ORIGINAL ARTICLE

High intensity interval training (HIIT) increases insulin-like growth factor-I (IGF-I) in sedentary aging men but not masters' athletes: An observational study.

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Abstract

Introduction: The aim of this investigation was to examine the impact high intensity interval training (HIIT) on serum insulin-like growth factor-I (IGF-I) in active compared with sedentary aging men.

Methods: 22 lifetime sedentary (SED; 62 ± 2 years) and 17 masters' athletes (LEX; 60 ± 5 years) were recruited to the study. As HIIT requires preconditioning exercise in sedentary cohorts, the study required three assessment phases; enrolment (phase A), following preconditioning exercise (phase B), and post-HIIT (phase C). Serum IGF-I was determined by electrochemiluminescent immunoassay.

Results: IGF-I was higher in LEX compared to SED at baseline (P=0.007, Cohen's *d*=0.91), and phase B (P=0.083, Cohen's *d*=0.59), with only a small difference at C (P=0.291, Cohen's *d*=0.35). SED experienced a small increase in IGF-I following preconditioning from 13.1 ± 4.7 to 14.2 ± 6.0 ug·dl^{-1} (P=0.376, Cohen's *d*=0.22), followed by a larger increase post-HIIT (16.9 ± 4.4 ug·dl^{-1}), which was significantly elevated compared with baseline (P=0.002, Cohen's *d*=0.85), and post-preconditioning (P=0.005, Cohen's *d*=0.51). LEX experienced a trivial changes in IGF-I from A to B (18.2 ± 6.4 to 17.2 ± 3.7 ug·dl^{-1} [P=0.538, Cohen's *d*=0.19]), and post-HIIT (18.4 ± 4.1 ug·dl^{-1} [P=0.283, Cohen's *d*=0.31]). Small increases were achieved in fat free mass in both groups following HIIT (P<0.05, Cohen's *d*=0.32-0.45).

Conclusions: In conclusion, HIIT with preconditioning exercise abrogates the age associated difference in IGF-I in SED and induces small improvements in both SED and LEX.

Key words: Exercise, growth hormone, HIIT, IGF-I, training

INTRODUCTION

Insulin-like growth factor (IGF-I) is an endocrine and autocrine/paracrine growth factor expressed by multiple cell types. In humans, serum IGF-I peaks during adolescence and displays a gradual decline during middle-age. The reduction in circulating anabolic hormones, namely growth hormone (GH) and IGF-I, has been termed 'somatopause', and suggested as a potential mechanism for the atrophic sequelae of aging [1]. IGF-I is considered to play a central role in the age-associated compromise of both skeletal [2], and muscle [3] integrity.

Exercise plays an integral role in maintaining muscle mass and function during advanced age [4]. Furthermore, exercise can improve cardiovascular function, metabolic health, muscular function, body composition, and quality of life, in aging cohorts [5, 6, 7]. For example, Fiatarone and colleagues [8] reported significant increases in maximal strength and gait speed following eight weeks of high-intensity resistance training in nonagenarians. Favorable adaptations to endurance training in elderly populations center on cardioprotective benefits [9], whilst high intensity interval training (HIIT) is a form of exercise largely untested in aging populations despite resurgent interest younger cohorts [10, 11]. HIIT involves repeated bouts of high-intensity exercise, interspersed with recover periods, proclaimed as a time-efficient healthogenic strategy [10, 11] despite falling short of the recommended exercise volume to improve and maintain cardiovascular health [12]. However, prior to undertaking HIIT in sedentary aging cohorts, it is prudent to undertake a programme of preconditioning exercise [13].

