Paraxanthine Provides Greater Improvement in Cognitive Function and Psychomotor Vigilance Prior to and Following Running Than Caffeine

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Background: Paraxanthine (PX,1,7-dimethylxanthine) is a natural dietary component and the main metabolite of caffeine in humans. Acute ingestion of PX improves some measures of cognition, executive function, and vigilance. The purpose of this study was to compare the effects of caffeine (CA), PX, and the combined ingestion of PX and CA prior to endurance exercise on pre- or post-exercise cognition, executive function, and/or vigilance in trained runners.

Methods: In a double-blind, placebo controlled, crossover, and counterbalanced manner, 13 trained runners (27.1 ± 5 years, 68.6 ± 9 kg, 22.2 ± 2.7 kg/m^2, 15.7 ± 5% fat, 53.7 ± 11 ml/kg/min VO_{2peak}) were randomly assigned to consume 400 mg of placebo (PL); 200 mg of PL + 200 mg of CA; 200 mg of PL+ 200 mg of PX (ENFINITY™, Ingenious Ingredients); or, 200 mg CA + 200 mg of PX (CA+PX) with a 7-day washout between treatments. Participants donated fasting blood samples and completed pre-supplementation (PRE) side effects questionnaires (SE); the Berg Card Sorting task test (BCST) that assesses long thought, including reasoning, learning, executive control, and attention shifting; and, the Psychomotor Vigilance Task Test (PVTT) that assesses sustained attention reaction times through responses to visual stimuli. Participants then rested for 60-min, repeated tests (PRE-EX), performed a 10-km run on a treadmill (48.4 ± 6.7 min) and

then repeated tests (POST-EX). Data were analyzed using General Linear Model (GLM) univariate analyses with repeated measures using weight as a covariate and mean and percent changes from baseline with 95% confidence intervals.

Results: GLM analysis revealed no significant treatment x time interaction effects in variables assessed using weight as a covariate although moderate effect sizes (ES) and significant pairwise differences were observed among several variables. BCST analysis revealed moderate interaction ES in Error Rate (η_p^2 = 0.07) with a significant difference (p = 0.03) observed in between PX and CA+PX PRE-RUN values as well as Perseverative Errors following PAR rules (η_p^2 = 0.07) with participants in the PX treatment observing a 12% reduction (p = 0.03) in errors from PRE-EX to POST-EX while error rate increased by 22% with CA (p = 0.03). Analysis of PVTT data revealed medium ES in Trial 2 (η_p^2 = 0.09), Trial 10 (η_p^2 = 0.06), Trial 20 (η_p^2 = 0.06), and Mean (η_p^2 = 0.09) Vigilance Reaction Times. Pairwise comparison revealed that PRE-RUN Mean Reaction Time was significantly faster (p = 0.02) in the PX treatment compared to PL and that Trial 2 POST-RUN 2-Letter Length Reaction time in the PX treatment was significantly faster than PL (p = 0.03). Moreover, POST-EX vigilance during trial 20 in the PX treatment tended to be different than PL (p = 0.07) and CA. In terms of safety, one participant withdrew after ingesting the CA treatment while others reported minimal side effects with no significant treatment x time effects observed in the frequency or severity of headaches, dizziness, racing heart rate, palpitations, shortness of breath, nervousness, blurred vision, or clinical chemistry panels.

Conclusions: Results suggest that PX supplementation is safe and improves prefrontal cortex function, attenuates attention, and mitigates cognitive fatigue prior to and following exercise. PX showed greater improvements than CA independently, while adding CA to PX did not provide any additional benefit.

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