Prediction of one-year change in knee extension strength by neuromuscular properties in older adults

Running title

One-year strength change explained by neuromuscular properties

Authors

Tetsuya Hirono[1,2], Ryosuke Takeda[1], Taichi Nishikawa[1], Kohei Watanabe[1]

1. Laboratory of Neuromuscular Biomechanics, School of Health and Sport Sciences, Chukyo University
   101 Tokodachi, Kaizu-cho, Toyota, Aichi, Japan
2. Human Health Sciences, Graduate School of Medicine, Kyoto University
   53 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto, Japan

Corresponding author

Tetsuya Hirono, Ph.D., R.P.T.

Human Health Sciences, Graduate School of Medicine, Kyoto University

53 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto, Japan

Email: hirono.tetsuya.4r@kyoto-u.ac.jp

ORCID: 0000-0002-4337-6249

ABSTRACT

Improving muscle strength and preventing muscle weakness are important for older adults. The change in strength can be effectively explained by skeletal muscle mass and neural factors. Neural factors are important for older adults because the variation of neural components is greater in older than in young adults, and any decline in strength cannot solely be explained by a decrease in skeletal muscle mass. The purpose of the present study was to investigate whether skeletal muscle mass or motor unit firing properties could explain the change in muscle strength after one year. Thirty-eight older adults (75.0±4.7 years, 156.6±7.7 cm, 55.5±9.4 kg, 26 women) performed maximum voluntary knee extension and their skeletal muscle mass was measured using a bioimpedance device. During a submaximal contraction task, high-density surface electromyography was recorded and the signals were decomposed into individual motor unit firing. As an index of motor unit firing properties, the slope and y-intercept (MU intercept) were calculated from the regression line between recruitment thresholds and firing rates in each participant. After one year, their maximum knee extension torque was evaluated again. A stepwise multiple regression linear model with sex and age as covariates indicated that MU intercept was a significant explanation with a negative association for the one-year change in muscle strength (β=-0.493, p=0.004), but not skeletal muscle mass (p = 0.364). The results suggest that neural components might be predictors of increasing and decreasing muscle strength rather than skeletal muscle mass.

KEYWORDS

Aging, Motor unit, Central nervous system, Skeletal muscle mass, High-density surface electromyography

INTRODUCTION

With aging, muscle atrophy and muscle weakness are ongoing and lead to poor muscle functions, reduced performance, and impaired activities of daily living. The variability of muscle functions among older adults is typically wider [1, 2]; thus, it is important to prevent loss or maintain muscle functions with a consideration of individual characteristics. The variability is caused by neural mechanisms in aging muscle [3, 4]. Since neuromuscular mechanisms with such variability are basic factors that influence muscle strength change, it is possible that basic factors of neuromuscular properties could determine a longitudinal change in muscle strength.

Generally, skeletal muscle mass loss is focused on aging muscular physiology, such as sarcopenia [5-7]. Muscle size decreases with aging, which is associated with a reduction in the number of muscle fibers [8], and also with neuromuscular remodeling, as characterized by a loss of motor neurons and instability of neuromuscular junction transmission [4, 9]. Whereas skeletal muscle mass, some of the main contributors to muscle force generation are neural factors in older individuals. Manini, Hong [10] pointed out that the decline of muscle strength in older individuals cannot solely be explained by the decline in muscle mass, suggesting that the reduction in neural factors also contributes to muscle weakness. Even in community-dwelling older adults who live independently and without any support, aspects of neural degeneration accompany declines in skeletal muscle mass [11]. Immobilization and skeletal muscle disuse induce degenerations of motor unit firing properties [12, 13], and with aging, neural component degeneration, such as denervation and reinnervation, is observed in older individuals in early stages [14, 15]. Additionally, neural components may show plasticity by changing after low-intensity training [16] and reportedly adapt in the early phase of resistance training [17-19], suggesting that focusing on neural components is important when considering the variability of motor functions among older adults, and neural components are also essential components to maintain and improve physical functions in older adults.

The motor unit is the basic functional unit of the neuromuscular system that produces force and facilitates movement [20]. Varying the number of motor units recruited and firing rate determines muscle contraction and strength. A non-invasive method to assess motor unit firing is high-density surface electromyography (HDsEMG). A specific analysis of HDsEMG signals can identify motor unit firing properties [21, 22]. This method has recently been used to identify individual differences in neural components of older populations [11, 23] and it may be applicable to predict motor functions in the future.

Longitudinal research is important to clarify the mechanism of neuromuscular degeneration associated with aging. The purpose of the present study was to investigate whether neuromuscular properties, including skeletal muscle mass and motor unit firing properties, could explain the change in muscle strength after one year in older adults. The hypothesis was that motor unit firing properties could explain the one-year change in muscle strength. Such knowledge would be useful for the prevention of a decline in the physical function or sarcopenia in the early stage in healthy older adults, and also useful for proposing program prescriptions of physical training for older populations.

