

Spinal neuromotor rehabilitation using a portable isokinetic training robot

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Most lower-extremity assistive robots are designed to actively assist gait^{1–7} without considering long-term neuromuscular adaptations^{8–11}. Here we present a lightweight (0.96 kg) robot that administers isokinetic resistance training to sustain neuromuscular rehabilitation after removal. The device integrates a variable stiffness mechanism with a back-drivable damping motor to make available safe, portable and customizable resistance training to juveniles with spinal muscular atrophy (SMA) type II. In a study involving six such juvenile participants, substantial improvements in lower-extremity motor ability were observed after 6 weeks of robot-assisted training in a clinical trial (NCT06648486). Participants gained the ability to perform sit-to-stand transitions with hands on knees but without external support from an average seated knee flexion angle of 111° to 104°, representing a 7° improvement from pre-intervention. This improvement was accompanied by greatly increased bilateral knee joint function (peak torque: +130%; range of motion (ROM): +51%; work: +97%). Marked physiological quadriceps muscle hypertrophy was observed (anatomical cross-sectional area (ACSA): +12%; volume: +19%; physiological cross-sectional area (PCSA): +21%) alongside enhanced femoral nerve conduction (compound muscle action potential (CMAP): +19%), representing physiological changes consistent with the observed functional improvements. Notably, participants were able to retain their gains after discontinuing isokinetic training and returning to their conventional physiotherapy routines. These results indicate that even temporary exposure to isokinetic resistance training through wearable robotics may facilitate enduring neuromuscular recovery.

SMA ranks among the most prevalent autosomal recessive diseases, with an incidence of approximately 1 in 6,000–10,000 live births and a carrier frequency of around 1 in 50 (refs. 12–14). It is clinically classified into four subtypes based on the age of onset and achieved motor milestones. SMA type I is the most severe, with affected individuals only ever achieving limited head control. SMA type II is milder, with individuals capable of sitting independently but unable to walk. SMA types III and IV are milder yet, with those affected typically capable of walking early in the course of the disease and later with mobility aids. At present, medications only slow disease progression and no therapy can fully cure SMA (ref. 15).

Resistance training has emerged as a promising rehabilitation approach to managing the symptoms of SMA. Four clinical studies involving individuals with SMA and other neuromuscular disorders have reported substantial improvements in muscle strength and motor function following structured resistance training programmes^{16–19}. Furthermore, physical exercise has previously sustained motor function and demonstrated a 57.3% improvement in longevity, alongside reductions in muscle atrophy, apoptosis and neuronal mortality in type II SMA-like mouse models compared with controls without such training²⁰. These findings suggest that physical rehabilitation may preserve

motor function in patients with SMA (ref. 19), especially through physical exercise that actively stimulates muscle contraction²¹. In particular, isokinetic resistance training enforces dynamic muscular contractions at a constant movement speed, ensuring that the muscles generate maximal tension throughout the entire range of joint motion^{22–26}, thus leading to optimal rehabilitation outcomes²⁵.

However, isokinetic resistance training is predominantly available only in specialized institutions that focus on athlete rehabilitation and muscle strength assessment^{27,28}. It is typically administered using training systems such as Biodex²⁹, Kineo³⁰, CON-TREX MJ (ref. 31) and IsoMed 2000 (ref. 32). The minimum resistance levels provided by these machines are often too high for individuals and, in particular, juveniles with SMA. The bulky designs of these devices and the high cost of entry into their hosting facilities further limit accessibility.

So far, rehabilitation interventions specifically targeting juveniles with SMA remain poorly studied, with limited high-quality evidence available to systematically evaluate their efficacy. Although physical therapy and exercise are routinely recommended to preserve muscle strength and function, existing studies largely focus on adult populations³³ or animal models²⁰, leaving paediatric rehabilitation under-represented³⁴. Neuromodulation methods, including non-invasive

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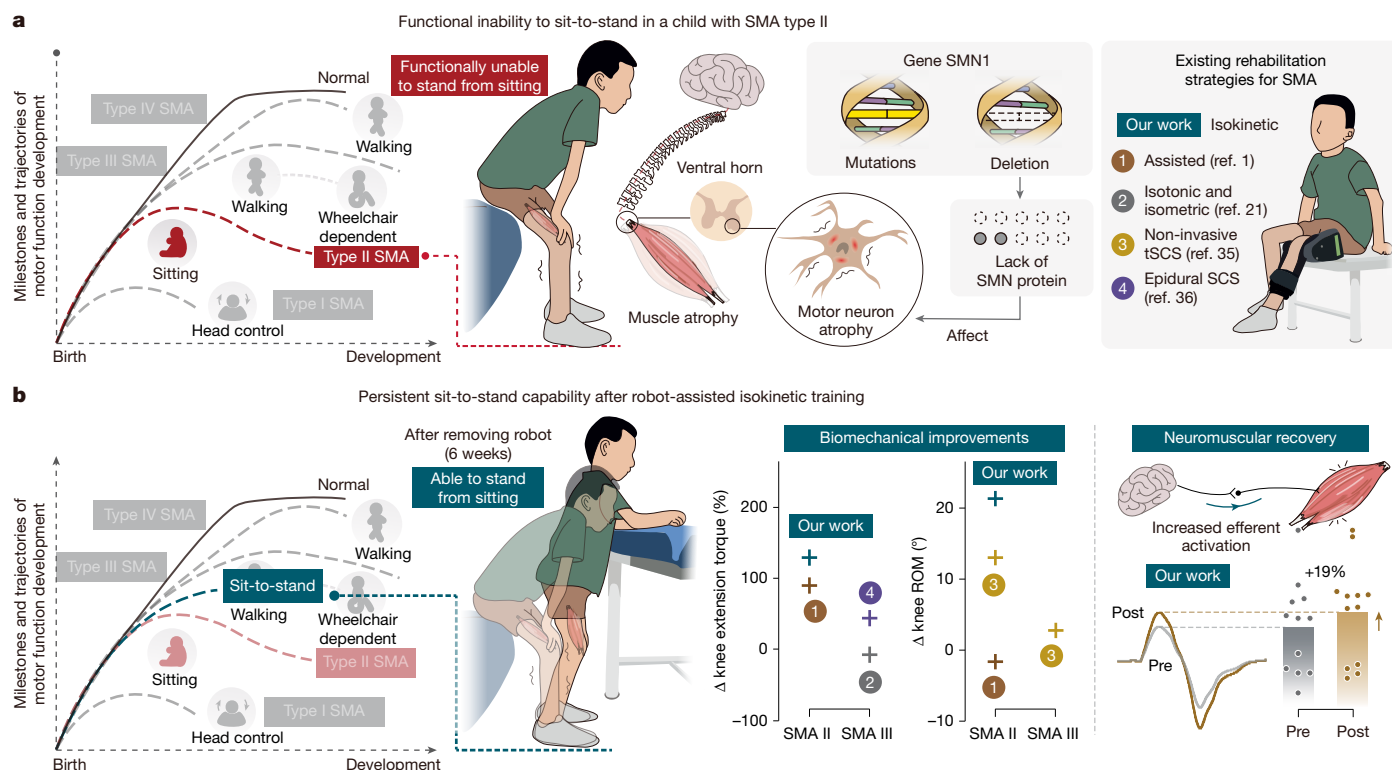


Fig. 1 | Isokinetic resistance training with a wearable robot enables juveniles with SMA type II to perform unassisted standing movements. a, Juvenile subjects with SMA type II were initially unable to stand without external support (self-assist allowed) from a typical seated position. In the absence of intervention, their motor function typically plateaus or declines progressively with age following disease onset. The deletion or mutation of the survival motor neuron 1 (SMN1) gene results in a deficiency of the SMN protein, leading to muscle wasting and weakness. Existing rehabilitation strategies primarily involve isotonic and isometric training²¹, neuromodulation approaches such as non-invasive transcutaneous spinal cord stimulation (tSCS)³⁵ and epidural

spinal cord stimulation (SCS)³⁶, as well as assistive robots¹. **b,** The ability to stand without external support (self-assist allowed) was achieved after isokinetic knee extension training with our experimental wearable robot. Subjects demonstrated improved knee extension strength and ROM as well as increased efferent muscle activation, correlating with a sustained ability to independently transition from sitting to standing. The panels describing neuromuscular milestones and trajectories in SMA were adapted from ref. 13 with modifications under a Creative Commons Attribution 4.0 International License.

transcutaneous spinal cord stimulation³⁵ and epidural spinal cord stimulation³⁶, have also shown potential in improving motor function in individuals with SMA. However, these stimulation techniques require supplementation with active motor training to be effective, as stimulation alone may be insufficient to promote functional recovery³⁶. There remains an urgent need for a portable solution that can provide adaptable-resistance isokinetic training to improve the lives of juveniles with SMA.

Wearable lower-extremity robots present an ideal form factor to deliver neuromuscular rehabilitation³⁷, but no such device exists at present to provide isokinetic resistance training to juveniles with SMA. Most wearable lower-extremity robots are primarily designed for adults to actively assist walking by decreasing efferent muscle activation^{1–7}. Rehabilitation-oriented devices may aim to assist individuals with complete spinal cord injuries in standing and walking^{38,39}, whereas others focus on improving gait for patients with stroke^{40–42}. Although these devices may provide short-term performance improvements in users, it remains unclear whether these benefits translate into long-term functional recovery or neuromuscular adaptation once the device is removed^{8–11}. Their benefit may be even more limited for individuals with conditions such as SMA types II and III who require increased efferent muscle activation for proper neuromuscular function (Fig. 1a).

In this study, we designed and implemented a lightweight (0.96 kg), untethered wearable knee robot to provide isokinetic training to juveniles with SMA type II. The robot features variable resistance control and integrated torque sensing to enforce isokinetic concentric contraction

of the quadriceps during knee extension. To enhance user engagement and comfort, a mobile application was also developed to gamify training sessions. We hypothesized that regular and appropriate use of the robot would promote sustained muscle development and improve motor coordination in individuals with SMA type II even after cessation of training with the robot.

To validate the hypothesis, six juveniles with SMA type II (aged 6–10 years; three males and three females) were recruited into a customized training programme. Following 6 weeks of high-intensity isokinetic training, all individuals achieved progressive improvements in standing up from seats of decreasing height, with some continuing to improve during a subsequent 6-week low-intensity isokinetic training phase (follow-up 1). Notably, motor gains were largely retained during a final >30-day follow-up without isokinetic training (follow-up 2).

Throughout the study, we observed substantial increases in peak knee extension torque, ROM, work per extension, quadriceps ACSA, quadriceps volume, quadriceps PCSA and bilateral femoral nerve CMAP, suggesting physiological adaptations underlying the sustained improvements in functional ability. In contrast to most robot training approaches that emphasize short-term motor recovery through assistance towards normative movements³⁷, we achieved this result by using a heterodox approach that increased the difficulty of movement during exercise. Together, these findings establish the feasibility of applying resistive robot training to deliver targeted rehabilitation across other joints, such as the elbow and hip, and to paediatric populations with other neuromuscular conditions. This new class of rehabilitative

