Studies of Twin Responses to Understand Exercise Therapy (STRUETH): Body Composition

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ABSTRACT

THOMAS, H. J., C. E. MARSH, B. A. MASLEN, K. J. SCURRAH, L. H. NAYLOR, and D. J. GREEN. Studies of Twin Responses to Understand Exercise Therapy (STRUETH): Body Composition. *Med. Sci. Sports Exerc.*, Vol. 53, No. 1, pp. 58–67, 2021. **Purpose:** We studied individual variability in exercise responses in twins. We hypothesized that 1) endurance (END) training would reduce fat mass whereas resistance (RES) training would increase lean mass, 2) individuals who did not respond to one modality would respond to the other, and 3) cross-sectional heritability estimates would be higher than estimates based on training responses. **Methods:** DXA was undertaken in 84 same-sex untrained twins (30 monozygotic [MZ], 12 dizygotic [DZ]). Participants underwent 3 months of END and RES training, separated by 3 months washout. Twins trained in pairs. **Results:** RES ($P < 0.001$) and END ($P = 0.002$) increased lean mass, with a greater change in RES ($P < 0.001$). Similarly, RES ($P = 0.04$) and END ($P = 0.006$) decreased fat mass. Eighty-four percent of subjects responded positively to RES for lean mass and 58% to END ($P < 0.001$). For fat mass, RES and END induced 56% and 66% responder rates, respectively ($P = 0.28$). Cross-sectional intraclass correlations, used to assess the similarity in twin responses, were higher for MZ than DZ pairs for all variables. Following training, only MZ pairs were significantly correlated ($P < 0.001$) for change in lean mass to RES. **Conclusion:** To our knowledge, this study is the first to report individual responsiveness in body composition to both RES and END in the same subjects. Although RES and END induced favorable changes in fat mass, RES was superior for lean mass. The frequency of lean mass responders to RES exceeded that for END, whereas response rates for fat mass were similar. Cross-sectional heritability estimates were higher than training response estimates, and shared environment had the largest influence on changes in body composition. This study suggests that exercise professionals should consider modality and environmental factors when optimizing exercise interventions. **Key Words:** HERITABILITY, GENETICS, DUAL-ENERGY X-RAY ABSORPTIOMETRY, ENDURANCE TRAINING, RESISTANCE TRAINING

Obesity is associated with increased risk of several chronic diseases, including type 2 diabetes, hypertension, and cardiovascular disease (1). Age-related decline in skeletal muscle mass is an independent risk factor for adverse outcomes, including difficulties in carrying out tasks of daily living, falls, fractures, hospitalization, and death (2). Regular exercise can decrease obesity and increase skeletal muscle mass (3), with these advantageous but countervailing effects on body composition resulting in modest decreases in body weight and body mass index (BMI) (4,5). Defining optimal strategies for facilitating favorable changes in body composition remains a major public health challenge (6). Although some guidelines advise individuals to focus on resistance (RES)-based exercise to combat declines in muscle mass (3), others favor endurance (END)-based exercise to reduce total fat mass and visceral adiposity (6). However, the relative effects of RES and END training on fat and lean body mass have not been well characterized in humans. This is particularly important given that standardized exercise interventions can confer different levels of response between individuals (7–9). Although characterizing the proportion of high and low responders to specific training modalities would provide information relevant to individualizing desired health outcomes, the high versus low response rates of individuals to RES and END training in terms of body composition have not previously been experimentally addressed. An associated issue, relevant to optimizing and individualizing exercise prescription, is whether nonresponders

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to one mode of exercise are necessarily nonresponders to alternative forms of training.

Another important question is whether changes in body composition with exercise training are dictated by heredity, that is, whether individuals are genetically predisposed to respond. Comparing monozygotic (MZ) and dizygotic (DZ) twins provides an opportunity to estimate genetic and environmental contributions to variation in phenotypic traits (10). In relation to body composition, there is a lack of research employing twin studies that have used dual-energy x-ray absorptiometry (DXA), the "gold-standard" for quantification of lean and fat mass (11). Heritability estimates based on subcutaneous (skinfold) fat distribution (1) and BMI (12) have ranged from ~30% to ~85%, but these are not ideal measures of body composition. The few studies that have used DXA have estimated heritability based on cross-sectional (CX) comparisons of twins (11,13). These may not accurately represent the genetic contribution to exercise training. The current study used a classic twin paradigm, combined with a randomized crossover design of two exercise modalities commonly used in the fitness industry that we prescribed at levels consistent with physical activity guidelines (14–16).

We aimed to investigate 1) whether RES or END training have a greater effect on measures of body composition within individuals, 2) whether the responder rate for change in body composition differs according to exercise modality, and 3) what the contribution of genetic versus environmental factors is to variation in body composition response to RES and END. We hypothesized that 1) END would result in a greater reduction in total fat mass and visceral adipose tissue (VAT), whereas RES would result in a larger increase in total lean mass; 2) individuals who did not respond positively to one form of training would respond to the alternate mode of training; and 3) CX estimates of genetic and environmental effects derived from the intraclass correlation coefficient (ICC) between twin pairs would be higher than those associated with responses to training.

METHODS

Full details of the study design and experimental procedures can be found in our protocol paper (17) and in the study registration (ACTRN12616001095459), which was published before recruitment and randomization. A summary is provided below.

