How does stress induce headache?

An Experimental Study

Juanita K. Miller Berry

B.A.(Hons) B.Ed.

This thesis is presented for the degree of Doctor of Psychology
of Murdoch University

Faculty of Psychology and Exercise Science

June 2020

Declaration

I declare that this thesis is my own account of my research and contains as its main content work that has not previously been submitted for a degree at any tertiary education institution.

Juanita K. Miller Berry

25th June 2020

Abstract

Psychological stress triggers headaches, but how this happens is unclear. To explore this, 38 episodic migraine sufferers, 28 with tension-type headache (T-TH) and 20 controls rated nausea, negative affect, task-expectancies and headache at 5-minute intervals during an unpredictable and uncontrollable 25-minute mental arithmetic task with a non-contingent failure rate. Blood pressure and pulse rate were measured every 3 minutes and salivary cortisol was sampled before and after the task. Trigeminal activation was measured by nociceptive blink reflex measures during each of the three experimental phases.

Multiple regression analyses indicated that negative affect (NA) was the strongest predictor of headache intensity during the task. Increases in stress-headache were unrelated to consistent changes in cardiovascular activity but were related to declines in cortisol and increased post-task trigeminal activity. In repeated measures ANOVAs, participants who developed headache had higher nausea, NA and self-efficacy expectancies than those with no-or-low headache ($p < .05$ to $p < .001$). In further multiple regression analyses to identify which aspects of the stress process contributed to the high NA preceding headache, discouragement, anxiety, irritation and tension mediated the relationship between headache intensity during the stressful task and primary and secondary appraisal processes (stressor exposure and stressor reactivity). Avoidant coping, perceived inability to decrease pain, and outcome expectancy independently predicted headache intensity during the stressful task. Anxiety mediated the relationship between headache intensity and the coping tactics of wishful thinking, self-criticism, pain catastrophizing and praying/hoping. Attachment anxiety and the personality traits of openness, agreeableness and conscientiousness moderated the relationship between stress appraisals and headache. Results were discussed using the model of stress-headache as allostatic load.

Findings suggest that headache developed when participants overextended themselves during a stressful task, adopting an information processing style which impeded emotional adjustment to changing situational demands. Learning to modify perceptions of threat and adopting a more flexible, less outcome-dependent processing style which avoids response conflict might help to prevent headache from spiralling upward.

Table of Contents

List of Figures

List of Tables

Abbreviations

AAI	Adult Attachment Interview
ACC	anterior cingulate cortex
ACT	Acceptance and Commitment Therapy
ACTH	adrenocorticotrophic hormone
AUC	area under the curve
BR	blink reflex
CNS	central nervous system
CRF	corticotrophin releasing factor
CRH	corticotropin releasing hormone
CSQ	Coping Strategies Questionnaire
CSQ-R	Coping Strategies Questionnaire (Revised)
DBP	diastolic blood pressure
DLPT	*dorsolateral pontomesencephalic tegmentum*
DNIC	diffuse noxious inhibitory controls
ECR	Experiences in Close Relationships Questionnaire
EPQ	Eysenck Personality Questionnaire
FFM	Five Factor Model
FPI	Freiburg Personality Inventory
GR	glucocorticoid receptor
HPA	hypothalamic-pituitary-adrenal
ISI	interstimulus interval
MMPI	Minnesota Multifactorial Personality Inventory
MRI	magnetic resonance imaging
NA	negative affect
nBR	nociceptive blink reflex
NE	norepinephrine
PAG	periaqueductal gray
PNS	parasympathetic nervous system
PR	pulse rate
PVN	paraventricular nucleus
RVM	rostroventral medulla
SAM	sympathetic-adrenal-medullary

SBP	systolic blood pressure
SNS	sympathetic nervous system
SSN	superior salivatory nucleus
STAI	State-Trait Anxiety Inventory
TNC	trigeminal nucleus caudalis
TPA	temporal pulse amplitude
VAS	visual analogue scales
VPM	ventral posteromedial nucleus
WCQ-R	Ways of Coping Questionnaire (Revised)
ZKPQ	Zuckerman-Kuhlman Personality Questionnaire

List of Publications

Paper 1 (Chapter 4)	
Title:	Does attachment anxiety increase vulnerability to headache?
Authors:	Juanita K. M. Berry, B.A. (Hons); Peter D Drummond, PhD
Status:	Published
Journal:	Journal of Psychosomatic Research
Reference:	Berry J.K.M., Drummond P.D. Does attachment anxiety increase vulnerability to headache? *Journal of Psychosomatic Research*, (2014) 76(2):113-120.
DOI:	http://dx.doi.org/10.1016/j.jpsychores.2013.11.018
Notes:	© 2013 Elsevier Inc. All rights reserved., LLC 2017. ISSN 0160-7715 0022-3999/$ – see front matter

Paper 2 (Chapter 6)	
Title:	Psychological generators of stress-headaches
Authors:	Juanita K. M. Berry, B.A. (Hons); Peter D Drummond, PhD
Status:	Published
Journal:	Journal of Behavioural Medicine
Reference:	Berry J.K.M., Drummond P.D. Psychological generators of stress-headaches. *Journal of Behavioural Medicine*, (2018) 41(1):109–121.
DOI:	https://doi.org/10.1007/s10865-017-9872-9
Notes:	Published online July 14, 2017 © Springer Science+Business Media, LLC 2017. ISSN 0160-7715

Statement of Contribution of Others

Paper 1 (Chapter 4)

Title: Does attachment anxiety increase vulnerability to headache?

Authors: Juanita K. M. Berry, B.A. (Hons); Peter D Drummond, PhD

Contributions to work:

JKMB collected the data, ran statistical analyses and wrote the first draft.
PDD designed the study, ran statistical analyses and contributed to the manuscript.

Paper 2 (Chapter 6)

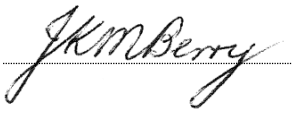
Title: Psychological generators of stress-headaches

Authors: Juanita K. M. Berry, B.A. (Hons); Peter D Drummond, PhD

Contributions to work:

JKMB collected the data, ran statistical analyses and wrote the first draft.
PDD designed the study, ran statistical analyses and contributed to the manuscript.

Student Signature

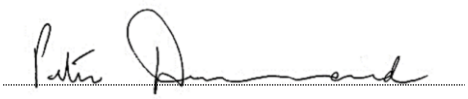


Juanita K. Miller Berry

25th June 2020

Co-Author Signature

I hereby certify that the above declaration correctly reflects the nature and extent of the student's and co-author's contributions to this work.



Dr. Peter Drummond

25th June 2020

Acknowledgements

The completion of this thesis would not have been possible without the academic support, guidance, help and patience of my academic supervisor and mentor Professor Peter Drummond. I would like to thank him for his expert scientific leadership and his knowledge that has shaped me as researcher. I will miss the mentor-student relationship that has developed over the years of working together and hope that in some small way I have shown myself worthy of the tremendous investment of his time and energy in me.

I would also like to thank the staff within the School of Psychology and Exercise Science, especially the Technicians Man and Francis. Due to the technical calibre of this research, it would not have been possible without their expert technical assistance. I want to thank David Nicholson for writing the computer program used during the stressful task and Katie Brocx for helping quantify the photoplethysmograph data. Additionally, I am grateful for the fantastic help from Shiree and Anna who chaperoned and assisted me during the testing sessions and with so many other lab tasks. I would also like to thank Dr Neville Bruce and his staff at UWA who patiently coached and mentored me in the collection and analysis of salivary cortisol samples, Dr Tim Fairfield who offered encouragement and helpful suggestions for getting the thesis finalised and Dr Brody Heritage who offered tips and statistical information in the new (to me) area of regression-based path analysis.

I would also like to sincerely acknowledge the role of all participants who completed the research. None of the testing sessions were a pleasant experience for participants who volunteered themselves to undergo a stressful task that gave them a headache. These altruistic people sacrificed their comfort and time in the name of science, which left me in awe of their participation.

During my candidature I have had the privilege of sharing the Lab with many inspiring and intelligent colleagues including Shiree T-H, Anna CG, Dean, Lone, Katie and Lechi. I have also shared my D Psych journey with other candidates and staff who offered collegial support and generally eased the burden with practical help, conversation, hugs, encouragement, writing groups and coffee, including Frankie, Renee, Anna, Tracey, Lechi and Lone. My late friend and support person Vreni offered me the use of her Chicago apartment for six weeks while I analysed the blink reflex results. You are sadly missed.

Sally Knowles and Cecily Scutt were instrumental in helping me get words onto paper and encouraging a “You can do this” attitude in me.

I am also very thankful for the formatting and graphic art work from Michael Done who helped get the numerous tables (indeed the whole thesis) sorted into a readable format. He went ‘over and beyond’ and provided generous assistance at a time when I needed it most. This task was made easier during the recent stressful COVID period by the much-appreciated thesis whispering of Liana Christensen.

My final but far from least heart-felt thanks go to my family and friends. My family has expanded during the period of my candidature but we have also experienced loss with my Dad passing away mid-way in my candidature. I know he would have been proud, if nothing else but for my perseverance. My husband Peter, children Alison and Laurie and grandchildren Miette, Jackson, Blake and Keira gave my life another purpose outside of work and research, and continued to give me love, lightness, humour and encouragement throughout this journey. My Mum. brother and sister also deserve a thank you for keeping my feet firmly on the ground and ensuring I see the broader picture in life. I am very grateful to my special friends Peggy (who kept me sane with coffee, walking and conversation), Rhonda (who helped me out with my planning and encouraged me to persevere while getting some semblance of a work-life balance) and Annie (who never stopped believing in me).

What an amazing journey!

To my late father, Raymond Stewart Middleton, for his unfailing practical and moral support.

Your "can do" attitude, love and encouragement made this possible.

Love you Dad.

SECTION 1: OVERVIEW

Chapter One

1

Introduction

1.1 Background, terminology and rationale

Sensitivity to psychosocial stress represents a possible psychobiological vulnerability for the ubiquitous primary headaches of migraine and tension-type headache or T-TH (1; 2), where primary headaches are those without structural abnormalities (3).

Migraine is a common headache disorder of neurovascular origin (4), occurring in 18% of women and 6% of men (5; 6). It is characterised by recurrent and disabling episodes of moderate to severe headache associated with nausea, vomiting, phono- and/or photophobia. Its most prominent feature is throbbing, often unilateral headache, which can last from 4-24 hours and is aggravated by activity (7). The migraine experience may comprise four stages: the prodrome (e.g. fatigue and irritability), the aura, the headache phase and the postdrome (e.g. thirst, somnolence, visual disturbances, food craving, parasthesias and ocular pain) (8; 9). Neurological aura symptoms occur in approximately one third of migraineurs (10).

Fewer than 15 headaches per month represents an episodic rather than a chronic headache condition. Median attack frequency is around one attack per month, median duration around 24 hours, although women report a longer migraine attack duration, increased risk of headache recurrence, greater disability and a longer period of time required to recover (11).

In contrast to migraine, T-TH is a featureless headache in which migrainous focal neurological symptoms are absent. The pain is bilateral with a pressing, tightening quality, often described as aching or cramping, with diffuse localisation (7). T-TH affects some two-thirds of adult males and over 80% of females (12).

Links between stress and headache

Clinical, prospective and laboratory studies confirm the link between stress and primary headache. Psychosocial stress or tension – as distinguished from environmental and physical stress such as the bodily reactions to extremes of temperature, noxious fumes, flickering lights or strong and unpleasant odours – was retrospectively endorsed as a significant ‘trigger’ of primary headache across different cultures by 60-90% of male and female, child as well as adult, headache patients, ahead of fasting, sleep deprivation and alcohol (13-21). From prospective headache diary studies, self-reported ‘stress’ precedes a migraine attack by some 3-4 days (22; 23) and a greater-than-normal frequency of subjectively stressful events precedes a migraine attack (24-26).

In laboratory studies, both stress and negative affect (NA) have been implicated as significant headache precipitants that exacerbate the painful component of migraine and T-TH (27-33). Headache developed in 91% of patients with chronic tension-type headache (T-TH) during an hour-long stressful mental arithmetic task compared with only 4% of healthy controls (28), and headache was observed to develop more frequently in patients with T-TH than in controls or migraine sufferers during stressful mental arithmetic (33).

Neurological studies have demonstrated greater stress sensitivity in migraineurs, showing reduced habituation to stimulation between attacks (and thus greater excitability), as measured by increased amplitude and reduced or delayed habituation of cortical evoked potentials (34; 35). Hypersensitivity in the visual and auditory systems of migraineurs has been demonstrated during and between attacks (36; 37). Also, in migraineurs, hypo-excitability in the thalamocortical circuits which process sensory experience has been associated with attack initiation and sensory hypersensitivity (38). A lack of habituation has also been described in migraineurs for a brainstem reflex, the nociceptive blink reflex (nBR), interictally (39; 40) and a global amplitude increase was reported during attacks (41). Migraineurs are thought, therefore, to have an inherited central neuronal sensitivity or hyper-excitability to stress (2; 3; 42). Taken together, this research suggests that migraineurs (and possibly also T-TH sufferers) are generally more sensitive to stress than those who do not suffer recurrent headaches (1; 2).

However, how and at what points the components of the stress process are linked with migraine and T-TH are relatively understudied and therefore poorly understood (43).

1.1.1 Difficulties and directions in research

A widely-used definition of *psychological stress* is of the processes occurring when environmental demands tax or exceed one's perceived coping resources (44). Nevertheless, 'stress' is a 'slippery' construct (45), and there is a "serious lack of agreement" regarding how best to define its psychological aspects (46, p.113). The three main branches of stress science – environmental, physiological, psychological – have different 'languages', research foci and discipline-specific definitions (45), and none offer a linguistic equivalent of the nociception-pain distinction. In lay circles, 'stress' is an overused term, denoting NA or any stimulus with the capacity to elicit NA (45)[1]. This stimulus-response confusion complicates stress measurement by self-report, especially as

[1] Vingerhoets (2004, p. 114) cites the pithy comment of a journalist that "stress, in addition to being itself, and the result of itself, is also the cause of itself".

there is no ‘gold standard’ for determining when a person is in a state of ‘stress’. There is also poor correspondence between its physiological, cognitive, emotional and behavioural aspects (46).

Thus, it is frequently unclear which aspect or aspects of the stress process, singly or in combination, may predict headache in migraine and T-TH, especially if pain is conceptualised from the narrow viewpoint of nociceptive processing. Do headache sufferers experience more frequent stressors, appraise them differently, cope differently and less effectively, have stronger physiological reactions to a stressor or perhaps experience more intense (or different) negative affects than those who seldom suffer from headaches? And how might distal psychological factors such as personality or attachment style impact stress-related headache? Fortunately, recent advances have provided clarification of some otherwise ‘muddy’ areas in stress research, which will be reviewed later.

1.1.2 Value of study

Both migraine and T-TH carry a heavy burden of suffering and disability (47). Repeated headache attacks and often the constant fear of the next one can damage employment, social and family life (48; 49). In a 2010 Global Burden of Disease survey, T-TH and migraine were the second and third most prevalent disorders in the world, respectively, and migraine was the seventh highest cause of disability in the world, particularly in women (50). Clearly, it is imperative to find ways to reduce this burden.

In this respect, of all headache precipitants or ‘triggers’, psychological stress is one of the most modifiable (51), even of a genetically-influenced condition such as migraine (52). This is evidenced by the efficacy of non-pharmacological approaches including stress management in the treatment of primary headache (53-55). Better knowledge of how stress induces headache may assist headache treatment and management in other ways, for example patients seeking non-pharmacological options and physicians aiming to avoid medication side-effects, including rebound headache (56-58). Furthermore, such knowledge may illuminate the role of psychosocial stress on disease outcome or progression in other disorders similarly affected — including episodic neuromuscular disorders such as fibromyalgia with which the migraines share similar clinical characteristics, and with which migraine may be comorbid (52; 59-61).

For these reasons, this research aimed to investigate how psychological stress induces headache in those with a history of (episodic) migraine or T-TH.

In the sections to follow, the neural correlates of headache will be reviewed, and research on relevant perspectives of the stress construct will be described. This will be followed by discussion as to how stress impacts pain processing in headache. Finally, a biopsychosocial model of headache is presented.

1.2 Nociception and pain in headache

Nociception refers to the transduction, transmission and spinal cord modulation of a noxious stimulus (62; 63), while its psychological counterpart, *pain* – the perception of unpleasant or aversive bodily sensations – results from the activation patterns of a wide range of cortical structures, the pain 'neuromatrix' (64; 65), within which nociceptive stimuli are screened and edited. Nociceptors may be active at low levels in humans without the perception of pain (66-68). Conversely, after an injury and in chronic pain conditions, benign activity from non-nociceptive receptors may be interpreted as pain (69).Thus, pain is not the end result of nociceptive signals arriving at the threshold of consciousness, but an individual and subjective *construction* of the brain from numerous inputs, including sensory input, appraisals, attention, memory, coping and expectations based on environmental context (64; 70; 71). This nociceptive input is transmitted to the brain via first, second and third order neurons, culminating in the perception of headache.

1.2.1 First order neurons

Headache is thought to begin with the stimulation of small diameter Aδ or C-fibre meningeal nociceptors which transmit impulses to cell bodies in the trigeminal ganglia. The antidromic release of inflammatory and vasoactive neurotransmitters, including the key excitatory transmitter glutamate, activates sensory receptors, including those in small blood vessels branching from the middle cerebral (pial) and middle meningeal (dural) arteries (72-76), which swell. Extracranial dilatation adds nociceptive input in some migraineurs (77) as does myofascial tension in T-TH (78) and occipital nerve compression (79). This sensory information is conveyed to the *trigeminal (sub)nucleus caudalis* (TNC) in the spinal cord via the trigeminal nerve fibres which innervate the cerebral arteries.

