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Similar muscle hypertrophy following eight weeks of resistance training to momentary muscular failure or with repetitions-in-reserve in resistance-trained individuals

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ABSTRACT

This study examined the influence of resistance training (RT) proximity-to-failure, determined by repetitions-in-reserve (RIR), on quadriceps hypertrophy and neuromuscular fatigue. Resistance-trained males ($n = 12$) and females ($n = 6$) completed an 8-week intervention involving two RT sessions per week. Lower limbs were randomised to perform the leg press and leg extension exercises either to i) momentary muscular failure (FAIL), or ii) a perceived 2-RIR and 1-RIR, respectively (RIR). Muscle thickness of the quadriceps [rectus femoris (RF) and vastus lateralis (VL)] and acute neuromuscular fatigue (i.e., repetition and lifting velocity loss) were assessed. Data was analysed with Bayesian linear mixed-effect models. Increases in quadriceps thickness (average of RF and VL) from pre- to post-intervention were similar for FAIL [0.181 cm (HDI: 0.119 to 0.243)] and RIR [0.182 cm (HDI: 0.115 to 0.247)]. Between-protocol differences in RF thickness slightly favoured RIR [−0.036 cm (HDI: −0.113 to 0.047)], but VL thickness slightly favoured FAIL [0.033 cm (HDI: −0.046 to 0.116)]. Mean volume was similar across the RT intervention between FAIL and RIR. Lifting velocity and repetition loss were consistently greater for FAIL versus RIR, with the magnitude of difference influenced by the exercise and the stage of the RT intervention.

Key Points

- Terminating RT sets with a close proximity-to-failure (e.g., 1- to 2-RIR) can be sufficient to promote similar hypertrophy of the quadriceps as reaching momentary muscular failure in resistance-trained individuals over eight weeks, but the overall influence of proximity-to-failure on muscle-specific hypertrophy may also depend on other factors (e.g., exercise selection, order, and subsequent musculature targeted).
- Due to high repetition loss (from the first to final set) when sets are terminated at momentary muscular failure, performing RT with 1- to 2-RIR allows for similar volume load and repetition volume accumulation as reaching momentary muscular failure across eight weeks, possibly influencing the overall RT stimulus achieved.
- Performing RT to momentary muscular failure consistently induces higher levels of acute neuromuscular fatigue versus RT performed with 1- to 2-RIR; however, improved fatigue resistance overtime may attenuate acute neuromuscular fatigue and subsequent repetition loss (but may depend on the exercise performed).

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Resistance training; fatigue; proximity-to-failure; repetitions-in-reserve; muscle hypertrophy

1. Introduction

Skeletal muscle hypertrophy is a physiological adaptation to resistance training (RT), specifically driven by the repeated exposure of muscle fibres to mechanical tension (Wackerhage et al., 2019). To promote meaningful muscle hypertrophy, it is accepted that resistance-trained individuals should terminate RT sets with a close proximity-to-failure (defined as the number of repetitions remaining in a set prior to momentary muscular failure) (Hickmott et al., 2022; Refalo, Helms, Trexler, et al., 2022). Whether closer proximities-to-failure during RT *always* promote greater muscle hypertrophy, however, is contentious. For example, RT sets to momentary muscular failure may incur high levels of i) neuromuscular fatigue that impairs the stimulus acheived within a RT session (Alix-Fages et al., 2022), and ii) muscle damage that compromises protein synthesis directed towards muscle hypertrophy (Damas et al., 2016). Therefore, prescribing RT with a repetitions-in-reserve (RIR) scale to terminate sets close to, but not at momentary muscular failure has become common (Refalo, Helms, Hamilton, et al., 2022; Zourdos et al., 2016). The lack of research employing RIR prescription, however, and the uncertainties surrounding the relationship between proximity-to-failure, neuromuscular fatigue, and muscle hypertrophy, highlight key areas for future research to explore.

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To investigate the influence of proximity-to-failure on muscle hypertrophy, previous research has compared either i) RT performed to momentary muscular failure versus non-failure (Lacerda et al., 2020; Lasevicius et al., 2019; S. Martorelli et al., 2017; Nobrega et al., 2018; Santanielo et al., 2020), or ii) RT performed to different percentages of velocity loss from the first (or fastest) repetition (Andersen et al., 2021; Pareja-Blanco et al., 2017; Pareja-Blanco, Alcazar, Cornejo-Daza, et al., 2020; Pareja-Blanco, Alcazar, SA-V, et al., 2020; Rissanen et al., 2022; Rodiles-Guerrero et al., 2022). Specifically, meta-analysis (Refalo, Helms, Trexler, et al., 2022) of this relevant literature shows no statistically significant difference between RT performed to momentary muscular failure versus non-failure for muscle hypertrophy, and that performing RT to high velocity loss thresholds (>25%) likely promotes greater muscle hypertrophy than low velocity loss thresholds (<20%) but similar muscle hypertrophy to moderate (20–25%) velocity loss thresholds (i.e., closer versus further proximities-to-failure). Although these data suggest that it is possible for proximity-to-failure to influence muscle hypertrophy in a *non-linear* manner (i.e., as sets are terminated closer to momentary muscular failure, muscle hypertrophy increases, but only to a certain point), the specific RIR achieved in non-failure conditions is unclear (Pelland et al., 2022; Refalo, Helms, Hamilton, et al., 2022). Nonetheless, (Robinson et al., 2023). conducted an *exploratory* analysis of the relationship between RIR and muscle hypertrophy by estimating specific RIR values for each non-failure RT group from the relevant literature (Pelland et al., 2022; Refalo, Helms, Hamilton, et al., 2022). Muscle hypertrophy increased as sets were terminated closer to momentary muscular failure in the resulting meta-regression, but uncertainty surrounding i) the accuracy of RIR estimations of non-failure RT groups, and ii) the variability in RIR between participants and across sets within a given study (Pelland et al., 2022; Refalo, Helms, Hamilton, et al., 2022), renders the exact relationship between RIR and muscle hypertrophy, unclear. As a whole, the literature suggests that RT to momentary muscular failure is effective for promoting muscle hypertrophy (within the timeframes studied); however, reaching close proximities-to-failure may also be sufficient even in resistance-trained individuals (Andersen et al., 2021; Pareja-Blanco et al., 2017; Pareja-Blanco, Alcazar, Cornejo-Daza, et al., 2020; Pareja-Blanco, Alcazar, SA-V, et al., 2020; Rissanen et al., 2022; Santanielo et al., 2020). Overall, deriving practical recommendations that inform the proximity-of-failure of set termination is challenging due to the limitations of the current literature.

To monitor and control the proximity-to-failure achieved during RT, sets can be terminated at specific RIR values (e.g., 3 sets x 10–15 repetitions at 2-RIR). Although RIR prescription is commonly used in practice, however, few studies (Arede et al., 2020; Graham & Cleather, 2021; Helms et al., 2018; Mangine et al., 2022) have investigated the influence of intra-set RIR predictions on RT adaptations and short-term responses. This research gap may be due, in part, to concerns relating to individual RIR accuracy (i.e., the proximity of actual set termination from the target RIR). Consequently, most RIR-related research (to date) focuses on RIR accuracy (Helms et al., 2016; Ormsbee et al., 2019; Zourdos et al., 2016, 2021), with one meta-analysis concluding that individuals underpredict RIR by approximately one repetition on average (Halperin et al., 2021) and a recent experimental trial observing that resistance-trained individuals were within 0.40 (±0.68) and 0.90 (±0.81) repetitions from 1-RIR or 3-RIR targets, respectively (Refalo, Remmert, et al., 2023). These data indicate that RIR prescription may be an efficacious set termination strategy for controlling proximity-to-failure in RT interventions, at least in resistance-trained samples. Indeed, future research comparing RIR prescription with reaching momentary muscular failure during RT can advance the understanding of the relationship between proximity-to-failure and outcomes of interest (i.e., muscle hypertrophy and neuromuscular fatigue) and subsequently improve practical recommendations.

1.1. Objectives

Proximity-to-failure in RT is a continuous variable as RIR values range from 0–10+. However, proximity-to-failure has only been investigated dichotomously, with previous research comparing RT to "set failure" versus non-failure. As such, previous research does not describe the relationship between RIR and muscle hypertrophy, and is therefore practically limited, as set termination does not have to be binary (i.e., set failure or non-failure). Therefore, the primary objective of this study was to examine the influence of RT proximity-to-failure, determined by RIR, on quadriceps hypertrophy following eight weeks of RT performed to either momentary muscular failure or with RIR in resistance-trained individuals. Importantly, only one (Santanielo et al., 2020) out of five (Lacerda et al., 2020; Lasevicius et al., 2019; S. Martorelli et al., 2017; Nobrega et al., 2018) studies comparing RT performed to momentary muscular failure versus non-failure on muscle hypertrophy has been conducted in a resistance-trained sample. We employed a Bayesian approach for data analysis to directly model uncertainty and intuitively present the results through posterior probabilities to allow meaningful inferences to be made regarding the influence of proximity-to-failure on muscle hypertrophy (Kruschke & Liddell, 2018). We also explored changes in lifting velocity and repetitions performed during RT, and volume accumulation to quantify acute neuromuscular fatigue.

2. Methods

2.1. Experimental approach

Resistance-trained participants completed an 8-week unilateral RT intervention (within-participant design), whereby each lower limb was randomised to perform the unilateral leg press and leg extension exercises either to i) momentary muscular failure (FAIL), or ii) a perceived 2-RIR and 1-RIR, respectively (RIR) (Figure 1). Prior to the RT intervention, two pre-testing sessions were conducted to obtain baseline measurements of muscle thickness, determine individual load selection, and familiarise participants with predicting intra-set RIR and reaching momentary muscular failure.

