The significance of CYP1A2 genotype on caffeine metabolism and exercise performance

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Abstract

Objective: The objective of this study was to investigate whether a single nucleotide polymorphism (C to A transversion at position -163 downstream of the first transcribed nucleotide) in the enzyme that metabolizes caffeine (CYP1A2), would explain the variability seen in caffeine related responses in endurance exercise performance. In a double blind crossover trial, well trained male endurance athletes (n=11, mean VO_2 max 69±4 $mL.kg^{-1}.min^{-1}$) ingested either caffeine (5 $mg.kg^{-1}$) or a placebo 60 minutes prior to performing a lab based experimental protocol involving a two hour steady state cycle (70% VO_2 max) followed by a 30 minute time trial to measure performance. The rate of caffeine metabolism over seven hours (inclusive of exercise period) was also determined by the HPLC analysis of plasma caffeine and its major metabolites, paraxanthine, theophylline and theobromine. Caffeine metabolism at rest over a similar seven hour period was also determined in the same manner.

Results: Caffeine improved endurance performance by 7.1% (p=0.037) compared to a placebo. Caffeine also significantly elevated heart rate during the time trial (p=0.003); and RPE (p=0.010) and VO_2 (p=0.047) during steady state exercise. There was no correlation between caffeine or paraxanthine concentrations at the start of the time trial and subsequent performance and the rate of caffeine metabolism was not significantly different between resting or exercising trials. Furthermore there was no significant interaction between caffeine treatment and CYP1A2 genotype on performance or any other

variables measured. However there was a trend for carriers of the C allele showing faster metabolism than those homozygous A/A (p=0.097).

Conclusions: Caffeine is ergogenic during endurance exercise, however individual responses were variable. In this study this variability could not be explained by CYP1A2 genotype. However the small sample size in this study especially when subjects were divided into genotype groups, makes drawing conclusions difficult.

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Approval for the research was obtained from Massey University Human Ethics Committee (HEC: Southern A Application 11/35) for the experiments described in this thesis.

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Abbreviations

137X	1,3,7-trimethylxanthine (caffeine)
17U	1,7-dimethyluric acid
17X	1,7-dimethylxanthine (paraxanthine)
1U	1-methyluracil
1X	1-methylxanthine
AFMU	5-acetylamino-6-formylamino-3-methyluracil
AUC	Area Under the Curve
BW	Body Weight
Caffeine-Ex	Exercise trial with Caffeine
Caffeine-Rest	Resting trial with Caffeine
cAMP	cyclic adenosine monophosphate
CNS	Central Nervous System
CYP1A2	Cytochrome P450 1A2
DNA	Deoxyribonucleic Acid
EDL	Extensor digitorum longus muscle
EDTA	Ethylenediaminetetraacetic acid
FFA	Free Fatty Acids
HIT	High Intensity Training
HPLC	High Performance Liquid Chromatography
HR	Heart Rate
NMR	Nuclear Magnetic Resonance
PAH	Polycyclic aromatic hydrocarbons
PCR	Polymerase Chain Reaction
Placebo- Ex	Exercise trial with Placebo
PX	Paraxanthine
RER	Respiratory Exchange Ratio
RPE	Rating of Perceived Exertion
SNP	Single Nucleotide Polymorphism
TB	Theobromine
TFA	Trifluroacetic Acid
TP	Theophylline

USDA	United States Department of Agriculture
VO_2	Volume of Oxygen
VO_2 max	Maximal Oxygen Uptake
WADA	World Anti-Doping Agency