Whilst acute exercise-induced elevations in IGF-I are consistently reported [14], the effect of exercise training on basal IGF-I is poorly understood, particularly in aging cohorts. For example, eight weeks of endurance training resulted in a 19% increase in systemic IGF-I in males aged 66 ± 2 years [15], yet Vitiello et al. [16] observed no change in IGF-I following six months of endurance training in males aged 67 ± 1 years. Furthermore, a recent

investigation reported decreased systemic IGF-1 following 12 weeks resistance exercise in older adults (74 ± 6 years), yet an increase in lean mass [17]. As such, the role of IGF-I in the adaptive process to exercise during middle and older age remains unclear.

One way to identify whether a relationship exists between basal IGF-I and exercise during advancing age is to compare masters' athletes with age matched sedentary counterparts. Similarly, subjecting a sedentary cohort to structured exercise training may establish whether basal IGF-I is influenced by an exercise intervention. A single study to date has directly compared serum IGF-I in masters' athletes with controls [18], where the authors outline a lack of difference between endurance runners, speed-power athletes compared with moderately active controls. However, comparisons between masters' athletes and sedentary aging men have not been established. Similarly, no study has examined the influence of HIIT, either with or without conditioning exercise on serum IGF-I in sedentary aging men compared with masters' athletes.

With these aspects in mind, the aims of this study were to; 1) establish whether masters' athletes and sedentary controls have different serum IGF-I concentrations, and 2) determine whether HIIT preceded by preconditioning exercise would impact basal IGF-I concentrations in aging men. We hypothesized that: 1) IGF-I would be greater in masters' athletes compared to sedentary older males, and 2) six weeks of HIIT, preceded by 6 weeks of preconditioning would increase IGF-I in sedentary aging men compared with masters' athletes.

METHODS AND MATERIALS

Participants

Following approval to exercise by their general practitioner, participants provided informed written consent prior to the study which was approved by the institutional ethics committee. Twenty two males (62 ± 2 years, with a stature of 175 ± 6 cm, body mass of 91 ±

16 kg, and peak oxygen uptake of 28 ± 6 ml·kg·min^{-1}) comprised the lifelong sedentary group (SED). Seventeen males (60 ± 5 years, with a stature of 173 ± 6 cm, body mass of 78 ± 12 kg, and peak oxygen uptake of 39 ± 6 ml·kg·min^{-1}) were enrolled as lifelong exercisers (LEX) and acted as a positive control group. Participants recruited for the SED group did not participate in organized exercise programmes and had not done so for >30 years. The LEX group were highly active exercisers and had been so for the previous >30 years. They consisted of current masters' athletes in sports including water-polo, triathlon, track cycling, road cycling, and distance running.

