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Effects of L-Tyrosine Ingestion on Endurance Performance in Mentally Fatigued Cyclists

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ABSTRACT

This study investigated whether L-tyrosine supplementation enhances endurance performance in mentally fatigued cyclists. Twelve recreational cyclists completed two constant-workload tests to exhaustion cycling tests under two experimental conditions at 80% of maximal endurance power output: L-tyrosine ingestion (300 mg/kg) under mental fatigue (TYR-MF), and placebo under mental fatigue (PLA-MF). Mental fatigue (MF) was induced by a 60-min Stroop task (ST). Oxygen consumption (VO_2), rating of perceived exertion (RPE), and heart rate (HR) were measured throughout the cycling test. Time to exhaustion in the TYR-MF condition (459.9 ± 199.6 s) was higher when compared to the PLA-MF experimental condition (398.7 ± 222.1 s) ($p = 0.008$). The increase (i.e., slope technique) of RPE throughout the cycling to exhaustion was lower in the TYR-MF (0.560 ± 0.184 a.u.) than in PLA-MF (0.673 ± 0.251 a.u.) ($p = 0.03$) experimental condition. No differences were observed between conditions for VO_2 and HR data ($p > 0.05$). L-tyrosine ingestion increased endurance performance by approximately 16% in mentally fatigued cyclists. This effect was accompanied by a reduction in RPE slope during cycling to exhaustion. Therefore, these preliminary findings suggest that L-tyrosine supplementation may offer moderate benefits in performance for cyclists under mental fatigue conditions, although confirmatory studies with larger samples are needed.

1 | Introduction

Whole-body endurance tasks involving repetitive contractions of large muscle groups impose both physical and mental demands that can limit performance (Chamari and Padulo 2015; Lepers et al. 2000; Pageaux 2014). Endurance performance depends on both physiological capacity and the cognitive ability to sustain effort despite mounting discomfort (Marcora et al. 2009a; Martin et al. 2018). During prolonged, continuous effort, various changes in physiological variables are observed, including increased heart rate, oxygen consumption, and accumulation of metabolic byproducts (Azevedo et al. 2016; Marcora et al. 2009a). These physiological alterations occur alongside cognitive strain from maintaining focus, making tactical decisions, and sustaining motivation throughout prolonged exercise bouts (Schiphof-Godart et al. 2018). Thus, changes in psychological variables are also observed, specifically the rate of perceived exertion (RPE) (Marcora et al. 2009a; Martin et al. 2018). Therefore, it is reasonable to suggest that athletes engaged in endurance sports may experience both neuromuscular and mental fatigue (MF), often accompanied by discomfort, tiredness, and reduced motivation (Ishii et al. 2014; Tanaka et al. 2014).

Specifically, MF is defined as a psychobiological state characterized by subjective feelings of tiredness, reduced alertness, and

Highlights

- Ingestion of L-tyrosine (300 mg/kg) before exercise improves endurance performance under mentally fatiguing conditions.
- The rate of perceived exertion (RPE) increase during cycling to exhaustion is lower after L-tyrosine ingestion.
- L-tyrosine supplementation may help athletes maintain performance when mental fatigue is present.

diminished cognitive capacity resulting from cognitive activity (Boksem and Tops 2008). MF can be induced experimentally through extended low-intensity cognitive tasks (≥ 30 min) or briefer high-intensity cognitive demands (≥ 10 min) requiring sustained attention, inhibitory control, or working memory (Brown et al. 2020; Lopes et al. 2023; Schampheleer et al. 2025). Regardless of the induction method, MF has been consistently shown to impair whole-body endurance performance across various athletic populations, with time-to-exhaustion reductions ranging from 5% to 15% (Brown et al. 2020; Giboin and Wolff 2019; Habay et al. 2023). Importantly, the performance decrements induced by MF occur predominantly through altered perception rather than peripheral physiological limitation. Thus, while MF does not substantially alter maximal cardiorespiratory variables or metabolic responses at submaximal workloads, athletes terminate exercise prematurely due to higher RPE at the same relative exercise intensity (Marcora et al. 2009a).

From a mechanistic perspective, contemporary psychobiological models propose two primary pathways through which MF impairs endurance performance. First, MF increases the perceived effort required for a given task, meaning that identical absolute workloads will be more demanding after cognitive exertion (Schiphof-Godart et al. 2018). Second, MF may diminish the perceived value of performance-related rewards (e.g., achieving personal records, competitive success), thereby reducing motivation to tolerate high effort levels (Schiphof-Godart et al. 2018). In time-to-exhaustion protocols at fixed intensities, typical of laboratory assessments and certain real-world scenarios such as breakaway attempts in cycling, the effort perception pathway appears dominant, as athletes disengage when perceived exertion reaches intolerable thresholds regardless of external incentives (Marcora et al. 2009a; Pageaux 2014).

Neurophysiologically, although the underlying mechanisms are not yet fully understood, researchers suggest that mentally fatigued individuals exhibit increased RPE and reduced motivation during endurance exercise due to increased extracellular adenosine and decreased cerebral dopaminergic activity in the anterior cingulate cortex (ACC) (Boksem and Tops 2008; Lorist et al. 2005; Martin et al. 2018; Schiphof-Godart et al. 2018). Given that these neural alterations can impair both physical output and perceptual responses during exercise (Pires et al. 2018), interventions capable of counteracting such changes at the neural level may be particularly valuable. This is especially relevant because both recreational and professional athletes commonly encounter cognitively demanding activities before training or official competition, including extended travel to event venues (Zhao et al. 2012), work-related demands (Wiehler et al. 2022), and screen-based activities such as video gaming or social media engagement (L. S. Fortes et al. 2019, 2023). Consequently, identifying practical countermeasures to prevent or reverse MF-induced performance losses holds direct relevance for optimizing training quality and competitive outcomes.

Various researchers have investigated behavioral, physiological, and psychological countermeasures to mitigate the deleterious effects of MF on human performance (Ferreira et al. 2023; Proost et al. 2022). In summary, several countermeasures have shown promise in combating MF, including sensory interventions (e.g., peppermint odor), auditory stimuli (e.g., self-selected music), pharmacological approaches (e.g., caffeine ingestion at doses of 3–6 mg/kg), and psychological strategies (e.g., monetary incentives) (Proost et al. 2022). Importantly, the most commonly proposed mechanism by which these diverse countermeasures exert their effects is through modulation of the dopaminergic neurotransmission (Proost et al. 2022). The dopaminergic system comprises different anatomical pathways (Kok 2022; Tam et al. 1990; Yang et al. 2022). Specifically, these pathways are referred to as the mesocortical pathway (ventral tegmental area to the prefrontal cortex), mesolimbic pathway (ventral tegmental area to the nucleus accumbens and ventral striatum), and nigrostriatal pathway (substantia nigra to the dorsal striatum), which regulate motivation, reward processing, motor planning, and effort-based decision making (Kok 2022; Meeusen and Roelands 2018). Therefore, interventions capable of enhancing dopaminergic signaling may mitigate the increase in RPE and provide greater tolerance to prolonged physical effort, thereby counteracting the detrimental effects of MF on physical performance (Meeusen and Roelands 2018). While pharmacological agents such as caffeine have demonstrated efficacy through dopaminergic mechanisms (Azevedo et al. 2016; Franco-Alvarenga et al. 2019), the potential for amino acid-based nutritional supplements to modulate catecholamine synthesis and thereby mitigate MF-related performance decrements remains largely unexplored.

