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Medium chain triglycerides with a C8:C10 ratio of 30:70 enhances cognitive performance and mitigates the cognitive decline associated with prolonged exercise in young and healthy adults

Jake S. Ashton [a,*], James W. Roberts [b], Caroline J. Wakefield [a], Don P.M. MacLaren [b], Simon Marwood [a], James J. Malone [a]

[a] School of Health and Sport Sciences, Liverpool Hope University, Liverpool, UK
[b] School of Sport and Exercise Sciences, Liverpool John Moores University, Liverpool, UK

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ABSTRACT

Introduction: Prolonged exercise has been linked to a decline in cognitive function due to a variety of factors, such as a drop in oxygen in the prefrontal cortex and an increase in stress hormones and neurotransmitters. Medium chain triglycerides (MCTs) may possibly offset this decline as they provide energy for the brain via both direct and indirect pathways, alongside promoting chronic physiological adaptations within the brain.

Methods: Participants were divided into two groups; MCT ($n = 9$) and Placebo ($n = 10$). The MCT gels contained 6 g of MCT with a C_8:C_{10} ratio of 30:70, whereas the placebo gels contained carbohydrates of similar calorific value to the MCT gels. Participants visited the laboratory on three occasions (familiarisation/fitness test, pre-supplementation, post-supplementation), during which they performed a battery of cognitive tasks assessing domains such as processing speed, working memory, selective attention, decision making and coordination, before and after a prolonged bout of exercise (60 mins at 90% gas exchange threshold (GET). A 2-week supplementation period between visits 2 and 3 involved the ingestion of 2 gels per day.

Results: Exercise resulted in detriments in most cognitive tasks pre-supplementation for both groups, and post-supplementation for the Placebo group (main effect ps$<$ 0.05). Post-supplementation, the effect of exercise was mediated in the MCT group for all cognitive tasks (main effect ps$<$ 0.05), except for the Digit and Spatial Span Backwards test phases (main effect ps$>$ 0.05). Furthermore, MCT supplementation enhanced before-exercise cognitive performance and in some measures, such as working memory, this was maintained after-exercise (interaction effect ps$>$ 0.05).

Conclusions: Chronic MCT supplementation enhanced before-exercise cognitive performance and offset the cognitive decline caused by a prolonged bout of exercise. In some cases, improvements in before-exercise cognitive performance were maintained after-exercise.

1. Introduction

The principles of the "inverted-U" relationship between arousal and performance was originally proposed by Davey [1], based from Yerkes and Dodson [2], s hypothesis. It suggests that exercise is a stressor which may also present a "inverted-U" relationship with cognition, so that relative to low and high intensities, moderate exercise is associated with enhanced cognitive performance [3–5]. Meta-analyses support this proposal, with cognitive performance improving after exercising at moderate intensities, compared to rest/low and high intensities [6–9]. For example, Covassin et al. [10] demonstrated declines in verbal memory and both immediate and delayed memory recall following maximal incremental running, whereas moderate exercise has been evidenced to increase cognitive parameters such as choice reaction time [11–13], simple reaction time [14], and coincidence-timing and stimulus detection [15]. Since low intensity exercise has little or no effect on cognitive performance versus resting conditions [6,16], the relationship between exercise intensity and cognitive performance may be more accurately represented by an "inverted-J" [17]. This was supported by Duncan et al. [18] who observed that as treadmill running intensity

* Corresponding author at: School of Health and Sport Sciences, Liverpool Hope University, Hope Park Campus, Liverpool, L16 9JD, UK.
E-mail address: 16001857@hope.ac.uk (J.S. Ashton).

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increased, cognitive performance incrementally improved before declining rapidly at 90% heart rate reserve.

Despite the potential for moderate exercise intensities to enhance cognitive performance, the duration of exercise has been shown to exert a modifying role. For example, 20 min of moderate exercise has been shown to facilitate enhanced performance in the Stroop task, whereas shorter (10 mins) and longer (45 mins) periods only produced negligible effects [19,20]. Indeed, it is plausible that an interaction between exercise intensity and duration underpins any impairment of cognitive performance during ~~high intensity~~ exercise, such that the total metabolic work completed is of central importance. For instance, a two-hour bout of moderate intensity exercise has been shown to be detrimental to performance in cognitive tests such as visual target detection, auditory go no/go tasks [21], perceptual response and an increase in errors in a complex task [22]. Due to these studies utilising well trained populations, it is plausible that a shorter duration, i.e. 45–60 mins of exercise, may lead to similar results in untrained individuals. However, exercise duration and intensity are inherently linked, e.g. very high intensity exercise is also very short in duration by nature, hence each are not mutually exclusive so both need to be carefully considered when designing a protocol. Indeed, Moore et al. [23] demonstrated decrements in cognition, such as in tests of memory vigilance and complex visual perceptual-discrimination immediately following 60 min cycling at 90% ventilatory threshold (a non-invasive estimation of the lactate threshold [24]) in healthy but untrained participants. Although such exercise is defined as "moderate", long duration exercise has been shown to cause fatigue in the brain's neurons involved in central motor drive [25,26], potentially underpinning the notion of a decline in cognitive performance due to prolonged exercise [27]. The study of Moore et al. [23] is also of importance because exercise intensity was determined with respect to a specific physiological threshold (i.e. lactate threshold), rather than arbitrary indices of exercise intensity such as age-predicted heart rate [28] and the heart-rate reserve [18]. These latter methods of exercise intensity prescription do not permit clarity on which exercise intensity domain participants are exercising in and are thus a confounding factor when examining the effect of exercise on cognitive performance.

The literature on the effect of exercise on cognitive performance is equivocal [29–31]. A confounding factor is likely due to the varied means by which exercise intensity has been defined. Most studies examining the effect of training status on cognitive performance during exercise have defined exercise intensity via arbitrary factors, such as age predicted heart rate [28]. By not indexing exercise intensity to accurate measures such as lactate threshold and/or critical power, there remains a lack of clarity of which exercise intensity domain participants are exercising in. Accordingly, the notion that cognitive performance does not decline in trained populations when moving between intermediate and higher exercise intensities [28] might be artefactual of weak definitions of exercise intensity.

