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RESEARCH

Ketone Monoester Supplementation Effects on a Comprehensive Cognitive Test Battery Following Non-Exhaustive Exercise

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Abstract
Ketone monoester (KME) supplementation has been suggested to preserve or enhance cognitive performance, but its effects across cognitive domains during non-exhaustive exercise remain unclear. We aimed to investigate whether KME improves cognitive performance during moderate-intensity exercise in healthy young men. In a randomized, double-blind, placebo-controlled, crossover study, 9 recreationally active healthy males (mean ± SD: age: 26 ± 5 year, $\dot{V}O_{2max}$: 47 ± 4 mL·kg^{-1}·min^{-1}) completed two experimental trials involving 90 min of cycling at 60% $\dot{V}O_{2max}$. Participants consumed either KME or tasted-matched placebo (PLA) drinks around exercise (total 0.75 g·kg^{-1}). A comprehensive cognitive test battery (CTB) of validated tests assessed memory, attention, inhibitory control, and visual processing before and after exercise (tests included delayed recall, spatial span, digit span, endogenous and exogenous covert shift of attention, Stroop task, psychomotor vigilance task, global form perception, and global motion perception). Post-exercise blood β-Hydroxybutyrate concentrations were higher in the KME (3.3 ± 0.5 mM) vs. PLA (~0.1 ± 0.0 mM; $P<0.01$). Only global motion perception showed a time x condition interaction ($P=0.044$), whereby KME rescued the decay observed in PLA. Moderate-intensity exercise of 90 min did not affect other cognitive performance metrics ($P>0.05$) and KME did not enhance cognitive function relative to PLA in any other domain tested ($P>0.05$). KME supplementation during 90-min of moderate-intensity non-exhaustive exercise preserved global motion perception but did not improve other cognitive performance in healthy young males.

Keywords Cognitive performance · Cycling · Ketosis · Ketone monoester

Introduction

Athletic performance relies on a complex interplay of physiological and cognitive processes (Scharfen & Memmert, 2019). Consequently, identifying strategies to mitigate exercise-induced cognitive decline or to enhance cognitive function during exercise important for athletes, even when physiological systems are not at the limit of their capacity. To optimise physical performance, nutritional interventions — particularly carbohydrate-based strategies— have been developed and refined over the last six decades (Burke & Hawley, 2018). However, recent evidence suggests that while carbohydrate ingestion can enhance physical performance, it does not consistently prevent cognitive decline following exercise (Yang et al., 2023).

Emerging research indicates that ketone monoesters (KME) may offer a promising alternative. These novel supplements induce rapid nutritional ketosis, elevating blood β-hydroxybutyrate (βHB) levels to ~3 mM within 60 min (Clarke et al., 2012), without requiring adherence to a low-carbohydrate ketogenic diet. This results in a unique metabolic state where both ketones and carbohydrates are available as energy substrates (Evans et al., 2017).

Notably, ketones are preferentially utilized by the brain even in the presence of ample glucose (Cunnane et al., 2016), and have been associated with increased cerebral blood flow and a higher Gibbs free energy yield for ATP synthesis compared to glucose metabolism (Mujica-Parodi et al., 2020; Poffé et al., 2023; Svart et al., 2018; Walsh et al., 2021). Although the exact mechanisms are not clear,

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these metabolic advantages may underpin the cognitive-enhancing effects reported in recent studies.

Indeed, multiple investigations have shown that KME supplementation can mitigate exercise-induced cognitive decline and enhance cognitive function even in the absence of physical fatigue. For example, KME reduced errors on a multitasking inhibitory control task following fatigue in male team sport athletes (Evans & Egan, 2018), and preserved reaction time during high-intensity intermittent exercise (Quinones & Lemon, 2022). Similarly, KME maintained attention and motor speed following a 100-km ultramarathon (Poffé et al., 2023), and improved inhibitory control and sustained attention in trained females after a 10-km cycling time trial (Waldman et al., 2024). Outside of athletic contexts, Graybeal et al. (2025), observed improvements in inhibitory control and working memory in the absence of exercise-induced fatigue.

Together, these findings suggest that KME may enhance or preserve cognitive performance particularly in the domains of inhibitory control, working memory, and sustained attention. However, whether KME exerts similar effects across a broader range of cognitive domains, and whether these benefits are consistent in both fatigued and non-fatigued states, remains unclear.

Therefore, we aimed at conducting an exploratory study to evaluate the effects of acute KME supplementation on cognitive performance before and after exercise using a comprehensive cognitive test battery (CTB). We specifically assessed the domains of memory, attention, inhibitory control, and visual processing, and hypothesized that KME would either enhance or sustain attention and inhibitory control following prolonged non-exhaustive exercise, as measured by validated cognitive tests.

