Concurrent brain endurance training improves endurance exercise performance
Dallaway, Neil; Lucas, Sam; Ring, Chris

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Abstract

Objectives: Mental fatigue impairs endurance exercise. Brain endurance training (BET) – engaging in cognitively fatiguing tasks during exercise - can develop resilience to mental fatigue and improve physical performance over physical training alone. The mechanism for this effect is unknown. This experiment examines if BET enhances performance over physical training and investigates potential underlying physiological mechanisms.

Design: A mixed design randomised control trial.

Methods: Pre- and post-testing: 36 participants completed dynamic rhythmic muscular endurance handgrip tasks requiring generation of as much force as possible once a second for 300 s, performed under 3 counterbalanced conditions: following 600 s of a 2-back memory/attention task (subsequent); while performing a 2-back task (concurrent); and on its own (solo). Cardiac activity, electromyographic forearm activity, pre-frontal cerebral haemodynamics (near infrared spectroscopy), and force were recorded. Training: Participants (randomised to a Control or BET group) completed 24 (6 weeks) submaximal hand contractions sessions. The BET group also completed concurrent cognitive tasks (2-back, Stroop). Measures of motivation, physical and mental exertion and mental fatigue were collected throughout.

Results: Endurance performance, across the 3 tasks, improved more following BET (32%) than Control (12%) (p<0.05). The better performance following BET occurred with a higher pre-frontal oxygenation during the post-training physical tasks over time relative to Control (p<0.05).

Conclusions: Concurrent BET improved endurance performance over physical training alone. This was accompanied by a training-induced maintenance of pre-frontal oxygenation, suggestive of reduced mental effort during physical activity.

Keywords: Mental fatigue, muscle fatigue, prefrontal cortex, attention, psychobiological model, near infrared spectroscopy
Introduction

Mental fatigue, defined as a “psychobiological state caused by prolonged periods of demanding cognitive activity and characterised by subjective feelings of tiredness and a lack of energy”¹, can impair endurance exercise² and skilled motor performance³. Accordingly, individuals should avoid mental fatigue when seeking optimal physical performance and performing activities associated with high cognitive and physical demands, such as those faced by the military and rescue services⁴. Marcora and colleagues¹ demonstrated that task-induced mental fatigue reduced time to exhaustion by 18%, together with a higher rate of perceived exertion (RPE), without any differences in blood lactate, respiratory and cardiovascular activity, compared to control. Although the neurophysiological mechanism underlying this fatigue-related effect has yet to be established, several candidates have been proposed, including changes to muscle and brain function. Electromyographic (EMG) recordings confirmed increased knee extensor muscle activity during an endurance cycling task whilst mentally fatigued⁵ and increased flexor muscles during a submaximal isometric handgrip task after completing a mentally fatiguing response inhibition task⁶. Reduced oxygenated haemoglobin levels in the prefrontal cortex (PFC), suggestive of lower PFC activation, have been observed at exhaustion following a simultaneous submaximal handgrip and cognitive task relative to handgrip alone⁷. Additionally, 30-min of continuous engagement in a 2-back working memory task has been shown to decrease vagal and increase sympathetic nerve activity based on beat-to-beat electrocardiographic recordings⁸.

Marcora⁹ hypothesised that building resilience to the negative effects of mental fatigue by repetition of mentally fatiguing tasks would reduce RPE and thereby improve endurance performance. He introduced the term brain endurance training (BET) to describe such fatigue inoculation interventions. Marcora tested his hypothesis by comparing a control group, who completed 12 weeks of cycle training (3 times a week at 65% VO₂max for 60 minutes), and a BET group who concurrently completed a mentally demanding cognitive task with the cycle training. Both groups exhibited similar increases in VO₂max from pre- to post-training, presumably due to the same exercise volume. Notably, however, time to exhaustion (cycling at 75% of VO₂max) increased by 113% in the BET compared to 43% in the control group, coupled with a reduction in RPE. To date, this preliminary
report is the only evidence, to our knowledge, that demonstrates the effectiveness of BET. Based on
the abovementioned evidence, any intervention which reduces RPE, while maintaining the same
workload, should improve exercise performance. Likewise, workload should increase during self-
paced exercise at the same RPE.