METHODS

Participants

Physical test measurements were held in May of 2022 and 2023. At baseline and one-year follow-up physical test measurement, 51 and 71 community-dwelling older adults took part in. Thirty-eight participants of them took part in both measurements (Fig. 1). The analyzed participants were 12 men and 26 women, and their age was 75.0±4.7 years, height was 156.6±7.7 cm, and body mass was 55.5±9.4 kg at the baseline. According to a previous study that evaluated proportional hazards regression analysis using simulation techniques [24], it appears most prudent for the value of events per variable to be 10. Therefore, a sample size of 30 participants is considered sufficient. They received an explanation of the experimental procedures prior to providing informed written consent. This study was approved by the Research Ethics Committee of Chukyo University and conducted in accordance with the Declaration of Helsinki.

Procedure

In May 2022, knee extension strength, skeletal muscle mass, and motor unit firing properties were measured. At the one-year follow-up, only knee extension strength was measured again.

Knee extension strength

A custom-made chair with a dynamometer (Takei Scientific Instruments Co., Ltd., Niigata, Japan) and force transducer (LU-100KSE; Kyowa Electronic Instruments, Aichi, Japan) was used to measure knee extension strength. The participants were seated on the chair with their hip and knee angles at 90 degrees, and performed maximum voluntary isometric contraction (MVC) of knee extension twice following a familiarization session consisting of 50 to 90% of maximum voluntary contraction several times. The greater value was used for further analysis. Knee extension strength was defined as multiplying the force value and arm length, which was determined as the distance between the knee joint axis and force transducer.

Skeletal muscle mass

Appendicular lean mass was estimated using a bioelectrical impedance analysis device (Inbody 430, Inbody Japan Inc., Tokyo, Japan). The device assesses the resistance and reactance of arms, the trunk, and legs with a segmental multifrequency approach (5, 50, and 250 kHz). Their feet and hands were cleaned with an alcohol swab, and were wiped to be dry. After they were seated with being relaxed, they were instructed to stand on and grip the electrodes of the device and to be relaxed during measuring bioimpedance. Since muscle strength and motor unit firing properties were assessed for the right lower limb, skeletal muscle mass of the right lower limb was calculated and used for further analysis.

Motor unit firing properties

The participants were seated on the same chair as for evaluation of knee extension strength. Submaximal isometric ramp-up contraction to 50% of MVC, consisting of a 17-sec increasing phase and 10-sec sustained phase, was performed. The exerted force and target level were shown on a monitor in real-time. During the submaximal ramp-up contraction, HDsEMG was recorded from the vastus lateralis using an EMG acquisition device (Sessantaquatro, OT Bioelettronica, Torino, Italy) with a force signal. A 64-channel electrode grid (GR08MM1305, OT Bioelettronica) was attached on the skin over the vastus lateralis with a bi-adhesive sheet (KITAD064, OT Bioelettronica) and conductive paste (Elefix Z-181BE, Nihonkohden, Tokyo, Japan). After the skin had been cleaned with alcohol, the grid was attached along the line between the head of the greater trochanter and superior and lateral edge of the patella, and the center of the grid was placed at the midpoint of the line. A reference electrode (WS2, OT Bioelettronica) was attached on the tibial tuberosity. Monopolar EMG signals were filtered with a bandpass filter from 10 to 500 Hz, amplified by a factor of 150, and sampled at 2,000 Hz. Recorded EMG signals were transferred to analysis software (MATLAB R2019a, MathWorks GK, MA, USA), and the signals were differentiated between adjacent electrodes in the longitudinal direction. Thus, 59-channel differentiated signals were decomposed and individual motor units were identified by the Convolution Kernel Compensation (CKC) technique using Decomposition of Motor Unit Surface EMG (DEMUSE) software (ver. 6; The University of Maribor, Slovenia) [25, 26]. A single experimental investigator (TH) manually inspected all decomposition results. Any physiologically irregular motor unit discharge (less than 4 Hz or more than 50 Hz) and motor units showing a coefficient of variation of the firing rate over 30% were discarded [27-29]. Recruitment thresholds of motor units were determined from the force level when the motor units first discharged.

The median firing rate of individual motor units at 45-50% of MVC was calculated from the interspike intervals, and the regression line between recruitment thresholds and firing rates was described. The slope (MU slope) and y-intercept (MU intercept) were calculated from the regression line (Fig. 2). To ensure the motor unit firing property with individual participants, data of participants from whom 5 or more motor units were detected were analyzed and used for further analysis [30]. Normally, the motor unit firing rate increases as the recruitment threshold decreases. Thus, we calculated MU intercept to normalize the firing rate depending on the recruitment threshold [30, 31].

Statistical analysis

All statistical analyses were performed using Statistical Package for the Social Sciences ver. 28.0, IBM Japan Inc., Japan). Significance was set at $p < 0.05$.

To identify the relationship at the baseline between knee extension strength and neuromuscular properties as skeletal muscle mass, MU slope and MU intercept, a stepwise multiple linear regression model with variables adjusted for age and sex was used with independent variables of skeletal muscle mass of the right lower limb, MU slope, and MU intercept.

Knee extension torque at the one-year follow-up measurement was divided by that at the baseline, and the percentage change in knee extension strength was calculated. Partial correlation coefficients with sex as a covariate were performed to identify whether knee extension strength change was correlated with skeletal muscle mass, MU slope, or MU intercept at the baseline. Additionally, a stepwise multiple linear regression model with variables adjusted for age and sex was used to identify the most important individual neuromuscular parameters (skeletal muscle mass of the right lower limb, MU slope, and MU intercept) in determining knee extension strength change with consideration of the interrelationships among independent variables.