Materials and methods

Participants

Nine recreationally active males, classified as tier 1 according to the participant categorization framework (McKay et al., 2022), (Age: 26 ± 5 (means ± SD); height: 1.80 ± 0.07 m; body mass: 80 ± 9 kg; $\dot{V}O_{2max}$: 47 ± 4 mL·kg^{-1}·min^{-1}) were included in the analysis after excluding one participant due to a technical error in the provision of the treatment drinks. Prior to the start of trials, participants provided informed written consent. The study was approved by the local Research Ethics Committee of Liverpool John Moores University (ref. no. H23/SPS/043) and conducted in accordance with the Declaration of Helsinki.

General Study Design

A randomized, double-blind, placebo-controlled, crossover study design was employed, with participants attending the laboratory on three separate occasions, with all testing taking place in the morning and early afternoon. On the first visit, participants completed assessments for participant characterisation, including a $\dot{V}O_{2max}$ test with the initial workload was set at 125 W, followed by 25-W increments per min, until exhaustion (Bishop et al., 1998). Participants then performed a CTB test run for familiarisation to avoid learning effects. Participants were randomized by a researcher external to this project to ensure allocation concealment and minimize bias. The two subsequent experimental testing visits were separated by a washout period of 7 days, and comprised a pre/post exercise CTB, with 90 min of cycling at 60% $\dot{V}O_{2max}$. Subjects received either 0.75 g·kg^{-1} of KME [>96% (*R*)−3-hydroxybutyl (*R*)−3-hydroxybutyrate] or a volume and taste-matched placebo (PLA). Both drinks were spread in two doses to be ingested at min 45 of the cycling session (0.5 g·kg^{-1}, 1.2 mL·kg^{-1}) and immediately after exercise completion (0.25 g·kg^{-1}, 0.6 mL·kg^{-1}). An outline of the study protocol is shown in (Fig. 1).

Experimental Protocol

Fourty-eight to twenty-four hours before each experimental sessions, participants maintained their usual food intake and exercise habits. Any exercise performed prior to the first trial was recorded and replicated for the second trial. Twenty-four hours before the experimental sessions, subjects abstained from alcohol, caffeine, and exercise or strenuous physical activity, and participants were provided prepackaged diet containing 5 g·kg^{-1}·day^{-1} carbohydrate, 1.5 g·kg^{-1}·day^{-1} protein, and 1 g·kg^{-1}·day^{-1} fat.

On trial days participants arrived fasted (0730 to 0830 h), completed a CTB upon arrival approximately 90-min pre-exercise, and were cannulated on the antecubital vein of either arm (Becton Dickinson (BD) Nexiva Closed IV Catheter 22G, Midmeds, Hertford, UK) for blood sampling. Venous blood samples were drawn into 6 mL serum vacutainers (BD, Midmeds, Hertford, UK) at 30 min pre-exercise and immediately after exercise. Subjects consumed a standardized breakfast (1 g·kg^{-1} carbohydrate, 0.1 g·kg^{-1} protein, 0.03 g·kg^{-1} fat) 30 min pre-exercise. Subjective perception of gastrointestinal symptoms was assessed during the experimental session with a 0–8 Likert scale questionnaire (Pfeiffer et al., 2009). Body mass was measured 5 min pre-exercise and after post-exercise CTB completion (704, SECA, Hamburg, Germany). Baseline measurements and measurements taken during

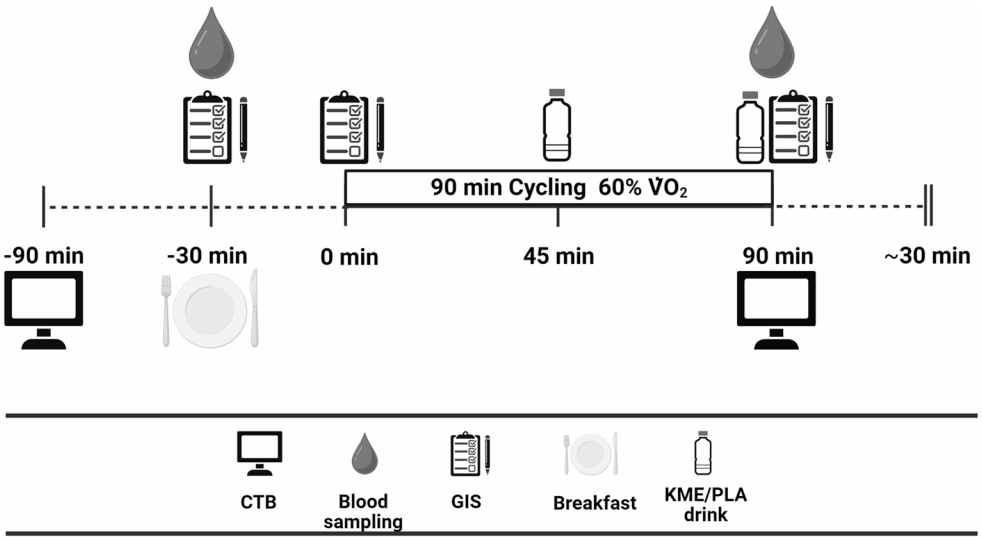

Fig. 1 Schematic of the study protocol. The study involved two experimental sessions following a randomized, double-blind, crossover design. During each visit, subjects completed a pre- and post-exercise cognitive test battery (CTB). Exercise consisted of 90-min steady state cycling at 60% $\dot{V}O_{2max}$. Participants consumed two doses of a KME or PLA drink at 45-min into the exercise session (0.5 $g \cdot kg^{-1}$) and immediately after completing the cycling session (0.25 $g \cdot kg^{-1}$), respectively. CTB, cognitive test battery; GIS, gastrointestinal symptoms scale; KME, ketone monoester; PLA, placebo

