The role of oxidative, inflammatory and neuroendocrine systems during exercise stress in athletes

A thesis submitted for the degree

Doctor of Philosophy

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By

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Certificate of Authorship and Originality of Thesis

I certify that the work contained in this thesis has not been previously submitted either in whole or in part for a degree at the University of Technology, Sydney or any other tertiary institution.

I also certify that the thesis has been written by me, Katie May Slattery. Any help that I have received in my research work and in the preparation of this thesis has been acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

__________________________________

Katie Slattery

__________________________________

Date Submitted
Acknowledgements

‘A man [women] is not an island’, and PhD is not done alone. Many people have contributed to the completion of this thesis and I am sincerely thankful and appreciative to you all.

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Finally, to my family and friends, a huge thank you for all of your encouragement, well-wishes, patience and unwavering support.
Preface

This thesis for the degree of Doctor of Philosophy is in the format of published or submitted manuscripts and abides by the ‘Procedures for Presentation and Submission of Theses for Higher Degrees – University of Technology, Sydney; Policies and Directions of the University’. All manuscripts included in this thesis are closely related in subject matter and form a cohesive research narrative.

Based on the research design and data collected by the candidate, three manuscripts have been submitted for publication and one manuscript has been accepted, in peer-reviewed journals. These papers are initially brought together by an Introduction, which provides background information, defines the research problem and the aim of each study. A Literature Review then follows to provide an overview of previous knowledge regarding the effect of intensified training periods and antioxidant supplementation on the oxidative, inflammatory and neuroendocrinological response to exercise. The body of the research is presented in manuscript form (Chapter 3 to Chapter 6), in a logical sequence following the development of research ideas in this thesis. Each manuscript outlines and discusses the individual methodology and the findings of each study separately. The General Discussion chapter provides an interpretation of the collective findings and practical applications from the series of investigations conducted. Finally, a Summary and Recommendations chapter is a synopsis of the research hypothesis tested and conclusions from each project. Based on these findings, directions for future research are suggested. Author-date reference style has been used throughout the document and the reference list is at the end of the thesis.
List of Articles Submitted for Publication

Refereed Journal Publications


Conference Proceedings & Abstracts


Statement of Candidate Contribution

The contribution of each author to the investigations undertaken as part of the thesis is outlined in Table A below.

Table A: Percentage contribution (%) of each author to the investigations conducted during the candidature

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Abstract

Introduction: Exercise induces a stress reaction that initiates adaptive processes, which can be modified by intensive physical training and/or exogenous antioxidant supplementation. However, the optimal exercise training strategy and corresponding level of antioxidant support for positive adaptation remains unclear. Therefore, the overall aim of this thesis was to investigate the interactions between exercise-induced changes within the oxidative, inflammatory and neuroendocrinological systems and antioxidant supplementation on athletic performance during intensive physical training. Three separate studies were undertaken and reported in four manuscripts. Study 1: In Study 1, well-trained athletes (n = 23) completed a 4 day food record during a period of intensified physical training. Collectively, the participants consumed a sufficient dietary intake of antioxidants (vitamin A, C and E) according to the Australian recommendations. Study 2: Study 2 used a crossover experimental design to examine the effect of intensive physical training on oxidative damage, inflammation, hormonal disturbances and performance capacity. Participants (n = 7) completed a high-intensity intermittent running protocol following both a reduced (LOW) and intensive (HIGH) 4 day physical training period. The results demonstrated that HIGH physical training led to an increased amount of muscle damage, decreases in sprint velocity (P < 0.001) and a reduction in total distance covered (P < 0.05) during the high-intensity intermittent running protocol. HIGH physical training also induced a greater increase in oxidative damage (xanthine oxidase) markers 2 h post-exercise (paper 1). Neuroendocrinological measures (growth and thyroid hormones) were not altered by training-induced fatigue (paper 2). These findings suggest that 4 day HIGH training can impair high-intensity running performance and exacerbate oxidative damage. Study 3: Study 3 used a double blind randomised placebo-controlled crossover design to investigate the effect of 9 d oral N-acetylcysteine (NAC) supplementation (1200 mg/day) in eight well-trained triathletes. Changes in performance (cycle ergometer race simulation) and pre- to post-exercise biochemistry measures were taken to determine the ergogenic effect of NAC and associated reaction within the oxidative and inflammatory systems. It was demonstrated that oral NAC supplementation enhanced repeat sprint cycling performance via an improved redox balance and promoted adaptive processes in well-trained triathletes undergoing intensive physical training. NAC supplementation was also effective at blunting the inflammatory response to exercise. Conclusion: Collectively, this thesis provides novel information regarding the dose-response relationship between training-induced fatigue, antioxidant supplementation and athletic performance.
Keywords