Since many of these nociceptive signals are short-lived, peripheral signals must be prolonged and amplified for headache to occur (80). Signals are prolonged through the process of *windup*, wherein repetitive stimulation causes a cumulative increase or summation in pain rating (temporal summation) which does not return to baseline between stimulations (81; 82). They are amplified through the process of *sensitisation*, in which nociceptive neurons become over-responsive to normal afferent input (83-88), reducing

the firing threshold and enhancing excitatory efficiency at the synapse (89-92). This change may provide the cellular basis for learning and memory in brain neuronal circuits (93). The sum of windup and sensitisation processes can be the fatiguing and possibly the death of inhibitory interneurons from excess glutamate so that the area is rendered increasingly sensitive to incoming nociceptive stimuli (hyperalgesia). The scalp, for example, can become tender even to low-level stimulation (94). Previously neutral stimuli are then perceived as painful (allodynia), and this sensitisation can last for months or longer (95; 96).

1.2.2 Second order neurons

Nociceptive and other impulses synapse in the TNC, the first site at which head pain processing occurs (92; 97). The TNC represents the first of the spinal 'gates' – i.e. lamina II of the dorsal horn, which consists of mostly inhibitory interneurons (65). Here neurotransmitters and neuromodulators in the endogenous pain control system can alter signal transmission to the somatosensory cortices. The release of opiates or endorphins for example can cancel or reduce the perception of pain (98), although endogenous μ-opioid transmission is impaired in chronic migraineurs (99).

In the case of T-TH, the upper cervical nerves innervate the infratentorial dura mater, and impulses from dorsal root ganglia of the upper cervical segments arrive at the brainstem, particularly via the greater occipital nerve (80). Hence the TNC, which is functionally an extension of the dorsal horn into the lower brainstem, also receives synaptic input from the cervical (C_2) spinal afferents (100-102). As a result, neck pain can spread into the head and headaches can involve soreness in the neck. This may be one reason why many migraineurs report episodes of T-TH (103).

Thus the essential substrate for primary headache is the *trigeminovascular system* – which, by definition, consists of the trigeminal nerve, extracranial and intracranial arteries and the TNC in the brainstem (104-107).

Meanwhile, the perception of headache can be facilitated or enhanced by descending pathways that converge in the periaqueductal gray (PAG) (108; 109) and project through the rostroventral medulla (RVM). Neurons from the RVM project to the face area of the somatosensory cortex on the inferior portion of the postcentral gyrus where initial cortical processing takes place (110). For example, the *spinoparabrachial* pathway transmits impulses to the amygdala and hypothalamus via brain stem nuclei responsible for arousal and preparation for threat (the parabrachial nucleus). A circuit comprising the PAG, 5-

hydroytryptamine (5-HT) neurons of the RVM and norepinephrine (NE) neurons of the *dorsolateral pontomesencephalic tegmentum* (DLPT) is particularly important in pain modulation (97). It has been hypothesised that anxious/stressful feelings may trigger activation in the PAG and paraventricular hypothalamic nucleus, activating a series of events in the superior salivatory nucleus and trigeminovascular system that results in migraine pain (111). While a reverberant loop of activation from the parabrachial nucleus to the TNC can prolong nociceptive stimulation (112), a functional connection between the parabrachial nucleus and pain modulation areas of the RVM also allows this pathway to access descending control systems as part of a recurrent circuit (113). Thus, by modulating the activity of TNC neurons that process and relay peripheral nociceptive input (114-116), variables such as emotion and memories can influence whether the pain 'gate' is 'open'(117), and allow stress to modulate nociceptive processes (118).

1.2.3 Third order neurons

From the TNC, input from the trigeminovascular system is conveyed to third-order trigeminal neurons in the ventral posteromedial (VPM) nucleus of the thalamus (113; 119). At the thalamic level, the spinothalamic tract bifurcates into a lateral pathway which encodes the sensory dimension of pain and a medial pathway which encodes its affective-motivational qualities (120), both of which end up in Brodmann Area 24 of the anterior cingulate cortex. Area 24 is involved in softening pain distress while leaving its sensory features intact. It is also deactivated by pleasant emotions and a decrease in pain unpleasantness (121).

Via ascending spinothalamic and spinoparabrachial nociceptive pathways, impulses are further transmitted to the PAG, hypothalamus and lateral thalamic nuclei – areas of the CNS involved in sensory, emotional, autonomic and motor processing (122). Burstein & Jakubowski (111) maintain that headache is only perceived once the nociceptive signals originating in the meninges reach the somatosensory cortex, after being conveyed through the trigeminal ganglion, medullary dorsal horn (TNC) and thalamus.

1.3 Perspectives on stress

Modern stress theory has emerged as a confluence of biomedical, neuro-affective and psychological research, beginning with the biomedical tradition which borrowed the terms stress and strain from 17th century engineering: *stress* was the amount of force applied to an object, *strain* the resultant wear-and-tear.

1.3.1 Biomedical stress research

Harvard physiologist Walter Cannon (123) first described the primary sympathetic-adrenal-medullary (SAM) stress response. Within seconds of a stressor, the sympathetic nervous system (SNS) is activated, with corresponding suppression of the parasympathetic nervous system (PNS). Via a neural pathway arising from the hypothalamus and descending to the spinal cord, sympathetic efferents activate the release of the catecholamines epinephrine and norepinephrine from the adrenal medulla. These hormones prepare the organism for fight or flight, by increasing respiration, elevating heart rate and blood pressure, redistributing blood from the extremities and internal organs to the muscles, increasing sweating, dilating the pupils and causing changes in immune functioning. The catecholamines also help to break down liver glycogen rapidly and make abundant blood sugar available for the stressed organism.

The second 'arm' of the stress response, arising from the slower-acting hypothalamic-pituitary-adrenal (HPA) axis, was identified by Hans Selye – considered the 'father' of modern stress theory (124). The HPA response is activated within 10 minutes from the paraventricular nucleus (PVN) of the hypothalamus, releasing the stress hormone CRF (corticotrophin releasing factor) which, in turn, triggers the release of ACTH (adrenocorticotrophic hormone) from the anterior pituitary, which then releases cortisol (17α-hydroxy-corticosterone) from the adrenal cortex (125). Cortisol acts to increase blood glucose levels, enhance metabolism and reduce inflammatory and immune responses. These pituitary-adrenal changes constitute the background effect of stress and cannot be detected by the individual (126). They are considered the (biological) hallmark of the stress response, since everything that is typically considered to be a stressor in humans generates this response and the SAM response is not specific to stress (127). As the end result of the cascade of hormones through the HPA axis and as the primary peripheral stress hormone, the glucocorticoid cortisol is considered a good indicator of HPA axis activity and a vital link between stress and its health consequences (125; 128).

The arms of the stress response emanate from a cluster of brain structures including the locus coeruleus at the top of the brain stem, the midbrain and limbic system structures of thalamus, hypothalamus, hippocampus and amygdala, and adjacent structures such as anterior cingulate cortex (129). They communicate with the rest of the body about how to respond to the stressor. Each system alters the functioning of other systems, stimulating the cardiovascular and respiratory systems and inhibiting the digestive and immune

systems (124). Hence, stress in the biomedical tradition is a body-brain response, since practically all visceral organs and immune responses are also recruited during stress.

Homeostasis and allostasis

In the 19th century, the French physiologist Claude Bernard described the bodily response to stress as an homeostatic process, in which body states are actively stabilised against outside disturbances though negative feedback mechanisms (130). The concept of homeostasis followed a long tradition which recognised that disease states could result from alterations in the ability of an organism to maintain bodily homeostasis when stressors or responses exceeded a certain magnitude, or where responses were inadequate in duration (130; 131).

For Selye, stress was the non-specific response of the body to any demand placed upon it; a 'General Adaptation Syndrome' with three phases – alarm, resistance and exhaustion – although his non-specificity theory has since been discredited (132). Each phase was designed to achieve homeostatic balance and caused distinctly different physiological changes (124). Sterling & Eyer's concept of *allostasis* – stability through change (133) – challenged Selye's homeostatic concept of stress, arguing that biological stress responses were not just negative feedback loops associated with disrupted homeostasis, but a response to a prediction (134). For example, when rats are forced to swim against a current for 15 minutes, repeated exposures result in a decline in HPA response (135). Since a laboratory-bred rat has never previously been exposed to a swimming pool, the stimulus can be considered as unpredictable and uncontrollable. With repeated experience, the magnitude of the SAM and HPA response, particularly its speed of recovery (136), alters to become more attuned to the metabolic demands of a 15-minute swim. A better prediction of the demands shifts the integrated response.

Since the situation has now become controllable and predictable it may no longer be perceived as a stressor – "a stimulus or environmental condition in which the response demands exceed the *adaptive capacity* of the organism" (134, p.1298), i.e. its capacity to adapt behaviourally and physiologically to a situation. A stressor is perceived as uncontrollable if it exceeds one's adaptive capacity (as when one's personal or social resources are inadequate), and as unpredictable if it exceeds the organism's *regulatory range* – the range of environmental conditions within which regulatory processes operate adequately without requiring adaptive changes (137). Physiologically speaking,

perceptions of unpredictability are characterised by the absence of an anticipatory response; uncontrollability by a reduced recovery of the neuroendocrine reaction (134).

Thus, from an allostatic perspective, stress involves the biopsychosocial processes occurring when response demands exceed either the organism's adaptive capacity or natural regulatory range (137). An individual is in a state of stress when environmental demands exceed one's natural regulatory capacity. As will be seen, this view of stress brings biomedical and psychological conceptions of stress into greater alignment.

1.3.2 Neuroaffective research

Affective neuroscience (126) offers a further and profound perspective on the nature of stress. This body of research has illuminated the hallmark changes in the cognitive processing of affective information and subcortical emotional circuits that underpin the phenomenological experience of stress.

1.3.2.1 Cognitive processing in stress

Phenomenologically, stress is characterised by disrupted cognitive processing of affective information (126). When our lives are calm, there is a reciprocal control between cognitive and emotional processes, so that the spontaneous behavioural and affective dictates of the more primitive brain control systems are kept in check. During stress, however, the upward influence of subcortical emotional circuits on the higher reaches of the brain is stronger than top-down controls. Sympathetic and HPA axis responses are running 'at full tilt' (126), and the 'disorganizing aspects of emotion' prevail. Thought and action are fragmented as a result of a temporary 'disconnect' from those higher appraisal processes which help us make sense of what is happening, plan, decide our options and regulate our emotions. The functioning of pre-frontal cortical centres involved in regulating emotions and defining our sense of self is impeded (126), including the infralimbic region of the medial prefrontal cortex that plays a role in stress controllability (138) and exerts an inhibitory influence on emotional responsiveness (139). Although the specific cognitions associated with stress-related NA are seldom reported (and difficult to verbalise), they may reflect awareness of emotional and physical dysregulation and difficulty 'thinking straight'. They parallel the primary stress appraisal processes identified by Lazarus – the emotional impact, subjective 'stressfulness', goal salience and perceived controllability of the stressor (140).

1.3.2.2 Affective reactivity to stress

Therefore, although NA is an integral part of the stress response, psychological stress is strictly a state distinct from its affective components (141). NA accompanies activation of the threat-defence system – subjectively experienced distress which comprises emotions, feelings and action tendencies (142). NA arises initially as an *emotion*, a rapid, hardwired, minimally processed pre-cognitive 'affective computation' regarding the significance of the stimulus (143), and a sense of immediate unpleasantness related to threat triggered by the arousal of hierarchically arranged emotional circuits in the limbic system (126). This emotion is followed by feelings, or 'cognitive computations' about the relations between such stimuli (143), which are derived from meanings arising from higher-level deliberations that characterise the conscious contents of a human mind dwelling on how to deal with personally significant situations (126; 144). Ultimately, feelings arise from the interaction of the various emotion systems with the fundamental brain substrates of "the Self" – neurally-based self-representation systems, possibly centred in the PAG (126; 145), the site of the purported 'migraine generator' (146).

While emotions follow the 'low road' to the amygdala – a 'quick and dirty route', feelings follow the slower 'high road' to the auditory, somatosensory, gustatory and olfactory cortices (143). The perceptual information connected with feeling states and projections from the cortices to the amygdala allow responses to stimuli in a single sensory modality (143; 147). The amygdala finally receives inputs from brain regions associated with full-blown, polymodal, perceptual representations of the stimulus situation and with memory, allowing the emotional response to be triggered by complex, contextual features of the stimulus (143; 147). Feelings can thus be modified by visceral activity (148) and neurocognitive processes (142). Affect is the overt expression of emotions and feelings (142), which are usually aversive in the case of stress and pain. Investigations of the relationship between NA and headache are the subject of Chapter 6 of this thesis.

1.3.2.3 Subcortical emotional command systems in the stress process

The affective 'drivers' of the stress process arise from subcortical 'emotional command centres' (126). These systems orchestrate and coordinate perceptual behavioural and physiological changes that promote survival in the face of danger: to approach when *Seeking*, to escape from *Fear*, to attack when in *Rage*, to seek social support and nurturance when in *Panic* from the threat of social loss, to enjoy *Play* and *Lust* and

dominance. The four most salient systems involved in the stress process are detailed in Table 1.1 and are described as follows:

1. Activation of the *FEAR* circuit may accompany all forms of stress and creates the phenomenological experience of anxiety. This genetically ingrained function of the nervous system is generated by pain or the threat of destruction and experientially is an aversive state, characterised by apprehensive worry and tension which tells creatures that their safety is threatened. Depending on the type of fear, i.e. whether or not punishment is involved and whether or not the fear is learned or spontaneous, activation of the *FEAR* circuit prompts animals to hide (freeze) or flee (126). Neuro-chemistries in the *FEAR* emotional system include glutamate[2] (important for the mediation of memory and cognitive processes) and a variety of neuropeptides, including corticotrophin-releasing factor (CRF). CRF controls the pituitary-adrenal stress response that accompanies virtually all emotions, including depression (149-151).

2. The *PANIC* circuit is activated by interpersonal stressors which threaten the loss of those with whom we have social bonds and mediates negative feelings such as sorrow, grief and, at high levels of intensity, panic. It is neurochemically related to the processes that create social attachments and dependencies – processes that tonically sustain emotional equilibrium and promote mental and physical health throughout our lifetime. The system is so termed because panic can emerge from precipitous arousal of the separation-distress system (126). CRF is a common neurochemistry in both *FEAR* and *PANIC* circuits, which overlap. However, separation anxiety differs from the fearful anxiety of the *FEAR* system in being accompanied by feelings of weakness and depressive lassitude, with autonomic symptoms of a parasympathetic nature, such as strong urges to cry and seeking the company of special loved ones.

3. The *RAGE* circuit is thought to arise from the neural circuits that orchestrate affective attack (129) and has close anatomical and neurophysiological linkages to the *SEEKING* system, with which it is complementary. The *RAGE* circuit is aroused by a rapid suppression of activity within the *SEEKING* system, when rewarding brain stimulation is terminated (152).

[2] When secreted in excessive amounts, glutamate damages receptive neurons, although underactivity in this system may also be neurotoxic (Olney & Farber, 1995).

4. The mesolimbic/cortical dopamine circuits at the heart of the *SEEKING* or exploratory system can *inhibit* stress (and pain). During stimulation of the lateral hypothalamic circuits of this system, people report feeling challenged and invigorated (153; 154) as these anticipatory-appetitive arousal dopamine circuits tend to energise and coordinate the functions of many higher brain areas that mediate planning and foresight. Underactivity of this system results in a form of depression, a feeling of sluggishness (155). Over-arousal can also occur, a response to the uncertainty when an expected reward is not forthcoming. This system also appears to respond to the anticipation of aversive events – emotional challenges where solutions must be sought (156; 157), so that deactivation may result when circumstances are ambiguous or important life goals are thwarted. Depending on secondary appraisals, feelings of disappointment or sluggishness may follow. Long-term stress can sensitise the *SEEKING* system and reduce stress tolerance (126).

Therefore, stressor unpredictability/uncontrollability may activate the *RAGE* circuit if the stressor is appraised as signifying an attack on self or significant others, the *FEAR* circuit if the stressor involves pain or threat of destruction or the *PANIC* circuit if a survival-relevant emotional tie to significant others is threatened (126).

Table 1.1 Four emotional command systems potentially activated during pain and stress Adapted from Panksepp (126).

Neural circuit (affective experience)	Function	Neural pathway	Activators	Behaviours	Neuro-transmitters
FEAR (Anxiety, terror, anticipatory anxiety)	Generate a major form of trepidation leading to freezing and flight; reduce pain and possibility of destruction	Central amygdala to periaqueductal gray (PAG) of midbrain	Pain; Threat of destruction (e.g. predator) or to sustainability of our way of life (45).	Freeze if danger distant or inescapable; flee when danger close but can be avoided	Glutamate and a variety of neuropeptides (e.g. CRF, ACTH, CCK, DBI, α-MSH), each of which may instigate slightly different anxieties
PANIC (Interpersonal: loneliness, sadness, psychic pain, separation distress)	Maintain important social bonds which are survival-relevant	Midbrain PAG, very close to where physical pain responses are generated; medial diencephalon, esp. dorsomedial thalamus, ventral septal area, preoptic area, stria terminalis, amygdala, hypothalamus. Emerged from pre-existing pain & thermo-regulatory circuits in course of evolution)	Threat of separation or social loss (of those with whom we have social bonds);	Stimulus-bound attachment behaviours; distress vocalisations	CRF, β-endorphins; Endogenous opioids, oxytocin and prolactin suppress this system
SEEKING (Invigoration, interest, excitement, anticipation, curiosity; eagerness; depression and sluggishness if underactive)	Appetitive motivational; promotes exploration and foraging, survival abilities, facilitates learning	Specific two-way circuits between midbrain and frontal cortex; involves lateral hypothalamus. System more active in response to cues that predict reward than to the reward itself.	Smells, sights, novel environmental cues, anticipation of rewards or pleasurable activity, emotional challenge where organism must seek solutions	Searching, foraging, investigating, sniffing, discriminative learning, anticipatory behaviour	Dopamine, norepinephrine (NE) and epinephrine (E) play modest facilitatory roles while serotonin generally inhibits (except at some sites in mesencephalon)
RAGE (anger, frustration at attempts to curtain freedom of action)	Energises body to angrily defend its territory and resources	Medial areas of the amygdala through discrete zones of the hypothalamus and down into the PAG of the midbrain; Linked with reward systems of cortex	Body surface irritation, restraint, frustration, concern about distribution of resources	Invigoration of musculature; increases in heart rate, blood pressure, muscular blood flow; Tendency to strike at offending object; Threatening behaviour/ aggression – 3 distinct circuits exist: predatory, '*internale*' and affective attack	Enkephalin Substance P Norepinephrine (NE) Serotonin (5-HT) suppresses anger

Abbreviations: CRF = corticotrophin releasing factor; ACTH = adrenocorticotropic hormone; CCK=cholecystokinin; DBI= diazepam-binding inhibitor; MSH=melanocyte-stimulating hormone

1.3.3 Psychological stress research

Psychological stress research focuses on the role of cognitions, affect and behaviours in the stress response.