the last 3-min of every 15-min stages of the exercise session included respiratory gas exchange (Vyntus™ CPX metabolic cart, Vyaire, Mettawa, Illinois, USA), heart rate (H10 Polar, Polar Electro Oy, Kempele, Finland), and rating of perceived exertion (RPE, 6–20 scale, ((Borg, 1982). During exercise participants consumed water *ad libitum*, and hydration status, defined as % body mass loss (%BML), was monitored through changes in pre and post-exercise body mass and total fluid intake (Maughan et al., 2007). Post-exercise CTB was assessed immediately after exercise completion.

Ketone and Placebo Drinks

Double-blinding and randomization of KME and PLA drink were performed by an investigator external to this study. KME drink contained water, KME (TdeltaS Ltd, Thame Oxfordshire, UK), 5% w/v sucralose (MyProtein, Northwich, UK), and 1% v/v strawberry flavour drops (Myprotein, Northwich, UK). PLA drink contained water, bitter sucrose octaacetate (Sigma-Aldrich, Bornem, Belgium), 5% w/v sucralose, and 1% v/v strawberry flavour drops, dissolved and in proportion to water volume. To avoid potential visual identification, both drinks were provided in non-transparent bidons.

Venous Blood Analysis

βHB and glucose were measured in serum using the RX Daytona+ (Randox Laboratories, Crumlin, UK: assay codes RB1007 and GL8319, respectively).

Cognitive Test Battery

The CTB was developed and administered using Labvanced (Scicovery, Paderborn, Germany), an online reliable platform for conducting cognitive studies (Kolyasnikov et al., 2019). The CTB assessed working memory (Graybeal et al., 2025; Stalmans et al., 2025), inhibitory control (Quinones & Lemon, 2022), and sustained attention (Waldman et al., 2023) in line with previous KME research, and additionally including higher-order visual processing tasks. All CTB tasks were selected for their established validity and reliability in measuring these cognitive domains (Ho et al., 2005; Jasinski et al., 2011; Lo et al., 2012; Nasreddine et al., 2005; Ro & Rafal, 1999; Sanabria et al., 2019; Stroop, 1935; Zwicker et al., 2006). During the familiarization session, participants completed the CTB pre- and post-exercise. Electronic devices and music were prohibited until the post-exercise CTB was completed. The battery included standardized tests assessing memory: *i*) short-term memory, *ii)* phonological working memory, and *iii)* visuo-spatial working memory), attention: *iv*) covert exogenous shift of attention, *v*) covert endogenous shift of attention (CSoA), and *vi*) sustained attention), inhibitory control: *vii*) Stroop task, and higher-order visual processing: v*iii*) global form perception and *ix*) global motion perception. For short-term memory, phonological and visuo-spatial working memory, trials were excluded from analysis if participants scored zero, as this likely indicated an error in response registration and/or failure in the participant to simply follow the task. For CSoA and Stroop task, incorrect response reaction times, anticipation reaction times (< 100 ms), and values above +2SD the intra-individual mean were removed for

subsequent analyses. While for PVT anticipatory reaction times (< 150 ms) and failed responses or + 2SD above the intra-individual mean were regarded as lapses in attention, and thus removed for subsequent analyses.

Delayed Recall

Short-term memory was assessed using a delayed recall task (adapted from the Montreal Cognitive Assessment (*MoCA*); (Nasreddine et al., 2005), which is often used for screening cognitive impairment or dementia onset. Participants were shown with a list of 5 words to remember, and recalled the words after completing the digit and spatial span tasks (~ 7 min). To avoid any familiarity, different word lists consisting of similar semantic (i.e., meaning and/or themes) and phonological (i.e., no. of syllables) features were used for each of the experimental conditions. Short-term memory was measured by the total number of correctly recalled words (max score: 5).

Memory Span

Phonological working memory was assessed using the digit span (DS) test (Jasinski et al., 2011), and visuo-spatial working memory was evaluated using the spatial span (SS) test (Lo et al., 2012); both of which comprise the widely-used Wechsler Memory Scale (WMS) (Wechsler, 1945). For the DS test, participants were presented with a sequence of numbers and asked to type them in the same order. For the SS test participants were presented with a sequence of 9 squares that lit up in a pre-determined order. Therein, participants had to tap the squares in the corresponding order in which they were lit up. Each task included 2 trials per sequence length, starting with two items and increasing to nine. The task ended when participants failed both trials at any sequence length. Performance was quantified by the maximum number of sequences correctly recalled (max 16).

