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Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

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 (*n*) 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 *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒ 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. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐ 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 *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

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 (AIIS) 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

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

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
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

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

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

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

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

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_(α/2)+t_β)*S/δ]^2 #(S1) Given α=0.05 and β=0.1, the critical values t_(α/2) and t_β are calculated as: t_(α/2)=1.96, t_β=1.28 #(S2) From the Ref. [58], S=16.1, δ=32.3. After calculation, we obtained N>5.21 #(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

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☐	☒ MRI-based neuroimaging

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	NCT06648486

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, theta 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