The precise physiological mechanisms underpinning the effects of exercise on cognitive performance remain unclear. McMorris [32] showed that decrements in a central executive task with higher exercise intensities was associated with increases in plasma adrenocorticotropic hormone, suggesting the involvement of the hypothalamic-pituitary-adrenal axis in the inhibition of performance. Plasma catecholamine concentration tracks exercise intensity [32], and an increase in catecholamines activates the limbic system at the expense of the prefrontal cortex, leading to possible decrements in tasks requiring executive function [32,33]. Exercise also progressively increases the concentration of specific neurotransmitters [5,34–36]. Although moderate secretion of these neurotransmitters has a positive influence on cognition [5], higher intensity/longer exercise leads to cerebral neurotransmitter levels to increase to a level that negatively impacts cognition [5], due to damage being caused to neural networks [37]. Increased cerebral oxygenation is linked to enhanced executive function [38–40] and the relationship of cerebral oxygenation to exercise intensity approximates an "inverted-U" [41–43], i.e. cerebral oxygenation and blood flow in the pre-frontal cortex increases with exercise before declining at intensities above the respiratory compensation point (an estimate of critical power) [42]. This mirrors the effect of exercise intensity on cognitive performance [44], suggesting that the effect of exercise intensity on cognitive performance is, at least in part, mediated by cerebral oxygenation. If exercise is long enough in duration, blood glucose homoeostasis may come under threat [45,46]. Although glucose storage in neuronal tissue is limited, necessitating a continuous supply of glucose for brain function [47], brain glucose uptake has been observed to decrease with increases in exercise intensity [48]. When arterial glucose concentration falls below ~3.6 mM, cerebral glucose uptake declines due to the endothelial glucose transport becoming rate limiting [49], with further reductions associated with cognitive dysfunction [50]. The cerebral cortex is the most sensitive region in the brain to hypoglycaemia [51], so fatigue due to hypoglycaemia may be linked to motor cortices having an insufficient glucose supply [52] and/or depletion of brain glycogen stores [53].

Many sports, in particular team sports and Olympic events such as the winter biathlon (which combines cross-country skiing and rifle shooting) rely on the athlete's capability of combining their physical prowess with high cognitive control. Due to research highlighting the fact that prolonged exercise can decrease cognitive capabilities [23,54], it highlights the need for an intervention to maintain cognitive ability post exercise, without diminishing athletic performance itself. Medium Chain Triglycerides (MCT) supplementation offers a possible solution to the cognitive decline linked to prolonged exercise. MCT ingestion, and C_8 in particular, provokes an increase in ketosis, resulting in elevated circulating ketones such as βHB [55,56] which can cross the blood-brain-barrier via monocarboxylic acid transporters [57]. Additionally, free fatty acid derivatives of MCTs also become present in the body, directly crossing the blood-brain barrier owing to their short carbon chain length [58–60]. Furthermore, MCT supplementation has been shown to provoke chronic physiological adaptations in the brain, with C_{10} supplementation strongly linked to increasing mitochondrial biogenesis, as shown by Hughes et al. [61] using a neuronal cell line. Hence, MCT supplementation of both C_8 and C_{10} may provoke enhanced energy metabolism in the brain via mechanisms of enhanced substrate supply and an increased capacity for energy production. MCT supplementation has previously been shown to improve cognition at rest in individuals with reduced baseline cognition linked to age and cognitively debilitating diseases such as Alzheimer's [62–66]. These individuals benefit from MCT supplementation as the brain maintains its ability to utilise ketones despite the decreased cerebral metabolism and/or cerebral insulin resistance due to age/disease inhibiting glucose metabolism [62,66,67]. Furthermore, our previous work demonstrated that MCT supplementation with a C_8:C_{10} ratio of 30:70 enhanced cognition performance in tasks requiring working memory, executive function and task switching in a young and healthy cohort at rest after 2–3 weeks of supplementation [68]. It is therefore plausible that MCT supplementation may offset the cognitive decline associated with prolonged exercise.

The purpose of the present study was to evaluate the effects of a 2-week supplementation period of MCTs with a C_8:C_{10} ratio of 30:70 on the decline in cognitive performance associated with a prolonged bout of moderate intensity exercise. We hypothesised that this chronic MCT supplementation would offset the cognitive decline associated with such exercise.

2. Methods

2.1. Participants

20 university students volunteered to take part in the study. Their names were changed to numeric codes and a random number generator was used to divide them into 2 equal groups, although 1 participant from

the MCT group dropped out due to injury (MCT group: 6 males and 3 females, age: 20.1 ± 1.5 years, height: 174 ± 9 cm, weight: 75.0 ± 13.7 kg, VO_{2max}: 32.5 ± 3.0 ml/kg/min; Placebo group: 7 males and 3 females, age: 20.5 ± 1.8 years, height: 173 ± 9 cm, weight: 70.6 ± 9.2 kg, VO_{2max}: 34.3 ± 3.8 ml/kg/min). An independent *t*-test of VO_{2max} indicated that the two groups were matched for fitness as $p = .259$. All participants were clear of neurological and health impairments and were instructed not to partake in any unnecessary cognitively or physically demanding tasks for 24 h prior to each laboratory visit, such as exercising or playing computer games. Participants were instructed to otherwise follow their habitual diet, but with the exception that they should be fasted and avoid alcohol and excessive caffeine overnight for 12 h prior to each laboratory visit. The study was approved by the local University research ethics committee (S 22–11–19 PA 053) and designed and conducted in accordance with the Declaration of Helsinki (2013).

2.2. Experimental procedure

The study involved a repeated-measures design involving three visits to the laboratory (Fig. 1), of which the first was a familiarisation session where study procedures were outlined, and the cognitive tests were firstly demonstrated and then practised once in full. Thereafter, participants completed an incremental ramp exercise test on an electronically braked cycle ergometer (Lode Excalibur Sport, Lode BV, Groningen, Netherlands) until the limit of tolerance for the determination of the maximal oxygen uptake and gas exchange threshold (GET).

Between the second (pre-supplementation) and third (post-supplementation) visits to the laboratory, participants ingested a gel twice daily (30 min prior to breakfast and evening meals) for a 2-week period. The MCT gels (Nuroco, London, UK) were 15 g and contained 6 g of MCT per gel and were each 59 kcal, with a C_8:C_{10} ratio of 30:70. Meanwhile, the Placebo group ingested a carbohydrate gel (Energel+, Nutrition X, Gloucester, UK) with a similar calorific value (94 kcal). These supplements were administered in a double-blind protocol, with all gels being completely covered with black tape. We have previously demonstrated that cognitive performance has improved after ingesting two 6 g MCT gels with a C8:C10 ratio of 30:70 for two weeks, possibly due to the combination of C_8 and C_{10} increasing the levels of plasma ketones and medium chain fatty acids, as well as causing chronic physiological adaptations to the brain, respectively [68].

During their second and third visits to the lab, participants undertook a battery of cognitive and sensorimotor tests before and immediately after a 1-hour bout of exercise on the cycle ergometer at 90% of the individual participants' GET (for similar procedures, see Moore et al. [23]).

2.3. Gas exchange threshold (GET)

During the familiarisation visit, GET (a non-invasive estimate of the lactate threshold) was determined. Exercise was initiated at a baseline intensity of 50 W for 2 mins, which thereafter progressively increased by 20 $W.min^{-1}$ whilst sustaining a cadence of 60–70 RPM. The test was terminated volitionally or when cadence could not be sustained above 50 RPM. Pulmonary gas exchange was measured breath-by-breath via an online gas analysis system (Ergostick, CPET, Bad Kissingen, Germany). Breath-by-breath gas analysis was examined and errant breaths removed [69]. Using 10-s averages, VO_2 was plotted against VCO_2 with GET determined via the 'v-slope' method [70,71]; that is, identification of a disproportionate increase in VCO_2 compared with VO_2. This point was confirmed by coincidence of this point with (i) an increase in the ventilatory equivalent for O_2 without a concomitant increase in the ventilatory equivalent for CO_2, and (ii) an increase in end-tidal PO_2 without a concomitant increase in end-tidal PCO_2. The power output associated with 90% GET was determined via regression of the VO_2 – time relationship, with a correction of 40 s made to account for the mean response time and power output determined accordingly.