CSoA

Exogenous (stimulus-driven) and endogenous (goal-directed) attention were assessed using a covert attention paradigm (Ro & Rafal, 1999). In the exogenous task, a cross (X) was initially presented in a left or right square within a short (100 ms) or long (800 ms) time of a subsequent response target. The short time typically manifests in a quicker response when the target appears at the previously cued compared to uncued location (*cue facilitation*), while the long-time typically manifests in the reverse (*inhibition of return*) (Posner, 1984). In the endogenous task, arrows were initially presented pointing left (<<) or right (>>) from centre. Therein, for both tasks, a green target was presented in the left or right squares to cue the participants to tap left ('G') or right ('J'). The cuing effect (mean uncued reaction time – mean cued reaction time) for each of the tasks was calculated and forwarded for analysis.

Psychomotor Vigilance Task

Sustained attention was measured using a 5-min psychomotor vigilance task, which is shown to be highly sensitive to acute bouts of exercise (González-Fernández et al., 2017) and aerobic fitness levels (Luque-Casado et al., 2016). Participants were instructed to react to a circle that began to change colour by pressing the spacebar on the keyboard with the index finger of their dominant hand. The stimulus was presented at random intervals between 2,000 and 10,000 ms (Sanabria et al., 2019), and for a period of 1,500 ms or until response was given. The slope from a linear polynomial fit to the degree of 1 was taken as a measure of vigilance while lapses were considered as a measure of failure to sustain attention.

Stroop Task

Inhibitory control—a component part of executive function (Miyake et al., 2000)—was assessed using the Stroop task (Stroop, 1935). Participants were presented with a list of colour words (e.g.,"red", "blue" or "green") displayed in either compatible ink colour (e.g., cued: "red" in red ink) or incompatible ink colour (e.g., uncued: "red" in blue ink). Once a word appeared on screen, participants were instructed to ignore the meaning of the word and respond to the colour of the ink. The Stroop effect was calculated and forwarded for analysis. Shorter reaction times are expected from compatible trials compared to incompatible trials.

Global Perception Tasks

Coherent global perception is a key characteristic of higher-level visual processing, where multiple local stimulus details can become perceptually unified into a single pattern. It generally reflects how the human visual system can transmit signals from initially small neural receptive fields at the retina to large ones nearer the striate cortex (V1) (Mather, 2023). There are two test variants of global perception including form and motion, which have been previously shown to discriminate typically-developing persons and a series of neurodiverse populations including dyslexia (Hansen et al., 2001), autism (Pellicano et al., 2005), and William's syndrome (Atkinson et al., 1997).

The global form perception task features a series of static arrows pointing either in a single left or right direction (signal), while other arrows point in random different

directions (noise). In a none-to-dissimilar vein, the global motion perception task features a series of square dots moving in a single left or right direction (signal) at a constant velocity (~6°/sec), while other dots move in random different directions (noise). Participants judge the direction of the signal by pressing a left ('G') or right ('J') key as the level of coherence from the signal progressively decreases between 100%, 75%, 50%, 25%, 12.5%, and 6.25% for the form task, and 100%, 50%, 25%, 12.5%, 6.25%, 3.12%, and 1.6% for the motion task (Ho et al., 2005; Zwicker et al., 2006). Each coherence level comprised of 8 trials, while the task ceased once there were ≥4 incorrect or no responses at a particular coherence level. The coherence threshold was determined by initially fitting a Weibull function to the data using a maximum-likelihood estimation procedure, which was performed using the Palamedes toolbox (Prins & Kingdom, 2018). Therein, the threshold was taken as the point of inflection (maximum slope) that is synonymous with 82% correct within a two-alternative force choice (Strasburger, 2001).

Exit Survey

After the final experimental trial, participants completed an exit interview and were asked *i*) if they could differentiate the KME and PLA drink, *ii)* in which trial they received the KME or PLA drinks, *iii*) in which trial they thought their cognitive performance was better.

Statistical Analysis

Using a large effect size (f=0.75) derived from a previous study evaluating the effect of KME on sustained attention through PVT and inhibitory control via incongruent flanker task (Waldman et al., 2024), the power analysis indicated that a sample size of 8 participants would be sufficient to demonstrate a significant difference with an α level of P<0.05 and expected power (1–β) of 0.90 for a repeated-measures design. Firstly, we assessed the validity of the tests where possible including CSoA, PVT and Stroop tasks by analysing the pre-exercise results from both treatment groups combined. That is, cuing effects (cued vs. uncued) from each of the exogenous CSoA, endogenous CSoA, and Stroop tasks were analysed using a paired-sample test. Meanwhile, the slope coefficients from the PVT were compared with a theoretical value of zero using a single-sample t-test. Normality was tested using the Shapiro-Wilk test, and results were expressed as mean ± standard deviation. Sphericity was tested using Mauchly's test, and Greenhouse-Geisser correction was applied if violated. Due to missing data points a general linear mixed modelling (LMM) was used to analyse all metrics for each cognitive task and CTB completion time. Models included fixed effect for time and condition with random intercepts for subjects. Statistical significance of the fixed effect was determined using type III tests with Satterthwaite approximation degrees of freedom. A two-way repeated-measures (2 × 2) RM-ANOVA was performed to analyse venous blood glucose and βHB, while a RM-ANOVA (2 × 7) analysed all cardiorespiratory metrics and RPE. Paired *t*-tests were used to analyse %BML, timing between exercise and CTB start. To assess potential learning effects, all cognitive tasks were analysed in chronological order, irrespective of condition with LLM. If significant interactions effects were observed, *post hoc* analysis was performed with Bonferroni´s correction. Significance was declared at $P \leq 0.05$. Effect size measures were reported for significant main effects as partial eta squared (n_p^2: small effect ≤ 0.05; moderate effect = 0.05–0.14; large effect ≥ 0.14) (Maher et al., 2013) for RM-ANOVA and semi-partial r^2 (Edwards et al., 2008) for LMM (r^2: small effect ≤ 0.02; moderate effect = 0.02–0.26; large effect ≥ 0.26) (Cohen, 1988). Analyses were performed in SPSS v27 (IBM Corp, Armonk, NY, USA), and figures were designed using GraphPad Prism v10 (GraphPad Software, San Diego, CA).