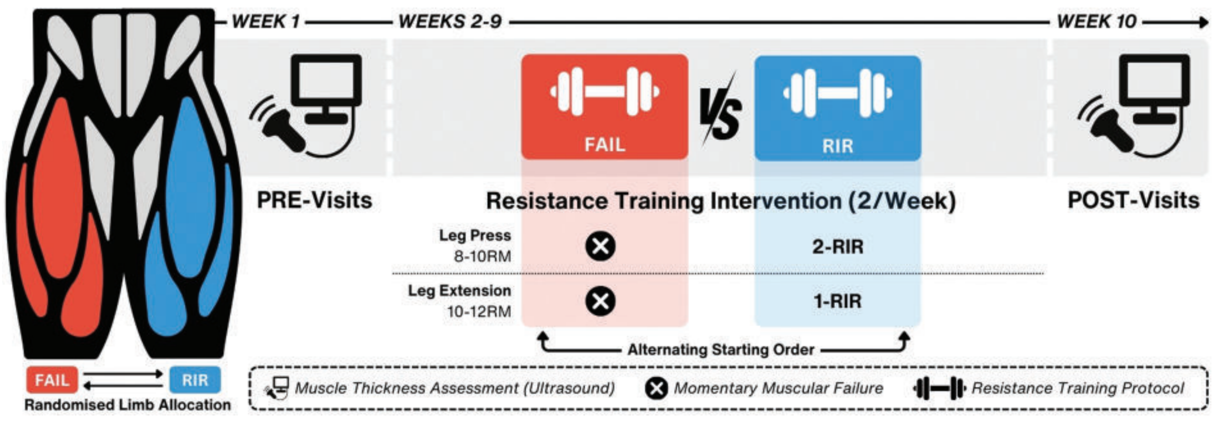

Figure 1. Schematic overview of study design and resistance training protocols. Participants completed two pre-testing sessions (involving two ultrasound assessments, and a repetitions-to-failure and repetition-maximum load assessment), 16 experimental sessions across the 8-week intervention (two times per week separated by ~72 h), and two post-testing sessions (involving two ultrasound assessments). *RIR, repetitions-in-reserve. RM, repetition-maximum.*

Participants then commenced the 8-week intervention involving two RT sessions per week (with each lower limb performing RT to either FAIL or RIR) separated by ~72 h (Figure 1). Muscle thickness of the quadriceps [rectus femoris (RF) and vastus lateralis (VL)] was assessed via ultrasound at baseline and following the 8-week RT intervention. To provide surrogate measures of neuromuscular fatigue, the change in lifting velocity (in weeks one, four, and eight) and repetitions performed from the first to final set, along with volume (i.e., volume load and repetition volume) accumulation were assessed.

2.2. Participants

Pre-exercise participant characteristics are presented in Table 1. Male (*n* = 12) and female (*n* = 7) participants were recruited i) between 18–40 years old, ii) with no existing musculoskeletal injuries or neuromuscular disorders, iii) who confirmed they had not used anabolic steroids, or illegal agents known to increase muscle size for the previous year, iv) with a minimum of three years RT experience (with at least three or more RT sessions per week) (Santos Junior et al., 2021). One female participant did not adhere to the nutritional requirements and was therefore not included in data analysis. However, a sensitivity analysis was conducted for our primary outcome measure (i.e., change in muscle thickness) with the full sample (*n* = 19) displayed in Supplementary Table 3.5. All 18 participants included in data analysis reported experience with intra-set RIR predictions, 16 (89%) had worked with a personal trainer face-to-face, and nine (50%) had previously competed in powerlifting or bodybuilding. Of the six female participants, four (67%) reported experiencing a regular menstrual cycle and five reported using oral contraceptives.

2.2.1. Sample size justification

The target sample size for this study was 18 participants; however, to account for a 20% dropout rate, we aimed to recruit 20 participants. Sample size was based on the following pragmatic considerations: i) recruiting more than 20 participants was not feasible due to resource constraints (time and associated costs to complete data collection and analysis), and ii) this sample size is greater than similar within-subject unilateral pre-post studies investigating the influence of RT proximity-to-failure on muscle hypertrophy (Andersen et al., 2021; Lacerda et al., 2020; Santanielo et al., 2020). We initially conducted a sensitivity power analysis in G*Power software (Version 3.1.9.7) with the pre-specified sample size. A minimum (critical) effect size (Cohen's *d* = 0.59) was calculated that based on findings from previous research (Santanielo et al., 2020) is sufficient to capture likely effect sizes for within-group changes in muscle hypertrophy (*d* = 0.7 to 0.8), but it is unclear whether between-group differences in muscle hypertrophy (*d* = 0.2) may be detected. The critical effect size is likely sufficient to detect between-group differences in other outcome measures like lifting velocity loss from

Table 1. Baseline participant characteristics. An overview of the relevant characteristics for each participant included in data analysis. Quadriceps set volume is reported as 20% higher than the initial volume that participants were assigned based on previous resistance training experience. *kg, kilograms; p/w, per week; y, years.*

	Males (*n* = 12)		Females (*n* = 6)	
Variable	Mean ± *SD*	Range	Mean ± *SD*	Range
Age (y)	26.9 ± 3.1	20–31	30.0 ± 5.8	24–38
Bodyweight (kg)	82.6 ± 6.0	75–94	62.8 ± 5.4	57–72
RT experience (y)	7.8 ± 2.6	4–13	7.5 ± 2.3	5–10
RT frequency (p/w)	4.8 ± 0.9	3–6	4.7 ± 0.8	4–6
Quadriceps set volume	12 ± 1	10–14	14 ± 2	12–17

the first to the final set (d = 2.5 (Sanchez-Medina & Gonzalez-Badillo, 2011)). Nonetheless, our final decision was to employ Bayesian statistical methods to generate posterior distributions that i) account for uncertainty in parameter estimates where limited data may be available, and ii) provide a full probability distribution that allows for the interpretation of not only point estimates (or single effect sizes) but also the entire range of plausible values (Kruschke & Liddell, 2018).

2.3. Procedures

2.3.1. Exercise and nutrition control

Participants were asked to not perform i) any high-intensity aerobic exercise during the RT intervention, and specifically, ii) any lower-body RT or aerobic exercise in the 24 h period before each study visit. Participants were allowed to perform additional moderate-intensity RT involving muscle groups other than the quadriceps, but exercise constraints were employed to minimise potential confounding influences (described in Supplementary Table S1.1). Participants were required to track their nutritional intake and bodyweight using a mobile application (MacroFactor; Stronger By Science Technologies LLC, Raleigh, NC, USA), which provided each participant individualised macronutrient (i.e., protein, carbohydrate, dietary fat) and energy (i.e., kilocalories) targets based on a monthly rate of weight gain equal to 1% of their starting body weight (kg) for the duration of the study period (10-weeks). Data retrieved from MacroFactor are reported in Table 2.

2.3.2. Menstrual cycle considerations

Considering that all female participants completed both unilateral protocols, thus acting as their own "controls", and that recent meta-analyses indicate that both i) menstrual cycle phase (D'Souza et al., 2023; McNulty et al., 2020), and ii) modern oral contraceptive use (D'Souza et al., 2023; Elliott-Sale et al., 2020), have at most trivial effects on exercise performance at the group level, females commenced the intervention period at any time-point throughout their menstrual cycle and no timing considerations were made for post-testing. If participants experienced menstrual symptoms during the study period that they believed affected RT performance, study visits were rescheduled as necessary.

2.3.3. Pre-testing sessions

2.3.3.1. Exercise technique. For the leg press (Hammer Strength), participants were seated with one foot positioned on the plate whilst ensuring that the foot, knee, and hip were in line. Participants held the handles and maintained contact with the seat whilst lowering the plate until knee angle was less than 90 degrees and contact was made with the safety mechanism. The safety mechanism was individualised for each participant to standardise range-of-motion. For the leg extension, participants were seated with their back flush against the back rest and hands gripping the support handles. Toes were pointed upwards, and participants were required to reach full knee extension by ensuring their shin contacted – or was at least within sufficient proximity of – the standardised implement (see yellow dotted lines in Supplementary Figure S1.2). Participants were instructed to perform the concentric (lifting) phase of each repetition with maximal lifting velocity (i.e., as fast as possible), followed by a controlled eccentric (lowering) phase (~2 s). See Supplementary Figure S1.2 for images of equipment and demonstration of exercise technique.

2.3.3.2. Repetition-maximum load assessment. To determine starting loads, participants completed four repetition-maximum (RM) assessments (8–10-RM for the leg press and 10–12-RM for the leg extension per limb) in pre-visit one. To begin, a warm-up consisting of three sets of eight repetitions was performed on a randomly selected lower limb with the minimum load on the leg press exercise (55 kg) and with 70 and 80% of the approximate 8–10-RM load determined for the leg press based on participant training history. Participants then rested two minutes before attempting a set to momentary muscular failure with the predicted 8–10-RM load. If the participant appeared i) able to (as determined by an experienced supervisor) perform more than 10 repetitions without reaching momentary muscular failure, or ii) unable to complete eight repetitions, the set was immediately terminated. The load was then increased or decreased (5–10 kg on the leg press and 2.5–5 kg on the leg extension), and after a five-minute recovery period, another set was attempted. This was repeated until the participant reached momentary muscular failure on the 9th, 10th, or 11th repetition. Once the 8–10-RM load was established on the leg press, the same procedures were used to determine the 10–12-RM load on the leg extension. This procedure was completed on both limbs. An experienced supervisor ensured participant safety and encouraged maximum lifting velocity with strong verbal encouragement.

Table 2. Nutritional intake and bodyweight change. An overview of nutrition (energy, protein, carbohydrate, and dietary fat intake) and body weight data extracted from MacroFactor for males and females, separately. *BW, bodyweight; g, grams; kcal, kilocalories; kg, kilograms.*

	Males (n = 12)		Females (n = 6)	
Variable	Mean ± *SD*	Range	Mean ± *SD*	Range
BW change (kg)	3.1 ± 2.5	−0.2–9.3	2.2 ± 1.8	0–5.4
BW change (%)	3.6 ± 2.9	−0.3–10.2	3.5 ± 3	0–8.8
Energy Intake (kcal)	3149 ± 234	2722–3535	2523 ± 352	2102–3173
Protein (g)	208 ± 18	178–234	145 ± 24	111–173
Protein (g) per kg/BW	2.5 ± 0.3	2.1–3	2.3 ± 0.4	1.7–2.8
Carbohydrate (g)	390 ± 59	299–511	293 ± 81	217–440
Dietary fat (g)	86 ± 17	56–115	82 ± 19	62–119

2.3.3.3. Repetitions-to-failure assessment. In pre-visit two, participants completed two sets to momentary muscular failure with the loads determined in pre-visit one for the leg press and leg extension. An overview of the procedures and participant instructions can be found elsewhere (Refalo, Remmert, et al., 2023). All procedures were performed on both limbs, in a randomised manner.