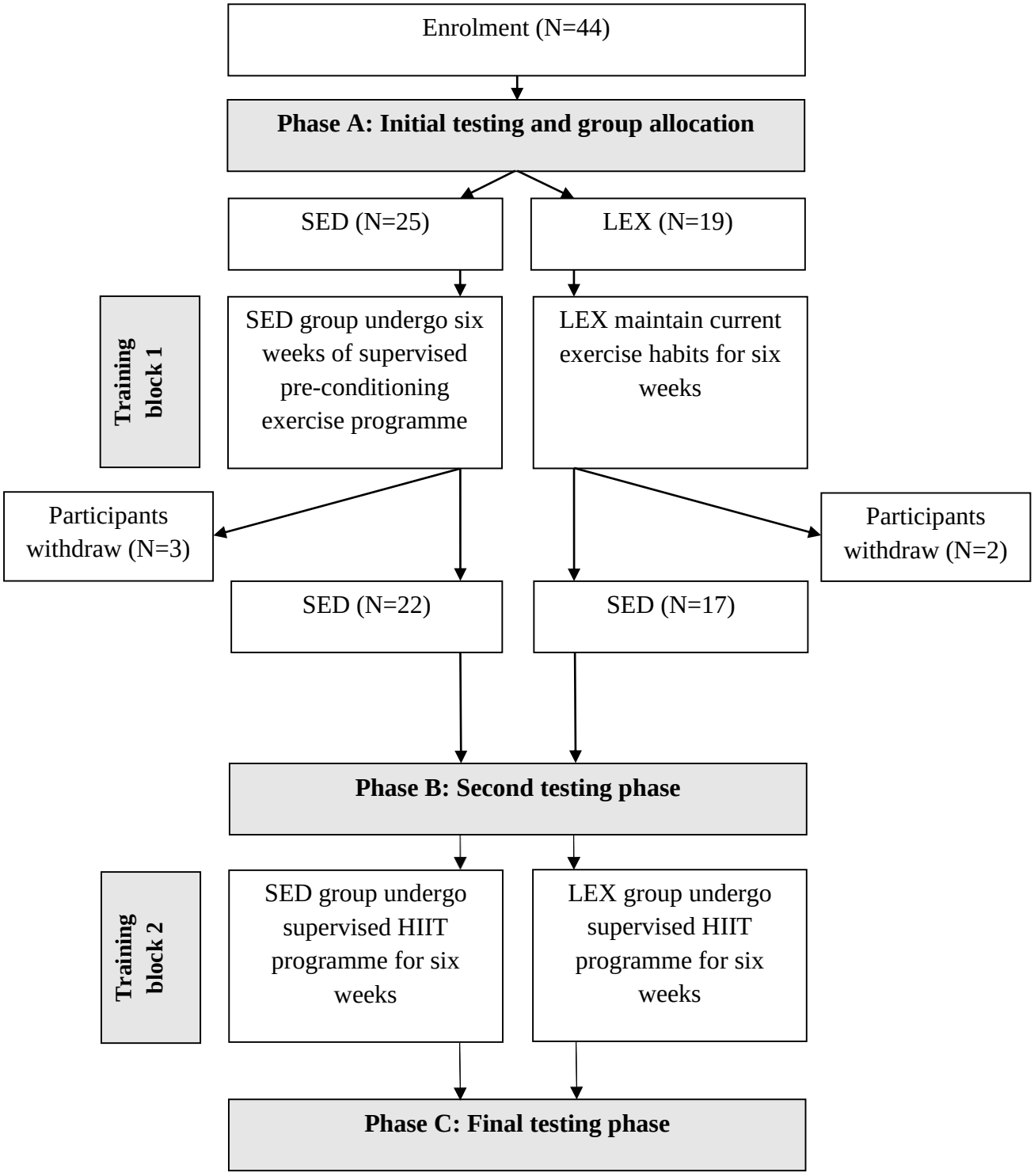
Exercise Training

To account for the contribution of aerobic conditioning exercise, participants were tested at three time points (phase A, B, and C), interspersed with two six weeks training blocks (12 weeks training in total [Figure 1]). As preconditioning, (training block 1), a six week exercise programme that reflected the ACSM guidelines of 150 mins·wk^{-1} of moderate to vigorous exercise was prescribed to SED. SED were advised to achieve a minimum of two sessions per week in accordance with the ACSM guidelines for older persons [19]. Participants were given verbal instructions on the use of a Polar FT1 heart rate monitor (Polar, Kempele, Finland) and exercise intensities were self-monitored, enabling recording of exercise time, and average and peak heart rate. The aim was to achieve an average heart rate reserve (HRR) of approximately 55% for the first two weeks of the intervention. This was increased to 60% of HRR for the subsequent weeks including 5-10 s of increased intensity every 10 min. The final two weeks required vigorous periods of exercise every 5 min achieving a HRR of 60-65%. The mode of training was optional, and included walking, walk/jogging, jogging, and cycling. Over the six week intervention, 160 ± 15 min·wk^{-1} exercise were achieved. Whilst SED underwent preconditioning, LEX maintained their habitual training. LEX recorded their weekly exercise,

which included type, frequency, intensity (recorded by heart rate telemetry), and duration of training. Time spent in low to medium intensity (<65% heart rate reserve [HRR]), and high-intensity (>65% HRR) training totalled 214 ± 131 min·wk^{-1} and 67 ± 52 min·wk^{-1} respectively.