1.3.3.1 Stress-related cognitions, affect and behaviour

By profoundly challenging the behaviourist view of stress as a property of the events and situations we face (e.g.158), Richard Lazarus' influential transactional model of stress represented a watershed in stress science. He argued that stress depends on a transaction, a goodness-of-fit, between the individual and the environmental demands (159). Stress was described as a 'distressing, goal-incongruent condition', arising when important personal goals are threatened (160).

At the core of the cognitive model of stress is the notion that for an event to be stressful it must first be appraised as such (159). Primary appraisals: "What is at stake here?" evaluate whether a potential stressor is irrelevant, benign-positive or stressful-negative, based on the personal goal relevance of the stressor to self or significant other, type of ego involvement, its likely impact, controllability and subjective 'stressfulness' (161; 162). Secondary appraisals consider whether the stressor requires a problem or an emotion focus and how readily one can successfully implement and move flexibly between them (163).

Appraisals affect physiological activation, both the SAM and HPA systems and NA. An event congruent with an individual's goals is evaluated as positive (164). If not, then NA is generated (165). For example, depression may arise from making no progress toward the realisation of a goal, anger from a demeaning offense against 'me and mine', anxiety from facing uncertain, existential threat and fear from facing an immediate, concrete and overwhelming physical danger (166). Such feelings may also arise when overuse of the threat and drive systems, absent self-soothing, lead to exhaustion, anxiety, shame or helplessness, resulting in persistent low moods (167). Ongoing NA can itself generate threat appraisals (168).

The appraisal process is constantly changing as the individual updates perceptions of stressor controllability and of success or failure in meeting a challenge or threat (outcome appraisal) (159). Stress and headache vulnerability may increase or decrease depending on the reappraisal, for example if secondary appraisals of coping options result in the adoption of more active or more confrontational strategies.

The more recent affective psychology perspective extends this argument: stress arises from a pre-cognitive appraisal of a *future* threat to our wellbeing and is any process which increases uncertainty about the sustainability of our way of life. In the stress process, normally separate positive and negative emotion systems 'collapse', nullifying positive emotions. The degree of threat depends on the salience and perceived level of uncertainty the stressor may pose (45).

Also important in the stress process are behavioural coping responses – constantly changing cognitive and behavioural efforts to manage specific external and/or internal demands that are appraised as taxing or exceeding the resources of the person' (159,p.141). Optimal stress coping involves confronting the problem and/or managing its emotional impact; non-optimal coping involves avoidance of either or both (159). Non-optimal coping increases headache risk and is greater in headache sufferers than controls (169; 170), possibly because such coping methods fail to regulate or mis-regulate (have adverse outcomes) (171).

1.3.3.2 Personality and the stress process

Personality dispositions – individual differences in characteristic patterns of thinking, feeling and behaving (172) – have long been viewed as distal vulnerability factors for migraine and T-TH. The experience of being 'at the mercy' of unbridled emotions whilst bereft of our usual top-down controls can be experienced as threat to the 'self' (126) or 'ego', is likely to elicit habitual responses or behaviours designed to manage this threat (166), thereby increasing stress sensitivity in headache sufferers.

Historically speaking, personality research in headache has focused on trait rather than process conceptualisations of personality (173; 174). Examples of the latter are 'middle-level' constructs such as locus of control (175), self-efficacy (176), hardiness (177) or dispositional optimism (178). At least two difficulties can however be identified in personality-headache research to date. Firstly, global trait perspectives such as the Five Factor Model (FFM) have been criticised for being descriptive rather than explanatory (179). Secondly, inter-relationships between traits and those personality processes which may impact on headache are frequently unclear. Research which links both global and 'middle-level' personality constructs with the headache experience is needed (180).

Nevertheless, a small body of research has established that stable personality traits such as neuroticism (negative affectivity) and extraversion (positive affectivity) reliably relate to the frequency and/or intensity of short-term mood states, to emotional information

processing across different cognitive tasks and how well emotions are regulated (181-183). In relation to stress, personality expression has been linked to stressor exposure, the likelihood of making threat appraisals of an event, and to stressor reactivity, the emotional and physiological reactivity to a stressor (184). In this thesis therefore, the inter-relationship between headache, stress, global traits and the possible moderating effects of appraisal processes and coping behaviours on both stress and headache (184; 185) is explored. The relationship between trait conceptualizations of personality, headache and stress are investigated in Chapter 3, and their putative relationship to these particular 'middle-level' personality processes in Chapters 7 and 8.

1.3.3.3 Attachment style and the stress process

The temporary loss of top-down cognitive controls characteristic of the stress experience may prompt appeals to our significant others for regulatory assistance, as without social support we are forced to 'ride the whirlwind alone – usually with less rather than more skill' (126). Thus, attachment style – one's characteristic way of behaving in close relationships – is a second potential distal influence on the stress process, and may also reflect one's level of perceived as well as received social support, which are known to buffer the effects of stress on health (186). The influence of an anxious and avoidant attachment style in headache is investigated in Chapter 4 of this thesis.

A synthesis of these perspectives conceptualises stress as a biopsychosocial process where the elements: stressor—appraisal—coping—stress response—strain (46), may interact to activate the physiological, cognitive, affective and behavioural changes that promote headache. (Figure 1.1). Distal influences (personality, attachment status, prior experience) can interact at any point with these elements. Of course, lifestyle factors such as sleep quality (187; 188), diet/eating patterns (189), exercise (135) and one's general state of health may moderate the relationship between stress and headache. However, since the aim of this study was to examine psychological influences in stress and headache, while as far as possible separating out stressors which may equally result from, as well as cause, stress, lifestyle factors were excluded from analysis in this study.

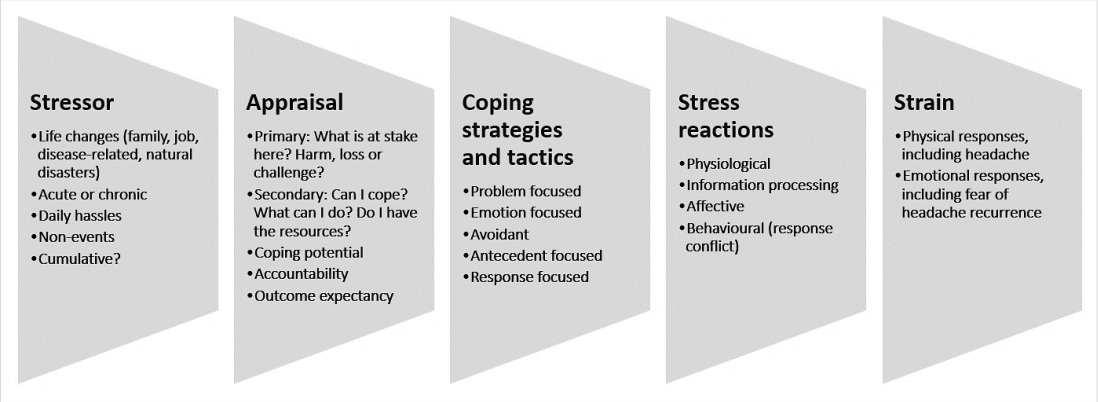


Figure 1.1 Stages of the stress process in psychological stress theory (cf 46). Stressor-appraisal-coping strategies and tactics, stress reactions (physiological, information processing, affective and behavioural)-strain.

1.4 Stress sensitivity and pain processing in headache

We are now well placed to consider the effects of stress on headache, using the synthesis of perspectives diagrammed in Figure 1.1. In this section, the components of the stress process will be considered in relation to each stage of pain processing in headache, i.e. sensory-discriminative (pain intensity), affective-motivational (pain affect and unpleasantness), cognitive-evaluative (pain cognitions and beliefs) and pain behaviour stages (190; 191). Specifically, it will be argued that stress sensitivity may increase headache pain perception by increasing (i) stressor exposure, (ii) activity in peripheral pain producing mechanisms, (iii) pain affect/unpleasantness, (iv) negative pain cognitions, (v) pain behaviours. The end result can be long-term wear-and-tear on the organism, i.e. strain, as migraine attacks are stressful events in their own right, and attacks with recurrent episodes of pain, central sensitisation, and concomitant hormonal and inflammatory changes may alter brain structure and function (192).

1.4.1 Increased stressor exposure

Prior experiences of headache and perhaps predisposing psychobiological factors such as neuroticism may mean that headache sufferers are exposed to more, or more frequent, stressors (184), are more likely to appraise a stressor (including headache) as threatening (185), and to have greater expectancies of goal disruption (193).

Greater headache frequency and intensity has been associated with major life events (such as death, divorce, job loss) and ‘daily hassles’ (187; 194-196) – the short-lived ‘irritating, frustrating, distressing demands that to some degree characterise everyday transactions with the environment’ (197; 198). Examples are environmental events (e.g.

noisy gatherings, crowded rooms), work issues (e.g. deadlines, tension with co-workers) or interpersonal problems, e.g. an argument with a relative or close friend (199).

Major environmental stressors (e.g. an earthquake) may increase allostatic load (the burden of stress adaptation) (200) by exceeding the individual's regulatory range (194; 201), whereas the cumulative effect of daily hassles may exceed the individual's adaptive capacity. Ambiguous stressors – those lacking clear indications of situational contingencies or likely outcomes which can aid coping choices – also increase allostatic load (202-206). The more stressors and the greater their salience to the individual, the greater the allostatic load.

1.4.2 Increased activity in peripheral pain-producing mechanisms

Both arms of the stress response (negative affect and physiological arousal) are activated as part of the pain response (207) and communicate with the rest of the body about how to respond to the stressor. Each system alters the functioning of other systems, stimulating the cardiovascular and respiratory systems and inhibiting the digestive and immune systems (124). Cortisol levels also increase.

The net effect of the activation of these systems can be to increase pain intensity – the location, quality, duration and intensity of pain (208). Although multiple brain regions are activated and modulated by nociceptive stimuli (209), the insula, a limbic-related cortex, is associated with general interoceptive awareness of body states and is where the sensation of pain is judged as to its degree (118). It is believed to play a role in mapping visceral states that are associated with emotional experience, giving rise to conscious feelings (144). Stress-related changes in cardiovascular and cortisol activity can intensify these responses. Persistence or fatigue of these responses may alter the brainstem excitation-inhibition balance, increasing trigeminal activation and cortical hyperarousal. This interplay means that headache and nausea can potentiate each other (210), autonomic arousal by itself can produce emotional experiences (211) and neurocognitive processes such as expectancies and reappraisal (212) can influence headache more than NA alone (213).

Thus, at the sensory-discriminative stage of pain processing, stress-headache may be caused by:

1. *Increased activity in peripheral pain producing mechanisms*, including:

    a) Increased pre-synaptic nociceptive input or increased peripheral or central sensitisation. These may be greater in headache sufferers than controls.

b) Greater cardiovascular activity which may increase vascular distension and/or responsiveness in cranial arteries, causing regional blood flow changes and greater blood flow through distended scalp arteries. Such changes may be greater in headache sufferers than controls.
c) Increased (or decreased) cortisol secretion. Greater cortisol secretion may act to sensitise nociceptors; although results are inconsistent as to whether hyper- or hypo-cortisolism is exaggerated during stress (214) and whether cortisol might act on the pain-producing mechanisms of headache to a greater extent in headache sufferers than controls (215).

2. *Persistence or fatigue of autonomic or neuroendocrine responses* activated to restore homeostasis after a stressful event. Prolonged stress may result in either exhaustion of pain modulation processes or an excess of inflammatory substances implicated in trigeminal sensitisation, contributing to recurrent headache.

1.4.3 Affective-motivational factors in headache pain processing

Nociception is a triggering mechanism for massive, parallel, distributed, preconscious processing in the limbic brain (64), and prolonged nociception may itself cause a sustained, maladaptive stress response (216). For example, the *spinohypothalamic* and *spinopontoamygdaloid* nociceptive pathways pass through the medial temporal lobe (which contains the amygdala and hippocampus) and activate the emotional response to pain and the fight-flight reflex (217). Therefore, nociception, pain and negative moods may be considered to exist on a single continuum of aversion (118).

Subcortical emotion circuits

Affective pain processing is linked in different ways with the subcortical 'emotional command centres' (Section 1.3.2):

1. The *FEAR* circuit is generated by pain or the threat of destruction, and influences pain sensitivity. Nevertheless, pain and fear can be dissociated (218). For example, animals and humans do not focus on their bodily injuries when they are frightened (219) and fear-induced analgesia emerges, at least in part, from arousal of pain-inhibition pathways that employ neurotransmitters such as serotonin and endogenous opioids (220; 221).

2. Since the *PANIC* or separation-distress circuit appears to have evolved, in part, from pre-existing pain circuits, opioid systems can modulate the intensity of both physical pain and separation distress (126). CRF is a common neurochemistry in both *FEAR* and *PANIC* circuits, so that the anticipatory anxiety of pain (part of the *FEAR* circuit) and the threat of social loss may show considerable overlap and interaction in pain processing.

3. The *RAGE* circuit has close anatomical and neurophysiological linkages to the *SEEKING* system, to which it is complementary. It is aroused by a rapid suppression of activity within the *SEEKING* system, when rewarding brain stimulation is terminated (152). Animals then show an elevated tendency to bite (222) while humans in comparable situations tend to clench their jaws and swear epithets (126). This may relate to the jaw clenching associated with T-TH and migraine (223).
4. Activation of the mesolimbic/cortical dopamine circuits at the heart of the *SEEKING* or exploratory system can inhibit stress and pain. Underactivity of this system results in sluggishness, a form of depression (155), frequently reported in the migraine prodrome and 'let down migraine' (Section 1.4.6).

Therefore, headache may result from the interaction of emotions and feelings connected with activation of the *FEAR, PANIC* or *RAGE* circuits. Consistent with this, increases in tension, irritability, annoyance, depression and fatigue have been reported during the migraine prodromal period (27; 224). Headache may also be inhibited by activation of the *SEEKING* circuit (e.g. when attention is diverted to something interesting) and by the interaction of the *FEAR/PANIC* and *RAGE/SEEKING* circuits which govern fight-flight reactions and are mutually inhibitory at low levels of arousal (126). These circuits also govern behaviourally nonspecific chemistries of the brain such as norepinephrine and serotonin (220; 221), which are implicated in headache (33; 225) and are targeted by certain migraine medications.

Pain affect and unpleasantness

Stress can increase pain unpleasantness, the drive to seek relief from uncomfortable sensations, by increasing the negative valence of pain stimuli. Conversely, positive emotional valence (pleasant rather than unpleasant ratings) of a stimulus contributes to decreased pain intensity and even analgesia, particularly if the stimulus is associated with the relief of pain (226; 227).

Stress also increases pain affect, the degree of emotional arousal or changes in action readiness caused by the sensory experience of pain (208). The 'triumvirate' of pain affects – anxiety, anger, depression – are central to the experience and expression of pain (228). Anxiety results from an inability to predict pain and may exacerbate it (229), perhaps due to sensitisation of peripheral nociceptors through the release of noradrenaline (230). Depression or feelings of hopelessness may likewise enhance the release of noradrenaline, increasing nociceptor excitation and pain intensity (231), and may arise when one is unable to prevent or terminate pain (232). Anger has been found to precipitate headache in laboratory studies (29), although whether this is due to associated effects (e.g. cardiovascular activation) or the possible effect of noradrenaline is not known. Unlike pain intensity, pain affect ratings are highly susceptible to contextual and psychological factors (e.g. social or work situations, a history of prior injury), so show large inter-individual differences (233). As with any pain experience, a headache attack gives rise to new peripheral and spinal cord nociceptive learning/sensitisation and emotional learning that is potentiated by its salience and perceived value (118). As a result, pain affect may be more intense in headache sufferers than controls.

In addition, the affective response to pain is moderated by personality and social support from attachment figures (234). Neuroticism has been reliably identified in epidemiological studies as a headache vulnerability factor (235; 236). Although results are not always consistent, studies of clinical populations have also identified low extraversion (sociability) (237-239), low openness to experience (conservatism) (240), aggression–hostility (241) and impulsivity or 'sensation seeking' (242) as relevant to headache, via their associations with emotional regulation capacity (181). An insecure attachment style was postulated to influence headache since associations have been reported between insecure attachment and headache in clinical populations (243; 244). (Chapters 3,4 & 7).

In sum, during stress, the capacity of the fronto-cortical system to effectively regulate meso-limbic system activity is compromised (126; 245), and both limbs of the stress response – negative affect and physiological arousal – may, by different mechanisms, disrupt inhibitory pain control. The sum of multiple aspects of pain processing can thus increase headache intensity by exacerbating the affective response to pain, altering functional connectivity between cortico-thalamic pain modulating circuitry (246), the PAG (247), amygdala and viscероceptive cortex (248).

In migraine patients, disruptions in limbic functional connectivity to pain-related regions of the modulatory and encoding cortices are reported, such as decreased functional

connectivity between the right amygdala and contralateral orbitofrontal cortex and significant functional connectivity consolidation between the bilateral hippocampus and cerebellum (249). Hence, migraineurs may be more susceptible to the characteristically disrupted emotional processing during stress (126).