In the current study we sought to understand the effects of BET on exercise performance. We
had two study purposes. The first was to investigate the effects of BET on the performance of a
rhythmic force production task. Based on preliminary evidence\(^9\) we expected that concurrent mental
and physical training would improve exercise performance compared to physical training alone. The
second was to investigate cortical, muscular, and cardiac based mechanisms. Based on past evidence,
we expected that any BET performance improvements would be associated with increases in pre-
frontal cortex activation\(^7\), decreases in muscular activation patterns\(^6\), and increases in heart rate
variability\(^8\).

Methods

We employed a mixed experimental design, with group (BET, control) as the between-
participant factor, and both test (pre-test, post-test) and task (solo, subsequent, concurrent) as within-
participant factors. Participants attended 26 sessions over eight weeks, consisting of a pre-test (week
one), 24 training sessions (weeks two to seven) and post-test (week eight).

Participants were 36 (15 females, 21 males) healthy undergraduate students aged 20 ± 2
years. Exclusion criteria included dominant hand injury and changes in habitual exercise during the
study. In the 24-hours prior to testing, participants were requested to abstain from exercise and
alcohol consumption, and to sleep for 7-hours. They were asked to refrain from eating (1-hour) and
caffeine (3-hours) before all sessions. Participants were randomly assigned to either a control group \((n = 18)\) or BET group \((n = 18)\). Ethical approval was obtained from the University of Birmingham
Research Ethics committee. Informed consent was obtained from participants. Each received a £50
voucher and course credit.
Pre- and Post-Testing: Following instrumentation, determination of MVC\textsuperscript{10}, and one minute of task familiarisation, participants completed a 5-min endurance task under three counterbalanced conditions. In each task, participants were asked to generate as much force as possible by squeezing a handgrip dynamometer with their dominant hand once per second as cued by a metronome. The three tasks were completed: 1) following 600 s of a 2-back \textsuperscript{11} working memory task (subsequent); 2) while performing a 2-back task (concurrent), and 3) on its own (solo). The tasks were separated by 5-min, during which participants completed self-report questionnaires and baseline physiological measures recorded. No additional rest was given to the participants between tasks. The experimental protocols are depicted in Figures S1 and S2 (Supplementary Material).

Participants completed the 2-back test for a period of 10-min in the pre- and post-testing session prior to the physical task in the subsequent condition. The 2-back task presented a random consonant in the centre of a computer monitor for half a second followed by a blank display for three seconds requiring participants to respond indicating if the current letter displayed was the same (target) or different (non-target) as the letter displayed two previously using a computer keyboard with their non-dominant hand. Letters were displayed with a 1:2 target to non-target ratio. Performance was determined by the percentage correct responses. Participants were verbally briefed on the task and presented with written instructions prior to the familiarisation period and performance task. All cognitive tasks were implemented using E-Studio (Psychology Software Tools, USA).

Force (N) was recorded continuously throughout all sessions. In the pre- and post-test tasks, physical performance was calculated from the area under the force-time curve of each squeeze and averaged over 30-s intervals.

An electrocardiogram was recorded using surface electrodes in a modified chest configuration and an amplifier (509, Morgan, USA). Heart rate variability (HRV) measures were used as an indicator of physiological demands \textsuperscript{12}. HRV was calculated from the R-to-R wave interval period for each minute of the pre- and post-testing tasks. The root mean square of the successive differences (RMSSD) and the standard deviation (SDNN) of the R-to-R wave interval were calculated (for further detail see Cooke et al \textsuperscript{10}).
The electromyographic (EMG) activity of extensor and flexor carpi radialis forearm muscles were recorded using differential surface electrodes and an amplifier (Bagnoli-2, Delsys, USA). The EMG signals were rectified, averaged over 30-s, and normalised as a percentage of EMG during MVC.