Results

Physiological and Metabolic Responses

Participants exercised at ~63% of $\dot{V}O_{2max}$, which elicited 148 ± 12 bpm HR, and 12 ± 1 RPE. There were no significant differences between treatments for exercise-related parameters assessed such as HR, RPE, $\dot{V}O_2$, and $\dot{V}CO_2$.

We observed a significant main effect for condition (P<0.01, η_p^2 = 0.98 —large—), time (P < 0.01, η_p^2 = 0.95 —large—), and an interaction (P<0.01, η_p^2 = 0.95 —large—) in serum βHB concentrations. As expected, pre-exercise serum βHB concentrations were similar ~0.1 mM in both conditions (P = 0.09) but were significantly higher in the KME condition (3.3 ± 0.5 mM) compared to the PLA condition (~0.1 mM) post-exercise after KME drink provision (P < 0.01).

There was a significant interaction (P=0.03, η_p^2 = 0.49 —large—), but no main effect of condition (P = 0.09) or time (P=0.06) for serum glucose concentrations. Baseline serum glucose at PRE was similar in both conditions (KME = 4.9 ± 1.0 mM, PLA = 4.8 ± 0.8 mM). Serum glucose concentrations were lower in KME compared to PLA (KME: 3.9 ± 0.5, PLA: 4.7 ± 0.6 mM, P = 0.01) post-exercise.

There was no significant difference (P>0.05) between KME and PLA condition on %BML (P=0.30;

KME = 1.68 ± 0.60%, PLA = 1.57 ± 0.54%), suggesting no difference in hydration status between trials.

The reader may find further details of other physiological and metabolic responses reported in an accompanying manuscript to this work (Mosquera-Lopez et al., 2025),

GI Symptoms

The average incidence of GI symptoms at 30 min pre-exercise (KME = 0 ± 0, PLA = 1 ± 2 on a 96-point scale) and immediately before exercise (KME = 0 ± 1, PLA = 1 ± 2) were low, increasing marginally immediately post-exercise for both conditions (KME = 5 ± 3, PLA = 3 ± 3), but remaining low, suggesting no concerns of either conditions on incidence of gastrointestinal problems.

Cognitive Test Battery

There was no difference between KME and PLA in the delay to start the CTB after exercise (263 ± 75 s and 269 ± 107 s, respectively, $P = 0.81$).

For CTB completion time, there was no significant interaction ($P = 0.90$) or main effect of condition (KME: 1446 ± 91 s, PLA: 1415 ± 109 s, $P = 0.20$). However, there was a significant effect of time ($P < 0.01$, $r^2 = 0.29$ — large—) where POST (1391 ± 102 s) was faster than PRE (1471 ± 82 s, $P < 0.01$).

There was no visit order effect (visit 1 vs. visit 2, $P > 0.05$) for spatial and digit span, delayed recall, exogenous and endogenous CSoA, Stroop effect, and global form and motion coherence thresholds.

Memory

In the spatial span task, one trial from one participant was excluded from analysis for scoring zero in PLA POST condition. There was no significant interaction or main effects ($P > 0.05$) for spatial span (KME PRE: 9 ± 2, KME POST: 9 ± 2, PLA PRE: 9 ± 3, PLA POST: 8 ± 3) (Fig. 2A) and digit span task (KME PRE: 11 ± 2, KME POST: 10 ± 2, PLA PRE: 10 ± 2, PLA POST: 10 ± 3) (Fig. 2B).

In the delayed recall task, two trials from one participant were excluded from analysis for scoring zero in KME condition. There was no significant interaction or main effects ($P > 0.05$) for delayed recall task (KME PRE:5 ± 1, KME POST: 5 ± 0, PLA PRE: 4 ± 1, PLA POST: 4 ± 1) (Fig. 2C).