2.3.4. Resistance training intervention

Participants performed both exercises in a unilateral manner on both lower limbs twice per week for eight weeks (Figure 1), with each limb randomly assigned to perform either the FAIL or RIR protocol. FAIL performed all sets to momentary muscular failure. Considering RT sets do not have to beterminated at the same proximity-to-failure, and that proximity-to-failure may be prescribed based on the complexity of the exercise performed (Refalo, Helms, Hamilton, et al., 2022), RIR performed the leg press to 2-RIR and leg extension to 1-RIR. For RIR, participants were provided the following standardised instruction: *"you will be required to stop the set when you perceive to have reached the RIR target"*. Conversely, during FAIL, momentary muscular failure occurred when despite attempting to do so, participants were unable to complete the concentric portion of their current repetition with a full range-of-motion and without deviation from the prescribed form of the exercise (Refalo, Helms, Hamilton, et al., 2022) (participants had up to two seconds to progress past the "sticking point" before sets were ceased). To explore individual responses and increase the precision of RT effects on muscle hypertrophy (Scarpelli et al., 2022), set volume for each participant was equal to the weekly number of quadriceps sets they typically performed in their most recent training routine and was equally distributed between the leg press and leg extension. Where a participant was assigned ≥ 15 sets, a 20% decrease in volume was implemented (e.g., 16 sets − 20% = 13 sets) to mitigate potential injury risk, excessive fatigue, and prolonged session durations. Halfway through the intervention (commencement of week five), all participants increased set volume by 20%.

2.3.4.1. Resistance training protocol.. Participants commenced the first RT session on a random limb, with the starting limb alternated each session. Both exercises were completed on the starting limb before training the alternate limb. Four warm-up sets were performed on the leg press, starting with the minimum load, working up to 50, 65, and 85% of the 8–10-RM load (for ten, eight, six and four repetitions, with two-minute inter-set rest periods). Only two warm-up sets were performed on the leg extension (50 and 65% of the 10–12-RM load for five repetitions). Participants then performed their specified number of sets on each exercise with their individualised load. For both protocols, if the participants performed more repetitions than the RM load range, the load was adjusted on the subsequent set by 2.5–5 kg on the leg press and 1.25–2.5 kg on the leg extension. Four minutes rest was given between working sets on the leg press, two minutes for the leg extension, and five minutes between exercises. If a participant experienced musculoskeletal discomfort that prevented them from performing either exercise, if feasible, all sets were allocated to the exercise they could perform. For example, if a participant needed to complete 10 sets but was unable to perform the leg press, the FAIL protocol would perform all 10 sets to momentary muscular failure on the leg extension and the RIR protocol would perform the first five sets to 2-RIR (4 min rest) and the remaining five sets to 1-RIR (2 min rest) on the leg extension (for a total of 10 sets). To ensure recovery and minimise residual fatigue, ~72 h was allocated between RT sessions; however, 48 to 96 h were allowed for scheduling flexibility (in case participants were unable to schedule 72 h between sessions). All RT sessions were monitored by a qualified exercise professional (MR), and strong verbal encouragement was provided during each working set. Participants that completed 90% of scheduled sessions (14 out of 16 RT sessions) were included in the final analysis.

2.4. Outcome measures

2.4.1. Repetitions-in-reserve prediction accuracy

The difference between the predicted (i.e., 1- or 3-RIR) and actual RIR (i.e., number of repetitions performed after the prediction was given until momentary muscular failure was reached) achieved during the repetitions-to-failure assessment was defined as RIR accuracy (Refalo, Remmert, et al., 2023). This was calculated as both *raw* RIR accuracy, which accounts for directionality of error, and *absolute* RIR accuracy, an absolute value representing the magnitude of error (Refalo, Remmert, et al., 2023).

2.4.2. Volume accumulation

Volume of RT, measured as repetition volume (sets x repetitions) and volume load (sets x repetitions x load), was deliberately not equalised between FAIL and RIR. Volume completed in each protocol was recorded, and the percentage decrease in repetitions performed from the first to final set was also calculated.

2.4.3. Change in lifting velocity from the first to final set

Mean concentric velocity (MV) for each repetition (described herein as "lifting velocity") was measured (on the starting limb in both sessions in weeks one, four, and eight) using a linear position transducer (GymAware, Kinetic Performance Technology, Canberra, Australia) attached to the loading bar of the leg press. The mean lifting velocity of the first three repetitions completed in each of the leg press sets was used to determine the change in mean lifting velocity from the first to final set to investigate acute neuromuscular fatigue (Refalo, Helms, et al., 2023; Sanchez-Medina & Gonzalez-Badillo, 2011). The result was expressed as percentage change, with negative values (i.e., decreased lifting velocity from the first to final set) used to indicate acute neuromuscular fatigue.

2.4.4. Muscle thickness

Ultrasound imaging [SONOSITE M-Turbo (probe size = 5 cm, scanning frequency = 15–16 MHz); FUGIFILM, Bothell, Western Australia] was used to determine left and right RF and VL thickness. Two separate scans were performed during both pre-testing and post-testing (separated by 48–72 h) at least 72 h after RT to assess the reliability of the measurement and minimise any confounding effect of residual intramuscular swelling.

Participants lay in a supine position and images were obtained at 50% of the distance between the lateral epicondyle and greater trochanter for the vastus lateralis and 50% on the distance between the anterior spina iliaca superior (ASIS) and the superior part of the patella for the rectus femoris. Accurate repositioning of the probe in subsequent scans was ensured by marking measurement sites and transferring the markings to a transparent plastic sheet (when apparent, blemishes and tattoos were also marked to replicate its positioning). Scans were taken three times at the same site with the probe positioned longitudinally (i.e., lengthwise on the thigh, not perpendicular to it) with the skin layer located in the most superior portion of the image to standardise probe pressure. Images were transferred to a computer and analysed using open-source software (OsiriX, version 3.2.1; OsiriX Imaging Software, Geneva, Switzerland) by generating an average measurement (i.e., largest distance between the superficial and deeper aponeuroses) of the proximal, central, and distal portions of images (Sarto et al., 2021) as shown in Supplementary Figure S1.3. The average of the three images for each site was used for analysis. The typical error (TE) and intraclass correlation (ICC) of the two pre- and post-testing ultrasound assessments are summarised in Supplementary Figure S1.3. As the same investigator (MR) supervised all RT sessions during the study, it was not possible to blind the ultrasound assessments and data analysis.

2.5. Statistical analysis

To provide a more flexible modelling approach and an intuitive results interpretation by reporting probabilities (Kruschke & Liddell, 2018), we analysed data with Bayesian linear mixed-effect models using the "brms" (Bürkner, 2023) package in R (v 4.0.2; R Core Team, https://www.r-project.org/). Posterior draws were extracted using "tidybayes" (Kay, 2023), estimated marginal effects were calculated using "emmeans" (Lenth, 2023), and the probability (i.e., percentage value ranging from 0% to 100%) that an estimate was in favour of a given protocol was calculated manually by examining the proportion of posterior draws that met the criteria of interest (e.g., >0) and denoted as the probability of direction (*pd*). For our primary outcome (i.e., change in muscle thickness) a model was generated to assess mean differences in outcome measures between protocols for the quadriceps (average of RF and VL) and for the RF and VL individually. We also calculated the probability that a certain change in muscle thickness exceeded the TE and denoted it as "*pd* > TE". For change in lifting velocity, a model was generated to explore differences at three time points throughout the RT intervention between protocols. For change in repetitions performed, volume load, and repetition volume, models were generated to calculate the slopes for each protocol (i.e., change in the variable assessed per session) and explore differences in longitudinal trends between protocols. Further model details, population-level effects, and final group-level slope structures are displayed in Supplementary Table S2.2. Non-informative priors (i.e., default "brms" priors) were used for all model parameters across all outcome measures. Inferences from all analyses were made from posterior samples generated using the Hamiltonian Markov Chain Monte Carlo method and via the use of high-density credible intervals (HDI). Model diagnostics were conducted as per the WAMBS-Checklist (Depaoli & van de Schoot, 2017) (Supplementary Table S2.1). All raw data of outcome measures (in text and figures) are presented as mean and standard deviation. A comprehensive overview of the statistical analysis along with the R code used can be found on the Open Science Framework (https://osf.io/34d92/).

3. Results

3.1. Intervention adherence

Mean participant adherence was 97.5% (87.5–100%). In some instances, sessions were completed over 11 weeks instead of 10 due to scheduling constraints. No sessions had to be rescheduled due to menstrual symptoms in females. To maintain adherence, minor protocol modifications were made if a participant experienced musculoskeletal discomfort (e.g., muscular strains or knee joint pain) but was able to continue the study as mutually decided by the participant and supervisor. Eight participants experienced minor musculoskeletal discomfort (FAIL = 5, RIR = 3), with two of the eight unable to perform the leg press in some weeks (in which case the remaining set volume was allocated to the leg extension). One participant experienced a muscular strain (limb = RIR) in the second week and had to cease participation, but once recovered (~12-weeks), recommenced the study from the start. All participants completed the study. Tracked nutritional variables and body weight change are reported in Table 2. Out of the 18 participants, 16 (89%) increased bodyweight, as intended by MacroFactor.

