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The Umeå HIT Study - A Randomized Controlled Trial

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Editor's choice

Research Article

Effects of Controlled Supramaximal High-Intensity Interval Training on Cardiorespiratory Fitness and Global Cognitive Function in Older Adults: The Umeå HIT Study—A Randomized Controlled Trial

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Abstract

Background: This study examined the effects of regulated and controlled supramaximal high-intensity interval training (HIT) adapted for older adults, compared to moderate-intensity training (MIT), on cardiorespiratory fitness; cognitive, cardiovascular, and muscular function; and quality of life.

Methods: Sixty-eight nonexercising older adults (66–79 years, 44% males) were randomized to 3 months of twice-weekly HIT (20-minute session including 10 × 6-second intervals) or MIT (40-minute session including 3 × 8-minute intervals) on stationary bicycles in an ordinary gym setting. Individualized target intensity was watt controlled with a standardized pedaling cadence and individual adjustment of the resistance load. Primary outcomes were cardiorespiratory fitness ($V\dot{O}_2$peak) and global cognitive function (unit-weighted composite).

Results: $V\dot{O}_2$peak increased significantly (mean 1.38 mL/kg/min, 95% CI [0.77, 1.98]), with no between-group difference (mean difference 0.05 [−1.17, 1.25]). Global cognition did not improve (0.02 [−0.05, 0.09]), nor differed between groups (0.11 [−0.03, 0.24]). Significant between-group differences in change were observed for working memory (0.32 [0.01, 0.64]), and maximal isometric knee extensor muscle strength (0.07 N·m/kg [0.003, 0.137]), both in favor of HIT. Irrespective of the group, there was a negative change in episodic memory (−0.15 [−0.28, −0.02]), a positive change in visuospatial ability (0.26 [0.08, 0.44]), and a decrease in systolic (−2.09 mmHg [−3.54, −0.64]) and diastolic (−1.27 mmHg [−2.31, −0.25]) blood pressure.

Conclusions: In nonexercising older adults, 3 months of watt-controlled supramaximal HIT improved cardiorespiratory fitness and cardiovascular function to a similar extent as MIT, despite half the training time. In favor of HIT, there was an improvement in muscular function and a potential domain-specific effect on working memory.

Clinical Trial Registration: NCT03765385

Keywords: Aerobic capacity, HIIT, Moderate-intensity training, SIT, Sprint interval training

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Engaging in regular physical exercise has been shown to delay age-related physiological and cognitive decline, reduce the risk of common diseases, and improve the subjective quality of life (1–3). Meanwhile, a large proportion of older adults are insufficiently physically active (4,5), potentially increasing societal health-related challenges connected to a growing older population (6). It is, therefore, important to provide both effective and attractive exercise methods adapted for this group.

One of the proposed key factors in maximizing exercise effects is to exercise beyond moderate intensities, as in high-intensity interval training (HIT) (7,8). Although aerobic moderate-intensity training (MIT) is performed at intensities below the anaerobic threshold, HIT is broadly defined as short repeated work intervals at an external intensity close to (80%–100%), or above (>100%) the intensity that elicits maximum oxygen uptake ($\dot{V}O_2$max), with passive or low-intensity recovery between intervals (9). In supramaximal HIT, the focus is solely on external intensities above the intensity that elicits $\dot{V}O_2$max (10).

Supramaximal HIT is characterized by intervals of short duration (≤30 seconds) performed at external target intensities reaching up to 5 times the intensity reached during MIT, and stresses both the cardiovascular and muscular systems closer to maximal capacity (11). Studies show similar to superior cardiorespiratory and cardiometabolic improvements in supramaximal HIT compared to MIT, but in less time (12,13), as well as additional anaerobic and muscular adaptions (14,15). HIT can also be more enjoyable and less monotonous than MIT (16,17). In addition, supramaximal HIT with repeated all-out efforts of shorter interval durations (≤6 seconds) has been favored over fewer but longer intervals (15–30 seconds), both in terms of reducing negative affect and drop-out rates, as well as increasing exercise compliance (18–20). However, most studies on supramaximal HIT have so far been performed among young and middle-aged adults.

Existing studies on supramaximal HIT for older adults have shown promising results (21–23). However, they suffer from small sample sizes, the use of inactive control groups or lack of control conditions entirely, strict experimental settings, and one-to-one supervision. Consequently, interpretations of the results are limited, and the opportunity for large-scale implementation is reduced. In addition, concerns have been raised regarding the safety and feasibility of repeated all-out sprint intervals with uncontrolled target intensity for older and untrained individuals (24,25). These include an increased risk of overshooting exercise interval intensity (26) that may lead to physical discomfort and nausea (27), and potentially decrease adherence to the exercise program (25).

In a previous study (10), we developed a group-based supramaximal HIT protocol consisting of 10 × 6-second cycling intervals adapted for older adults. Key characteristics of this protocol were the use of standardized pedaling cadence and individual adjustment of resistance load, which allowed for controlled and easy regulation of a stipulated target intensity. By prescribing the intensity as external target power output (TPO) in watts, issues of time delay in heart rate response and excessive perceived exertion were avoided (9), thus reducing the risk of both over- and undershooting the interval TPO (26). The use of interval intensity escalation criteria further allowed a standardized and individualized procedure to progress exercise intensity over time.

The present study aimed to examine the effects of regulated and controlled supramaximal HIT, compared to MIT, on cardiorespiratory fitness, cognitive, cardiovascular, and muscular function, as well as quality of life among nonexercising older adults.