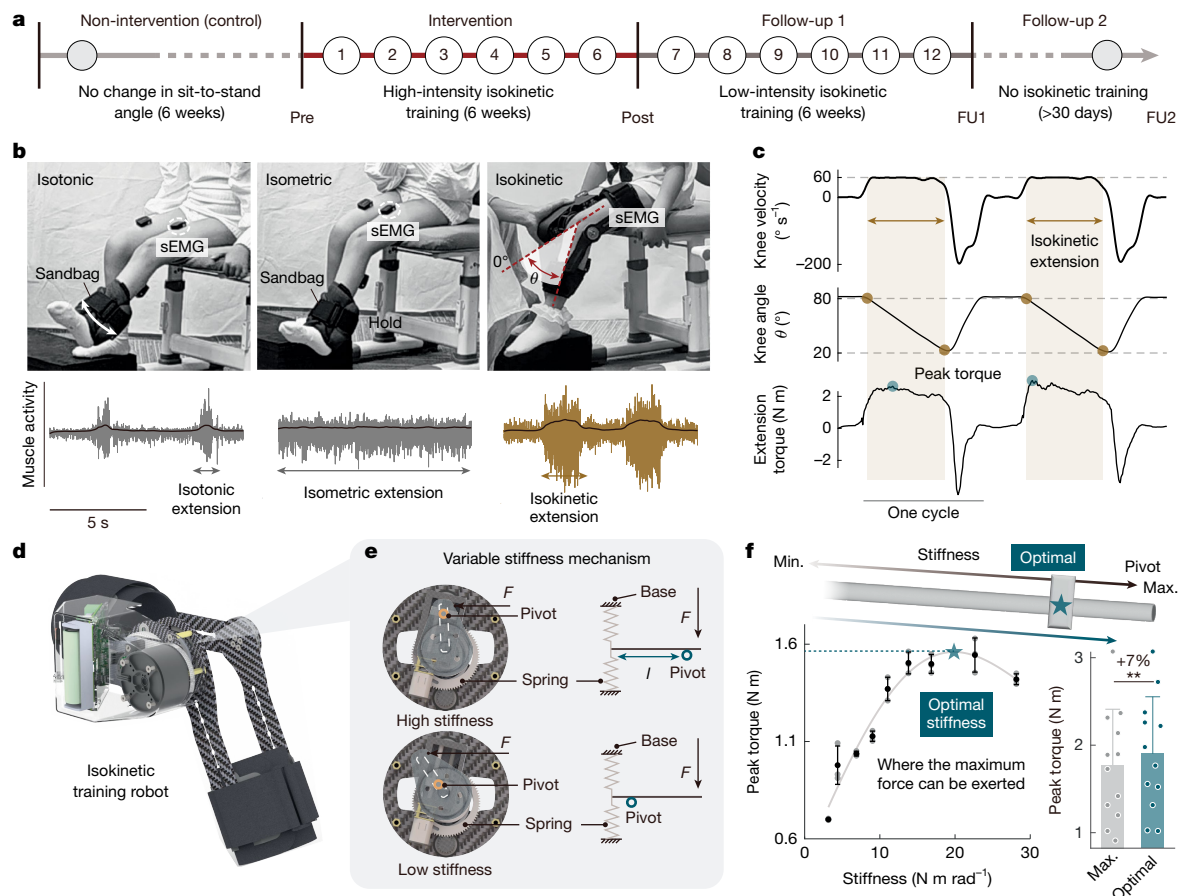


Fig. 2 | Isokinetic training robot with a variable stiffness mechanism for juveniles with SMA type II. **a**, Training and evaluation timeline. A cohort of six juveniles with SMA type II underwent a 6-week control period in which no change in initial sit-to-stand angle was observed ('Non-intervention'), followed by a 6-week high-intensity isokinetic training phase ('Intervention'), a 6-week low-intensity isokinetic training phase ('Follow-up 1') and a >30-day no isokinetic training phase ('Follow-up 2'). **b**, Quadriceps muscle activation in a representative juvenile (subject 2) with SMA type II during isotonic, isometric and isokinetic knee extension. **c**, Representative trajectories of knee velocity, knee angle and extension torque recorded during two isokinetic training repetitions. **d**, 3D rendering of the isokinetic robot. **e**, Variable stiffness mechanism used in the isokinetic robot. The stiffness of the mechanism is

wearable robots may enhance quality of life not by actively assisting difficult movements but by sustaining enduring neuromuscular recovery that empowers individuals through their own capabilities (Fig. 1b).

Clinical study design

To evaluate the feasibility and therapeutic potential of the portable isokinetic training robot, a clinical study (NCT06648486, <https://clinicaltrials.gov/study/NCT06648486>) was conducted involving six non-ambulatory juveniles with SMA type II (aged 6–10 years; three males and three females). SMA type II was selected as the most severe form of the disease in which patients can perform training with the robot. All participants were unable to perform sit-to-stand transitions from a seated position at 90° hip and knee flexion using voluntary quadriceps activation.

Participants first completed a 6-week non-intervention period while maintaining their usual physiotherapy routines (conventional rehabilitation): three received regular rehabilitation at a designated facility and three received home-based rehabilitation. No participant demonstrated improvement in their lowest sit-to-stand initial knee angle,

modulated by altering the position of a pivot. The centre-line distance between the pivot and the joint axis is denoted as l . **f**, Peak torque generated by a representative subject (subject 3, left leg) at different stiffness settings during isokinetic knee extensions. A fourth-order polynomial fit is applied to the discrete stiffness–peak torque data points (bars, mean; error bars, s.d.; scatters, each extension; $n = 3$). The stiffness corresponding to the maximum point on the fitted curve is the optimal stiffness for the subject and the associated parameter l is the corresponding optimal mechanical lever arm for the robot. Peak torque generated at the optimal stiffness is greater than at the maximum stiffness at Pre (bars, mean; error bars, s.d.; scatters, each leg; $n = 12$; $**P = 0.0094$, Cohen's $d = 0.91$, two-sided paired-sample t -test).

a clinical indicator of quadriceps strength and neuromuscular control, suggesting that their usual care routines and ageing-related development were insufficient to enhance functional muscle performance.

Subsequently, all participants underwent an acute 6-week phase of high-intensity isokinetic knee extension training using our portable robot (30 intervention trials; each trial consisting of ≥ 6 sessions per leg, ten movement repetitions per session), followed by a 6-week low-intensity isokinetic training phase (follow-up 1; 18 trials) and a final >30-day follow-up without isokinetic training (follow-up 2) (Fig. 2a). All trials were matched in duration to participants' previous routines and were conducted at home under caregiver supervision using a standardized robotic training protocol. Five participants trained at an isokinetic knee extension angular velocity of 60° s^{-1} , a target setting commonly applied in similar rehabilitation protocols^{43,44}. However, owing to limited ROM and insufficient muscle strength, subject 3 was assigned a lower target velocity of 45° s^{-1} to accommodate their specific physical capability. The device itself is capable of controlling resistance to maintain isokinetic angular speed in the range 15 – 150° s^{-1} (Supplementary Fig. 1). A mobile application provided real-time gamified feedback on knee extension torque, velocity and joint angle to promote interactive engagement.

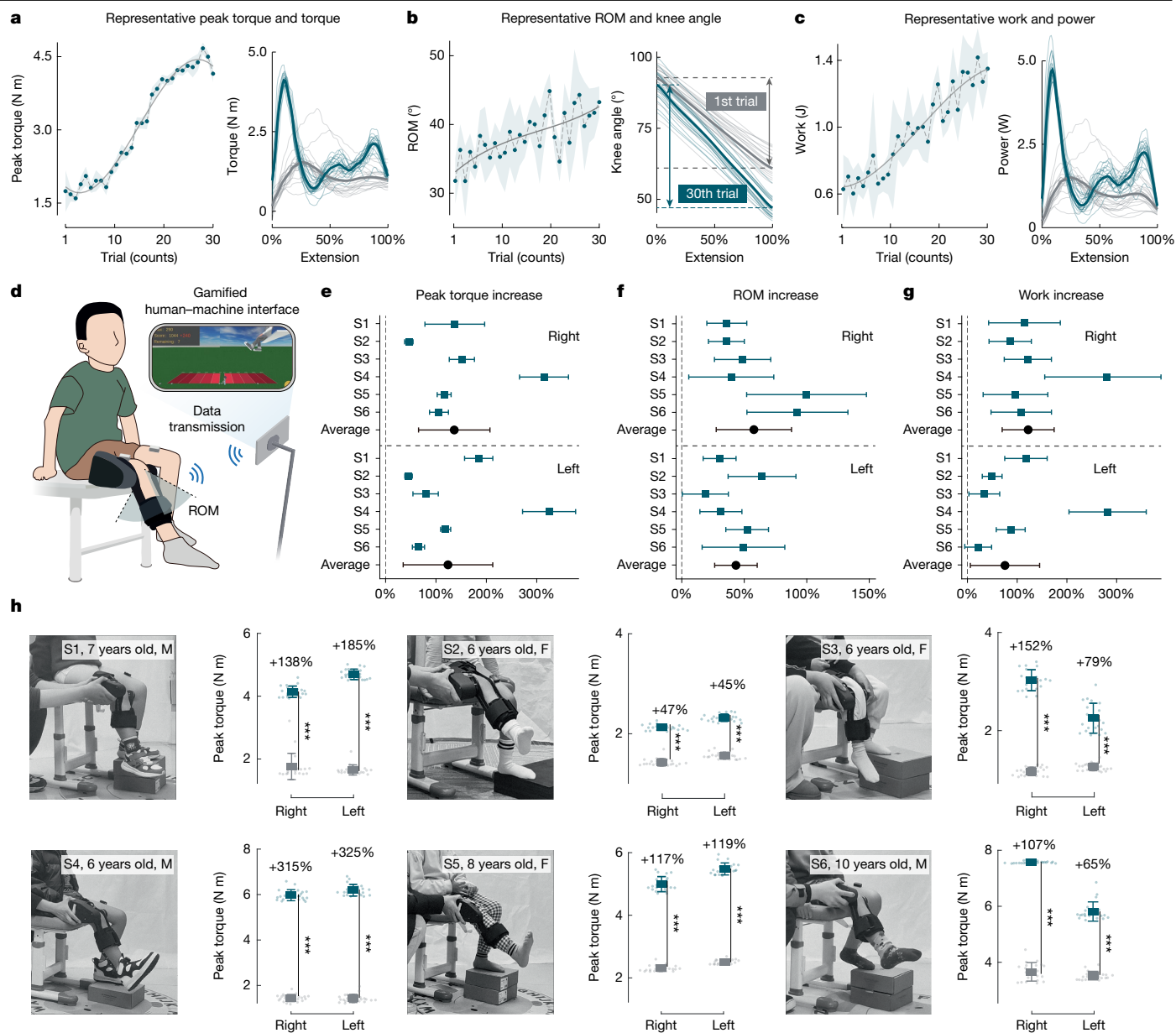


Fig. 3 | Biomechanical improvements associated with isokinetic knee extension training. **a–c**, Representative functional metrics from the right leg of subject 1. In each panel, data are presented in two parts: the left plot illustrates the longitudinal progression of peak torque, ROM and per-movement work over 30 high-intensity training trials spanning 6 weeks (scatters, mean; shaded regions, s.d.; $n = 20$); the right plot compares the associated biomechanical profiles (torque, knee angle and power) between the initial (1st) and final (30th) trials, with the x -axis representing the normalized extension phase (0–100%). Light lines denote a single knee extension repetition, whereas thick lines

indicate the means across repetitions. **d**, Isokinetic training set-up using the robot. Five subjects in the experimental cohort performed knee extension using the robot at an angular velocity of 60° s^{-1} , whereas one subject (subject 3) trained at 45° s^{-1} . **e–g**, Improvements in peak torque, ROM and work during isokinetic knee extension training across all participants (rectangles, mean; error bars, s.d.; $n = 6$). **h**, Details of peak torque improvements in left and right legs for each participant (rectangles, mean; error bars, s.d.; scatters, each repetition; $n = 20$; *** $P < 0.001$, two-sided independent samples t -test). All P -values and effect sizes are provided in Supplementary Table 2.

Comprehensive assessments were conducted at the end of each of four experimental phases at discrete time points designated as Pre, Post, FU1 and FU2 (Fig. 2a). Assessments included bilateral measurements of knee extension torque, ROM, work per extension, magnetic resonance imaging (MRI) of the thigh and femoral nerve conduction studies. The ability of each participant to perform hands-on-knees standing from progressively deeper-seated initial knee angles without external support was also documented at each assessment point (Supplementary Table 1).

After FU2, all participants underwent assessments including isotonic, isometric and isokinetic training trials. Wireless surface electromyography (sEMG) was used to quantify quadriceps muscle activation across

modalities. Among the three training modalities, isokinetic training elicited the greatest muscle activation under matched intensity conditions, further distinguishing it as the high-activation exercise modality relative to the two low-activation alternatives (Fig. 2b). Real-time monitoring of knee velocity, joint angle and extension torque during isokinetic trials enabled detailed profiling of movement dynamics and loading characteristics (Fig. 2c).