Both groups undertook supervised HIIT programmes from phase B to C. HIIT sessions were performed every five days, for six weeks (nine sessions in total). Rationale for this programme is provided by our previous work which identified that five days recovery was required for recovery of peak power output (PPO) post-HIIT amongst older males [20]. Sessions consisted of 6 x 30 s sprints at 40% PPO (determined during familiarization) interspersed with 3 min active recovery on a cycle ergometer (Wattbike Ltd., Nottingham, UK). Sessions were conducted in groups of 4-6 and were the sole exercise performed by both groups during this time. To allow for comparison with other literature, training intensities were compared with power achieved at VO_{2peak}. In the majority of cases, 40% of PPO exceeded power at VO_{2peak}; in 4 cases (1 SED; 3 LEX), it exceeded 90% of power at VO_{2peak} (92; 92; 96; 98% respectively). In SED, mean training intensity equated to 141 ± 27% of power at VO_{2peak}, whilst in LEX, mean training intensity equated to 126 ± 22% of power output at VO_{2peak}.

FIGURE 1:


Enrolment (N=44)
Phase A: Initial testing and group allocation
SED (N=25)
LEX (N=19)
Training block 1
SED group undergo six weeks of supervised pre-conditioning exercise programme
LEX maintain current exercise habits for six weeks
Participants withdraw (N=3)
Participants withdraw (N=2)
SED (N=22)
SED (N=17)
Phase B: Second testing phase
Training block 2
SED group undergo supervised HIIT programme for six weeks
LEX group undergo supervised HIIT programme for six weeks
Phase C: Final testing phase

Blood draws and analysis

Blood samples from each participant were collected at each phase between 07:00-09:00 h, 48-72 hours following the last exercise session as previously described [21, 22]. Samples were obtained using a 20-gauge disposable needle equipped with Vacutainer tube holder (Becton Dickinson, Oxford, UK) following an overnight fast and 20 min supine rest. Blood draws were conducted from the antecubital vein, by the same phlebotomist to control for biological variation, and inter- and intra-subject variation. Approximately 14 mL of blood was drawn into two 10 mL serum separator tubes and allowed to clot at room temperature prior to being centrifuged at 6,000 rpm at 15°C for 15 min. Resultant serum was divided into appropriate aliquots and stored at -80°C until analysis. Serum concentrations of IGF-I were measured by electrochemiluminescent immunoassay on the E601 module of the Roche Cobas 6000 (Burgess Hill, West Sussex, U.K.). Inter-assay coefficients of variation (CV) over a 6 month period were <5%. Analysis was conducted in the Clinical Biochemistry Laboratory at Royal Glamorgan Hospital (Wales, UK).

Body composition

Stature was measured to the nearest 0.1 cm using a stadiometer (Seca, Birmingham, UK), and body mass and body composition was determined by a multi frequency bioelectrical impedance analyzer (BIA [Tanita MC-180MA Body Composition Analyzer, Tanita UK Ltd.]). GMON software (v1.7.0, Tanita UK Ltd.) was used to determine absolute and relative body fat. Fat free mass (FFM) was calculated by subtracting fat mass from total body mass.

Peak oxygen uptake and peak power output

Peak oxygen uptake (VO_{2peak}) was determined using a Cortex II Metalyser 3B-R2 (Cortex, Biophysik, Leipzig, Germany) utilizing methods previously described [23] and a

modified Storer Test [24]. PPO was established using the 6 s Herbert test [25] on an air-braked cycle ergometer (Wattbike Ltd., Nottingham, UK). Order of measurement was; blood sampling, body composition, PPO determination, and VO_{2peak} assessment.