Method

Trial Design

The Umeå HIT Study was a randomized controlled superiority trial of parallel design conducted in Umeå (Sweden), with a 1:1 group allocation to 3 months of supramaximal HIT or MIT. Ethical approval was given by the Regional Ethics Review Board in Umeå (2018-307-31M, 2018-421-32M). The study protocol was registered at ClinicalTrials.gov (NCT03765385).

Participants and Recruitment

Participants were recruited through a local newspaper advertisement. Eligible participants were nonexercising adults aged 65 years or older with the ability to undertake a twice-weekly training program for 3 months. Individuals without engagement in regular physical exercise at moderate or high intensity over the past year, regardless of exercise experience earlier in life, were considered nonexercisers. Exclusion criteria were movement-related dysfunction (eg, pain prohibiting participation in physical tests or exercise); heart or lung conditions with exercise-induced symptoms; poor blood pressure control or untreated arterial hypertension (≥140/90 mmHg); insulin-treated diabetes; a Mini-Mental State Examination (MMSE) score below 27; chronic or progressive neurological disease; or sharing a household with a participant already included in the study.

Telephone screening was conducted by a physical therapist or sport scientist, and applicants deemed eligible received further in-depth oral and written information about the study. Medical screening was conducted at the Clinical Research Centre in Umeå, where each applicant provided written informed consent, completed the MMSE, and underwent a medical examination by an experienced cardiologist (B.J.), which included a 12-lead electrocardiography. The enrollment period spanned from December 2018 to September 2019 and resulted in 4 waves of participants.

Study Timeline and Assessment Procedures

For each wave of participants, the study procedure started with baseline assessments, followed by randomization, a 3-month-long exercise intervention (supramaximal HIT or MIT), and subsequent follow-up assessments (3-month follow-up). Detailed descriptions of assessment procedures, outcomes and measures, and the exercise intervention are provided in Supplementary Material.

Outcomes and Measures

Primary outcomes were cardiorespiratory fitness (peak oxygen uptake, $\dot{V}O_2$peak), and global cognitive function. Secondary outcomes were domain-specific cognitive functions, cardiovascular and muscular function, and quality of life.

Cardiorespiratory fitness

$\dot{V}O_2$peak (mL/kg/min) was assessed as the highest recorded oxygen uptake during a standardized ramp test on an electronically braked cycle ergometer (Monark 839E Monark Exercise AB, Vansbro, Sweden). The test started at 30 watts for females and at 40 watts for males, and was kept constant for the first 3 minutes. This was followed by a ramp protocol with a continuous increase in the workload of 10 watts/min for females and 15 watts/min for males (see Supplementary Material for more detailed descriptions and test termination criteria). Expired air was analyzed continuously during the test with a mixing chamber-based ergo-spirometry system (AMIS 2001 Innovision A/S, Odense, Denmark) and registered as means of

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30-second intervals. For additional medical clearance purposes, another 12-lead electrocardiography (MAC 5000, Schiller AG, BAAR, Switzerland) was recorded during the test and subsequently examined (B.J.).

Cognitive function

To capture a broad range of cognitive abilities and minimize floor and ceiling effects (28), we derived global and domain-specific cognitive composites from a test battery comprising 11 cognitive tests. The tests were administered in the following order: (1) Digit symbol, (2) Free recall, (3) Automated Operation Span, (4) Word recognition (encoding), (5) Backward digit span, (6) Stroop, (7) n-back, (8) Word recognition (retrieval), (9) Trail Making Test (TMT) 2–4, (10) Paired associates, and (11) Form boards. For each test and time point, participant raw scores were *z*-transformed, using the baseline mean and standard deviation (*SD*) of the entire sample. The *z*-transformed scores were then averaged to form unit-weighted composites. A higher composite score indicated better cognitive function. The tests selected for the global and domain-specific composites were based on previous research (29,30). Descriptions of each test and composite score computations are found in Supplementary Material.

Global cognitive function.

The global cognitive composite was calculated from the tests targeting the cognitive domains processing speed, episodic memory, working memory, and executive function (specified later). Participants missing no more than 1 *z*-transformed score within each of the 4 cognitive domains were assigned a global composite.

Domain-specific cognitive function.

Domain-specific composites were calculated for 5 different domains: (1) Processing speed (Digit symbol, 1-back, TMT 2 and 3), (2) Episodic memory (Free recall, Word recognition, Paired associates), (3) Working memory (Automated Operation Span, Backward digit span), (4) Executive function (Stroop, 2-back, TMT 4), and (5) Visuospatial ability (Form boards). Domain-specific composite scores were calculated only for participants missing no more than 1 *z*-transformed score within that domain.

Cardiovascular function

Average systolic and diastolic blood pressure (mmHg) were based on 6 days of home-based measurements with a validated automatic upper arm blood pressure monitor (Omron M2, (31)). Only participants with at least 30 valid measurements were included (32).

Muscular function

Maximal isometric knee extensor muscle strength (normalized joint torque in N·m/kg) was assessed with a load cell (Lutron FG-5100, Lutron Electronic Enterprise Co., Ltd., Taipei, Taiwan) positioned in a Biodex dynamometer chair (Biodex System Pro X, Biodex Medical Systems, Shirley, New York, NY). After submaximal practice, participants performed 2 maximum trials for each leg with 2 minutes of rest between trials. For each leg, the maximal torque (N·m) was calculated from the highest obtained force (N) of the 2 trials multiplied by the moment arm (m), and then averaged across both legs and divided by weight (kg). For participants with complete values only for 1 leg ($n = 4$) at baseline or follow-up, the single values for that leg were used instead of an average across both legs.