Supplementation with the amino acid L-tyrosine (ALT) can cross the blood-brain barrier and acts as a biochemical precursor to the catecholamines dopamine and norepinephrine (Jongkees et al. 2015). Animal studies have demonstrated that tyrosine administration (25–50 mg/kg) selectively increased dopamine synthesis in the prefrontal and cingulate cortex, with enhanced effects on dopamine metabolism when neurons were pharmacologically activated (Tam et al. 1990). The theoretical rationale for tyrosine supplementation in performance contexts rests on the "depletion hypothesis": high-demand cognitive stress accelerates catecholamine turnover, potentially depleting the tyrosine precursor pool and thereby limiting neurotransmitter synthesis (Jongkees et al. 2015). Supporting this framework, human studies have shown that tyrosine supplementation (100–300 mg/kg) improves cognitive performance specifically under stressful conditions, such as cold exposure, sleep restriction, or demanding multitasking, which presumably tax catecholaminergic systems (Jongkees et al. 2015). Importantly, human dose-response studies demonstrated that 300 mg/kg bodyweight is more effective than 150 mg/kg for preserving executive function under cold stress (Mahoney et al. 2007) and

maintaining plasma tyrosine concentrations during prolonged heat exposure (Tumilty et al. 2020).

Regarding whole-body endurance performance, although previous literature supports the biological plausibility of this nutritional supplement as a potential ergogenic aid (Tumilty et al. 2011), its effects have not been confirmed in a recent meta-analysis (effect size [ES]: −0.01; 95% confidence interval [CI] [−0.32, 0.29]) (Solon-Júnior et al. 2023). However, this null finding may reflect a limitation in the existing evidence base: none of the included studies assessed participants under conditions of MF (Solon-Júnior et al. 2023). This represents a substantial research gap because the theoretical rationale for tyrosine supplementation, enhancing catecholamine synthesis when demands are elevated, predicts that benefits should emerge specifically when dopaminergic systems are challenged (Jongkees et al. 2015). Thus, considering its neural mechanism of action, it would be expected that the impact of tyrosine supplementation on the central nervous system (CNS) may be more pronounced during MF. Therefore, since dopaminergic activity is thought to be reduced in mentally fatigued individuals (Martin et al. 2018), and previous findings suggest beneficial effects of tyrosine on the CNS under stress conditions (Jongkees et al. 2015), it is plausible that tyrosine ingestion could counteract the deleterious effects of MF on whole-body endurance performance.

For recreational cyclists who frequently experience pre-training or pre-competition MF from daily life demands, the tyrosine supplementation could represent a practical and accessible ergogenic strategy to preserve training quality and competitive performance. Therefore, the present study aimed to examine whether acute L-tyrosine supplementation (300 mg/kg) could attenuate the performance-impairing effects of MF on time-to-exhaustion cycling at 80% of maximal power output in recreational cyclists. Based on the mechanistic framework outlined above, we hypothesized that: (1) tyrosine would increase time-to-exhaustion following MF compared to placebo; (2) this performance benefit would be accompanied by a delay for the increase of RPE (RPE slope) throughout the exhaustive bout, reflecting normalized effort processing; and (3) cardiorespiratory responses (heart rate, oxygen consumption) during exercise would not differ between experimental conditions, as MF and tyrosine effects are hypothesized to operate primarily through perceptual rather than metabolic pathways.

2 | Methods

2.1 | Experimental Design

A randomized, double-blind, counterbalanced, and crossover experimental design was used in the present study. The study protocol and reporting adhere to the CONSORT guidelines for randomized crossover trials. The experimental procedures were designed based on previous studies investigating the impact of countermeasures for MF on endurance cycling performance (Azevedo et al. 2016; Ferreira et al. 2023). The cyclists participated in four laboratory visits that took place in the morning (approximately 08:30 a.m.) to avoid any circadian interference.

2.1.1 | Visit 1: Familiarization

Visit 1 consisted of familiarization with all experimental procedures, including abbreviated versions of cognitive tasks [5-min Stroop word-color test (ST), 3-min psychomotor vigilance task (PVT)], practice with subjective rating scales [that is, Visual Analogue Scale for MF (VASmf), RPE, and Gastrointestinal Discomfort Questionnaire (GIDQ)], and accommodation to cycling equipment. This visit established individualized Stroop task parameters (see Cognitive Manipulation section) and ensured participant competency with all assessment tools. Also, during the first visit, participants received a checklist that they were instructed to follow before visits 2, 3, and 4. For example, participants were instructed to abstain from consuming any substances (e.g., caffeine and/or maltodextrin, chocolate, soft drinks, ginseng, vitamins/minerals/guaraná bars, among others) 12 h before arriving at the laboratory (Proost et al. 2022); to maintain their training routine from the beginning to the end of the study; to avoid physical exercise and alcohol consumption 48 h before the experimental visits; and to avoid using social media or other sources of MF in the hours immediately preceding each laboratory session so that the baseline MF level upon arrival would not exceed 25 mm on the VASmf scale. This criterion ensured that participants began each experimental trial in a comparable low-MF state, with any subsequent MF being experimentally induced rather than carried over from pre-session activities.

Also, the participants were instructed to maintain their habitual sleep patterns rather than adhering to a rigid duration, minimizing disruption while ensuring basic sleep adequacy. Importantly, participants were required to consume a standardized, decaffeinated breakfast on all experimental mornings, composed of approximately 60% carbohydrate, 25% fat, and 15% protein (e.g., 50 g of wheat bread + 1 whole egg = 222 kcal, 30.3 g carbohydrate, 12.3 g protein, 5.8 g fat, 2 g fiber). This breakfast was consumed at home, and verbal confirmation of adherence was obtained upon laboratory arrival. While on-site breakfast consumption would have provided superior control, logistical constraints and ecological validity considerations (athletes typically consume pre-training meals at home) informed this decision.

2.1.2 | Visit 2: Baseline Assessment and Maximal Testing

During the second visit, each subject completed a 24-h dietary recall to enable dietary replication before each experimental trial (Solon-Júnior et al. 2025). This ensured dietary consistency, minimizing variability in substrate availability (Jeukendrup 2017). After the dietary recall, cyclists were invited to perform a maximal incremental test on a cycle ergometer to measure maximal oxygen consumption (VO_{2max}) and maximal endurance power output (W_{max}). After the second visit, cyclists were blindly assigned by an independent researcher to participate in two experimental visits with a 7-day washout period. Condition order (TYR-first vs. PLA-first) was randomized using a computer-generated sequence (www.randomization.com) by an independent researcher not involved in data collection or outcome assessment, ensuring allocation concealment and blinding integrity.

2.1.3 | Visits 3 and 4: Experimental Trials (TYR and PLA, Counterbalanced)

Initially, participants arrived at the laboratory at 08:30 a.m. only after confirming that they had followed all the checklist recommendations, completed the dietary recall, and consumed the standardized breakfast. Before supplementation, the cyclists reported their level of subjective MF prior to prolonged cognitive effort, performed the 3-min PVT, completed the 5-min ST, and had blood collected. These 5 min of ST were performed to define the individual response time thresholds for the 60-min Stroop experimental task. This individualization ensured equivalent task intensity relative to each participant's basal processing speed, thus reducing daily interindividual variability. After the 5-min ST, the cyclists ingested the supplementation and waited seated for 60 min before starting the cognitive task, which lasted for 60 min. Finally, before starting the cycling test, the cyclists again responded to the VASmf, performed the psychomotor vigilance task (PVT), and had blood collected. The 80% Wmax cycling test was adopted based on previous MF studies that found consistent detrimental effects on time-to-exhaustion in recreational cyclists (Azevedo et al. 2016; Marcora et al. 2009a; Martin et al. 2016; Salam et al. 2018). After the time-to-exhaustion (TTE, at 80% of Wmax) task, the GIDQ was also administered.