1.4.4 Pain suffering: Cognitive-evaluative pain processing

The old saying "pain is inevitable, but suffering is optional" (apparently mis-attributed to Buddha) refers to the reciprocal relationship between the pain experience and neurocognitive processes such as attention, reappraisal and expectancies (212). Stress can increase 'negative' self-talk/beliefs, focusing attention on the affective qualities of pain (121; 250; 251), altering threat appraisal (212; 250) and amplifying pain signals – leading to more negative self-talk, pain affect and suffering (252). The degree of suffering will also depend on current as well as future goals (253), the extent of perceived goal interference, the desire for and perceived likelihood of success and whether the goal requires approach or avoidance. All determine the meaning and implications of the stressor (254).

Thus, pain perception is influenced by meanings and beliefs. Famously, recuperating soldiers told they were returning to the battlefield had higher pain report than soldiers with more severe injuries who were being discharged home (255). Pain self-efficacy, the belief that one can effectively control or decrease pain or headache (176; 256) can moderate both headache and the impact of stressful events on headache (176; 257). Expectancies can also increase pain perception, as occurred for example with the aversive labelling of cold pressor stimuli (258). Likewise, by predisposing to threatening interpretations of ambiguous stimuli, pain perception is increased by rumination and pain-catastrophizing – an exaggerated negative orientation towards noxious stimuli (259). These cognitive processes are more common in headache sufferers than controls (169; 260-263).

Stress disrupts cognitive processing including self-efficacy because, bereft of the usual top-down processes which strengthen and empower us and give us a sense of self-mastery, we may experience loss of the "ineffable feeling of experiencing oneself as an active agent in the perceived events of the world" (126,p.310). Events are perceived as no longer within our control – a shift associated with increased NA and subjective stress, increased autonomic arousal (256), physiological changes such as norepinephrine (NE) depletion and increased serotonin (5-HT) sensitisation (225; 264). Appraisals of noxious stimuli involving harm, threat, or loss were associated with dependent coping, higher pain intensity and greater levels of depression (265). Headache self-efficacy can be reduced by

prior experiences of recurrent and uncontrollable headache, particularly if social supports are lacking (266; 267). The result can be a 'learned helplessness' response (268) to headache, which may generalise to other stressors perceived as uncontrollable. This possibility is investigated in Chapter 8 of this thesis.

In sum, stress-related cognitive processes may exacerbate headache by:

1. Reducing perceived control over pain
2. Lowering headache self-efficacy
3. Interfering with important goals or the capacity to manage such interference.

Each of these factors is itself threatening, increasing NA and the use of threat-based coping strategies which may only increase pain sensitivity.

1.4.5 Pain coping & pain behaviours

The disruption of cognitive processing of affective information associated with stress reduces the frequency of active coping behaviours (232; 269; 270) and of proactive pain coping methods such as positive self-statements, reinterpreting or ignoring pain sensations. Migraine-without-aura patients also showed significantly reduced use of the "turning to religion" approach, an emotion-focused coping strategy (271). Stress also reduces the effectiveness of distraction, since distraction can reduce pain-related distress and pain intensity (272) if the task leading to distraction results in a positive emotional outcome (273) and when the level of pain intensity is relatively mild and has risen gradually (274). Instead, stress may increase the use of passive methods of pain management such as analgesic medication, worrying, resting, hoping/wishing and dependence on others for coping, which predict a decrease in functional status and greater levels of disability (275). Stress also increases ruminations about pain ("Why me?"), which are usually associated with depressed mood, cognitive deficits and the use of maladaptive coping strategies such as praying/hoping for a cure or pain relief and catastrophising (265). An unwillingness to accept one's pain is related to greater depression, disability, anxiety and poorer adjustment (276).

The fear-avoidance model (Figure 1.2) is commonly used in explaining the inter-relationship between coping and (chronic) pain.

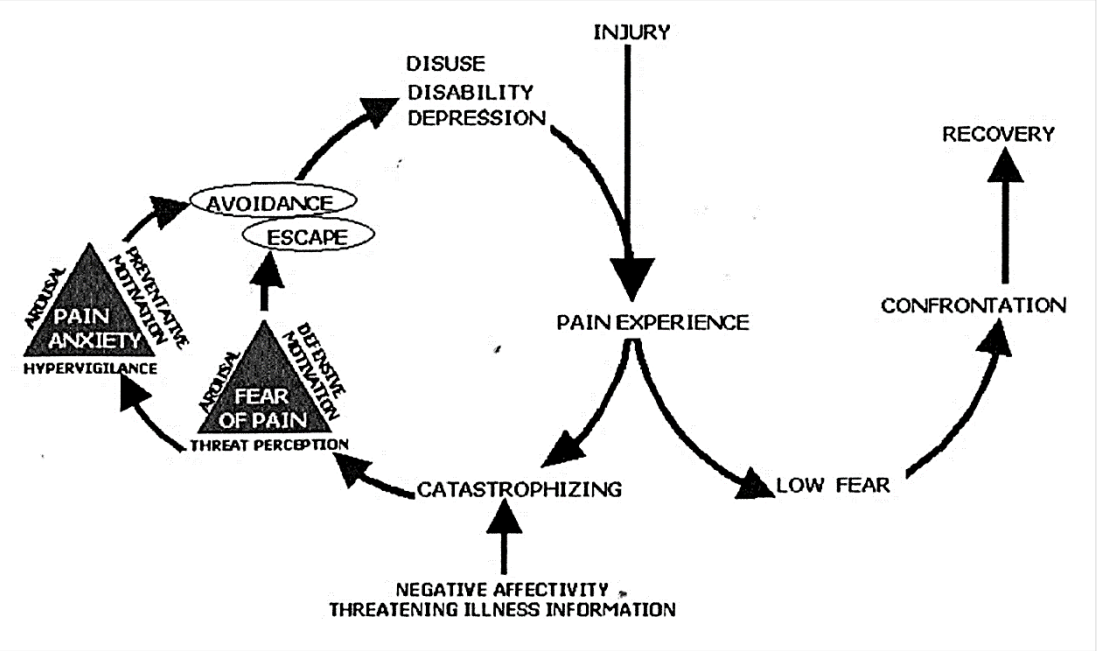


Figure 1.2 **The Fear Avoidance model of chronic pain** Adapted from Eccleston **(277)**.

In this model, an individual's coping response to pain occurs on a spectrum from confrontation to avoidance, depending on their fear of pain. Those with low fear or who confront their pain display behaviours that promote optimal functioning. Contrastingly, individuals who have high levels of pain-related fear avoid activities or experiences they perceive to contribute to pain. In the long term, continued avoidance or escape behaviours lead to chronicity of pain, disuse or disability, which perpetuates the negative cycle of pain-related cognitions and behaviours **(277; 278)**.

In headache patients, dysfunctional coping, characterised by fear and avoidance, was frequent and was not confined to chronic forms of headache (279). Social avoidance behaviour and pain-related disability in migraine were also associated (280).

In addition, depending on the interpersonal context and one's attachment style, headache pain report may represent a pain behaviour, signalling to significant others the desire to be left alone or perhaps to receive supportive care (281).

1.4.6 Strain

Long-term wear and tear on the organism – Selye's third and final phase of the General Adaptation Syndrome – may increase headache frequency or chronicity. The response system becomes fatigued, the pituitary-adrenal axis fails to respond, lymphatic structures become dysfunctional or enlarged, hormones such as cortisol increase and adaptive hormones are depleted (124). Since gluco-corticoids have anti-inflammatory and anti-

nociceptive effects, "let down" migraine may result from glucocorticoid withdrawal and reduced HPA activation when acute stress ends (282). Thus, a decline in stress from one evening diary to the next was associated with increased migraine onset over the subsequent 6, 12 and 18 hours (283).

This loss of restorative bodily functions may, however, be temporary (284). In this respect, "let-down migraine" may be part of a bodily signalling system to (in effect) "take it easy" – a signal motivating adaptive behaviour (285). Functional-evolutionary models of emotion posit that pain and negative affects which increase pain perception, such as anxiety, discouragement and irritation/anger (229; 286), or affective states which influence motivation (sluggishness, confusion, tension) may induce recuperative 'sickness behaviours' (287) until headache subsides.

1.5 A biopsychosocial model of headache

To guide investigations, a biopsychosocial model of headache was developed from perceptual and pain processing models (288-290), as diagrammed in Figure 1.3. It is consistent with the paradigm of biopsychosocial synergism, which encourages investigation of the activity and relationship among the multiple regulatory loops that influence the value of regulated variables (291), such as the multiple and reciprocal relationships between biological (neurophysiological), psychological (affective, cognitive, behavioural) and socio-cultural (environmental) factors in headache activity during a stressful episode. The model also fits with the notion that stress-headache may relate to allostatic load, the burden of stress adaptation (192).

Specifically, the model postulates that within a specific context, stress-headache results from interactions between distal tonic processes (e.g. headache history, personality and attachment anxiety) and proximal phasic responses such as the emotional-physiological responses evoked by a stressful stimulus.

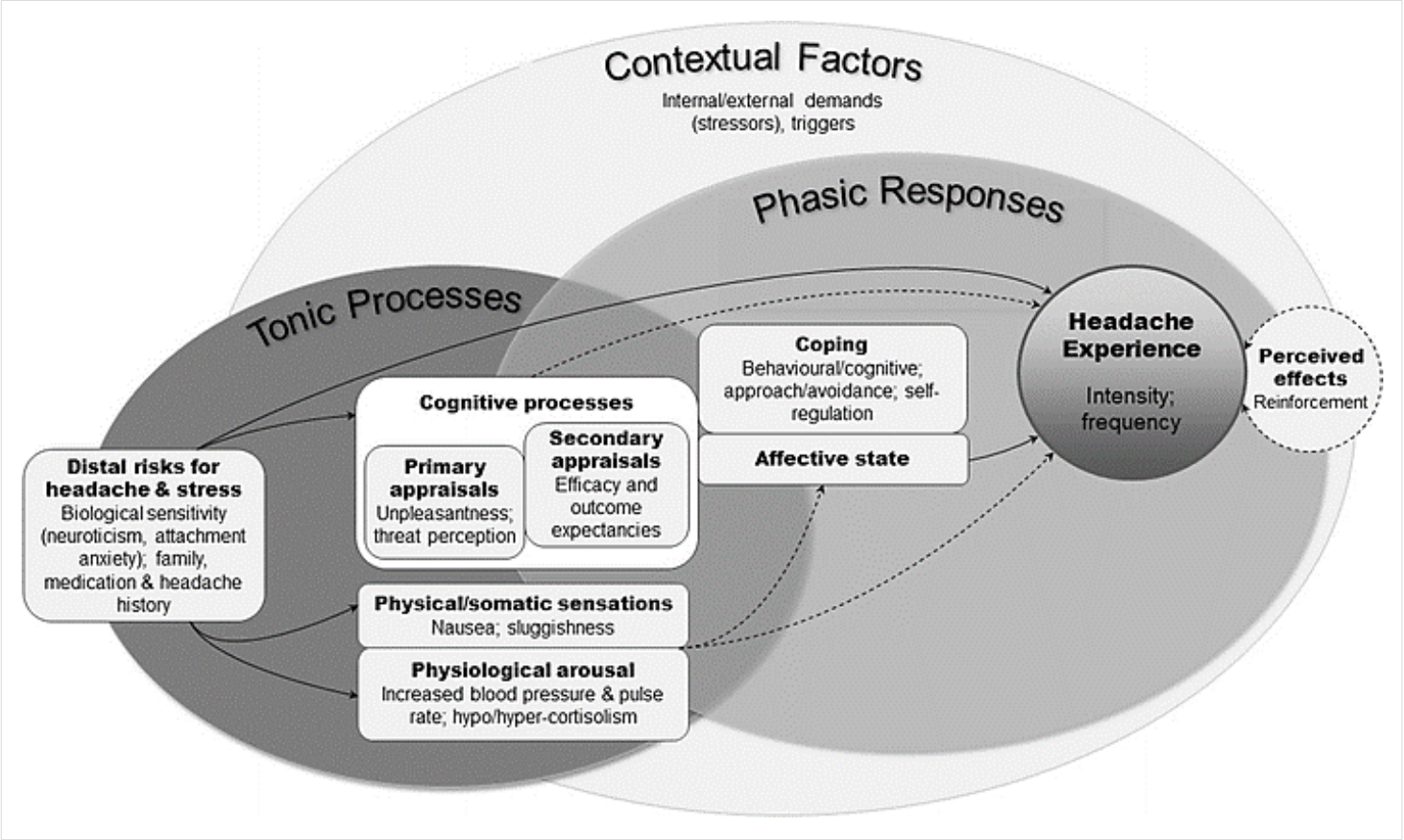


Figure 1.3 A biopsychosocial model of stress-headache adapted from perceptual and pain processing models The model posits that in a given context, stress-headache results from interactions between distal, tonic processes including headache history, personality or attachment anxiety, and proximal, phasic responses including the physical-emotional responses to a stressful stimulus. Inter-relationships between headache and other physical sensations, physiological arousal, appraisals, negative affect, self-efficacy and coping were examined in this research. Arrows indicate links but do not necessarily imply direction.

1.6 Summary of aims

The present study aimed to test some hypothesised aspects of a biopsychosocial model of headache during a 25-minute laboratory stressor designed to induce headache in episodic migraine and T-TH samples. The physiological aspects of the stress-headache interaction were salivary cortisol and cardiovascular (blood pressure, pulse rate) changes in response to the stressor. The psychological aspects of the stress-headache interaction were: stressor appraisal processes, personality traits, attachment style, NA, self-efficacy beliefs and stress/pain coping strategies. The aim was to determine which of these variables (if any) predicted stress-induced headache in headache sufferers compared with controls and whether and in what way these variables differentiated between migraine and T-TH participants. Specifically, we expected that migraine and T-TH participants would exhibit different processes at (i) the neurobiological level – cardiovascular, cortisol, trigeminal, and (ii) the psychological level: greater stressor exposure, more threat appraisals, reduced self-efficacy, greater NA and dysfunctional coping which either fails to regulate or 'misregulates' (has adverse outcomes) (171).

The following chapter structure was adopted.

- Chapter 2: Methodological considerations and methodology
- Chapter 3: Distal influence #1. Personality traits and headache
    a. Study 1: Personality and 'usual' headache severity: life stressor
    b. Study 2: Personality and headache intensity: laboratory stressor
- Chapter 4: Distal influence #2. Attachment style and headache (paper published in the *Journal of Psychosomatic Research*)
- Chapter 5: Proximal influence #1. Somatic and physiological responding in headache
- Chapter 6: Proximal influences #2. Negative affect and self-efficacy (paper published in the *Journal of Behavioral Medicine*)
- Chapter 7: Proximal influences #3: Primary and secondary appraisal: stressor exposure and reactivity, and the moderating effects of personality traits
- Chapter 8: Proximal influence #4. Coping choice, effectiveness and headache.
- Chapter 9: General discussion and conclusions.

Chapter Two

2

Methods

2.1 Methodological Issues

The aim of this chapter is to report the rationale for, and design of, the study and the selection of measurement instruments. As outlined in Chapter 1, research investigating the inter-relationship of stress responses and headache should:

- Involve multidimensional assessment: stressor, appraisal, coping and the four different levels of reactions to a stressor, i.e. physiological, cognitive, affective and behavioural
- Be 'cross analytic', i.e. involve simultaneous measurement at both physiological and psychological levels of analysis (292)
- Assess the impact of distal as well as proximal factors in headache
- Use the paradigm of biopsychosocial synergism which encourages the study of multiple interactions between variables (mediation and moderation effects).

2.1.1 Choosing a stressor

In line with critiques of the concept and measurement of stress (293), an established cognitive laboratory stressor (cf 28; 33) was modified to maximise the essential dimensions of uncontrollability and unpredictability. Unbeknown to participants, the task had an arbitrary and predetermined failure rate (uncontrollability component), was markedly time-pressured and accompanied by extraneous noises and head shocks (uncontrollability and unpredictability component). Consistent with a previous study in our laboratory by Frew & Drummond (286), in which a stressful arithmetic task increased distress, altered participant mood in a predictable way and initiated activity in opiate systems resulting in stress-induced analgesia, we postulated that such modifications could provoke headache by reducing both adaptive and regulatory capacities (28; 33; 294). Attempts at salience were made by promoting the experiment to participants as a potentially useful contribution to medical research.

2.1.2 Participant recruitment

A university undergraduate sample of 88 women and 18 men aged between 17 and 52 years were recruited by a general campus advertisement to participate in "a study of the relationship between stress and head pain". Two groups were recruited separately – those who "regularly or frequently suffered from headaches", and those who "seldom experienced headaches". The total sample consisted of undergraduates and alumni (n=101) and others from the wider community (n=6). This sample size was chosen to ensure that sufficient power was available to detect a large effect. Type 1 error was set at

the conventional alpha of $p<.05$ (295). A large effect size was chosen based on the results of related studies (296; 297).

In sampling for migraine, an attempt was made to replicate the 1:4 migraine gender ratio. Only episodic sufferers were selected: over months or years, episodic headaches can increase in frequency in susceptible individuals, becoming less intense but more disabling and less responsive to treatment (3). However, the clinical status for chronic headache is considerably more complex than for episodic sufferers (188; 298), with a higher incidence of comorbid psychopathology in chronic migraine (299-301) and T-TH (302), and greater subjective perception of headache pain (303). Hence episodic sufferers were selected to avoid the confounding effects of pain chronicity.

2.1.3 Headache Questionnaire

A standard clinical interview that addressed International Headache Society (I.H.S.) criteria (7) was used to assign people to the different diagnostic groups. Appendix A shows the interview questions. Headache type, frequency, severity and history were assessed by means of this interview. Where appropriate a medical opinion was sought.

Debate exists as to whether T-TH is a separate disorder or on a continuum with migraine, particularly as over half of those with a definite migraine diagnosis report having both T-TH and migraine at separate times (103; 304) and some 70% of those with definite T-TH have reported migraine-type symptoms (103). Regardless, the IHS definition of T-TH is exclusionary, sidestepping debate: T-TH is, broadly, everything that migraine is not. Thus, while there is evidence to suggest that the migraines and T-TH may be on a continuum, particularly as the chronification of migraine leads to a decrease in symptoms such as nausea, photophobia and phonophobia, it is worth considering them as two different categories according to the IHS criteria – the approach taken in this thesis.