Quality of life

Subjective health-related quality of life was assessed with the Swedish Short Form Health Survey (SF-36) as a composite mean of the 8 subscales, ranging on a scale of 0–100 (higher scores indicating better quality of life). Incomplete forms were handled with participant subscale means imputed for missing values (33). If more than half of a subscale's items were missing, imputation was not conducted, and the participant was not assigned a composite mean.

Randomization

An external researcher not involved in the study generated lists of random numbers using Research Randomizer (http://www.randomizer.org/). For each of the 4 waves of participants, randomization was performed after complete baseline assessments and stratified by biological sex and age (65–69 years, or ≥70 years) to ensure a good balance between groups.

Blinding

Participants were informed about the general study purpose but blind to study hypotheses and only received detailed information about their allocated exercise group. Outcome assessors were blinded to group allocation, and participants were repeatedly instructed to withhold any details of their group allocation during follow-up assessments. The primary outcome analyses used a masked data set, with the code key administered by a researcher not involved in the study.

Exercise Intervention

For both HIT and MIT, exercise was performed in groups of 8–10 participants on Tomahawk IC7 indoor bicycles (Indoor Cycling Group, Nürnberg, Germany) at a local exercise facility. The exercise was conducted twice weekly, with at least 72 hours of recovery between sessions, for 3 months. In total, 25 sessions were provided, of which the first 2 were shorter introductory sessions aimed at familiarizing participants with the equipment and designated exercise protocol. From Session 3, the full exercise protocol and procedure to progress interval intensity were applied (Figure 1).

The training was computer guided, with 2 supervisors (educated in sports medicine or physiotherapy) always present to prepare the equipment (Supplementary Material, Supplementary Figure 1), monitor, and collect data on adherence, adverse events (AE), and escalation/de-escalation criteria (Figure 1). Heart rate was continuously sampled with Polar H10 sensors, monitored via the Polar Club application, and evaluated in Polar Flow between sessions (Polar Electro Oy, Kempele, Finland). Self-rated perceived exertion was assessed with the 15-point (6–20) Rating of Perceived Exertion (RPE) scale (34). Detailed descriptions of the data sampling are provided in Supplementary Material.

Exercise intensity was individually prescribed as external TPO in absolute watts, and regulated by standardized pedaling cadence and individual adjustment of the brake resistance level. The TPO during warm-up, between-interval active recovery, and cool-down corresponded to 33% of the participant's maximum aerobic power (MAP; the watts produced at $\dot{V}O_2$peak during the baseline cycle ergometer ramp test), with a set pedaling cadence of 60 revolutions per minute (RPM). Although the interval TPO for MIT also was a percentage of MAP, the interval TPO for supramaximal HIT was based on the participant's maximum mean power output for 6 seconds (MPO^6). The maximum MPO^6 was estimated at baseline from a modified

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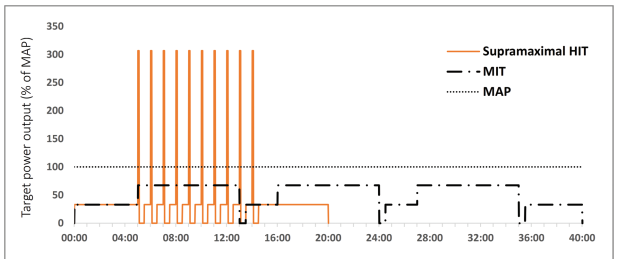

Exercise setup	Supramaximal HIT	MIT
Total duration	20 minutes	40 minutes
Number of intervals x duration	10 x 6 seconds	3 x 8 minutes
Standardized pedaling cadence		
Warm-up, active recovery and cool-down	60 RPM	60 RPM
Intervals	85 RPM	60 RPM
Stipulated interval TPO		
Warm-up, active recovery and cool-down	33% of MAP	33% of MAP
Intervals (session 1-3)	60% of MPO[6]	40% of MAP
TPO escalation criteria (from 3rd session)		
Maintained cadence during last interval	85 RPM	60 RPM
Rated perceived exertion (RPE)	RPE ≤ 16	RPE ≤ 14
Peak HR during last interval	≤ 95% HRR	≤ 70% HRR
Possible to do an additional (11th) interval	YES	-
Participant ready to escalate load	YES	YES
TPO de-escalation criteria		
Maintain cadence during the last interval	RPM < 85	RPM < 60
Rated perceived exertion (RPE)	RPE ≥ 18	RPE ≥ 16
Peak HR during last interval	> 95% HRR	> 70% HRR
Possible to do an additional (11th) interval	NO	-
Participant ready to escalate load	Wants to de-escalate	Wants to de-escalate
Between-session regulation of interval TPO		
Escalation/de-escalation (one step)	4% of MPO[6]	4% of MAP

Figure 1. Exercise protocol characteristics of controlled supramaximal HIT and MIT. The plotted lines represent the group means values of target power output, expressed as a percentage of MAP, at the end of the training period for supramaximal HIT (solid line) and MIT (dot-dashed line). The full protocols were applied from session three and onwards. The escalation/de-escalation step was equally large in absolute terms (watts) during the entire intervention. All escalation criteria had to be fulfilled to increase intensity 1 step for the next session, whereas decrease of intensity only required fulfillment of 1 de-escalation criterion or the participant explicitly asking to decrease intensity. In cases when all escalation criteria were met except RPE, and the rated RPE was 17 for HIT, and 15 for MIT, the exercise intensity was maintained for the next session. HIT = high-intensity interval training; HRR = heart rate reserve; MIT = moderate-intensity training; MAP = maximum aerobic power at baseline; MPO[6] = maximum mean power output for 6 seconds estimated at baseline; Peak HR = peak heart rate (10-second mean during last interval for HIT, average of 60 seconds of the last interval for MIT); RPE = rating of perceived exertion on the Borg (6–20) scale; RPM = revolutions per minute; TPO = target power output.

version of the Borg Cycle Strength Test, and multiplying the highest obtained power output by 1.75 (10).