2.2 | Participants

The sample size was estimated using G*Power 3.1.9.2 (Universität Kiel, Kiel, Germany) with the following parameters: repeated-measures ANOVA (within-subjects), $\alpha = 0.05$, power = 0.80, effect size $f = 0.33$ (equivalent to Cohen's $d = 0.65$), correlation among repeated measures = 0.70, two conditions (TYR vs. PLA). This effect size was derived from Tumilty et al. (2011), who reported that tyrosine supplementation increased time-to-exhaustion by 16% (11.1 min, from 69.2 to 80.3 min; $p < 0.01$) during submaximal cycling in heat stress (30°C) in recreationally trained individuals ($n = 8$). The analysis indicated that 13 participants were required to achieve 80% power. While Tumilty et al. examined tyrosine under heat stress rather than mental fatigue, we considered this effect size appropriate for several reasons: (1) Both heat stress and mental fatigue are theorized to impair performance through reduced central dopaminergic activity (Martin et al. 2018; Meeusen and Watson 2007), creating comparable neurobiological conditions where tyrosine supplementation might exert benefits; (2) Both stressors produce similar performance decrements (5%–15%) compared to control conditions; (3) The population (recreationally trained cyclists) was comparable; and (4) no prior studies had examined tyrosine specifically under mental fatigue conditions, making Tumilty et al. (2011) dopaminergic intervention study the most relevant available precedent.

Although 14 volunteers were initially recruited, two withdrew from the study before completing all tests due to time constraints and external commitments. Consequently, data were collected and analyzed from the 12 male participants who completed all experimental sessions [mean (± SD) age, 32 ± 6 years; body weight, 80 ± 9 kg; height, 176 ± 5 cm; $VO2_{max}$ from ramp incremental test, 62.7 ± 12.6 mL/(min·kg); maximal endurance power output 346.9 ± 56.7 W; maximal heart rate during ramp test, 180 ± 10 beats·min^{-1}; 3 ± 1.4 training sessions per week; training volume per week:112 ± 47 km; > 6 years of cycling experience], in line with the estimated sample size. The participants were classified as level 3 (i.e., recreationally trained) according to sports science guidelines (McKay et al. 2022; Pauw et al. 2013). The eligibility criteria were as follows: 2 to 4 sessions of regular weekly cycling training, totaling around five hours per week; covering ~70 km per week; having an average of three years of cycling experience; competing in regional or national tournaments; being non-smokers; not taking any medication or dietary supplements; being free of cardiovascular diseases, sleep disorders (i.e., insomnia), cognitive, brain, and visual impairments; and having had no injuries in the past 3 months. Written information was given on the protocol, and participants were allowed to ask questions before providing written informed consent to proceed with the study. The study was approved by the local ethics committee (Number: 6.330.647) and was conducted according to the Declaration of Helsinki.

3 | Cognitive Manipulation (Mental Fatigue Protocol)

The computerized version of the Stroop word-color task (PsychoPy v1.85.6, United Kingdom) was used to induce MF in the experimental conditions. The participants performed the cognitive task for 60 min before the TTE. The ST was conducted in a quiet and well-lit room, with the cyclists seated comfortably in a chair in front of a 20-inches monitor. Indeed, studies that induce MF using the ST have shown high inter-individual variability in self-reported post-cognitive task MF levels (Lopes et al. 2020; Penna et al. 2021), likely due to differences in individual cognitive capacity and resilience to the demanding nature of incongruent stimuli, which require continuous inhibition of automatic responses. Therefore, in an attempt to reduce this variability, we proposed individualizing task complexity (Martin et al. 2016) based on the participants' average response time previously collected in a 5-min test (see Figure 1). For example, a participant with a mean response time of 1200 ms was required to respond within 1200 ms during the 60-min Stroop experimental task; responses exceeding this threshold were recorded as “time limit losses”. This individualized response time constraint was designed to maintain consistent task intensity across participants while accounting for baseline differences in processing speed. By requiring each participant to respond within their individually determined time limit, we ensured that all participants experienced a similarly challenging cognitive demand relative to their baseline capacity. The two alternating forms of incongruent stimuli (responding to the meaning of the word vs. responding to the color) appeared consistently on the screen throughout the task in a randomized sequence.

The incongruent stimuli appeared on the monitor in two alternating forms: (a) Participants had to respond to the meaning of the word (i.e., red, blue, green, and yellow) but not its color when the stimulus appeared inside the rectangle; and (b) Participants had to respond to the color (i.e., red, blue, green,

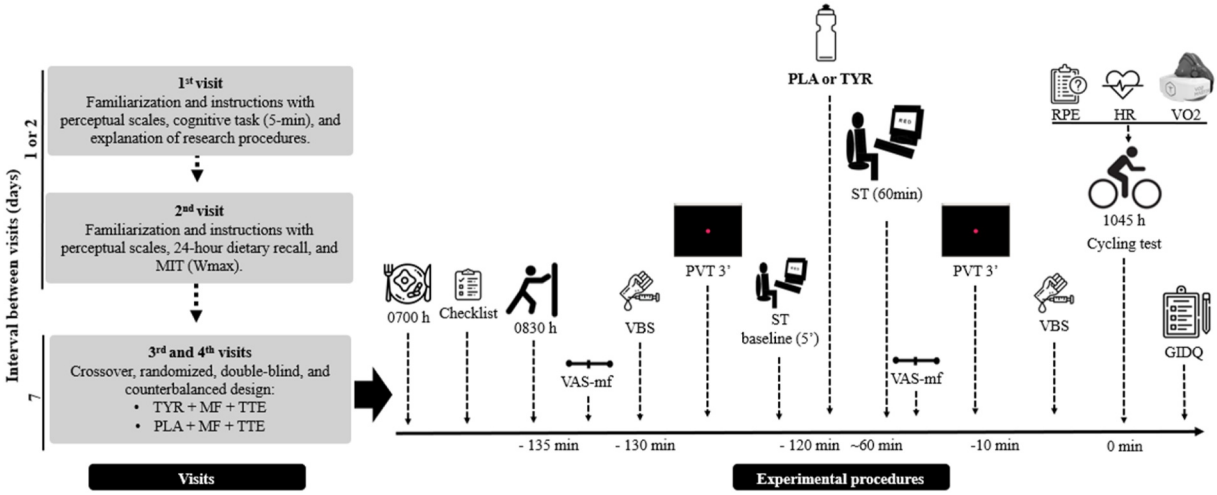

FIGURE 1 | Experimental design of the study. MIT = Maximal Incremental Test; MF = Mental Fatigue; TYR = L-tyrosine; PLA = Placebo; VASmf = Subjective mental fatigue; VBS = Venous blood sampling; ST = Stroop task; PVT = psychomotor vigilance task; RPE = Rating of Perceived Exertion; HR = heart rate; VO2 = Oxygen consumption; GIDQ = Gastrointestinal Discomfort Questionnaire.

and yellow) in which the word was written when no rectangle appeared around the word. It is important to highlight that all stimuli were incongruent, meaning that the text color did not match the word's meaning. Response time, percentage of correct responses (i.e., accuracy), and number of stimuli responded to after the time limit (i.e., time limit loss) were the behavioral outcomes evaluated and compared between experimental conditions. This dual-format paradigm increases task complexity beyond standard Stroop by requiring frequent rule-switching (Monsell 2003), thereby enhancing MF induction efficacy.