Stiffness relates to training efficacy

To improve both compliance and training efficacy, a variable stiffness mechanism was integrated in series within the wearable robot

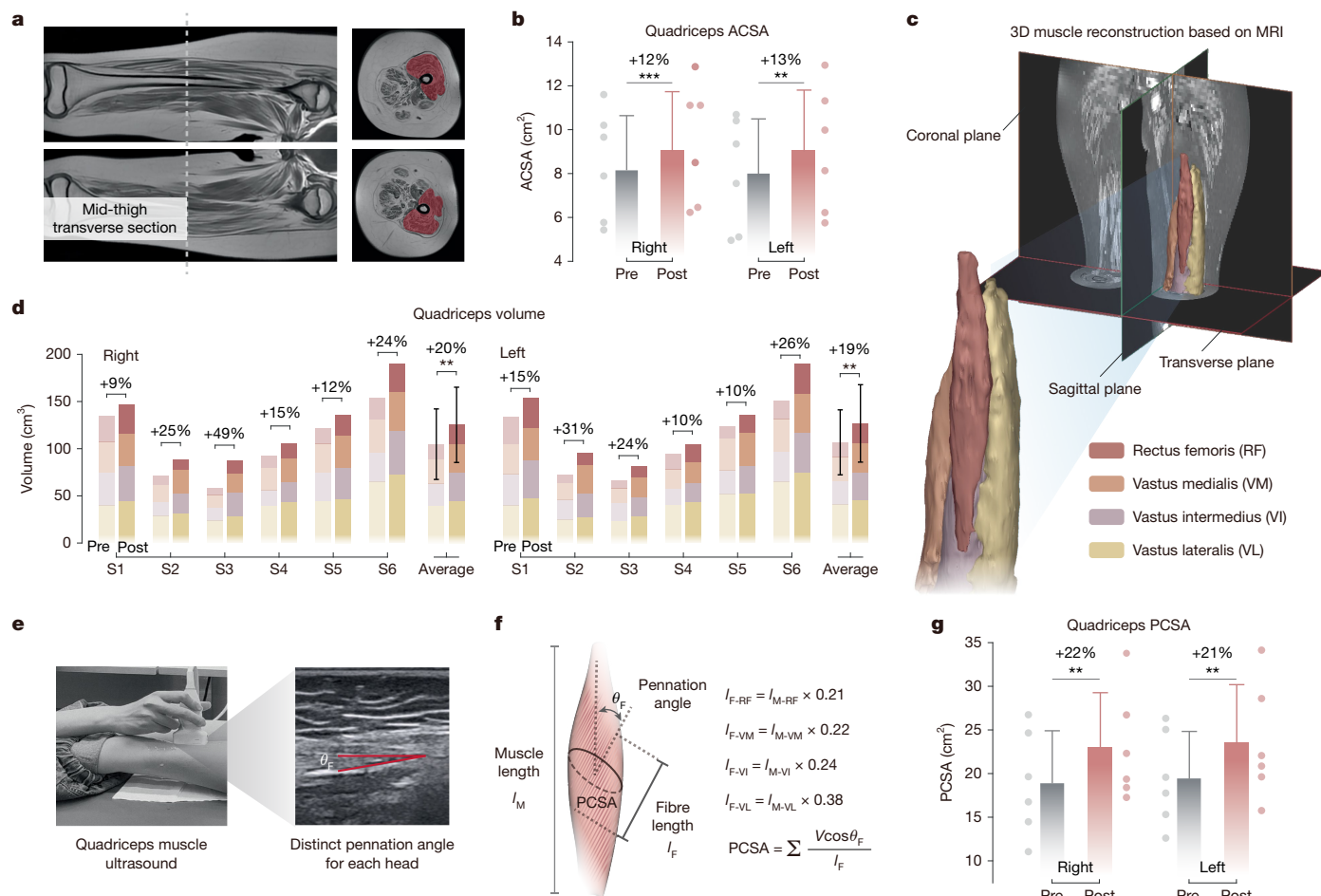


Fig. 4 | Measurement of post-intervention quadriceps hypertrophy. **a**, ACSA of the quadriceps obtained by MRI. The midpoint of the thigh was selected as the cross-sectional plane for assessing the ACSA. **b**, Changes in ACSA of the left and right quadriceps muscles in each participant (bars, mean; error bars, s.d.; scatters, each participant; $n = 6$; right leg, $***P < 0.001$; left leg, $**P = 0.0088$). Grey bars indicate pre-intervention mean ACSA ('Pre') and red bars indicate mean ACSA after high-intensity isokinetic training ('Post'). **c**, 3D reconstruction of the quadriceps based on MRI data. **d**, Changes in quadriceps muscle volume of left and right legs from pre-intervention to post-intervention across all participants ($n = 6$; right leg, $**P = 0.0038$; left leg, $**P = 0.0060$). Each bar colour corresponds to a specific muscle within the quadriceps group. **e**, Measurement of quadriceps pennation angle. Ultrasound imaging was used to measure the pennation angle of each individual muscle within the

quadriceps. **f**, Estimation of the PCSA of the quadriceps femoris. l_{M-RF} , l_{M-VM} , l_{M-VI} and l_{M-VL} represent the lengths of the rectus femoris, vastus medialis, vastus intermedius and vastus lateralis muscles, respectively. Correspondingly, l_{F-RF} , l_{F-VM} , l_{F-VI} and l_{F-VL} denote the fibre lengths of the rectus femoris, vastus medialis, vastus intermedius and vastus lateralis, respectively. For each muscle, the ratio between muscle fibre length and muscle length is assumed to be constant⁵⁰. **g**, Changes in PCSA of the left and right quadriceps muscles in each participant (bars, mean; error bars, s.d.; scatters, each participant; $n = 6$; right leg, $**P = 0.0048$; left leg, $**P = 0.0065$). Grey bars indicate pre-intervention mean PCSA and red bars indicate post-intervention mean PCSA. Statistical significance was assessed with a two-sided paired-sample *t*-test. All *P*-values and effect sizes are provided in Supplementary Table 3.

(Fig. 2d). The stiffness of the robotic joint is regulated by adjusting the position of the pivot along the elastic element (Fig. 2e and Supplementary Video 1). Participants demonstrated distinct torque output profiles while performing isokinetic knee extensions under varying stiffness conditions (Supplementary Fig. 2), suggesting the existence of an individual optimal stiffness, defined as the stiffness level at which maximal voluntary torque output is achieved. Notably, torque generation at this optimal stiffness was greater than that at the device's maximum stiffness setting by an average of 7% at Pre (from 1.77 to 1.90 N m, $P < 0.01$, paired-sample *t*-test) (Fig. 2f). The value of optimal stiffness varied not only between individuals but also between limbs of the same individual, indicating inherent neuromuscular heterogeneities. Values of optimal stiffness increased dynamically following each user's individual improvement trajectory, highlighting the potential of the metric as an adaptive training parameter for personalized rehabilitation (Extended Data Fig. 1).

Universal functional improvements

Throughout the acute 6-week high-intensity isokinetic training phase, all participants demonstrated increasing trends in functional metrics of the bilateral knee, including peak torque (+130%), ROM (+51%) and work per extension (+97%) (Fig. 3).

Across the six participants, peak torque of the right knee increased by 136% (from 1.96 to 4.63 N m, $P < 0.01$, paired-sample *t*-test) and peak torque of the left knee increased by 123% (from 2.00 to 4.46 N m, $P < 0.01$) by the end of the high-intensity training phase (Fig. 3e). Subject 4 exhibited the most pronounced improvements in peak torque, with that of the right knee increasing by 315% (from 1.44 to 5.97 N m, $P < 0.001$, independent samples *t*-test) and that of the left knee by 325% (from 1.46 to 6.20 N m, $P < 0.001$) (Fig. 3h). On average, participants' ROM of the right knee increased by 58% (from 42.45° to 66.94°, $P < 0.01$), along with a 122% increase in work per extension (from 1.00 to 2.23 J, $P < 0.01$). Participants' ROM of the left knee increased by 43% (from

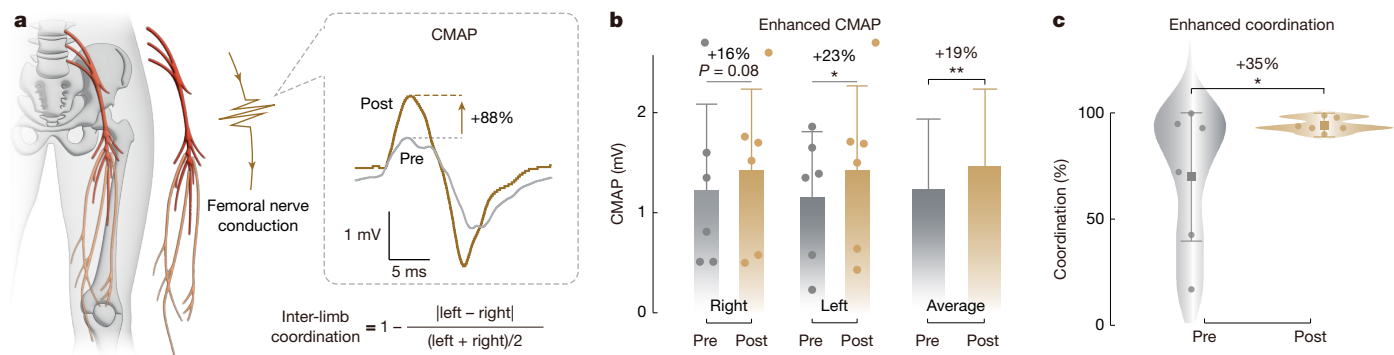


Fig. 5 | Enhancement of femoral nerve conduction. **a**, Evaluation of femoral nerve conduction. CMAP amplitude, measured in millivolts (mV), was used as an indicator of neuromuscular excitability. Left, schematic illustration of the femoral nerve. Right, representative CMAP waveform from the right leg of subject 4 and formula for inter-limb coordination. **b**, Enhancement of CMAP from pre-intervention to post-intervention across all participants (bars, mean;

error bars, s.d.; scatters, each participant; $n = 6$; right leg, $P = 0.0817$; left leg, $*P = 0.0413$; $n = 12$; average, $**P = 0.0087$). **c**, Enhancement of inter-limb coordination from pre-intervention to post-intervention (squares, mean; error bars, s.d.; scatters, each participant; $n = 6$; $*P = 0.0417$). Statistical significance of any increase was assessed with a one-sided paired-sample t -test. All P -values and effect sizes are provided in Supplementary Table 4.

41.83° to 59.95°, $P < 0.01$), with a 75% improvement in work per extension (from 1.12 to 1.97 J, $P < 0.05$) (Fig. 3f,g).

By the 30th and final training trial in the high-intensity isokinetic training phase, all participants exhibited marked improvements in all measured metrics compared with their first training trial (Supplementary Figs. 3–5). Notably, even the participant with the smallest gain in each metric demonstrated a meaningful positive response: subject 2's peak left knee torque increased by 45% (from 1.59 to 2.31 N m, $P < 0.001$) (Fig. 3h); subject 3's left knee ROM increased by 19% (from 35.67° to 42.40°, $P < 0.001$); subject 6's left knee work per extension increased by 22% (from 2.09 to 2.54 J, $P < 0.001$). Despite variability in magnitude of effect, no participant showed a decline in any functional indicator after the high-intensity isokinetic training phase.

Evidence of quadriceps hypertrophy

To evaluate muscle-level adaptations following training, quadriceps ACSA (Fig. 4a,b), muscle volume (Fig. 4c,d) and PCSA were quantified using MRI and ultrasound imaging (Fig. 4e–g). PCSA was estimated by combining MRI-derived muscle volume with pennation angle measurements obtained with ultrasound. Substantial increases in all three parameters (ACSA: +12%; volume: +19%; PCSA: +21%) were observed after 6 weeks of high-intensity isokinetic training across all participants.

Specifically, quadriceps ACSA measured at the mid-thigh level increased by an average of 12% in the right leg (from 8.15 to 9.09 cm², $P < 0.001$, paired-sample t -test) and 13% in the left leg (from 8.01 to 9.05 cm², $P < 0.01$) (Fig. 4b). Quadriceps muscle volume increased by an average of 20% in the right leg (from 105.09 to 125.60 cm³, $P < 0.01$) and 19% in the left leg (from 106.74 to 126.80 cm³, $P < 0.01$) (Fig. 4d), whereas PCSA increased by 22% in the right leg (from 18.92 to 23.01 cm², $P < 0.01$) and 21% in the left leg (from 19.41 to 23.48 cm², $P < 0.01$) (Fig. 4g).

