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The Effects of Rapid and Prolonged Changes in Blood Pressure on Cerebral Blood Flow in Healthy Humans

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Abstract

The regulation of blood flow to the brain is complex and incompletely understood. Many local and systemic factors modulate cerebral perfusion, one of which is arterial blood pressure. The brain possesses intrinsic mechanisms which act to protect against rapid and also prolonged changes in perfusion pressure. However, recent evidence indicates that this supposedly powerful regulatory mechanism/s may not be as efficient as traditionally believed and that changes in arterial blood pressure have a profound effect on cerebral blood flow (CBF). This thesis explored different non-pharmacological means of perturbing mean arterial blood pressure (MAP) both rapidly (dynamic) and for prolonged steady-state periods (~5 min; static). Dynamic changes in blood pressure were induced via upright resistance exercise (**Chapter Five**) and standing Valsalva manoeuvres (VM; **Chapter Six**), while static changes were induced via lower body positive pressure (**Chapters Seven and Eight**). The effects of these changes in MAP on cerebral blood flow were assessed via transcranial Doppler ultrasound of the blood velocity in middle cerebral artery (MCAv). The findings of **Chapter Five** illustrated that *during* resistance exercise the peak mean MCAv ($MCAv_{mean}$) was unchanged between loads despite the increasing MAP with the increasing relative load. Following resistance exercise, however, the hypotension observed was matched by concomitant reductions in $MCAv_{mean}$, the magnitude of which was load dependent. **Chapter Six** investigated the role of the Valsalva manoeuvre (VM) alone in the stability of the MCAv response whilst standing. **Chapter Six** highlights that the VM protects the cerebral vessels during acute hypertension. In addition, more intense straining during a VM produced a similar response following the release of the manoeuvre to that seen following the resistance exercise. Thus, more pronounced decreases in blood pressure,

whilst upright, do result in concomitant decreases in $MCAV_{mean}$. The steady-state elevations in MAP examined in **Chapters Seven** and **Eight** increased $MCAV_{mean}$ with and without hypercapnia. Thus, illustrating that even when the regulatory mechanisms were functionally intact (normocapnia) the brain demonstrated a pressure passive relationship during relatively small increases in MAP. Overall, both abrupt and steady-state changes in perfusion pressure were coupled with alterations in $MCAV_{mean}$. This thesis contributes to the notion that the cerebral circulation is not independent of changes in MAP, and that sustained hypercapnia impairs the autoregulatory capacity of the cerebral circulation. Importantly, this thesis shows these effects without the use of pharmacological agents to confound the interpretation of the data.

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Table of Contents

Abstract.....	ii
Acknowledgments.....	iv
Table of Contents.....	v
List of Abbreviations.....	ix
List of Tables.....	xii
List of Figures.....	xiii
Chapter One: Introduction.....	1
Chapter Two: Literature Review.....	4
2.1 Cerebral Blood Flow.....	4
2.1.1 Arterial Carbon Dioxide Content.....	8
2.1.2 Arterial Oxygen Content.....	12
2.1.3 Arterial Blood Pressure.....	14
2.1.3.1 Static Cerebral Autoregulation.....	17
2.1.3.2 Dynamic Cerebral Autoregulation.....	19
2.1.3.3 Role of Arterial Gases in Cerebral Autoregulation.....	21
2.1.3.3.1 Carbon Dioxide.....	21
2.1.3.3.2 Oxygen.....	22
2.1.4 Cardiac Output.....	24
2.1.5 Neurovascular Coupling.....	25
2.1.6 Autonomic Nervous System.....	25
2.2 Cardiovascular Function.....	28
2.2.1 Baroreflex.....	29
2.2.2 Baroreflex During Exercise.....	32
2.2.3 Low Pressure Baroreceptors.....	33
2.2.4 Chemoreception and Arterial Blood Pressure.....	35
2.2.5 Blood Pressure Regulation and the Cutaneous Circulation.....	37
2.2.6 Stroke Volume.....	39
2.2.6.1 The Frank-Starling Mechanism.....	39
2.2.6.2 Arterial Blood Pressure.....	40
2.2.6.3 Contractility.....	41
2.2.6.3.1 Autonomic Activation.....	41
2.2.6.3.2 Heart Rate.....	42
2.3 Control of Ventilation.....	43
2.3.1 The Chemoreflex Drive to Breathe.....	43
2.4 Orthostasis.....	46
2.4.1 Syncope/Cerebral Hypoperfusion.....	47
2.4.1.1 Initial Orthostatic Hypotension.....	48
2.4.1.2 Prolonged Orthostasis.....	49
2.4.2 Cerebro- and Cardiovascular Control at Vasovagal Syncope.....	50
2.4.2.1 Cerebral Autoregulation.....	51
2.4.2.2 Sympathetic Nervous Activity.....	53
2.4.2.2.1 Muscle Sympathetic Nervous Activity.....	53
2.4.2.2.2 Cerebral Sympathetic Nervous Activity.....	55
2.4.2.3 Arterial Blood Gases.....	55