Prefrontal cortical haemodynamics were assessed using near infra-red spectroscopy (NIRS; NIRO-200NX, Hamamatsu Photonics KK, Japan). The NIRO-200 device measures changes in chromophore concentrations of oxyhaemoglobin and deoxyhaemoglobin ($\Delta$O$_2$Hb and $\Delta$HHb) via the modified Beer-Lambert law and provides depth-resolved measures of tissue O$_2$ saturation [total oxygenation index (TOI)] and tissue Hb content (i.e., relative value of the total haemoglobin normalized to the initial value, nTHI) using the spatially resolved spectroscopy (SRS) method. The SRS-derived NIRS parameters limit contamination from superficial tissue via depth-resolved algorithmic methods, providing an index of targeted local tissue saturation (TOI) and perfusion (nTHI), see Davies et al. for a recent review. Probes were enclosed in light-shielding rubber housing that maintained emitter-to-detector optode spacing (4 cm), positioned over the right pre-frontal electrode site (Fp2 in 10-20 system) and secured to the head. Before each task participants were instructed to sit still, relax, clear their mind, and look at a fixation cross for 2 minutes. Measures of TOI, nTHI, O$_2$Hb and HHb were averaged over 30-s calculated relative to the last 30 s of the prior baseline.

All signals were acquired via a Power 1401 (Cambridge Electric Design Limited, UK) digital-to-analogue convertor (16-bit resolution, 2.5 kHz sample rate) running Spike2 (version 6.06) software. Physiological measures were recorded only in the testing sessions.

Success motivation was measured prior to each task using a 5-point scale with anchors of “0 = not at all” and “4 = extremely”; example items included “I will be disappointed if I fail to do well on this task” and “I am eager to do well”. Exertion and fatigue were measured following each task using 11-point scales: the mental exertion (ME) scale had anchors of “0 = nothing at all” and “10 = maximal mental exertion” whereas the mental fatigue (MF) scale had anchors of “0 = nothing at all” and “10 = totally exhausted”. A baseline measure of MF was also taken. Following each task, interest
and enjoyment were measured using a 7-point scale with anchors of “1 = not true at all” and “7 = very true”, with example items including “I enjoyed doing this activity very much” for enjoyment and “I would describe this activity as very interesting” for interest. RPE was measured every minute during the solo and subsequent tasks and after the training sessions.

Training: The physical task required participants to squeeze the handgrip dynamometer once per second (cued by metronome) at approximately 30% MVC until they reached a pre-determined cumulative force production target. Target attainment was calculated by summing the force generated, normalised to MVC, every second. Based on pilot testing, the initial target was 12000 (1 unit representing 1% MVC per second), which incremented 500 points every week (every fifth session) to account for training-related improvements in strength. 6-weeks of rhythmic handgrip training at 30% MVC has been shown to substantially improve muscular endurance performance. Every fourth session, participants completed the first 5000 points as quickly as possible to replicate the solo task (described above). In session one, visual feedback was provided in the first 5-mins for guidance. The BET group completed the computer-based cognitive tasks using a mouse in their non-dominant hand; tasks became progressively more difficult each week. Training session time and psychological self-report measures were averaged each week in conjunction with the progressive physical and cognitive task demands.

The cognitive tasks during the training period for the BET group consisted of the pre-test concurrent 2-back (sessions 1-4, 9, 11), colour word Stroop (sessions 5-8, 10, 12), modified colour word Stroop (sessions 13,14,15,16), 2-back test with a 2500 ms letter refresh rate (sessions 17,18,19,20), and double incongruent colour word Stroop task (sessions 21,22,23,24). The colour word Stroop required participants to indicate the font colour (red, blue, green and yellow) of a colour word from two possible answers displayed in a black font in the bottom left and right corners of the display with a corresponding left or right mouse click. Participants received verbal and written instructions displayed to participants prior to the training task. The modified version displayed answers in a green font whereas the double incongruent version presented the incorrect answer in a random colour and the correct answer in the same colour of the word presented. The Stroop test
requires response inhibition and working memory. Performance was measured by response time and accuracy. For all Stroop tasks the stimulus was presented for 2500 ms or until a response was given followed by a fixation cross for 500 ms. The sequence and increased difficulty of the cognitive tasks were designed to minimise any learning effects.

Statistical analysis. To evaluate the study hypotheses, we used mixed model analysis of variance (ANOVA) to examine the effects on our parametric task measures (described above) of group (BET, control), our between-participants factor, together with training week (1, 2, 3, 4, 5, 6), test (pre, post), task (subsequent, concurrent, solo), and/or time (various), our within-participants factors. These analyses were performed using SPSS (v24, IBM, United States). The multivariate solution to ANOVAs has been reported. Significance was set at $p<0.05$, Data were expressed as mean ± standard deviation, unless otherwise stated. Partial eta-squared ($\eta^2$) was reported as a measure of effect size, with values of .02, .13 and .26 representing small, medium, and large effect sizes, respectively.
averages) ANOVA on force produced per second, revealing a group-by-test interaction effect ($F_{1,34}=6.064$, $p<0.05$, $\eta^2=.15$). The BET group showed a greater increase in force production (Figure 1) from pre-to-post ($\Delta=32\%$) than the control group ($\Delta=12\%$). There were no group-by-time interaction effects indicating that pacing performance was common to both groups in both testing sessions.

