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Metabolic Alterations in Skeletal Muscle Following Eccentric Exercise Induced Damage

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Abstract

Eccentric exercise-induced muscle damage (EEIMD) is experienced following unaccustomed eccentric-biased exercise. Gaps in knowledge on aspects of the metabolic response to EEIMD exist, particularly on *in vivo* metabolism. The aim of this thesis is to provide empirical evidence to advance the scientific knowledge and understanding of EEIMD by investigating the metabolic responses following acute and adaptive bouts of eccentric exercise. Eccentric exercise causes changes to the ultrastructure of skeletal muscle and may alter the ability of the muscle to store and utilise intracellular substrates such as glycogen and intramyocellular lipid (IMCL). Using expired respiratory gases collected during one legged cycling to estimate whole body substrate utilisation, the first study showed that acute bouts of eccentric exercise alter the pattern of substrate selection. The effect of EEIMD on substrate utilisation during one legged cycling revealed significantly higher rates of CHO oxidation in EEIMD and that the CHO oxidation further increased during one legged cycling at 48 hours. This is suggestive of greater reliance upon muscle glycogen during subsequent bouts of exercise. The utilisation of nuclear magnetic resonance (NMR) spectroscopy to measure phosphate compounds and IMCL content of the *vastus lateralis* allowed for examination of changes in substrate storage following exposure to an acute bout of eccentric exercise. The second study showed that, following EEIMD, using proton spectroscopy (^{1}H-MRS), alterations occur in the IMCL pool within skeletal muscle with a higher concentration evident in the eccentric leg at 24 hours but the trend had been reversed at 48 hours with higher concentrations of IMCL in the concentric leg at 48 hours. Using phosphorous spectroscopy (^{31}P-MRS) there was also a significant alteration for resting phosphate stores with increases in inorganic phosphate concentration ([P_i]) in EEIMD. Eccentric exercise also alters the physiological response to normal levels of insulin and can be defined as 'transient insulin resistance'. Repeated eccentric exercise training initiates a protective adaptation so that recovery results in reduced symptoms of damage in the repeat bout compared to the initial bout. The third study investigated; via a standard 75g oral glucose tolerance test (OGTT), whether disruptions to glucose and insulin responses following eccentric exercise could be attenuated after a repeated bout of eccentric exercise. There was no change in the insulin response, in comparison to a control trial, 48 hours after a bout of 100 squats of 30% body mass; this formed the eccentric exercise for the study. A subsequent bout of

the same eccentric exercise did not attenuate the insulin response. It is not known if repeated exposure to eccentric exercise can attenuate increases in indirect measures of intracellular metabolism (P_i / PCr) following EEIMD, as seen in study two. Study four utilised ^{31}P-MRS to examine the effect of EEIMD on intramyocellular phosphate stores in skeletal muscle, which had been concentrically or eccentrically trained. The data revealed that increases in skeletal muscle phosphate metabolism were not attenuated following exposure to repeated bouts of eccentric exercise and decrements in force generating capacity of muscle following EEIMD must be mediated by central factors. The four studies have provided novel insights into the influence of eccentric, muscle-damaging exercise on the metabolic response of skeletal muscle.

Summary Table

	Study 1 (Chapter 3)	Study 2 (Chapter 4)	Study 3 (Chapter 5)	Study 4 (Chapter 6)
Participants	8 males	6 males	8 males	5 males 1 female
Measure	Whole body substrate oxidation	IMCL, P_i, P_i /PCr	Glycaemic response	P_i, P_i /PCr
Measurement Tools	Indirect calorimetry	^{1}H-MRS, ^{31}P-MRS	75g 2 hour OGTT	^{31}P-MRS
Eccentric Exercise	Bench Stepping	Isokinetic dynamometry / Quads	Squat exercise	Isokinetic dynamometry / Quads
1st Outcome measure	Increased RER (Reliance on glycogen)	Higher IMCL in EEIMD at 24 hrs.	No change in whole body insulin or glucose response	Increased P_i and P_i / PCr in both conditions
2nd Outcome measure	Muscle performance decrease in EEIMD	Increased P_i and P_i / PCr in EEIMD	CK increase but attenuated in second bout	Attenuated muscle performance and volume

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List of publications and presentations

Peer Reviewed Journals

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Conference Papers

Hughes, J. D., Johnson, N. A., Brown, S. J., Chapman, P. G. and Stannard, S. R. (2009). Substrate utilisation in eccentric exercise induced damaged muscle. *Proceedings of the New Zealand Sports Medicine & Science Conference*, pp. 74.

