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## Accepted Manuscript

Title: Resistance training enhances delayed memory in healthy middle-aged and older adults: A randomised controlled trial

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**Title**

Resistance training enhances delayed memory in healthy middle-aged and older adults: A randomised controlled trial.

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**Abstract**

**Objectives:** High-intensity exercise is a potential therapeutic tool to postpone or prevent the onset of cognitive decline. However, there is a lack of sufficient evidence regarding the longitudinal effects of structured resistance training on cognitive function in healthy adults. The purpose of this study was to investigate the effect of two ecologically valid, intense 12-week resistance training programs on cognitive function in late middle-aged adults.

**Design:** Single-site parallel randomised controlled trial at the Department of Exercise Science strength and conditioning laboratory. Groups allocated by minimisation randomisation.

**Methods:** Forty-five healthy adults (age range=41-69 years) were enrolled and randomised into A.) high-load, long rest resistance training (n=14), or B.) moderate-load, short rest resistance training (n=15) twice per week for 12 weeks, or a non-exercising control (n=16). Follow-up within 7 days. Data were collected September 2016-December 2017. Cognitive function assessed using the CogState computerised battery. Assessors were blinded to participant group allocation. Secondary outcomes were maximal muscle strength and body composition.

**Results:** Forty-four participants were analysed in 2018. Delayed verbal memory performance was improved ( $p=0.02$ ) in resistance training groups ( $g=0.67-0.79$ ) when compared to the control group, with no differences between training groups. Likewise, increases in maximal muscle strength were observed ( $p<0.01$ ) in resistance training groups when compared to the control group, with no differences between training groups. No differences in body composition were observed. There were no adverse events or side-effects of the intervention.

**Conclusions:** 12 weeks of intense resistance training improves delayed verbal memory irrespective of training design (i.e., high-load vs. moderate-load).

**Trial registration:** This study is registered at [www.anzctr.org.au](http://www.anzctr.org.au) ACTRN12616000690459.

**Funding:** Department of Exercise Science student stipend.

**Keywords:** resistance training, cognitive function, middle-aged adults

## **Introduction**

Physical inactivity is amongst the greatest modifiable risk factors for progressive cognitive decline in ageing adults.<sup>1</sup> Within the literature, aerobic exercise demonstrates promise in postponing cognitive decline through reductions in vascular disease risk,<sup>2</sup> improved cognitive function,<sup>3-5</sup> and elevated expression of peripheral neurotrophins integral to the growth and maintenance of neural tissue.<sup>6</sup> While data surrounding the impact of aerobic exercise on cognitive function are growing,<sup>5-7</sup> limited data are available regarding the impact of resistance training on cognitive health. This is surprising given that most health organisations worldwide recommend older adults undertake regular resistance training,<sup>8,9</sup> and acute resistance exercise has been demonstrated to mediate the expression of neural-acting growth factors.<sup>10-12</sup> The lack of longitudinal studies examining the impacts of resistance training on cognitive health warrants additional research.

Similar to aerobic exercise,<sup>13</sup> the effects of resistance exercise on cognition are likely intensity-dependent,<sup>14</sup> and related specifically to the intensity of an entire session (i.e., session intensity) rather than the load intensity (i.e., percentage of repetition maximum [RM]) in isolation. Indeed, Chang and Etnier<sup>14</sup> demonstrated a linear relationship ( $p < 0.05$ ,  $r^2 = 11\%$ ) between session intensity and acute cognitive processing speed, and a positive association has been noted between session intensity and physiological mediators of cognitive function (i.e., brain-derived neurotrophic factor).<sup>10,15</sup> Furthermore, we recently reported a strong association ( $r = 0.70$ ,  $p < 0.01$ ) between serum neurotrophin expression and blood lactate concentration,<sup>10</sup> (a physiological

measure of exercise intensity<sup>16</sup>) following an intense session of 10RM resistance exercise with short inter-set recovery durations. Session intensity is complex, influenced by; the number of repetitions and sets performed, load intensity and the inter-set recovery duration.<sup>17</sup> As such, it is possible to design a resistance training session with greater session intensity using a moderate-intensity load (i.e., 60-70% of 1RM) with short inter-set recovery duration, when compared with a session using a high-intensity load (i.e., 80-90% of 1RM) and long inter-set recovery duration.<sup>17</sup>