Attention & Inhibitory Control

In the exogenous CSoA, 70 out of 1152 trials (6.1%) were removed prior to analysis due to anticipatory responses < 100 ms (0.2%), incorrect responses (2.0%), and intra-individual lapses (3.9%). Pre-exercise long and short cuing effect were in agreement with the hypothesized direction (long: cued > uncued, short: cued < uncued, $P < 0.05$). There were no significant interactions, nor main effects of condition and time ($P > 0.05$) for exogenous CSoA long cuing effect (Fig. 3A) or short cuing effect (Fig. 3B).

In the endogenous CSoA, 80 out of 1440 trials (5.6%) were eliminated prior to analysis due to anticipatory responses < 100 ms (0.1%), incorrect responses (1.1%), and intra-individual lapses (4.4%). Pre-exercise cuing effect favoured the cued trials compared to the uncued trials ($P < 0.05$). There was no interaction or main effect for

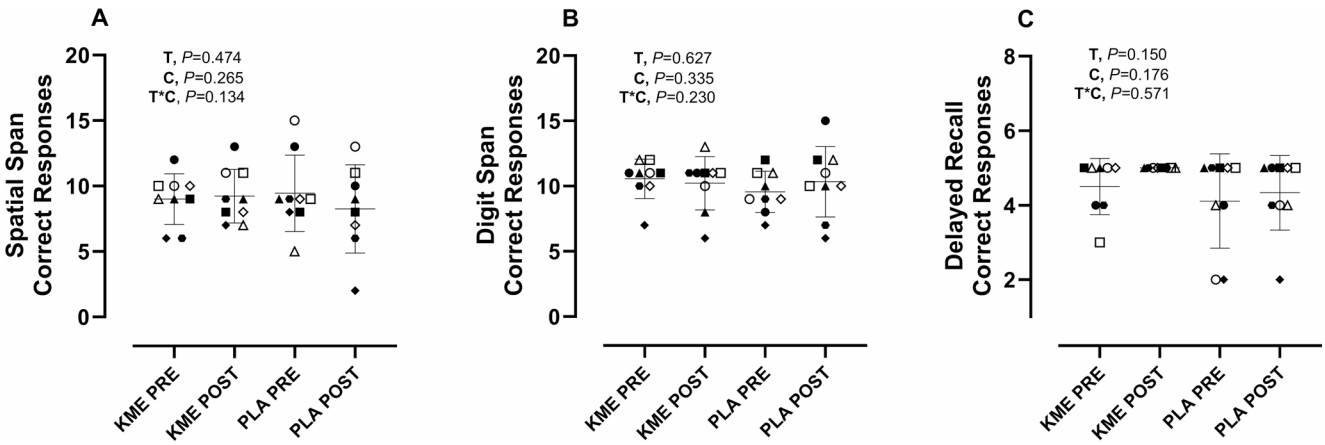

Fig. 2 Cognitive tests related to memory. Comparing KME vs. PLA pre-post exercise for spatial span correct responses (**A**), digit span correct responses (**B**), and delayed recall correct responses (**C**). Data presented as mean ± SD and values identifying each individual are represented with a unique symbol each. PRE, pre-exercise; POST, post-exercise

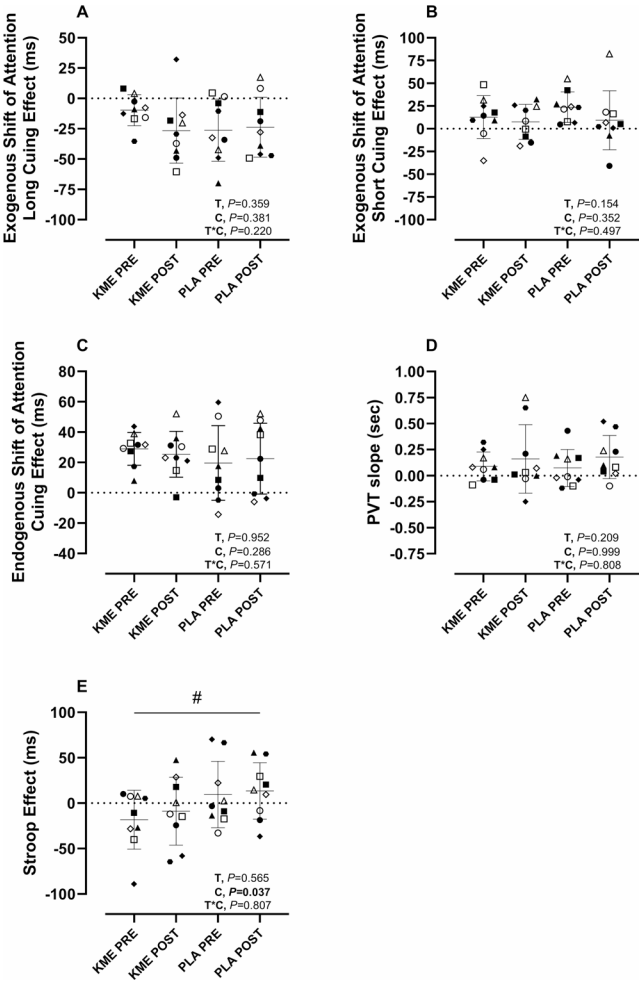

Fig. 3 Cognitive tests related to shifting of attention, sustained attention and inhibitory control. Comparing KME vs. PLA pre-post exercise for exogenous shift of attention long cuing effect (**A**), exogenous shift of attention short cuing effect (**B**), endogenous shift of attention cuing effect (**C**), PVT slope (**D**), Stroop effect (**E**). Data presented as mean ± SD and individual values identifying each individual are represented with a unique symbol each. $^{\#}P<0.05$ PLA vs. KME

condition and time for endogenous CSoA cuing effect ($P>0.05$) (Fig. 3C).

