

A 4-week endurance training program improves tolerance to mental exertion in untrained individuals

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Objectives: The aim of this study was to investigate whether 4 weeks of endurance training could 30 31 improve tolerance to mental exertion in untrained participants. Design: Longitudinal training study. 32 Method: Twenty untrained young adults (14 F, 6 M; 27.6±6.2 years) completed a 4-week training 33 protocol in a randomised and counterbalanced order. Baseline and follow-up assessment were 34 conducted over three sessions in the week preceding and following the training period. During session 1, participants completed an incremental maximal ramp test. During sessions 2 and 3 participants 35 36 completed a 15 min cycling time trial preceded by either a mental exertion or control conditions. 37 Following baseline assessments, participants were randomised into a physical training or placebo 38 group that completed the training intervention thrice weekly over four weeks. **Results:** The physical 39 training resulted in increases in VO₂peak relative to the placebo group (p=0.003). Linear mixed 40 models utilising the control condition time trial performance as a covariate found the physical training group increased their time trial distance following the mental exertion condition to a greater extent 41 42 than the placebo group (p=0.03). RPE during the time trial and perceptual measures of mental exertion did not significantly change between groups (all p>0.10) although interaction effects were observed 43 44 when considering the RPE-power output relationship during the time trial. Conclusions: Four weeks 45 of endurance training increased tolerance to mental exertion in untrained participants during a subsequent physical performance, but not during prolonged cognitive performance. This finding 46 47 suggests that the ability to tolerate mental exertion is trainable in at least some contexts and highlights 48 the far-reaching benefits of endurance training.

49 Keywords: mental fatigue, endurance training, resilience, brain adaptations, cycling

50 **Practical implications**

51 The ability to tolerate mental exertion appears to be trainable, highlighting that endurance 52 training could have potential benefit not only in sports, but also in many sporting, 53 occupational, and military settings.

54 A reduction in mental fatigue could improve physical work capacity and, consequently, 55 encourage the use of physical exercise as a good practice in many occupational contexts.

56 Introduction

Endurance exercise training results in adaptations to the neuromuscular, metabolic, cardiovascular, respiratory and endocrine systems as reflected in improvements in key parameters of aerobic fitness, exercise economy and lactate/ventilatory threshold¹. Aside from these traditional, peripherally-based adaptations, endurance exercise is linked to cognitive benefits^{2,3} as well as structural⁴ and functional changes in the brain⁵. These observations appear consistent with adaptations that, among other benefits, would confer improved efficiency and/or capacity for mental work. Brain adaptations to physical training could therefore also be important in our resistance to mental fatigue.

Acute mental fatigue is defined as a psychobiological state that may arise during or after prolonged 64 cognitive activities; it is characterized by feelings of tiredness or exhaustion, and a decreased 65 commitment and increased aversion to continue the current activity⁶. Acute mental fatigue has an 66 adverse effect on cognitive function^{7,8} and endurance performance⁹. Mental fatigue appears to impair 67 endurance performance through an increased perception of effort during subsequent physical 68 exercise⁹. However, a physiological reason for an increase in perceived exertion has, to date, only been 69 postulated¹⁰. Beyond the physiological mechanism of mental fatigue, it is important to understand 70 71 whether the ability to resist mental fatigue is associated with a genetic predisposition or displays a trainable phenotype. In a recent study, we observed an impairment of endurance performance 72 73 (measured as distance covered during a cycling time trial) after mental exertion in recreational and under 23 but not in professional cyclists^{11,12}. In addition, the professional cyclists performed better 74 75 during the cognitive challenge than recreational athletes, suggesting a potential association between 76 resistance to mental fatigue and cognitive capacity in this context. This observational snapshot of 77 cohorts does not, however, distinguish between heritability and trainability.

To date, no studies have investigated the effect of endurance training on the ability to tolerate mental exertion. Therefore, the primary aim of this study was to determine whether 4 weeks of endurance training could improve tolerance to mental exertion, as determined by the difference in time trial cycling performance after a mental exertion task compared to a control condition, in previously

untrained participants. We also sought to investigate if this physical training would have a measurable impact on cognitive function. The physical training group was compared to a placebo intervention group that watched a series of documentaries with recall questions to replicate the contact time of the training group, but not the physical demands.