Statistical Analysis

Following a Shapiro-Wilk test of normality and Levene's test for homogeneity of variance, a 2 x 3 (group [SED, LEX] x time [phase A, B, C]) repeated measures analysis of variance (ANOVA) with *post hoc* Tukey's LSD tested for differences between groups and between time points. To determine relationships between variables, a Pearson's correlation coefficient was conducted. Alpha level was set *a priori* at $P \leq 0.05$, and effect size is displayed, and classified as <0.2=trivial, 0.2-0.49=small, 0.5-0.79=moderate, and >0.8=large. Data are presented as mean ± standard deviation (SD). As LEX maintained their current exercise habits between phase A and B, we used these two samples to determine the absolute minimum threshold for a meaningful change in IGF-I (expressed as a percentage).

RESULTS

Basal IGF-I concentrations at phase A, B, and C for both groups are displayed in Figure 2A, and in SED in Figure 3. IGF-I was largely higher in LEX compared to SED at baseline (P=0.007, Cohen's *d*=0.91), moderately higher after preconditioning (P=0.083, Cohen's *d*=0.59), whilst a small difference existed post-HIIT (P=0.291, Cohen's *d*=0.35).

SED IGF-I increased post-HIIT compared to baseline (16.9 ± 4.4 and 13.1 ± 4.7 $ug \cdot dl^{-1}$ respectively [~29% increase; P=0.002, Cohen's *d*=0.85]) and compared to preconditioning (~21% increase; 14.2 ± 6.0 $ug \cdot dl^{-1}$ [P=0.005, Cohen's *d*=0.51]). Preconditioning accounted for ~8% of the increase from baseline (P=0.376, Cohen's *d*=0.22).

LEX experienced a trivial ~1% difference in IGF-I post-HIIT compared to baseline (18.4 ± 4.1 and 18.2 ± 6.4 ug·dl^{-1} respectively [P=0.901, Cohen's *d*=0.04), and a ~7% increase post-HIIT compared to phase B (17.2 ± 3.7 ug·dl^{-1} [P=0.283, Cohen's *d*=0.31). A trivial change in IGF-I was observed in LEX from phase A to B, equal to 5% (P=0.538, Cohen's *d*=0.19).

FIGURE 2:

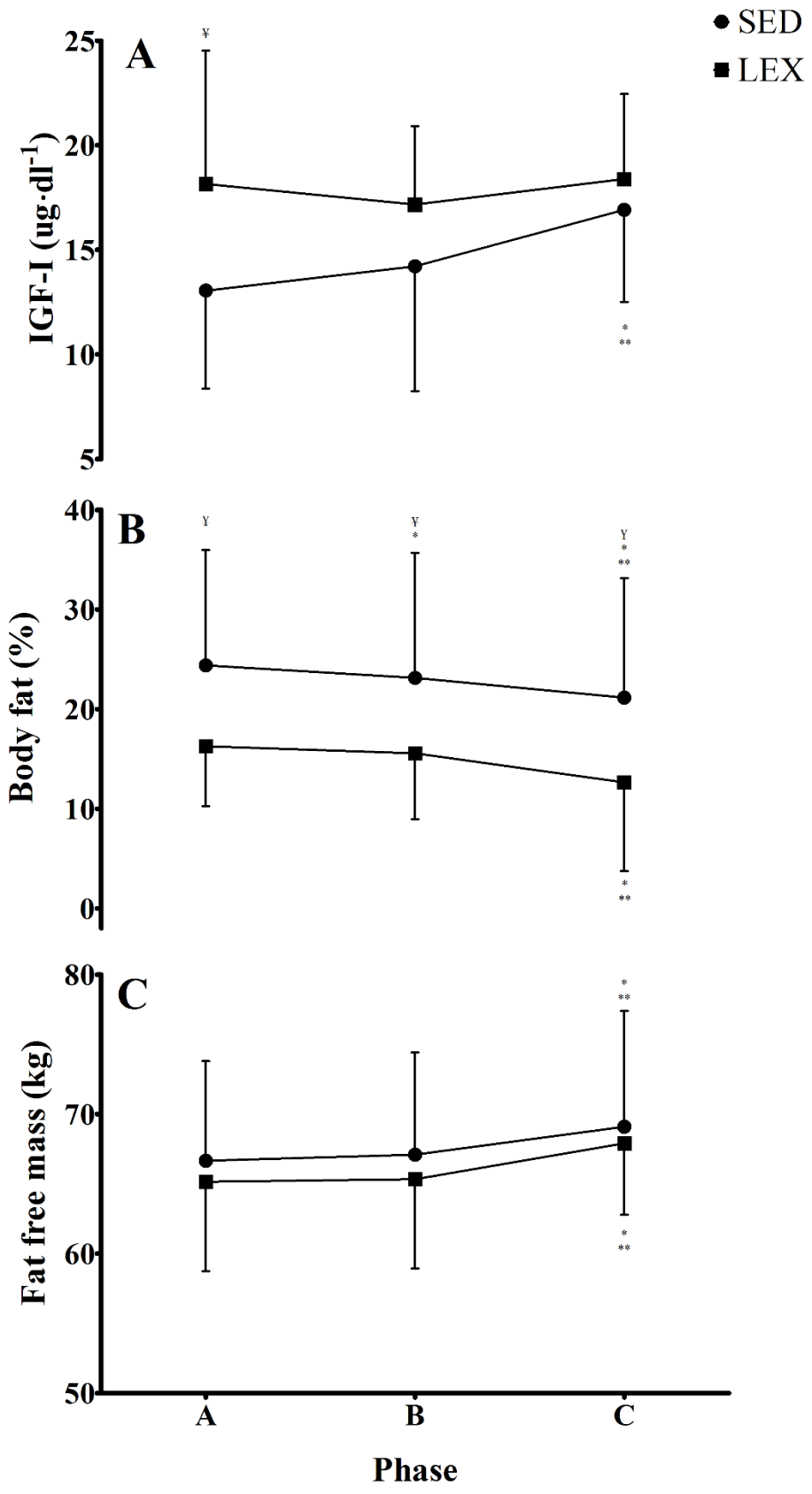
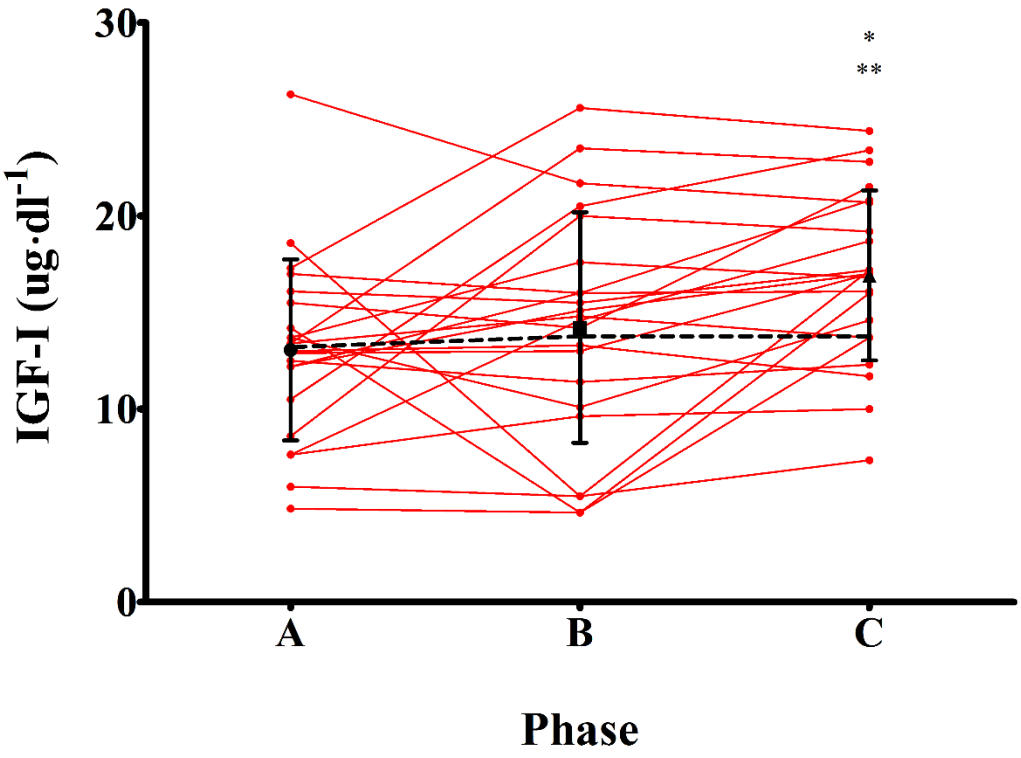