In light of the limited evidence examining the impact of resistance training on cognitive function, the purpose of this study was to investigate the effect of theoretically work-matched, yet contrasting in session intensity, 12-week resistance training programs on cognitive function in late middle-aged adults. Resistance training was either moderate-load intensity with short recovery, or high-load intensity with long recovery; ecologically valid (i.e., resistance training approach that contributes to enhanced tolerability and adherence in ageing populations) resistance training methods to develop maximal muscle hypertrophy or strength, respectively. We hypothesised that cognitive function would improve in moderate-load intensity (i.e., high session intensity) and high-load intensity (moderate session intensity) resistance training groups when compared to a non-exercising control group. Further, we hypothesised that the moderate-load group would experience greater improvements in cognitive function when compared to the high-load group.

## **Methods**

This study was a single-site parallel randomised controlled trial in a cohort (n=45) of adults aged 41-69 years old. The outcomes of 12 weeks of resistance training were assessed via baseline, six-week (mid-intervention) and post-intervention testing for cognitive function, maximal muscle

strength and body composition in a high-load, moderate-load or control condition. Data were collected from September 2016-December 2017.

Individuals attended an initial screening visit to determine eligibility. During this visit, a trained rater assessed global cognitive abilities using the Montreal Cognitive Assessment (MoCA;<sup>18</sup>), whereby scores below 26 were considered outside a normal range and required study exclusion. Likewise, individuals were deemed ineligible if they; i.) presented with musculoskeletal disorders or injuries that would prevent resistance training, ii.) were categorised as high risk for adverse events by an adult pre-exercise screening tool,<sup>19</sup> or iii.) had partaken in resistance training within the prior six months. There was no racial or gender bias in the selection of participants. Apolipoprotein E (*APOE*) genotype was determined for each participant as carriage of at least one copy of the *APOE*  $\epsilon$ 4 allele (e.g.,  $\epsilon$ 3/ $\epsilon$ 4) predisposes an individual to a greater risk of cognitive decline and AD.<sup>20</sup> Genotype was utilised solely as a stratifying variable for group randomisation. Eligible participants were cognitively normal, categorised as low to moderate risk for moderate to intense exercise, and deemed untrained in resistance training.<sup>21</sup> Individuals were informed of the potential benefits and risks associated with participation and all participants provided written informed consent. The procedures of this study were approved by the institutional Human Research Ethics Committee and, therefore, were performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. This study complied with CONSORT guidelines (Supplementary File 1). Data were collected at the Murdoch University Mind and Body laboratory.

Participants attended a familiarisation session, two baseline sessions, one mid-intervention session and two post-intervention sessions. Within 10 days of completing the familiarisation session, participants attended a baseline assessment, where they completed a computer based

neuropsychological assessment and provided a fasted blood sample. No greater than 10 days following the first baseline session, participants completed a baseline maximal strength and body composition assessment. General self-reported physical activity at baseline and post-intervention was assessed by the seven-day retrospective International Physical Activity Questionnaire.<sup>22</sup> Participants were then randomised into one of three groups; i.) high-load intensity, long recovery, ii.) moderate-load intensity, short recovery, or iii.) non-exercising control. At six weeks during the 12-week intervention, participants completed a single testing session to re-assess body composition only. Within seven days post-intervention, participants completed two testing sessions under the same conditions as the baseline assessments.

During the familiarisation visit, participants were instructed in regards to correct lifting technique for all exercises, and performed light-load repetitions for each. Weights machines were adjusted appropriately for each participant, and were recorded to allow consistency between maximal strength testing time-points.

The intervention comprised of 12 weeks of resistance training, or a non-exercising control condition for comparison, whereby participants were encouraged to maintain their typical lifestyle habits. Participants randomised to an exercise condition performed either high-load or moderate-load resistance training twice per week for 12 weeks at the Murdoch University Strength and Rehabilitation Laboratory. The high-load protocol consisted of five sets of five repetitions of bench press, leg press, lat pull-down and leg curl at a load intensity of 85% of 1RM, recorded during the baseline maximal strength assessment, and resting passively for 180s between sets. The moderate-load protocol consisted of three sets of 10 repetitions at a load intensity of 70% of 1RM, and resting passively for 60s between sets. The sets, repetitions and percentage of 1RM of the high-load and moderate-load protocols were designed such that they were theoretically work-matched *a priori*.