A research-relevant factor in the interview is that headache diagnosis requires accurate self-report and some patient introspection. In our interview, we noted that some 56% of migraineurs with and without aura were initially unaware that they met criteria for migraine. Logic would suggest that it is unlikely for such patients to visit their GP with an adequately detailed headache diary, and migraine is often managed in the primary care setting where the major resource that is lacking is time (305). Thus, particularly when non-clinical samples are used, a headache interview must be both generous with time and carefully structured to allow for this lack of awareness.

2.1.4 Participants

Eligible participants were scheduled for two appointments, approximately a week apart. 86 of the 106 participants completed both testing sessions. Details of all 106 participants are listed in Table 2.1.

2.1.4.1 Participant group #1: Whole sample (n = 106)

In the initial sample of 41 female and 8 male migraineurs, 24 met criteria for migraine without aura. All but three of the migraineurs reported concurrent episodic T-TH. The T-TH sample consisted of 28 females and 4 males who met IHS criteria for episodic T-TH (<15 days per month) and one participant who at 16 headache days per month just met the criterion for chronic T-TH. The 25 healthy controls reported less than six mild headaches per year, lasting on average an hour. Headache history data are included in Table 2.1 below.

Table 2.1 Participant and headache history data

	Migraine	T-TH	Control	Total N
N	49	32	25	106
Gender:				
Female	41	28	19	89 (83%)
Male	8	4	6	18 (17%)
Mean age years (± SE)	24.96 ±1.9 (18 – 52)	21.74 ± 0.76 (18 –40)	23.44 ± 5.3 (17 – 36)	23.6 ± 6.8 (17 – 52)
Aura or 'warning'	24	3*	0	27
Nausea	31	3	1	35 (33%)
Strictly unilateral	21 (43%)	8 (25.2%)	8 (32%)	37
One-sided, but alternating sides	13 (26.5%)	4 (12.5%)	nil	17
Frequency per month	4.19 ±.57	2.28 ±.35	0.29±.05	2.81±.33
Headache duration (hours) ± SE	16.5 ± 3.25	5.6 ± 2.1	1 ±.16	9.8 ± 1.8
Family members with migraine	28 (57%)	16 (50%)	11 (44%)	55 (52%)
GP visits re headache	22 (39%)	11 (34%)	2 (8%)	35 (33%)

* "Warning", e.g. dizziness

2.1.4.2 Participant group #2: Experimental subgroup (n = 86)

Of the 106 initial participants, 7 completed the initial interview and psychological testing but did not participate in the experiment a week later, citing work and other commitments. A further 13 participants were excluded from further testing because they were taking headache or psychiatric medication, had a chronic medical or psychological condition or had used mood-altering drugs including alcohol in the previous 24 hours. Table 2.2 details these reasons for exclusion.

Table 2.2 Excluded participants

Reason for exclusion	Migraine	T-TH	Control	Total* (n=13)
Chronic medical condition	5	Nil	nil	5
Headache or other medication (including psychotropic)	2	Nil	nil	2
Co-morbid psychopathology				
a) Depression	2	Nil	nil	2
b) Anxiety/Panic	1	2	1	4
c) Adult ADHD	nil	1	nil	1

* Note: One participant fitted into more than one category.

Of the final experimental sub-sample of 72 women and 14 men, 38 met diagnostic criteria for episodic migraine and 28 for episodic T-TH (7). Another 20 with no more than 6 mild headaches per year, maximum duration 2 h, formed a control group. Participant details are shown in Table 2.3.

Table 2.3 Participant and headache history data (means and standard deviations) for experimental sample.

	Migraine	T-TH	Controls	Total/Mean
Females	31	24	17	72 (83.7%)
Males	7	4	3	14 (16.3%)
Mean age (years)	24.6 ± 7.9	22.1 ± 5.0	23.7 ± 5.8	23.6 ± 6.6
Age range	18 – 52	18 – 40	17 – 36	17 – 52
Headache onset (year)	13.5 ±8.5	10.8 ±3.7	n/a	
Aura or warning, e.g. dizziness	24 (aura)	3 (warning)	0	27
Nausea[a]	24	2	0	26
Headache days per month[b]	4.6 ± 4.2	2.4 ± 2.2	0.3 ± 0.2	–
Headache duration (hours)[c]	14.7 ± 18.1	5.8 ± 13.7	1.0 ± 0.8	–
High school education	2	0	0	2
University education	36	28	20	84

[a] Nausea was reported more frequently by migraine than T–TH sufferers or controls, $\chi^2(2) = 35.3$, $p < .001$.
[b,c] Headache days/month and duration of headaches were greater in migraine than T–TH sufferers; headache days/month $t(58.6) = 2.74$, $p < .01$, and headache duration $t(64) = 2.17$, $p < .05$.

Most participants were altruistically motivated, understanding that the study findings could potentially reduce the burden of headache. Each participant provided informed consent for the procedures, all of which were approved by the Murdoch University Human Research Ethics Committee. Participants were reimbursed AUD $30 for participating and awarded course credits if appropriate. Participants were debriefed at the end of the experiment.

2.2 Experimental procedures

Testing was conducted in two sessions, a week apart. In the first session, participants completed a structured headache interview and psychological questionnaires. They were told that the following session would comprise a computer-scored "moderately stressful mental arithmetic task" designed to measure their "ability to handle mental stress". They were also informed that as part of the procedure they would receive "a series of mild electrical stimuli to the forehead akin to a series of pinpricks", but that this would have no lasting effects. To ensure their continued participation, their attention was drawn to a newspaper article on the use of shocks in headache treatment (306). Participants were invited to ask questions, after which they signed the informed consent form.

In the second session, prior to the experiment, a series of questions was asked regarding food and intake of alcohol or other drugs, and, for females, their menstrual cycle. Participants who were not initially headache-free on that day or females in days 22-28 of their menstrual cycle were rescheduled for testing.

The experiment comprised three phases, each of 25 min duration— (i) preliminary (pre-stressor), (ii) stressful task and (iii) post-stressor. Throughout the three phases of the experiment, pain processing was measured by recording nociceptive blink reflexes, and stress response levels were monitored via measures of autonomic activity – systolic and diastolic blood pressure, pulse rate, facial blood flow (temporal pulse amplitude, TPA) and immunological response (salivary cortisol levels). During the recording session, the participants were seated in a desk chair without armrests in a Faraday cage. The room was quiet, the lighting muted, the room air conditioned and kept at 23° ± 2ºC.

In the preliminary phase, the experimenter interacted with participants in a friendly manner, offering encouragement and engaging them in conversation about themselves and their work or studies. During the pre- and post-stressor phases, participants verbally rated headache, nausea and distress after each series of shocks using a 10 cm visual analogue scale, where 0 corresponded to no sensation or distress, 1 to awareness of sensation or distress, 2–3 to mild, 4–6 to moderate, 7–8 to somewhat severe, 9 to severe, and 10 to extremely severe. Participants also rated electrically-evoked pain for each of the ten trials of the 30 s shock series (a mean pain rating was later computed). In addition, an overall pain rating was obtained following the series of 20 shocks delivered at 2 s intervals. At the end of each set of shocks, to ensure that we were measuring headache and not simply pain from the electrode prick, participants were asked to rate their

headache, nausea and distress “right now”. At the end of phase 1, the experimenter checked in with each participant, ensuring that equipment was correctly attached, that they understood the purpose of the shocks, were not experiencing undue discomfort, and were answering relevant questions appropriately.

The second experimental phase, the stressful task, consisted of 25 min of difficult mental arithmetic. After two practise trials, participants were asked to rate headache and nausea on an electronic visual analogue scale by moving a cursor along a 10 cm line, with descriptors as above. Participants were told that their final test score would be compared with those of others but were given no further information about the nature of the task, particularly its pre-determined 50% maximum success rate. At no point during the arithmetic task did the experimenter interact with participants.

Mental arithmetic problems were delivered by a purpose-written computer program (shown in Appendix E) consisting of four five-minute sets of addition and subtraction exercises at three levels of difficulty, with each level corresponding to an extra digit (e.g. Level 1 = 6 + 8 – 2; Level 2: 27 − 19 + 3; Level 3 = 116 + 118 – 12). Participants were required to type answers within a designated time – 8, 12 and 15 seconds for each level of difficulty respectively. Incorrect answers or delay beyond the allotted time elicited a continuing loud and unpleasant beeping noise. Correct answers within the time frame earned a softer, more musical sound and terminated the beeping. Following three successful responses, subsequent arithmetic questions were automatically raised to the next difficulty level, or dropped a level following three incorrect answers. To maintain an overall 50% success rate, those participants who consistently scored correct responses within the time frame at the highest difficulty level were informed on screen that their responses were “too slow” and were subjected to aversive beeping regardless of their actual success.

To add to the stressfulness of the task, an audio recording of a crying baby was played, which steadily increased in volume and intensity.

In all three phases, participants received three series of 2 milliamp electric shocks, 10 at 30 second intervals, 20 shocks at 2 second intervals and a further 10 at 30 second intervals, giving a total of 120 shocks throughout the entire procedure. (The 30s inter-stimulus interval was designed to minimise opportunity for habituation.)

Prior to testing, face makeup was removed, then using an alcohol wipe, the experimenter cleaned the temple area and the eye and neck area on the side to be

stimulated. To ensure skin penetration of the 2 mA electric shock, an electrode preparation pad was used to exfoliate skin on the forehead on the side to be stimulated. A concentric electrode was attached to one side of the forehead above the supra-orbital notch with a double adhesive ring, placed on the usual side of headache for migraineurs, alternate left or right side for other participants. The electrode consisted of a copper wire cathode (0.5 mm diameter) centered within a stainless steel annular anode (internal diameter 10 mm and external diameter 20 mm), set to deliver monopolar square-wave pulses (pulse width 0.3 ms, current intensity 2 mA). (At this intensity R1 of the blink reflex is absent, and R2 is mediated by superficial (Aδ and C) nociceptive fibres rather than Aβ fibres (307).

The 2 mA shocks were delivered during each 5-min arithmetic set, as follows: first set—no shocks; second set—ten shocks at 30 s intervals; third set—20 shocks at 2 s intervals 2 min into the set; and fourth set—ten shocks at 30 s intervals. The recordings and procedures were performed by the same researcher throughout the study using standardised methodology and were similar during the pre- and post-stressor phases. Blood pressure readings were taken throughout the three phases, as shown in 2.3.1, and salivary samples (Section 2.3.3) at four points during the experiment: after a 15-minute relaxation period after entry, then after a ten-minute rest period at the end of each phase. Care was taken to ensure that participants did not receive a blood pressure reading during a shock.

Following each of the four arithmetic sets, using a centrally-positioned cursor to move along an (on-screen) 10cm Visual Analogue Scale, participants rated themselves along dimensions of head pain, nausea, anxiety, confusion, discouragement, irritation, sluggishness, tension and self-efficacy (see Section 2.4.1). To avoid interrupting the task, participants did not rate electrically evoked pain. No shocks were delivered during this ratings period. In the third (post-stressor) phase of the experiment, participants again rated headache, nausea and distress after each series of electric shocks. They were debriefed about the nature of the experiment, offered pain relief as needed and encouraged to ask questions. A timeline of the experiment is illustrated in Figure 2.1. The data collection sheet is shown in Appendix B.

Figure 2.1 Timeline of Experiment

2.3 Biological measures

2.3.1 Blood pressure and pulse rate

Blood pressure and pulse rate were measured at approximately 3 min intervals via a cuff on the non-dominant arm attached to an Omron M4 digital blood pressure monitor. Three measures were displayed: systolic and diastolic blood pressure in mmHg and pulse rate/minute. A total of 25 readings were taken throughout the procedure at baseline then at approximately one and four minutes during each shock series (Table 2.4). Time of measure is expressed as minutes from the beginning of the experiment.

Table 2.4 Time of measure for blood pressure and pulse rate readings across the three phases of the experiment.

Phase 1 (Baseline)		Phase 2 (Stressful Task)		Phase 3 (Recovery phase)	
Time	**Context**	**Time**	**Context**	**Time**	**Context**
3min	Upon arrival	**43min**	1 min prior to stressful task	**70min**	1 min after completion of task
15min	Following application of electrodes	**46min**	One min into first math set	**73 min**	Four minutes after completion of task
		49min	Four minutes into first math set		
18min	1 min after start of 30-second inster-stimulus - interval stimuli (30second- ISI)	**52min**	1 min into 2nd math set (30-second- ISI stimuli)	**83 min**	1 minute after start of 30-second-ISI stimuli
21min	4 min after start of 30 second- ISI stimuli	**55 min**	4 minutes into 2nd math set (30second- ISI stimuli)	**86 min**	4 min after start of 30s ISI stimuli
24min	1 min following 30s-ISI stimuli	**58 min**	1 min into 3rd math set (2second-ISI stimuli)	**89 min**	1 min following 30second-ISI stimuli
27min	1 min following 2 second-ISI stimuli	**61 min**	4 min into 3rd math set (2second-ISI stimuli)	**92 min**	During the 2 min period following 2 second-ISI stimuli
30min	1 min after start of 2nd set of 30sec ISI stimuli	**64 min**	1 min into 4th math set (30second-ISI stimuli)	**95 min**	1 min after start of 2nd set of 30-second-ISI stimuli
33min	4 min after start of 2nd set of 30second- ISI stimuli	**67 min**	4 min into 4th math set (30second-ISI stimuli)	**98 min**	4 min after start of 2nd lot of 30-second-ISI stimuli

Note: *ISI* = inter-stimulus interval

2.3.2 Temporal pulse amplitude (TPA)

This was measured by means of pulse transducers (photo-plethysmographs, Grass Instruments Company) attached with double-sided adhesive rings to the forehead, 1 cm above the eyebrows and 3 cm from the midline. To prevent room lighting from interfering

with photo-electric signals, the pulse transducers were covered with a black cloth band which was secured lightly at the back of the participant's head with Velcro tape. Pulse waveforms were displayed on the computer monitor in separate channels of the AcqKnowledge software program referred to below. Where movement artefacts due to electric shocks and facial movements interfered with recordings, the better of the two measures was used.

2.3.3 Salivary cortisol

Saliva samples were collected at four intervals: (i) upon arrival; (ii) prior to the mental arithmetic following the first complete shock series; (iii) 10 minutes after the completion of the mental arithmetic task and modified *Ways of Coping Scale*, and (iv) upon completion of the whole procedure. These time intervals were chosen because the cortisol response takes place over a much longer time course than other physiological systems, and a change in cortisol levels may not be detected until 10-30 minutes after completion of a stressful task (308). Initial measures were taken immediately upon arrival to allow for both time of day (cortisol response has its own circadian rhythm) and to offer a baseline measure for hyper- or hypo-cortisolism resulting from chronic long-term stress.

2.3.4 Measuring trigeminal transmission: Nociceptive blink reflexes

Many cranial nerves have some general somatic afferent fibres and these nerve fibres will terminate in the trigeminal spinal nucleus regardless of the nerve that they follow in the head (110). Thus, measurement of activity at brainstem level offers a way of ascertaining neuronal activity in deeper cranial structures. The spinal trigeminal nucleus is also important on the sensory side of many cranial reflex pathways. One trigeminofacial brainstem reflex, the blink reflex, offers a non-invasive measure of trigeminal nerve transmission in humans. It is usually elicited by electrical stimulation of the supraorbital nerve. The efferent arm of the reflex is the facial nerve, so recording from the *orbicularis oculi* muscle enables study of the trigeminal nerve and its brainstem connections. Quantitative analysis for functions that involve the dorsolateral pons, lateral medulla and the fifth and seventh cranial nerves can be provided (309).

The blink reflex has three components: an early ipsilateral, pontine R1, with an onset latency of 11 ms, and two bilateral medullary components, the R2 and the R3, with onset latencies of 33 and 84 ms, respectively (310; 311). R1 is mediated by pontine inter-neurons located in the principal sensory nucleus of the spinal trigeminal nucleus and R2 is probably

mediated by inter-neurons in the caudal part of the spinal trigeminal nucleus (312; 313). R2 latency is particularly useful in detecting differences in reactivity to noxious stimuli as well as length of time to return to baseline. The neuronal origin of R3 is uncertain, but it is possibly part of the startle reaction (314).

Methods for studying the nociceptive system are based on the employment of stimuli which activate preferentially the Aδ and C afferents. In contrast to the bipolar surface electrode used in early blink reflex (BR) studies, which depolarised the Aδ fibres but also reached the deeper layers containing Aβ fibres, the nociceptive Blink Reflex (nBR), utilises a concentric electrode with high current density that rather selectively activates Aδ fibres, eliciting the R2 component (41; 315). Although this stimulation modality lacks the selectivity to evoke reliable pain-related cortical responses (316), it may be efficaciously employed for the elicitation of a muscle response under trigeminal nociceptive activation (307; 315). Hence the nBR is touted as a more accurate and nociception-specific reading of trigeminal activity than the standard BR (317; 318) and represents a sensitive marker for the functional state of the trigeminal nociceptive system (41; 319; 320). It has thus been used to test for the role of peripheral and central sensitisation in migraine and T-TH (320; 321). A pivotal study on migraine pathophysiology described amplitude and habituation abnormalities of the nBR in asymptomatic subjects with first-degree inheritance for migraine; these were similar to the abnormalities found interictally in subjects with active disease, indicating nBR dis-habituation as a genetic predisposing trait (40).

The nociceptive electrical stimuli were delivered using a Grass SD9 stimulator. The custom-built planar concentric electrode assembly comprised a central metal cathode (Diameter: 10.5 mm), an isolation insert (Diameter: 5 mm), and an external anode ring (Diameter: 6 mm) providing a stimulation area of 19.6 mm^2). It provided a high current density at low intensities to stimulate the supra-orbital region. Adhesive surrounds of disposable “Cleartrode” EMG electrodes were trimmed to fit over the orbicularis oculi muscle below the lower eyelid and outer canthus of the eye on the stimulated side, and a ground electrode was attached to the side of the neck below the hairline on that side.