86

87 Materials and methods

Twenty initially untrained participants completed the study. Although twenty-two originally 88 89 volunteered, two participants withdrew due to personal reasons after the first visit. Participants 90 confirmed that they were not involved in regular vigorous physical activities (≤ 2.5 hours of 91 moderate/vigorous physical activity per week) and completed a pre-exercise screening (Exercise and 92 Sport Science Australia Adult Pre-Exercise Screening Tool) before entering the study. Participants 93 were excluded from enrolling in the study if they declared any medical condition or injury that would 94 prohibit them from completing the physical components of the study, had a diagnosed sleep disorder, 95 known colour-vision impairments, or were shift-workers. The study design and procedures were approved by the University of Canberra Human Research Ethics Committee (HREC-2018-76) and 96 followed the ethical principles for medical research involving human participants set by the World 97 98 Medical Association Declaration of Helsinki. Participants were provided with written instructions 99 outlining the procedures and risks associated with the study and gave informed written consent.

A randomised counterbalanced design was used. Group, physical training or placebo group, and order of the experimental treatments, mental exertion or control conditions, were randomly assigned based on balanced permutations generated by a web-based computer program. While participants were aware of their allocation to the physical training or placebo group, they were blinded to the true aims of the study. Participants were told the study sought to compare the effects of a physical and a mental training program on cycling time trial performance.

An overview of the experimental protocol is shown in Figure 1. Participants attended the laboratory on
eighteen occasions over six weeks. During baseline (week 1) and follow up (week 6), participants

108 completed the same three sessions. During the first session, weight and height were assessed before 109 participants completed an incremental maximal test on an SRM cycle ergometer (High-Performance Ergometer, Schoberer Rad MeBtechnik, Germany) to determine peak oxygen consumption and heart 110 111 rate. The test began with a 3 min stage at 50 W, then increased by 25 W every minute to volitional 112 exhaustion. Participants were then familiarised with the procedures and measures employed during the 113 next two sessions. During the second and third visits participants completed either the mental exertion 114 or control condition in a randomised counterbalanced order. During the mental exertion condition, 115 participants completed a cognitive task which aimed to assess cognitive performance, induce a state of 116 mental fatigue, and provide manipulation checks. This task consisted of 90 min of computerised 117 cognitive tasks presented on a laptop using specialist software (E-Prime, Psychology Software Tools 118 Inc., United States). The task was divided into three parts: a) an initial 45-min cognitive battery 119 assessing cognitive domains including working memory, response inhibition and task-switching; b) a 40-min modified incongruent Stroop colour-word task¹¹; and c) 5-min of the same task-switching 120 (flanker) task as in the cognitive battery. The 45-min cognitive battery comprised four different tasks: 121 1) 15-min of the flanker task¹³; 2) 10-min of a go/no-go task¹⁴; 3) 10-min of a 2-back task¹⁵, and; 4) 122 10-min of a working memory task¹⁶. Further details of the cognitive tasks and assessments are 123 124 available in the supplementary material (Supplementary material 1). After the mental exertion 125 condition, participants recorded their subjective sensation of mental fatigue and motivation toward the 126 upcoming physical endurance test using a visual analogue scale (VAS). Participants marked their 127 response on a 10 cm line anchored by 0 (no mental fatigue at all) and 100 (maximal mental fatigue), and 0 (no motivation at all) and 100 (maximal motivation) for the mental fatigue and motivation scales 128 129 respectively. Participant responses were measured from the left anchor and expressed in mm. 130 Participants recorded subjective workload of the mental exertion condition using the National Aeronautics and Space Administration Task Load Index scale (NASA-TLX)¹⁷. Participants completed 131 132 the NASA-TLX immediately after the other perceptual scales.

133 During the control condition participants watched a white screen for 15 min. At the end of the task, 134 they were required to record their subjective sensations of mental fatigue, motivation and workload, as 135 described following the mental exertion condition.