Each training session commenced with a five-minute rowing ergometer warm-up at a self-selected intensity, and a single set of 10 repetitions at 50% of 1RM prior to each exercise. Resistance was progressively increased by 2.5-5% as per individual tolerance, and no greater than 10% per week, using the 2-for-2 progression method (i.e., on two consecutive training sessions, progression is recommended if two or more repetitions can be performed on the last set of an exercise).<sup>23</sup>

We assessed cognitive function using the CogState (CogState Ltd, Melbourne, Australia) computerised battery, administered by a trained rater. The battery is comprised of tasks in the following order: i.) international shopping list learning (ISL-learning; immediate verbal memory), ii.) Groton Maze learning (GML; problem solving), iii.) detection (DET; processing speed), iv.) identification (IDN; attention and vigilance), v.) One Card Learning (OCL; visual memory), vi.) One-Back Task (ONB; working memory), vii.) continuous paired associate learning (CPAL; visual memory), viii.) Groton Maze recall (GMR; visual memory) and ix.) international shopping list recall (ISL-recall; delayed verbal memory).

Maximal strength was assessed via a 1RM test for bench press, leg press, lat pull-down and leg curl within a single visit in order of mention. Warm-up sets were performed as per a previous methodology.<sup>23</sup> Participants were instructed to lift a pre-determined resistance, aiming for a single repetition through full range of motion. Successful attempts were adjusted in small increments until either the researcher was required to intervene for assistance, exercise technique was compromised, or full range of motion was not achieved. Participants rested for 120-240s between each 1RM attempt to ensure maximum recovery. All 1RM assessments were conducted by the same rater.

Body composition assessed via dual-energy x-ray absorptiometry (Discovery™, Hologic®, Marlborough, MA, U.S.A) determined total fat mass, total lean mass and total appendicular lean mass.

A fasted 4.0 ml venous blood sample was collected from the antecubital vein. Whole blood was prepared into 200 µl aliquots and frozen at -80° C. DNA was extracted from whole blood as per manufacturer instructions using QIAamp DNA Blood Mini Kits (Qiagen, Hilden, Germany). Genotyping was performed as described previously.<sup>24,25</sup> Briefly, TaqMan® genotyping assays were used to determine apolipoprotein E (*APOE*) genotype (Life Technologies, Carlsbad, CA, U.S.A.) and were performed on a QuantStudio 12K Flex™ Real-Time-PCR system (Applied Biosystems, Foster City, CA, U.S.A.) using the TaqMan® GTXpress™ Master Mix (Life Technologies) methodology as per manufacturer instructions.

Participants were enrolled into the study, and randomly allocated to one of three experimental groups using minimisation randomisation software (QMinim;<sup>26</sup>) following baseline assessment. Randomisation was stratified by age, sex and *APOE* ε4 allele carriage (i.e., carrier of at least one ε4 allele or a non-carrier) at an equal ratio (Table 1). A third party not involved in the project was responsible for randomising each participant to a group. Research personnel conducting cognitive assessments were blinded to the group allocation of each participant.

The sample size was based upon pilot data of changes in cognitive function (via the CogState assessment battery) following high-intensity aerobic training. A moderate effect (Cohen's  $d=0.68$ ) was observed in the change in CPAL performance following 12 weeks of high-intensity cycling when compared to moderate-intensity cycling. Assuming  $d=0.68$ ,  $\beta=0.20$ ,  $\alpha=0.05$  and comparison across three groups, we required a sample size of 45 participants (15 per group).