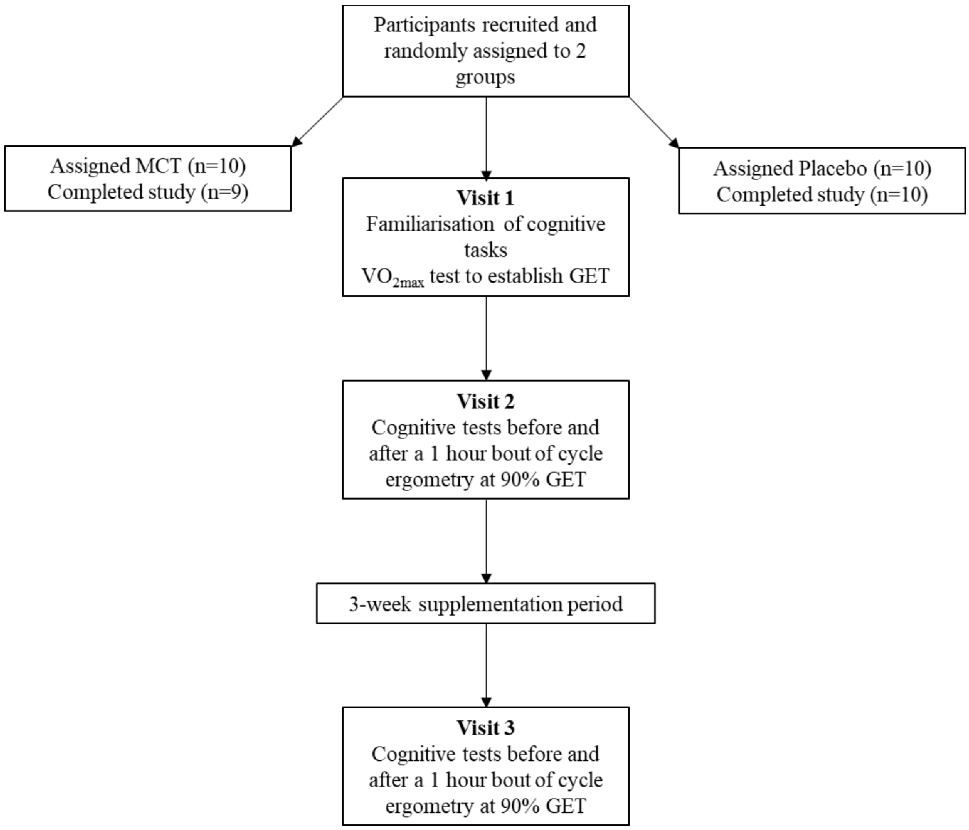

Fig. 1. Schematic view of study design and participant flow.

2.4. Cognitive and sensorimotor assessments

2.4.1. Trail making

Trail Making broadly assesses visual motor skills, processing speed and sequencing abilities [72]. Using pen/pencil and paper, participants were required to connect a series of numbered circles as quickly as possible. Part A involved drawing lines to connect numbers (1–25) in ascending order. Meanwhile, part B involved drawing lines to connect alternate pairs of both numbers (1–13) and letters (A-L) in ascending order (i.e., 1-A, 2-B, 3-C, etc.). Any errors were immediately identified by the experimenter so that participants could correct for them. Participants were able to initially practise each part, comprising of 8 circles. In line with clinical administration of the test (e.g. [73]), the time it took to complete the task was recorded by the experimenter using a stop-watch.

2.4.2. Memory span

Digit span and spatial span were used to collectively assess working memory's verbal and visuo-spatial components, respectively [74]. For digit span, a series of numbers were read aloud by the experimenter in a predetermined order. Meanwhile, for spatial span, a series of blocks on a Corsi Block tapping apparatus were tapped by the experimenter in a predetermined order. Participants were then required to repeat the sequence in the corresponding (forwards test phase) or reverse order (backwards test phase). The span length increased by one item for each iteration of span length, and there were two trials devoted to each span length. Once participants were incorrect in the recall of both trials for one particular span length, the test was terminated. There was one point assigned for each correct response, and the maximum number of points in each test phase was 16. No practice trials were necessary as the first trial had only 2 numbers, allowing for full understanding of the task.

2.4.3. Stroop task

The Stroop task assesses inhibitory control, underlying selective attention and decision-making abilities [75]. The colour words 'red', 'yellow' or 'blue' were presented using coloured text that would appear either *red, yellow* or *blue* on an LCD monitor (1280 × 1024-pixel resolution). Participants had to respond as quickly as possible by pressing one of three keys on a keyboard according to the visual rather than semantic properties of the word (*red* = 'V', *yellow* = 'B', *blue* = 'N'). The semantic and visual properties of the word were either congruent (e.g., word 'red' presented in *red* text) or incongruent (e.g., word 'red' presented in *yellow* text) with each other. Typically, individuals take longer to respond to the incongruent trials as they find difficulty in inhibiting a response to the semantic rather than solely visual properties. Hence, the ability to limit this difference renders enhanced inhibitory control.

The stimuli were generated and controlled using an in-house designed routine courtesy of Matlab (MathWorks, Natick, MA, USA) running Psychtoolbox (version 3.0.11; [76]. Following a random fore period (2200–3200 ms), the stimuli were presented on the monitor. As soon as participants responded to the stimuli, the stimuli were removed, and the screen appeared blank. Following a practice phase lasting 12 trials, the test trials were completely randomised. There were 4 trials per combination of colour word and coloured text (total trials = 36). Any trials that featured a reaction time <100 ms were discarded prior to any subsequent analysis as they indicated an anticipatory response. The number of response errors and within-participant mean reaction time difference between congruent and incongruent trials were calculated for subsequent analysis. For reaction time analyses, only correct responses were used.

2.4.4. Reciprocal aiming task

The reciprocal aiming task assesses sensory-motor control and coordination [77,78]. Participants were required to execute back-and-forth, target-directed aiming as quickly and accurately as possible using their dominant upper-limb across the medio-lateral axis (i.e., left-to-right, right-to-left). Each trial consisted of 10 individual movement segments (5 cycles). Moving a limb more quickly tends to decrease movement accuracy [79]; hence, individuals exhibit enhanced performance when their movement times are shorter while still hitting the target.