3.1 | Tyrosine Administration

TYR or placebo supplementation was administered 60 min before the cognitive manipulation and approximately 120 min before the TTE. This timing was selected to ensure that the peak plasma tyrosine concentrations, which occur approximately 60–120 min post-ingestion (Solon-Júnior et al. 2023; Tumilty et al. 2020), coincided with both the Stroop task and the cycling performance test. Participants ingested a dose diluted in an opaque bottle containing 300 mg·kg^{-1} body weight of TYR (pure powder - Free-Form, NOW Foods, USA) or microcrystalline cellulose (PLA) with 500 mL of sugar-free lemon water, as previously suggested (Solon-Júnior et al. 2023). The 300 mg/kg dose maintained executive function in humans exposed to demanding environmental conditions (Mahoney et al. 2007), and other researchers showed that plasma TYR levels were higher when participants ingested 300 mg·kg^{-1} when compared with 150 mg·kg^{-1} (Tumilty et al. 2020). For this reason, we selected a dose of 300 mg·kg^{-1}, which totaled approximately 24 g per subject based on the mean body weight of our sample. All beverages were blindly administered in opaque bottles with a dosing spout and prepared by an independent supervisor who was not involved in the data collection. Beverage blinding was verified in a prior pilot trial (n = 5 individuals not participating in the main study) using a triangle test procedure: participants tasted three samples and attempted to identify the different sample.

3.2 | Maximal Cycling Incremental Test and Cycling Workload Constant Tests

Both the maximal incremental test and the TTE test followed methods similar to previous studies (Azevedo et al. 2016; Salam et al. 2018). Both tests were performed on a stationary bike with an accuracy > 97% for speed, cadence, and power output measurements during the cycling task (Tacx FLUX 2 Smart, Italy) (Matta et al. 2022). The equipment was calibrated before each test session, and the seat height was individually adjusted for the subject's comfort, ensuring that their legs were almost fully extended during each pedal stroke. After a 3-min warm-up at 100 W, the maximal incremental test increased by 25 W every 1 min until participants reached exhaustion. Participants exercised at a pedal cadence between 60 and 70 rpm, and the test was finalized when the participant was unable to maintain a minimum cadence of 60 rpm for 6 s despite verbal encouragement. Participants received standard instructions for overall RPE using Borg's 15-point scale and strong verbal encouragement to continue for as long as possible. Gas exchange was measured breath-by-breath using a portable gas analyzer (VO2 Master Health Sensors Inc., Vernon, British Columbia, CA) with 30-s averaging intervals throughout the test (Montoye et al. 2020). Before each test, the gas analyzer was calibrated according to the manufacturer's recommendations. Maximum HR (HRmax) was defined as the highest value recorded at the end of the test, and maximal endurance power output (Wmax) was determined using the following equation: 'Wmax = Wc + [(t/60) × 25],' where Wc is the load of the last completed stage, t is the time completed in the stage (s), 60 is the stage duration, and 25 is the power increment. The HR was continuously monitored throughout the test using a chest strap monitor (Polar H10 Electro, Brazil) connected via Bluetooth to the VO_2 Master app.

For the cycling constant workload test, participants were instructed to perform a standardized warm-up consisting of 5 min of cycling at 40% of Wmax (138 ± 22 W) at a pedal cadence of 60 rpm. Immediately after the warm-up, the power output corresponding to 80% of Wmax (277 ± 45 W) was set,

and participants were instructed to maintain a pedal cadence between 60 and 70 rpm. Exercise tolerance was measured from the beginning of the rectangular workload until the pedal cadence dropped below 60 rpm for more than 6 s despite standardized verbal encouragement. TTE was recorded as the primary outcome using the Tacx trainer's (Tacx FLUX 2 Smart, Italy) internal timer, with concurrent manual stopwatch measurement serving as verification. In all cases, measurements agreed within ± 1 s; trainer-recorded values were used for analysis. The HR was recorded continuously throughout all TTE tests, and RPE was collected during the last 5 s of each 30 s.

3.3 | Manipulation Checks

3.3.1 | Mental Fatigue Assessment

Subjective MF was assessed using a VASmf, with responses ranging from 0 mm (none at all) to 100 mm (maximal), as suggested by previous studies (L. D. S. Fortes et al. 2022; L. d. S. Fortes et al. 2024). Participants were asked, "How mentally fatigued do you feel now?". Participants drew a vertical line on the scale to report their level of MF. These responses, expressed as arbitrary units (a.u.), were compared between pre- and post-ST.

3.3.2 | Cognitive Performance Monitoring (Psychomotor Vigilance Task)

The PVT is a simple visual reaction time test that was used and configured (i.e., 3-min duration) according to previous recommendations (Smith et al. 2019). In this test, a red circle with a millisecond counter starting at zero appeared in the center of the screen. Participants were instructed to press the 'space' button as quickly as possible when the circle appeared. Pressing the button stopped the counter and displayed the reaction time (RT). The time between stimuli varied randomly from 2 to 10 s. If the response button was pressed within the first 100 ms, an error was signaled on the notebook screen. Cyclists performed the test for 3 min before and after the 60-min Stroop task. The PVT was included as a validated, objective marker of sustained attention and reaction time, sensitive to mental fatigue (Smith et al. 2019).

3.3.3 | Biochemical Verification of Tyrosine Supplementation

Venous blood samples (10 mL) were collected via antecubital venipuncture at two time points: pre-supplementation (baseline) and 60 min post-supplementation (immediately before the Stroop task). This timing corresponds to the expected peak in plasma tyrosine concentrations following oral administration (Tumilty et al. 2020). Plasma was obtained by centrifugation at 3000 rpm for 15 min. Plasma aliquots were equally distributed into three Eppendorf tubes and frozen at −80°C until biochemical analysis. The analysis performed in the present study aimed to assess total proteins using the Bradford assay (Bradford 1976; Dusseldorf 2019), with L-tyrosine as the standard substance. While this approach does not provide direct measurement of free tyrosine concentrations, which would require high-performance liquid chromatography (HPLC), it served as a pragmatic verification that supplement ingestion influenced plasma composition. For this, the Bradford reagent was prepared with 50 mg of Coomassie Brilliant Blue G-250 dye dissolved in 50 mL of ethanol (96%), and 100 mL of phosphoric acid (85% w/v) was added. Immediately afterward, 850 mL of distilled water was added to the mixture, and the reagent was filtered using qualitative filter paper (80 G). For the analyses, 100 μL of the samples were diluted at a 1:100 ratio in distilled water, and then 1000 μL of the Bradford reagent was added. After 5 min, 200 μL of the samples were transferred to a 96-well plate (flat-bottom TPP) and analyzed at 595 nm using a plate reader (Biotek-Synergy HT, Winooski, Vermont, USA). The standard curve was constructed using serial dilutions of a tyrosine standard solution ranging from 0.01 to 1 mg· mL^{1}, and the blank consisted of the Bradford reagent with distilled water. All samples were analyzed in triplicate.