2.5 Resistance Exercise	57
2.5.1 Blood Pressure Response	58
2.5.1.1 During Resistance Exercise	58
2.5.1.2 Following Resistance Exercise	59
2.5.2 Cerebrovascular Response	60
2.5.2.1 During Resistance Exercise	60
2.5.2.2 Following Resistance Exercise	62
2.5.3 Role of the Valsalva Manoeuvre	62
2.5.4 Circulatory Adaptations to Resistance Exercise	65
2.6 Lower Body Positive Pressure	68
2.6.1 Blood Pressure Response	69
2.6.2 Cerebrovascular Response	70
2.7 Summary	70
Chapter Three: Review of Techniques and General Methodology	72
3.1 Measurement of Cerebral Blood Flow	72
3.1.1 Transcranial Doppler Ultrasound: Ultrasonography Principles	73
3.1.2 Validity	75
3.2 Measurement of Arterial Blood Pressure	77
3.2.1 Beat-to-beat Arterial Blood Pressure	77
3.2.2 Validation of Non-Invasive Beat-to-beat Arterial Blood Pressure	79
3.2.3 Non-invasive Stroke Volume and Cardiac Output Estimates	80
3.2.4 Validation of Modelflow Estimates of Stroke Volume and Cardiac Output	82
3.3 General Methodology	84
3.3.1 Insonation of the Middle Cerebral Artery (MCA) using Transcranial Doppler (TCD) Ultrasonography	84
3.3.2 Calculation of Mean MCAv	86
3.3.3 Calculation of Area Under the Curve	87
3.3.4 Cerebrovascular Conductance/Resistance	87
3.3.5 Technique of Photoplethysmography	88
3.3.6 Calculation of Mean, Systolic and Diastolic Arterial Blood Pressures	89
3.3.7 Electrocardiogram	89
3.4 Physiological Stressors	90
3.4.1 Valsalva Manoeuvre (VM)	90
3.4.2 Lower Body Positive Pressure (LBPP)	91
Chapter Four: Research Aims and Hypotheses	92
4.1 Chapter Five	92
4.2 Chapter Six	93
4.3 Chapter Seven	94
4.4 Chapter Eight	94
Chapter Five: Haemodynamic Response to Upright Resistance Exercise: Effect of Load and Repetition	96
5.1 Introduction	96
5.2 Methods	98
5.2.1 Participants	98
5.2.2 Study Design	98
5.2.3 Experimental Protocol	100
5.2.4 Measurements	101

5.2.5 Data Analyses	102
5.2.6 Statistical Analyses	103
5.3 Results	104
5.3.1 Haemodynamic Responses During Upright Resistance Exercise	104
5.3.2 Cerebrovascular and Cardiorespiratory Variables at $MCAv_{mean}$ Nadir	105
5.3.3 Cerebrovascular and Cardiorespiratory Variables at MAP Nadir	107
5.3.4 Recovery Following Exercise	108
5.4 Discussion.....	112
5.4.1 MAP Response During Upright Resistance Exercise.	112
5.4.2 The Restraint of $MCAv$ During Resistance Exercise	113
5.4.3 The Reduction in $MCAv_{mean}$ is Due to a Selective Decrease in Diastolic Flow Velocity.....	114
5.4.4 The Role of Arterial CO_2 During and Following Heavy Resistance Exercise.....	115
5.5 Conclusion	116
Chapter Six: The Cerebrovascular Response to Graded Valsalva Manoeuvres Whilst Standing.....	118
6.1 Introduction	118
6.2 Methods	121
6.2.1 Participants.....	121
6.2.2 Study Design.....	121
6.2.3 Experimental Protocol.....	122
6.2.4 Measurements	122
6.2.5 Data Analyses	123
6.2.6 Statistical Analyses	123
6.3 Results	124
6.4 Discussion.....	130
6.4.1 The Haemodynamic Response During Phase I of the VM.....	131
6.4.2 The Haemodynamic Response During Phase III of the VM.....	133
6.4.3 The Effect of Posture on the VM.....	134
6.4.4 Contribution of $P_{ET}CO_2$	135
6.4.5 Implications for Resistance Exercise	135
6.5 Conclusion	137
Chapter Seven: Middle Cerebral Artery Blood Flow Velocity in Response to Lower Body Positive Pressure	139
7.1 Introduction	139
7.2 Methods	141
7.2.1 Participants.....	141
7.2.2 Study Design.....	141
7.2.3 Experimental Protocol.....	142
7.2.4 Measurements	142
7.2.5 Data Analyses	143
7.2.6 Statistical Analyses	144
7.3 Results	144
7.4 Discussion.....	146
7.4.1 LBPP Induced Changes in MAP and Static Cerebral Autoregulation	147
7.4.2 Role of the Sympathetic Nervous System.....	148
7.5 Conclusion	150

