MASTER OF PHILOSOPHY

THESIS

Individual differences in coping style influence acute endocrine and neurobiological responses to psychosocial stress.

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B Biomed Sci

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Statement of Originality

This work contains no material, which has been accepted for the award of any other degree or diploma in any university or other tertiary institution to the best of my knowledge and belief. The work embodied in this thesis does form the basis of a scholarly work of which I am a joint author, and I have included a statement endorsed by my supervisor clearly outlining the extent of my contribution to the joint publication. I give consent to this copy of my Thesis being made available for loan and photocopying, when deposited in the University Library, subject to the provisions of the Copyright Act 1968.

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Candidate signature: Louise Masters

Acknowledgement of authorship/collaboration

I hereby certify that the work embodied in this Thesis is the result of original research, the greater part of which was completed subsequent to admission to candidature for the degree and comprises the major contribution of behavioural testing and analysis, tissue collection and processing, immunohistochemistry, hormone detection assays, brain imaging, Fos detection, statistical analysis, and academic writing to the joint scholarly work.

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Supervisor signature: Trevor Day

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Thesis Synopsis

The psychosocial stress of social conflict contributes to the development of depression and anxiety in those individuals vulnerable to its effects, yet the factors that contribute to vulnerability remain unclear. Researchers investigating factors such as behaviour and physiology have used the animal resident/intruder social conflict model whereby a young male rodent (intruder) is placed into the home cage of an older male (resident) that is trained to attack and defeat all intruders. Findings reported previously have shown that defeated intruders displayed medium to longer-term stress-related changes in behaviour and physiology, with considerable variability in the severity of these changes reported from one individual to another. Interestingly, a reduction in severity of behavioural and physiological changes was associated most significantly with intruders that deployed 'active coping' behaviours during the social defeat interaction than animals that deployed 'passive coping'. However, these findings do not describe the short-term effects, raising the question; does coping style also influence the short-term stress response?

We investigated the relationship between coping behaviour adopted by intruders during a 10 minute social conflict culminating in defeat and both acute peak plasma corticosterone (CORT) stress hormone levels and number of cells expressing Fos protein in eight brain regions. Our investigations revealed that higher levels of fight and guard behaviours were associated with lower peak plasma CORT levels compared to ready submission, and that higher levels of fight were associated with fewer numbers of Fos-ir cells in prefrontal cortex (PFC), amygdala (Am), and paraventricular nucleus (PVN) brain regions. In general terms, these findings indicate that coping behaviour deployed *during*

social conflict influences the endocrine and neurobiological elements of the acute phase of the HPA axis response to psychosocial stress. Intruders that deploy an ‘active’ coping style including fight behaviours display significantly smaller physiological and neurobiological alterations in the acute response than intruders that deploy a ‘passive’ coping style during social conflict. These results demonstrate that the vulnerability to the effects of psychosocial stress are ameliorated by actively engaging with the perpetrator rather than passively taking the attack, and that adopting the behaviour fight is most protective. Further elucidation of the neural mechanisms that underpin the reduction in stress-induced effects is warranted.

Abbreviation	Definition
ABC	Avidin:Biotinylated enzyme Complex
ACEC	Animal Care and Ethics Committee
ACTH	adrenocorticotrophic hormone
aHyp	anterior hypothalamus
AHipA	amygdalohippocampal area
Am	amygdala
ANOVA	analysis of variance
AUC CORT	area under the curve for plasma corticosterone
AVP	arginine vasopressin
Base CORT	plasma corticosterone levels prior to defeat encounter
BNST	bed nucleus of the stria terminalis
BSA	bovine serum albumin
CA	catecholamine
CeA	central amygdala
CG	cingulate gyrus
CN	cuneiform nucleus
CORT	corticosterone
CRF	corticotrophin-releasing factor
DAB	diaminobenzidine
dBNST	dorsal bed nucleus of the stria terminalis
dmH	dorsomedial hypothalamus
dR	dorsal raphe
fMRI	functional magnetic resonance imaging
h	hour
HPA	hypothalamic-pituitary-adrenal
IEG	immediate early gene
IL PFC	infralimbic medial prefrontal cortex
ITF	inducible transcription factor
LC	locus coeruleus
lHyp	lateral hypothalamus
lPAG	lateral periaqueductal grey
lPOA	lateral preoptic area
LS	lateral septum
MeA	medial amygdala
mPFC	medial prefrontal cortex
mPOA	medial preoptic area
mR	medial raphe
mRNA	messenger ribonucleic acid
NSRI	noradrenaline serotonin reuptake inhibitor
NTS	nucleus of the solitary tract
OT	oxytocin
PACAP	pituitary adenylate cyclase-activating polypeptide
PAG	periaqueductal grey
PBS	phosphate buffered saline
Peak CORT	maximum plasma corticosterone level 15 or 30 min after onset of the defeat encounter
PFC	prefrontal cortex
PL PFC	prelimbic medial prefrontal cortex
PVN	paraventricular nucleus

S	septum
s	second
SEM	standard error of the mean
SHypN	septohypothalamic nucleus
SNS	sympathetic nervous system
SON	supraoptic nucleus
SSRI	selective serotonin reuptake inhibitor
TH	tyrosine hydroxylase
vBNST	ventral bed nucleus of the stria terminalis
VLM	ventrolateral medulla
vlPAG	ventrolateral periaqueductal grey
vLS	ventral lateral septum
vmHyp	ventromedial hypothalamus