Consistent with observed functional improvements, none of the participants exhibited reductions in any measured anatomical parameter (Extended Data Fig. 2 and Supplementary Figs. 6 and 7). These image-based physiological measurements offer a potential physiological explanation for the functional improvements observed in joint torque, ROM and work capacity.

Enhanced nerve and limb coordination

To assess the effects of training on motor neuron and axonal function, bilateral femoral nerve conduction assessments were performed on all participants before and after the acute intervention. CMAP values were measured in millivolts (mV) as an indicator of neuromuscular excitability (Fig. 5a).

A significant 19% increase in mean CMAP amplitude was measured following 6 weeks of high-intensity isokinetic training (from 1.21 to 1.44 mV, $P < 0.01$, paired-sample t -test), suggesting enhanced motor neuron recruitment and improved axonal conduction in aggregate, even if CMAP increases were not significant in both legs individually. Specifically, CMAP increased by 16% in the right leg (from 1.25 to 1.44 mV, $P = 0.08$) and 23% in the left leg (from 1.18 to 1.45 mV, $P < 0.05$) (Fig. 5b). We also quantified inter-limb CMAP symmetry as an indirect measure of bilateral neuromuscular coordination. Post-intervention data showed a significant 35% improvement in inter-limb symmetry (from 0.70 to 0.94, $P < 0.05$) (Fig. 5c).

Notably, in terms of bilateral averages, the participants exhibited increased CMAP amplitudes relative to pre-intervention levels (Supplementary Figs. 8 and 9). These consistent improvements suggest that high-activation isokinetic exercise supports both beneficial peripheral nerve plasticity and improvements in bilateral motor coordination.

Sustained improvements in follow-ups

Training-induced benefits were sustained by the study cohort throughout both follow-up phases, as indicated by all functional and physiological metrics assessed.

In respect to joint-level functional performance, the mean normalized peak torque of both knees (Fig. 6a) showed slight further increases during the low-intensity isokinetic training phase (follow-up 1) and remained stable throughout the monitoring phase (follow-up 2), maintaining statistically significant improvements compared with pre-intervention values ($P < 0.05$, paired-sample t -test). Although the average ROM and normalized work per extension of some subjects declined slightly relative to immediate post-intervention values (Fig. 6b,c and Supplementary Figs. 10–12), they remained significantly elevated from pre-intervention values ($P < 0.05$) to suggest meaningful retention of training gains.

Concerning quadriceps morphology, improvements in normalized ACSA (Fig. 6d), muscle volume (Fig. 6e) and PCSA (Fig. 6f) were maintained over time. No significant declines were observed after follow-up 1 or follow-up 2 and all measures remained significantly higher than pre-intervention values ($P < 0.05$) to suggest persistent structural muscle adaptation.

In reference to femoral nerve conduction and inter-limb neuromuscular coordination (Fig. 6g), positive trends persisted during both follow-up phases. In terms of CMAP amplitude, significant increases compared with Pre were observed in the left leg at Post and both follow-up points (Post, FU1, and FU2; $P < 0.05$). Increased CMAP amplitudes of the right leg reached statistical significance during

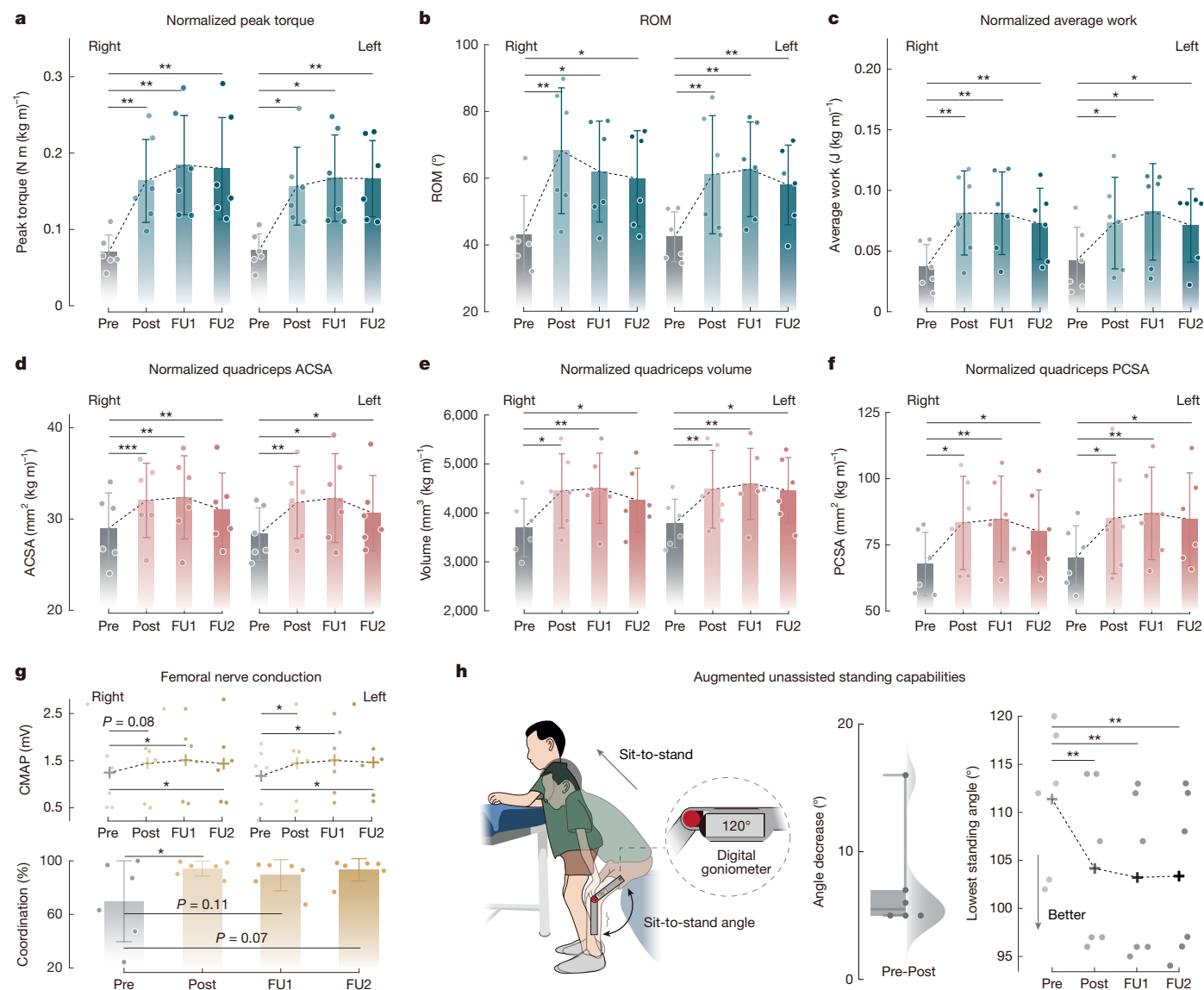


Fig. 6 | Retention of training-induced improvements during follow-up periods. **a–c**, Retention of improvements in knee functional metrics (bars, mean; error bars, s.d.; scatters, each participant; $n = 6$). **d–f**, Retention of improvements in muscle morphology (bars, mean; error bars, s.d.; scatters, each participant; $n = 6$). **g**, Retention of improvements in femoral nerve conduction (bars, mean; error bars, s.d.; scatters, each participant; $n = 6$). **h**, Improvement and retention of sit-to-stand ability without external support (self-assist allowed). Left, definition of the sit-to-stand initial knee angle, defined as the thigh-shank angle measured immediately before initiation of movement. Box plot of changes in sit-to-stand initial knee angles from Pre to

Post: the centre line indicates the median; the bounds of the box represent the 25th and 75th percentiles; whiskers extend to the absolute minimum and maximum. Right, changes in the lowest sit-to-stand initial knee angle across all participants throughout the entire study period ($n = 6$). For relevant subfigures, peak torque, work, ACSA, muscle volume and PCSA were normalized by the product of each subject's height and weight. For panel **g**, statistical significance was assessed with the one-sided paired-sample t -test; for all other subfigures, the two-sided paired-sample t -test was used: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. All P -values and effect sizes are provided in Supplementary Table 5.

both follow-up points (FU1 and FU2; $P < 0.05$). For coordination differences, although the values at FU1 ($P = 0.11$) and FU2 ($P = 0.07$) did not reach strict statistical significance, the values remained elevated, suggesting a possible trend of sustained neuropsychological adaptation.

For task-based functional capacity, sit-to-stand performance without external support (self-assist allowed) improved after the acute intervention, as reflected by a lower average minimum initial knee angle (from 111° to 104° , -7° , Post, $P < 0.01$) (Fig. 6h). This functional improvement was retained throughout both follow-up phases (both $P < 0.01$) (Supplementary Fig. 13 and Supplementary Table 1) and is corroborated by improvements observed during real-world activities (Supplementary Table 6).

Together, these findings associate sustained beneficial neuromuscular adaptations with a period of high-activation isokinetic resistance training in juveniles with SMA type II. The long-term retention of functional, morphological and neuropsychological gains suggests the translational potential of similar approaches to rehabilitation and motor maintenance for individuals with neuromuscular impairments.

Discussion

Extending the application domain of wearable robots

Many wearable lower-extremity robots have emerged that acutely assist gait. By decreasing muscle activation, these robots aim to increase metabolic efficiency and provide support to increase endurance and

reduce exertion^{1–7}. By contrast, the goal of rehabilitation and physical training is often to temporarily increase muscle exertion for sustained long-term neuromuscular development³⁷. Acute power assistance may hinder muscle development in the context of patients recovering from injury or individuals with conditions requiring muscle-strengthening interventions such as SMA. For these users, resistive, rather than assistive, wearable robots may be more suitable for fostering progressive neuromuscular growth over time. This approach represents an inversion of the classical applications of wearable lower-extremity robots to suggest a rich area of potential research.

Resolving conflicting outcomes in resistance training

Although a body of evidence exists to support the general efficacy of resistance training for patients with SMA¹⁹, other recent studies have reported mixed results in specific instances^{1,21,36,45}. Several studies have suggested that physical training has no notable impact on the strength of patients with SMA, with one having indicated a potential 7% decline in joint torque as a result^{21,36}. In our study, juveniles with SMA type II first underwent 6 weeks of conventional isometric and isotonic resistance training of the knee muscles, during which no changes were observed in minimum sit-to-stand initial knee angle. They subsequently completed 6 weeks of interventional high-intensity isokinetic training of the knee extensors using a wearable robotic device, resulting in a 7° decrease in minimum sit-to-stand initial knee angle (Fig. 6h). This functional gain was accompanied by substantially increased muscle strength, muscle volume and neuromuscular excitability relative to pre-intervention values. The cohort then demonstrated maintenance of these metrics without obvious further improvement after a follow-up period (FU2) of isometric and isotonic training (Fig. 6). 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 notable strength improvements and hypertrophy. If so, the enhanced effectiveness of isokinetic training probably originates from sustaining maximal muscle tension throughout the full ROM of a joint as a consequence of enforcing constant velocity.

Growth confounding

To distinguish the therapeutic effects of the intervention from those of somatic development, we compared our participants to data from the literature detailing the functional abilities of healthy juveniles⁴⁶ and those progressing according to the natural history of SMA (refs. 47,48). To facilitate direct comparison, reported changes^{46–48} were linearly interpolated to estimate changes at exactly 6 weeks (Supplementary Fig. 14). In the natural history of paediatric SMA, ageing-related development is often accompanied by minimal muscle hypertrophy or even progressive atrophy, with reported reductions in muscle size of roughly 1.1% over 6 weeks in SMA type II populations⁴⁷ (Supplementary Fig. 14). By contrast, the cohort in this study demonstrated increasing quadriceps ACSA, volume and PCSA throughout the high-intensity isokinetic training phase, followed by maintenance rather than continued age-typical atrophy^{47–49}. The timing and magnitude of these morphological changes were consistent with concurrent improvements in strength, mechanical work, ROM and CMAP amplitude, suggesting coordinated neuromuscular adaptations rather than passive developmental outcomes. Notably, increases of 19% in quadriceps volume and 12% in ACSA observed within 6 weeks substantially exceed reported growth-related changes in healthy juveniles of similar age and time durations (volume: +1.8%; ACSA: +1.0%)⁴⁶. Together, these observations are consistent with our hypothesis that intensive resistance training administered by a wearable robot can sustain increased muscle development and improved motor function in juveniles with SMA type II beyond levels expected from ageing-related development alone.