A bubble plot was constructed to show the relationships among the change in knee extension strength, skeletal muscle mass, and MU intercept. Skeletal muscle mass and MU intercept were normalized with a consideration of sex differences by calculating standard scores, as shown below, in each sex:

Standard score = 50 + 10 x (individual value – mean value) / standard deviation

RESULTS

Eight participants (1 man and 7 woman) were excluded from analyses using the MU slope or MU intercept because fewer than 5 motor units could be detected. The mean and standard deviation of the number of detected motor units in each participant were 12.0±9.3 among the participants in whom more than 5 motor units were detected. Finally, 30 participants were used for analyses using motor unit data, whereas 38 participants data were used for only correlation analysis between the change in knee extension strength and skeletal muscle mass at baseline.

Table 1 shows stepwise multiple regression analysis for knee extension strength at the baseline, indicating a significant explanation of skeletal muscle mass of the right lower limb ($p = 0.011$), but not MU slope ($p = 0.605$)

nor MU intercept (p = 0.082).

Figure 3 shows the results of partial correlation analyses. There was a significant negative correlation between knee extension strength change and MU intercept (p = 0.005), but no significant correlation between the change in knee extension strength and skeletal muscle mass (p = 0.995) nor MU slope (p = 0.479).

Multiple regression analysis indicated that MU intercept was significantly correlated with knee extension strength change (p = 0.004), but neither skeletal muscle mass (p = 0.364) nor MU slope (p = 0.871) was selected as a significant variable (Table 1). Figure 4 shows bubble plots indicating the change in knee extension strength (size of bubble), standard score of skeletal muscle mass of the bright lower limb on the x-axis, and standard score of MU intercept on the y-axis.

DISCUSSION

The present study investigated whether the one-year change in muscle strength could be explained by neuromuscular properties at the baseline in community-dwelling older adults with a longitudinal study design. The results indicated that MU intercept significantly explained the change in knee extension strength (Fig. 3 and Table 2) although skeletal muscle mass was related to knee extension strength at the baseline on cross-sectional analysis (Table 1). These results suggest that the motor unit firing rate may be an important variable related to the one-year change in muscle strength. This is the first study, to our best knowledge, to report that the one-year longitudinal change in muscle strength could be explained by baseline motor unit firing properties, and not baseline skeletal muscle mass. As previous studies pointed out the importance of neural properties [32-34], our results support the importance of neural properties in the muscle strength of older adults.

At the baseline, knee extension strength was only related to skeletal muscle mass, not motor unit firing properties (Table 1). Of course, muscle mass is important to explain muscle strength in community-dwelling older adults [35, 36]. With aging, the neuromuscular system degenerates [3, 4], and its variability among older adults was greater than that in young adults [1, 2]. Therefore, motor unit firing properties were not selected as significant to explain muscle strength at the baseline (Table 1). While the greater variability of neural properties among older individuals may not relate to muscle strength based on cross-sectional analysis (Table 1), MU intercept was a significant contributor to the one-year change in muscle strength in the longitudinal analysis (Table 2 and Fig. 3).

The one-year change in muscle strength was explained by MU intercept at the baseline in community-dwelling older adults in the present study (Table 2). In a previous longitudinal study investigating changes in muscle strength and muscle mass for about 10 years [37], muscle mass change influenced the magnitude of muscle strength over time. Previous studies [10, 32-34, 37, 38] also reported that the decline of strength could not be explained solely by muscle mass, suggesting that other factors, including neural factors, may contribute to the strength change. Indeed, nervous system degeneration assessed by voluntary activation or motor corticospinal excitability contributed to muscle weakness in older adults [32]. Since neural factors can exhibit plasticity [16, 39, 40], neural excitability might increase after one year in individuals with a low MU intercept, and MU intercept was selected as an explanatory variable to determine the one-year change in muscle strength by stepwise regression analysis in the present results.

The negative association of the present results indicated that a greater MU intercept could lead to a decline in muscle strength after one year (Fig. 3 and Table 2). The assessment of motor unit firing properties in the present study was conducted during a submaximal 50% of MVC task. Lower neural excitability during the same relative force production could be interpreted as greater efficiency of neural input to muscle exertion output during submaximal force production [41], involved in the control of synergistic muscles [42] and MU firing synchronization [43]. Although a greater MU intercept means greater neural input to muscle [30, 44], the phenomenon of a lower MU firing rate during submaximal contraction might indicate an effective strategy to promote force exertion. There was no significant change between knee extension torque at the baseline and follow-up (according to Wilcoxon signed-ranked test; $p = 0.245$), meaning that some participants showed improved muscle strength and others showed reduced strength, like bubble colors indicating the various situations in Fig. 4. Previous studies reported a decline in strength with advancing age [37, 38, 45, 46], while one study reported no change in 8 years [47], and another reported that not all participants showed a decline in muscle strength after 10 years [37]. In the present study, one year might be too short a period to observe significant age-related decline, and some older adults rather showed the improvement of knee extension strength. Regarding the negative correlation (Fig. 3 and Table 2), lower neural input to muscle at the baseline could lead to the improvement of muscle strength, whereas greater neural input could lead to the attenuation of muscle strength following one year of conducting daily activities. Considering the interpretation as greater efficiency of neural input during submaximal force production [41], older individuals who exhibited an effective force production strategy with lower neural excitability may show future improvement of muscle strength. We did not assess motor unit firing properties at the follow-up, which is a limitation of the present study, but older individuals with a lower MU intercept might have capacities for neural excitability and muscle strength developments. Since older adults show trainability regarding neural components [10, 18, 34], MU intercept may be a good predictor of one-year change in muscle strength.

