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

A thesis presented in partial fulfilment of the requirements for the degree of

Doctor of Philosophy

Massey University, Manawatu, New Zealand

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2014

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.

Acknowledgments

I would firstly like to thank my supervisors Drs. Toby Mündel, Samuel Lucas and Darryl Cochrane. I am forever grateful for your guidance, advice and time that has made this journey all the more enjoyable. In particular, Toby, without your contagious enthusiasm it would be highly unlikely I would have undertaken postgraduate study, let alone a PhD! A special thank you to Drs. Zachary Schlader and Matthew Barnes for your advice, input and critique of the experiments comprising this thesis. I would also like to thank Massey University for awarding me a doctoral scholarship to complete this degree. Furthermore, I would like to formally thank the individuals who participated in the experiments required for this thesis. Your willingness was greatly appreciated; after all it is hard to conduct human research without eager participants! Finally, I would like to thank my family; Graeme, Annie, Kent, Joel and Kay. Without you this thesis would not have been possible and I am forever indebted to the love and support you have given me over my entire student life.

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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_2O	Water

I

ICA	Internal carotid artery
ICP	Intracranial pressure

K

kg	Kilograms

L

LBNP	Lower body negative pressure
LBPP	Lower body positive pressure
$L \cdot min^{-1}$	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

O_2	Oxygen

P

P_aCO_2	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

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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