The regulation of interval intensity followed standardized escalation and de-escalation criteria (Figure 1) to ensure a safe progression according to the participant's own ability. The de-escalation criteria were applied already at the first session, whereas the escalation criteria were applied from the third session. All escalation criteria had to be fulfilled in order to increase intensity at the next session. A decrease in intensity required fulfillment of only 1 de-escalation criterion or the participant explicitly asking to decrease the intensity. Each escalation/de-escalation step was equally large in absolute terms in watts during the entire intervention (ie, 4% of MPO[6] for supramaximal HIT and 4% of MAP for MIT).

Supramaximal HIT

The supramaximal HIT protocol, in total 20 minutes per session, consisted of 10 × 6-second intervals interspersed with a 54-second recovery period (24 seconds of passive recovery, followed by 30 seconds of active recovery). During the last 5 seconds of active recovery, participants were instructed to increase pedaling cadence from 60 to 85 RPM and prepare to adjust the brake-level resistance for the upcoming interval. The interval TPO for the first 3 sessions was 60% of MPO[6], and the progression of interval TPO beginning after the third session, implemented in absolute steps of 4% of baseline MPO[6] (Figure 1). If a participant rated their RPE ≥ 18 at any time during the exercise session, they completed the rest of the session at 33% of MAP, and interval TPO was de-escalated 1 step (ie, 4% of MPO[6]) at the following session.

Moderate-intensity training

The MIT protocol, in total 40 minutes per session, consisted of 3 × 8-minute bouts interspersed with a 3-minute recovery period (30 seconds of passive recovery, followed by 150 seconds of active recovery). The interval TPO for Sessions 1–3 was 40% of MAP, and the progression of interval TPO started after the third session in absolute steps of 4% of MAP (Figure 1). If a participant in MIT rated their RPE of ≥16 at any time during the session, the interval TPO was immediately de-escalated 1 step (ie, 4% of MAP), and maintained for the next session. The MIT protocol was divided into 3 longer bouts (instead of a continuous constant-load setup) in order to prevent AEs, boredom, and drop-out (35), as well as make it more similar to exercise protocols at training facilities.

Compliance to protocols

To minimize discomfort, participants in both groups were allowed to dismount the bike during the passive recovery period. Supervisors monitored each participant's pedaling cadence and produced power output at least once per session, with additional instructions provided if necessary.

Adverse Events

AEs were documented at the beginning of each training session (any discomfort experienced since the previous training session), and at the end of the session (any discomfort experienced during the current training session). All AEs were categorized based on symptom descriptions. Two reviewers (a medical doctor and a sports medicine researcher) not involved in the study assessed whether each AE was considered a serious AE (SAE). An SAE was defined as an event resulting in death; risk of death; hospitalization; disability or permanent damage; or a required intervention to prevent permanent impairment, damage, or other medical events. The assessment was first conducted individually, after which the reviewers discussed until reaching a mutual conclusion. The reviewers also assessed whether each case of discontinuation from the exercise intervention and study withdrawal was related to the intervention, and if so, whether the case was considered an SAE.

Sample Size

Power calculations (80% power, $\alpha = 0.05$, 2-sided) based on estimated between-group differences in primary outcome variables peak oxygen uptake (Vo_2peak, MD = 3.5 mL/kg/min, *SD* 4.0) and global cognition (effect size [ES] = 0.793 (30)), with an estimated drop-out rate of 15%, revealed a need to include 70 participants.

Statistical Analysis

All analyses were conducted in R 4.0.5 (36), and RStudio 1.1.463 (RStudio Team, 2016), using the lme4 (37) and lmerTest (38) packages with 2-tailed testing and $\alpha = 0.05$.

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All available participant data were analyzed according to participants' original group allocation in agreement with the intention-to-treat principle. For each outcome, linear mixed-effects models (LMM) were applied to examine the between-group difference in change, within-group change, and change over time irrespective of group. Group, time (baseline and 3-month follow-up), and a group × time interaction were used, with adjustment for age and sex as fixed effects, and individual as a random effect. Analyses of cognitive functions were also adjusted for education level as a fixed effect. Results are reported as LMM-estimated mean change, with either standard error (*SE*) or 95% confidence interval (95% CI). ES were calculated from the model estimates of the between-group difference in change divided by the unadjusted pooled *SD*.

A prespecified sensitivity analysis was performed for Vo2peak by removing participants not meeting age-adjusted Vo_2max-criteria (RER ≥ 1.0, and/or post-test blood lactate of ≥3.5 mmol/L for females and ≥4.0 mmol/L for males (39)), as well as a stricter post hoc analysis removing participants not meeting an RER of ≥1.1. For global cognitive function, participants with the extreme change in scores from baseline to 3-month follow-up (≥3 *SD* in a cognitive test) were removed.

Results

Recruitment and Participant Flow

In total, 68 out of 233 applicants were deemed eligible, completed baseline assessments, and were randomized to either supramaximal HIT or MIT (Figure 2, Table 1). A total of 3 participants voluntarily withdrew from the study, none of which presented reasons considered related to the intervention. Three participants discontinued the exercise intervention but participated at a 3-month follow-up, 1 of which (in HIT) was discontinued by the doctor's request (B.J., a precautionary measure due to thrombophlebitis being re-diagnosed by primary health care). The other 2 discontinued voluntarily, with 1 of the cases (MIT) considered related to the intervention (musculoskeletal AE; back pain arising from trying to adjust the bicycle handlebar that had got stuck).