As presented in Fig. 4, individuals showing a decline of strength (blue circles) tend to be scattered in the area where both standard scores of the MU intercept and skeletal muscle mass exceeded mean values, while individuals with improved strength (red circles) tend to be scattered in the area where both scores or especially MU intercept score were below mean values. The bubble plot suggests the individual characteristics and trainability for the change in muscle strength could be dependent on the chart area. When considering the determination of muscle strength, the muscle contractile property is also a factor [48] and this is related to MU firing properties [49]. Depending on degeneration of the muscle contractile property with aging, MU firing is altered [9, 50]. We measured only skeletal muscle mass estimated by bioelectrical impedance analysis, and not contractile properties. In the upper and right areas of Fig. 4, with both showing high scores, a decline in muscle strength of all older individuals was observed. Even if an older adult has greater skeletal muscle mass, greater neural input could prevent any increase in muscle strength because of the muscle contractile properties of the individual. Focusing on an individual with the lowest score of skeletal muscle mass but high score of MU intercept, or another individual with the highest score of skeletal muscle mass but low score of MU intercept, the two individuals would show reduced muscle strength after one year (Fig. 4). Such traits could be signs of declining muscle strength. This is of interest but the sample size is small; therefore, further study is needed to investigate such signs of declining muscle strength. In order to consider the details of relationships among muscle strength, skeletal muscle mass, and motor unit firing properties, large sample sizes and longer investigation periods are needed in future studies.

A limitation of the present study was that hydration status and water consumption were not strictly controlled. These variables can influence the bioimpedance measurements. Another limitation was that we did not measure both motor unit firing properties and skeletal muscle mass changes at follow-up. The changes could be useful assumptions for muscle strength change. We did not investigate their physical activities or whether their lives had changed in one year, which is also a limitation of the present study. Habitual physical activities may be key to explaining the relationship between a change in muscle strength and neural excitability at the baseline. In future study, large sample size and long duration could be investigated to evaluate more detail physiological age-related changes.

In conclusion, the present study investigated neuromuscular properties to assess any one-year change in knee extension strength in community-dwelling older adults, and found that neural excitability assessed by MU intercept was a significant factor explaining one-year change in muscle strength with a negative association. Our findings support the previous conclusion that neural components are important for older adults [4, 10, 32], and suggest that neural components might be useful as predictors of future changes in muscle strength that cannot be solely explained by changes in skeletal muscle mass. This knowledge may be useful for the prevention of muscle weakness and decline of physical function in the early stage in healthy older adults, and also useful for proposing physical training programs with an emphasis on the neural components.

Acknowledgments

We would like to thank Dr. Shun Kunugi, Dr. Masamichi Okudaira, Ms. Saeko Ueda, Dr. Akito Yoshiko, Ms. Yoko Kawakami, and lab. members for helping with data collection. We also appreciate Prof. Aleš Holobar of the University of Maribor, Slovenia, for supporting the analyses of motor unit firing properties using the DEMUSE tool.

This study was financially supported by a Grant-in-Aid from the Japan Society for the Promotion of Science Fellows (21J00674 and 22KJ2973).