Participants

Eighty-four healthy same-sex twins (n = 42 pairs; 30 MZ and 12 DZ; mean ± SD, 24.9 ± 5.4 yr old) were recruited to participate in the study (see Figure, Supplementary Digital Content 1, consort diagram, http://links.lww.com/MSS/C61). After recruitment and initial CX testing, 31 of these pairs (n = 62; 42 MZ and 20 DZ) completed the training intervention. In six participants (two pairs MZ males and one pair MZ females), VAT results were not included due to being younger than 18 yr. Recruitment was facilitated by Twins Research Australia (formerly the Australian Twin Registry [18]), whereby twin pairs in metropolitan Perth were sent e-mails, newsletters, and mail regarding participation in the study. Other recruitment strategies included advertising in Perth-based newspapers, online and via social media, university e-mail lists, and word-of-mouth referral. Inclusion criteria were healthy, relatively unfit individuals who did not meet Australian guidelines for physical activity recommendations (<150 $\text{min}\cdot\text{wk}^{-1}$), nonsmokers, and medication-free individuals. This study was approved by the University of Western Australia Human Research Ethics Committee (reference number RA/4/7031). Oral and written consent was obtained from all subjects before participation in the study, which conformed to the Declaration of Helsinki. Baseline demographic data are displayed in Table 1. A DNA test was administered to determine the zygosity of each twin pair (EasyDNA AU, Springwood, QLD) at study entry.

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Study Design

All participants underwent baseline testing of outcome measures, including body composition measures, physical activity monitoring, and a food diary. Following this, twins were randomized, together as a pair, to commence with either the 3-month RES or the 3-month END training intervention (see Figure, Supplementary Digital Content 2, study design, http://links.lww.com/MSS/C62). Participants then underwent a 3-month washout period, during which they were instructed to return to their usual activities and diet. Participants then crossed over to complete 3 months of their second, alternate, exercise intervention (RES or END). Twins within a pair trained together at matched relative intensities for each exercise modality and completed their exercise interventions in the same period. Participants were instructed to maintain their

TABLE 1. Baseline characteristics of participants enrolled in the study.

	Monozygotic (MZ)	Dizygotic (DZ)	*P*
	n = 60 (30 pairs; 17 F, 13 M)	n = 24 (12 pairs; 8 F, 4 M)	
Age (yr)	26 (6)	24 (5)	0.07
Height (cm)	174 (7.1)	172 (8)	0.29
Weight (kg)	74 (17.9)	63 (11)	0.01
BMI ($\text{kg}\cdot\text{m}^{-2}$)	24 (5)	21 (3)	0.01
Daily caloric intake (kJ)	8929 (2445)	8323 (2372)	0.22
TEE (kJ)	8015 (1885)	7001 (1477)	0.62
AEE (kJ)	3237 (1256)	2965 (1107)	0.16
Lean mass (g)			
Total	48,554 (10,146)	43,671 (9025)	0.11
Arms	5551 (1818)	4713 (1590)	0.13
Legs	17,395 (3,783)	15,498 (3167)	0.08
Trunk	22,354 (4,456)	20,389 (4269)	0.17
Android	3,244 (667)	2954 (558)	0.13
Gynoid	7,727 (1,639)	6999 (1375)	0.12
Fat mass (g)			
Total	21,269 (8,189)	16,521 (7123)	0.03
Arms	2,250 (775)	1804 (781)	0.04
Legs	7,863 (2617)	6942 (3,014)	0.31
Trunk	10,279 (5101)	6953 (3763)	0.01
Android	1569 (958)	965 (626)	0.01
Gynoid	3915 (1457)	3305 (1558)	0.20
VAT	482 (496)	150 (179)	<0.001

Data are presented as mean (SD).

usual activity levels and diet, as well as refrain from the use of medications or supplement use throughout the study.

Exercise Interventions

The two exercise interventions (RES and END) consisted of 3 × 1 h sessions per week for 12 wk. The programs included progressive overload and consisted of specified training phases. END used 2× running and 1× cycling session per week progressing from 60% to 90% $\dot{V}O_{2max}$, and RES alternated between upper and lower body each session progressing from 60% to 90% one-repetition maximum. Attendance to training sessions was 94% for RES and 95% for END. Detailed explanation of the exercise interventions is provided in our protocol paper (17).

Primary Outcome Measures

Body composition was measured in the supine position using DXA (Lunar iDXA, GE Healthcare Madison, WI). Standard calibration and quality assurance procedures were used (www.gehealthcare.com). Indices of body composition derived from iDXA analysis included fat mass (total, arms, trunk, legs, android, gynoid, and VAT) and lean mass (total, arms, trunk, legs, android, and gynoid). VAT is not reported for individuals younger than 18 yr ($n = 6$). Participants arrived at the laboratory at the same time of day for each of the four measurements (before and after each exercise intervention) and were instructed to fast for 3 h before their scan and maintain normal hydration. iDXA outcomes are highly reproducible (ICC > 0.99) (12).

Secondary Outcome Measures

Physical activity monitor. A physical activity monitor (Actiheart 4; CamNtech Ltd., Cambridge, UK) was used to measure total (TEE) and active (AEE) energy expenditure the week before or immediately after each exercise intervention to quantify incidental changes in physical activity levels. Participants wore the monitor for a 5-d period, removing it for showering and during sleep. The Actiheart was placed on the participant with two ECG electrodes (40 × 34 mm; AgCl, Red Dot 2560, 3 M) either above or below the nipple line with the medial electrode placed in the center of the chest (usually on the sternum) and the lateral electrode placed horizontally to the left side with the wire straight but not taut. A signal test was performed to determine the best positioning of the electrodes for each participant. Electrode positioning was noted and repeated at subsequent time points.

Food diary. A food diary was given to each participant to complete the week before, or immediately after, each exercise intervention. Participants were instructed to complete the diary on four consecutive days, including one weekend day. Participants were required to record the type, brand, cooking method, portion size, and timing of ingested food and beverage in detail, to assess whether eating habits had remained constant throughout the study. Mean total daily energy intake was determined from these records using a commercially available software program (Foodworks 9; Xyris Software, Queensland, Australia).