A 2 group (BET, Control) by 2 test (pre, post) by 2 task (subsequent, concurrent) ANOVA on correct responses during the 2-back memory task yielded a group-by-test interaction effect ($F_{1,34}=4.56$, $p<0.05$, $\eta^2=.12$). The BET group improved their cognitive task performance, indexed by percent correct responses, in the subsequent task from 89±4% to 96±3% whilst the Control group improved from 87±7% to 90±7%. In the concurrent task, the BET group improved from 88±6% to 94±5% whereas Controls were unchanged from 86±7% to 85±18%. These values represent an overall improvement in working memory performance of 7% for BET and 1% for control.

A 2 group (BET, Control) by 2 test (pre, post) by 2 task (subsequent, concurrent) by 5 time (one minute averages) ANOVA on RPE revealed a test-by-task-by-time interaction effect ($F_{1,34}=8.36$, $p<0.05$, $\eta^2=.20$) (Figure 2). A series of 2 group (BET, control) by 2 test (pre, post) by 3 task (subsequent, solo, concurrent) ANOVAs were conducted on self-reported interest, enjoyment, success motivation, ME, and MF. These analyses yielded a test-by-task interaction effect for interest/enjoyment ($F_{1,34}=9.21$, $p<0.05$, $\eta^2=.21$), dropping from 3.5±0.9 to 2.6±0.8 (subsequent), 3.8±0.9 to 2.8±0.8 (concurrent) and 3.4±0.8 to 2.7±0.8 (solo) and a group-by-test interaction ($F_{1,34}=10.15$, $p<0.05$, $\eta^2=.23$), changing from 3.6±1.2 to 2.3±1.0 (BET) and 3.5±1.2 to 3.1±1.0 (Control); We also detected a test-by-task interaction effect for success motivation ($F_{1,34}=10.70$, $p<0.05$, $\eta^2=.24$), reducing from 2.5±0.9 to 2.3±1.0 (subsequent), 2.5±1.0 to 2.2±1.0 (concurrent) and 2.3±1.0 to 2.3±1.0 (solo), but no group interactions.

Measures of prefrontal cortical haemodynamic responses were analysed with a series of group (BET, control) by test (pre-test, post-test) by task (solo, subsequent, concurrent) by 10 time (30 s averages) mixed design ANOVAs revealing a group-by-test-by-time interaction for TOI ($F_{1,34}=5.35$, $p<0.05$, $\eta^2=.14$) (Figure 3A), a group-by-test-by-task-by-time interaction for nTHI ($F_{1,34}=4.84$, $p<0.05$, $\eta^2=.14$).
p<0.05, η²=.13) (Figure 3B), a group-by-task-by-time interaction for O₂Hb ($F_{1,34} = 4.31, p<0.001, η²=.1$) (Figure 3C), and a task-by-time interaction for HHb ($F_{1,34} = 4.65, p<0.05, η²=.12$) (Figure 3D).

Flexor carpi radialis and extensor carpi radialis electromyographic activity during the physical tasks were analysed with a series of group (BET, control) by test (pre-test, post-test) by task (solo, subsequent, concurrent) by 10 time (30 s averages) mixed design ANOVAs. Analyses revealed a test-by-task-by-time interaction effect the flexor carpi radialis ($F_{18,612} = 1.679, p<0.05, η²=.0.047$, Figure S3). Analyses yielded test-by-task ($F_{2,68} = 5.403, p<0.05, η²=.0.137$) and task-by-time ($F_{18,612} = 4.368, p<0.001, η²=.114$) interaction effects for the extensor carpi unilaris (Figure S4).