Statements and Declarations

None

Competing Interests

None

REFERENCES

1. Vanden Noven, M.L., et al., *Motor Variability during Sustained Contractions Increases with Cognitive Demand in Older Adults.* Front Aging Neurosci, 2014. **6**: p. 97.
2. Degens, H. and M.T. Korhonen, *Factors contributing to the variability in muscle ageing.* Maturitas, 2012. **73**(3): p. 197-201.
3. Hunter, S.K., H.M. Pereira, and K.G. Keenan, *The aging neuromuscular system and motor performance.* J Appl Physiol (1985), 2016. **121**(4): p. 982-995.
4. Piasecki, M., et al., *Age-related neuromuscular changes affecting human vastus lateralis.* J Physiol, 2016. **594**(16): p. 4525-36.
5. Yoshiko, A., et al., *Applicability of the seated step test for assessing thigh muscle sarcopenia in older individuals.* Exp Gerontol, 2023: p. 112283.
6. Chen, L.K., et al., *Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia.* J Am Med Dir Assoc, 2014. **15**(2): p. 95-101.
7. Cruz-Jentoft, A.J., et al., *Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People.* Age Ageing, 2010. **39**(4): p. 412-23.
8. Wilkinson, D.J., M. Piasecki, and P.J. Atherton, *The age-related loss of skeletal muscle mass and function: Measurement and physiology of muscle fibre atrophy and muscle fibre loss in humans.* Ageing Res Rev, 2018. **47**: p. 123-132.
9. Piasecki, M., et al., *Age-dependent motor unit remodelling in human limb muscles.* Biogerontology, 2016. **17**(3): p. 485-96.
10. Manini, T.M., S.L. Hong, and B.C. Clark, *Aging and muscle: a neuron's perspective.* Curr Opin Clin Nutr Metab Care, 2013. **16**(1): p. 21-6.
11. Hirono, T., et al., *Motor unit firing patterns in older adults with low skeletal muscle mass.* Arch Gerontol Geriatr, 2023. **116**: p. 105151.
12. Duchateau, J. and K. Hainaut, *Effects of immobilization on contractile properties, recruitment and firing rates of human motor units.* J Physiol, 1990. **422**: p. 55-65.
13. Inns, T.B., et al., *Motor unit dysregulation following 15 days of unilateral lower limb immobilisation.* J Physiol, 2022. **600**(21): p. 4753-4769.
14. Sirago, G., et al., *Loss of neuromuscular junction integrity and muscle atrophy in skeletal muscle disuse.* Ageing Res Rev, 2023. **83**: p. 101810.
15. Piasecki, M., et al., *Failure to expand the motor unit size to compensate for declining motor unit numbers distinguishes sarcopenic from non-sarcopenic older men.* J Physiol, 2018. **596**(9): p. 1627-1637.
16. Hirono, T., et al., *Effects of home-based bodyweight squat training on neuromuscular properties in community-dwelling older adults.* Aging Clin Exp Res, 2023.
17. Kamen, G. and C.A. Knight, *Training-related adaptations in motor unit discharge rate in young and older adults.* J Gerontol A Biol Sci Med Sci, 2004. **59**(12): p. 1334-8.
18. Moritani, T. and H.A. deVries, *Potential for gross muscle hypertrophy in older men.* J Gerontol, 1980. **35**(5): p. 672-82.

19. Pearcey, G.E.P., et al., *Chronic resistance training: is it time to rethink the time course of neural contributions to strength gain?* Eur J Appl Physiol, 2021. **121**(9): p. 2413-2422.
20. Duchateau, J. and R.M. Enoka, *Human motor unit recordings: origins and insight into the integrated motor system.* Brain Res, 2011. **1409**: p. 42-61.
21. Holobar, A. and D. Zazula, *On the selection of the cost function for gradient-based decomposition of surface electromyograms.* Annu Int Conf IEEE Eng Med Biol Soc, 2008. **2008**: p. 4668-71.
22. Holobar, A. and D. Zazula, *Correlation-based decomposition of surface electromyograms at low contraction forces.* Med Biol Eng Comput, 2004. **42**(4): p. 487-95.
23. Feeney, D.F., D. Mani, and R.M. Enoka, *Variability in common synaptic input to motor neurons modulates both force steadiness and pegboard time in young and older adults.* J Physiol, 2018. **596**(16): p. 3793-3806.
24. Peduzzi, P., et al., *Importance of events per independent variable in proportional hazards regression analysis. II. Accuracy and precision of regression estimates.* J Clin Epidemiol, 1995. **48**(12): p. 1503-10.
25. Holobar, A., et al., *Estimating motor unit discharge patterns from high-density surface electromyogram.* Clin Neurophysiol, 2009. **120**(3): p. 551-62.
26. Farina, D., et al., *Decoding the neural drive to muscles from the surface electromyogram.* Clin Neurophysiol, 2010. **121**(10): p. 1616-23.
27. Adam, A. and C.J. De Luca, *Firing rates of motor units in human vastus lateralis muscle during fatiguing isometric contractions.* J Appl Physiol (1985), 2005. **99**(1): p. 268-80.
28. Fuglevand, A.J., D.A. Winter, and A.E. Patla, *Models of recruitment and rate coding organization in motor-unit pools.* J Neurophysiol, 1993. **70**(6): p. 2470-88.
29. Hirono, T., et al., *Acute changes in motor unit discharge property after concentric versus eccentric contraction exercise in knee extensor.* J Electromyogr Kinesiol, 2022. **67**: p. 102704.
30. Okudaira, M., et al., *Longitudinal development of muscle strength and relationship with motor unit activity and muscle morphological characteristics in youth athletes.* Exp Brain Res, 2023. **241**(4): p. 1009-1019.
31. Watanabe, K., et al., *Neuromuscular characteristics of front and back legs in junior fencers.* Exp Brain Res, 2022. **240**(7-8): p. 2085-2096.
32. Clark, L.A., et al., *Reduced Neural Excitability and Activation Contribute to Clinically Meaningful Weakness in Older Adults.* J Gerontol A Biol Sci Med Sci, 2021. **76**(4): p. 692-702.
33. Clark, B.C. and T.M. Manini, *What is dynapenia?* Nutrition, 2012. **28**(5): p. 495-503.
34. Manini, T.M. and B.C. Clark, *Dynapenia and aging: an update.* J Gerontol A Biol Sci Med Sci, 2012. **67**(1): p. 28-40.
35. Fukumoto, Y., et al., *Skeletal muscle quality assessed from echo intensity is associated with muscle strength of middle-aged and elderly persons.* Eur J Appl Physiol, 2012. **112**(4): p. 1519-25.
36. Taniguchi, M., et al., *Increase in echo intensity and extracellular-to-intracellular water ratio is independently associated with muscle weakness in elderly women.* Eur J Appl Physiol, 2017. **117**(10): p. 2001-2007.

