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Supplementation with a low-dose of octopamine does not influence endurance cycling performance in recreationally active men

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ABSTRACT

Objectives: The aim of this study was to examine the influence of octopamine supplementation on endurance performance and exercise metabolism.
Design: Double-blind cross-over study.
Methods: Ten healthy, recreationally active men (Mean ± SD; age: 24 ± 2 years; body mass: 78.4 ± 8.7 kg; VO_{2peak}: 50.5 ± 6.8 mL kg^{-1} min^{-1}) completed one VO_{2peak} test, one familiarisation trial and two experimental trials. After an overnight fast, participants ingested either a placebo or 150 mg of octopamine 60 min prior to exercise. Trials consisted of 30 min of cycle exercise at 55% peak power output, followed by a 30 min performance task whereby participants completed as much work (kJ) as possible.
Results: Performance was similar between the experimental trials (placebo: 352.8 ± 39 kJ; octopamine: 350.9 ± 38.3 kJ; Cohen's *d* effect size = 0.05; $p = 0.380$). Substrate oxidation and circulating concentrations of free fatty acids, prolactin and cortisol were similar between trial conditions (all $p > 0.05$). There were also no differences across trials for heart rate or perceived exertion during exercise (both $p > 0.05$).
Conclusions: Acute supplementation with a low dose of octopamine did not influence endurance cycle performance, substrate oxidation or circulating hormonal concentrations, which could be due to the low serum octopamine concentrations observed. Future studies should investigate the influence of larger doses of octopamine in recreationally active and well-trained individuals during prolonged exercise in temperate and high ambient conditions.

1. Introduction

Octopamine is a naturally occurring amine structurally similar to the neurotransmitter noradrenaline.[1] It was first isolated from the salivary glands of the octopus[2] and is synthesised from the amino acid tyrosine with tyramine as an intermediate.[3] The function of octopamine is well-characterised in invertebrates, where it modulates signal transduction processes through the activation of octopamine receptors.[1] Vertebrates, including humans, are absent of these receptors, which led to the suggestion that endogenous octopamine exerts no major role in human physiology.[1] However, low circulating concentrations are observed in plasma,[4] leading octopamine to being classified as one of the primary trace amines.[5] A unique group of G protein-coupled receptors known as trace amine-associated receptors (TAAR) have been identified in recent years.[6] Importantly, octopamine can bind to the TAAR1 subtype,[6] a receptor which modulates the release of monoamines from presynaptic terminals in the brain.[7] This confirms previous reports of the presence of octopamine in mammalian nerve tissues and brain.[8] Furthermore, octopamine is suggested to play a role in the pathogenesis of Parkinson's disease.[4] Therefore, octopamine may, in part, modulate normal and abnormal neurophysiological processes[5] and possess stimulant-like properties capable of influencing exercise performance.[9]

Octopamine was studied as a therapeutic agent to treat hypotensive disorders, with doses of 450–600 mg day^{-1} resulting in mild increases in blood pressure without the presence of adverse effects.[10] Subsequent studies demonstrated the ability of octopamine to activate β_3 adrenoreceptors and stimulate lipolysis,[11] suggesting octopamine could influence fat metabolism. Furthermore, intracerebroventricular administration of octopamine increased locomotor activity in rats.[12] Despite these observations, no human study has examined the influence of

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octopamine on exercise performance or substrate metabolism. Therefore, the aim of this investigation was to determine whether a low dose of octopamine could influence endurance performance and/or exercise metabolism in a group of healthy volunteers.

2. Methods

Ten healthy, recreationally active men (age: 24 ± 2 years; body mass: 78.4 ± 8.7 kg; height: 1.81 ± 0.07 m; VO_{2peak}: 50.5 ± 6.8 mL kg^{-1} min^{-1}; peak power output: 295 ± 41 W) participated in this study, which employed a double-blind, randomised, cross-over design. Before the study, all participants received written and verbal information regarding the nature of the investigation. Following an opportunity to ask questions, a written statement of consent was signed. All participants were free from chronic disease and deemed eligible to take part following the completion of a health screen questionnaire. The experimental protocol was approved by the Ethics Approvals (Human Participants) Sub-Committee of Loughborough University, UK (Ref: R15-P072).

All participants completed one incremental maximal exercise test, one familiarisation trial and two experimental trials. The initial visit consisted of incremental cycle exercise to volitional exhaustion on an electronically braked cycle ergometer (Lode Corival, Groningen, Holland) to determine peak power output at VO_{2peak} (W_{max}) and the power output required to elicit 55% and 75% of W_{max}. Following this, participants completed a familiarisation trial. This was undertaken to ensure all participants were accustomed to the procedures employed during the investigation and to minimise any learning or anxiety effects. This visit was identical to the experimental trials in all respects, with the exception of no treatment being administered. All visits to the laboratory were separated by 5–7 days and were performed at the same time of day to minimise circadian-type variance. Participants were instructed to record their dietary habits and physical activity patterns during the 24 h before the familiarisation trial and to replicate this in the 24 h preceding the subsequent experimental trials. Additionally, no strenuous exercise, alcohol ingestion or excessive caffeine consumption (i.e. above habitual intake) was permitted during the 24 h before each experimental trial. Compliance to these measures was verified upon arrival at the laboratory, prior to any data collection.