Cardiac measures during the physical tasks were analysed using a series of group (BET, control) by test (pre-test, post-test) by task (solo, subsequent, concurrent) by 5 time (60 s averages) mixed design ANOVAs. For heart rate (Figure S5) we found test by task ($F_{2,68} = 13.673, p<0.001, η²=.287$), test by time ($F_{4,136} = 3.983, p<0.05, η²=.105$), and task by time ($F_{8,272} = 13.807, p<0.001, η²=.289$) interaction effects. There were no group effects. For RMSSD (Figure S6), we obtained test by task ($F_{2,68} = 5.530, p<0.05, η²=.140$) and test by time by group ($F_{2,34} = 2.586, p<0.05, η²=.071$) interaction effects. The analysis for SDNN (Figure S7) yielded test by task ($F_{2,68} = 8.179, p<0.001, η²=.194$) and test by time by group ($F_{4,34} = 3.686, p<0.05, η²=.098$) interaction effects.

A 2 group by 2 training by 10 time mixed design ANOVA on the cardiac measures during the cognitive component of the subsequent task only yielded time main effects (Figure S6) for heart rate ($F_{9,306} = 4.150, p<0.001, η²=.0.109$), SDNN ($F_{9,306} = 2.373, p<0.05, η²=.065$), and RMSSD ($F_{9,306} = 2.186, p<0.05, η²=.060$).

**Discussion**

Our study was designed to evaluate the effects of concurrent fatigue inoculation training on endurance performance and to explore underlying mechanisms. We demonstrated that 6-weeks of BET improved dynamic rhythmic handgrip performance over physical training alone and found
evidence that changes in prefrontal cortical haemodynamics accompanied this effect. In addition, BET facilitated greater performance scores in post-testing cognitive tasks relative to control.

Our finding of greater improvements in a physical performance following BET is consistent with Marcora. The 32% overall task improvement found in the current study compares to 41% in Marcora’s study at the 6-week test. This small discrepancy in performance improvement could be due to a number of protocol differences between the two studies, including the shorter cognitive task engagement during BET (60 versus 180 min per week), differing modes of endurance exercise (muscular endurance versus whole-body), and test type (time trial versus time to exhaustion). In contrast to Marcora’s study we did not observe lower RPE in the BET group, relative to control, during post-training testing probably due to our use of a maximal, compared to a sub-maximal and fixed workload performance test. We also observed that increases in post-test performance by both groups were achieved with the same pacing strategy, RPE, and success motivation. Task interest/enjoyment decreased more in the BET group than control group.

Our secondary aim was to explore potential mechanisms underlying the benefits of six weeks of BET relative to physical training alone. We found that performance improvements were achieved for the same heart rate and motivation as the control group. In support of our hypothesis, we observed increases in heart rate variability in the BET group over time, during the post training tasks, relative to controls. This finding reveals a reduction in sympathetic nervous system activity and indicates that participants found the physical tasks less physiologically demanding. Contrary to our hypothesis, no changes were observed in muscular activity. The post training reduction in ratings of interest and enjoyment for BET relative to control suggests that more challenging and exciting tasks are needed to engage participants. Additionally, pre-frontal oxygenation was unchanged in the BET group but decreased in the control group.

The PFC comprises interconnected areas that communicate with various subcortical structures in order to exert executive control, such as response inhibition, working memory, and facilitate goal directed behaviour. These cognitive processes are utilised extensively during the progressively challenging mentally demanding tasks, as would be the case during the training period in the BET
group in addition to the executive control and effort required to complete the physical task. It has been suggested that during exercise the PFC interprets physiological information in combination with psychological factors, such as arousal and motivation, to facilitate a top-down effect on motor unit recruitment and is involved in the capacity to tolerate high levels of exertion \(^{21}\). World-class endurance athletes have demonstrated an ability to maintain cerebral oxygenation during 5-km running time trials \(^{22}\), whereas well-trained recreational athletes exhibit declines in cerebral oxygenation \(^{23}\). Moreover, PFC oxygenation declines at the point of fatigue \(^{24}\) \(^{25}\), particularly in chronic fatigue patients \(^{26}\). Several studies have shown increases in PFC activity, indicated by reduced cerebral oxygenation, during exercise and a reduced physical and cognitive performance in a concurrent executive function cognitive task during 20 km of high intensity (~70% VO\(_2\) peak) cycling, \(^{27}\) and 9 minutes of cycling at 85% peak power \(^{28}\). Taken collectively, these studies suggest a role of the PFC in regulating endurance exercise performance.