The movements were captured using a hand-held stylus in contact with a graphical digitising tablet that was connected to a computer via serial port (GTCO Calcomp Drawing Board VI, temporal resolution = 125 Hz (8 ms per sample, spatial resolution = 1000 lpi). These movements were translated to an LCD monitor (1280 × 1024-pixel resolution) in the form of a cursor dot (3 mm width) with the movement-to-stimulus mapping set at 1:1. The intended targets were presented on the same screen and featured two circles that were separated at an amplitude of 16 cm (centre-to-centre); that is, 8 cm left and right of the midline. Each trial featured one of four possible sizes for both of the presented targets including 4, 2, 1, and 0.5 cm, which equated to an Index of Difficulty of 3, 4, 5, and 6 bits, respectively ($\log_2$(2 x Amplitude / Width; see [79]).

The stimuli were once again generated and controlled using an in-house designed routine courtesy of Matlab (MathWorks, Natick, MA, USA) running Psychtoolbox (version 3.0.11; [76]). The trials were randomly presented within each permutation of target size meaning each size appeared once every four trials. There were 5 trials for each target size (total trials = 20). Participants were able to initially practice for 5 trials with a 1.4 cm target; that is, equivalent to the median from the possible range of IDs within the actual experiment (i.e., 4.5 bits). Because the first and last movement segments did not feature a continuing movement segment both before and after their execution, they were removed from any subsequent calculations prior to the analysis [80]. The participant's mean proportion of target errors (as indicated by radial error exceeding the target radius), and movement times from all of the trials combined were calculated for subsequent analysis.[1]

2.4.5. Statistical analysis

The data were analysed using a three-way mixed-measures ANOVA courtesy of the statistical package IBM SPSS Statistics (Version 25, Chicago, IL, USA). Specifically, there was one between-measures factor of group (MCT, Placebo), and two repeated-measures factors of supplementation (pre-, post-supplementation) and exercise (before-, after-exercise). Significant effects featuring more than two means were further decomposed via a post hoc analysis using the Holm-Bonferroni method. Significance was set at $p < .05$.

3. Results

3.1. Trail making

Trail making A performance showed no significant main effect of group ($F(1,17) = 3.18$, $p = .092$), although there was a significant main effect of exercise ($F(1, 17) = 18.3$, $p < .001$, $\eta^2 = 0.519$), as cognitive performance decreased due to exercise. There was no significant group x exercise interaction ($F(1, 17) = 1.08$, $p = .314$), although there was a significant group x supplementation interaction ($F(1, 17) = 27.3$, $p < .001$, $\eta^2 = 0.617$). However, these effects were superseded by a significant group x exercise x supplementation interaction ($F(1, 17) = 7.54$, $p = .014$, $\eta^2 = 0.307$).

Trail making B performance showed no significant main effect of

[1] For purposes of the present study, we have isolated the handling and analysis of the reciprocal aiming task data to the main measures of performance; that is, mean proportion of target errors and movement time taken across all the target conditions combined (0.5-4-cm width; 3-6 bits). However, the more in-depth movement kinematics are subject to further investigation within a separate study, where there is sufficient scope to elaborate.

group (F(1, 17) = 0.122, p = .731), although there was a significant main effect of exercise (F(1, 17) = 25.5, p< .001, η^2 = 0.600), as cognitive performance decreased due to exercise. There was no significant group x exercise interaction (F(1, 17) = 3.14, p = .094), although there was a significant group x supplementation interaction (F(1, 17) = 35.1, p< .001, η^2 = 0.674). However, these effects were superseded by a significant group x exercise x supplementation interaction (F(1, 17) = 4.94, p = .04, η^2 = 0.225).

Post-hoc analyses revealed for both trail making A and B that the exercise induced decline in performance at pre-supplementation, as seen for both groups, was mitigated post-supplementation for the MCT group, but not the placebo group (Fig. 2). Furthermore, there was an improvement in performance in both measures from pre- to post-supplementation before-exercise (rested) for the MCT group, but not the placebo group.

3.2. Memory span

Digit span forwards performance showed a significant main effect of group (F(1, 17) = 10.0, p = .006, η^2 = 0.371), as the MCT group outperformed the placebo group overall, and exercise (F(1, 17) = 145, p< .001, η^2 = 0.895), as cognitive performance decreased due to exercise. There was significant group x supplementation (F(1, 17) = 60, p< .001, η^2 = 0.779) and group x exercise (F(1, 17) = 12.8, p = .002, η^2 = 0.431) interactions. However, these effects were superseded by a significant group x exercise x supplementation interaction (F(1, 17) = 6.62, p = .02, η^2 = 0.280). Post-hoc analyses revealed that the exercise induced decline in performance at pre-supplementation, as seen for both groups, was mitigated post-supplementation for the MCT group, but not for the placebo group (Fig. 3). Furthermore, there was an improvement in performance from pre- to post-supplementation before-exercise (rested) for the MCT group, but not the placebo group.

Digit span backwards performance showed no main effect of group (F(1, 17) = 2.83, p = .111), although there was a main effect of exercise (F(1, 17) = 44.7, p< .001, η^2 = 0.724), as cognitive performance decreased due to exercise. There was a significant group x supplementation interaction (F(1, 17) = 14.2, p = .002, η^2 = 0.456), although there was no significant group x exercise (F(1, 17) = 0.009, p = .926), nor group x exercise x supplementation (F(1, 17) = 0.643, p = .434) interactions. Post-hoc analyses revealed that the exercise induced decline in performance at pre-supplementation, as seen for both groups, was also present post-supplementation (Fig. 3). Furthermore, there was an improvement