3.2. Repetitions-in-reserve prediction accuracy

Participants had a high absolute RIR accuracy; on average less than one repetition from the 1- and 3-RIR targets on both exercises (Table 3). There was a slight trend for overestimation

Table 3. Repetitions-in-reserve prediction accuracy. Summary of absolute repetitions-in-reserve prediction accuracy (raw values) for both exercises on each lower limb. Arrow symbols inform the raw repetitions-in-reserve accuracy and indicate whether the average prediction was an overestimation (up arrow = ↑) or underestimation (down arrow = ↓). Data shown are presented as mean ± *SD. RIR, repetitions-in-reserve.*

	Leg Press		Leg Extension	
RIR Target	Left	Right	Left	Right
1-RIR	↑ 0.44 ± 0.51	↑ 0.44 ± 0.78	↑ 0.56 ± 0.51	↑ 0.44 ± 0.70
3-RIR	↑ 0.61 ± 0.70	↓ 0.94 ± 1.16	↓ 0.83 ± 0.99	↓ 0.89 ± 1.08

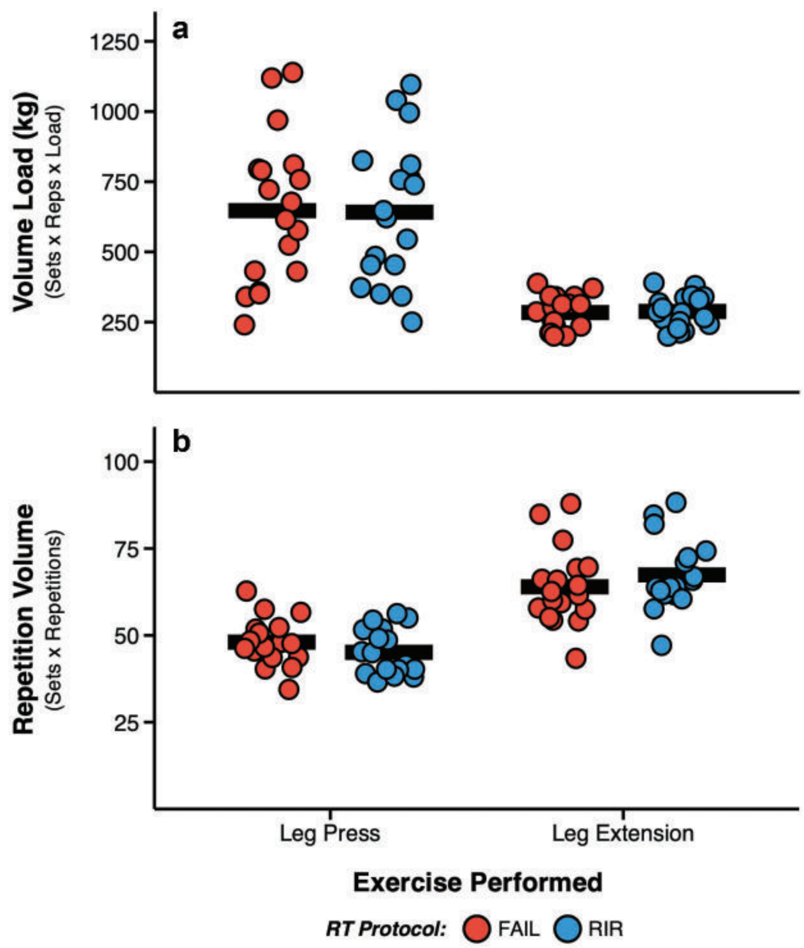

Figure 2. Volume load (a) and repetition volume (b) completed across the resistance training intervention for FAIL and RIR and for both exercises. Volume load calculated as: sets x repetitions x load. Repetition volume calculated as: sets x repetitions. Data shown are raw values presented as both protocol means (with individual values), and the *SD* of protocol means can be found in supplementary tables 3.1 and 3.2.

on 1-RIR predictions (i.e., participants were more likely to over-predict RIR closer to momentary muscular failure) and under-estimation on 3-RIR predictions (i.e., participants were more likely to underpredict RIR further from momentary muscular failure) excluding the left limb leg press.

3.3. Resistance training variables

Average volume load and repetition volume across all sessions of the RT intervention were similar between FAIL and RIR (Figure 2). Table 4 displays a summary of all RT variables recorded for each week (average values from both sessions completed) across the intervention.

3.4. Muscle thickness

Raw quadriceps thickness (average of RF and VL) is displayed in Figure 3(a,b). Similar increases in quadriceps thickness were estimated for FAIL [0.181 cm (HDI: 0.119 to 0.243); *pd* = 100%] and RIR [0.182 cm (HDI: 0.115 to 0.247); *pd* = 100%] from pre- to post-intervention (Figure 3(c)). The probability of change in quadriceps thickness above the TE of measurement (0.055 cm) was also similar between FAIL (*pd* > TE = 100%) and RIR (*pd* > TE = 100%). Raw measures of RF and VL thickness from pre- to post-intervention are displayed in Supplementary Table S3.3. Slightly greater increases in RF thickness were estimated for RIR [0.193 cm (HDI: 0.114 to 0.264); *pd* > TE = 100%] versus FAIL [0.156 cm (HDI: 0.080 to 0.227); *pd* > TE = 100%] from pre- to post-intervention (Figure 4(a)). However, slightly greater increases in VL thickness were estimated for FAIL [0.205 cm (HDI: 0.134 to 0.277); *pd* > TE = 100%] versus RIR [0.172 cm (HDI: 0.097 to 0.250); *pd* > TE = 100%] from pre- to post-intervention (Figure 4(a)). Estimates for between-protocol differences are shown in Table 5 and posterior distributions in Figure 4(b).

3.5. Change in lifting velocity from the first to final set

Raw measures of change in lifting velocity (as percentage change) from the first to final set for weeks one, four, and eight are displayed in Figure 5a. Larger decreases in lifting velocity were estimated for FAIL [–9.9% (HDI: –14.8% to –5%); *pd* = 100%] versus RIR [–4.4% (HDI: –9.1% to 0.7%); *pd* = 98%] in Week 1, for FAIL [–12.6% (HDI: –18% to –7.2%); *pd* = 100%] versus RIR [–5.8% (HDI: –11.1% to –0.5%); *pd* = 99%] in Week 4, and for FAIL [–9.6% (HDI: –15.1% to –3.7%); *pd* = 100%] versus RIR [–6.4% (HDI: –12% to 0.6%); *pd* = 99%] in Week 8. Estimates for between-protocol differences are shown in Table 5 and posterior distributions in Figure 5b.

Table 4. Descriptive characteristics for each resistance training protocol. Repetition values are rounded to the nearest whole number. Percentage decrease from the first to final set is calculated from instances where the load was not adjusted across sets (i.e., not calculated from repetition data shown in table). Data shown are calculated as the average result from both resistance training sessions completed in each week and are presented as mean ± *SD. kg, kilograms; reps, repetitions.*

	FAIL		RIR		FAIL		RIR	
Variable	LP	LE	LP	LE	LP	LE	LP	LE
	Week 1				**Week 2**			
Total Reps	46 ± 10	57 ± 10	42 ± 7	63 ± 10	47 ± 8	59 ± 11	46 ± 9	63 ± 10
Reps (first set)	11 ± 3	11 ± 2	9 ± 2	12 ± 2	11 ± 2	12 ± 2	10 ± 2	12 ± 2
Reps (final set)	8 ± 2	8 ± 1	8 ± 1	9 ± 2	8 ± 2	8 ± 1	8 ± 2	10 ± 1
% Decrease Reps	*23.5%*	*32%*	*8.7%*	*23.5%*	*17.9%*	*32.4%*	*11.6%*	*19%*
Load Lifted (kg)	101 ± 45	32 ± 10	98 ± 43	31 ± 8	105 ± 44	31 ± 8	102 ± 42	31 ± 7
Volume Load (kg)	546 ± 289	254 ± 71	527 ± 273	253 ± 55	574 ± 268	244 ± 48	555 ± 254	246 ± 46
	Week 3				**Week 4**			
Total Reps	49 ± 11	60 ± 10	44 ± 9	64 ± 10	46 ± 8	63 ± 12	43 ± 8	63 ± 10
Reps (first set)	11 ± 4	12 ± 2	10 ± 2	13 ± 1	10 ± 2	13 ± 2	9 ± 2	13 ± 1
Reps (final set)	8 ± 2	8 ± 1	8 ± 2	10 ± 1	8 ± 2	9 ± 1	8 ± 2	9 ± 1
% Decrease Reps	*21.6%*	*29%*	*8.1%*	*22.3%*	*21.4%*	*28.5%*	*11%*	*25.4%*
Load Lifted (kg)	110 ± 46	31 ± 8	107 ± 43	31 ± 7	110 ± 47	32 ± 8	112 ± 44	32 ± 7
Volume Load (kg)	599 ± 282	248 ± 47	582 ± 266	252 ± 46	592 ± 266	257 ± 52	582 ± 255	264 ± 55
	Week 5				**Week 6**			
Total Reps	52 ± 11	63 ± 15	49 ± 11	66 ± 14	49 ± 12	65 ± 11	48 ± 10	65 ± 11
Reps (first set)	9 ± 2	12 ± 3	9 ± 1	12 ± 2	9 ± 2	13 ± 2	8 ± 2	12 ± 1
Reps (final set)	8 ± 1	8 ± 1	8 ± 1	9 ± 2	7 ± 2	8 ± 1	7 ± 1	9 ± 2
% Decrease Reps	*20.2%*	*28.9%*	*10.6%*	*21%*	*26.8%*	*31.5%*	*15.2%*	*20.1%*
Load Lifted (kg)	104 ± 41	34 ± 8	104 ± 42	34 ± 8	114 ± 45	34 ± 8	112 ± 43	35 ± 8
Volume Load (kg)	669 ± 225	303 ± 110	668 ± 227	313 ± 111	709 ± 237	300 ± 76	701 ± 219	307 ± 78
	Week 7				**Week 8**			
Total Reps	51 ± 8	67 ± 9	48 ± 10	69 ± 13	48 ± 10	68 ± 13	44 ± 9	73 ± 12
Reps (first set)	10 ± 2	13 ± 2	9 ± 2	12 ± 2	9 ± 3	13 ± 2	8 ± 2	13 ± 2
Reps (final set)	7 ± 2	8 ± 1	7 ± 2	9 ± 3	7 ± 2	8 ± 2	7 ± 2	9 ± 3
% Decrease Reps	*32%*	*33.7%*	*21.7%*	*23%*	*25.6%*	*35.4%*	*20.7%*	*24.3%*
Load Lifted (kg)	121 ± 45	36 ± 8	124 ± 44	37 ± 8	121 ± 48	37 ± 8	122 ± 47	37 ± 8
Volume Load (kg)	740 ± 274	344 ± 82	776 ± 253	331 ± 68	768 ± 287	330 ± 76	770 ± 277	338 ± 74

3.6. Change in repetitions performed from the first to final set

Predicted longitudinal trends for change in repetitions performed (as percentage change) from the first to final set for FAIL and RIR for each session and exercise are displayed in Figure 6. When averaged across all sessions, greater repetition loss was found for FAIL [–20.4% (HDI: –27% to – 13.9%); *pd* = 100%] versus RIR [–15.8% (HDI: –22.8% to –9.3%); *pd* = 100%] on the leg press, and FAIL [–29.9% (HDI: –33.8% to –25.9%); *pd* = 100%] versus RIR [–21.4% (HDI: –25.8% to –17.6%); *pd* = 100%] on the leg extension. Slope estimates of the change in repetitions performed for each exercise were also calculated for FAIL [Leg Press = –0.3% (HDI: –1% to 0.2%); *pd* = 86%, Leg Extension = 0.4% (HDI: 0% to 0.7%); *pd* = 98%] and RIR [Leg Press = –0.6% (HDI: –1.2% to 0.1%); *pd* = 97%, Leg Extension = 0.3% (HDI: 0.1% to 0.7%); *pd* = 94%]. Posterior distributions for between-protocol differences are shown in Supplementary Figure S4.1 and estimates for between-protocol differences in Table 5.