Applicability of Intervention

In supramaximal HIT, the stipulated interval intensity of 60% of MPO[6] for the first exercise session corresponded to an average workload of 235 watts (*SD* 62.9), and 174% of MAP (*SD* 32.2). By the end of the intervention, the interval TPO had increased to 428 watts (*SD* 117.3), which corresponded to 110% of baseline MPO[6] (*SD* 13.7) and 316% of MAP (*SD* 54.3). In MIT, the average workload was 54 watts (*SD* 15.6) for the first session and 84 watts (*SD* 23.6) by the end of the intervention. The latter corresponded to 69% of baseline MAP (*SD* 11.8).

Exercise session attendance was 88.0% for HIT, with a median of 23 out of 25 attended sessions per participant (range, 11–25 sessions). Corresponding numbers for MIT were 88.1% and 23 out of 25 (range, 0–25 sessions).

Of the 1 497 attended sessions, participants reported discomfort experienced since the previous training in 83 sessions (5.5%) and discomfort experienced during the current training in 63 sessions (4.2%). Of these 146 AEs, 52 were reported in HIT and 94 in MIT. The majority were musculoskeletal (70%, eg, pain/soreness/numbness in muscles/joints). No AE was considered an SAE.

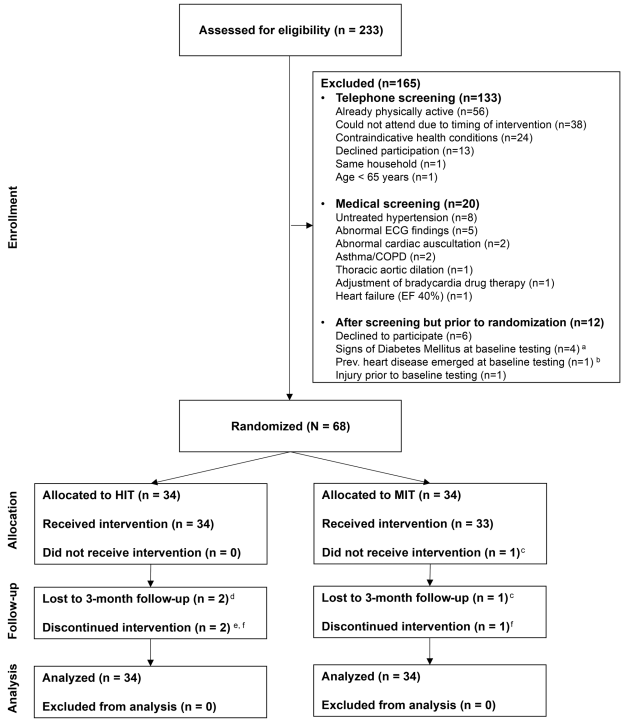

Figure 2. CONSORT flow diagram of Umeå HIT Study. The enrollment period spanned from December 2018 to September 2019, and resulted in 4 waves of participants. The first wave started in January 2019 and finished in May 2019, and the fourth and last waves started in September 2019 to be completed in February 2020. COPD = chronic obstructive pulmonary disease; ECG = electrocardiogram; EF = ejection fraction; HIT = high-intensity interval training. [a]Unexpected signs of diabetes mellitus during baseline testing in need of further medical investigation. [b]Unexpected history of previous heart disease emerging at baseline familiarization visit. [c]Withdrawal from study during intervention without having attended any exercise sessions. [d]Withdrawal from study, of which 1 during ongoing intervention period and 1 after the intervention period but prior to 3-month follow-up. [e]Discontinued the exercise intervention at doctor's request (re-diagnosed with thrombophlebitis) with continued participation in 3-month follow-up. [f]Discontinued the exercise intervention at own request with continued participation in 3-month follow-up.

Primary Outcomes

After 3 months of exercise, no statistically significant between-group differences in change were observed for Vo_2peak (MD = 0.05 mL/kg/min, 95% CI [−1.17, 1.25]) or global cognitive composite score (MD = 0.11, 95% CI [−0.03, 0.24]). Overall, irrespective of group, a significant mean increase in Vo_2peak of 1.38 mL/kg/min (95% CI [0.77, 1.98]) was observed and corresponded to 5.9%. Global cognitive function did not change (*M* = 0.02, 95% CI [−0.05, 0.09]). See Table 2 for detailed LMM estimates, and Figure 3 for grouped distributions and individual trajectories in primary outcomes.

Sensitivity analyses

For Vo2peak, the results remained essentially the same after removing participants not meeting age-adjusted Vo_2max criteria (39), for both between-group difference in change (*n* = 56, MD = 0.26, 95% CI [−0.94, 1.45]) and change over time (*M* = 1.64, 95% CI [1.04, 2.23]). The results for global cognition also remained the same after removing participants with extreme change (*n* = 66, MD = 0.11, 95% CI [−0.03, 0.25], and *M* = 0.03, 95% CI [−0.04, 0.11]). More

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Table 1. Participant Characteristics at Baseline