Participants arrived at the laboratory in the morning (7–9 am) following an overnight fast (8–12 h) with the exception of ingesting 500 mL of plain water approximately 90 min before arrival. Post-void nude body mass was recorded upon arrival (Adam AFW-120K, Milton Keynes, UK) and a heart rate telemetry band (Polar Beat, Kempele, Finland) was positioned. Participants then rested in a seated position for 15 min before a 21-g cannula was inserted into an antecubital vein to enable repeated blood sampling; this was flushed with a small volume of saline after each sample to ensure patency. A baseline venous sample (12 mL) was collected before participants ingested a capsule containing either 150 mg of starch (placebo) or 150 mg of octopamine (Blackburn Distributions, Lancashire, UK) with a small volume of water (50 mL). The purity of octopamine was certified at >99% (HFL Sport Science, Fordham, UK; Ref: LGC255966). The 150 mg dose was chosen to avoid hypertensive effects reported after oral intakes of 450–600 mg in hypotensive patients.[10] All capsules were visually identical and blinded by an external party not involved in any stage of data collection. Following ingestion of the capsules, participants rested in a comfortable environment for 60 min; this timeframe is sufficient to elicit peak octopamine concentrations in the blood.[13] After the rest period, a second venous sample (12 mL) was collected before participants began cycle exercise for 30 min at a workload corresponding to 55% W_{max}. During this period heart rate and rating of perceived exertion (RPE) were recorded every 5 and 10 min, respectively.[14] Expired gas samples (1 min) were collected into Douglas bags at 15 and 30 min to determine the rates of fat and carbohydrate oxidation.[15] Oxygen and carbon dioxide concentrations in each bag were determined with a paramagnetic analyser (Servomex 1400, Sussex, UK) calibrated against gases of known concentration on the morning of each trial. Total volume was quantified (Harvard Dry Gas Meter, Harvard Apparatus, USA) and gas values were expressed as STPD. Following the collection of each sample, participants were provided with 100 mL of plain water. After the 30 min, a third venous sample (12 mL) was collected while participants remained seated on the ergometer.

Subsequently, there was a 2–3 min delay while the ergometer was set up for the performance task. Participants were instructed to complete as much work (kJ) as possible within 30 min. This method of measuring performance is consistent with previous studies which examined the performance benefits of stimulants such as caffeine.[16,17] Furthermore, this performance test elicits a coefficient of variation of approximately 3% in recreationally active participants following one familiarisation trial,[18] indicating a similar test-retest reliability to the energy-based time-trial protocols.[19] Participants began exercise at a workload corresponding to 75% W_{max}, but were free to adjust their workload as desired from the outset. During this period participants received feedback regarding time elapsed and cadence, but no other information or verbal encouragement was provided and contact was limited to the recording of the physiological and perceptual variables. Heart rate was recorded every 5 min and RPE at 10 and 20 min, respectively. A final venous sample (12 mL) was collected upon completion of exercise while participants remained seated on the ergometer. After this, the cannula was removed.

All venous samples were drawn directly into dry syringes. A small volume (2 mL) was dispensed into tubes containing K_2EDTA. Duplicate 100 μL aliquots were rapidly deproteinised in 1 mL of ice-cold 0.3 N perchloric acid. These were centrifuged and the resulting supernatant used to determine blood glucose concentrations (GOD-PAP, Randox Ltd., UK). Haemoglobin (cyanmethemoglobin method) and haematocrit (microcentrifugation) values were used to estimate percentage changes in blood and plasma volumes relative to the resting sample.[20] A separate 5 mL was dispensed into tubes containing K_2EDTA and a further 5 mL was dispensed into tubes containing clotting activator; both aliquots were left on ice for 60 min prior to centrifugation at 1750 g for 10 min at 4 °C. The resulting plasma from the K_2EDTA treated blood was stored at −21 °C for the subsequent determination of free fatty acids (FFA; Randox laboratories Ltd., Crumlin, UK) by colorimetric methods. The resulting serum from the clotted blood was stored at −21 °C for the subsequent determination of prolactin and cortisol with ELISA (DRG diagnostics, Germany) and octopamine with a modified reverse-phase HPLC method as previously described.[21]

All data were analysed using IBM SPSS statistics version 21.0. Normality was assessed with the Shapiro Wilk test. To evaluate differences in exercise performance, pre-exercise nude body mass, and fasting plasma glucose across trial conditions, a paired *t*-test was employed. Cohen's *d* effect size (ES) for differences in total work produced during the performance task was determined ([mean 1–mean 2]/pooled SD) and interpreted as trivial (0–0.19), small (0.2–0.49), medium (0.5–0.79) or large (>0.8) as previously described.[22] Variables measured throughout each trial were analysed using a two-way (trial × time) repeated-measures ANOVA. Where the assumption of sphericity had been violated, the degrees of freedom were corrected with a Greenhouse-Geisser as appropriate. Main effects and interactions were followed up with Bonferroni adjusted paired *t*-tests for normally distributed data or Bonferroni adjusted Wilcoxon Signed Rank tests for non-normally distributed data. Data are presented as means ± SD throughout. Statistical significance was accepted at $p < 0.05$.

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