Statistical Analysis

Statistical analyses were performed with SPSS 20.0 (IBM Australia Ltd., New South Wales, Australia) and STATA 11 software (StataCorp, College Station, TX). CX results for each outcome measure refer to baseline entry (week 0) data. Differences in means of CX measurements (Table 1) and responses to the exercise interventions (Fig. 1; for more details on body segments, see Table and Figures, Supplementary Digital Content 3, Changes in body composition, physical activity and caloric intake, http://links.lww.com/MSS/C63; Supplementary Digital Content 4, Changes in arm, leg and trunk lean masses, http://links.lww.com/MSS/C64; and Supplementary Digital Content 5, Changes in arm, leg and trunk fat masses, http://links.lww.com/MSS/C65) between MZ and DZ pairs were assessed for each outcome measure using a linear mixed model, which adjusted for twin correlation and covariates of age and sex. Carryover and order effects were also assessed using linear mixed models adjusting for twin correlations. A z-test was used to assess the differences between percentages of responders for exercise interventions (RES vs END) for each variable. A responder was defined as any positive response in an outcome variable, whereas a nonresponder was defined as a negative response in an outcome variable.

The classic twin model and analysis is based on the fact that MZ twins theoretically share 100% of their DNA whereas DZ twins only share 50%. A phenotype that is purely explained by genetics would hold a ratio of 2:1, with correlations of 1 for MZ and 0.5 for DZ (19). If the 2:1 ratio remains the same, but the correlations are lower than 1.0 and 0.5, then both shared and unshared components may be influencing results. This modeling approach has advantages over other heritability estimation methods as extensive variance information (i.e., difference between twins) and covariance information (i.e., common characteristics between twins) are deduced (20). From this, we can determine what proportion of the variation is due to genes (A, additive genetic effects) and environment. The environmental proportion can be broken down into shared (C, common shared environmental effects) or unique (E, individual unshared environmental effects) to twin pairs. A crucial assumption of this model is that C is equal for MZ and DZ pairs; that is, MZ and DZ pairs share their environments to the same extent on average (the "equal environments" assumptions [21]). All components represent unmeasured effects, after adjustment for all relevant measured covariates. In STATA, mixed-effects models were used to calculate ICC (r) for MZ and DZ twin pairs. The subsequent rMZ and rDZ, and their respective P values and 95% confidence intervals (CI), are presented in Table 2 (for specific body segments, see Table, Supplementary Digital Content 6, ICCs and heritability for body composition indices, http://links.lww.com/MSS/C66). Significant differences between ICC (rMZ vs rDZ) were assessed using the likelihood ratio test in STATA

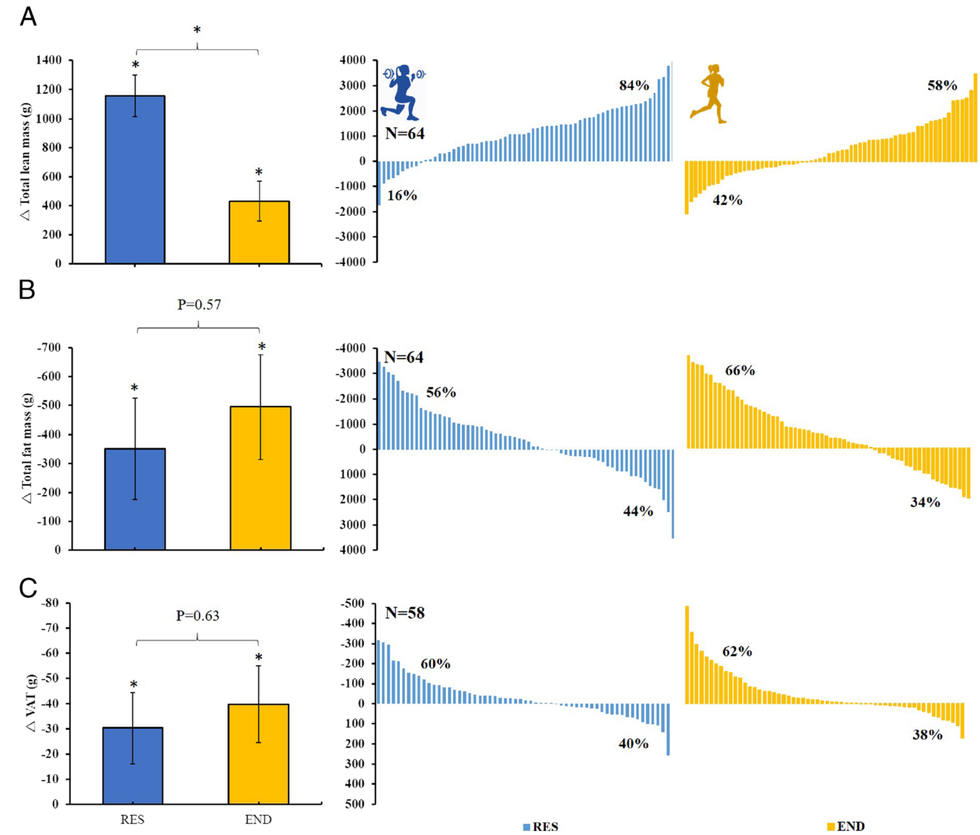

FIGURE 1—Changes (Δ) with RES (*blue*) and END (*yellow*) training for total lean mass (*top panel*, A), total fat mass (*second panel*, B), and VAT (*third panel*, C) in regard to group responses (left) and individual response to RES (middle) and END (right) training. **P* < 0.05.

to compare mixed-effects models constraining covariances for MZ and DZ pairs to be equal with models, allowing different covariances for MZ and DZ pairs (Table 2; for specific body segments, see Table, Supplementary Digital Content 6, ICCs and heritability for body composition indices, http://links.lww.com/MSS/C66) (22). If rMZ was significantly different to rDZ, then A, C, and E were calculated, and CI values for A, C, and E were estimated using the delta method. When rMZ and rDZ were not significantly different, then a single model that included all twin pairs but constrained the covariance to be equal for MZ and DZ pairs was used in STATA to calculate C and E components only and their respective 95% CI. An additional model that estimated covariance for MZ twins but fixed the DZ covariance to be zero was fitted if the estimated correlations suggested that the equal environments assumption may have been violated and rDZ was approximately 0.