Maximal strength measurement reliability between baseline and post-intervention sessions was determined for the control group participants from ICCs; an ICC greater than 0.90 was interpreted as excellent reliability.<sup>27</sup> Integrity of the cognitive variables was assessed using accuracy as a criterion (i.e., accuracy less than 50% to 90% depending on the task). Values violating data integrity criteria as per CogState guidelines were removed prior to analysis. Due to the number of cases not meeting the criteria for DET (n=21), IDN (n=10) and OCL (n=10) tasks, these tasks were excluded from analysis. Baseline characteristics across groups were compared using a one-way analysis of variance (ANOVA) for continuous variables and chi-square for categorical variables. Self-report physical activity levels within the control group at baseline, six weeks and post-intervention were analysed using a one-way repeated measures ANOVA. Differences between groups for changes (i.e., baseline to post-intervention change) in maximal strength, body composition and cognitive function were assessed using an analysis of covariance (ANCOVA) incorporating the baseline value of each variable as a covariate. Age, sex, and *APOE*  $\epsilon 4$  carriage were not incorporated as covariates as they were included as stratifying variables for randomisation. A Sidak adjustment was applied for multiple pairwise comparisons. Statistical analyses were performed using SPSS analytical software (Version 24, IBM®, U.S.A) with a significance of  $p < 0.05$ . Hedge's  $g$  effect sizes and 95% confidence intervals (CI) were calculated to represent the magnitude of difference in cognitive outcomes between groups. Data are presented as mean  $\pm$  SD unless otherwise noted. Data were analysed in 2018.

## Results

Total session attendance was 93.5% for high-load (1.6 $\pm$ 1.2 missed sessions) and 95.8% for moderate-load (1.0 $\pm$ 1.1 missed sessions). Total session compliance was 99.7% for high-load

(7.1±18.2 missed repetitions) and 99.3% for moderate-load (4.3±9.6 missed repetitions). No adverse events occurred as a consequence of the intervention, and no side-effects of exercise training were reported. Of the 45 individuals recruited, 44 completed the post-intervention testing (Supplementary File 1; one withdrawal from the control group due to time restrictions).

There were no significant differences between continuous variable characteristics at baseline (Table 1). As expected, chi-squared tests revealed no differences in the distribution of *APOE* ε4 carriers ( $\chi^2=0.14$ ) or sexes ( $\chi^2=0.21$ ) between groups. The cognitive outcomes from baseline to post-intervention are detailed in Table 2. The ANCOVA revealed greater change in ISL-recall correct responses in high-load ( $p=0.02$ ;  $g=0.67$  [95% CI:  $g=0.06-1.28$ ]) and moderate-load ( $p=0.02$ ;  $g=0.79$  [95% CI:  $g=0.23-1.35$ ]) when compared to control, with no difference ( $p=0.99$ ;  $g=0.05$  [95% CI:  $g=-0.68-0.79$ ]) between high-load and moderate-load groups observed (Figure 1). No differences in changes from baseline to post-intervention on the CPAL, Groton Maze learning and recall or One Back task were observed between groups.

Maximal strength assessments for the control group demonstrated high agreement between baseline and post-intervention visits (ICC=0.995; 95% CI:0.991-0.997). No differences were observed in baseline maximal strength between groups in any exercise (Table 1). Following the 12-week intervention period, changes in maximal strength for the bench press were greater ( $p<0.01$ ) in high-load (9.7±2.8 kg [33.1±11.6%]) and moderate-load (7.0±3.9 kg [25.0±12.0%]) when compared to the control group (0.1±2.1 kg [-0.2±6.2%]), with no difference ( $p=0.06$ ) between high-load and moderate-load groups observed. Likewise, changes in maximal leg press strength were greater ( $p<0.01$ ) in high-load (39.1±18.0 kg [40.7±23.4%]) and moderate-load (36.7±20.2 kg [35.3±13.9%]) groups when compared to the control group (5.4±4.8 kg [5.5±5.0%]), with no difference ( $p=0.99$ ) between the high-load and moderate-load groups. Lat

pull-down maximal strength changes were greater ( $p<0.01$ ) in high-load ( $8.1\pm 2.9$  kg [ $23.3\pm 10.5\%$ ]) and moderate-load ( $5.6\pm 3.1$  kg [ $15.5\pm 9.0\%$ ]) groups when compared to the control group ( $-0.2\pm 2.5$  kg [ $-0.6\pm 7.8\%$ ]), with no difference ( $p=0.09$ ) between the high-load and moderate-load groups. Finally, changes in leg curl maximal strength were greater ( $p<0.01$ ) in high-load ( $7.8\pm 4.8$  kg [ $17.5\pm 11.2\%$ ]) and moderate-load ( $11.3\pm 5.8$  kg [ $27.8\pm 15.7\%$ ]) groups when compared to the control group ( $0.2\pm 4.7$  kg [ $-0.4\pm 9.5\%$ ]), with no difference ( $p=0.17$ ) between the high-load and moderate-load groups observed.