136 Within 10 min of the completion of the mental exertion and control conditions participants performed a 3 min standardised cycling warm-up followed by a 15 min time trial using an SRM cycle ergometer. 137 138 The ergometer was setup to replicate the participants' preferred bike position in the initial session and 139 replicated thereafter. Participants were instructed to cover as much distance as possible during the 15 min. A timer was placed in front of participants and remained visible during the time trial. Participants 140 141 were blinded to all other performance and physiological data. A member of the research team who was 142 blind to the experimental treatment received by the participants provided standardised verbal encouragement during the time trial. Heart rate was recorded at the end of the warm-up, and during the 143 final 15 s of every 3rd minute throughout the time trial using a heart rate monitor. At the same time 144 points, a rating of perceived exertion (RPE) was recorded using the Borg 6-20 scale¹⁸. Mean values for 145 146 power, speed and cadence were calculated for each 3 min block of the time trial, and the total distance 147 calculated using the speed recorded by the ergometer.

148 For both the physical training and placebo groups, the intervention took place during weeks 2-5 149 (lasting 4 weeks). The physical training group completed 3x60 min sessions per week on an air-braked 150 cycle ergometer (Wattbike Pro Trainer, Wattbike Ltd, United Kingdom). Each week training consisted of: a) 1x60 min at 65-70% of the peak heart rate recorded during the incremental maximal ramp test; 151 152 b) 1x20 min at 65-70%, plus 6x3 min at 85-90% of the peak heart rate, with 2 min of active rest 153 between repetitions; and c) 1x20 min at 65-70% followed by 40 min at 75-80% of the peak heart rate. 154 During each session, heart rate, power output and cadence were recorded, and participants provided a 155 session RPE (Supplementary material 2). The placebo group attended the laboratory on the same 156 number of occasions and for the same duration as the physical training group. However, participants 157 watched an assortment of documentaries lasting approximately 50-60 min sourced from local free-to-158 air broadcasting. The documentaries were viewed by the research team prior to the start of the study 159 and were chosen so that they were interesting but not likely to generate strong emotive responses. To

ensure that the participants attended to the documentary, at the end of each viewing participants were
asked to answer four simple questions pertaining to the content of each video (participants' maximum
mistake rate was 1 out 4).

All the testing and intervention sessions were performed in an isolated air-conditioned room (20 ± 1) °C). Prior to each visit, participants were instructed to sleep for at least 7 h, refrain from the consumption of alcohol and caffeine, and avoid any vigorous exercise the day before visiting the laboratory. Participants were also instructed to avoid any mentally demanding tasks on the day of the training and testing sessions. Each participant carried out the sessions individually and at the same time of day (within 1 h period, between 9:00 and 13:00).

Statistical analysis was conducted with R version $3.4.2^{19}$. The mean and standard deviation of the 169 170 outcome measures at baseline and follow up were calculated for each group. Group differences in 171 baseline characteristics were assessed with Chi-square tests for categorical data and t-tests for continuous data. To investigate intervention effects, data were analysed by General Linear Mixed 172 Models with a random intercept fitted for participants to take into account the repeated measures 173 nature of the data and interindividual variability using the lme4 package²⁰. For each model, the 174 175 dependent variable was the outcome measured during the mental exertion condition. The independent 176 variables were time (baseline and follow up) and group (training and placebo) with the corresponding 177 control condition outcome as a covariate. The interaction terms between group and time were included 178 in each model. A significant interaction term indicated the change from baseline to follow up was 179 different by group. Visual inspection of QQ-plots generated for each model showed no obvious 180 deviations from normality. Statistical significance was accepted at p<0.05.

181

182 **Results**

Participants were similar between groups at baseline regarding anthropometric characteristics, VO_{2peak} and distance covered during the time trial (Table 1). At baseline, participants completed significantly less distance following the mental exertion condition compared to the control condition (mean diff: -

186 223 m; 95% CI: -137 to -309; p<0.001). Using the NASA-TLX scale, participants reported that the 187 mental exertion condition was more mentally demanding (mean diff: 6.4; 95% CI: 5.5 to 7.4; p<0.001) 188 than the control condition. The VAS scales showed mental fatigue (mean diff: 53 mm; 95% CI: 42 to 189 65; p=0.001) was significantly greater, while motivation (mean diff: -3 mm; 95% CI: -12 to 7; p=0.55) 190 was not significantly different, following the mental exertion condition compared to the control 191 condition.