3.3.4 | Perceptual and Physiological Measures Throughout TTE

RPE was obtained through a 15-point Borg scale (Borg 1982). Each participant was then subsequently asked to rate their perceived effort at each 30s during the test, as suggested elsewhere (Salam et al. 2018). For statistical analyses, to account for the different TTE durations, RPE data were subsequently plotted against TTE, with the slope of the relationship being calculated (Salam et al. 2018). Gas exchange during TTE was measured breath-by-breath using a portable gas analyzer (VO2 Master Health Sensors Inc., Vernon, British Columbia, CA), with 1-min averaging intervals throughout the test until the end of the test (Montoye et al. 2020). The HR was recorded at the end of the warm-up and every minute during TTE in visits 3 and 4 using a HR monitor fitted with a chest strap (Polar H10 Electro, Brazil). To include all tests in the statistical analyses, a 4-min isotime was adopted.

3.3.5 | Gastrointestinal Discomfort Questionnaire (GIDQ)

Few studies that investigated the effects of tyrosine intake evaluated its possible side effects, an important analysis in studies with sports supplementation (Solon-Júnior et al. 2023). Therefore, the GIDQ was adopted based on a previous study on nutritional supplementation (Too et al. 2012). The questionnaire includes 7 categories (abdominal pain, heartburn, regurgitation, bloating, nausea, belching, and flatulence) to be answered using a seven-point Likert scale, classified as: 0 (none), 1 (mild), 2 (moderate), three (quite a lot), 4 (severe), 5 (very severe) and 6 (unbearable). The GIDQ was administered only immediately post-exercise (within 2 min of TTE termination) to assess gastrointestinal symptoms experienced during the supplementation period and cycling bout. Baseline GIDQ was not collected as participants were asymptomatic at study entry (per inclusion criteria).

3.4 | Statistical Analysis

All data are presented as mean ± one SD. Normality was assessed using the Shapiro-Wilk test ($p < 0.05$ indicating non-normality) and visual inspection of Q-Q plots. All variables exhibited non-normal distributions (positive skew), supporting the use of generalized models. All repeated-measures outcomes were analyzed using Generalized Estimating Equations (GEE), which provide population-averaged effect estimates robust to misspecification of the within-subject correlation structure. For all models, the following specifications were used: 1) Repeated subject identifier: Participant ID ($n = 12$); 2) Working correlation structure: Exchangeable (assumes equal correlation between any two measurements from the same participant); 3) Standard errors: Robust to account for potential misspecification of the correlation structure; 4) Model fit criterion: Quasi-likelihood under Independence Model Criterion (QIC); 5) lower values indicate better fit; 6) Distribution family and link function: Gamma distribution with log link. The distribution family was selected based on: (1) QIC values (lower = better fit), (2) visual inspection of residual Q-Q plots, and (3) theoretical appropriateness for the outcome type (e.g., time and response time variables are bounded at zero and typically right-skewed, favoring Gamma). In all cases, the Gamma distribution provided superior fit (lower QIC) for positively skewed variables. Significant main effects or interactions were compared using Bonferroni-adjusted pairwise comparisons. Mean differences and 95% confidence intervals (CIs) were calculated from GEE estimated marginal means (model-based predictions) rather than raw data means to account for the within-subject correlation structure. In the model, the intercept of the "subjects" was added as a random factor, allowing for a better interpretation of individual variability. Given the small sample size ($n = 12$) and expected high inter-individual variability in response to dopaminergic interventions, we report individual-level data alongside group averages for primary outcomes (Slope RPE and endurance performance). All data analyses were performed using the Statistical Packages for Social Sciences (SPSS version 25.0, IBM Company) with a significance level of 5%, and the graphs were created in GraphPad Prism (version 8.0). The mean differences presented in all figures were used to report the effect size.

4 | Results

4.1 | Methods

Manipulation checks pre-and post-cognitive effort (i.e., Stroop task) and pre-and post-TYR supplementation (i.e., total proteins).

4.1.1 | Subjective Mental Fatigue

Although there was a significant main effect of time ($W = 123.83$, df = 1, $p = 0.001$), no main effect of condition was found for subjective MF ($W = 0.90$, df = 1, $p = 0.34$), indicating that tyrosine supplementation did not attenuate the subjective experience of MF induced by the Stroop task. Subjective MF increased in both conditions, rising from 12.6 ± 12.9 a.u. To 81.4 ± 24.6 a.u. in the TYR condition and from 12.6 ± 11.4 a.u. To 77.6 ± 24.1 a.u. in the PLA condition ($p > 0.05$). Also, a significant condition × time interaction effect was not found for subjective MF (see Figure 2a; $W = 0.48$, df = 1, $p = 0.48$), as shown in Figure 2A.

4.1.2 | Response Time in the PVT

A significant main effect of time ($W = 24.42$, df = 1, $p = 0.001$) was observed for PVT response time, indicating that participants became slower from pre-to post-Stroop regardless of the condition ($p < 0.05$). In practical terms, the prolonged cognitive task impaired vigilance and reaction speed. Response times increased from 342.8 ± 58.2 ms to 394.7 ± 58.9 ms in the TYR condition and from 342.6 ± 34.4 ms to 384.5 ± 44.6 ms in the PLA condition (Figure 2B). Importantly, there was no main effect of condition ($W = 0.30$, df = 1, $p = 0.58$) and no condition × time interaction effect ($W = 0.47$, df = 1, $p = 0.49$). This means that tyrosine did not differ from placebo overall, nor did it alter the pattern of change over time. Both groups showed a similar decline in response time following the Stroop task.

4.1.3 | Accuracy in the PVT

A significant main effect of time ($W = 12.39$, df = 1, $p = 0.001$) was observed for PVT accuracy, indicating that accuracy declined from pre-to post-Stroop in both conditions. Specifically, accuracy decreased from 92.2 ± 7.5% to 82.7 ± 14.8% in the TYR condition and from 94.0 ± 6.3% to 86.5 ± 11.4% in the PLA condition (Figure 2C). However, no main effect of condition ($W = 1.78$, df = 1, $p = 0.18$) and no condition × time interaction effect ($W = 0.44$, df = 1, $p = 0.50$) were detected, indicating that tyrosine supplementation did not differ from placebo overall when averaging across time points.

4.1.4 | Total Proteins Pre-SUPP and Post-SUPP

A significant main effect of condition ($W = 8.44$, df = 1, $p = 0.004$) and a significant main effect of time ($W = 7.06$, df = 1, $p = 0.008$) were observed for total protein levels. These results indicate that (1) the two conditions differed overall, and (2) total protein levels changed over time. Post-hoc Bonferroni analyses showed that total protein significantly increased from pre-to post-supplementation in the PLA condition ($p = 0.03$), whereas no significant change was observed in the TYR condition ($p > 0.05$), as shown in Figure 2D.