No differences in fat mass or lean mass were observed between groups at baseline (Table 1). Following the 12-week intervention period, changes in fat mass were not different ( $p=0.87$ ) between high-load ( $-0.1\pm 1.3$  kg), moderate-load ( $-0.3\pm 1.7$  kg) or control ( $-0.1\pm 1.5$  kg) groups. Likewise, no differences ( $p=0.51$ ) in total lean mass change were observed between high-load ( $0.3\pm 1.5$  kg), moderate-load ( $0.1\pm 1.4$  kg) or control ( $-0.3\pm 1.2$  kg) groups. No differences ( $p=0.34$ ) in appendicular lean mass changes were observed between high-load ( $0.1\pm 0.7$  kg), moderate-load ( $0.4\pm 0.7$  kg) or control ( $0.1\pm 0.5$  kg).

There were no differences between groups for baseline to post-intervention change in self-reported physical activity ( $p=0.63$ ) between high-load ( $-666.4\pm 284.1$  MET-min-week<sup>-1</sup>), moderate-load ( $-325.6\pm 272.3$  MET-min-week<sup>-1</sup>) or control ( $-342.9\pm 271.9$  MET-min-week<sup>-1</sup>) groups

## Discussion

The purpose of this study was to examine the influence of 12 weeks of intensive resistance training on cognitive function in healthy late middle-aged adults. We utilised two different methods of resistance training to determine whether resistance training intensity plays a role in enhancing

cognitive function. Here, we report participants undertaking a resistance training intervention demonstrated greater improvements in delayed verbal memory (regardless of specific resistance training condition), compared with the control group.

We hypothesised a stronger effect of resistance training on cognition in the moderate-load (i.e., high session intensity) group compared with the high-load (i.e., moderate session intensity) group, based on the notion that high-intensity exercise is more effective in enhancing cognitive health than moderate- and low- intensity exercise. Contrary to our hypothesis, participants improved in delayed verbal memory performance irrespective of resistance training condition, when compared to control (Figure 1). This is one of few resistance training studies to demonstrate significant between-group improvements in delayed verbal memory performance in healthy adults, when compared with a non-exercising control group.<sup>28</sup> The observed difference in ISL-recall across groups was in contrast to ISL-learning performance, in which no differences were noted. Memory consists of four sub-stages occurring largely in the hippocampus; acquisition, formation (consolidation), storage and retrieval.<sup>29</sup> In the context of our investigation, the ISL-learning task likely represents memory acquisition and formation, while the ISL-recall task likely represents the latter stage of memory retrieval. Therefore, our findings indicate that intense resistance training can influence memory; yet, the influence is not consistent across all memory domains.

In this study, we have demonstrated that, in a group of healthy late middle-aged adults, intense resistance training can positively influence delayed memory recall. The two resistance training protocols used in this study were designed to provide intense training sessions consistent with muscular hypertrophy (moderate-load) or strength gains (high-load). By design,<sup>17</sup> the session intensity of the moderate-load condition was greater than the high-load condition; however, no differences were noted between intensity conditions for any of the cognitive outcomes. It is

possible that we underestimated the difference in session intensity between the two protocol designs.<sup>30</sup> A competing and more likely argument is that, similar to recent findings in our laboratory,<sup>17</sup> the short rest durations in the moderate-load condition did, as anticipated, result in a greater session intensity compared with the high-load condition. However, the lack of differences in ISL-recall measure between the moderate-load and high-load conditions reflects a possible ‘intensity threshold’ through which memory is influenced; beyond this threshold no additional benefits are provided. Though, we concede that cognitive health is more complicated than cognition in isolation. For instance, contributing factors that promote later life cognitive decline (i.e., vascular disease or type 2 diabetes mellitus)<sup>31</sup> may indeed benefit from additive session intensity whilst demonstrating no measureable change to cognitive function.