RESULTS

Participant Characteristics

Zygosity-based participant demographics, indices of body composition, physical activity, and caloric intake CX data are presented in Table 1. The MZ group had greater total fat mass (P = 0.03; including arm fat mass P = 0.04, trunk fat mass P = 0.01, and android fat mass P = 0.01) and VAT (P < 0.001), resulting in greater total body weight (P = 0.01) and BMI (P = 0.01), than the DZ group, who were somewhat younger on average. Height (P = 0.29), total lean mass (P = 0.11), daily caloric intake (P = 0.22), and physical activity levels (TEE P = 0.62 and AEE P = 0.16) were not different between zygosities. Although there were some differences between the MZ and the DZ groups, responder and concordance analyses compare within individuals and heritability analysis

TABLE 2. ICC and heritability ACE contributions for MZ and DZ twins for body composition indices.

		rMZ	rDZ	*P* rMZ vs rDZ	A	C	E
Lean mass (g)							
Total	CX^{ACE}	0.95*	0.85*	0.04	0.13	0.82	0.05
	$ΔRES^{C}$	0.68*	0.29			0.68	0.32
	ΔEND	0.00	0.00				
Fat mass (g)							
Total	CX^{CE}	0.72*	0.48*	0.23		0.69	0.31
	ΔRES	0.00	0.31				
	ΔEND	0.21	0.44				
VAT	CX^{C}	0.67*	0.27			0.62	0.38
	ΔRES	0.05	0.25				
	ΔEND	0.02	0.00				

**P* < 0.05. A, additive genetic effects; C, common (shared) environmental effects; E, individual (unshared) environmental effects; ^{ACE} ACE method, normal method used when rMZ and rDZ and likelihood ratio test (*P* rMZ vs rDZ) are all significant; ^{CE} CE method, a method used to calculate C and E when rMZ and rDZ are not significantly different (using the likelihood ratio test), assumes that all correlation is due to shared environmental effects (C); ^{C} Revised model C, a new method to calculate revised rMZ when rDZ is not significant, and it only assumes correlation for MZ pairs. Note that the estimate of C from this model has a different meaning and interpretation from the estimate of C from the usual CE model. Note that variance components models were not fitted when neither rMZ nor rDZ were significantly different from 0.

within twin pairs; it was not necessary nor our intention to match twin groups.

Effect of RES and END on Body Composition: Group Means

Lean mass. Group means in response to RES and END training are shown in Figure 1 (for individual body segments, see Table and Figures, Supplementary Digital Content 3, Changes in body composition, physical activity and caloric intake, http://links.lww.com/MSS/C63; Supplementary Digital Content 4, Changes in arm, leg and trunk lean masses, http://links.lww.com/MSS/C64; and Supplementary Digital Content 5, Changes in arm, leg and trunk fat masses, http://links.lww.com/MSS/C65). In response to RES training, there was a significant increase in total lean mass (Δ 1156 ± 1132 g, $P < 0.001$), reflected by a significant increase in all body segments (all $P < 0.001$). END training also resulted in a significant increase in total lean mass (Δ 430 ± 1111 g, $P = 0.002$), driven by a significant increase in the legs and gynoid regions (both $P < 0.001$), but not the trunk ($P = 0.10$) or android ($P = 0.34$) regions. Of note, END training resulted in a significant reduction in arm lean mass (Δ −67 ± 215 g, $P = 0.01$). The magnitude of change after RES training compared with END training was significantly greater in total ($P < 0.001$), arms ($P < 0.001$), android ($P < 0.001$), and gynoid lean mass ($P = 0.003$).

Fat mass. There was a significant reduction in total fat mass in response to END training (Δ −495 ± 1464 g, $P = 0.006$), driven by a significant decrease in all regions (including arms $P = 0.003$, trunk $P = 0.009$, android $P = 0.007$, and gynoid $P = 0.003$), except leg fat mass ($P = 0.08$). RES training also elicited a significant reduction in total fat mass (Δ −351 ± 1403 g, $P = 0.04$), mainly due to changes in trunk ($P = 0.007$) and VAT regions ($P = 0.03$). The magnitude of change after END training compared with RES training in fat mass was significantly greater in arm fat mass only ($P = 0.03$). Both RES and END resulted in a statistically significant reduction in VAT (Δ −30 ± 108 g, $P = 0.03$, and Δ −40 ± 120 g, $P = 0.009$), respectively.

Physical activity and caloric intake. There were no significant changes after RES and END training in daily caloric intake ($P = 0.99$ and $P = 0.80$, respectively), AEE ($P = 0.60$ and $P = 0.22$, respectively), or TEE ($P = 0.42$ and $P = 0.24$, respectively). However, there were significant differences in the magnitude of change between RES and END training for both AEE ($P = 0.049$) and TEE ($P = 0.03$).

Responder Rate and Concordance of Response to RES and END Interventions

Individual responses to each exercise intervention are plotted in Figure 1 for total lean mass, total fat mass, and VAT (for VAT and individual body segments, see Figures, Supplementary Digital Content 7, VAT changes for twin pairs, http://links.lww.com/MSS/C67; Supplementary Digital Content 4, Changes in arm, leg and trunk lean masses, http://links.lww.com/MSS/C64; and Supplementary Digital Content 5, Changes in arm, leg and trunk fat masses, http://links.lww.com/MSS/C65). For total lean mass, simple positive response rates (>0) to RES training and END training were 84% and 58%, respectively ($P < 0.001$ for difference between modes). For total fat mass, positive response rates to RES and END training were 56% and 66%, respectively ($P = 0.28$ for difference between modes). For VAT, positive response rates to RES and END training were 60% and 62%, respectively ($P = 0.85$ for difference between modes). Only five individuals were nonresponders to both RES and END in more than one body composition outcome (total lean mass, total fat mass, and VAT), with only one subject a nonresponder to all three outcome measures.

Lean mass. Concordance graphs are displayed in Figure 2, which present each individual's response for change following both RES and END. Percentages for each quadrant, concordant (positive or negative), and discordant, for RES and END interventions, are also presented. For total lean mass responses to RES and END, positive concordance was 50%, negative concordance was 8%, and discordance was 34% and 8%. Nonresponders to RES for total lean mass (16% of individuals) had an equal chance (8:8) of responding to END, whereas nonresponders to END (42% of individuals) had an almost 4:1 (34:8) chance of responding to RES.

