscular atrophy II: a case series. *J. Neuroeng. Rehabil.* **19**, 75 (2022).

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21. Montes, J. et al. Single-blind, randomized, controlled clinical trial of exercise in ambulatory spinal muscular atrophy: why are the results negative? *J. Neuromuscul. Dis.* **2**, 463-470 (2015).

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35. Novikov, A., et al. First use of non-invasive spinal cord stimulation in motor rehabilitation of children with spinal muscular atrophy. *Life* **13**, 449 (2023).

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36. Prat-Ortega, G. et al. First-in-human study of epidural spinal cord stimulation in individuals with spinal muscular atrophy. *Nat. Med.* **31**, 1246–1256 (2025).

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Supplementary Table 25 | Comparison of nerve conduction metrics with other studies

	Type	Nerve conduction metrics	Journal
[36]	Adults: 3 Type III	Unclear	Nature Medicine, 2025
[35]	Juveniles: 2 Type II, 3 Type III	×	Life, 2023
[19]	Juveniles: 6 Type II, 3 Type III	×	Muscle Nerve, 2015
[1]	Juveniles: 3 Type II	×	J Neuroeng Rehabil, 2022
This study	Juveniles: 6 type II experiment group, 6 healthy reference group	√ (Femoral nerve conduction)	

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References [1], [19], [35] and [36] consistent with main text

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1. Cumplido-Trasmonte, C. et al. Effects of ATLAS 2030 gait exoskeleton on strength and range of motion in children with spinal muscular atrophy II: a case series. *J. Neuroeng. Rehabil.* **19**, 75 (2022).

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19. Lewelt, A. et al. Resistance strength training exercise in children with spinal muscular atrophy. *Muscle Nerve* **52**, 559-567 (2015).

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35. Novikov, A., et al. First use of non-invasive spinal cord stimulation in motor rehabilitation of children with spinal muscular atrophy. *Life* **13**, 449 (2023).

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36. Prat-Ortega, G. et al. First-in-human study of epidural spinal cord stimulation in individuals with spinal muscular atrophy. *Nat. Med.* **31**, 1246–1256 (2025).

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Supplementary Table 26 | Daily training time

Subject Activity	1	2	3	4	5	6
Suspended squat (min)	0	20	0	0	0	0
Knee extension (min)	30	0	20	20	20	10
Wall sit (min)	0	15	20	10	25	20

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Supplementary Table 27 | Comparison between the revised and the first version

	Firstly	Revised
Torque	√	√
Sit-to-stand test	√	√
Work/power	√	√
Surface electromyography (sEMG)	√	√
Anatomical Cross-Sectional Area (MRI)	√	√
Physiological Cross-Sectional Area (MRI)	×	√
Volume (MRI)	×	√
Range of motion (ROM)	×	√
Femoral nerve conduction	×	√
Baseline group (non-intervention)	×	√
Follow-up study	×	√ (2 phases)
Ultrasound	×	√
Healthy subjects	×	√ (6)
RHS	×	√
Isotonic training	×	√
Isometric training	×	√
Number of Subjects	1	6(SMA)+6(Healthy) >5.5 months
Duration	2 months (training)	(6 weeks + 6 weeks + 6 weeks + >30 days)

1308 MRI: Magnetic Resonance Imaging

1309 RHS: Revised Hammersmith Scale

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Supplementary Table 28 | Comparison of patient numbers with previous studies

	Sample size	Type	Duration	Journal
[36]	3	Adults: 3 Type III	4 weeks	Nature Medicine, 2025
[35]	5	Juveniles: 2 Type II, 3 Type III	10-14 days	Life, 2023
[38]	1	1 juvenile with cerebral palsy	10 visits	IEEE BioRob, 2022
[1]	3	Juveniles: 3 Type II	9 sessions, bi-weekly	J Neuroeng Rehabil, 2022
This study	6+6	Juveniles: 6 type II experiment group, 6 healthy reference group	>5.5 months (SMA)	

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1313 **References [1], [35] and [36] consistent with main text**

1314 1. Cumplido-Trasmonte, C. et al. Effects of ATLAS 2030 gait exoskeleton on strength and range of
1315 35. Novikov, A., et al. First use of non-invasive spinal cord stimulation in motor rehabilitation of
1316 children with spinal muscular atrophy. *Life* **13**, 449 (2023).
1317 36. Prat-Ortega, G. *et al.* First-in-human study of epidural spinal cord stimulation in individuals with
1318 spinal muscular atrophy. *Nat. Med.* **31**, 1246–1256 (2025).
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Study	Journal	Original Text
Ref. [45]	Cochrane Database of Systematic Reviews (2019)	“It is uncertain whether combined strength and aerobic exercise training is beneficial or harmful in people with SMA type 3, as the quality of evidence is very low .”
Ref. [1]	Journal of NeuroEngineering and Rehabilitation (2022)	“..., all of them (hip and knee extension and ankle dorsiflexion) improved after the use of the exoskeleton compared to the initial state.” “..., knee ROM did not increase after the training sessions in our study.”
Ref. [21]	Journal of Neuromuscular Diseases (2015)	“Table 3. HHD knee extension (kg) Baseline: 4.44 (1.58); Month 6: 3.54 (1.52)” (Decrease)
Ref. [36]	Nature Medicine (2025)	“Even though exercise is known to be ineffective in SMA, ...”

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References [1], [21], [36] and [45] consistent with main text

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Study	Journal	Original Text
Ref. [8]	Wearable Technologies (2025)	“Additionally, we highlight critical gaps in current research, such as the lack of sufficient long-term evaluations and studies assessing sustained therapeutic impacts.”
Ref. [9]	Annals of Biomedical Engineering (2025)	“It is not clear from our data whether any longer-term changes to movement behaviors may have occurred over exposure durations of the order of several hours or over multiple days/sessions occurring over several weeks/months.”
Ref. [10]	Journal of neuroengineering and rehabilitation (2021)	“In addition, evidence supporting their benefits is still limited to short-intervention trials with few participants and diversity among their clinical protocols.”
Ref. [11]	Systematic Reviews (2025)	“However, current evidence regarding long-term follow-up as well as pediatric and elderly subgroups remains limited , ...”

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References [8-11] consistent with main text

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Supplementary Table 31 | Literatures on small sample trial challenges

Study	Journal	Original Text
Ref. [52]	Orphanet journal of rare diseases (2018)	“..., especially when traditional randomised control trial designs are not possible due to limited number of available patients.”
Ref. [53]	Orphanet journal of rare diseases (2019)	“The classical randomized controlled trial (RCT) cannot always be conducted , because of small numbers of eligible patients and the heterogeneity of the patient groups.”

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Note: Spinal Muscular Atrophy (SMA) is a typical rare neurodegenerative disease⁵⁴⁻⁵⁸.

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1351 **Supplementary Videos**

1352 **Video 1: Robot design and structure.**

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1354 **Supplementary References**

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