This study provides important information on the impact of intense resistance training on delayed memory recall; however, we do acknowledge limitations to the study that may have impacted our outcomes. The participants we recruited were high functioning adults with an average education of 14.8 yr (high-load), 17.7 yr (moderate-load) and 16.7 yr (control), and average MoCA score of 27.8 (high-load), 28.3 (moderate-load) and 27.7 (control). Although mean total years of education and MoCA score were not different between groups, it is possible that participants were capable of performing a number of the cognitive tasks proficiently at baseline; thus, limiting the potential for post-intervention improvements (i.e., a ceiling effect). We also note that 12 weeks of resistance training remains a relatively acute period. In healthy adults, it is possible that improvement in short-term memory or attention takes months or even years to manifest in a measurable difference. Despite detecting a significant improvement in ISL recall performance following the interventions, the direct clinical relevance in terms of contribution to long-term cognitive health remains to be determined. Intervention studies utilising a long-term

follow-up will be essential in determining the whether exercise-induced neural changes are associated with decreasing risk of dementia. Finally, there was no measure of dietary habits in this investigation. As intake of certain foods may be protective (e.g., flavonoids) or detrimental (e.g., refined sugar) to long-term cognitive health, diet should be a consideration for future studies. The current study also has strengths that provide us with confidence in our research findings. These strengths include a carefully designed intervention administered in a controlled exercise lab setting, a well-characterised cohort and a comprehensive neuropsychological battery.

## **Conclusions**

Cognitive decline is a hallmark symptom of ageing and neurodegenerative disease. In cognitively healthy late middle-aged adults, 12 weeks of intense resistance training improves short-term memory irrespective of the training approach. Based on our findings, intense moderate- to high-load resistance training should be considered in programs aiming to enhance short-term memory.

## **Practical Implications**

- Intensive resistance training twice per week for 12 weeks improves delayed verbal memory in healthy late middle-aged adults.
- If sufficiently intense, high-load ( $5 \times 5$  at 85% of 1RM) or moderate-load ( $3 \times 10$  at 70% of 1RM) training methods are likely to stimulate cognitive improvement.
- Resistance training should be based upon maximal strength data such as the 1RM implemented here to accurately design an intense training stimulus.

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ACCEPTED MANUSCRIPT

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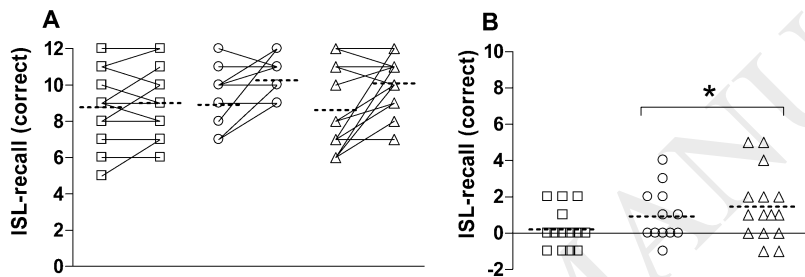
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### Figure captions

**Figure 1:** A) Paired pre-post intervention comparisons about the mean (---) for total correct responses during the International Shopping List recall (ISL-recall) task in control ( $\square$ ), high-load ( $\circ$ ) and moderate-load ( $\triangle$ ) groups, and B) Mean pre-post intervention differences about the mean (---) for total correct answers given during the ISL-recall task in control ( $\square$ ), high-load ( $\circ$ ) and moderate-load ( $\triangle$ ) groups. \*Greater than control group  $p=0.02$  (ANCOVA pairwise comparisons).