In the PVT task, 96 out of 1614 trials (6.0%) were removed prior to analysis due to anticipatory responses < 150 ms (1.4%) and intra-individual lapses (4.5%). There was no significant interaction or main effects ($P>0.05$) for PVT lapses (KME PRE: 2 ± 1, KME POST: 2 ± 1, PLA PRE: 2 ± 1, PLA POST: 2 ± 1). PVT pre-exercise slope was significantly different to zero ($P<0.05$). There was no significant interaction or main effects for PVT slope ($P>0.05$) (Fig. 3D).

In the Stroop task, 121 out of 1620 trials (7.5%) were removed prior to analysis due to anticipatory responses < 150 ms (0.1%), incorrect responses (2.5%), and intra-individual lapses (4.8%). There was no difference between pre-exercise cued and uncued trials for Stroop task ($P>0.05$). For Stroop effect, there was no significant interaction or time effects ($P>0.05$), but there was a condition effect ($P=0.04$, $r^2=0.13$ —moderate—) with PLA obtaining higher Stroop effect values than KME ($P=0.04$) (Fig. 3E).

Visual Processing

There were no significant main effects of time, treatment or interaction ($P>0.05$) for global form coherence threshold (Fig. 4A). For motion perception coherence threshold there was a significant interaction ($P=0.04$, $r^2=0.16$ — moderate—), but no main effect of condition ($P=0.38$) or time ($P=0.07$). *Post hoc* analysis revealed that PLA POST (38 ± 34%) was significantly higher ($P=0.02$) than PLA PRE (17 ± 13%) (Fig. 4B).

Exit Survey

Two participants (22%) were able to differentiate the KME from the PLA based on their perception of the organoleptic characteristics of the drinks. Five participants (56%) adequately identified the trial in which the KME drink was

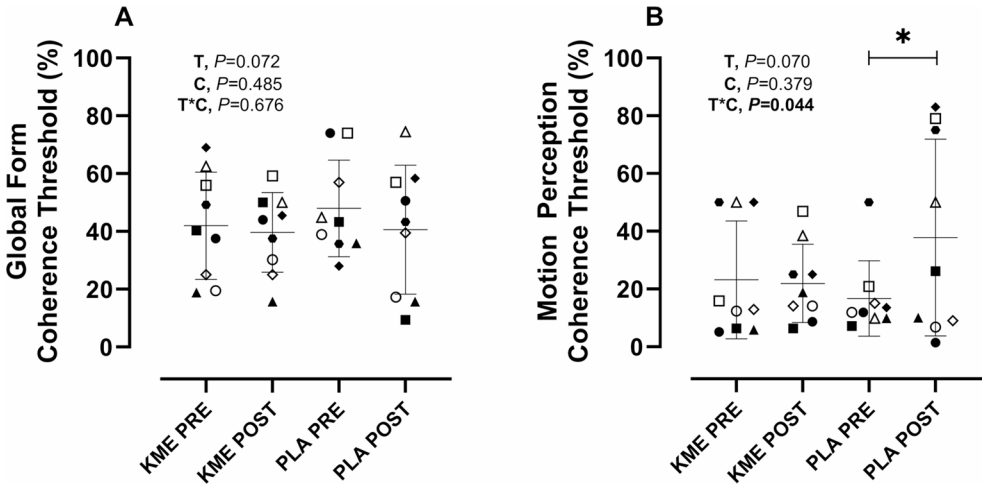

Fig. 4 Cognitive tests related to visual processing. Comparing KME vs. PLA pre-post exercise for global form coherence threshold (**A**), motion perception coherence threshold (**B**). PRE, pre-exercise; POST, post-exercise. Data presented as mean ± SD and individual values identifying each individual are represented with a unique symbol each. * $P<0.05$ PLA PRE vs. PLA POST

provided. The remaining four participants (44%) incorrectly identified the trial in which they received KME. Given the binary nature of the question, the trial identification outcome can be attributed to chance. Retrospective evaluation of the individuals upon unblinding showed that 3 participants (33%) considered that their performance improved on the KME trial, 4 participants (44%) considered their performance superior in the PLA trial, and 2 participants (22%) perceived no difference in their performance across the two trials.

Discussion

The aim of this study was to explore the effect of ketone monoesters on enhancing or preserving a wide range of cognitive abilities in individuals following a non-exhaustive exercise bout. The main finding is that KME did not affect metrics of cognitive performance related to memory, attention, and inhibitory control but attenuated the post-exercise decline in visual motion perception. Our findings suggest that, in the absence of an exercise-induced cognitive decline, KME supplementation may only have a small effect on cognitive performance in healthy young participants.