SED
LEX
A
B
C
IGF-I (ug·dl-1)
Body fat (%)
Fat free mass (kg)
25
20
15
10
5
40
30
20
10
0
80
70
60
50
A
B
C
Phase

FIGURE 3:



Body composition is displayed in Figure 2B and 2C. Body fat percentage was greater in SED than LEX at baseline (P=0.013, Cohen's *d*=0.862), after preconditioning (P=0.031, Cohen's *d*=0.74), and post-HIIT (P=0.020, Cohen's *d*=0.80).

HIIT decreased SED body fat percentage by ~3.3% compared to baseline (21.1 ± 12.0% and 24.4 ± 11.6% respectively [P<0.001, Cohen's *d*=0.28]) and ~2.2% compared to preconditioning (23.1 ± 12.6% [P=0.008, Cohen's *d*=0.16]). A ~1.3% decrease occurred as a result of preconditioning alone (P=0.006, Cohen's *d*=0.10). LEX body fat percentage decreased from 16.3 ± 6.0% at baseline to 12.6 ± 8.9% post-HIIT (P=0.006, Cohen's *d*=0.48), which was also lower than at phase B (15.6 ± 6.6% [P=0.020, Cohen's *d*=0.37]. LEX body fat percentage was trivially decreased from phase A to B (P=0.079, Cohen's *d*=0.11).

FFM was not significantly different between SED and LEX at A, B, or C (P=0.439-0.61). SED FFM was similar at baseline and following preconditioning (66.7 ± 7.1 kg and 67.1 ± 7.3 kg respectively [P=0.336, Cohen's *d*=0.06]). This was followed by a ~3.0% increase post-HIIT (69.1 ± 8.3 kg [P=0.005, Cohen's *d*=0.26]), which was ~3.6% greater than at baseline (P=0.001, Cohen's *d*=0.32). LEX FFM was unchanged from phase A to B (65.2 ± 6.4 kg and 65.3 ± 6.4 kg respectively [P=0.590, Cohen's *d*=0.03]), followed by a ~4.0% increase post-HIIT (67.9 ± 5.1 kg [P=0.008, Cohen's *d*=0.45]), which was ~4.1% greater than at baseline (P=0.006, Cohen's *d*=0.48).

At baseline, a weak negative correlation was present between IGF-I and BMI (P=0.016, *r*=-0.385), and IGF-I and body fat percentage (P=0.030, *r*=-0.345), whereas a moderate relationship existed between IGF-I and FFM (P=0.087, *r*=0.600). The change in IGF-I from pre- to post-HIIT was not significantly associated with change in FFM (P=0.860, *r*=0.029) or body fat percentage (P=0.860, *r*=-0.029). There was a strong significant correlation between change in FFM and body fat percentage from baseline to post-HIIT (P<0.001, *r*=-0.904).

DISCUSSION

The main findings from the present study were that 1) masters' athletes (LEX) have higher basal IGF-I concentrations than age-matched sedentary (SED) counterparts and that 2) a programme of HIIT training that includes preconditioning exercise increases IGF-I concentrations in SED compared with LEX. These data provided preliminary evidence for the positive influence of HIIT on tissue growth factors in lifelong sedentary aging men.