**Table 1:** Baseline characteristics of high-load (HL), moderate-load (ML) and non-exercising control (CON) groups.

Variable	CON (n = 15) Mean (SD)	HL (n = 14) Mean (SD)	ML (n = 15) Mean (SD)	Difference (p)
Age, yr*	59.1 (7.4)	55.2 (6.8)	58.0 (5.5)	0.28
<i>APOE</i> $\epsilon$ 4, % (n)*	46.6 (7)	42.8 (6)	40.0 (6)	0.93
Female, % (n)*	80.0 (12)	85.7 (12)	80.0 (12)	0.90
Height, cm	164.2 (9.3)	166.2 (4.6)	167.0 (9.0)	0.64
Mass, kg	73.4 (13.3)	71.5 (13.0)	69.2 (12.0)	0.66
BMI, kg·m <sup>2</sup>	27.3 (4.4)	25.9 (4.2)	24.9 (4.1)	0.30
Total fat mass, kg	24.6 (8.0)	22.6 (7.1)	21.5 (7.8)	0.54
Total lean mass, kg	42.8 (8.7)	42.8 (7.9)	41.8 (9.2)	0.93
APN lean mass, kg	19.6 (5.0)	19.4 (4.0)	19.1 (5.2)	0.96
IPAQ, MET-min-week	3073.8 (1621.3)	3858.3 (2270.3)	3006.3 (2340.4)	0.51
Education, y	16.7 (4.1)	14.8 (3.6)	17.7 (4.8)	0.18
MoCA, score	27.7 (1.1)	27.8 (1.0)	28.3 (1.0)	0.26
1RM BP, kg	29.6 (12.2)	31.3 (10.8)	30.3 (14.7)	0.93
1RM LP, kg	114.2 (43.8)	107.0 (40.7)	102.7 (36.5)	0.73
1RM LT, kg	38.2 (11.1)	37.1 (9.5)	39.5 (15.3)	0.87
1RM LC, kg	49.5 (16.2)	48.4 (15.4)	44.2 (16.2)	0.64

*Note:* Differences across groups were determined by ANOVA for continuous variables and chi-square for categorical variables. **APOE** = Apolipoprotein E, **APN** = appendicular, **BMI** = body mass index, **BP** = bench press, **IPAQ** = International Physical Activity Questionnaire, **LC** = leg curl, **LP** = leg press, **LT** = lat pulldown, **MoCA** = Montreal Cognitive Assessment, **RM** = repetition maximum, **SD** = standard deviation. \*Included as stratifying variables for randomisation by minimisation.



**Table 2:** Mean ( $\pm$  standard deviation) baseline cognitive function values and mean changes from baseline to post-intervention.

Variable	CON (n = 15)		HL (n = 14)		ML (n = 15)		ANCOVA <sup>†</sup>
	BL	BL-POST $\Delta$	BL	BL-POST $\Delta$	BL	BL-POST $\Delta$	Group (p)
CPAL (total errors) <sup>a</sup>	124.1 (40.2)	-26.2 (48.9)	118.0 (62.8)	-21.8 (68.2)	100.8 (66.3)	-24.1 (55.3)	0.89
Groton Maze							
Learning (total errors) <sup>a</sup>	60.8 (8.2)	-9.6 (15.1)	56.6 (8.2)	-6.8 (14.2)	55.5 (7.9)	-10.2 (14.0)	0.58
Recall (total errors) <sup>a</sup>	10.9 (2.1)	-1.1 (5.5)	8.9 (2.1)	0.7 (6.0)	8.4 (2.3)	-1.2 (4.6)	0.52
One Back (lmm) <sup>a</sup>	1.324 (0.065)	-0.049 (0.089)	1.361 (0.048)	0.003 (0.063)	1.318 (0.059)	-0.036 (0.099)	0.61
ISL							
Learning (total correct) <sup>b</sup>	8.9 (0.7)	-0.2 (4.0)	8.6 (0.7)	0.8 (3.1)	8.6 (0.7)	1.7 (4.4)	0.48
Recall (total correct) <sup>b</sup>	8.7 (1.0)	0.2 (1.1)	8.9 (1.5)	1.4 (2.1)*	8.6 (1.2)	1.5 (1.9)*	< 0.01

*Note:* ANCOVA = analysis of covariance, BL = baseline, BL-POST  $\Delta$  = baseline to post-intervention change, HL = high-load resistance training group, CON = control group, CPAL = continuous paired associate learning, ISL = international shopping list task, lmm = Log<sub>10</sub> milliseconds, ML = moderate-load resistance training group. <sup>†</sup>Baseline score included as covariate for ANCOVA.

<sup>a</sup>Lower values indicated greater performance. <sup>b</sup>Higher values indicate greater performance. \*Greater than CON group p=0.02 (ANCOVA pairwise comparisons).