4.2 | Response Time, Accuracy, and Loss of Time Limit in the Stroop Task (Cognitive Manipulation)

No significant main effect of condition was found between TYR and PLA conditions for response time ($W = 0.11$, df = 1, $p = 0.73$; TYR = 822.2 ± 75.1 ms; PLA = 816.2 ± 90.1 ms; Figure 3A), accuracy ($W = 0.31$, df = 1, $p = 0.57$;

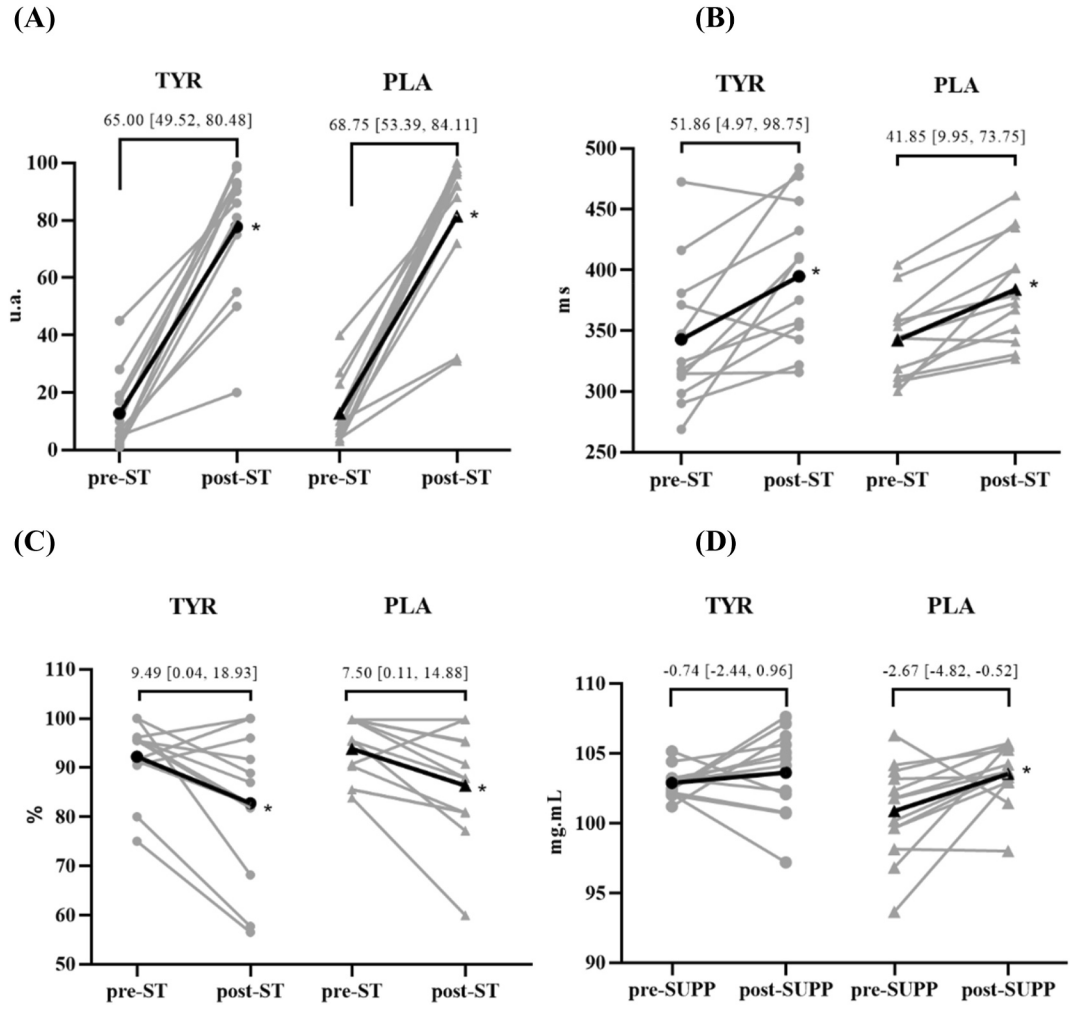

FIGURE 2 | Manipulation checks pre- and post-cognitive effort (i.e., Stroop task) and pre- and post-supplementation (i.e., total proteins). TYR Tyrosine ingestion group, PLA Placebo ingestion group. Subjective MF (A), response time PVT (B), accuracy PVT (C), and total proteins (D). The numbers in the figure before and between the brackets refer to the mean differences between the measures for each comparison performed. *$p < 0.05$ a significant main time effect.

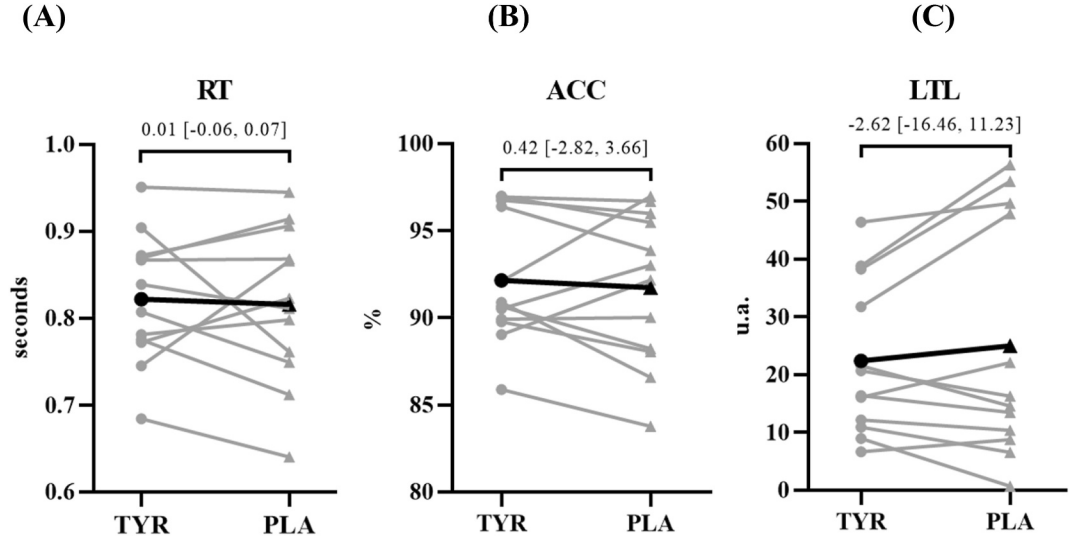

FIGURE 3 | Response time, accuracy, and lost of time limit in the Stroop task (Cognitive manipulation). TYR Tyrosine ingestion group, PLA Placebo ingestion group. The numbers in the figure before and between the brackets refer to the mean differences between the measures for each comparison performed.

TYR = 92.1 ± 3.7%; PLA = 91.7 ± 4.3%; Figure 3B), and loss of time limit (W = 1.05, df = 1, p = 0.30; TYR = 22.3 ± 13.2 u.a.; PLA = 24.9 ± 20.5 u.a.; Figure 3C) throughout the 60 min of the Stroop task, as shown in Figure 3.

4.3 | Physiological Measures Throughout TTE

4.3.1 | HR Isotime

A main effect of condition was not found for HR (W = 3.69, df = 1, p = 0.051). However, there was a significant main effect of time for HR (see Figure 4A; W = 370.90, df = 3, p = 0.0001). Post-hoc analysis revealed an increase in HR throughout the TTE in both conditions (p < 0.05). Also, there was no time × condition interaction effect for HR (W = 1.05, df = 3, p = 0.99).

4.3.2 | VO2 Isotime

There was a significant main effect of time for VO_2 (see Figure 4B; W = 364.52, df = 4, p = 0.0001). Post-hoc analysis revealed an increase in oxygen consumption throughout the TTE in both conditions (p < 0.05), but no main effect of condition was found (W = 0.52, df = 1, p = 0.82). There was no time × condition interaction effect for VO_2 (W = 1.47, df = 4, p = 0.83).