Fat mass. For total fat mass responses to RES and END, positive concordance (fat loss) was 39%, negative concordance was 17%, and discordance was 17% and 27%. Nonresponders to RES for total fat mass (44% of individuals) had a slightly higher than even chance 1.5:1 (27:17) of responding to END, whereas nonresponders to END (34% of individuals) had an equal chance (17:17) of responding to RES.

For VAT responses to RES and END, positive concordance was 34%, negative concordance was 12%, and discordance was 26% and 28%. Nonresponders to RES for VAT (40% of individuals) had an almost 2:1 (28:12) chance of responding to END and nonresponders to END (38% of individuals) had a similar almost 2:1 (26:12) chance of responding to RES.

Heritability of Body Composition: CX and in Response to Training

The ICC (r) and the proportions of variance calculated for A, C, and E components are presented in Table 2 and represented in Figures 3 and 4 (for VAT, see Figure, Supplementary Digital Content 7, VAT changes for twin pairs, http://links.lww.com/MSS/C67).

Comparison between twin pairs at baseline. CX rMZ and rDZ were significant for total lean mass (rMZ = 0.95, 95% CI = 0.90–0.98, $P < 0.001$; rDZ = 0.85, 95% CI = 0.63–0.95, $P < 0.001$) and total fat mass (rMZ = 0.72, 95% CI = 0.52–0.86, $P < 0.001$; rDZ = 0.48, 95% CI = 0.14–0.84, $P = 0.04$). VAT showed a significant rMZ (0.67, 95% CI = 0.44–0.84, $P < 0.001$) but not rDZ (0.27, 95% CI = 0.02–0.86, $P = 0.19$). Subsequent analysis revealed a predominant C (shared environment) contribution for total lean mass (0.82, 95% CI = 0.56–0.95), total fat mass (0.69, 95% CI = 0.53–0.85), and VAT (0.62, 95%

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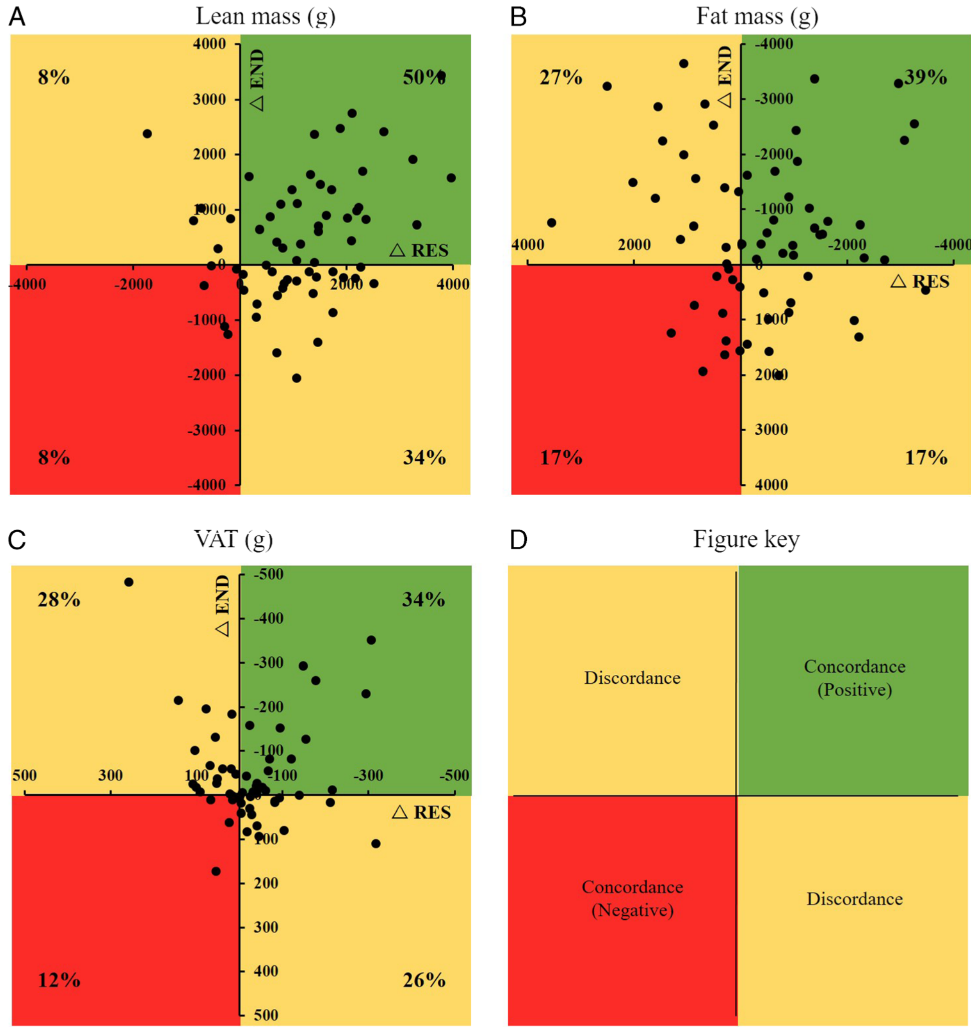

FIGURE 2—Individual subject exercise intervention change score (Δ) data plotted against one another with response to END on the *y*-axis and RES on the *x*-axis. Total lean mass is shown in panel A. Total fat mass is shown in panel B, and VAT is shown in panel C. A figure key (D) depicts concordance and discordance for response to RES and END with percentages of responders for each quadrant reported for each variable (A–C).

CI = 0.43–0.81). Results for individual body segments of lean and fat mass are presented in Table, Supplementary Digital Content 6, ICCs and heritability for body composition indices, http://links.lww.com/MSS/C66.