Chapter Eight: The Effect of Hypercapnia on Static Cerebral Autoregulation.....	152
8.2 Methods	154
8.2.1 Participants.....	154
8.2.2 Experimental Protocol.....	154
8.2.3 Measurements	155
8.2.4 Data analysis.....	156
8.2.5 Statistical Analysis	157
8.3 Results	157
8.4 Discussion.....	161
8.4.1 The Efficacy of Static Cerebral Autoregulation	162
8.4.2 Role of the Sympathetic Nervous System	164
8.4.3 Interaction Between Sympathetic Activation and Arterial CO ₂	165
8.5 Conclusion	165
Chapter Nine: General Discussion	167
9.1 Dynamic Changes in MAP	167
9.2 Static Changes in MAP	172
9.3 Limitations.....	175
9.3.1 Transcranial Doppler	175
9.3.2 Participants.....	178
9.3.3 Implications for Special Populations.	179
9.4 Conclusions	179
9.5 Future Directions.....	180
9.5.1 Lower Body Positive Pressure	180
9.5.2 The Valsalva Manoeuvre	181
References	183
Appendix A.....	220
A: Ethical Approval Documentation.....	220
Chapter Five: Haemodynamic Response to Upright Resistance Exercise: Effect of Load and Repetition	220
Chapter Six: The Cerebrovascular response to Graded Valsalva Manoeuvres Whilst Standing.....	221
Chapter Seven: Middle Cerebral Artery Blood Flow Velocity in Response to Lower Body Positive Pressure	222
Chapter Eight: The Effect of Hypercapnia on Static Cerebral Autoregulation.....	223
Appendix B.....	224
B: Statements of Contribution	224
Appendix C.....	227
C: Published Papers.....	227
Appendix D	230
D: Copyright Agreements.....	230

List of Abbreviations

A

ABP	Arterial blood pressure
ACA	Anterior cerebral artery
ANOVA	Analysis of variance
AVM	Arteriovenous malformation

B

BA	Basilar artery
beats·min ⁻¹	Beats per minute

C

CBF	Cerebral blood flow
cm	Centimetres
cm·s ⁻¹	Centimetres per second
CO ₂	Carbon dioxide
CPP	Cerebral perfusion pressure
CVC	Cerebrovascular conductance
CVP	Central venous pressure
CVR	Cerebrovascular resistance

D

DBP	Diastolic blood pressure
DMCAv	Diastolic middle cerebral artery blood flow velocity

E

ECG	Electrocardiogram
-----	-------------------

H

HR	Heart rate
H ₂ O	Water

I

ICA Internal carotid artery
ICP Intracranial pressure

K

kg Kilograms

L

LBNP Lower body negative pressure
LBPP Lower body positive pressure
L·min⁻¹ Litres per minute
L-NMMA N^G-monomethyl-L-arginine

M

m Metre
MAP Mean arterial blood pressure
MCA Middle cerebral artery
MCAv Middle cerebral artery blood flow velocity
MCAv_{mean} Mean middle cerebral artery blood flow velocity
min Minute
mL Millilitres
mm Hg Millimetres of mercury
MVC Maximal voluntary contraction
MSNA Muscle sympathetic nerve activity

N

NTS Nucleus tractus solitarius

O

O₂ Oxygen

P

P_aCO₂ Partial pressure of arterial carbon dioxide

P_aO_2	Partial pressure of arterial oxygen
PCA	Posterior cerebral artery
$P_{ET}CO_2$	Partial pressure of end-tidal carbon dioxide
$P_{ET}O_2$	Partial pressure of end-tidal oxygen

Q

\dot{Q}	Cardiac output
-----------	----------------

R

RM	Repetition maximum
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S

SBP	Systolic blood pressure
SD	Standard deviation
SE	Standard error
SMCAv	Systolic middle cerebral artery blood flow velocity
SV	Stroke volume