	All (N = 68)	HIT (n = 34)	MIT (n = 34)
Demographics			
Women, No. (%)	38 (56)	19 (56)	19 (56)
Age, y	69.7 (2.95)	69.7 (3.15)	69.6 (2.8)
Education, y	14.4 (3.3)	14.4 (3.5)	14.3 (3.13)
Anthropometrics			
Body mass, kg	76.5 (14.4)	77.2 (14.8)	75.8 (14.2)
BMI, kg/m^2	26.2 (3.94)	26.1 (3.53)	26.4 (4.37)
Basic hemodynamics			
* Systolic BP, mmHg [No.]	126 (10.8) [59]	127 (11.2) [30]	126 (10.7) [29]
* Diastolic BP, mmHg [No.]	80.0 (6.08) [59]	80.0 (5.77) [30]	79.9 (6.49) [29]
Physical activity			
BHW PA, median (min.; max.), score	9 (4; 19)	9 (4; 14)	9 (4; 19)
Cardiorespiratory fitness			
Vo_2peak, L/min	1.74 (0.44)	1.81 (0.47)	1.67 (0.4)
Vo_2peak, mL/kg/min	22.9 (4.91)	23.6 (5.19)	22.3 (4.58)
MAP, W	131 (41)	139 (44.6)	124 (36.2)
Anaerobic work capacity			
Maximum MPO^6, W	386 (99.7)	392 (105)	380 (95.6)
Muscular function			
Isometric muscle strength (N·m/kg)	1.69 (0.36)	1.66 (0.35)	1.72 (0.37)
Quality of life			
SF-36 [No.]	86.13 (9.69) [67]	83.96 (9.88) [34]	88.37 (9.1) [33]
Diagnoses, no. (%)			
Any	53 (78)	28 (82)	25 (74)
Hypertension	38 (56)	17 (50)	21 (62)
Hypothyroidism	8 (12)	5 (15)	3 (9)
Diabetes	6 (9)	3 (9)	3 (9)
Hip prosthesis	5 (7)	2 (6)	3 (9)
Medication, no. (%)			
Any	47 (69)	23 (68)	24 (71)
BP-lowering	37 (54)	17 (50)	20 (59)
Beta-blockers	8 (12)	5 (15)	3 (9)
Statins	13 (19)	5 (15)	8 (24)
Levaxin	8 (12)	5 (15)	3 (9)
Diabetes treatment	5 (7)	2 (6)	3 (9)
Tablets	3 (4)	1 (3)	2 (6)
Diet	2 (3)	1 (3)	1 (3)
ASA/antiplatelet	5 (7)	2 (6)	3 (9)

Notes: Numbers are presented as mean (*SD*) unless stated otherwise. [no.] indicates the number of participants contributing to the mean value, in cases when single-participant values are missing. Specified diagnoses and medications are those occurring more prevalent. ASA = acetylsalicylic acid; BHW = the Swedish National Board of Health and Welfare; BMI = body mass index; BP = blood pressure; bpm = beats per minute; HRmax = maximum heart rate; HRrest = resting heart rate; MAP = maximum aerobic power; MPO^6 = mean power output for 6 seconds; Vo_2peak = peak oxygen uptake; W = watts.

*Calculated as average systolic and diastolic blood pressure from six days of repeated morning and evening measurements.

details are given in Supplementary Material and Supplementary Table 1.

Secondary Outcomes

Statistically significant between-group differences in change were observed for the working memory composite score (MD = 0.32, 95% CI [0.01, 0.64]), and maximal isometric knee extensor muscle strength (MD = 0.07 N·m/kg, 95% CI [0.003, 0.137]), and indicated an advantage for the HIT group. For HIT, the within-group mean change was 0.20 (95% CI [−0.03, 0.43]) for working memory and 0.07 Nm/kg (95% CI [0.02, 0.12]) for muscle strength. Corresponding figures for MIT were −0.12 (95% CI [−0.34, 0.12]) for working memory and −0.004 (95% CI [−0.05, 0.04]) for muscle strength. No other significant between-group effects were observed (Table 2).

Overall, irrespective of group, there was a negative change in the episodic memory composite score (M = −0.15, 95% CI [−0.28, −0.02]), a positive change in visuospatial ability (M = 0.26, 95% CI [0.08, 0.44]), and no change in processing speed (M = 0.11, 95% CI [-0.02, 0.24]) and executive function (M = 0.03, 95% CI [−0.09, 0.14]). There was a significant decrease in systolic blood pressure (M = −2.09 mmHg, 95% CI [−3.54, −0.64]) and in diastolic blood pressure (M = -1.27 mmHg, 95% CI [−2.31, −0.25]). Subjective quality of life did not change significantly (M = −0.07, 95% CI [−3.05, 2.93]).

Discussion

The present study shows that supramaximal HIT with controlled target intensity is a viable exercise program to improve cardiorespiratory fitness and cardiovascular function to a similar extent as MIT, in nonexercising older adults. Specifically, after 3 months of exercise, we observed no significant between-group difference in change for

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Table 2. Within-Group Change and Between-Group Differences in Change From Baseline to 3-Month Follow-Up