Limitations and future implications

Although a randomized clinical trial with large cohort sizes would be the ideal study design for determining intervention efficacy, subject recruitment was limited owing to SMA being a rare disease with poor prognoses. Further, no guardians were willing to consent their children as possible participants in a non-intervention cohort. MRI was omitted at the start of the non-intervention phase to minimize clinical interference and preserve the participants' pattern of daily activities. Although this omission limits the ability of the study to control for the influence of developmental neuromuscular changes, findings are presented in context with the literature detailing the absence of functional development in people with SMA type II to mitigate developmental hypertrophy as a confounding factor^{46–48} (Supplementary Fig. 14). With regard to device capabilities, the prototype restricts resistance to concentric isokinetic knee extension to specifically isolate quadriceps function. Although eccentric and isometric training modalities may also be clinically relevant, isokinetic concentric training was given priority in this initial study owing to its suitability for portable, home-based applications. The positive outcomes observed in this study are sufficient to justify an extended investigation on continuous isokinetic training for children with SMA type II to determine its long-term influence on functional development throughout adolescence. Finally, the design of both the device and the study may be extended to include those affected by conditions that impair executive function, such as stroke, to further validate the efficacy of this rehabilitative approach across broader populations.

Online content

Any methods, additional references, Nature Portfolio reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at <https://doi.org/10.1038/s41586-026-10642-0>.

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Methods

Further details on the clinical trial, mechatronic system, acquisition and analysis of experiment metrics and MRI processing and analysis can be found in the Supplementary Information.

Clinical study

Clinical trial. All experimental protocols were approved by the Biological and Medical Ethics Committee of Beihang University (no. BM20240173) and the Medical Science Research Ethics Committee of Peking University Third Hospital (no. 2024-973-02). The study protocol is publicly available on ClinicalTrials.gov (NCT06648486, <https://clinicaltrials.gov/study/NCT06648486>). Six juveniles with SMA type II were enrolled in the study. Six other juveniles with typical neuromuscular development were recruited to provide reference data. Certain experimental procedures were adjusted for participants with specific physical limitations and these instances are clearly indicated. 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.

Inclusion and exclusion criteria. The following inclusion criteria were applied for study enrolment: individuals aged 6–12 years; diagnosed with SMA type II owing to a deletion or mutation in the SMN1 gene. Individuals were excluded on the basis of any one of the following criteria: severe comorbidities; MRI-incompatible implanted medical devices; claustrophobia; refusal to provide informed consent or inability to complete the entire study protocol, among other factors; uncontrolled hypertension (systolic blood pressure ≥ 160 mmHg and/or diastolic blood pressure ≥ 95 mmHg) or congestive heart failure classified as New York Heart Association (NYHA) Class III or IV; cognitively impaired or unable to comprehend the requirements of study participation.

Participant information. A total of 12 juveniles participated in this study, consisting of six juveniles diagnosed with SMA type II and six age-matched juveniles with typical physiological neuromuscular development. The SMA group consisted of six clinically stable juveniles (three females, three males) aged 6–10 years (mean: 7.2 ± 1.60 years). Motor function was assessed using the Revised Hammersmith Scale (RHS), with scores ranging from 29 to 42. Height ranged from 109 to 130 cm and weight from 15 to 33 kg. A detailed summary of the clinical and demographic characteristics of the SMA participants is presented in Supplementary Tables 7 and 8. The age-matched group of six healthy juveniles was recruited to provide reference data for quadriceps muscle activation during isometric, isotonic and isokinetic knee extension tasks and to enable comparative analysis of isokinetic knee extension torque and sEMG signals (Extended Data Fig. 3). These participants were free of neuromuscular or orthopaedic conditions and exhibited physiological motor development. The participants ranged in age from 6 to 10 years (mean: 7.3 ± 1.75 years), with heights ranging from 113 to 147 cm and weights ranging from 20 to 40 kg. Detailed biophysical characteristics are provided in Supplementary Table 9.

Physiological metrics

Knee joint torque, ROM and work. The robot's embedded torque sensor, located at the knee joint, measured the interaction torque that the human participant exerts on the frame (that is, human-to-robot torque). This torque was recorded in real time at a sampling frequency of 100 Hz. Knee joint angles were simultaneously measured at 100 Hz using an angular encoder integrated into the robot. Knee joint velocity was derived in real time. The work generated during knee extension training was calculated by means of the discrete-time integration of gravity-compensated knee joint torque with respect to angular displacement.

sEMG. sEMG was used to quantify and compare quadriceps muscle activity in juveniles with SMA and their age-matched healthy juveniles during isometric, isotonic and isokinetic knee joint exercises, as well as the sit-to-stand task. Electromyographic activity of selected muscles was acquired at a sample rate of 1,259 Hz using 16-channel wireless Delsys Trigno sensors (Delsys Inc.), with surface electrodes placed over the quadriceps muscles. Quadriceps muscle activity during isokinetic knee movements was recorded using sEMG while participants wore the isokinetic training robot. During isometric and isotonic exercises, participants performed the tasks while wearing an ankle-mounted sandbag (Supplementary Methods).

MRI. Thigh MRI scans were acquired using a 3.0-Tesla superconducting MRI scanner (uMR 880, United Imaging Healthcare). Imaging parameters were as follows: repetition time = 7,398 ms, echo time = 30.96 ms, slice thickness = 4 mm, interslice gap = 0.8 mm, field of view = 400 mm and phase field of view = 280 mm. The scan coverage spanned from the anterior inferior iliac spine to the distal margin of the patella to capture the full volume of the quadriceps muscles. Bilateral thigh MRI was conducted with participants lying in the supine position to ensure standardized acquisition conditions.

PCSA and ACSA. PCSA is considered a key determinant of muscle strength, as it accounts for muscle volume, pennation angle and fibre length⁵¹. PCSA was calculated using the following formula:

$$PCSA = \sum \frac{V \cos \theta_f}{l_f} \quad (1)$$

in which V is muscle volume, θ_f is the pennation angle and l_f is fibre length. On the basis of bilateral thigh MRI data, 3D models of the individual muscles comprising the quadriceps femoris were reconstructed using Mimics Medical version 21.0 (Materialise) to facilitate volumetric and morphological analysis. Muscle lengths were extracted from the 3D reconstructions of each individual muscle. Fibre lengths were subsequently estimated using established scaling ratios, reflecting the proportional relationship between muscle length and fascicle length⁵⁰. Ultrasound imaging was used to quantify the muscle pennation angles (Supplementary Methods). The ACSA was assessed at the central region of the thigh^{52,53}. The measurement was derived from MRI data and analysed using Mimics Medical version 21.0 for precise segmentation and quantification.

Femoral nerve conduction. The stimulation site chosen at which to measure femoral nerve conduction was slightly lateral to the femoral pulse, below the inguinal ligament (Supplementary Fig. 15). The stimulator (cathode) was placed over a site on which the femoral nerve was expected to run on the basis of anatomic landmarks. The active recording electrode (G1) was placed on the muscle belly of the rectus femoris and the reference electrode (G2) was placed over the patella at the quadriceps tendon. The ground electrode was attached to either the patient's thigh or wrist. The stimulus intensity was slowly increased until the first small submaximal potential was recorded. After determining this value, the stimulus current was held constant and the stimulator was moved parallel to the initial stimulation site, both slightly laterally and then slightly medially. The position that yielded the highest response was determined to be the position closest to the nerve. Because the stimulus intensity was low, this procedure was not painful for any patient. Once the optimal position was determined, the current was increased to supramaximal stimulation⁵⁴. To achieve supramaximal stimulation, the current intensity was slowly increased until the amplitude of the recorded potential reached a plateau. The current intensity was then increased an extra 20% to ensure that the potential no longer increased. The recorded potential, known as the CMAP, represents the summation of all underlying individual muscle fibre action potentials.

Sit-to-stand test

A standardized initial sitting posture was established for all participants, defined by the lower legs being positioned perpendicular to the ground and the trunk aligned parallel to the backrest of the chair. In this standardized sitting posture, the angle formed between the thigh and shank (that is, $<180^\circ$) served as the metric for evaluating sit-to-stand performance. Before the beginning of the study, all participants were administered a test to determine each individual's lowest initial sit-to-stand angle. The procedure for determining the lowest initial sit-to-stand angle was as follows.

During the initial sit-to-stand assessment, participants began in the standardized sitting posture. A starting angle was identified at which the participant could successfully complete the sit-to-stand movement using bilateral hand support on the knees (self-assist allowed). The sit-to-stand angle was then gradually decreased in 1° decrements in each subsequent test. Participants were allowed to rest between tests to mitigate fatigue. This process was repeated until the participant could no longer initiate the movement, defined as the inability of the hips to lift off the seat despite hand support. The final angle at which the participant successfully completed the task was designated as the pre-intervention angle for subsequent sit-to-stand evaluations. At the beginning of each training trial, a sit-to-stand assessment was performed. If the participant was able to complete the task at the current angle, the angle was subsequently reduced, allowing for progressive evaluation of functional improvement.

Wearable mechatronics for rehabilitation

The isokinetic training robot comprises a back-drivable motor (GIM4310, SteadyWin), a variable stiffness mechanism, power electronics and several sensors for kinetic and kinematic monitoring (Supplementary Figs. 16–18 and Supplementary Video 1). A back-drivable motor is used to provide the damping required for isokinetic control, whereas the variable stiffness mechanism is incorporated to adjust the human–robot interface compliance. For subject 6, owing to a substantial increase in torque output in follow-up 1, the original motor was no longer able to provide sufficient resistance for isokinetic training. Therefore, the training device was upgraded with a higher torque motor (RobStride 01, RobStride Dynamics) to meet the increased demand.

The back-drivable motor's rotor is connected to a set of reduction gears that amplify the resistance provided by the motor. Individualized gear transmission ratios were assigned according to each participant's knee extension torque capacity (Supplementary Methods). This approach allowed for appropriate scaling of output motor torque to match the resistance requirements of each user. The motor's stator is mechanically grounded to one carbon fibre composite plate affixed to the lateral side of the thigh and the output shaft of the variable stiffness mechanism is affixed to a second carbon fibre composite plate on the calf. Comfortable, compliant straps are fitted to both carbon fibre composite plates to ensure contact with the device during use. During isokinetic training, forces are transmitted from the user's leg, first to the variable stiffness mechanism, then to the torque sensor and reduction gear and finally to the back-drivable motor. The baseline mass of the system is 0.96 kg, incorporating the battery (3.7 V, 3,800 mA h), GIM4310 motor, transmission module (ratios: 3, 3.5 or 4), and carbon-fibre elements. Any modifications to the motor or transmission setup will vary this total mass.

Isokinetic control

The computational controller uses a microcontroller unit (STM-32F405RGT6, STMicroelectronics), with angular position and torque data sampled at a frequency of 100 Hz. For motor control, a motor driver (DRV8323S, Texas Instruments) is used to drive six power MOSFETs (BSC123N08NS3, Infineon) (Supplementary Figs. 19 and 20).

The controller performs two functions. First, it modulates the braking torque generated by the primary motor to enforce isokinetic movement. Second, it regulates the position of the secondary motor to control the variable pivot point that modifies overall stiffness. During passive motor rotation, activating the low-side MOSFETs allows current to flow within the motor winding circuits, resulting in a counter-electromotive force (back EMF) torque generated by the magnetic field of the motor stator that opposes the direction of rotation. By controlling the duration of low-side MOSFET activation through pulse-width modulation (PWM), the primary motor is able to vary back EMF torque to achieve the closed-loop speed control necessary for isokinetic training. A higher duty cycle produces increased damping torque from the motor. The duty cycle is regulated by the difference between the target and actual joint velocities, which is fed into a proportional–integral–derivative controller. Specifically, when the PWM signals are active (creating a closed loop across the windings), energy is stored in the inductance of the two motor phases, generating a braking torque. When the PWM signals are inactive, the circuit is open and the motor enters a free-spinning state, in which the only resistance is because of mechanical friction. Also, a supercapacitor can be integrated into the circuit to enable regenerative braking and recover the energy generated during braking (Supplementary Methods). As only isokinetic knee extension training was allowed, the low-side MOSFETs remained off during the knee flexion phase, allowing the motor to rotate freely without generating braking torque from back EMF.