37. Hughes, V.A., et al., *Longitudinal muscle strength changes in older adults: influence of muscle mass, physical activity, and health.* J Gerontol A Biol Sci Med Sci, 2001. **56**(5): p. B209-17.
38. Metter, E.J., et al., *Muscle quality and age: cross-sectional and longitudinal comparisons.* J Gerontol A Biol Sci Med Sci, 1999. **54**(5): p. B207-18.
39. Martinez-Valdes, E., et al., *Tracking motor units longitudinally across experimental sessions with high-density surface electromyography.* J Physiol, 2017. **595**(5): p. 1479-1496.
40. Del Vecchio, A., et al., *The increase in muscle force after 4 weeks of strength training is mediated by adaptations in motor unit recruitment and rate coding.* J Physiol, 2019. **597**(7): p. 1873-1887.
41. Pucci, A.R., L. Griffin, and E. Cafarelli, *Maximal motor unit firing rates during isometric resistance training in men.* Exp Physiol, 2006. **91**(1): p. 171-8.
42. Rutherford, O.M. and D.A. Jones, *The role of learning and coordination in strength training.* Eur J Appl Physiol Occup Physiol, 1986. **55**(1): p. 100-5.
43. Semmler, J.G. and M.A. Nordstrom, *Motor unit discharge and force tremor in skill- and strength-trained individuals.* Exp Brain Res, 1998. **119**(1): p. 27-38.
44. Herda, T.J., *Resistance exercise training and the motor unit.* Eur J Appl Physiol, 2022. **122**(9): p. 2019-2035.
45. Fukumoto, Y., et al., *Association of physical activity with age-related changes in muscle echo intensity in older adults: a 4-year longitudinal study.* J Appl Physiol (1985), 2018. **125**(5): p. 1468-1474.
46. Daly, R.M., et al., *Association between changes in habitual physical activity and changes in bone density, muscle strength, and functional performance in elderly men and women.* J Am Geriatr Soc, 2008. **56**(12): p. 2252-60.
47. Greig, C.A., J. Botella, and A. Young, *The quadriceps strength of healthy elderly people remeasured after eight years.* Muscle Nerve, 1993. **16**(1): p. 6-10.
48. Van Vossel, K., et al., *Can muscle typology explain the inter-individual variability in resistance training adaptations?* J Physiol, 2023. **601**(12): p. 2307-2327.
49. Piotrkiewicz, M., et al., *Age-related change in duration of afterhyperpolarization of human motoneurones.* J Physiol, 2007. **585**(Pt 2): p. 483-90.
50. Dalton, B.H., et al., *Differential age-related changes in motor unit properties between elbow flexors and extensors.* Acta Physiol (Oxf), 2010. **200**(1): p. 45-55.

Table 1. Multiple regression analysis of knee extension strength at baseline

Dependent variable: Knee extension strength at baseline

Model: $R^2 = 0.608$, adjusted $R^2 = 0.563$

Independent variables	B	Standard error	95%CI Lower	Upper	Standardized β-coefficients	t	p
Skeletal muscle mass	12.057	4.419	2.974	21.140	0.565	2.728	0.011
Age	-0.098	0.881	-1.908	0.912	-0.014	-0.111	0.912
Sex	-16.056	13.332	-43.461	11.349	-0.249	-1.204	0.239

Excluded variables: MU slope, MU intercept

Forced entry variables: Age, Sex

MU slope and MU intercept were calculated from the regression line between recruitment thresholds and firing rates of motor units.

Table 2. Multiple regression analysis of one-year change in muscle strength

Dependent variable: Change rate of knee extension strength

Model: $R^2 = 0.376$, adjusted $R^2 = 0.304$

Independent variables	B	Standard error	95%CI Lower	Upper	Standardized β-coefficients	t	p
MU intercept	-2.286	0.721	-3.768	-0.803	-0.493	-3.17	0.004
Age	0.492	0.359	-0.245	1.229	0.213	1.373	0.181
Sex	-5.862	3.243	-12.527	0.803	-0.281	-1.808	0.082

Excluded variables: Skeletal muscle mass of right lower limb, MU slope

Forced entry variables: Age, Sex

Figure 1

A timeline of the study

Figure 2

A: Representative motor unit firing data from one participant. Blue lines represent individual motor unit firing rates during ramp-up contraction to 50% of maximum voluntary contraction (MVC). The recruitment threshold was defined as the force level when the motor unit fired first. The firing rate was calculated as the median value at 40-50% of MVC. B: Regression lines described from the recruitment threshold and firing rate. From the regression lines, slope (MU slope) and y-intercept (MU intercept) were calculated and used for further analyses.

Figure 3

Partial correlations between change in knee extension strength after one year and skeletal muscle mass of right lower limb, MU slope, and MU intercept, with sex as a covariate. MU slope and MU intercept were defined as regression lines of motor unit recruitment threshold and firing rate.