Antioxidant
Fatigue
Inflammation
Intensified physical training
Muscle Damage
N-acetylcysteine
Nuclear factor – kappaB
Oxidative damage
Performance
Hormone
List of Abbreviations

8-OHdG 8-hydroxy-deoxyguanosine
AMP adenosine monophosphate
AP-1 activating protein-1
AU arbitrary units
CAT catalase
Cdmax maximum amount of conjugated dienes
CI confidence interval
COX-2 cyclooxygenase
CR-10 category ratio 10
CV coefficient of variation
d Cohen’s d effect size
DAG diacylglycerol
DALDA Daily Analysis of Life Demands for Athletes
F2-isoprostane 15-isoprostane F2 concentration
FRAP ferric reducing ability of plasma
FT3 free triiodothyronine
FT4 free thyroxine
g Hedge’s g effect size
GH growth hormone
Gr glutathione reductase
GPX glutathione peroxidise
GSH reduced glutathione
GSH:GSSG reduced glutathione to glutathione ratio
GSSG glutathione
HIGH intensified training period
H2O2 hydrogen peroxide;
HSF heat shock factor
HSP heat shock protein
ICC intra-class correlation
IκB inhibitor -kappaB
IκK inhibitor - kappaB kinase
IL-6 interlukin-6
iNOS inducible nitric oxide synthase
ISAK International Society for the Advancement of Kinanthropometry
JNK c-Jun N-terminal kinases
LDH lactate dehydrogenase
lipid-ox lag time in lipid peroxidation
LOH redox inert alcohol
LOOH lipid hydroperoxide
LOW low training load
Lp length of lag phase
MAPK mitogen-activated protein kinase
MCP-1 monocyte chemoattractant protein-1
MDA malondialdehyde
MKK MAP kinase kinase
MnSOD manganese superoxide dismutase
mRNA messengerRNA
η2p partial eta squared
NAC N-acetylcysteine
<table>
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<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>NADPH</td>
<td>nicotinamide-adenine dinucleotide phosphate</td>
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<td>NF-κB</td>
<td>nuclear factor-kappaB</td>
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<tr>
<td>nm</td>
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<td>NMT</td>
<td>non-motorised treadmill</td>
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<td>O₂</td>
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<td>ORAC</td>
<td>oxygen radical absorbance capacity</td>
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<td>protein C kinase</td>
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<td>double-stranded RNA protein kinase</td>
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<td>PLC</td>
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<td>PPARγ</td>
<td>peroxisome-proliferators-activated receptor gamma</td>
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<tr>
<td>PPAR</td>
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<tr>
<td>PUFA</td>
<td>poly unsaturated fatty acid</td>
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<tr>
<td>RDI</td>
<td>recommended daily intake</td>
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<td>Redox</td>
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<td>superoxide dismutase</td>
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<td>SRM</td>
<td>Schoberer Rad Meßtechnik</td>
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<td>T</td>
<td>training load period</td>
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<td>TAC</td>
<td>total antioxidant capacity</td>
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<td>TBARS</td>
<td>thiobarbituric acid-reactive substances</td>
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<td>typical error</td>
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<td>TEAC</td>
<td>trolox-equivalent antioxidant capacity</td>
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<td>TNF-α</td>
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<td>thyroid stimulating hormone</td>
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<td>training load</td>
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<tr>
<td>UA</td>
<td>uric acid</td>
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<tr>
<td>XO</td>
<td>xanthine oxidase</td>
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