Our data are in agreement with some [26], but not all [17, 27] previous investigations in reporting increased IGF-I following exercise interventions. However, it is evident that a) previous exercise training, and b) exercise intensity, mediate the IGF-I response to training. LEX exhibited greater IGF-I compared to SED at baseline, supporting our hypothesis that

lifelong exercise would be associated with higher basal IGF-I concentrations. Preconditioning accounted for ~8% of the IGF-I increase in SED, whereas HIIT accounted for a further ~21%, despite a reduction in training volume from ~160 min·wk^{-1} to ~3-6 min·wk^{-1}. As such, it appears that HIIT likely induces greater increases in basal IGF-I compared with a higher volume of lower intensity exercise in SED. However, this remains preliminary until confirmed by a randomized controlled trial.

Arnarson et al. [17] observed that following 12 weeks resistance training, lean body mass increases were negatively associated with IGF-I changes, leading these authors to hypothesize that during periods of anabolism, IGF-I was redistributed from circulation into tissue. However, our data do not support such a redistribution, as SED FFM was increased post-HIIT, concomitantly with an increase in systemic IGF-I. Moreover, changes in FFM were not associated with changes in IGF-I in either group. Hofmann and colleagues [27] add further ambiguity to the relationship between lean mass and IGF-I, reporting increased muscle quality and chair stand performance after six months of resistance training, without serum IGF-I perturbations at three, or six months. As such, despite the *in vitro* evidence demonstrating IGF-I to be critical for muscle hypertrophy [28], further research is required to untangle the known associations between exercise, IGF-I, and lean body mass, in older adults.

HIIT appears to induce a number of favorable adaptations in older adults, including vascular function [23], quality of life [7], muscle power [29], and mitochondrial function [30]. Despite the evident benefits of HIIT to older adults, we suggest caution when inducting older adults onto a HIIT programme, as we have previously demonstrated delayed recovery in older, compared to young, males [20]. Moreover, Donath et al. [31] reported increased postural sway following a single HIIT session in seniors (70 ± 3 years), suggesting an increased likelihood of falls acutely post-HIIT. As such, pragmatic periodization is necessary to allow adequate recovery and mitigate risk arising from HIIT [13].

One limitation of the present investigation is that groups were not BMI-matched (SED were heavier than LEX). As such, differences in IGF-I between groups could have been caused by differences in body composition, rather than differences in habitual exercise, which is supported by the moderate correlations between IGF-I and body composition parameters. However, given the interrelationship between exercise and body composition, delineating these effects was outside the scope of the present study and requires further investigation.

Conclusion

In conclusion, lifelong sedentariness was associated with lower systemic IGF-I compared to masters' athletes. However, a programme of HIIT training that includes preconditioning exercise increases IGF-I concentrations in SED compared with LEX and provides preliminary evidence for the positive influence of HIIT on tissue growth factors in lifelong sedentary aging men.

Authors declare they have no conflict of interest.

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FIGURE LEGENDS

Figure 1: The CONSORT (Consolidated Standards of Reporting Trials) flow chart depicting transit of lifelong sedentary (SED) and lifelong exercising (LEX) participants though the study. HIIT = high intensity interval training.

Figure 2: (A) Insulin-like growth factor (IGF-I), **(B)**, body fat percentage, and **(C)** fat free mass in a group of sedentary (SED) and lifelong exercising (LEX) older males. Data are presented as mean ± SD. *Denotes significant differences from phase A ($P<0.05$). **Denotes significant difference between phase B and C ($P<0.05$). ¥Denotes significant difference between groups at this experimental phase.

Figure 3: Insulin-like growth factor (IGF-I) in a group of sedentary older males. Data are presented as individual data points in addition to mean ± SD. The minimum threshold for a meaningful change compared to baseline has been added as a dashed line. *Denotes significant differences from phase A ($P<0.05$). **Denotes significant difference between phase B and C ($P<0.05$).