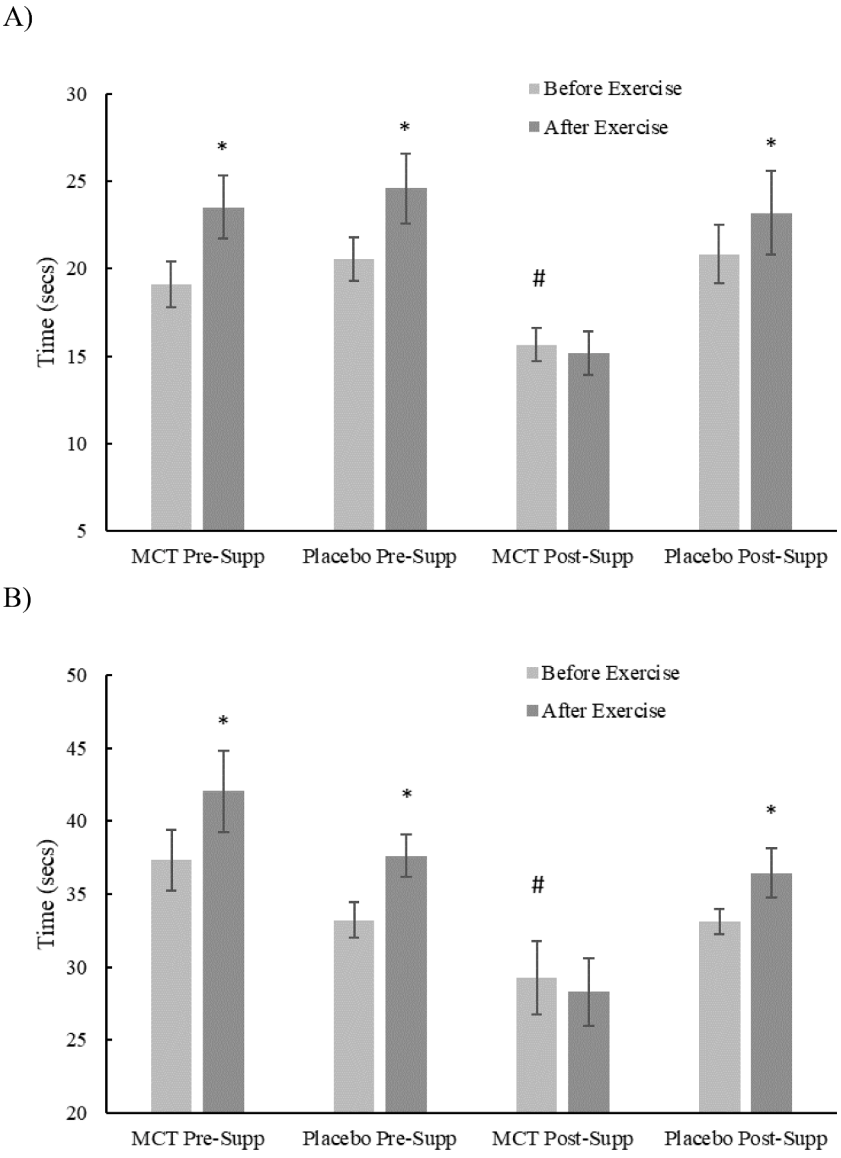

Fig. 2. Trail making performance in conditions A) Trail Making A and B) Trail Making B. * denotes a significant difference within a group due to exercise; # denotes a significant difference within a group due to the supplementation period. Significance was set at p< .05. Data represented as mean ± SE.

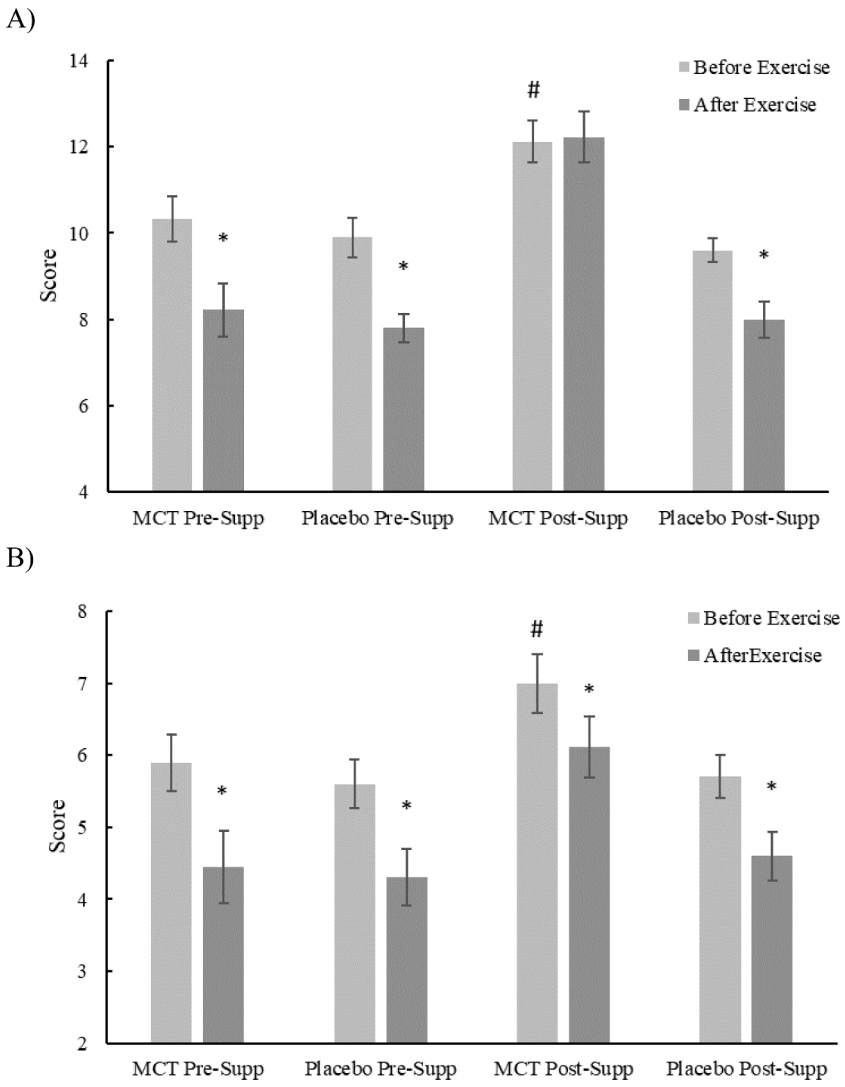

Fig. 3. Digit span performance in conditions A) Digit Span Forwards and B) Digit Span Backwards. * Denotes a significant difference within a group due to exercise; # denotes a significant difference within a group due to the supplementation period. Significance was set at $p < .05$. Data represented as mean ± SE.

in performance from pre- to post-supplementation before-exercise (rested) for the MCT group, but not the placebo group.

Spatial span forwards performance showed no significant main effect of group ($F(1, 17) = 0.744$, $p = .400$), although there was a significant main effect of exercise ($F(1, 17) = 66.2$, $p < .001$, $\eta^2 = 0.796$), as cognitive performance decreased due to exercise. There was a significant group x supplementation ($F(1, 17) = 7.80$, $p = .013$, $\eta^2 = 0.314$) and group x exercise ($F(1, 17) = 8.79$, $p = .009$, $\eta^2 = 0.341$) interaction. However, these effects were superseded by a significant group x exercise x supplementation ($F(1, 17) = 8.63$, $p = .009$, $\eta^2 = 0.337$) interaction. Post-hoc analyses revealed that the exercise induced decline in performance at pre-supplementation, as seen for both groups, was mitigated post-supplementation for the MCT group, but not the placebo group (Fig. 4).

Spatial span backwards performance showed no significant main effect of group ($F(1, 17) = 1.29$, $p = .271$), although there was a significant main effect of exercise ($F(1, 17) = 81.1$, $p < .001$, $\eta^2 = 0.827$), as cognitive performance decreased due to exercise. There was no significant group x supplementation ($F(1, 17) = 3.00$, $p = .102$), group x exercise ($F(1, 17) = 1.22$, $p = .286$), nor group x exercise x supplementation ($F(1, 17) = 2.37$, $p = .142$) interaction.