Comparison between the effects of training within twin pairs. For response to training, significant rMZ but not rDZ was present for total lean mass response to RES (rMZ = 0.68, 95% CI = 0.37–0.84, $P < 0.001$) with a predominant C (0.68, 95% CI = 0.48–0.90) contribution (Fig. 3). There were no significant rMZ or rDZ correlations for total lean mass response to END, total fat mass (Fig. 4), and VAT (see Figure, Supplementary Digital Content 7, VAT changes for twin pairs, http://links.lww.com/MSS/C67) response to RES or END.

Carryover and Order Effects for Total Fat and Lean Mass

The 12-wk washout period between training interventions was sufficient for all variables. There were no carryover effects present when the two baseline periods were compared (week 0 vs week 24) for any variable (see Figure, Supplementary Digital Content 8, Washout and order effects, http://links.lww.com/MSS/C68). There was no order effect for magnitude of change in total lean mass (for RES P = 0.86 or END P = 0.28 training) or total fat mass (for RES P = 0.81 or END P = 0.80 training).

DISCUSSION

This study of MZ and DZ twins used a randomized crossover design to assess changes in lean and fat mass in response to RES and END training. We found that 1) both RES and END training result in a significant increase in total lean mass and reduction in total fat mass and VAT; however, RES results in a significantly higher increase in total lean mass than END. 2) The responder rate for changes in total lean and total fat mass differs according to exercise modality. 3) CX correlations of MZ and DZ twins are higher than those seen in

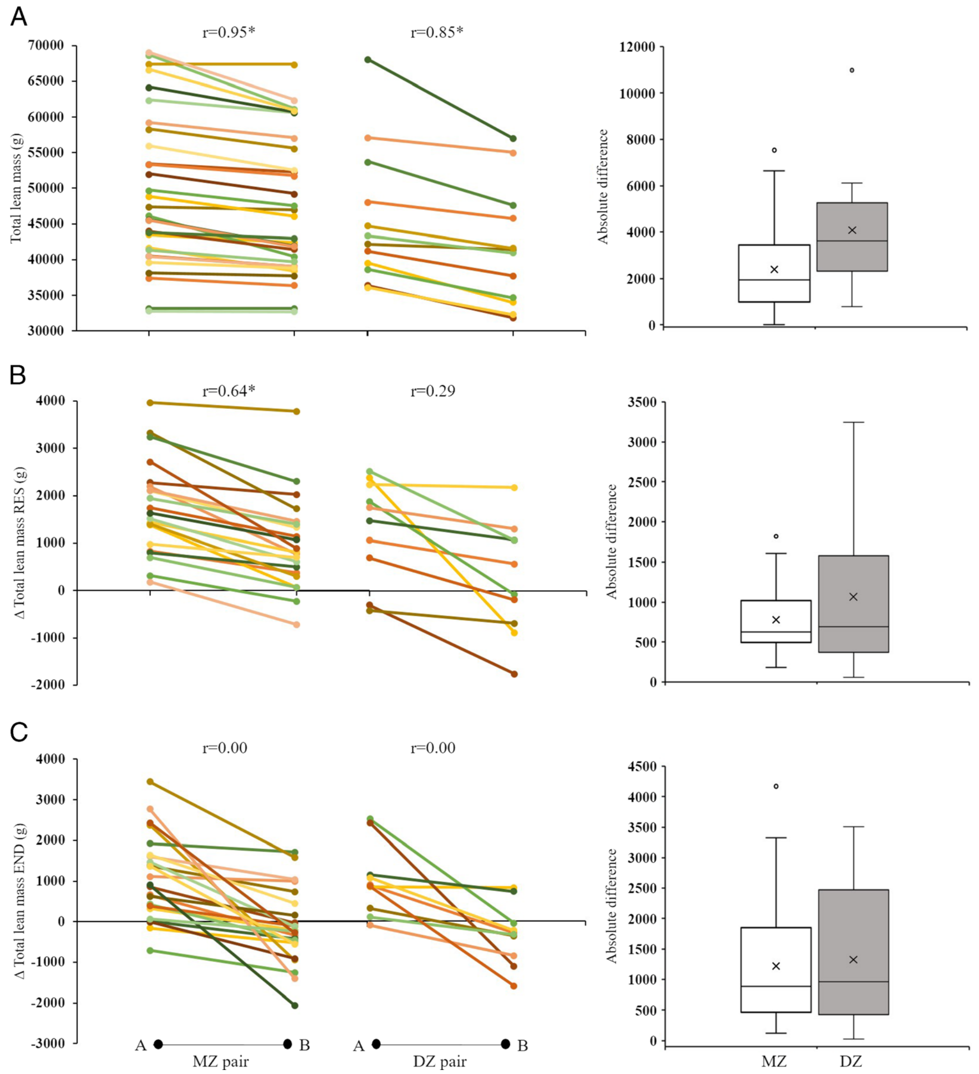

FIGURE 3—Total lean mass results displayed as CX (A) and response (Δ) to RES (B) and END (C) training. Individual results for twin A and B are represented (*left panel*) as the higher (left) and lower (right) result within a twin pair, respectively, with each individual within a pair joined by a line. The respective ICC (*r*) values for MZ and DZ twin pairs are above the paired figures. A box plot of the absolute differences for each twin pair (twin A − twin B) for MZ and DZ, respectively, is displayed (*right panel*).

response to exercise training, and similarities between twins are predominantly due to shared environmental contributions.

We chose to assess responses to RES and END training in this study as they are two modes of exercise training that are commonly recommended and are generally considered to result in distinct physiological and health-related outcomes. Typically, RES training is prescribed to elicit increases in lean mass, whereas END training, which involves higher energy expenditure, is preferred to decrease fat mass (3,6,9). We found that both RES and END training resulted in a significant increase in total lean mass; however, RES training elicited a significantly greater increase than END. When we considered regional changes in lean mass, we observed that RES stimulated significant increases in all regions (arms, legs, trunk, android, and gynoid), whereas END resulted in significant increases because of the changes localized to the legs and gynoid compartments. There were no END-mediated changes in trunk or android lean mass, and there was a significant reduction in the arms. This suggests that, whereas END training can increase total lean mass, changes are localized to the predominantly active muscle beds.