Optimal stiffness

The optimal stiffness for a subject is defined as the stiffness at which they generate maximal torque during isokinetic knee extensions. The mechanical stiffness of the system can be tuned by varying the effective length of the rotary elastic element through parameter l (0–25 mm), which directly influences the system's compliance (Supplementary Figs. 16–18). Stiffness–torque data were collected at intervals of 1.25 mm (range from 15 to 25 mm) as participants, equipped with the isokinetic training robot in a seated posture, performed five knee extension repetitions at each predefined stiffness level. Stiffness settings at $l < 15$ mm remained uninvestigated owing to being too compliant for administering effective isokinetic training. The peak torque values from the three trials with the greatest torque outputs were averaged to determine the representative peak torque for that specific stiffness level. A fourth-order polynomial was fitted to the scatter plot with stiffness as the independent variable (x -axis) and peak torque as the dependent variable (y -axis). The stiffness corresponding to the maximum value on the fitted curve was identified as the optimal stiffness for the participant, corresponding also to the setting that allows maximum power transfer to the robot during isokinetic exercise. The optimal stiffness is bounded by a physical upper limit of $28.16 \text{ N m rad}^{-1}$.

Training regimen

The training regimen comprised four phases: a 6-week non-intervention phase (phase 1), a 6-week high-intensity isokinetic training phase (phase 2), a 6-week low-intensity isokinetic training phase (follow-up 1) and a >30 -day follow-up phase without isokinetic training (follow-up 2). First, all subjects were jointly recruited by Peking University Third Hospital and Beihang University. In phase 1, each subject maintained their usual care routines: three received regular rehabilitation at specific institutions and three received in-home rehabilitation. In phase 2, subjects completed 30 trials in 6 weeks, with five trials per week. Each isokinetic training trial included a minimum of six isokinetic training sessions per leg, with ten repetitions per session. On days when isokinetic training with the experimental robot was performed, further knee-related rehabilitation activities were reduced or withheld to ensure the same training intensity as during phase 1 (measured in time consumed). In follow-up 1, the training was reduced to 18 trials in total, with three trials per week. In follow-up 2, subjects stopped

isokinetic training and returned to their original training protocols used before the intervention, which primarily involved conventional, non-isokinetic exercises. This phase was designed to evaluate the retention of training-induced improvements following the withdrawal of the isokinetic training intervention.

Gamified human-machine interface

A mobile application was developed to enhance subject engagement of the experimental process and improve the visualization of results. The application communicates with the isokinetic training robot through a Bluetooth module (HC-04, HuiCheng). At the start of training, experimenters used the application to configure parameters such as the number of repetitions and joint extension speed. During training, the robot transmitted real-time data on torque, angle and velocity to be shown on the mobile device. On completion of each training trial, the application automatically uploaded all training data to a cloud server.

The application features two distinct interface designs (Supplementary Figs. 21 and 22 and Extended Data Fig. 4). One interface provides a real-time display of torque, angle and velocity data, primarily for debugging and visualizing the overall training process. The second interface offers a gamified environment simulating the isokinetic training process as a seated juvenile kicking a ball. In the game, the angle between the thigh and shank corresponds in real time to the actual angles measured by the robot and the ball's travel distance is a function of the peak knee extension torque, with greater torque resulting in more distance covered.

Gravity compensation

The embedded torque sensor located at the knee joint measured the interaction torque that the participant exerted on the robot (that is, human-to-robot torque τ_{hr}). This torque reflects the user's voluntary effort against the velocity maintained by the isokinetic controller. Therefore, the measured torque (τ_m) corresponds directly to the torque the human applies to the robot, that is:

$$\tau_m = \tau_{hr} \quad (2)$$

However, this does not yet reflect the full torque generated by the human knee joint, as it does not include the gravitational torque component caused by the weight of the lower leg. To obtain the total torque generated by the knee joint muscles, we compensate for the gravitational moment owing to the lower leg segment (Supplementary Fig. 23). The total torque (τ_{kn}) is calculated as:

$$\tau_{kn} = \tau_m + \tau_g \quad (3)$$

in which τ_m is the measured torque exerted by the participant against the robot and τ_g is the gravitational torque owing to the mass of the lower leg acting about the knee joint axis. The gravitational torque is estimated using a standard anthropometric model:

$$\tau_g = m \times g \times l_{COM} \times \cos(\theta) \quad (4)$$

in which m is the estimated mass of the lower leg ($\approx 5\%$ of total body weight)⁵⁵, g is the gravitational acceleration, l_{COM} is the distance from the knee joint to the lower leg's centre of mass and θ is the knee joint angle, as defined in Fig. 2b.

Data collection and analysis

Representative data shown in the figures were selected from independently conducted experiments in six subjects, with both legs tested. Similar trends were observed across all subjects and both legs. The number of training repetitions per subject, per leg and per trial ranged from 80 to 112, with a mean of 93 (Supplementary Table 10). To assess knee joint performance, the 20 isokinetic knee extension cycles with

the highest peak torque were extracted from each trial. The mean and standard deviation of peak torque, joint work and angular displacement across these cycles were computed to serve as outcome metrics for the corresponding trial. To preclude mathematical artefacts arising from heterogeneous baselines, the overall percentage changes (for example, peak torque: +130%) were calculated using the ratio of means, with the standard deviation estimated using the delta method^{56,57}. All numerical values reported in the main text are rounded to a maximum of two decimal places for presentation. However, to maintain statistical rigour, all results were calculated directly from the raw, unrounded data taking into account the limits of measurement precision (see 'Data availability').

To account for the influence of growth and developmental factors, biomechanical and morphological indicators (including peak torque, work, ACSA, muscle volume and PCSA) were normalized by the product of each subject's height and weight (Fig. 6). All sEMG and inertial measurement unit data were collected using Delsys Trigno inertial measurement modules that were affixed to both of the subject's upper thighs (surface of the quadriceps) during experimental trials. Torque, angle, sEMG and inertial measurement unit data were processed with MATLAB R2020b (MathWorks Inc.). All MRI analyses, including ACSA, muscle volume and PCSA, were processed with Mimics Medical version 21.0. All *t*-tests were conducted using MATLAB. We proposed a directional increase in CMAP, given the substantial increases already observed in peak torque, ROM, work, ACSA, volume and PCSA, which were assessed using two-sided paired-sample *t*-tests. Consequently, a one-sided paired-sample *t*-test was applied to analyse the CMAP data. All sEMG data underwent direct current offset removal, band-pass filtering (20–450 Hz), full-wave rectification and low-pass filtering with a 1-Hz cut-off to create linear envelopes for visualization. To distinguish isokinetic cycles and reduce noise interference, all angular data were processed using a 5-Hz low-pass filter. All filtering procedures were performed using zero-phase filtering by applying the filters in both forward and reverse directions. Standing knee angles were measured using a digital goniometer.

Reporting summary

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

Data availability

The datasets generated and analysed during the present study are available within the study and its associated Supplementary Information. Comprehensive statistical results, encompassing all *P*-values and effect sizes, are reported in Supplementary Tables 2, 3, 4 and 5. Detailed subject profiles, including those of both the SMA and healthy groups, can be found in Supplementary Tables 7, 8 and 9. Due to paediatric patient confidentiality, the complete data underlying the figures are not available in public repositories, but the Supplementary information contains all the necessary data and protocols to fully reproduce the research. Also, to maximize privacy protection for our paediatric participants, certain figures and videos containing identifiable subject information have been excluded from the published materials. These materials are available from the corresponding author, Y.F., provided that the requesting party guarantees to strictly maintain participant confidentiality.

Code availability

All codes involved in this study have been deposited at GitHub (<https://github.com/YANGGANG1971/SMA-sit-to-stand>).

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Author contributions Y.F. conceptualized the study, directed the project and provided personal funding. T.S. and Y.F. led the experimental design. F.Y. and Y.F. oversaw clinical trials. Y.L., J.R. and Y.F. designed the robotic system and oversaw its use during experiments. Y.L. and J.R. analysed the data, with supervision from Y.F. and T.S. Visualization and main figures preparation were handled by J.R. and Y.F. Final claims and reported outcomes were curated by T.S. and Y.F. The manuscript was co-drafted by Y.L., J.R., T.S. and Y.F. All authors contributed to the discussion as well as the review and editing of the manuscript.

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Competing interests Y.F. has filed two patent applications related to this work (patent nos. CN121061820 and CN120148732). The remaining authors declare no competing interests.

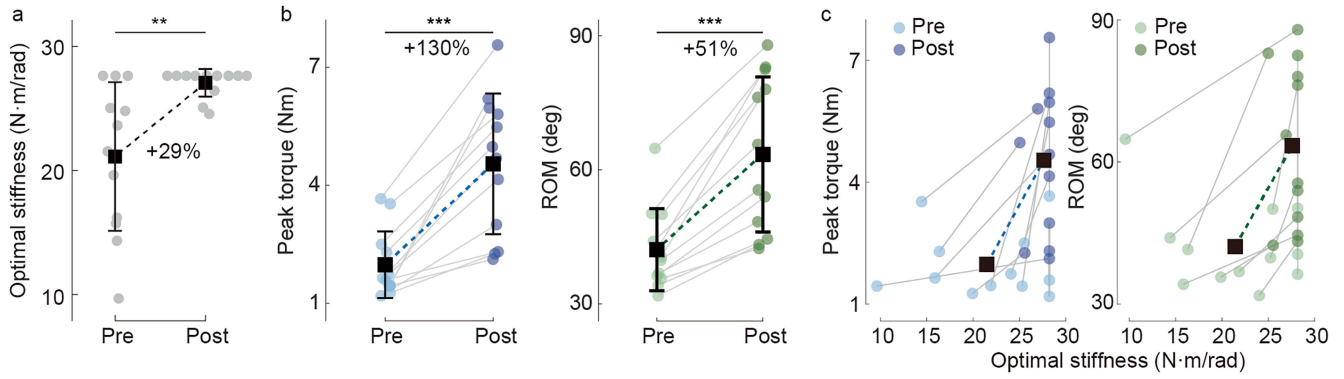
Additional information

Supplementary information The online version contains supplementary material available at <https://doi.org/10.1038/s41586-026-10642-0>.

Correspondence and requests for materials should be addressed to Yanggang Feng.

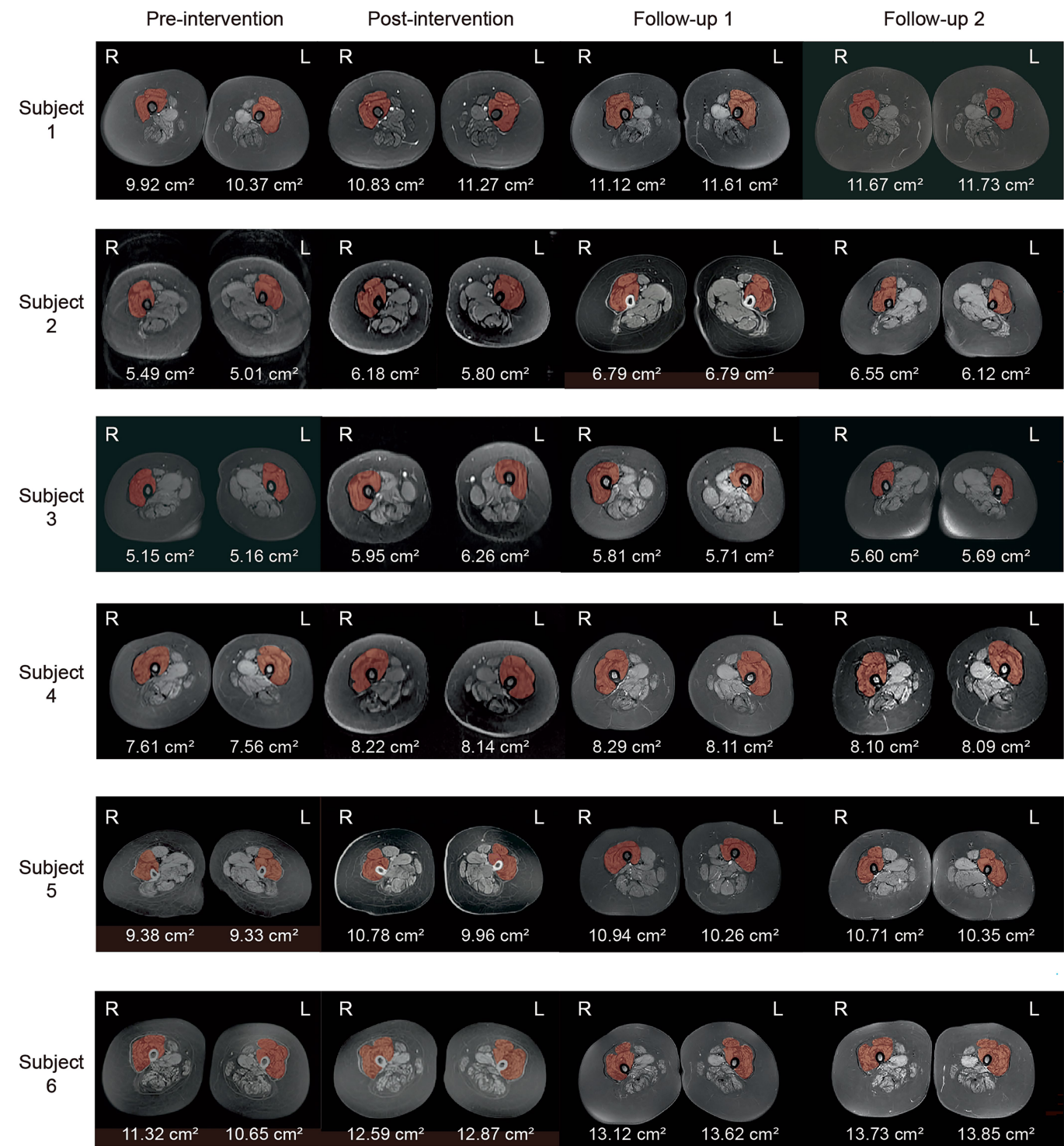
Peer review information *Nature* thanks Lorenzo Masia, Robert Muni-Lofra, Massimo Sartori and Marco (A.) Vaz for their contribution to the peer review of this work.