3.3. Stroop task

For reaction time difference, there was no significant main effect of group ($F(1,17) = 1.24$, $p = .281$), although there was a significant main effect of exercise ($F(1, 17) = 7.31$, $p = .015$, $\eta^2 = 0.301$), as cognitive performance decreased due to exercise. There was no significant group x exercise interaction ($F(1, 17) = 0.035$, $p = .854$), although there was a significant group x supplementation interaction ($F(1, 17) = 15.9$, $p < .001$, $\eta^2 = 0.483$). However, these effects were superseded by a significant exercise x group x supplementation interaction ($F(1, 17) = 31.3$, $p = .019$, $\eta^2 = 0.337$). Post-hoc analyses revealed that the exercise induced decline in performance at pre-supplementation seen by the MCT group was mitigated post-supplementation (Fig. 5).

For errors made (incongruent – congruent), there was no significant main effect of group ($F(1,17) = 0.937$, $p = .347$), although there was a significant main effect of exercise ($F(1, 17) = 13.9$, $p = .002$, $\eta^2 = 0.450$), as cognitive performance decreased due to exercise. There was no significant group x exercise ($F(1, 17) = 0.900$, $p = .356$), group x supplementation ($F(1, 17) = 1.96$, $p = .179$), nor group x exercise x supplementation ($F(1, 17) = 1.66$, $p = .215$) interaction. Post-hoc analyses revealed that the exercise induced decline in performance at pre-supplementation, as seen for both groups, was mitigated post-supplementation for the MCT group, but not the placebo group (Fig. 5).

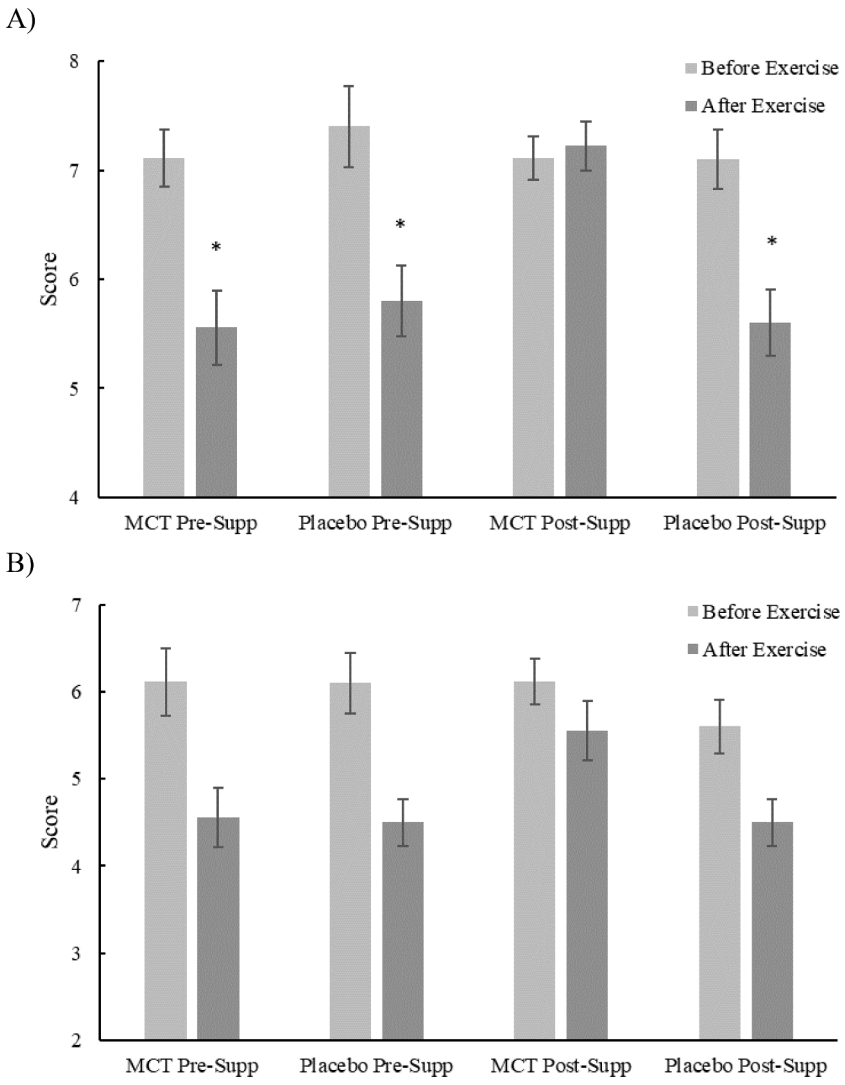

Fig. 4. Spatial span performance in conditions A) Spatial Span Forwards and B) Spatial Span Backwards.* denotes a significant difference within a group due to exercise; # denotes a significant difference within a group due to the supplementation period. Significance was set at $p < .05$. Data represented as mean ± SE.

3.4. Reciprocal aiming task

For movement time, there was no significant main effect of group ($F(1,17) = 2.19$, $p = .157$), although there was a main effect of exercise ($F(1, 17) = 13.2$, $p = .002$, $\eta^2 = 0.436$), as cognitive performance decreased due to exercise. There was no significant group x exercise interaction ($F(1, 17) = 0.358$, $p = .558$), although there was a significant group x supplementation interaction ($F(1, 17) = 16.5$, $p < .001$, $\eta^2 = 0.492$). However, these effects were superseded by a significant group x exercise x supplementation interaction ($F(1, 17) = 6.03$, $p = .025$, $\eta^2 = 0.262$). Post-hoc analyses revealed that the exercise induced decline in performance at pre-supplementation seen by the MCT group was mitigated post-supplementation (Fig. 6). Furthermore, there was an improvement in movement time from pre- to post-supplementation before-exercise (rested) for the MCT group, but not the placebo group.

For target errors, there was no significant main effect of group ($F(1, 17) = 0.356$, $p = .559$), although there was a significant main effect of exercise ($F(1, 17) = 22.4$, $p < .001$, $\eta^2 = 0.568$), as cognitive performance decreased due to exercise. There was no significant group x supplementation ($F(1, 17) = 3.79$, $p = .068$), nor group x exercise ($F(1, 17) = 1.78$, $p = .199$) interaction. However, there was a significant group x exercise x supplementation interaction ($F(1, 17) = 7.42$, $p = .014$, $\eta^2 = 0.304$). Post-hoc analyses revealed that the exercise induced decline in performance at pre-supplementation, as seen for both groups, was mitigated post-supplementation for the MCT group, but not the placebo group (Fig. 6).

4. Discussion

The present study investigated whether MCT supplementation could offset the decline in cognitive performance associated with a bout of prolonged exercise. Our results demonstrate that following a 2-week period of ingesting 12 g of MCTs per day, the cognitive decline caused by exercising for 60 min at 90% GET was significantly reduced, and in some cases, there was no significant cognitive decline following exercise. Moreover, MCT supplementation enhanced cognitive performance in rested (before-exercise) conditions and enabled this enhanced performance to be maintained after-exercise. The present data supports findings by Davis et al. [54] and Moore et al. [23] that prolonged exercise causes significant declines in cognitive measures requiring aspects of visual perception and memory, and that of previous work which found that transient declines in cognition are apparent both during [81, 82] and immediately following [10,83,84] exercise.