4.4 | Slope RPE and Endurance Performance

The RPE slope (see Figure 5A) was significantly lower in the TYR condition (0.560 ± 0.184 a.u./min) when compared to PLA (0.673 ± 0.251 a.u./min) (W = 4.37, df = 1, p = 0.03; g *Hedges* = 0.51; Figure 5A). This indicates that tyrosine supplementation attenuated the inclination for the increase of the RPE during exercise, meaning that participants in the TYR condition experienced a slower accumulation of effort sensations as they approached exhaustion. A significant difference between conditions was also observed for TTE (W = 7.08, df = 1, p = 0.008; g *Hedges* = 0.29), with participants in the TYR condition cycling for a longer duration (459.9 ± 199.6 s) when compared to those in the PLA condition (398.7 ± 222.10 s), as shown in Figure 5B.

4.5 | Gastrointestinal Discomfort Questionnaire (GIDQ)

No GI disturbances were reported by the cyclists and there was no statistical difference between experimental conditions (p > 0.05) [abdominal pain (PLA = 0.08 ± 0.28 a.u.; TYR = 0.08 ± 0.28 a.u.), heartburn (PLA = 0.41 ± 0.99 a.u.;

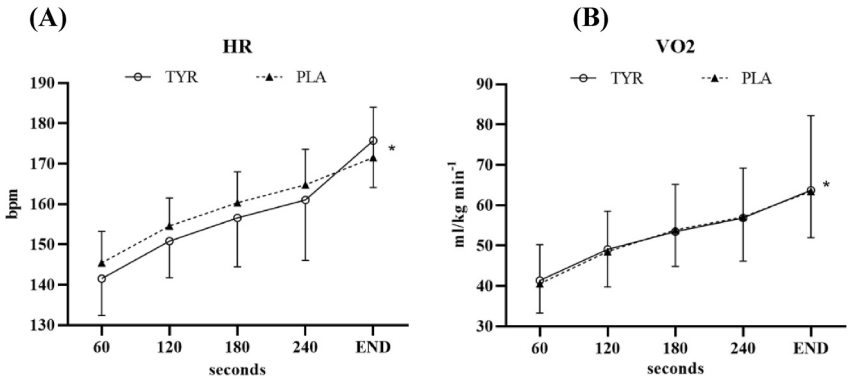

FIGURE 4 | Physiological measures throughout TTE cycling. TYR Tyrosine ingestion group, PLA Placebo ingestion group. HR (A) and VO2 (B). *denotes a significant main effect of time (p < 0.05).

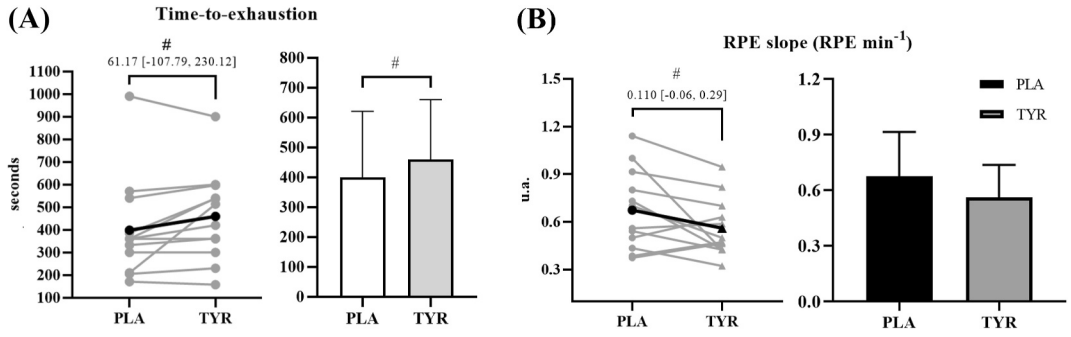

FIGURE 5 | Slope RPE (A) and endurance performance (B). TYR Tyrosine ingestion group, PLA Placebo ingestion group. The numbers in the figure before and between the brackets refer to the mean differences between the measures for each comparison performed. #denotes a significant main effect of condition (p < 0.05).

TYR = 0.16 ± 0.38 a.u.), regurgitation (PLA = 0.25 ± 0.62 a.u.; TYR = 0.00 ± 0.00 a.u.), bloating (PLA = 0.25 ± 0.62 a.u.; TYR = 0.16 ± 0.57 a.u.), nausea (PLA = 0.08 ± 0.28 a.u.; TYR = 0.00 ± 0.00 a.u.), belching (PLA = 1.41 ± 1.92 a.u.; TYR = 0.66 ± 0.88 a.u.), and flatulence (PLA = 0.08 ± 0.28 a.u.; TYR = 0.08 ± 0.28 a.u.)].

5 | Discussion

This study aimed to examine the effects of tyrosine ingestion on whole-body endurance performance, as well as on perceptual and physiological responses in mentally fatigued recreational cyclists. Considering that MF impairs whole-body endurance performance (Giboin and Wolff 2019; Habay et al. 2023), various countermeasures have been investigated in recent years (Proost et al. 2022), particularly in cycling (Azevedo et al. 2016; Ferreira et al. 2023; Franco-Alvarenga et al. 2019). However, although TYR supplementation has been shown to enhance executive function under stress by increasing catecholamine availability in the CNS (Jongkees et al. 2015), to the best of our knowledge, this is the first study to test the effects of TYR ingestion on endurance performance in mentally fatigued cyclists. Consistent with our hypothesis, TYR supplementation was associated with an approximately 16% improvement in time-to-exhaustion (mean difference: 61.2 s) following MF induction in recreational cyclists. This performance benefit was accompanied by a moderate reduction in RPE slope, suggesting attenuated perception of effort accumulation. This aligns with the interpretation that TYR may delay the rise in perceived exertion over time, rather than reducing its absolute level (Tumilty et al. 2011). However, these findings should be interpreted cautiously given the small sample size ($n = 12$), a small-to-moderate effect, and the absence of direct neurophysiological measurements.

The manipulation check findings indicated an increase in subjective MF, a longer response time in the PVT, and a decrease in PVT accuracy after the 60-min high-cognitive-demand task for both experimental conditions. These results are consistent with previous studies on MF, which used the same pre- and post-cognitive effort measures (Smith et al. 2019). Thus, it is clear that the present study successfully induced MF in the participants. On the other hand, it is important to note that there were no differences between the experimental conditions (MF-PLA vs. MF-TYR), either in the manipulation check measures collected before and after the cognitive effort (e.g., subjective mental fatigue, response time, and accuracy in PVT) or in the variables collected throughout the 60-min cognitive task (e.g., response time, accuracy, and number of missed responses beyond the time limit). In this sense, although the supplementation was administered 1 hour before of the mentally fatiguing task, it became evident that TYR had no effects on these subjective and behavioral outcomes, countering our initial hypotheses.

According to previous scientific literature, when individuals are exposed to cognitively challenging or stressful tasks, catecholaminergic neurons become more active, and their synthesis rate increases (Jongkees et al. 2015; Mahoney et al. 2007). In this context, as neurotransmitter production increases to meet cognitive demands, TYR is more heavily consumed, potentially leading to its depletion (Attipoe et al. 2015). However, it is important to acknowledge that direct evidence for catecholamine depletion in humans following standard laboratory cognitive tasks remains limited. Most supporting evidence derives from animal microdialysis studies showing reduced dopamine release after repeated stimulation (Tam et al. 1990) or indirect human studies measuring peripheral catecholamine metabolites (Deijen and Orlebeke 1994).