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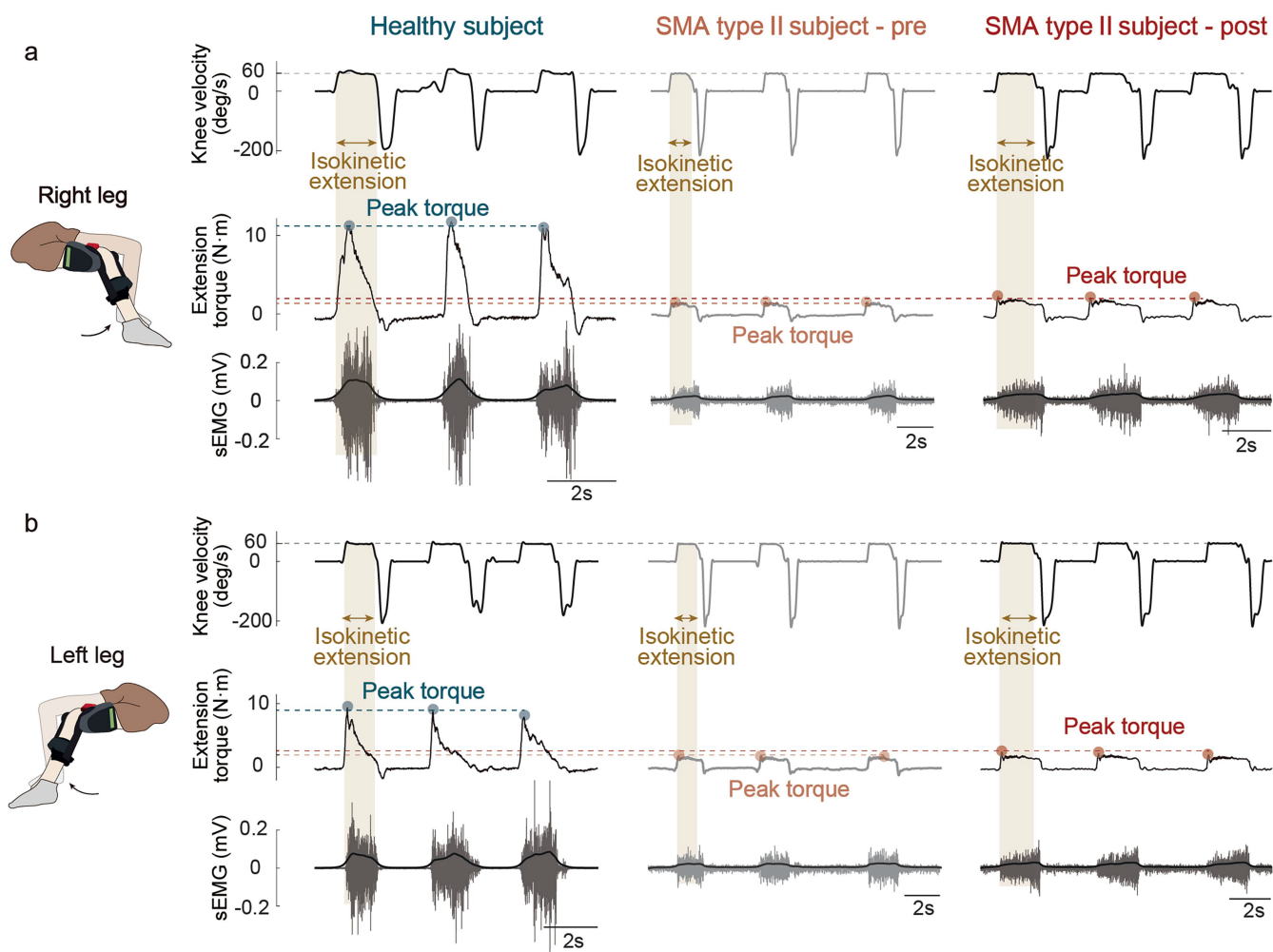


Extended Data Fig. 1 | Increases in optimal stiffness, peak torque and ROM from pre-intervention to post-intervention. a, Increases in optimal stiffness from pre-intervention to post-intervention ($n = 12$; $**P = 0.0040$, two-sided paired-sample t -test). **b,** Increases in peak torque and ROM from pre-intervention to post-intervention ($n = 12$; peak torque, $***P < 0.001$; ROM,

$***P < 0.001$, two-sided paired-sample t -test). **c,** Increases in peak torque and ROM with respect to optimal stiffness from pre-intervention to post-intervention. All paired squares and dashed lines represent group means and trends. Each pair of scatter points represents one leg (error bars, s.d.).

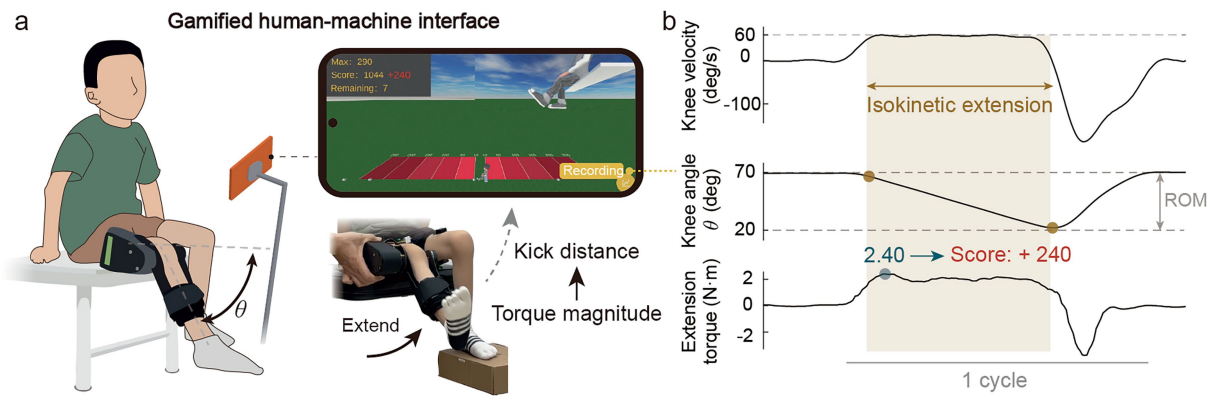


Extended Data Fig. 2 | ACSA of the left and right quadriceps in all participants. All participants underwent bilateral thigh MRI scans at the end of each experimental phase (pre-intervention, post-intervention, follow-up 1 and follow-up 2). The ACSA was measured at the mid-thigh. Red regions indicate the quadriceps muscle and corresponding ACSA values are listed immediately below.



Extended Data Fig. 3 | Comparisons of isokinetic knee extension torque and sEMG between representative SMA type II and healthy subjects. Data were collected during isokinetic extension at 60° s^{-1} from a representative healthy subject (subject H5) and an SMA type II participant (subject 2) before and after 6 weeks of acute isokinetic training (Pre and Post). Both subjects were

6-year-old females. **a**, Right leg performance. **b**, Left leg performance. In each panel, time-series plots show knee angular velocity (top row; $^\circ \text{ s}^{-1}$), extension torque (middle row; N·m) and sEMG amplitude (bottom row; mV). Shaded vertical bands indicate the first isokinetic extension phase.



Extended Data Fig. 4 | Gamified human-machine interface during isokinetic knee extension training. a, Gamified interface converting knee extension torque into the kick distance of a cartoon character, with current score, highest

score and remaining attempts shown in the top-left corner. Peak torque is proportional to kicked distance. **b,** Graphical user interface for recorded data.

Reporting Summary

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For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (<i>n</i>) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ The statistical test(s) used AND whether they are one- or two-sided <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☐	☒ A description of all covariates tested
☐	☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒ For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
☒	☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☐	☒ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒ Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i>), indicating how they were calculated

Our web collection on [statistics for biologists](#) contains articles on many of the points above.

Software and code

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Data collection	1. Data from the isokinetic training robot were collected using a smartphone software interface. To preclude mathematical artifacts arising from heterogeneous baselines, the overall percentage changes were calculated using the ratio of means, with the standard deviation estimated via the Delta method. 2. All sEMG and IMU data were collected using Delsys Trigno IM modules that were affixed to both of the subject's upper thighs (the surface of quadriceps) during experimental trials. 3. Thigh MRI scans were acquired using a 3.0 Tesla superconducting MRI scanner (uMR 880, United Imaging Healthcare, Shanghai, China). Imaging parameters were as follows: repetition time (TR) = 7398 ms, echo time (TE) = 30.96 ms, slice thickness = 4 mm, inter-slice gap = 0.8 mm, field of view (FOV) = 400 mm, and phase FOV = 280 mm. The scan coverage spanned from the anterior inferior iliac spine (AIIIS) to the distal margin of the patella to capture the full volume of the quadriceps muscles. Bilateral thigh magnetic resonance imaging was conducted with participants lying in the supine position to ensure standardized acquisition conditions. 4. All CMAP data were obtained through standardized examination at Peking University Third Hospital.
Data analysis	1. Torque, angle, sEMG, IMU and CMAP data were processed with MATLAB version 2020b (MathWorks Inc.) 2. All MRI analysis, including ACSA, muscle volume and PCSA, were processed with Mimics Medical 21.0. All code involved in this study are available at https://github.com/YANGGANG1971/SMA-sit-to-stand Software packages incorporated into the above code for data analysis included: MATLAB 2020b, https://ww2.mathworks.cn/products/matlab.htm Mimics Medical 21.0, https://www.materialise.com/en/healthcare/mimics

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All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
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The datasets generated and analyzed during the current study are available within the study and its associated Supplementary Information. Comprehensive statistical results, encompassing all P values and effect sizes, are reported in Supplementary Tables 2, 3, 4 and 5. Detailed subject profiles, including those of both the SMA and healthy groups, can be found in Supplementary Tables 7, 8 and 9. Owing to the sensitive nature of the pediatric biological data (aged 6–10 years), the datasets are not suitable for public repository deposition. To maximize privacy protection for our pediatric participants, certain figures and videos containing identifiable subject information have been excluded from the published materials. These materials are available from the corresponding author, Yanggang Feng, provided that the requesting party guarantees to strictly maintain participant confidentiality.

All codes involved in this study have been deposited at GitHub: <https://github.com/YANGGANG1971/SMA-sit-to-stand>.