Both RES and END resulted in a decrease in total fat mass, with no difference between modalities. However, RES resulted in a significant reduction in trunk fat and VAT, whereas END resulted in decreases in fat mass in all regions (except the legs). This would suggest that END training has a greater effect on overall fat loss, where RES training is most effective in core regions. These results show that, although both modalities can be effective overall for managing fat and lean body mass, specific exercise modalities can be important for targeting regional body composition goals.

Although group means can be useful in describing the effectiveness of an exercise intervention across a group of subjects, it is important when prescribing exercise to consider training efficacy on an individual level. Recent studies, notably by Bouchard and colleagues (23), have introduced the notion that

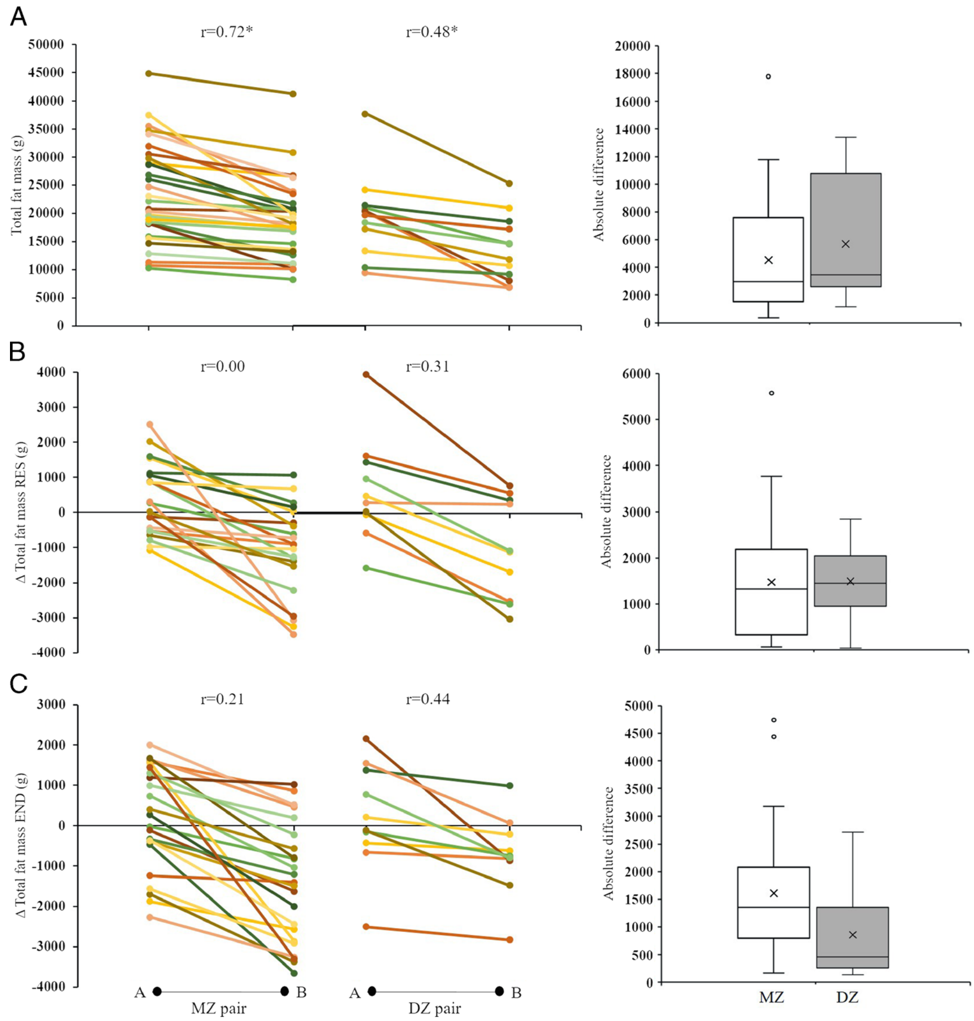

FIGURE 4—Total fat mass results displayed as CX (A) and response (Δ) to RES (B) and END (C) training. Individual results for twins A and B are represented (*left panel*) as the higher (left) and lower (right) result within a twin pair, respectively, with each individual within a pair joined by a line. The respective ICC (*r*) values for MZ and DZ twin pairs are above the paired figures. A box plot of the absolute differences for each twin pair (twin A − twin B) for MZ and DZ, respectively, is displayed (*right panel*).

individuals respond idiosyncratically to exercise interventions, even when these are adhered to and prescribed at similar levels. These studies have mostly focused on cardiorespiratory fitness outcomes (7,10,24,25), with fewer studies of RES-mediated changes (26–28). Although some investigators have proposed that increasing exercise intensity can ameliorate the low-responder phenomenon (10), others have shown that variability in response persists after exercise at different intensities (7) and that low responses can be observed in some subjects who undertake exercise at recommended guideline levels (8,29,30). Studies of responder rates to distinct modalities are rare. Hautala et al. (9) investigated the effects of both RES and END training, which showed a large individual responsiveness of $\dot{V}O_{2peak}$ to mode of training. However, this study only investigated fitness and had a relatively short, 2 wk, intervention period (9).

To our knowledge, this study is the first to investigate individual responsiveness in body composition to both RES and END. Our results (Fig. 2A) show that, despite there being an increase in total lean mass in response to both RES and END training, there is a significantly higher chance of an individual responding to RES (84%) compared with END (58%). The proportion of subjects who failed to respond to either mode was 8%. In addition, 80% of the individuals who were "nonresponders" to END were nonetheless able to respond positively and be "rescued" by adopting RES. In comparison, only 50% of the "nonresponders" to RES training were "rescued" following END training.