Figure 4

Bubble plot showing one-year change in muscle strength and baseline motor unit firing rate and skeletal muscle mass. The size of the bubbles indicates the individual change in knee extension strength; red bubbles mean improvements of strength, whereas blue bubbles mean declines of strength. The x- and y-axis represent standard scores for the motor unit firing rate and skeletal muscle mass in the right lower limb, respectively, which were calculated in each sex.

Fig1

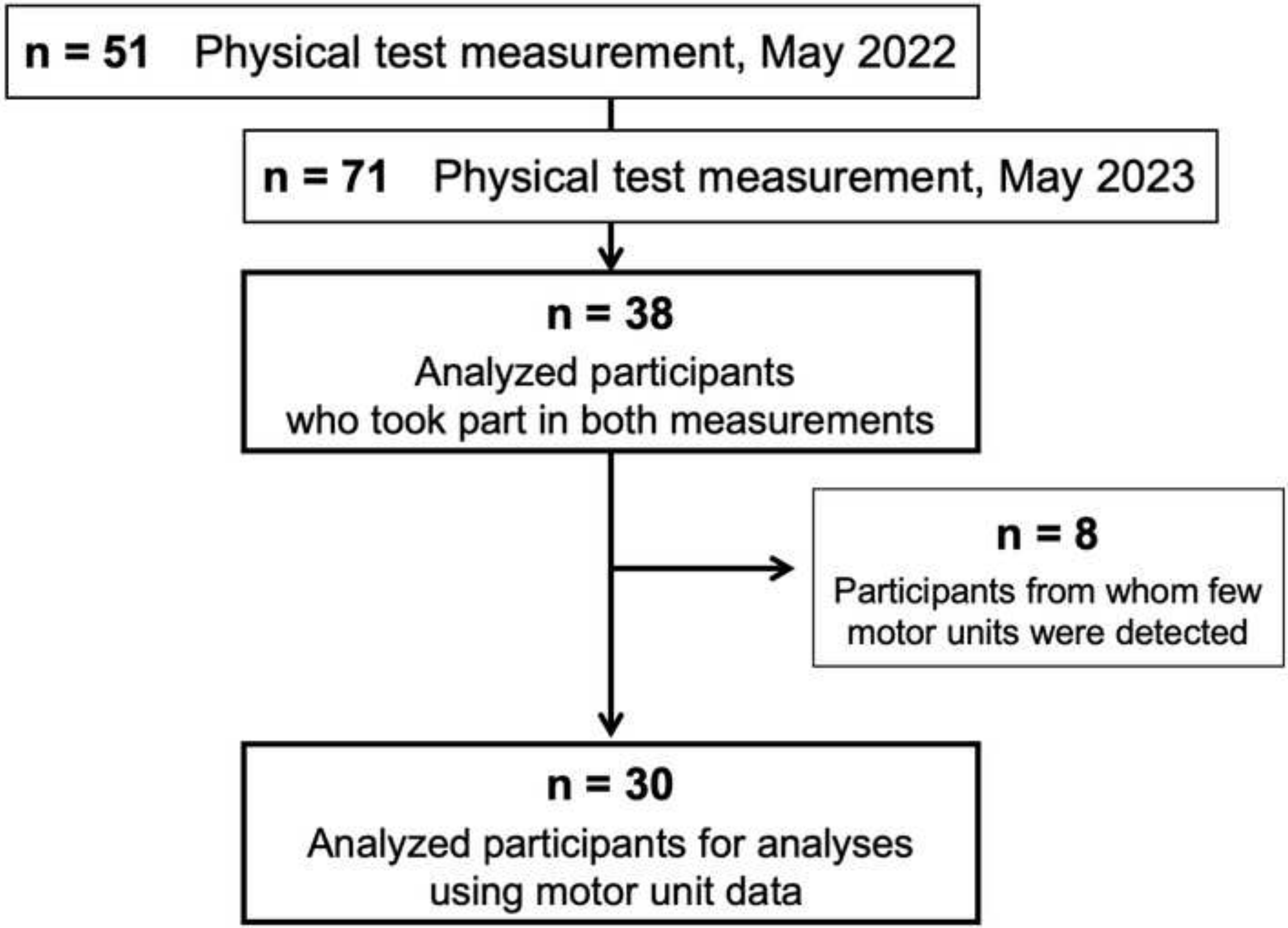
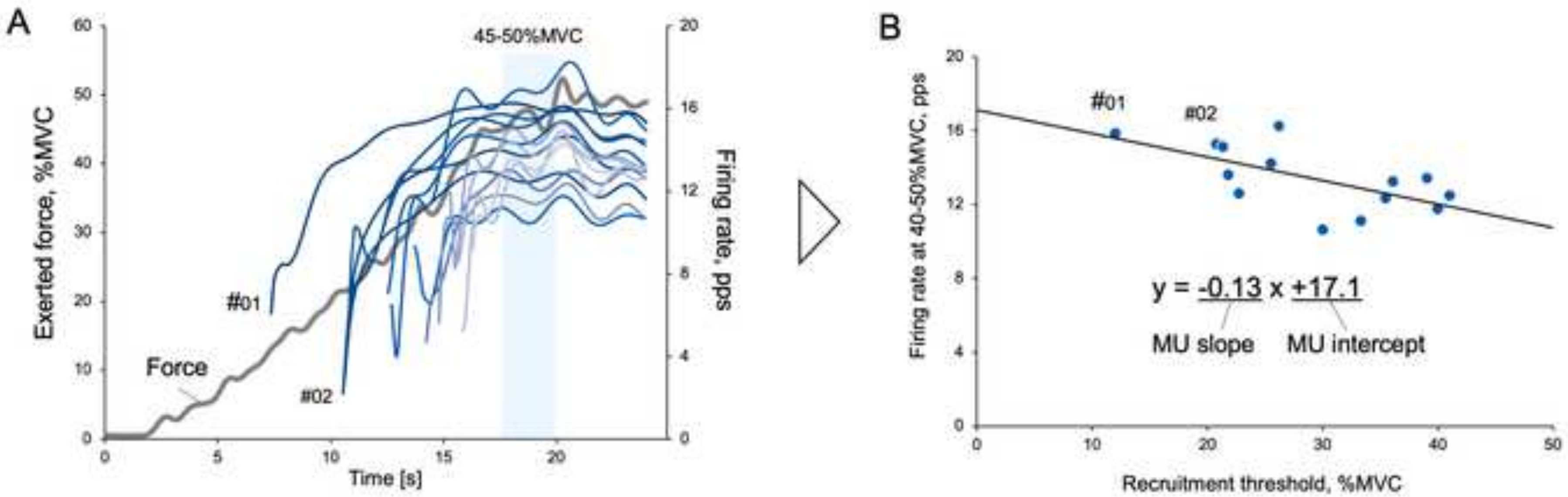