	Within-Group Change						Between-Group Difference in Change			
	Supramaximal HIT			MIT			Group × Time			
	No.[a]	Mean	*SE*	No.*	Mean	*SE*	Mean	95% CI	*p*	ES
Primary outcomes										
Vo_2peak (mL/kg/min)	34/30	1.40	0.44	34/32	1.36	0.43	0.05	[−1.17, 1.25]	.940	.019
Global cognition (composite score)	34/30	0.07	0.05	34/29	−0.04	0.05	0.11	[−0.03, 0.24]	.134	.395
Secondary outcomes										
Domain-specific cognitive function										
Processing speed (composite)	34/30	0.24	0.10	34/32	−0.02	0.09	0.26	[−0.002, 0.52]	.057	.490
Episodic memory (composite)	34/30	−0.03	0.10	34/31	−0.26	0.09	0.23	[−0.04, 0.49]	.097	.426
Working memory (composite)	34/30	0.20	0.12	34/32	−0.12	0.11	0.32	[0.01, 0.64]	.052	.500
Executive function (composite)	34/30	−0.09	0.08	34/30	0.14	0.08	−0.22	[−0.45, 0.005]	.062	−.496
Visuospatial ability (composite)	34/32	0.33	0.13	34/32	0.20	0.13	0.13	[−0.23, 0.49]	.491	.175
Cardiovascular function										
Systolic blood pressure (mmHg)	30/27	−1.95	1.06	29/27	−2.21	1.05	0.27	[−2.63, 3.16]	.860	.049
Diastolic blood pressure (mmHg)	30/27	−1.54	0.75	29/27	−1.02	0.75	−0.53	[−2.58, 1.52]	.621	−.122
Muscular function										
Isometric muscle strength (N·m/kg)	34/31	0.07	0.02	34/31	−0.004	0.02	0.07	[0.003, 0.14]	. 045	.517
Quality of life										
SF-36 (score)	34/32	−1.48	2.11	33/30	1.44	2.18	−2.92	[−8.85, 3.04]	.339	−.242

Notes: Values from linear mixed-effects models adjusted for age and sex as fixed effects and individual as random effect. Analyses of cognitive functions were adjusted also for educational level as a fixed effect. Data are reported as LMM-estimated mean change with their *SE* for within-group change, and 95% CI for between-group difference in change. ES was calculated from the model estimates of between-group difference in mean change and the unadjusted pooled standard deviation. CI, Confidence Interval; ES = effect size; HIT = high-intensity interval training; MIT = moderate-intensity training; *SE* = standard error; SF-36 = Short Form Health Survey-36; Vo_2peak = peak oxygen uptake.

*Number (No.) of available measurements at baseline and 3-month follow-up presented as baseline/follow-up.

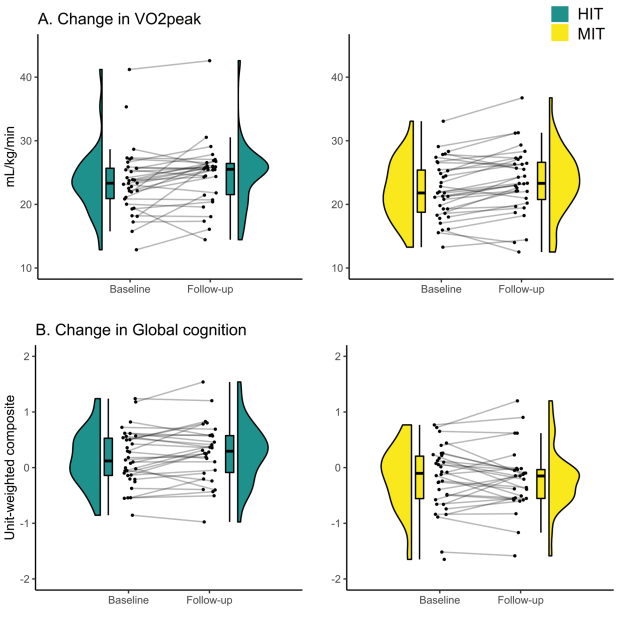

Figure 3. Visualization of change in primary outcomes. Raincloud plots of raw data group distributions and individual change in primary outcomes Vo_2peak (A) and global cognitive function (B) for supramaximal HIT (left) and MIT (right).

Vo_2peak, but a significant improvement irrespective of group. No effect was found on global cognition. For the secondary outcomes, we observed significant between-group differences in change in working memory performance and maximal isometric knee extensor muscle strength, both in favor of supramaximal HIT. No other significant between-group effects were observed. Overall, irrespective of group, there was also a negative change in episodic memory performance, a positive change in visuospatial ability, and a reduction in systolic and diastolic blood pressure.

The watt-controlled supramaximal HIT protocol increased Vo_2peak similar to aerobic endurance training at moderate intensity, despite half the training time. This is in line with previous nonwork-matched all-out sprint interval training studies in young and middle-aged adults (40,41), and favors our supramaximal HIT protocol as a time-efficient option for older adults. Although the change in Vo2peak was observed irrespective of group, the underlying physiological adaptations in supramaximal HIT and MIT may differ. Although MIT is suggested to primarily affect central adaptations, the Vo_2peak improvements in HIT may be driven by both central and peripheral adaptations (15,42,43). The change in Vo2peak was lower than we had anticipated, and the possible explanations are the initial exercise intensity and the lack of Vo_2max-confirmation during the testing. To increase the tolerability of the supramaximal HIT protocol, the exercise intensity for participants in HIT started at 60% of their estimated maximum MPO[6], with individual progression after the third session. We preferred this setup over the use of a preconditioning period of MIT. However, to observe Vo_2peak changes similar to previous all-out sprint interval studies (22,44), a longer intervention may have been necessary to ensure that all participants progressed and exercised closer to their MPO[6] for a larger proportion of the intervention.

The lack of improvement in global cognitive function may be due to insufficient physiological changes from our 3-month intervention (1). Although the relationship between physical exercise and cognition is complex, physiological changes have been proposed to

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precede changes in cognition (45). Recent meta-analyses have found the largest effects following interventions with longer session and intervention duration (46,47), indicating a longer intervention may have been needed to observe a significant group-level change in global cognition. Furthermore, we observed large individual differences in response to cognition similar to previous studies (30,48), and further in-depth analyses in future studies will aim to identify factors relevant to responders and non-responders.