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender	3 males and 3 females
Reporting on race, ethnicity, or other socially relevant groupings	No socially constructed or socially relevant categorization variables were used or are relevant for our manuscript.
Population characteristics	1. Diagnosed with SMA type II. 2. Aged 6 to 10 years (mean: 7.2 ± 1.6 years). 3. Motor function was assessed using the Revised Hammersmith Scale (RHS), with scores ranging from 29 to 42 (mean: 35.83 ± 4.62). 4. Height ranged from 109 to 130 cm (mean: 119.67 ± 7.45 cm) and weight from 15 to 33 kg (mean: 22.83 ± 7.03 kg). specifically, subject 1: Male, 7 years, 33kg, 124cm, RHS=35 subject 2: Female, 6 years, 15kg, 109cm, RHS=29 subject 3: Female, 6 years, 16kg, 114cm, RHS=42 subject 4: Male, 6 years, 20kg, 119cm, RHS=35 subject 5: Female, 8 years, 26kg, 130cm, RHS=34 subject 6: Male, 10 years, 27kg, 122cm, RHS=40
Recruitment	All participants were jointly recruited by Peking University Third Hospital and Beihang University through voluntary self-enrolment and were subsequently screened according to predefined inclusion and exclusion criteria. Inclusion criteria were: age 6–12 years and genetically confirmed SMA type II due to deletion or mutation of the SMN1 gene. Exclusion criteria included severe comorbidities, implanted medical devices preventing MRI, claustrophobia, refusal to provide informed consent, inability to complete the study protocol, uncontrolled hypertension, severe heart failure (NYHA class III or IV), and cognitive impairment preventing comprehension of study participation requirements. Due to the rarity of the disease and the limited pool of potential participants, all eligible individuals who applied were enrolled in the study (n=6). Thus, there was no secondary selection, precluding the possibility of selection bias during the recruitment phase.
Ethics oversight	Each subject was provided written informed consent, approved by the Biomedical Ethics Review Committee of Peking University, Third Hospital (No. 2024-973-02) and Beihang University (No. BM20240173).

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

Field-specific reporting

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☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

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Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	In this study, we recruited 6 juveniles with SMA type II based on a sample size calculation. The calculation was performed as follows, $N = 2 * [(t_{(\alpha/2)} + t_{\beta}) * S / \delta]^2 \quad \#(S1)$ Given $\alpha = 0.05$ and $\beta = 0.1$, the critical values $t_{(\alpha/2)}$ and t_{β} are calculated as: $t_{(\alpha/2)} = 1.96$, $t_{\beta} = 1.28 \quad \#(S2)$ From the Ref. [58], $S = 16.1$, $\delta = 32.3$. After calculation, we obtained $N > 5.21 \quad \#(S3)$ Therefore, the minimum required sample size $N_{\min} = 6$. Reference: 58. Zhang, X. et al. Impact of whey protein isolate and eccentric training on quadriceps mass and strength in patients with anterior cruciate ligament rupture: A randomized controlled trial. J. Rehabil. Med. 52, 1-8 (2020).
Data exclusions	Data from all 6 subjects were included.
Replication	The reliability of the isokinetic training robot was verified by the 6-week rehabilitation process (30 intervention trials). Before the formally reported study, we conducted one preliminary pilot study in an independently recruited subject with SMA type II under the same general intervention framework. In that pilot, knee extension torque, range of motion, work per extension, and hands-on-knees standing ability all improved markedly, which encouraged us to proceed with the present study. However, in accordance with the reviewer's suggestion, we have removed the content regarding the preliminary pilot study, as its experimental protocols and assessment metrics were inconsistent with those of the formal study. Should further information be required, please contact the corresponding author at yanggangfeng@buaa.edu.cn. No unsuccessful replication attempts were recorded.
Randomization	This was not a parallel-group trial, so allocation was not randomized. A parallel-group design was initially considered, but subjects and families were unwilling to accept assignment to a non-intervention control group, making random allocation impractical in this rare pediatric SMA population. We therefore adopted a within-subject, baseline-controlled design in which each participant served as their own control. In this design, between-group imbalance in fixed covariates was not directly relevant, and subject-specific baseline characteristics were inherently controlled through repeated within-subject comparisons over time. Our within-subject design included a baseline non-intervention phase, a high-intensity training phase, and two follow-up phases (low-intensity training phase and follow-up 2). A detailed set of complementary metrics was collected, encompassing functional performance (torque, range of motion, mechanical work), imaging-based quadriceps muscle morphology (ACSA and PCSA), neural function (CMAP), and inter-limb coordination. This detailed dataset was intended to maximize the scientific value of a small cohort and strengthen inference regarding training-associated changes.
Blinding	No blinding measures were intentionally implemented in this study. Unlike clinical drug trials, blinding was not feasible in this study because each subject received a customized portable isokinetic training robot, and the intervention required direct fitting, supervision, and adjustment, making both participant- and investigator-level blinding impractical.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

Methods

n/a	Involved in the study	n/a	Involved in the study
☒	☐ Antibodies	☒	☐ ChIP-seq
☒	☐ Eukaryotic cell lines	☒	☐ Flow cytometry
☒	☐ Palaeontology and archaeology	☐	☒ MRI-based neuroimaging
☒	☐ Animals and other organisms		
☐	☒ Clinical data		
☒	☐ Dual use research of concern		
☒	☐ Plants		

Clinical data

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Clinical trial registration

Study protocol

The full study protocol available for viewing at ClinicalTrials.gov (NCT06648486).

Six juveniles with SMA type II actively took part in the study. All participants were unable to perform sit-to-stand transitions from a seated position at 90° hip and knee flexion using voluntary quadriceps activation. Before their involvement, participants and their guardians underwent an informed consent process in accordance with the procedure approved by the Biomedical Ethics Review Committee of Peking University, Third Hospital.

The following inclusion criteria were applied for study enrolment: individuals aged 6-12 years; diagnosed with SMA type II due to a deletion or mutations in the SMN1 gene.

Individuals were excluded on the basis of any one of the following criteria: severe comorbidities; implanted medical devices preventing MRI; claustrophobia; refusal to provide informed consent or inability to complete the entire study protocol, among other factors; uncontrolled hypertension (systolic blood pressure ≥ 160 mmHg and/or diastolic blood pressure ≥ 95 mmHg) or congestive heart failure classified as New York Heart Association (NYHA) Class III or IV; cognitively impaired or unable to comprehend the requirements of study participation.

Participants first completed a 6-week non-intervention period while maintaining their usual physiotherapy routines (conventional rehabilitation): 3 received regular rehabilitation at a designated facility, and 3 received home-based rehabilitation.

Subsequently, all participants underwent an acute 6-week phase of high-intensity isokinetic knee extension training using the portable robot (30 intervention trials; each trial consisting of ≥ 6 sessions per leg, 10 movement repetitions per session), followed by a 6-week low-intensity isokinetic training phase (Follow-up 1; 18 trials), and a final 1-month follow-up without isokinetic training (Follow-up 2).

Comprehensive assessments were conducted at the end of each of four experimental phases at time points designated as Pre, Post, FU1 and FU2. Assessments included bilateral measurements of knee extension torque, range of motion, work per extension, thigh magnetic resonance imaging (MRI), and femoral nerve conduction studies. Each participant's ability to perform hands-on-knees standing from decreasingly flexed initial knee angles without external support was also documented at each assessment point.

Data collection

Peak torque, work, and ROM were collected during the home-based training process and were recorded in every trial using feedback from the portable isokinetic training robot via a mobile app.

Magnetic resonance imaging and femoral nerve conduction assessments were conducted at Peking University Third Hospital.

These assessments were performed at four time points: before the high-intensity isokinetic training phase (intervention), before and after the low-intensity phase (Follow-up 1), and after the phase without isokinetic training (Follow-up 2), to evaluate thigh cross-sectional morphology and femoral nerve conduction.

Time line: After recruitment, participants first completed a 6-week non-intervention period. Subsequently, all participants underwent an acute 6-week phase of high-intensity isokinetic knee extension training using the portable robot (30 intervention trials; each trial consisting of ≥ 6 sessions per leg, 10 movement repetitions per session), followed by a 6-week low-intensity isokinetic training phase (Follow-up 1; 18 trials), and a final 1-month follow-up without isokinetic training (Follow-up 2).

Outcomes

The primary outcomes were predefined to capture the main structural, functional, and neurophysiological effects of the intervention. These include:

Peak torque and work during isokinetic knee extension, cross-sectional area of the quadriceps and electromyographic (femoral nerve conduction) parameters.

Secondary Outcomes:

Additional confounding factors may render metrics such as knee range of motion, weight, and height insufficient for accurately reflecting the rehabilitation efficacy of the subjects. These parameters are less sensitive and intuitive compared to the primary indicators used in our study. Importantly, the prioritization of these indicators also aligns with the clinical recommendations provided by the consulting physicians.

Plants

Seed stocks

Not involved

Novel plant genotypes

Not involved

Authentication

Not involved

Magnetic resonance imaging

Experimental design

Design type

This study utilizes structural MRI to evaluate muscle morphology. No task-based functional MRI designs were employed.

Design specifications

MRI were performed at four time points: before the high-intensity isokinetic training phase (intervention), before and after the low-intensity phase (Follow-up 1), and after the phase without isokinetic training (Follow-up 2), to evaluate thigh cross-sectional morphology. Each MRI involved scans of the bilateral thighs. No behavioral trials or task blocks were involved during the scan.

Behavioral performance measures

Multiple physical performance metrics were recorded at each time point: bilateral knee extension torque, range of motion (ROM), and work per extension. Additionally, the ability to perform sit-to-stand transitions from varying angles and femoral nerve conduction studies were documented to correlate with MRI changes.

Acquisition

Imaging type(s)

Structural Muscle MRI of the thighs.

Field strength

3.0 Tesla (uMR 880, United Imaging Healthcare, Shanghai, China).

Sequence & imaging parameters

TR = 7398 ms, TE = 30.96 ms; Slice thickness = 4 mm with a 0.8 mm inter-slice gap; FOV = 400 mm, Phase FOV = 280 mm.

Area of acquisition

Bilateral thighs, with scan coverage extending from the Anterior Inferior Iliac Spine (AIIS) to the distal margin of the patella to ensure full volumetric capture of the quadriceps. Participants were scanned in a standardized supine position.

Diffusion MRI

☐ Used☒ Not used

Preprocessing

Preprocessing software

Mimics Medical version 21.0 (Materialise, Leuven, Belgium) was used for 3D reconstruction and volumetric analysis.

Normalization

No spatial normalization to a standard atlas. Instead, three-dimensional models of individual quadriceps muscles were reconstructed for each participant at each time point to allow for subject-specific morphological tracking.

Normalization template

Not involved

Noise and artifact removal

Precise manual segmentation within Mimics Medical to define individual muscle boundaries (RF, VL, VM, VI), followed by 3D surface smoothing to ensure accurate volume extraction

Volume censoring

Not involved

Statistical modeling & inference

Model type and settings

Longitudinal comparative analysis. A paired-sample approach was used to evaluate changes in muscle metrics across the four experimental time points (Pre, Post, FU1, and FU2). Paired t-tests were employed for head-to-head comparisons between phases.

Effect(s) tested

The primary effect of isokinetic training on Physiological Cross-sectional Area (PCSA), Anatomical Cross-sectional Area (ACSA), and Muscle Volume.

Specify type of analysis:

☐ Whole brain☒ ROI-based☐ Both

Anatomical location(s)

Individual muscles of the Quadriceps Femoris (Rectus Femoris, Vastus Lateralis, Vastus Medialis, Vastus Intermedius). ACSA was assessed at the central region of the thigh, while PCSA was calculated for each whole muscle.

Statistic type for inference

(See [Eklund et al. 2016](#))

ROI-based scalar values.

Quantitative analysis of:

1.PCSA : Calculated as $PCSA = (V/L) * \cos(\theta)$, where V is muscle volume, θ is pennation angle, and L is fiber length.

2.ACSA : Derived from the central thigh region via MRI segmentation.

3.Volume : Extracted from 3D models.

Voxel-wise/cluster-wise inference is not applicable.

Correction

No multiple comparison correction was applied.

Models & analysis

n/a | Involved in the study

☒ ☐ Functional and/or effective connectivity☒ ☐ Graph analysis☒ ☐ Multivariate modeling or predictive analysis