Monopolar square pulses of 0.3 ms duration and 2 mA intensity were delivered with pseudo-randomised interstimulus intervals (ISIs) of either 2 s or 30s. By means of surface electrodes, 2x10 blocks of EMG responses per phase with an interstimulus interval (ISI) of 30s with one block of 20 with an ISI of 2 s in between these were recorded over the orbicularis oculi muscle. Electromyograph signals were amplified with a Grass Instruments biopotential preamplifier (Quincy, MA, USA), digitised by an MP100 Biopac

Systems Analogue/ Digital Channel receptor (Goleta, CA, USA), sample rate 2000 Hz, and displayed on a computer monitor using AcqKnowledge software (Biopac Systems). Detailed procedures for calculation of the nBR are described in Appendix D.

2.4 Psychological measures

2.4.1 Self reports

Ten-point visual analogue scales (VAS) were employed for all self-reports during the stressful task as below. According to Price (322), VAS of sensory intensity and affective magnitude are valid ratio measures of sensation and affect, permitting comparison between (for example) chronic pain and experimental heat pain and between ratings by pain patients and volunteers.

2.4.1.1 Headache, nausea, distress, negative affect (NA)

To determine the time course of headache, during Phases 1 and 3 of the experiment, participants were asked to verbally rate their level of headache, nausea and distress on a ten-point VAS at three points: during and immediately following the first set of 10 shocks, following the second set of 20 shocks and following the third set of 10 shocks (Figure 2.1).

Pain intensity ratings were taken during Phases 1 and 3 of the experiment during and immediately following each set of shocks, where 0 = no sensation, 1 = awareness of pain, 2-3 = mild pain, 4-6 = moderate pain, 7-8 = somewhat severe pain, 9 = severe pain, 10 = extremely severe pain.

In Phase 2, after the practice trials and each mental arithmetic set, participants rated headache, anxiety, discouragement, irritation, confusion, tension and sluggishness/alertness by moving a cursor along a 10 cm electronic visual analogue scale. These affects were chosen to best represent the neuro-affective correlates of the stress experience (126). Zero corresponded to ‘‘no’’ or ‘‘none’’ and 10 to ‘‘extremely’’. Questions included: ‘‘How painful is your headache right now?’’, ‘‘How nauseated/anxious/confused (etc) do you feel right now?’’

At task-conclusion, participants rated the level of controllability, importance, emotional impact and stressfulness of the task on a seven-point scale, with ‘‘not at all (stressful/controllable)’’ at one end and ‘‘extremely stressful’’ at the other. Scoring was reversed for controllability.

2.4.1.2 Task self-efficacy

For self-efficacy, following two practice questions (addition and subtraction at the first and second levels of difficulty as above) participants were asked to "Please rate your ability to avoid mistakes for the remainder of the task" using a ten-point VAS rating scale as above. The initial rating corresponded to task expectancy whereas subsequent ratings reflected a reappraisal of the capacity to succeed in the face of failure feedback, distracting noises and intermittent electric shocks.

Since perceived control may trigger reappraisal processes that can change the pain experience (272), increasingly non-contingent failure feedback was provided as the stressful task progressed. Also, where initial expectations of success are followed by negative outcomes, stress levels may rise, whereas the converse ought to be true where subsequent feedback appears to confirm initial positive expectations of success. Therefore, we expected that as efficacy expectations fell, stress-headache and both pain and stress-related NA would increase. We also expected that low task and pain self-efficacy would be associated with higher headache intensity in those acquiring a headache during the laboratory stressor and in headache sufferers compared with controls.

2.4.2 Assessment instruments

The psychometric tests were filled out in the first week of testing following the administration of the Headache Questionnaire (2.1.3).

2.4.2.1 Personality traits: NEO-PI-R

The NEO Personality Inventory Revised (NEO-PI-R) (323), a U.S.-normed 240-item test, was developed from personality theory to operationalise the five factor model (FFM) of personality, "the most basic dimensions underlying the traits identified in both natural languages and psychological questionnaires" (Manual, p. 14). The scales have good construct, convergent and discriminant validity and test-retest reliabilities of between 0.75 and 0.83.

Items are scored along a five-point scale: Strongly Agree, Agree, Neutral, Disagree or Strongly Disagree. The NEO-PI-R scale represents continuous dimensions but is often summarised in terms of five levels: very low, low, average, high and very high.

The five factors of this "Big Five" model are: neuroticism-emotional stability, extraversion-introversion, openness to experience–conservatism, agreeableness-antagonism, conscientiousness-impulsivity.

2.4.2.2 Attachment style: Experiences in Close Relationships

The Experiences in Close Relationships (ECR) scale (324) was chosen over the Adult Attachment Interview (AAI) (325) for pragmatic and theoretical reasons. The ECR can be completed and computer scored in under 30 minutes, whereas the AAI takes considerable time (at least a one-hour face-to-face interview) and expertise in scoring. More importantly, each represents one of the two main lines of attachment research, and while the AAI is often considered the 'gold standard' in attachment research, the questions motivating research in each tradition are different – "the intergenerational transmission of attachment patterns versus social-cognitive dynamics affecting feelings and behaviour in close, especially romantic/marital, relationships" (326,p.18). For the purposes of this research, a measure of current adult attachment patterns as assessed by the ECR was considered more apposite.

The ECR has adequate validity and reliability (326) and offers four nominal and two continuous measures – a four-quadrant measure of attachment status: Secure, Dismissive, Preoccupied, Fearful-Avoidant, and measures of Attachment Anxiety (fear of separation and abandonment) and Attachment Avoidance (e.g. discomfort with intimacy and dependency). Participants complete statements such as "I often worry that my partner will not want to stay with me" along a 7-point scale of 1 = Disagree strongly, 4 = Neutral/mixed, 7 = Agree strongly.

Online scoring was available at www.authentichappiness.sas.upenn.edu/results

2.4.2.3 Stress coping during the laboratory stressor

Coping with the laboratory stressor was assessed by a modified version of the *Ways of Coping Questionnaire-Revised* (WCQ-R) (140) (Questions shown in Appendix C). The original 66-item empirically-based measure was designed to assess coping processes in a nominated stressful encounter. Still widely used, it was the first empirically-derived measure of coping devised and tested by Folkman & Lazarus (140).

The participant describes "the most stressful experience or event" they have encountered in the past month. On a 7-point scale, where 0 = not at all; 7 = maximum possible, participants rate each of the following:

- ability to control the event and/or its resolution (reversed scoring)
- importance of resolving situation (salience of stressor)
- emotional impact of event
- subjective stressfulness of event

Thereafter, the participant responds to a series of statements (e.g. "Just concentrated on what I had to do next – the next step") on a four-point Likert scale, where scale anchors were: 0 = does not apply and/or not used; 1=used somewhat, 2 = used quite a bit, 3 = used a great deal) on a four-point scale.

Unlike other coping scales, users of the WCQ-R are encouraged to add or drop items to suit the population under study (140).While it is acknowledged that this will affect the number of factors and the reliability of the measure, which is moderate at best (140), coping theory suggests that this is to be expected with a stressor-specific coping measure, and other, supposedly more theoretically-derived scales of intra-individual coping may not offer much improvement (327). Hence, the 'Adapted' WCQ-R was scored as for the original (140), only excluding items which could not apply in the laboratory situation, e.g. Item 66 "I jogged or exercised". The 'Seek Social Support' scale was also excluded (see Chapter 8). This 36-item test was administered 10 minutes after completion of the arithmetic task.

2.4.2.4 Pain Coping: Coping Strategies Questionnaire-Rervised (CSQ-R)

Pain coping refers to conscious, goal-directed and self-initiated actions, cognitive or behavioural, through which individuals attempt to control or tolerate pain. Although many pain coping strategies are idiosyncratic and differentiating between 'good' and 'bad' coping strategies is difficult (328), Rosenstiel & Keefe (329) designed the 50-item *Coping Strategies Questionnaire* (CSQ) which has been extensively explored in both its internal structure and its external correlates, and has accumulated a considerable amount of clinical data (330). It comprises six cognitive and two behavioural coping strategies including diverting attention, reinterpreting painful sensations, coping self-statements, ignoring painful sensations, praying or hoping, catastrophizing, increasing activity level and increasing pain behaviours. Two additional items tap perceived control over pain and the ability to decrease pain. Subsequent factor analysis has led to the removal of the two behavioural coping strategies scales (e.g. 330).

SECTION 2: DISTAL INFLUENCES IN HEADACHE

Chapter Three

3

Personality and headache

Background

Personality dispositions – individual differences in characteristic patterns of thinking, feeling and behaving (331) – have long been viewed as contributing directly to the primary headaches of migraine and T-TH and, historically speaking, formed the starting place for investigations into the ways in which stress may induce headache. Also, discussed earlier (section 1.3.3.2, page 17), historically speaking, personality has primarily been conceptualized in trait rather than process terms (332), with psychogenic explanations being the norm, i.e. where personality is viewed as having a direct relationship with headache. However, since traits tend to be descriptive rather than explanatory (179), few *a priori* explanations exist.

Thus, early psychoanalytic thinking maintained that headache resulted from a neurotic disorder characterised by internal conflict between dependency needs and the high negative affectivity, defensiveness, submissiveness and inhibition of anger expression induced by this conflict (333). The headache pioneer Harold Wolff commented:

> *The migraine headache represents a collapse of a way of dealing with life situations which are stressful to the individual. Up to a certain point the patient is able to cope with the accumulating tension and hostility resulting from the stress which he faces. Beyond this he cannot continue, and there ensues a period of disabling pain during which he is forced to halt. (131,p.430).*

Subsequent observations of headache sufferers in sub-specialty clinics characterized migraineurs as tense, driven, obsessional perfectionists with an inflexible personality and difficulties in dealing with, and expressing hostility and aggression (334; 335). T-TH patients were characterised as worrisome, depressed, anxious, chronically tense, hostile, dependent and psychosexually conflicted (336). The implication that headache patients had difficulties in stress management was clear and, from this psychogenic perspective, research focused on finding the 'migraine (or headache) personality'.

These research efforts were buttressed by studies using the psychoanalytically-oriented Minnesota Multifactorial Personality Inventory (MMPI) or its revised version, the MMPI-R (337; 338). Correlations between chronic migraine and the 'neurotic triad' – high scores on the MMPI hypochondriasis, depression and hysteria scales (e.g. 339) – were reported. However, apart from the obvious confound of referral bias in such samples (340; 341), the MMPI is of doubtful validity in assessing headache sufferers (342-344). Furthermore, the neurotic triad may fundamentally measure depression (345), with which migraine has a shared

aetiology (26; 340; 341; 346-348). The upshot of numerous investigations was that the better controlled studies offered little evidence of a clearly differentiated 'headache personality' (349).

Later prospective community surveys used a variety of measures, including the factorially-based Eysenck Personality Questionnaire (EPQ) with its two factors of neuroticism (N) and extroversion (E). As discussed further below, high-N scores were related to headache in community samples (350), although investigators warned that the EPQ structure was such that high-N scores may reflect general symptom-affirming (351). The revised version, the EPQ-R (352-355) improved the scoring process and included a third factor, that of psychoticism, which has however received little attention in relation to headache.

Subsequently, a consensus has developed around the Five Factor Model (FFM) framework – the "Big Five" – as providing a comprehensive account of major personality traits (356). Building on Eysenck's (353-355) research, the NEO-PI-R describes personality in terms of five broad dispositions, labelled: (i) neuroticism-emotional stability, (ii) extraversion-introversion, (iii) openness to experience-conservatism, (iv) agreeableness-antagonism and (v) conscientiousness-impulsivity. In an otherwise fragmented field with numerous single-factor constructs (357) – such as optimism, hardiness, Type A (178; 358; 359) – consistent use of the NEO has been called for to provide "commonalities, integration and a common language" (357, p.412). Nevertheless, this call has largely gone unheeded and research on the relationship of the Big Five to headache, particularly in community samples, is limited. Where associations between migraine and neuroticism, introversion, conservatism, antagonism and conscientiousness are reported in clinical populations (240; 360-363), the confounding effects of comorbid anxiety, depression or the effects of intractable headache itself (298; 364; 365) cannot be discounted.

In addition, research addressing the influence of personality on headache *during stress* is scarce. Stress disrupts the cognitive processing of affective information, increasing the strength of the upward influence of subcortical emotional circuits on the higher reaches of the brain relative to top-down controls (126). Hence, individual differences in personality traits may predispose to headache by influencing the strength and duration of responses to a stressor and/or by impeding regulatory processes during the stressor – thereby impacting the degree (or type) of affective, cognitive or physiological reactivity (184; 353; 366; 367) or the speed of post-stress adaptation (356). For example, a personality trait such as neuroticism can

positively predict subjective stress levels (184; 366), while extraversion and conscientiousness are negatively related to stress (368).

If, as part of headache treatment, sufferer and clinician are to identify processes by which personality traits may influence headache during stress, then a logical starting place is to assess relationships between traits, headache severity and intensity in a non-clinical sample during both a life stressor and a laboratory stressor. This was the aim of this chapter.

The 'Big Five' and headache

The following section reviews existing research on the relationship of headache in normal populations to the Five Factor Model (FFM) or "Big Five".

Neuroticism – Emotional stability

"Normal" neuroticism (N) – susceptibility to negative affect – concerns how easily and often an individual is distressed, with higher moodiness directly proportional to the degree of emotional instability. Neuroticism in the NEO-PI-R expanded conceptually on Eysenck's formulation to include facets of anxiety, angry hostility, depression, self-consciousness, impulsiveness and vulnerability (323).

Numerous studies using the EPQ, EPQ-R and various non-FFM measures have linked headache and neuroticism (negative affectivity) especially in clinical populations (339; 369; 370). Neuroticism (negative affectivity) as measured by the EPQ was predictive of migraine, especially in persons with migraine-with-aura (350; 351; 369; 371) and chronic T-TH (369; 371; 372) (235; 350; 351; 369; 371) – but only when chronicity and depression were controlled for. Similar results were reported using the Freiburg Personality Inventory (FPI) and Symptom Checklist 90 (SCL-90), although persons with migraine-with aura exhibited greater impairment than any of the other headache subtypes or controls on both measures (350). In an effort to separate out the issue of chronicity in T-TH, and using an alternative FFM questionnaire, the Zuckerman-Kuhlmann Personality Questionnaire (ZKPQ) (373), researchers compared episodic T-TH, chronic T-TH and migraine-without-aura with healthy controls (241). These researchers reported that greater 'neurotic anxiety' and depression appeared to be a defining factor of headache (241). Other researchers using trait measures of anxiety such as the State-Trait Anxiety Inventory (STAI) have likewise reported that anxiety relates to headache – albeit to headache frequency rather than headache type (372).

Thus, while neuroticism or some measure that heightens neuroticism – such as anxiety/distress – appears to contribute to headache, the diversity of measures of neuroticism potentially 'muddies' investigations. Nor is the extent to which neuroticism may contribute differentially to migraine rather than T-TH established. From prior research, it was expected that neuroticism scores would be higher in headache sufferers than controls and in those with than without an experimentally induced headache.

Extraversion- Introversion

This personality trait reflects social tendencies, encompassing characteristics such as sociability, assertiveness, high activity level, positive emotions, and impulsivity. For Eysenck (352), extroverts were more outgoing, uninhibited and socially active than introverts, whereas for Costa and McCrae (323), extraversion is somewhat broader and includes warmth, gregariousness, assertiveness, excitement-seeking and positive emotions.

Psychobiological mechanisms purportedly underlying extroversion include individual differences in condition-ability, arousal level, and sensitivity to rewarding stimuli. Thus, in Eysenck's cortical arousal theory (374; 375), introverts operate at higher tonic levels of cortical arousal, so require less external stimulation and are more responsive to 'internal' stimulation such as pain (342; 374; 375). In general, these hypotheses have been supported: introverts have lower pain thresholds and pain tolerance than extroverts, tend to rate stimuli of equal intensity as being more painful compared to extroverts and require greater analgesia (342; 376) – although if the pain is discrete rather than continuous, neuroticism rather than introversion was predictive of low pain tolerance (377). Hence, extraversion is thought to reduce headache vulnerability directly through decreasing pain sensitivity (353).

Sociability may also relate to headache (378). Thus, MMPI measures of introversion in clinical headache samples describe migraineurs as having a tendency toward social isolation and anxiety, while T-TH was associated with psychological distress including social discomfort and withdrawal (379-382). However, the direction of causation in these studies is unclear. Conceivably, introverted individuals may experience stress-related T-TH from pushing themselves to interact with others beyond their energy and comfort level (383) – as for example when a lack of desire to be sociable conflicts with the requirements of one's personal or occupational context (384; 385).

Despite these predictions, epidemiological studies report no relationship between migraine or T-TH and introversion, even when accepted factorial measures are used (235; 360; 386). It was expected therefore that extraversion would be unrelated to migraine and T-TH but would be linked with greater stress reactivity and higher pain report in experimentally induced headache.

Openness to experience – Conservatism

Openness (O) reflects intrapersonal tendencies, including active imagination, aesthetic sensitivity, attentiveness to inner feelings, preference for variety, intellectual curiosity and independence of judgment. Subscales are: Fantasy, Aesthetics (appreciation for art and beauty), Feelings (depth and differentiation of emotional states), Actions (willingness to try different activities), Ideas (intellectual curiosity) and Values (readiness to re-examine social, political and religious values).

High-O scorers are curious about both inner and outer worlds and have experientially richer lives. They are unconventional, willing to question authority, entertain novel ideas and are prepared to entertain new ethical, social and political ideas. They may be more likely to eschew conventional medicine in favour of alternative approaches. Low scorers tend to be overtly hostile, egocentric, sceptical of others' intentions and competitive rather than co-operative (323).