3.7. Volume load and repetition volume

Predicted longitudinal trends for volume load for FAIL and RIR for each session and exercise are displayed in Figure 6. When averaged across all sessions, similar mean volume load was found between FAIL [350 kg (HDI: 290 to 406); *pd* = 100%] and RIR [346 kg (HDI: 290 to 406); *pd* = 100%] on the leg press, and FAIL [129 kg (HDI: 114 to 143); *pd* = 100%] and RIR [131 kg (HDI: 116 to 145); *pd* = 100%] on the leg extension. Slope estimates of volume load for each exercise were also calculated for FAIL [Leg Press = 5.70 kg (HDI: 3.92 to 7.26); *pd* = 100%, Leg Extension = 0.71 kg (HDI: –0.12 to 1.47); *pd* = 96%] and RIR [Leg Press = 6.53 kg (HDI: 4.73 to 8.14); *pd* = 100%, Leg Extension = 0.81 kg (HDI: 0.02 to 1.63); *pd* = 97%].

Predicted longitudinal trends for repetition volume for FAIL and RIR for each session and exercise are displayed in Figure 6. When averaged across all sessions, similar mean repetition volume was found between FAIL [27 repetitions (HDI: 25 to 29); *pd* = 100%] and RIR [25 repetitions (HDI: 24 to 27); *pd* = 100%] on the leg press, and FAIL [31 repetitions (HDI: 29 to 32); *pd* = 100%] and RIR [32 repetitions (HDI: 31 to 34); *pd* = 100%] on the leg extension. Slope estimates of repetition volume for each exercise were also calculated for FAIL [Leg Press = –0.24 repetitions (HDI: –0.40 to –0.09); *pd* = 100%, Leg Extension = 0.25 repetitions (HDI: 0.13 to 0.37); *pd* = 100%] and RIR [Leg Press = –0.24 repetitions (HDI: –0.43 to –0.06); *pd* = 99%, Leg Extension = 0.13 repetitions (HDI: –0.04 to 0.30); *pd* = 94%]. Posterior distributions for between-protocol differences are shown in Supplementary Figure 4.2 and 4.3 and estimates for between-protocol differences in Table 5.

4. Discussion

4.1. Muscle hypertrophy

We found a similar increase in quadriceps thickness (i.e., average of RF and VL) after eight weeks of RT performed to either FAIL (+6.96%) or RIR (+6.98%) in resistance-trained males and females, with a 48% probability (*pd* > *TE* = 3%) that any potential difference (albeit negligible) between the protocols exists.

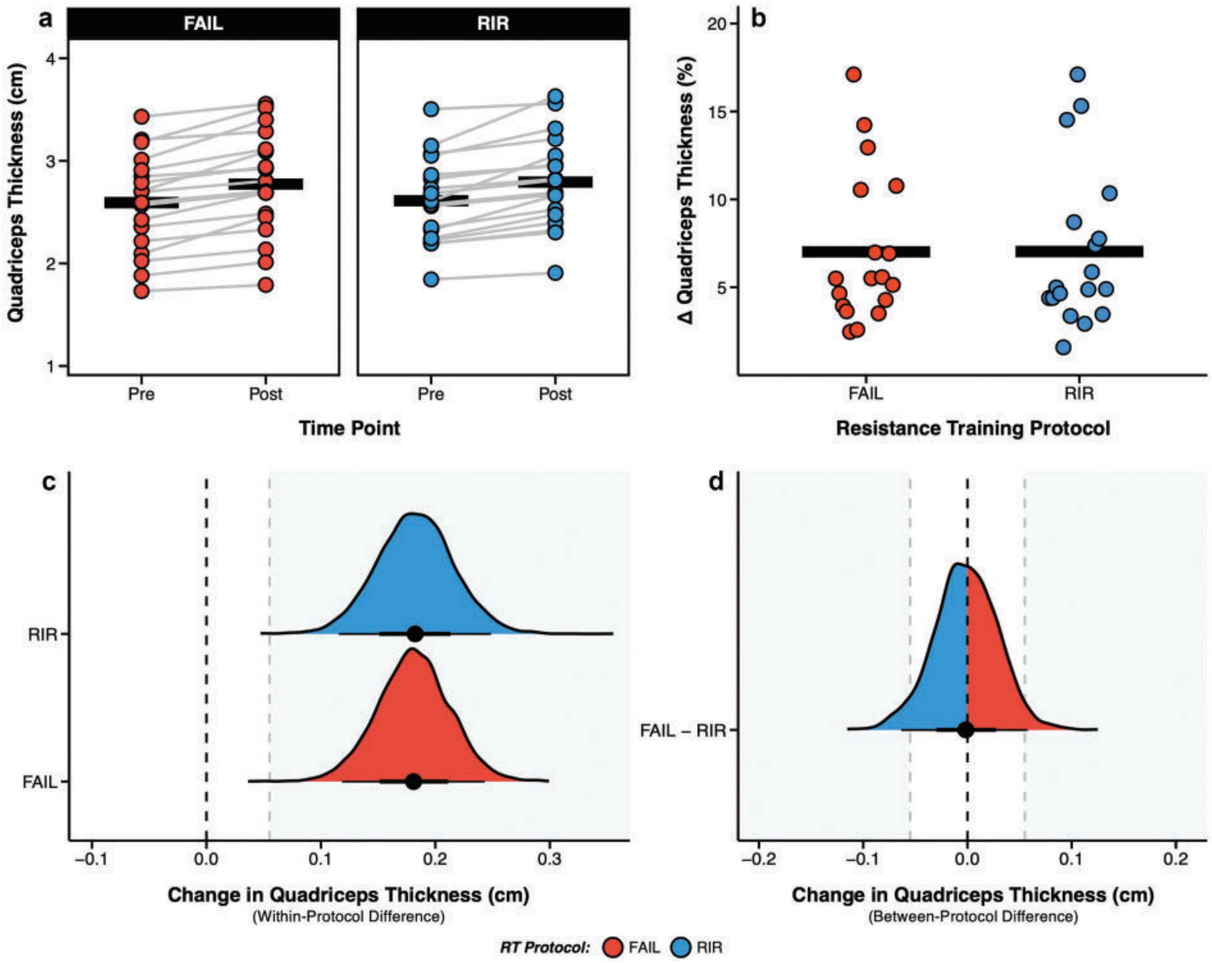

Figure 3. Quadriceps thickness at pre- and post-intervention for FAIL and RIR (a), percentage change (b), and with within-protocol (c) and between-protocol (d) posterior distributions. Quadriceps thickness calculated as the average result of raw rectus femoris and vastus lateralis measures. Data shown in figure A/B are raw values presented as both protocol means and individual values. The SD of protocol means can be found in supplementary table S3.3. Figure C and D display posterior distributions that show the central tendency (i.e., point estimate = mean) and highest density credible intervals, with the grey dotted lines indicating the typical error of the measurement and the shaded grey area representing the proportion of the change in quadriceps thickness above the typical error.

These changes in quadriceps thickness were unlikely due to measurement error, but rather, hypertrophy of the targeted musculature (Figure 3(c)). Moreover, we found an 81% probability ($pd > TE = 42\%$) of slightly greater RF thickness when RT was performed to RIR (+7.38%) versus FAIL (+5.98%), but a 79% probability ($pd > TE = 22\%$) of slightly greater VL thickness when RT was performed to FAIL (+7.95%) versus RIR (+6.59%). Overall, these findings demonstrate that in resistance-trained males and females, terminating sets at 1- to 2-RIR promotes similar overall quadriceps hypertrophy to reaching momentary muscular failure over eight weeks of RT, but the influence of proximity-to-failure on muscle-specific hypertrophy may depend on other factors (e.g., muscle group measured, exercises performed, etc.).