Although the brain utilises glucose as its main energy source, MCTs provide the brain with additional energy in the form of ketone bodies [85]. When blood ketone levels are high enough, the brain utilises

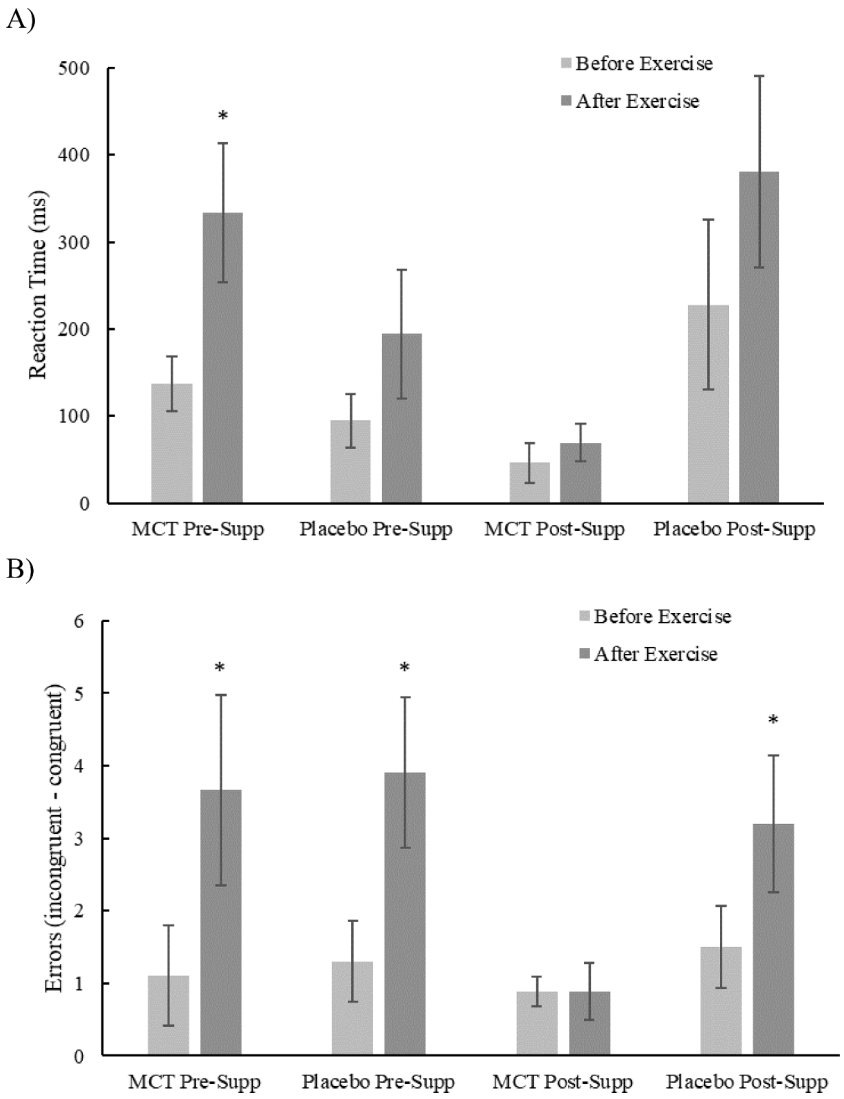

Fig. 5. Stroop task performance in conditions A) Reaction Time and B) Errors (incongruent – congruent). * Denotes a significant difference within a group due to exercise; # denotes a significant difference within a group due to the supplementation period. Significance was set at $p < .05$. Data represented as mean ± SE.

ketones preferentially over glucose, even at rest, with brain ketone metabolism being positively correlated with plasma ketone concentration [86,87]. Such increases in plasma ketone concentration is normally associated with ketosis, however, MCT ingestion allows this to occur without a radical change in diet [88–90]. Furthermore, free fatty acid derivatives from MCTs that bypass liver metabolism via the lymph system can directly cross the blood-brain barrier, providing a direct fuel source for the brain [59]. It is plausible that ketones/fatty acids present in the body due to the supplementation period mediated mechanisms causing cognitive decline, such as the depletion of brain glycogen stores [53]. There are no significant differences in brain ketone metabolism when comparing healthy young adults, older adults and adults with AD/mild cognitive impairment, [88,91–93], suggesting that ketone metabolism is preserved even when suffering from decreased cerebral metabolism/cerebral insulin resistance due to age/disease [62,66,67]. Therefore, it may be the case that the brain maintains its ability to utilise ketones despite the body being heavily fatigued by exercise, offsetting the cognitive decline associated with prolonged exercise. A further possible mechanistic explanation for the results of the study is an increased rate of mitochondrial biogenesis. This is due to the high concentration of C_{10} in the gels, paired with the fact that the doses of MCT were relatively low, meaning that the results cannon be solely explained via an increase in fuel sources for the brain [61,94,95].

The present MCT dosage and formula has been used previously [68,96]. Indeed, the improvement in cognitive performance following MCT supplementation in rested conditions mirrors our previous findings that daily MCT supplementation leads to improvements in the performance of trail making and digit span tasks in a similar population after a supplementation period of 2–3 weeks [68]. Moreover, the present data furthers these findings by showing that compared to baseline, MCT supplementation caused an improvement in after-exercise performance in all cognitive tasks. This effect was such that following MCT supplementation, with the exception of digit span backwards and spatial span backwards, there was no difference in cognitive performance before- versus after-exercise. Hence, not only was exercise-induced cognitive decline eliminated in such cases, but this was with a background of enhanced baseline performance. Therefore, not only did MCT supplementation enhance cognitive performance before-exercise, but this improvement was maintained despite the adverse effects of prolonged exercise. In contrast, the placebo group exhibited a consistent decline in cognitive performance with exercise unaffected by the supplementation period, thus precluding the possibility that the findings in the MCT group were due to a learning effect. Taken together with our previous study, this provides strong rationale to accept the hypothesis that MCT supplementation enhances baseline cognitive performance, in addition to offsetting the cognitive decline caused by a prolonged bout of