n = 51 Physical test measurement, May 2022
n = 71 Physical test measurement, May 2023
n = 38
Analyzed participants
who took part in both measurements
n = 8
Participants from whom few
motor units were detected
n = 30
Analyzed participants for analyses
using motor unit data

Fig2



A
45-50%MVC
Exerted force, %MVC
Firing rate, pps
Time [s]
Force
#01
#02
B
Firing rate at 40-50%MVC, pps
Recruitment threshold, %MVC
#01
#02
y = -0.13 x +17.1
MU slope
MU intercept

Fig3

Click here to access/download;colour figure;Fig3.png

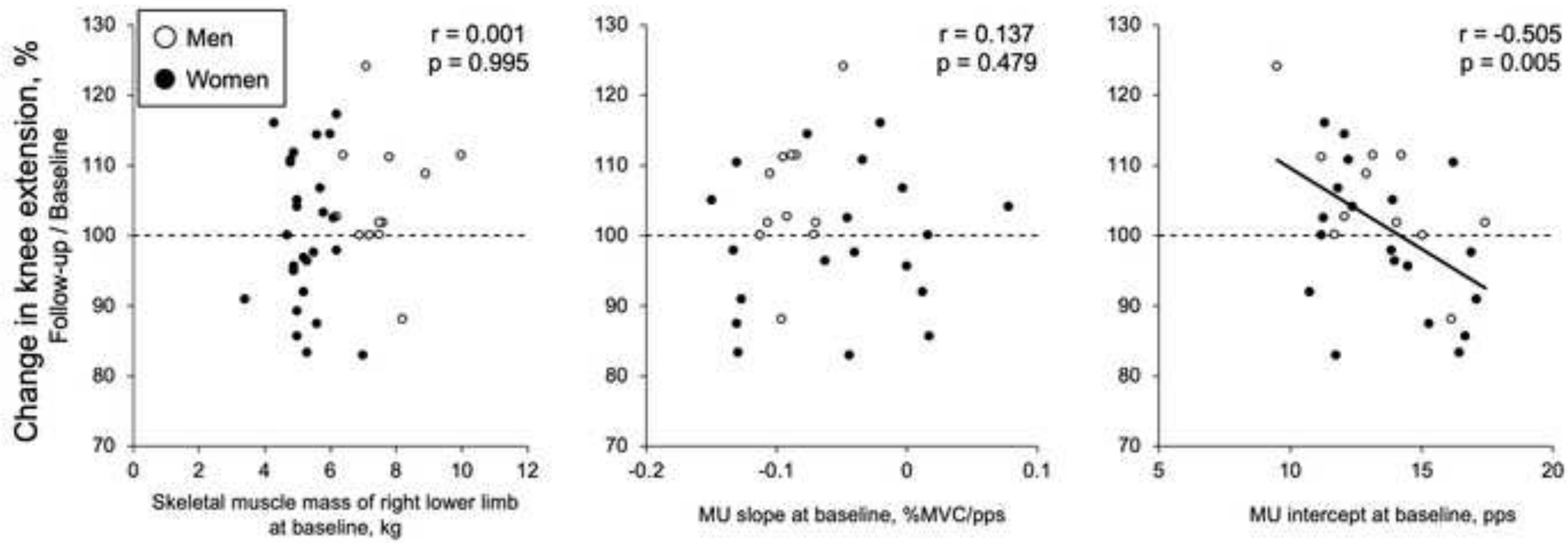


Fig4

Click here to access/download;colour figure;Fig4.png