Our findings of similar quadriceps hypertrophy between FAIL and RIR (Figure 3) align with previous studies (Andersen et al., 2021; Santanielo et al., 2020) and meta-analyses (Grgic et al., 2021; Refalo, Helms, Trexler, et al., 2022; A. F. Vieira et al., 2021) in resistance-trained individuals. For example, our meta-analysis (Refalo, Helms, Trexler, et al., 2022) found no statistically significant difference between i) RT performed to momentary muscular failure versus non-failure across five studies (n = 4 untrained; n = 1 resistance-trained), or ii) between moderate and high velocity loss thresholds across six studies in resistance-trained individuals. However, ambiguity of the proximities-to-failure achieved in non-failure RT groups, and different definitions of set failure used across studies (Jukic et al., 2023; Pelland et al., 2022; Refalo, Helms, Hamilton, et al., 2022), makes it difficult to confidently infer the influence of specific RIR values on muscle hypertrophy from previous research. Indeed, a recent meta-regression of estimated RIR values highlights that greater muscle hypertrophy seems to occur when sets are terminated closer to momentary muscular failure (Robinson et al., 2023), but whether closer proximities-to-failure are *always* better for muscle hypertrophy remains uncertain. For example, both Santanielo et al (Santanielo et al., 2020). and Andersen et al (Andersen et al., 2021). Also reported similar quadriceps hypertrophy (RF and VL) following RT performed to momentary muscular failure versus non-failure or high versus moderate velocity loss thresholds (i.e., closer versus further proximities-to-failure), respectively, in resistance-trained individuals. Taken as a whole, we provide further evidence that an adequate set volume coupled with

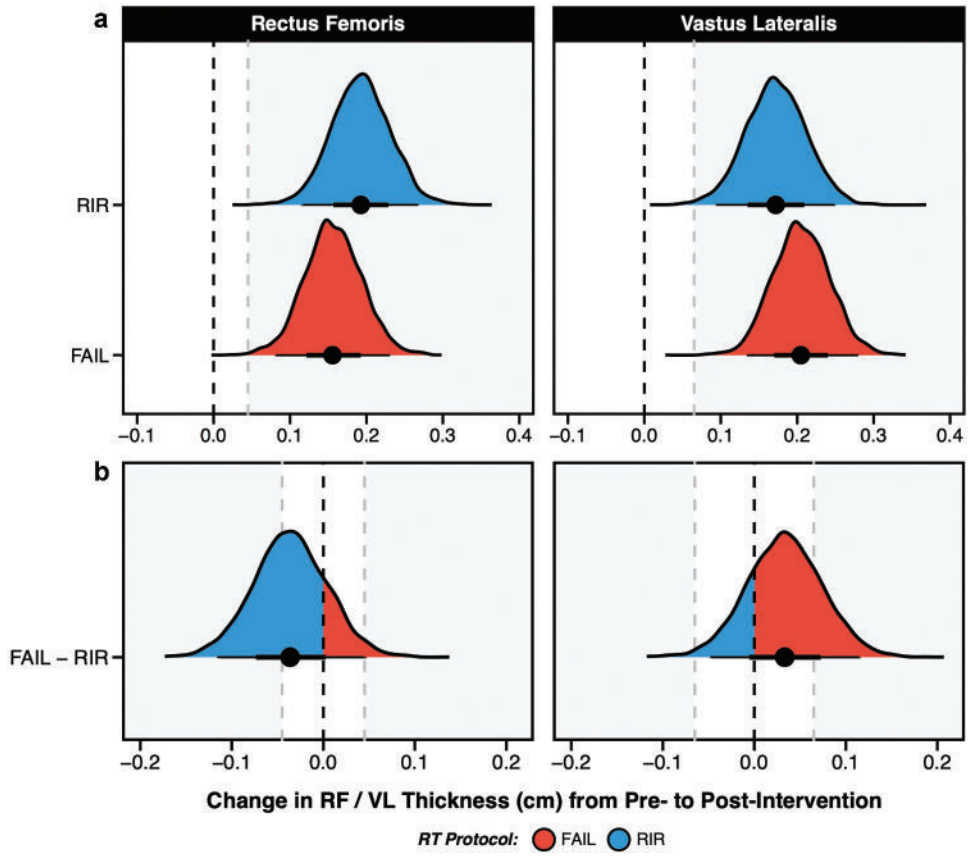

Figure 4. Posterior distributions of rectus femoris and vastus lateralis thickness for FAIL and RIR (a) along with between-protocol differences (b). Displayed are the posterior distributions for FAIL and RIR, along with the central tendency (i.e., point estimate = mean) and highest density credible intervals. Grey dotted lines indicate the typical error of the measurement, with the shaded grey area representing the proportion of the change in rectus femoris or vastus lateralis thickness above the typical error.

Table 5. Estimates of between-protocol differences (i.e., contrast between FAIL and RIR). Negative estimate values favour RIR, and positive estimate values favour FAIL. Probability that a certain estimate exceeded the typical error is only relevant for change in muscle thickness. *pd, probability of direction; TE, typical error.*

Outcome Measure	Estimate (Between-Protocol)	HDI	*pd*	*pd > TE*
Change in Muscle Thickness from Pre- to Post-Intervention				
Quadriceps Thickness	−0.001 cm	−0.063 to 0.058	48%	3%
Rectus Femoris	−0.036 cm	−0.113 to 0.047	81%	42%
Vastus Lateralis	0.033 cm	−0.046 to 0.116	79%	22%
Change in Lifting Velocity from the First to Final Set				
Week 1	−5.5%	−10.7% to − 0.2%	98%	
Week 4	−6.8%	−12.4% to 1%	99%	
Week 8	−3.2%	−9.2% to 3.1%	85%	
Change in Repetitions Performed from the First to Final Set (Slope Estimates)				
Leg Press	0.3%	−0.2% to 0.8%	86%	
Leg Extension	0.1%	−0.4% to 0.5%	66%	
Volume Load (Slope Estimates)				
Leg Press	−0.83 kg	−1.67 to 0.07	97%	
Leg Extension	−0.11 kg	−0.78 to 0.55	63%	
Repetition Volume (Slope Estimates)				
Leg Press	0 repetitions	−0.17 to 0.19	49%	
Leg Extension	0.13 repetitions	−0.02 to 0.29	95%	

close proximities-to-failure, rather than reaching momentary muscular failure *per se*, are key stimulators of muscle hypertrophy in resistance-trained individuals.

Despite similar quadriceps hypertrophy observed between protocols, slightly greater VL hypertrophy occurred in FAIL versus RIR while slightly greater RF hypertrophy occurred in RIR versus FAIL (Figure 4). Similarly, Andersen et al (Andersen et al., 2021). observed that RT performed to a high velocity loss (~40%) promoted slightly greater VL versus RF hypertrophy, and a moderate velocity loss (~20%) promoted slightly greater RF versus VL hypertrophy, but no between-group differences were found. Considering that the leg press was performed before the

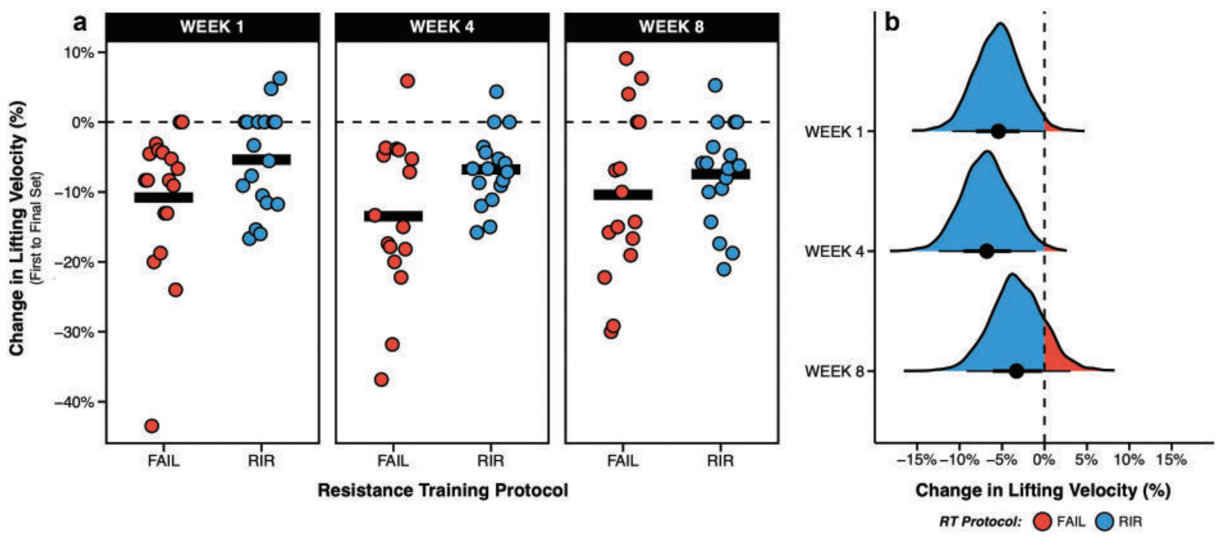

Figure 5. Change in lifting velocity (percentage) on the leg press from the first to final set for FAIL and RIR in weeks one, four, and eight (a) and posterior distributions of between-protocol differences (b). Percentage change in lifting velocity calculated as: first set lifting velocity − final set lifting velocity/first set lifting velocity. Data shown in figure a are raw values presented as both protocol means (with individual values), and the *SD* of protocol means can be found in supplementary table S3.4. Figure B displays the posterior distributions for FAIL and RIR, along with the central tendency (i.e., point estimate = mean) and highest density credible intervals.

leg extension in the present study and by Andersen et al (Andersen et al., 2021), it is possible that performing RT to, or very close to momentary muscular failure on the leg press maximised hypertrophy of the VL, but when the leg extension was subsequently performed in a fatigued state, hypertrophy of the RF was impaired. Conversely, performing RT further from momentary muscular failure on the leg press may have compromised hypertrophy of the VL but allowed for greater hypertrophy of the RF from the leg extension. Indeed, previous research has found that the RF is highly activated and subsequently hypertrophied from the leg extension compared to other quadricep exercises (e.g., squat and leg press) that involve simultaneous hip and knee flexion (Ema et al., 2016; Zabaleta-Korta et al., 2021). The findings of the present study thus highlight that it is possible for muscle-specific hypertrophy to be influenced by the proximity-to-failure reached in given exercises, their order within a RT session, and the subsequent musculature targeted.