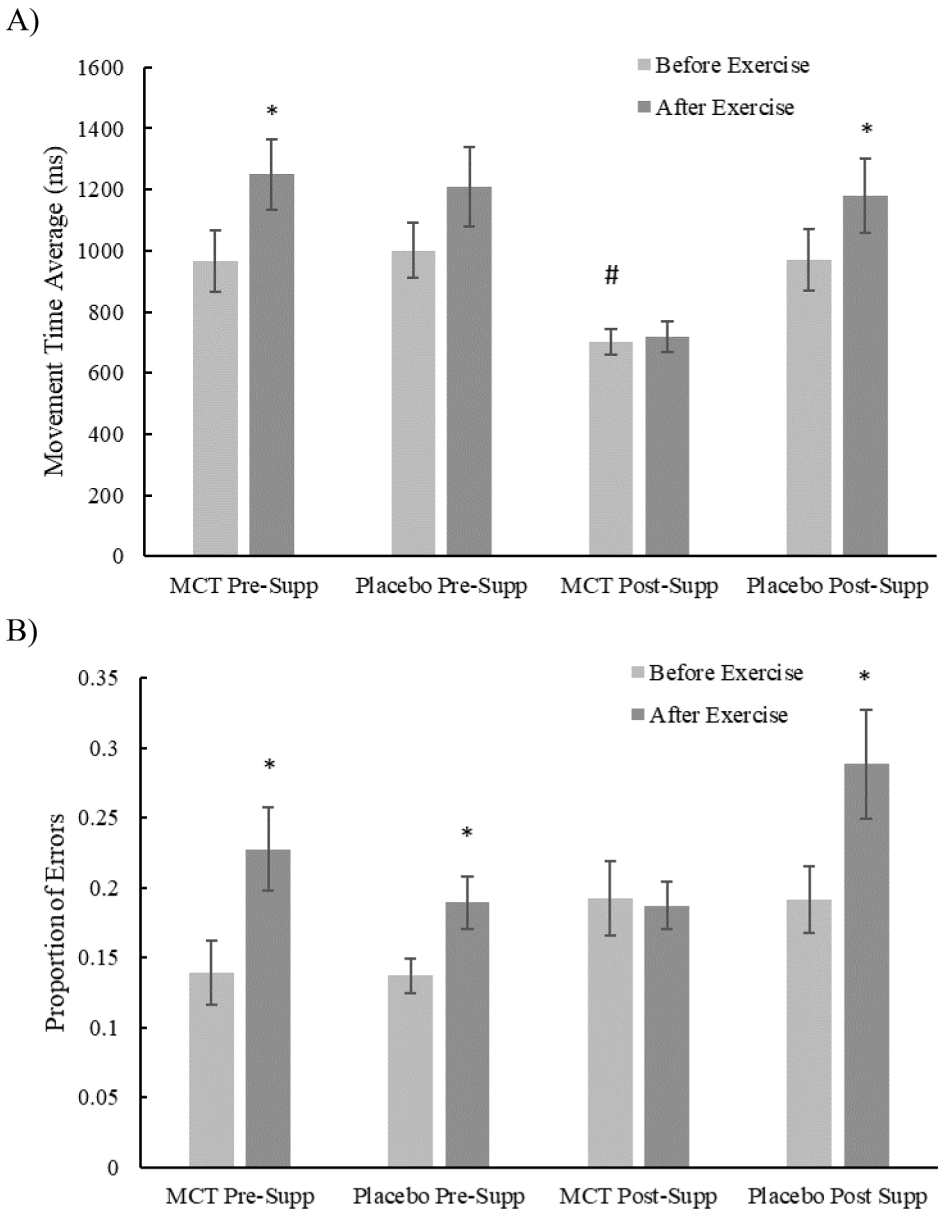

Fig. 6. Reciprocal Aiming Task performance in conditions A) Movement Time Average and B) Errors. * Denotes a significant difference within a group due to exercise; # denotes a significant difference within a group due to the supplementation period. Significance was set at $p < .05$. Data represented as mean ± SE.

prolonged exercise.

The enhanced performance for the MCT group in trail making A and B both before- and after-exercise suggests improvements in aspects of cognition such as processing speed, visual motor skills and sequencing [72]. This follows on from previous work showing that MCTs cause improvements in trail making performance in both elderly [65] and youthful [68] healthy participants. However, these improvements may be explained in part by the motor characteristics of the task following a similarly enhanced performance for the MCT group in the reciprocal aiming task. This particular task requires rapid manual movements toward a target without necessarily compromising the ability to hit it, which can prove somewhat challenging given that movement velocity is usually related to the movement's spatial variability [79,97]. More specifically, this task highlights the ability to more successfully feed-forward efferent motor signals in a coordinative fashion courtesy of a combination of the premotor and primary motor cortices [98] and cerebellum [99] respectively. At the same time, different sources of sensory feedback (e.g., vision, proprioception) must be processed via the relevant thalamic relay nuclei and primary sensory cortices with a view to modifying movement 'on-the-fly' [100,101]. Future research within our lab seeks to elaborate on the relative contribution of these underlying sensorimotor processes following the improvements caused by MCT supplementation.

MCT supplementation has also been previously demonstrated to improve performance in memory tests [62,63,65,66,96], including digit span and spatial span on young healthy participants [68]. The present data further supports these findings since after-exercise performance was enhanced for the MCT group for both the forwards and backwards test phases in digit span and spatial span, and also before-exercise performance in digit span forwards and backwards. However, in the backwards test phases, although performance was enhanced at rest and following exercise in the MCT group following supplementation, there remained a decline in performance with exercise. This could be explained due to the fact the backwards test phases are much more cognitively demanding. Whereas the forwards phases reflects solely memory storage, the backwards phases also require processing as the person must manipulate the stored numbers/blocks from their memory [102].

MCT supplementation had no impact on before-exercise (rested) performance for the Stroop task. However, post-supplementation, after-exercise performance was significantly improved from visit 1 for both reaction time and errors, and was unaffected by exercise per se, in contrast to pre-supplementation. This indicates that the MCT supplementation, although not directly impacting Stroop task performance, mediated the effect of exercise. Labelle et al. [103] observed that reaction times in the Stroop test increased in response to increasing exercise intensities, suggesting that 90% GET was not a high enough intensity to elicit negative effects. Alternatively, Alves et al. [104] actually showed an increase in Stroop performance due to high intensity exercise, although participants were given a short break between exercise and the cognitive tasks.

Notably, with a sufficient recovery duration following exercise, an enhancement in working memory may be observed [83], hence a strength of the present study is that cognitive tasks were conducted immediately post-exercise which simulates more closely the demands of sporting performance. A further strength of the study is the use of the gas exchange threshold by which to define exercise intensity, which permits a valid definition of relative exercise intensity and thus appropriately mitigates individual fitness differences. This is advantageous over previous literature, which used arbitrary measures such as age predicted heart rate max and the heart-rate reserve [18,28]. On the face of it, the sample size used in the present study appears to be relatively small, though seemingly sufficiently powered given the effects of exercise and MCT ingestion on cognitive performance. Furthermore, our previous work investigating the effects of these MCT gels on cognitive performance also rendered significant findings [68]. Nevertheless, our data do not necessarily permit the findings to be extrapolated to other populations, such as well-trained athletes.

5. Conclusion

The present study highlighted the positive effects of chronic MCT supplementation on cognition both at rest and following prolonged exercise. Our results suggest that MCTs with a 30:70 ratio of C_8:C_{10} mitigate the cognitive decline caused by a 1-hour bout of cycling at 90% GET. Future research should explore the mechanisms within the brain behind the ability of MCTs to improve cognitive performance and allow this level to be maintained following prolonged exercise. Furthermore, the applicability of the results from the present study in highly trained populations should be explored.

Author declaration

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Data availability

The data that has been used is confidential.

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