When considering individual responders in total fat mass (Fig. 2B), there was a similar rate of response following RES (56%) and END (66%). The proportion of subjects who failed to respond to either mode was 17%. There was a higher number of "nonresponders" to RES that could be saved by switching to END (61%) than "nonresponders" to END that could be saved by switching to RES (50%). In contrast to lean mass and fat mass, VAT had very similar response rates to both RES and END training and a similar level of rescued "nonresponders" after switching modality. The proportion of subjects who failed to respond to either mode in terms of VAT was 12%. Only one individual failed to respond to either mode for all body composition outcomes. Overall, these individual responsiveness results indicate that when prescribing an exercise intervention, it is important to understand the goals of the individual, the frequency of low responses, and the consequences of switching modality to achieve those goals.

Another factor that may be related to individual response to exercise is the question of genetic versus environmental impacts. To investigate this, we recruited both MZ and DZ twin pairs. The CX results for total lean mass and total fat mass revealed significant ICC coefficients for both MZ (0.95 and 0.72, respectively) and DZ (0.85 and 0.48, respectively) twin pairs, whereas VAT showed a significant ICC for MZ (0.67) twins only. The highest proportion of contribution to these ICC was shared environmental effects (ranging from 0.62 to 0.82), with a small contribution from both genetic effects and unshared environmental effects. There is a marked lack of studies employing twins that use DXA to characterize body composition. In addition, heritability estimates for body composition measures vary greatly in the literature. CX heritability estimates range from 30% to 85% for indicators of subcutaneous fat distribution (1), whereas heritability estimates for BMI range from 0.40 to 0.70. By contrast, studies using DXA suggest a heritability of 0.49–0.52 for lean mass (11,13), 0.48 for body fat percentage (11), and 0.76 for whole body fat mass (11). The variability seen across this literature emphasizes the importance of studies with larger sample sizes and those utilizing accurate measures of body composition such as DXA. In addition, our study highlights the importance of analyzing not just the ICC relationships between twin pairs but also the contributions of genetic, common environment, and external environment contributions, which are only possible in studies involving MZ and DZ twins.

Although this study shows high CX correlations between twins for measures of body composition, this does not necessarily suggest that the body composition responses seen with exercise will be as highly correlated. The HERITAGE family study investigated the heritability of the amount and the distribution of subcutaneous fat (skinfolds) in response to 20 wk of END training and found a low level of familial aggregation (0%–20%). The authors concluded that familial/genetic factors appeared to be greater when CX analysis of subjects was performed than when responses to END training were assessed (1). This concurs with our findings. HERITAGE was a familial study that could not distinguish between genetic and shared environmental effects, which can be achieved using twin studies (10). In addition, it relied on skinfolds, a relatively poor method of detecting changes in body composition (31). A previous pilot study by our group in different subjects to those in the present experiment (32) investigated the heritability of body composition using DXA in response to END training in MZ and DZ twins. This study suggested a moderate genetic contribution in the fat mass response to training. However, the study did not investigate the effect of RES training on the same individuals and did not DNA test their twin pairs. Results of the current study show that there is a significant ICC between MZ twins, but not DZ twins, in total lean mass response to RES training, with a predominant contribution from shared environmental effects. However, total lean mass in response to END and total fat mass and VAT in response to RES and END showed no significant ICC between MZ and DZ twins. These results suggest that, despite there being a high CX ICC, there is a low ICC for the response to an exercise stimulus in twin pairs. CX similarities are therefore not translatable to body composition adaptations to training in terms of genetic contribution to response. Furthermore, our study suggests that genetics do not play a predominant role in influencing the magnitude of an individual's body composition response, at least in response to 3 months of exercise training. Future research should assess whether the heritability of body composition is modulated by longer or more intense exercise interventions.

A limitation of the current study is the relatively low number of DZ twin pairs (n = 20, 10 pairs), which may have influenced the likelihood of rDZ being significant. When initially recruiting for the study, twin pairs self-reported their zygosity. However, DNA testing revealed that 10 pairs who initially self-reported as DZ were in fact MZ. DNA testing to determine zygosity of twin pairs was therefore a major strength of this study, which prevented us misclassifying zygosity, an integral component of all twin studies, emphasized by a systematic review which concluded that self-reported rather than DNA-tested zygosity has a significant effect on heritability results (33). Another strength of this study is that we only included same-sex twin pairs for DZ twins (no male–female pairs). This minimized any confounding sex-based influences (34). In addition, we used twin-based mixed models to determine the contributions of genetics (A), shared (C), and individual (E) environmental factors, which allowed us to determine what factors influenced ICC results. As previously stated, the use of DXA as the gold-standard technique for lean and fat mass assessment and the most sensitive method for assessing small changes in body composition (31) was also a strength of this study.

In conclusion, this is the first study to investigate changes in body composition to two distinct exercise modalities in a randomized crossover design using MZ and DZ twins. Our results indicate that differences exist between RES and END training in the magnitude of lean and fat mass changes and in individual responsiveness. Although RES and END induced favorable changes (on average) in fat mass, RES was superior for generalized gains in lean mass. The frequency of lean mass responders to RES (84%) exceeded that for END (58%), with 80% of END nonresponders capable of responding to RES but only 50% of RES nonresponders benefitting from a switch to END. Fat mass response rate was similar between RES (56%) and END (66%), with 61% of RES nonresponders capable of responding the END and 50% of END nonresponders benefitting for RES. We have shown that although "nonresponders" to training may exist (8% for lean mass, 17% for fat mass, and 12% for VAT; Fig. 2), switching to an alternate form of training may allow us to "rescue" a large proportion of those individuals. In addition, although an individual may be a nonresponder to training in one outcome (fat mass), they may be a responder in another outcome (lean mass). This finding raises the possibility of early assessment of exercise responsiveness to optimize training efficacy for individuals. Our results have also shown that CX comparisons of body composition between MZ and DZ twins produce higher heritability estimates than seen with response to both RES and END training and that shared environmental factors play the largest role in body composition adaptations. This study provides insight into body composition changes in response to different exercise modalities at an individual level and the significance of shared environmental factors over genetic contribution.

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The authors declare that they have no conflicts of interest. The results of the present study do not constitute endorsement by the American College of Sports Medicine. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

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