Research on the relation of this third Big Factor to headache is limited, so hypotheses regarding its relationship with headache rely on literature demonstrating the health risks of emotional suppression or inhibition (387). Those who express feelings about traumatic events have fewer subsequent health problems than those who repress their feelings, with a decrease in the number of physician visits, increased immune activity, changes in autonomic muscle activity, behavioural health markers, and self-reported wellbeing (388; 389). Thus, seropositive males who scored high in Openness and Agreeableness had significantly greater T-cell recovery than low scorers upon receipt of a new retroviral therapy (390). Likewise, female volunteers who scored high in a measure of "post traumatic growth" – psychological growth following a stressful experience – showed significantly reduced cortisol secretion by the third day after three hours of daily laboratory stress for three consecutive days (391).

To the extent therefore that attempting to hide one's feelings (low Openness) increases stress, then lower-O scores may be expected in headache sufferers than controls and in those who acquire a headache during the experimental task vs those who do not.

Agreeableness – Antagonism

In this dimension of interpersonal tendencies, high scorers are fundamentally altruistic, sympathetic to others and believe that others will be equally helpful in return, whereas low scorers tend to be overtly hostile, egocentric, sceptical of others' intentions and competitive rather than co-operative (323). Sub-scales are: Trust, Straightforwardness, Altruism, Compliance, Modesty, Tendermindedness.

Studies linking NEO agreeableness and headache suggest that more agreeable individuals are less often engaged in those interpersonal conflicts which may contribute to somatic symptoms including headache (194; 201; 392-394). This echoes the comments of Harold Wolff that his clinic-referred headache patients characteristically showed unexpressed and unresolved resentment and hostility (131). Using an alternative FFM measure, the ZPQ (241), elevated aggression-hostility in migraine-without-aura was reported when this group was compared with episodic T-TH, chronic T-TH, migraine-with-aura and healthy controls. Subsequent non-FFM investigations have supported the premise that anger – especially when repressed – can contribute to headache (169; 395-398), since the psychosomatic correlates of chronic anger may support a role for antagonism in creating a general stress vulnerability via heightened cardiovascular and neuroendocrine reactivity to environmental challenges and demands (204; 335; 399). For these reasons, a positive relationship may be expected between low-agreeableness, migraine and experimentally induced headache.

Conscientiousness- Impulsivity

An aspect of what once was termed "character", this factor deals with the control of impulses, but in the sense of planning, organizing and carrying out tasks relative to a goal. High-C scorers are scrupulous, purposeful, strong-willed, determined, punctual and reliable. Low scorers tend to be hedonistic and lackadaisical. High-C is associated with academic and occupational achievement, but it may also lead to annoying fastidiousness, compulsive neatness or workaholic behaviour. Sub-scales are: Competence, Order, Dutifulness, Achievement Striving, Self-discipline and Deliberation (323).

In the limited research in community samples, no direct relationship between conscientiousness and headache is reported. An indirect relationship may however be inferred between headache and low-C (impulsivity), since general ill-health is related to failure to implement positive health behaviours (400) and adhere to medical recommendations (401). Impulsive individuals may also fail to monitor and avoid known and idiosyncratic headache triggers, e.g. adopting an imprudent diet, using illicit drugs, smoking, having excessive alcohol intake (15). Impulsivity may also increase headache risk by fostering avoidance-related strategies which increase vulnerability to, and recovery from, stress, inhibiting the formation/maintenance of supportive social relationships able to mitigate stress and encourage coping (Chapter 9). In the present study no predictions were made about the relationship between conscientiousness and headache.

On the basis of prior research, therefore, we hypothesised that headache sufferers and those with experimentally induced stress-headache would score higher in neuroticism, lower in extraversion and open-ness, and lower in agreeableness than controls or those with than without a stress-headache.

STUDY 1: PERSONALITY TRAITS AND 'USUAL' HEADACHE SEVERITY

3.1 Method

3.1.1 Procedures

Where detailed descriptions have already been provided, these will not be repeated here.

Participants

Group #1: Whole sample (Table 2.1, p.33)

Measures

Personality as assessed by the NEO-PI-R (Section 2.4.2.1, p.43)

3.1.2 Data Analysis

Previous research indicates significant personality differences between migraine, T-TH and controls in headache. Hence, two planned contrasts compared personality trait measures in (i) headache sufferers v controls and (ii) migraine v T-TH. These differences were investigated in Group (planned contrast) multivariate analyses of variance. Although ratings were skewed, clustering in the lower end of the continuum, analysis of variance was employed to investigate these relationships as it is fairly robust to violations of normality. As the NEO has separate norms for males and females, and the number of males in the sample was small (n = 18), results were computed for females in the first instance, then recomputed for the whole sample.

3.2 Results

Personality traits in episodic migraine and T-TH

NEO personality traits and their facets were unrelated to headache category (migraine and T-TH). Table 3.1 shows results for the whole sample. As there are separate norms for males and females, means and standard errors are also shown for a female-only sample in Table 3.2. Table 3.3 and Table 3.4 show trait facets for the whole sample.

Table 3.1 Personality traits (NEO-PI-R) and headache category, means, standard errors, effects.

Personality trait	Headache sufferers v controls				Migraine v T-TH			
	Headache (n = 78)		Controls (n = 22)		Migraine (n = 46)		TTH (n = 32)	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Neuroticism	99.35	22.99	93.55	4.72	98.09	3.48	98.63	4.17
Extraversion	117.27	17.84	118.32	3.69	116.74	2.60	117.69	3.12
Openness	126.95	18.75	125.46	4.01	128.94	2.75	124.94	3.30
Agreeableness	119.39	17.94	117.96	4.04	118.09	2.81	120.13	3.37
Conscientiousness	111.65	17.4	116.27	4.19	114.02	2.64	110.53	3.17
	F	*df*	*p*	*η2*	*F*	*df*	*p*	*η2*
Neuroticism	1.17	(1, 95)	0.282	0.01	0.01	(1, 76)	0.921	0.00
Extraversion	0.06	(1, 95)	0.803	0.00	0.06	(1, 76)	0.803	0.00
Openness	0.11	(1, 95)	0.744	0.00	0.87	(1, 76)	0.355	0.01
Agreeableness	0.10	(1, 95)	0.756	0.00	0.22	(1, 76)	0.643	0.00
Conscientiousness	0.94	(1, 95)	0.335	0.01	0.72	(1, 76)	0.400	0.01

Table 3.2 Personality traits and headache category: Means, standard errors, main effects (females only)

Personality trait	*Planned contrast 1* Headache sufferers v controls				*Planned contrast 2* Migraine v T-TH			
	Headache (n = 65)		Controls (n = 17)		Migraine (n = 38)		TTH (n = 27)	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Neuroticism	100.38	2.69	95.53	5.26	100.03	3.71	100.89	4.4
Extraversion	119.29	2.12	120.06	4.14	119.63	2.85	118.81	3.38
Openness	126.78	2.33	126.12	4.56	128.74	3.0	124.04	3.56
Agreeableness	119.55	2.2	123.82	4.3	117.74	2.88	122.11	3.42
Conscientiousness	111.49	2.51	111.65	4.9	113.76	2.91	108.3	3.45
	F	*df*	*p*	*η2*	*F*	*df*	*p*	*η2*
Neuroticism	0.68	(1, 80)	0.414	0.01	0.02	(1, 63)	0.881	0.0
Extraversion	0.03	(1, 80)	0.869	0.0	0.03	(1, 63)	0.854	0.0
Openness	0.02	(1, 80)	0.897	0.0	1.02	(1, 63)	0.317	0.02
Agreeableness	0.78	(1, 80)	0.379	0.01	0.96	(1, 63)	0.332	0.01
Conscientiousness	0.00	(1, 80)	0.978	0.0	1.47	(1, 63)	0.230	0.02

Table 3.3 Personality facets and headache category: Means, standard errors (whole sample)

	Headache sufferers v controls				Migraine v T-TH			
	Headache (n = 78)		Controls (n = 22)		Migraine (n = 46)		T-TH (n = 32)	
Personality facets	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Neuroticism	**99.35**	**22.99**	**93.545**	**4.72**	**98.087**	**3.48**	**98.625**	**4.17**
n1 Anxiety	18.6	5.2	17.227	1.12	18.065	0.80	18.844	0.96
n2 Angry Hostility	15.35	5.06	14.318	1.12	15.109	0.76	15.750	0.91
n3 Depression	16.43	5.79	14.818	1.24	16.500	0.87	15.688	1.05
n4 Self Consciousness	16.88	5.36	17.182	1.14	16.370	0.82	17.000	0.98
n5 Impulsiveness	19.17	4.28	18.318	0.94	19.652	0.62	18.219	0.75
n6 Vulnerability	12.92	4.73	11.682	1.00	12.391	0.73	13.125	0.87
Extraversion	**117.27**	**17.84**	**118.318**	**3.69**	**116.674**	**2.60**	**117.688**	**3.12**
e1 Warmth	23.387	3.94	23.273	0.88	23.565	0.63	22.719	0.75
e2 Gregariousness	18.51	5.38	17.545	1.14	17.804	0.80	19.281	0.96
e3 Assertiveness	15.61	4.59	16.091	1.06	15.891	0.69	15.594	0.83
e4 Activity	17.28	3.77	17.545	0.86	17.239	0.56	17.438	0.67
e5 Excitement seeking	20.15	5.17	20.545	1.05	19.891	0.77	20.125	0.92
e6 Positive Emotions	22.33	4.53	23.318	0.93	22.283	0.66	22.531	0.79
Openness	**126.95**	**18.75**	**125.455**	**4.01**	**128.935**	**2.75**	**124.938**	**3.30**
o1 Fantasy	20.59	5.17	20.682	1.12	20.065	0.76	21.656	0.91
o2 Aesthetics	20.11	5.56	19.409	1.20	20.457	0.81	19.469	0.98
o3 Feelings	23.68	3.38	23.318	0.76	23.870	0.53	23.313	0.64
o4 Actions	17.09	4.13	16.000	0.93	17.587	0.61	16.406	0.73
o5 Ideas	21.4	6.09	21.864	1.29	21.891	0.91	21.188	1.09
o6 Values	23.61	3.63	24.182	0.77	24.304	0.53	22.906	0.64
Agreeableness	**119.39**	**17.94**	**117.955**	**4.04**	**118.087**	**2.81**	**120.125**	**3.37**
a1 Trust	19.05	4.4	19.045	0.99	19.000	0.68	18.969	0.81
a2 Straightforwardness	19.61	4.94	19.227	1.10	19.174	0.74	19.969	0.89
a3 Altruism	24.15	3.47	23.955	0.77	24.065	0.55	24.125	0.65
a4 Compliance	17.21	4.82	17.636	1.06	16.804	0.74	17.375	0.89
a5 Modesty	19.05	4.99	18.273	1.06	19.326	0.73	18.656	0.88
a6 Tendermindedness	20.4	4.26	19.818	0.89	19.870	0.63	21.031	0.75
Conscientiousness	**111.65**	**17.4**	**116.273**	**4.19**	**114.022**	**2.64**	**110.531**	**3.17**
c1 Competence	20.64	3.51	21.000	0.75	21.478	0.52	19.875	0.62
c2 Order	16.79	4.96	17.955	1.09	16.761	0.73	17.156	0.88
c3 Dutifulness	20.92	3.2	22.364	0.76	21.326	0.49	20.781	0.59
c4 Achievement Striving	18.83	4.72	19.455	1.03	19.609	0.69	18.000	0.83
c5 Self-Discipline	17.03	4.84	18.273	1.10	17.630	0.73	16.750	0.88
c6 Deliberation	16.89	4.61	17.136	1.01	16.304	0.68	17.969	0.81

Table 3.4 Personality facets and headache category: main effects (whole sample)

	Headache sufferers v controls				Migraine v T-TH			
	F	df	*p*	η^2	F	df	*p*	η^2
Neuroticism	**1.17**	**(1, 95)**	**0.282**	**0.01**	**0.01**	**(1, 76)**	**0.921**	**0.00**
n1 Anxiety	1.16	(1, 95)	0.285	0.01	0.38	(1, 76)	0.537	0.01
n2 Angry Hostility	0.65	(1, 95)	0.421	0.01	0.29	(1, 76)	0.590	0.00
n3 Depression	1.29	(1, 95)	0.258	0.01	0.35	(1, 76)	0.553	0.00
n4 Self Consciousness	0.05	(1, 95)	0.816	0.00	0.24	(1, 76)	0.624	0.00
n5 Impulsiveness	0.63	(1, 95)	0.428	0.01	2.17	(1, 76)	0.145	0.03
n6 Vulnerability	1.19	(1, 95)	0.279	0.01	0.42	(1, 76)	0.520	0.01
Extraversion	**0.06**	**(1, 95)**	**0.803**	**0.00**	**0.06**	**(1, 76)**	**0.803**	**0.00**
e1 Warmth	0.01	(1, 95)	0.910	0.00	0.75	(1, 76)	0.391	0.01
e2 Gregariousness	0.55	(1, 95)	0.459	0.01	1.40	(1, 76)	0.241	0.02
e3 Assertiveness	0.16	(1, 95)	0.694	0.00	0.08	(1, 76)	0.785	0.00
e4 Activity	0.07	(1, 95)	0.786	0.00	0.05	(1, 76)	0.821	0.00
e5 Excitement seeking	0.11	(1, 95)	0.740	0.00	0.04	(1, 76)	0.846	0.00
e6 Positive Emotions	0.86	(1, 95)	0.355	0.01	0.06	(1, 76)	0.811	0.00
Openness	**0.11**	**(1, 95)**	**0.744**	**0.00**	**0.87**	**(1, 76)**	**0.355**	**0.01**
o1 Fantasy	0.01	(1, 95)	0.941	0.00	1.82	(1, 76)	0.181	0.02
o2 Aesthetics	0.26	(1, 95)	0.611	0.00	0.60	(1, 76)	0.440	0.01
o3 Feelings	0.17	(1, 95)	0.678	0.00	0.45	(1, 76)	0.503	0.01
o4 Actions	1.07	(1, 95)	0.304	0.01	1.53	(1, 76)	0.220	0.02
o5 Ideas	0.10	(1, 95)	0.752	0.00	0.25	(1, 76)	0.620	0.00
o6 Values	0.42	(1, 95)	0.519	0.00	2.81	(1, 76)	0.098	0.04
Agreeableness	**0.10**	**(1, 95)**	**0.756**	**0.00**	**0.22**	**(1, 76)**	**0.643**	**0.00**
a1 Trust	0.00	(1, 95)	0.994	0.00	0.00	(1, 76)	0.976	0.00
a2 Straightforwardness	0.10	(1, 95)	0.757	0.00	0.47	(1, 76)	0.494	0.01
a3 Altruism	0.05	(1, 95)	0.827	0.00	0.00	(1, 76)	0.944	0.00
a4 Compliance	0.12	(1, 95)	0.725	0.00	0.24	(1, 76)	0.623	0.00
a5 Modesty	0.42	(1, 95)	0.520	0.00	0.34	(1, 76)	0.560	0.00
a6 Tendermindedness	0.33	(1, 95)	0.568	0.00	1.40	(1, 76)	0.240	0.02
Conscientiousness	**0.94**	**(1, 95)**	**0.335**	**0.01**	**0.72**	**(1, 76)**	**0.400**	**0.01**
c1 Competence	0.18	(1, 95)	0.673	0.00	3.92	(1, 76)	0.051	0.05
c2 Order	0.89	(1, 95)	0.349	0.01	0.12	(1, 76)	0.730	0.00
c3 Dutifulness	2.77	(1, 95)	0.099	0.03	0.50	(1, 76)	0.481	0.01
c4 Achievement Striving	0.29	(1, 95)	0.594	0.00	2.24	(1, 76)	0.139	0.03
c5 Self-Discipline	0.99	(1, 95)	0.323	0.01	0.59	(1, 76)	0.445	0.01
c6 Deliberation	0.04	(1, 95)	0.833	0.00	2.49	(1, 76)	0.119	0.03

Aim: To examine the relationship of NEO personality traits to headache induced during the three phases of a laboratory experiment.

3.3 Method

3.3.1 Procedures

Where detailed descriptions have already been provided, these will not be repeated here.

Participants

Group #2: the experimental sub-sample (Table 2.3, p.34).

Measures

1. Personality as assessed by the NEO-PI-R (Section 2.4.2.1, p.43).
2. Headache intensity ratings during experiment: a 10-point Visual Analogue Scale (described in Section 2.4.1.1, p.42)

Experimental design

See Sections 2.2, p.35.

3.3.2 Data analysis

Bivariate correlations were computed for the relationship between headache ratings at each phase of the experiment and the five NEO personality traits.

Multiple regression analyses computed the relationship between headache in each phase of the experiment and the component of each personality trait that is independent of the other personality factors.

3.4 Results

3.4.1 Correlational analyses

As shown in Table 3.5, there were significant correlations between neuroticism and headache before and after (but not during) the task, and these were particularly related to anxiety and depression.