Utilising a cohort of recreationally active healthy male adults, this is the first study to incorporate a comprehensive cognitive test battery to evaluate multiple cognitive domains, following the ingestion of KME during a 90-min moderate-intensity steady-state cycling protocol. The provision of 0.5 g/kg of KME halfway through the 90-min exercise bout elevated βHB to ~3.3 mM prior to the post-exercise CTB, and this appears to be the highest average value achieved when compared to research with similar experimental protocols where βHB concentrations have been reported to reach ~2.6 mM (Evans & Egan, 2018; Quinones & Lemon, 2022; Waldman et al., 2023). Cognitive domains that have been tested in separate studies using KME ingestion around exercise included inhibitory control (Evans & Egan, 2018; Evans et al., 2019; Quinones & Lemon, 2022; Waldman et al., 2024), attention (Evans & Egan, 2018; Poffé et al., 2023; Waldman et al., 2023, 2024), and working memory (Stalmans et al., 2025). For the first time we incorporate all these cognitive tests in one study and included new tests to evaluate visual processing utilizing validated methodology to provide a comprehensive assessment of cognitive capacity modulated by KME.

The main finding of our study was that KME did not modulate most of cognitive domains assessed but it attenuated the post-exercise decline in visual motion perception (Figs. 2, 3 and 4). The rescue of global motion perception by KME is a novel finding that guarantees further investigation. Findings on the other cognitive domains are comparable to previous research showing no positive effects of KME on post-exercise inhibitory control (Quinones & Lemon, 2022; Waldman et al., 2023), attention (Evans & Egan, 2018; Stalmans et al., 2025; Waldman et al., 2023), and working memory (Stalmans et al., 2025), but different from research reporting positive effects of KME supplementation on inhibitory control (Evans & Egan, 2018; Graybeal et al., 2025; Poffé et al., 2023; Waldman et al., 2024) and attention (Poffé et al., 2023; Waldman et al., 2024). Different results may be attributable to differences in methodology.

Differences in exercise protocol duration and intensity and co-ingestion of ketones with other nutrients may explain some of the differences from other research. Other studies showing positive effects of KME in the cognitive domains we tested included longer exercise duration (Poffé et al., 2023) or intensity (Evans & Egan, 2018; Quinones & Lemon, 2022) and had produced a decline in cognitive performance, which ketones rescued. Co-ingestion of KME with other nutrients may also play a role. While our participants were fed carbohydrates 30 min pre-exercise and did not become hypoglycaemic, KME ingestion resulted in a 20% decrease in circulating glucose post-exercise, similar to Poffé et al. (2023). In this context, it is noteworthy that other studies showing a positive effect of KME on cognitive performance, have also provided KME drinks with concomitant CHO intake (Evans & Egan, 2018; Poffé et al., 2023; Waldman et al., 2024). Nonetheless, two studies showing a positive effect on cognitive performance, provided KME without the co-ingestion with other nutrients (Graybeal et al., 2025; Quinones & Lemon, 2022). In any case, we believe that there may be more than just a difference in methodological details between our study and others, since it appears that the prevailing finding in the literature is that KME can mitigate the exercise-induced decline of some cognitive domains (Evans & Egan, 2018; Evans et al., 2019; Poffé et al., 2023; Quinones & Lemon, 2022; Waldman et al., 2023), but there is evidence showing enhancement of cognitive performance (Graybeal et al., 2025; Waldman et al., 2024), which our findings did not corroborate.

A limitation of this exploratory study is that it incorporated a small cohort ($n=9$), however this is consistent with other studies in this area, ($n=8$–12 (Evans & Egan, 2018; Evans et al., 2019; Graybeal et al., 2025; Poffé et al., 2023; Quinones & Lemon, 2022; Waldman et al., 2023, 2024). Given the sample size, we can only conclude that KME did not produce large effects in most of the variable assessed. Also, due to the nature of the cognitive capacity test, the tests could not be performed *during* exercise. Even though we purposefully minimised the transition time between the ergometer and CBT, there was still a small transition time and participants were not exercising during the test. Future studies investigating whether KME can enhance cognitive

performance during non-fatiguing exercise should involve larger cohorts to detect smaller effect sizes, and develop and/or include tests that can be conducted *during* exercise.

In conclusion, supplementation of KME during 90-min moderate-intensity exercise resulted in a significant increase in circulating ketones and mitigated the decline in global motion perception but showed no significant effects on cognitive performance related to memory, attention, and inhibitory control.

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Data Availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethical Approval This study was conducted in accordance with the principles of the Declaration of Helsinki. The study was approved by the local Research Ethics Committee of Liverpool John Moores University (ref. no. H23/SPS/043).

Consent To Participate Written informed consent was obtained from all the participants after complete explanation of the aims and protocols of this study.

Competing Interests The authors declare no competing interests.

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