In the current study, the post-training physical task improvements in the control group were associated with a decrease in right hemisphere PFC oxygenation (TOI), which did not occur in the BET group despite an even greater force production. It is possible that the increased cognitive workload during BET increased blood flow and resulted in subsequent neural adaptations within the PFC and other key cortical areas involved in exercise and cognitive processing. Few studies have investigated adaptations in the PFC following physical and cognitive training, making direct comparisons with our findings difficult and speculative. However, in support of this idea, the efficacy of cognitive tasks to induce such cerebral haemodynamic adaptations has been demonstrated during 12 weeks (~30 hours) of working memory training, which improved measures of intelligence and maintained oxygenation in the PFC relative to an active control group \(^{29}\). Similarly, three months of endurance training has been shown to maintain cerebral oxygenation during submaximal exercise in an overweight population \(^{30}\). Therefore, it is possible that the concurrent physical and cognitive tasks used in the current study induced greater central adaptations, resulting in an ability to maintain a higher PFC oxygenation during the post-training physical tasks. This could enable the BET participants to tolerate higher levels of perceived exertion (at the same absolute work rate), maintain
executive control, resist response inhibition during physical tasks and exert less mental effort,
ultimately resulting in increased performance. Finally, one might expect an effort-related drop in PFC
oxygenation during the physical performance tasks prior to training. However, due to the unfamiliar
nature of dynamic handgrip exercise the participants may lack the ability or experience to exert
maximal effort and perform well on this type of task, consequently PFC oxygenation was not
compromised for these pre-training measures.

Limitations: First, whilst we sought to control for physical training between groups with
regards to force production and task time, variations between participants resulted in small differences
in how long they engaged in the cognitive tasks during BET. Second, whilst we have demonstrated
the efficacy of BET, care must be taken when generalizing from a muscular endurance training
protocol to other exercise modes including whole-body endurance training, which should be further
investigated. Finally, further investigations should aim to determine the optimal cognitive training
volume during BET coupled with more detailed examination of the cortical adaptations using fMRI,
EEG, and whole-brain fNIRS, to better understand changes in neural activation and the coupled
vascular response, the latter only being examined here.

Conclusion

Our study provided evidence that supports the efficacy of concurrent fatigue inoculation
training (i.e., BET) as a means to improve muscular endurance and performance in a working memory
cognitive task. The finding that physical performance improvements were associated with a training-
induced maintenance of PFC oxygenation suggests that such training benefits could be attributable to
reduced mental effort during physical activity.

Practical Implications

• This study shows that adding an additional concurrent mentally demanding stimulus to sub-
maximal muscular endurance training requiring a high level of cognitive effort can improve
muscular endurance performance over matched physical training alone.
Performance improvements were associated with a training-induced maintenance of prefrontal cortex oxygenation, which could represent a reduced mental effort. Athlete’s engaging in prolonged sub-maximal endurance exercise who are either time constrained or not able to replicate the physical demands of their competing event in training (i.e. ultra-endurance) should consider the addition of a concurrent cognitive task to their training programme to illicit further performance improvements.

References


Fig. 1 Effect of brain endurance and physical training on absolute physical task performance averaged across the subsequent, concurrent, and solo tasks. # (p<0.05) Significant interaction effect of test-by-group. Data presented as M ± SEM.
Fig 2 Effect of brain endurance (BET) and physical training (Control) on RPE during the subsequent (A) and solo (B) tasks during pre-test and post-test. * Significant interaction effect of testing, time, and task (p<0.05). Data presented as M ± SEM.
Fig 3. Effect of brain endurance and physical training on prefrontal cortex haemodynamics indexed via total oxygenation index - TOI (A), total haemoglobin volume indexed via normalised tissue haemoglobin index - nTHI (B), oxyhaemoglobin volume - O2Hb (C) and cortex deoxyhaemoglobin volume - HHb (D). * Significant (p<0.05) interaction effect of group-by-test-by-time. + Significant (p<0.05) interaction effect of group-by-test-by-task-by-time. # Significant (p<0.05) interaction effect of group-by-task-by-time. & Significant (p<0.05) interaction effect task-by-time. See supplementary material for individual task data and associated interactions. Data presented as M ± SEM