The moderate between-group difference in change in working memory performance, in favor of supramaximal HIT, may be explained by the combined improvement of $V\dot{O}_2$peak and muscular strength in the HIT group. Aerobic and resistance training have overlapping as well as specific physiological effects, and a meta-analysis has shown positive effects from both aerobic and combined exercise, as well as a domain-specific interaction effect of resistance training on working memory (46). As our supramaximal HIT protocol taps into both aerobic and anaerobic processes, this finding should be directly addressed in future studies. However, although the 95% CI (0.01, 0.64) for working memory was separate from 0, indicating a between-group difference in change, the statistical method used for computing the p value (36) indicated nonsignificance (p = .0502). The preferred method for testing significance in LMM estimates is a subject for debate (37), and this finding should therefore be interpreted with caution.

The observed negative effect on episodic memory performance across groups was in the opposite of the expected direction (49), because a previous study utilizing the same tests observed a positive effect on episodic memory after a 6-month aerobic exercise intervention at moderate intensity (30). Our finding would have been easier to interpret if we had included a nonexercising control group. Consequently, this negative change and its potential neural underpinnings need to be confirmed in future studies.

The modest reduction in blood pressure for the whole group may be explained by the mean blood pressure being within a normal range already at baseline. Although this effect can be considered clinically relevant (50), future studies should include participants with clinically high blood pressure in order to conclude if this HIT protocol is a time-efficient alternative to reduce high blood pressure.

The between-group difference in change in isometric knee extensor muscle strength suggests that supramaximal HIT elicits additional effects on muscular function compared to MIT. A potential explanation is that HIT recruits both low- and high-threshold motor units, whereas MIT mainly recruits low-threshold motor units (51). The improvements could also be explained by muscle hypertrophy, as a recent study observed moderate increases in muscle mass among participants aged 50–68 years, after only 8 weeks of 4-second sprint interval training (23).

Our results incentivize making this watt-controlled supramaximal HIT protocol for older adults available for more people, as it may result in clinically meaningful improvements in both cardiorespiratory fitness, cardiovascular, and muscular function. For example, an increase in VO2peak of 1 mL/kg/min is associated with a reduced risk of cardiovascular mortality (52), and improvements in lower-limb muscle strength is important for fall prevention and maintained functional performance in daily living (53). Furthermore, in contrast to previous concerns and arguments against supramaximal HIT for nonexercising older adults (25), we observed high attendance, low drop-out rates (<6%), and no serious AEs during 3 months of controlled supramaximal HIT. The practical elements of the supramaximal HIT protocol, such as conducting the training in groups in a gym setting and participants independently adjusting the resistance load, provide a foundation for future large-scale implementation.

Methodological strengths of the present study include the relatively large sample size for a randomized controlled trial evaluating supramaximal HIT in older people, and the randomization and blinding procedure which reduce selection bias and detection bias. Also, due to the difficulty of fully blinding both participants and supervisors in an exercise intervention, performance bias was instead limited by concealing the study hypothesis from the participants, and by using standardized criteria to adjust the exercise intensity. Including a broad spectrum of outcome variables allowed us to evaluate the exercise protocol on several different aspects. One such example is the extensive cognitive test battery capturing a wider range of cognitive abilities (28).

This study also has limitations. Our sample size estimate and expected effect size were based on previous research using nonactive or low-active control groups. This may have been overly optimistic considering our use of an active control group conducting exercise at an intensity previously shown to benefit both aerobic capacity and global cognition. Also, despite our aim to recruit nonexercising individuals, the baseline assessments of physical activity level revealed that some participants may have been more active than we intended. Still, the baseline mean $V\dot{O}_2$peak for the whole group was lower than similar studies for this age group (22), implying that our participants were relatively inactive. Further, by using Vo2peak to assess cardiovascular function, instead of criteria-based maximal oxygen uptake (Vo2max), there is a risk that some participants did not reach their true Vo2max during the assessments. Even though our sensitivity analysis based on age-adjusted $V\dot{O}_2$max criteria did not significantly change the results, there was a tendency toward a greater effect in favor of the stricter RER criteria.

Although we observed some essential group-level improvements, the descriptive plots for the primary outcomes displayed large interindividual variability in response to exercise for both groups. Further exploration of the characteristics of our exercise protocols in relation to individual response is needed, as it is plausible that different individuals receive the best adaptations from MIT, supramaximal HIT, or from a combination of both. The implications of this study are limited to the particular population sample, with adults aged between 66 and 79 years old without a history of significant cardiac or neurological disease (ie, nonexercising but otherwise relatively healthy). Future studies should examine whether our supramaximal HIT program is viable and safe for people with more severe functional impairments and diseases.

Conclusion

In nonexercising older adults, 3 months of supramaximal HIT with controlled target intensity had a positive effect on cardiorespiratory fitness and cardiovascular function to a similar extent as MIT, despite half the training time. The effects of supramaximal HIT on cognitive functions appear limited, though with a potential domain-specific effect on working memory compared to MIT. The supramaximal HIT program also revealed a superior improvement in muscular function. These results support the use of watt-controlled supramaximal HIT for older adults.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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Conflict of Interest

None declared.

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Author contributions

E.S. and S.S. drafted the manuscript. E.R., C.-J.B., N.L., H.H., B.J., and M.H. are responsible for the conception of the study and study design. E.R and C.-J.B. provided fund procurement. E.S., B.J., N.L., and M.H. participated in data collection. E.S. participated as a supervisor during the exercise intervention. Data analyses were carried out by E.S., S.S., and H.H., with H.H. responsible for blinded analyses of primary outcomes. E.R., C.-J.B., M.H., N.L., H.H., and B.J. critically revised the article for important intellectual content. All authors read and approved the final manuscript.

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