192 There was a group*time interaction for VO_{2peak} (F_{18,1}=11.29; p=0.003), such that the physical training 193 group improved significantly more than the placebo group (b=3.8 ml·min⁻¹·kg⁻¹; 95% CI: 1.6 to 6.0).

The primary outcome measure was time trial distance following the mental exertion condition. Distance covered in the control condition was included in the model as a covariate to account for differences in time trial performance between groups following the intervention period. There was a significant group*time interaction ($F_{19,1}$ =5.66; p=0.03; Figure 2) and examination of the fixed effects showed the physical training group improved time trial distance in the mental exertion condition significantly more than the placebo group (b=264 m; 95% CI: 211 to 476).

200 RPE, power, and power relative to RPE, measured at each 3-min split during the time trial following mental exertion was then investigated (Supplementary material 3). To account for the structure of this 201 202 data, time trial split was initially included in the models as a three-way interaction with group and 203 time, with the control condition outcomes included as a covariate. Non-significant interaction terms 204 were dropped from the final models for ease of interpretation. Firstly, there were no significant 205 group*time*split interactions for RPE, power or power relative to RPE (all p>0.70). For RPE there 206 were no significant two-way interaction effects (all p>0.20). For power, the physical training group 207 improved during the mental exertion time trial to a greater extent than the placebo group (group *time: 208 F_{181.1}=20.86; p<0.001; b=16.12 watts; 95% CI: 8.76 to 22.82). Finally, the physical training group 209 increased power relative to RPE at iso-time (group*time: F_{179.1}=39.91; p<0.001; b=1.60 watts/RPE; 210 95% CI: 1.08 to 2.08) to a greater extent than the placebo intervention, indicating that participants in

the physical training group produced a higher power output for the reported RPE following the mentalexertion condition.

For the NASA-TLX scale, there were no significant group*time interactions for the mental demand ($F_{18,1}=2.20$; p=0.16), temporal demand ($F_{18,1}=1.39$; p=0.25), physical demand ($F_{18,1}=1.98$; p=0.18), performance ($F_{18,1}=0.05$; p=0.81), effort ($F_{18,1}=0.04$; p=0.85), or frustration ($F_{18,1}=0.16$; p=0.69) subscales. For the VAS, there were no significant group*time interactions for sensation of mental fatigue ($F_{17,1}=1.17$; p=0.29) or motivation ($F_{18,1}=0.54$; p=0.47) prior to completing the time trial in the mental exertion condition.

219 There were no significant group*time interactions for the cognitive performance outcomes220 (Supplementary material 4).

221

222 Discussion

The main finding of this study was that a 4-week physical endurance training program increased tolerance to mental exertion, showing an improved physical performance after a mental exertion condition compared to a placebo group. Further, power output during the time trial was higher for the reported RPE after the intervention period in the mental exertion condition, suggesting central as well as peripheral adaptations to the physical training. No other differences were found between the physical training and placebo groups for other perceptual or cognitive performance measures.

As expected, the endurance training protocol was effective in improving VO₂peak and performance in the cycling time trial. This improvement was accompanied by an increase in mental exertion tolerance in the physical training group, reflected in an almost negligible time trial performance decrement after the mental exertion condition following the physical training intervention. In the placebo-based intervention the mental exertion condition induced a similar reduction in time trial performance at both time points. Although this study was relatively small (n=10 in each group), our primary interaction effect has a large effect size (effect size calculated from F value, Cohen's d=1.122) and thus its