Although these mechanisms explain the potential benefits of TYR on brain function, studies investigating the effects of this supplementation on executive function under stress have produced inconsistent results, with some showing positive effects and others not (Jongkees et al. 2015). Another possible explanation might relate to the type of cognitive test used in this study. For example, in Mahoney et al. (2007) study, supplementation with 300 $mg.kg^{-1}$ of L-tyrosine attenuated cold-induced working memory decline (assessed using the Delayed Match-to-Sample test) but positive response was not observed in a visual vigilance test, which is similar to the PVT in the present study. This discrepancy may reflect fundamental differences in the cognitive processes underlying these tasks. Working memory tasks like the Delayed Match-to-Sample test require active maintenance and manipulation of information in prefrontal circuits heavily dependent on optimal dopamine signaling (Cools and D'Esposito 2011). In contrast, vigilance tasks primarily involve sustained attention and rely more on noradrenergic systems in parietal and thalamic regions (Coull et al. 2001; Martín-Signes et al., 2024). Consequently, tyrosine's dopaminergic effects may be more beneficial for tasks that specifically tax dopamine-dependent executive functions rather than sustained attention processes.

Indeed, although no effects were observed on behavioral outcomes, it is worth noting that our findings showed that total protein levels remained stable across time points in the L-tyrosine condition, whereas they increased significantly in the placebo condition from pre-to post-supplementation. Although the mechanisms underlying this pattern remain speculative (Jongkees et al. 2015), it may reflect differential protein mobilization responses to cognitive stress between conditions. Therefore, the increase in plasma proteins in the placebo condition could indicate a stress-induced mobilization response, whereas the stable levels in the tyrosine condition might suggest that supplementation attenuated this stress response (Deijen and Orlebeke 1994; Mahoney et al. 2007). However, we acknowledge that our assay measured total proteins rather than specific tyrosine concentrations (Tumilty et al. 2020), and that multiple physiological factors influence plasma protein levels. Therefore, while these findings provide indirect evidence that tyrosine supplementation reached the circulation and may have modulated the physiological response to cognitive stress, they should be interpreted cautiously as a manipulation check rather than a direct measure of tyrosine bioavailability. Thus, future studies should employ direct amino acid quantification methods to properly verify supplement absorption and estimate brain tyrosine availability.

Furthermore, our results demonstrated positive effects of TYR supplementation on TTE during a fixed-power cycling test in

mentally fatigued individuals. This is contrary to recent evidence suggesting that TYR supplementation does not enhance endurance activities (Solon-Júnior et al. 2023). However, a limitation of that meta-analysis is that none of the included studies assessed participants under mental fatigue conditions. In this case, our results align with the theoretical prediction that tyrosine's effects may be condition-specific, emerging primarily when particular stressors create demands on brain catecholamine systems (Jongkees et al. 2015). Also, though not directly demonstrated in humans, the MF has been theorized to involve altered dopaminergic signaling in motivation and effort-processing circuits (Martin et al. 2018). If this theoretical framework is correct, then mental fatigue would represent precisely the type of condition where tyrosine supplementation might confer benefits. However, we emphasize that this remains a theoretical proposition rather than an empirically confirmed mechanism in our study. The performance improvement was accompanied by a reduced RPE slope in the tyrosine condition. Given that mental fatigue typically increases the rate of perceived exertion rise during exhaustive exercise (Salam et al. 2018), this pattern suggests that tyrosine may have influenced perceptual rather than physiological aspects of exercise tolerance. However, the specific neurobiological processes underlying this perceptual change remain unknown.

Dopamine signaling has been implicated in motivation, reward processing, and effort-based decision-making through animal research and pharmacological studies in humans (Flagel et al. 2011; Kok 2022; Meeusen and Roelands 2018; Yang et al. 2022). In this case, while our study did not include direct neurophysiological measurements (e.g., neuroimaging, neurotransmitter quantification), this finding aligns with theoretical models proposing that dopaminergic signaling in the ACC influences effort-cost computations (Kok 2022). So, our data allow speculation that TYR supplementation may have increased dopamine and norepinephrine concentrations in the brain (Daubner et al., 2011; Tam et al. 1990), thus increasing the cognitive inhibitory system activity and modulating the excitability of neural circuits negatively impacted by mentally stressful activities (Ishii et al. 2014; Kok 2022; Kowalski and Anita 2020). As expected, no significant differences were found in cardiorespiratory variables between the experimental conditions. These findings confirm that the effects of TYR on endurance performance in mentally fatigued subjects may have been solely mediated by modulation of CNS function (Jongkees et al. 2015), which reduced RPE and allowed greater tolerance to prolonged physical exertion. However, further studies employing direct CNS measurements (e.g., functional neuroimaging, electroencephalography, or neurotransmitter quantification) are needed to confirm whether tyrosine ingestion improves endurance performance in mentally fatigued cyclists through central nervous system mechanisms, as theoretically proposed.

Although our study suggested that TYR is a promising ergogenic aid to improve endurance performance in mentally fatigued cyclists, some limitations must be acknowledged. First, the participants were recreationally trained for cycling (level 3) (Pauw et al. 2013). Therefore, these data cannot be generalized to elite athletes, untrained individuals, or other sports. Second, studies investigating the effects of acute TYR supplementation usually require participants to undergo overnight fasting (Solon-Júnior et al. 2023). This methodology aims to reduce competition at the blood–brain barrier between tyrosine and other neutral amino acids, such as phenylalanine and tryptophan (Fernstrom 1990). However, although this practice is recommended and commonly used (Tumilty et al. 2011, 2020), cycling athletes do not frequently train or compete in a fasted state, which limits the practical applicability of our findings. Additionally, although a dietary recall was used and participants were strongly advised to maintain the same diet across all experimental conditions, it was not possible to measure TYR dietary intake in this study, which prevents inferences regarding the impact of habitual intake of this amino acid on supplementation effects (Jongkees et al. 2015). Also, the reliance on self-reported dietary replication and home-based breakfast consumption represents a limitation. While we attempted to standardize nutritional status, we cannot fully exclude the possibility that inter-session dietary variation influenced tyrosine bioavailability or performance outcomes. Finally, it is important to acknowledge that we did not conduct direct measurements of CNS function (e.g., electroencephalography, functional near-infrared spectroscopy, and, most importantly, positron emission tomography, which quantifies cerebral metabolic processes). Thus, it is reasonable to suggest that further studies are needed to confirm the hypothesis that TYR ingestion can improve endurance performance in mentally fatigued cyclists through direct modulation of CNS function. Thus, given these limitations, our findings should be considered preliminary rather than definitive evidence for tyrosine's ergogenic efficacy in mentally fatigued athletes.

6 | Conclusion

In summary, this preliminary study provides initial evidence that acute L-tyrosine supplementation (300 mg/kg) may enhance endurance performance in recreational cyclists following mental fatigue induction. Tyrosine ingestion was associated with a 16% improvement in time-to-exhaustion and a reduced rate of perceived exertion increase during exhaustive cycling, with no differences in cardiorespiratory responses. These findings align with theoretical predictions that enhancing catecholamine precursor availability may attenuate MF-induced performance decrements.

Author Contributions

L.J.F.S.-J. and L.d.S.F. conceived and designed research. L.J.F.S.-J. and C.V.D. conducted experiments. D.B. and L.d.S.F. contributed analytical tools. L.J.F.S.-J. and C.V.D. analyzed data. L.J.F.S.-J. wrote the manuscript. All authors read and approved the manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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