T

TCD	Transcranial doppler
TPR	Total peripheral resistance

V

VA	Vertebral artery
VM	Valsalva manoeuvre

Y

Y	Years
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List of Tables

Table 5.1 Changes from baseline at MCAv nadir for 30, 60 and 90% 6RM loads.	110
Table 5.2 Hemodynamic changes from baseline at MAP nadir for 30, 60 and 90% 6RM loads.	111
Table 6.1 Changes from baseline at Peak (phase I) for 30, 60 and 90% VM intensities.	127
Table 6.2 Changes from baseline at Nadir (phase III) for 30, 60 and 90% VM intensities. ...	128
Table 7.1 Haemodynamic changes from baseline during 20 and 40 mm Hg of lower body positive pressure.	145
Table 8.1 Changes from baseline during hypercapnia and lower body positive pressure.	160

List of Figures

Figure 2.1 Diagrammatic representation of the arteries forming the circle of Willis (Franco Folino 2007).	5
Figure 2.2 The effect of key physiological stimuli on CBF. BP, Blood pressure; PCO_2 , partial pressure of carbon dioxide; SNA, sympathetic nerve activity (Ainslie & Duffin 2009).	6
Figure 2.3 Schematic representation of the neural response to changes in carotid sinus transmural pressure (CSTP) (Fadel et al. 2003)	30
Figure 2.4 Stimulus response curves during exercise of varying intensity (Raven et al. 2002)	33
Figure 2.5 Simplified illustration of the control of ventilation by the peripheral and central chemoreflexes (Duffin 2011)	44
Figure 2.6 The central (A) and peripheral (B) chemoreflex response to changes in PCO_2 (Duffin & Mahamed 2003)	45
Figure 3.1 Cross sectional of finger and cuff with blood pressure output including calibration (Physiocal, Finapres medical systems website, http://www.finapres.com).	78
Figure 3.2 Computation of aortic flow from arterial pressure (Harms et al. 1999).	81
Figure 3.3 Thermodilution and Modelflow derived stroke volume (SV) values in 10 participants (Harms et al. 1999).	84
Figure 3.4 Frontal view depicting standard probe placement over the temporal window during MCA insonation (Aaslid et al. 1982).	86
Figure 5.1 Photo depicting the squatting movement used in this experiment at starting point of the movement (left) and deepest point of the squat (right)	100
Figure 5.2 Experimental protocol	101
Figure 5.3 Average response of mean middle cerebral artery blood flow velocity ($MCAV_{mean}$), mean arterial pressure (MAP) and cerebrovascular conductance (CVC) following upright resistance exercise displayed every second.	106
Figure 5.4 Raw and averaged haemodynamic responses to 6 repetitions at 30% 6RM in one participant.....	107
Figure 6.1 The response of mean middle cerebral artery blood flow velocity ($MCAV_{mean}$), mean arterial pressure (MAP) and cerebrovascular conductance (CVC) during and following a Valsalva manoeuvre (VM) at 30, 60 and 90% of maximal VM pressure, displayed every second.....	129
Figure 6.2 Representative trace of middle cerebral artery blood flow velocity (MCAV), arterial blood pressure (ABP) and mouth pressure during a 90% 5s VM in one participant.....	129
Figure 6.3 The percentage change from baseline for mean middle cerebral artery blood flow velocity ($MCAV_{mean}$) and the absolute change in mean arterial pressure	

(MAP) during and following a Valsalva manoeuvre (VM) at 30, 60 and 90% of maximal VM pressure, displayed every second.	130
Figure 7.1 Cerebrovascular, cardiovascular and respiratory responses in the first minute (A) and in the fifth minute (B) to 40 mm Hg of lower body positive pressure (LBPP) in one individual.	143
Figure 7.2 Individual changes from baseline for mean middle cerebral artery blood velocity ($MCAv_{mean}$, A) and mean arterial pressure (MAP, B).....	146
Figure 8.1 Experimental protocol.	155
Figure 8.2 Absolute changes from baseline for mean middle cerebral artery blood flow velocity ($MCAv_{mean}$, A), mean arterial blood pressure (MAP, B) and cerebrovascular conductance (CVC, C).....	158
Figure 8.3 Individual mean middle cerebral artery blood flow velocity ($MCAv_{mean}$, A) and mean arterial blood pressure (MAP, B) responses to 5% CO ₂ (5%) alone and in combination with 20 and 40 mm Hg of lower body positive pressure.	161