236 practical meaning appears robust. To our knowledge, our study is the first to show that a physical endurance training program can increase resilience to prior mental exertion in this manner. We suggest 237 238 that given subjective reports of mental fatigue did not change, that is, participants still reported high 239 mental fatigue scores after the mental exertion condition, this result reflects an increased tolerance to 240 mental exertion. Increased tolerance to mental exertion may come about through the pursuit of 241 effortful tasks, such as endurance training. Indeed, cognitive control is often used to describe the 242 processes, or capacity, by which individuals manage goal-orientated behaviours against distractions, disincentives, habitual tendencies or in the face of many choices^{21,22}, and is thought to increase with 243 the pursuit of effortful behaviours. Unfortunately, we did not record how effortful participants 244 perceived the different interventions, but a change in tolerance was apparent and could be supported 245 246 mechanistically within our results. We observed an increase in the power output relative to RPE in the 247 physical training group during the training protocol (Supplementary material 2) and the time trials 248 (Supplementary material 3). Whereas this may just reflect a general adaptation to the physical training 249 stimulus, the physical training group increased power relative to RPE at iso-time following the mental 250 exertion condition relative to placebo suggesting that central adaptations were also generated. We have previously proposed¹⁰ how adenosine-reducing changes in cerebral fuel stores (e.g.,²³) and/or neural 251 recruitment patterns (e.g.,²⁴), perhaps reflecting altered mental efficiency, could account for this 252 253 increased tolerance. Hence there are possible physiological mechanisms that may explain our data 254 suggesting that - at least to some extent - resilience to mental exertion is a trainable trait. Our recent 255 research seems to support this hypothesis, showing that tolerance to mental exertion is higher in elite 256 athletes than in recreational ones, but also that sub-elite athletes have an intermediate ability to tolerate mental exertion compared to elite and recreational 11,12 . 257

We found no change in cognitive performance in our untrained, yet high-functioning healthy adult participants. Exercise training interventions that target cognitive performance in young and healthy adults are rare in the literature (e.g.,²⁵) although there is both cross-sectional²⁶ and randomized controlled trial²⁷ evidence that cognitive performance does benefit from exercise training in this population. The relative paucity of evidence, at least compared to investigations in older adults, may

be due to the typical high cognitive performance in this population, and this may explain the lack of cognitive improvements in our university-student based cohort. Future studies could confirm our findings using more demanding or prolonged cognitive tasks, or technologies such as electroencephalography to evaluate changes in neural processing and not just overt behavioural outcomes.

268 A possible limitation of this study was that we chose to include a placebo intervention which replicated the time spent by the training group, but not the physical demands. In doing so however, we 269 were conscious that cognitive and/or emotional control effort may have its own training effect and 270 271 thus chose relatively emotionally neutral, although reasonably interesting content. Although we 272 believe this met the aim of creating a placebo, we did not ask participants their expectations, nor about 273 the effort required for either intervention (outside RPE in the physical training group). Furthermore, 274 we acknowledge the limitation of the small sample size of the present study, however no studies have 275 been published on the effect of a training program on tolerance to mental fatigue. Therefore, we based our numbers on a practical solution that we thought we could achieve from a recruitment and 276 277 compliance perspective, and sought to inform future research of the effect sizes.

278

279 Conclusions

Four weeks of endurance training increased tolerance to mental exertion in untrained young adults during a subsequent physical task, with relative subjective ratings suggesting that central changes may account for this improvement. Cognitive performance assessments did not indicate any improvements in cognitive function as a result of endurance training.

284

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353	Figure legends
354	Figure 1. Schematic of the 6-week experimental design.

Figure 2. Time trial distance during the mental exertion condition. The change in control condition time trial distance was subtracted from the post intervention data to reflect the inclusion of this variable as a covariate in the Linear Mixed Models. Physical training group improved time trial distance in the mental exertion condition significantly more than the placebo group. Data are presented as mean \pm 95% Confidence Intervals.

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339

361 Table 1. Baseline characteristics of the study sample by group allocation.

	Training group (n = 10)	Placebo group (n = 10)	р
Females, n (%)	7 (70)	7 (70)	1.00

Age, y	27.6 (6.3)	27.5 (6.0)	0.97
Height, cm	169.4 (6.8)	169.5 (9.6)	0.98
Weight, kg	69.6 (18.4)	68.7 (14.3)	0.91
VO_{2peak} , ml·min ⁻¹ ·kg ⁻¹	32.9 (6.9)	32.8 (5.6)	0.98
TT in control condition, m	6823 (715)	6762 (701)	0.85

Note: Data are presented as mean (SD) or number of participants.