Although proximity-to-failure is a key RT variable that influences muscle hypertrophy, other variables like total volume and load also need to be considered in RT prescription. The set volume for each participant was equal to what they habitually performed in their previous training (Scarpelli et al., 2022) and was increased by 20% halfway through the RT intervention. Our results are therefore based on performing 10 to 17 sets for a given muscle group per week, indicating the relationship between proximity-to-failure and muscle hypertrophy may be stable across this range of set volumes, on average. This is an informative finding given set volumes employed in practice likely vary widely across individuals. Additionally, although a wide range of relative loads may induce muscle hypertrophy (Refalo et al., 2021), we employed 8–12-RM loads to reduce perceived discomfort, neuromuscular fatigue, and muscle damage (A. S. Martorelli et al., 2021; Pareja-Blanco, Rodriguez-Rosell, et al., 2020; Pareja-Blanco et al., 2019; Rodriguez-Rosell et al., 2018), and improve individual RIR accuracy (Zourdos et al., 2021). Whether similar muscle hypertrophy would be observed between FAIL and RIR if lower loads (>15-RM) were employed is unclear, as performing RT with closer proximities-to-failure may be more important for simulating muscle hypertrophy when lower versus higher loads are lifted (Lasevicius et al., 2019). Overall, the set volumes and loads we employed represent a practically-relevant RT intervention for resistance-trained individuals.

4.2. Neuromuscular fatigue

We observed greater decreases in lifting velocity from the first to final set for FAIL versus RIR in weeks one, four, and eight, indicating acute neuromuscular fatigue is higher when terminating sets at momentary muscular failure versus 1- to 2-RIR. For example, FAIL experienced decreases in lifting velocity on the leg press that ranged from −9.6% to −12.6%, with lower decreases in lifting velocity in RIR from −4.4% to −6.4%. Similarly, greater repetition loss from the first to final set (when averaged across all sessions of the RT intervention) was observed for FAIL versus RIR on the leg press (−20.4% versus −15.8%) and leg extension (−29.9% versus −21.4%). Indeed, greater repetition loss for FAIL versus RIR was sustained on both exercises across the RT intervention, with repetition loss gradually increasing for both RT protocols on the leg press but decreasing on the leg extension (Figure 6). These findings corroborate previous research (Refalo, Helms, et al., 2023; J. G. Vieira et al., 2021) showing that proximity-to-failure influences acute neuromuscular fatigue, with FAIL experiencing greater decreases in lifting velocity and repetitions performed across sets compared to RIR. To our knowledge, this is the first study to assess neuromuscular fatigue longitudinally between RT protocols differing in proximity-to-failure.

Similar to the findings of the present study, we previously examined the influence of specific proximities-to-failure on neuromuscular fatigue by employing an RIR-

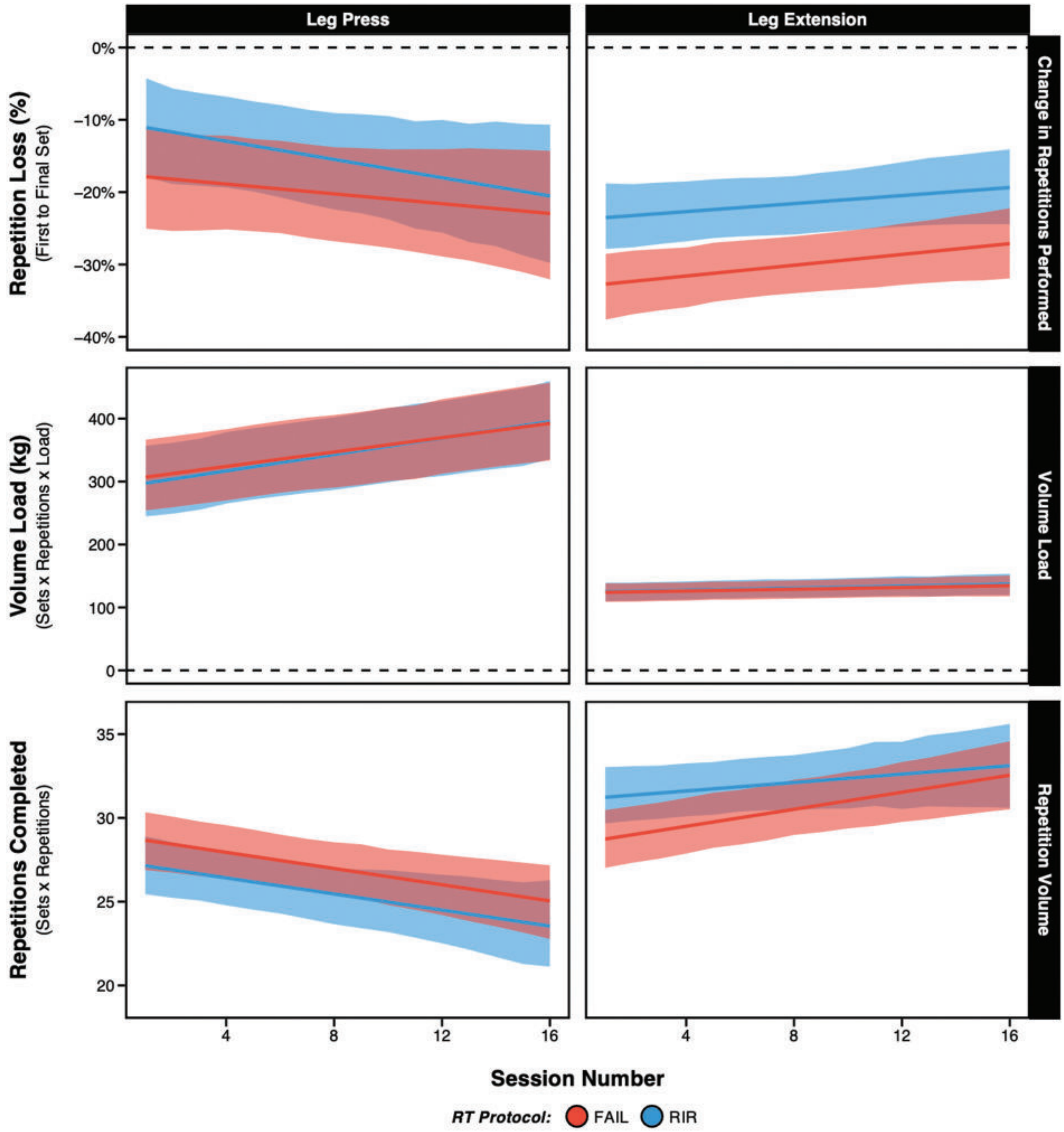

Figure 6. Predicted longitudinal trends for change in repetitions performed, volume load, and repetition volume on each exercise for FAIL and RIR across all sessions. Displayed are the predicted longitudinal trends (i.e., means marginalised across categorical variables) for each outcome measure analysed (i.e., indicated by the lines) and the highest density credible intervals (i.e., shaded area).

based approach to set termination and found greater decreases in lifting velocity when momentary muscular failure was reached versus a perceived 1-RIR and 3-RIR (Refalo, Helms, et al., 2023). Like much of the relevant literature, our previous study (Refalo, Helms, et al., 2023) was conducted acutely; this is relevant as the effect of proximity-to-failure on neuromuscular fatigue may be attenuated with repeated bouts of RT (Goodall et al., 2017). As such, the present study examined surrogate measures of acute neuromuscular fatigue across the whole RT intervention. Although the loss of lifting velocity on the leg press was consistently greater for FAIL versus RIR, the difference between protocols was smaller in week eight (−3.2%; *pd* = 85%) compared to week four (−6.8%; *pd* = 99%) and week one (−5.5%; *pd* = 98%). Similarly, we observed larger differences in repetition loss on the leg press between FAIL and RIR in the earlier stages of the RT intervention versus the latter (FAIL > RIR); repetition loss increased further for RIR overtime versus FAIL, suggesting that changes in intra-set fatigability or tolerance to the training stimulus (i.e., fatigue resistance) across the intervention differed between protocols. Conversely, although repetition loss for the leg extension was consistently greater across the RT intervention for FAIL versus RIR, both FAIL and RIR experienced less repetition loss as the RT intervention persisted, providing evidence for improved fatigue resistance overtime. Indeed, the lower acute neuromuscular fatigue experienced by RIR (versus FAIL) on the leg press may have been inadequate to promote fatigue resistance, but allowed for fatigue resistance on the leg extension, which was performed in a fatigued state. Overall, our primary findings highlight that i) acute neuromuscular fatigue is consistently greater over eight weeks when momentary muscular failure is reached versus when sets are terminated at 1- to 2-RIR, and ii) acute neuromuscular fatigue can decrease across weeks of a RT intervention but this may depend on the exercises performed and the RT stimulus.

4.3. Volume load and repetition volume

Repetition volume and volume load were deliberately not equalised to determine the potential influence of proximity-to-failure on volume accumulation. Nonetheless, we observed similar mean volume load and repetition volume for FAIL and RIR on both exercises with similar trends across the RT intervention (Figure 6). Although reaching momentary muscular failure theoretically maximises the RT stimulus experienced in a given set, the increased neuromuscular fatigue and muscle damage compared to non-failure RT (Refalo, Helms, Hamilton, et al., 2022) may reduce the volume completed across subsequent sets, and ultimately, the total RT stimulus experienced. Therefore, it is possible that the similar quadriceps hypertrophy observed between FAIL and RIR may be explained by the similar RT volumes achieved (Baz-Valle et al., 2022; Schoenfeld et al., 2017), rather than differences in proximity-to-failure *per se*. Further, although we found similar repetition volume on both exercises, it is possible that repetition volume may depend on exercise order, particularly if more than two exercises for the same muscle group are performed consecutively; for example, performing sets to momentary muscular failure may maximise repetition volume in earlier exercises of a RT session, but compromise it in subsequent exercises. Considering that RT to momentary muscular failure results in similar volume load and repetition volume as a perceived 1- to 2-RIR, possibly influencing the overall RT stimulus achieved, the potential interaction between proximity-to-failure and other RT variables needs to be considered in RT prescription for muscle hypertrophy.