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Hughes, J. D., Johnson, N. A. and Stannard, S. R. (2008). Eccentric exercise induced muscle damage and Intramyocellular lipid concentration. *Post Graduate Sport Research Conference*, pp. 30-32.

Contents

List of abbreviations

ADP	Adenosine diphosphate
AMARES	Advanced method for accurate, robust and efficient spectral fitting
AMP	Adenosine monophosphate
AMPK	AMP-activated protein kinase
ANOVA	Analysis of variance
ATP	Adenosine triphosphate
AUC	Area under the curve
B_0	Magnetic field
bFGF	Basic fibroblast growth factor
BSE	Bench stepping exercise
C	Carbon
Ca^{2+}	Calcium
CCB	Calcium channel blockers
CHO	Carbohydrate
CK	Creatine kinase
CMJ	Countermovement jump
CO_2	Carbon dioxide
COM	Centre of motion
Con	Concentric
ConTr	Concentric training
Cr	Creatine
CSA	Cross sectional area
CV	Coefficient of variance
DOMS	Delayed onset muscle soreness

E-C	Excitation-contraction coupling
Ecc	Eccentric
EccTr	Eccentric training
EE	Eccentric exercise
EEIMD	Eccentric exercise induced muscle damage
EMCL	Extramyocellular lipid
$FADH_2$	Flavin adenine dinucleotide
FFAs	Free fatty acids
FID	Frequency induction decay
GLUT-1	Glucose transporter type 1
GLUT-4	Glucose transporter type 4
H	Hydrogen
HL	Hydroxylysine
^{1}H-MRS	Proton magnetic resonance spectroscopy
HP	Hydroxyproline
HR	Heart rate
HSD	Honestly significant difference
HSL	Hormone sensitive lipase
IMCL	Intramyocellular lipid
IMTG	Intramuscular triacylglycerols
IRS-1	Insulin receptor substrates 1

IRS-2	Insulin receptor substrates 2
LDH	Lactate dehydrogenase
LED	Light emitting diode
LPL	Lipoprotein lipase
MG^{+2}	Magnesium
MRI	Magnetic resonance imaging
MRS	Magnetic resonance spectroscopy
MVC	Maximal voluntary contraction
NADH	Nicotinamide adenine dinucleotide
NMR	Nuclear magnetic resonance
NOE	Nuclear overhauser enhancement
O_2	Oxygen
OGTT	Oral glucose tolerance test
^{31}P-MRS	Phosphorus magnetic resonance spectroscopy
P	Phosphorus
PASW	Predictive analytics software
PCr	Phosphocreatine
PDE	Phosphodiesters
P_i	Inorganic phosphate
PI3-kinase	Phosphatidylinositol 3-kinase
P_i / PCr	Inorganic phosphate / phosphocreatine ratio
PME	Phosphomonosters

PRESS	Point resolved spectroscopy
QUEST	Quantitation based on quantum estimation
RBE	Repeat bout effect
RER	Respiratory exchange ratio
ROM	Range of motion
RPE	Ratings of perceived exertion
SD	Standard deviation
SR	Sarcoplasmic reticulum
T1	Longitudinal relaxation time
T2	Transverse relaxation time
TCr	Total creatine
$\mathbf{TCr_{BASAL}}$	Total basal muscle creatine
TE	Echo time
TG	Triacylglycerol
TNFα	Tumour necrosis factor-α
TR	Repetition time
VAS	Visual analogue scale
$\dot{V}\,\mathbf{O_{2max}}$	Maximal oxygen consumption
WL1	Work load 1
WL2	Work load 2

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