4.4. Strengths and limitations of current research

Our sample of participants had the highest reported RT experience (7.8 ± 2.6 and 7.5 ± 2.3 years for males and females, respectively) of any study comparing RT to set failure versus non-failure or to different velocity loss thresholds (Andersen et al., 2021; Karsten et al., 2021; Pareja-Blanco et al., 2017; Pareja-Blanco, Alcazar, Cornejo-Daza, et al., 2020; Pareja-Blanco, Alcazar, SA-V, et al., 2020; Rissanen et al., 2022; Rodiles-Guerrero et al., 2022; Santanielo et al., 2020). This included an average RT frequency of 4.72 days per week, and 50% of participants having competed in strength and/or physique sports. Although muscle hypertrophy following RT is likely similar between sexes (Roberts et al., 2020), measures of neuromuscular fatigue and volume accumulation may differ (Refalo, Helms, et al., 2023). Thus, our statistical models included "sex" as a population-level effect; however, we didn't specifically analyse sex differences as this was not a research question. To limit the potential influence of our unilateral design on the outcomes, we altered the starting limb of each session (i.e., the full RT protocol was completed on one limb, before the second RT protocol was completed on the following limb). This approach provided each limb an equal number of starting opportunities, as performance of the following limb may be impaired due to neuromuscular fatigue. Moreover, the change in lifting velocity was only measured on the starting limb to ensure standardised comparisons between RT protocols. Considering limb dominance may influence RT performance, we ensured an equal number of dominant limbs were assigned to each RT protocol. Our statistical models also accounted for dependency between observations (i.e., correlations between limbs), whereby observations for each limb were nested within each participant. Considering each participant's set volume varied and increased (by 20%) halfway through the intervention, we included "number of sets performed" as a population-level effect in the relevant statistical models. Although RIR accuracy throughout the RT intervention is unclear, the results of our initial RIR accuracy assessment (Table 3) provide confidence that set termination regularly occurred close to the target 1- and 2-RIR. Finally, whether our results can be generalised to other exercises and/or muscle groups is unclear as it is possible that muscles may respond differentially. Our ultrasound scans only involved one measurement site on the RF and VL, respectively, and as such, we are also unable to discern regional changes in muscle thickness.

4.5. Practical application of key findings

We designed an ecologically valid RT intervention that allowed for the assessment of multiple outcome measures over eight weeks that may inform the practical application of RT (Figure 7). Although we compared RT to momentary muscular failure versus with RIR, in practice one may choose to perform RT to various proximities-to-failure, including to momentary muscular failure. As such, a practical question of key importance is: *"How can proximity-to-failure maximise the RT stimulus (for a given muscle) across a whole session?"* To answer this question, RT variables (e.g., volume, load lifted, exercise order) other than proximity-to-failure that contribute to the RT stimulus, along with individual characteristics (e.g., fatigability), also need to be considered in RT prescription. For example, to limit neuromuscular fatigue that may compromise the volume achieved on subsequent sets and exercises, and ultimately, the RT stimulus imposed on the target musculature, sets may be terminated closer to, or at momentary muscular failure when i) performing subsequent exercises within a RT session or on the last set of an exercise or muscle group, ii) longer rest periods in-between sets are employed, iii) lower intra-session set volumes are completed, and iv) individual fatigability is low. Further, similar overall muscle hypertrophy between FAIL and RIR allows for individualised RT prescription options. For example: i) the

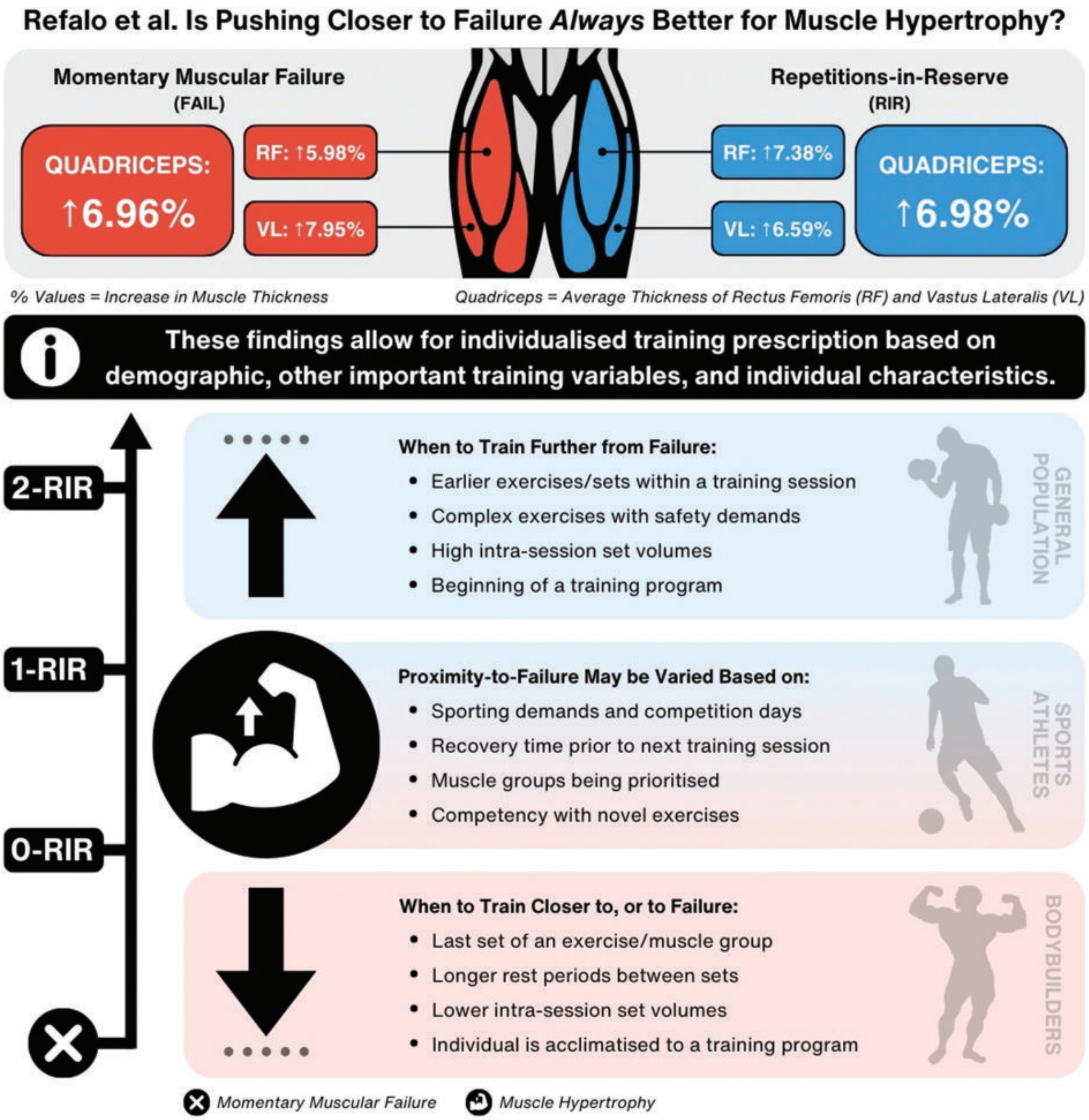

Figure 7. Graphical overview of key findings and practical applications. Resistance training variables (e.g., volume, load lifted, exercise order) other than proximity-to-failure that contribute to the resistance training stimulus, along with individual characteristics (e.g., fatigability), also need to be considered in resistance training prescription. Rather than being strict instructions, the demographic recommendations shown (via the silhouettes) are examples of how the target proximity-to-failure during resistance training may vary across individuals.

general population may choose to perform RT further from momentary muscular failure to limit negative perceptual responses (Refalo, Helms, et al., 2023), ii) athletes may choose to vary RIR based on the demands of their sport to maintain performance by limiting neuromuscular fatigue whilst stimulating muscle hypertrophy, and iii) bodybuilders and/or individuals looking to maximise muscle hypertrophy may choose to prioritise set termination close to, or at momentary muscular failure. Our findings also highlight that repeated exposure to the same RT stimulus may generate less acute neuromuscular fatigue overtime, as such, RT may be performed closer to, or to momentary muscular failure as an individual becomes more acclimatised to a given RT program. Further, whether an RIR prescription should be used to control set termination depends on individual RIR accuracy; based on our findings, if an individual is able to predict RIR within one repetition of the target, prescribing set termination between 0- to 2-RIR may be an effective approach to promote muscle hypertrophy.

5. Conclusion

Overall, we observed that terminating sets with a perceived 1- to 2-RIR can be sufficient to promote similar hypertrophy of the quadriceps as reaching momentary muscular failure in resistance-trained individuals over eight weeks. Our findings also highlight that muscle-specific hypertrophy may depend on exercise selection, exercise order, and subsequent musculature targeted. Importantly, our sample of participants were able to predict RIR within one repetition from the target RIR, and whether higher or lower RIR accuracy would influence our results is unclear. Performing RT with 1- to 2-RIR also allows for similar volume load and repetition volume accumulation as reaching momentary muscular failure, possibly influencing the overall RT stimulus achieved. Indeed, repetition loss from the first to the final set was greater when sets were terminated at momentary muscular failure versus with 1- to 2-RIR, likely contributing to the similar volume observed between protocols. Although performing RT to momentary muscular failure consistently induced higher levels of acute neuromuscular fatigue versus RT performed with 1- to 2-RIR, we observed improved fatigue resistance that may attenuate acute neuromuscular fatigue and subsequent repetition loss across eight weeks (but may depend on the exercise performed). To our knowledge, the present study is the first to compare RT performed to momentary muscular failure versus with 1- to 2-RIR (using RIR prescription) on muscle hypertrophy and neuromuscular fatigue over an 8-week intervention period in resistance-trained males and females, further advancing the understanding of proximity-to-failure and providing practical recommendations that can be applied across different demographics (i.e., general population, sports athletes, bodybuilders).

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Disclosure statement

Lee Hamilton and Jackson Fyfe declare that they have no conflicts of interest or competing interests. Martin Refalo, Eric Helms, and Zac Robinson are all coaches and writers in the fitness industry. No known companies will benefit from the results of the present study.

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Ethics approval

The study procedures were approved by the Deakin University Human Research Ethics Committee (reference number: 2022–329). All participants read and signed a plain language statement.

Consent for publication

All participants provided consent for their data to be published.

Availability of data and material

All data and code utilised will be openly available on Open Science Framework: https://osf.io/34d92/

Author contributions

Article conceptualisation: MCR, JJF, ERH, DLH; data collection: MCR; drafted manuscript: MCR and JJF; statistical analysis: MCR and ZPR; critically revised manuscript: all authors. All authors read and approved the final manuscript.

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