Table 3.5 Correlations between NEO personality traits and headache at each phase of the experiment

	Headache before task	Headache during task	Headache after task
Neuroticism	**0.248***	**0.169**	**0.241***
n1 Anxiety	0.245*	0.145	0.241*
n2 Angry Hostility	0.113	0.123	0.150
n3 Depression	0.310**	0.201	0.340**
n4 Self Consciousness	0.164	0.047	0.103
n5 Impulsivity	0.046	0.087	0.032
n6 Vulnerability	0.144	0.110	0.121
Extraversion	**0.009**	**0.139**	**–0.130**
e1 Warmth	0.127	0.266*	0.011
e2 Gregariousness	–0.006	0.163	–0.116
e3 Assertiveness	0.015	–0.080	–0.065
e4 Activity	0.160	0.267*	0.111
e5 Excitement seeking	–0.086	–0.048	–0.167
e6 Positive Emotionality	–0.141	–0.013	–0.225*
Openness	**–0.108**	**–0.187**	**–0.068**
o1 Fantasy	–0.174	–0.163	–0.209
o2 Aestheticism	–0.064	–0.027	–0.015
o3 Feelings	0.033	–0.079	–0.058
o4 Actions	–0.059	–0.080	–0.014
o5 Ideas	–0.062	–0.114	0.032
o6 Values	–0.108	–0.198	–0.135
Agreeableness	**–0.013**	**0.080**	**–0.008**
a1Trust	–0.021	0.159	–0.031
a2 Straightforwardness	0.047	–0.034	0.056
a3 Altruism	0.201	0.098	0.031
a4 Compliance	–0.029	0.069	–0.043
a5 Modesty	–0.111	–0.033	–0.017
a6 Tendermindedness	–0.080	0.027	0.000
Conscientiousness	**0.009**	**–0.077**	**0.052**
c1 Competence	–0.086	–0.109	–0.045
c2 Order	–0.061	–0.050	0.004
c3 Dutifulness	0.182	0.024	0.161
c4 Achievement striving	0.053	0.186	0.018
c5 Self discipline	–0.007	–0.114	–0.043
c6 Deliberation	–0.060	–0.094	0.019

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed)

3.4.2 Multiple regression analyses

As shown in Table 3.6 and Table 3.7, multiple regression analyses were conducted to determine which traits and their facets may predict headache before, during and after the task. Neuroticism predicted headache intensity before and especially after the task ($p<.05$), particularly its depression facet ($p<.0001$). The extraversion facets of warmth, activity and low 'positive emotionality' were significant predictors of headache – warmth predicted headache before and during the task ($p<.05$), the activity facet predicted headache at all points, especially during the task ($p<.001$) as did low positive emotionality, especially after the task ($p<.01$). Overall, low openness predicted headache during the task ($p<.05$), but none of its facets were significant predictors. Overall, conscientiousness did not predict headache, but its dutifulness facet predicted headache before the task ($p<.05$), while achievement striving ($p<.001$) and low self-discipline ($p<.05$) predicted headache during the task.

Table 3.6 Multiple regression analyses: NEO personality traits and headache intensity before, during and after the task

	Headache before task	Headache during task	Headache after task
R^2	0.079	0.103	0.091
Beta weights in each model			
Neuroticism	0.282*	0.146	0.295*
Extraversion	0.051	0.183	–0.097
Openness	–0.073	–0.237*	–0.001
Agreeableness	0.035	0.122	0.044
Conscientiousness	0.118	0.012	0.151

* Beta weight is significant at the 0.05 level

Table 3.7 Multiple regression analyses: NEO personality facets and headache intensity before, during and after the task

Traits and facets	Headache before task	Headache during task	Headache after task
Neuroticism			
R^2	0.125	0.063	0.190*
Beta weights in each model			
n1 Anxiety	0.184	0.184	0.218
n2 Angry Hostility	-0.004	-0.004	0.015
n3 Depression	0.410*	0.410	0.570***
n4 Self Consciousness	-0.142	-0.142	-0.306*
n5 Impulsivity	-0.077	-0.077	-0.120
n6 Vulnerability	-0.137	-0.137	-0.186

Traits and facets	Headache before task	Headache during task	Headache after task
Extraversion			
R^2	0.144	0.246***	0.164*
Beta weights in each model			
e1 Warmth	0.335*	0.330*	0.252
e2 Gregariousness	-0.115	0.055	-0.138
e3 Assertiveness	-0.051	-0.250*	-0.129
e4 Activity	0.299*	0.447***	0.319*
e5 Excitement seeking	-0.077	-0.117	-0.125
e6 Positive Emotionality	-0.336*	-0.301*	-0.358**
Openness			
R^2	0.048	0.066	0.078
Beta weights in each model			
o1 Fantasy	-0.190	-0.137	-0.222
o2 Aestheticism	-0.022	0.128	0.052
o3 Feelings	0.125	-0.046	0.023
o4 Actions	-0.054	0.012	-0.006
o5 Ideas	0.057	-0.041	0.173
o6 Values	-0.091	-0.200	-0.207
Agreeableness			
R^2	0.073	0.055	0.014
Beta weights in each model			
a1 Trust	-0.044	0.241	-0.075
a2 Straightforwardness	0.091	-0.190	0.122
a3 Altruism	0.237	0.097	0.029
a4 Compliance	-0.063	0.048	-0.083
a5 Modesty	-0.083	0.018	-0.029
a6 Tendermindedness	-0.110	-0.081	0.032
Conscientiousness			
R^2	0.076	0.164*	0.052
Beta weights in each model			
c1 Competence	-0.180	-0.240	-0.119
c2 Order	-0.111	0.023	0.010
c3 Dutifulness	0.258*	0.047	0.231
c4 Achievement striving	0.106	0.516***	0.078
c5 Self discipline	-0.045	-0.380*	-0.170
c6 Deliberation	-0.015	0.017	0.059

* Beta weight is significant at the 0.05 level, ** significant at the .01 level, *** significant at the .001 level.

3.5 Discussion

The aim of these investigations was to assess whether NEO personality traits differ among headache categories and relate to experimentally induced headache in an under-graduate sample of episodic migraine and T-TH participants.

Analyses of variance indicated that personality traits and their facets were similar in migraine, T-TH and controls in this sample. Multiple regression analyses also indicated that in combination, these personality variables explained only a small amount of variance in headache intensity during each phase of the experiment. This may have reflected the small size and composition of this sample, which may have been too homogeneous to adequately distinguish between headache categories. Some studies have, for example, found higher neuroticism scores in arts and humanities students compared with economics and business students (402), and the present sample consisted primarily of female psychology undergraduates.

Also, the predictive value of each trait to headache is limited to the component of that trait which is independent of other personality traits. In this respect, the Big Five personality traits are not entirely independent of each other (403) and appear to have a replicable higher-order structure, with the meta-trait of Plasticity reflecting the shared variance between Extraversion and Openness/Intellect, and the meta-trait of Stability reflecting the shared variance among Neuroticism, Agreeableness, and Conscientiousness. These higher order traits have been theorized to relate to individual differences in the functioning of the dopamine and serotonin systems, respectively (404). This suggests that a somatogenic or biopsychosocial paradigm may be more useful in uncovering relationships between personality and headache than a psychogenic paradigm (discussion below).

Nevertheless, when considered on its own, and consistent with findings in large scale community-based surveys (e.g. 300; 350), neuroticism was associated with headache intensity before and after the task. In the present context, this finding is also consistent with Eysenck's theory that high-N scorers have an easily activated neurological system– i.e. a low threshold to external stimuli (353). They may magnify negative symptoms (405; 406) and tend towards exaggerated harm appraisals which may confer stress vulnerability during threat (407) but which increase pain perception (344). They report more frequent physical illnesses as well as more frequent and severe physical symptoms (261; 408) which may at times be unfounded (i.e. without physiological basis) (409). Greater 'anxiety sensitivity' is also reported in high-N scorers – the tendency to avoid potentially painful

activity and catastrophically label anxiety-related body sensations in the belief that they are a signal of bodily harm or damage (410). Such sensitivity increases interpretive bias and negative pain perception (344; 411) and is related to headache (412).

Furthermore, personality neuroscience investigations, particularly those conducted from a cybernetic perspective, posit that neuroticism reflects individual differences in the sensitivity of defensive distress systems that become active in the face of threat, punishment and uncertainty (413). Uncertainty is innately threatening because it impedes the ability to confidently predict one's goal progress in a given situation, giving rise to anxiety (414). In this respect we saw that the neuroticism facets of proneness to worry ("anxiety") and especially the tendency to experience depressive affect ("depression") were associated with headache before and particularly after the task. Conceivably then, the head shocks, the unfamiliar and isolating environment of a Faraday cage (a steel-lined room to reduce electrical noise) and unpredictable procedures may have been perceived more adversely and raised higher negative affect in those scoring high in neuroticism.

However, why then was neuroticism not associated with headache during the task itself? We would expect neuroticism to be activated by the non-contingent feedback in the stressful task, since greater "feedback-related negativity" was reported in high-N individuals when feedback was ambiguous rather than when such feedback was negative, whereas the opposite was true with low-N individuals (415).

Perhaps therefore the cognitive task in phase 2 acted as a distractor (416), redirecting attention away from threat (407; 417) in high-N individuals. 'Mental" (rather than 'emotional') stressors have been shown to blunt the effects of negative affectivity (418). Thus, the higher pain report in high-N scorers before and after the task may reflect the absence of focused distractions in phases 1 and 3 of the experiment (419). However, in an emotional Stroop task, high trait anxiety individuals were less able than low trait anxiety individuals to shift attention away from the threatening content of anxiety-related words (417). This suggests that high-N individuals may have been less likely than low scorers to be distracted during the cognitive task.

Another possibility is that aspects of the stressful task itself influenced the expression of other FFM personality traits linked with headache, including the 'positive emotionality' and 'activity' facets of extraversion and the conscientiousness facet of "achievement striving", both of which are considered the inverse of neuroticism (420). Thus, the core function of extraversion is posited as sensitivity to reward, enabling the individual to be

energized by goals (413). In fMRI studies, extraversion has been shown to predict neural activation in response to emotionally positive or rewarding stimuli (421). Also, from a cybernetic perspective, the function of conscientiousness may be to facilitate the pursuit of non-immediate goals and rule-based behaviour (413). However, the task itself thwarted any sense of goal progress, possibly predisposing to headache. Thus, individuals with high "Activity" scores need to keep a rapid tempo and vigorous movement and to keep busy while individuals who score high on "achievement striving" have high aspiration levels, are diligent and purposeful and work hard to achieve their goals (323, p.17). This is consistent with early research suggesting that over-striving may be an aspect of personality which contributes to headache (131).

An alternative explanation therefore is that the task may have been stressful for all participants, extinguishing any differences between high and low scorers in neuroticism. Since the mean stressfulness rating of the task was 4.5 out of a possible 7, and only a small amount of variance in headache intensity was explained by personality traits, this seems the more likely explanation.

Study Limitations

A number of factors limit the conclusions to be drawn from this study, the most obvious being the small sample size. The associated low power increases the likelihood of Type II error rates (failure to detect real effects). Given that the middle third of effect sizes in psychology is between r =.2 and .3 (422), and that the average effect size in personality research is been estimated at .21 (423), researchers must ensure that they have the power to detect effects of at least r = .2. To have 80% power to detect a correlation of .2 at $p < .05$ requires a sample of 194 (422). As a result, only strong effects were detected in this study.

Conversely, small samples increase the likelihood of Type I errors (false positives) because of greater sampling variability and decreased precision. Nevertheless, as an exploratory rather than a confirmatory study, future research could use data from this study to select sample sizes able to more confidently test the hypotheses under investigation.

Another limitation is that the sample may have included undiagnosed mood disorders, since depression and anxiety were controlled for only through participant selection (i.e. relying on self-disclosure rather than psychometric testing). Headache frequency was also not measured. Future research should include more stringent checks on the presence of

mood disorders and also examine the relationship of personality and headache frequency, the latter ascertained by means of a headache diary.

Furthermore, this piece of research has implicitly adopted a psychogenic perspective on the relationship of personality and headache, particularly since personality was considered during the stress process only in Study 2. A somatogenic paradigm may be more apposite, which assumes that the relationship between personality and headache is indirect, i.e. occurs via shared underlying factors. The paradigm of biopsychosocial synergism is even more fitting – and more defensible from a stress theory perspective (424). This paradigm assumes that headache and personality are linked via multiple and interacting factors, such as stress appraisal processes, temporary emotional states and physiological reactivity. Investigations examine the social-cognitive processes by which personality traits may influence headache and stress. This paradigm is adopted in Chapter 7 of this thesis.

3.6 Conclusions

NEO personality traits were unrelated to 'usual' headache severity in those with a migraine or T-TH history. Neuroticism was associated with headache intensity before and after but not during a stressful laboratory task. Preliminary results suggest that negative mood may moderate headache during stress, particularly in the absence of distractions, and that the need to keep active and strive toward goal achievement may, when progress is thwarted, predispose to headache. Further research using a biopsychosocial paradigm is needed to investigate further the mechanisms and processes by which personality traits influence headache in migraine and T-TH. But first we will investigate the effect on headache of another distal psychological factor, that of attachment insecurity.

Chapter Four

4

Does attachment anxiety increase vulnerability to headache?

PAPER 1 – DOES ATTACHMENT ANXIETY INCREASE VULNERABILITY TO HEADACHE?

Manuscript details

Published Title:

Does attachment anxiety increase vulnerability to headache?

Authors:

Juanita K. M. Berry, B.A. (Hons) [a]; Peter D Drummond, PhD [a]

Author affiliations:

[a] School of Psychology, Murdoch University, Perth, Western Australia, Australia

Reference:

Berry J.K.M., Drummond P.D. Does attachment anxiety increase vulnerability to headache? *Journal of Psychosomatic Research* (2014) 76(2):113-120. http://dx.doi.org/10.1016/j.jpsychores.2013.11.018

Key words:

migraine; tension-type headache; attachment anxiety; attachment avoidance; psychological stress; personality

Conflict of interest statement:

The authors confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

Abstract

Background. Attachment-related anxiety and avoidance are potentially important aspects of pain experience and management, but have not been investigated in episodic headache sufferers or in relation to experimentally-evoked headache.

Objective. To determine whether adult insecure attachment styles were associated with sensitivity to pain or headache before, during or after stressful mental arithmetic in an episodic migraine and tension-type headache (T-TH) sample.

Methods. Thirty-eight episodic migraine, 28 episodic T-TH and 20 headache-free participants intermittently received a mild electric shock to the forehead before, during and after stressful mental arithmetic.

Results. A preoccupied attachment style and attachment anxiety, but not attachment avoidance, were associated with forehead pain and the intensity of headache before and after, but not during stressful mental arithmetic. These relationships were independent of Five Factor Model personality traits. Neither attachment anxiety nor avoidance was associated with episodic migraine or T-TH.

Conclusions. Anxiously attached individuals may express greater pain or show a stronger attentional bias toward painful sensations than securely attached individuals. However, distraction during psychological stress may override this attentional bias.

4.1 Introduction

The psychophysiological response to stress is one of the most commonly recognised triggers of headache. This link between stress and headache, identified in retrospective case studies and prospective diary studies (22; 26) has been verified in experimental investigations. For example, Cathcart *et al* (28) reported that headache developed in 91% of patients with chronic tension-type headache (T-TH) during an hour-long stressful mental arithmetic task compared with only 4% of healthy controls. Similarly, Stronks *et al* (33) observed that headache developed more frequently in patients with T-TH than in controls or migraine sufferers during stressful mental arithmetic. While the link between stress and headache seems clear, much remains to be learned about contextual and interpersonal vulnerability factors that may contribute to this link. Long-standing clinical observations suggest that relationship distress may play a role in migraine onset. For instance, Marcussen and Wolff (425) proposed that "the migraine headache represents a collapse of a way of dealing with life situations which are stressful to the individual" (p. 255) following accumulated tension and hostility. The neurologist Sacks (426) described a migraine sub-type driven by a chronic life situation in which the person feels caught up in a 'malignant emotional bind' (p. 221).

Bowlby's attachment theory (427-430) provides a theoretical base for examining the influence of interpersonal styles on stress-related headache. Attachment style – a trait-like pattern of relating to family and friends – reflects a mental representation of relationships arising from an individual's close relationship experiences. These styles strongly influence emotional bonds and reactions to social partners, reflect profound differences in sensitivity to social signals of support or conflict, and guide affect regulation and support-seeking in threatening situations (431; 432).

Research during the past two decades has converged on a definition of adult attachment based on two primary dimensions (433).These orthogonal dimensions are thought to reflect attachment-related anxiety, or a model of self, and attachment-related avoidance, or a model of others (324; 434; 435). According to Fraley and Shaver (436), attachment-related anxiety reflects an individual's predisposition toward "anxiety and vigilance concerning rejection and abandonment", whereas the avoidance dimension "corresponds to discomfort with closeness and dependency or a reluctance to be intimate with others" (pp. 142–143).

Four category measures can be derived from these dimensions, based on a high or low score on attachment anxiety or avoidance: Secure (low on both dimensions), Preoccupied (high anxiety, low avoidance), Dismissing (high avoidance, low anxiety) and Fearful (high on both dimensions) (434). The last three categories are deemed insecure styles of attachment.

Theoretical models link attachment orientations to the development and maintenance of chronic pain (e.g. 437; 438). In the *Attachment Diathesis Model of Chronic Pain* (438), attachment insecurity represents a vulnerability factor for both acute and chronic pain (439-441), as a temporary state and a more permanent trait (439; 441; 442). Based on repeated experiences of sensitive, reassuring and comforting responses from primary attachment figures, secure individuals are thought to have acquired self-efficacy in response to threat (443) and optimal regulation of negative emotions when pain is experienced (444). These experiences also influence pain report and pain-signaling to others (63; 445). Driven by a desire to have their attachment needs met, anxiously attached (preoccupied) individuals are thought to actively focus on or exaggerate their pain to elicit comfort and support, whereas avoidantly attached (dismissing) individuals inhibit distress caused by pain in order to minimize dependence on others whose responsiveness they distrust. In community surveys, secure attachment was associated with greater levels of control over pain and lower catastrophizing (437), while attachment anxiety was associated with greater pain intensity (446; 447) and with experiencing pain as highly threatening and distressing (431). In a painful cold-pressor task, attachment anxiety was associated with reduced pain thresholds, lower perceptions of control over pain, more stress and greater catastrophizing (440). Dismissing (and fearful) attachment was associated with less intense pain as well as increased cold pressor endurance (pain tolerance), albeit only in the presence of a known assessor (439). These associations were retained after controlling for measures of neuroticism, NA, age, and social desirability. Neuroticism (negative affectivity) correlates highly with attachment insecurity, so must be controlled for (448; 449).

Attachment-related neurobiological research suggests compromised regulatory functioning of the right orbitofrontal cortex in individuals with an insecure attachment history (450; 451). This area of the brain has been implicated in headache onset (452) and pain sensitivity in migraine sufferers (453). Correlational studies have reported an overrepresentation of insecure attachment styles in a combined migraine, T-TH and chronic daily headache clinic sample compared with controls (243). Attachment insecurity also predicted migraine-related disability (244). However, referral bias (12; 340) and

depression (454; 455) were possible confounds. Likewise, these studies did not control for personality traits which may contribute to pain or headache, including neuroticism – a headache vulnerability factor reliably identified in epidemiological studies (235; 236). Other major personality factors, such as extraversion (sociability) (237-239), low openness to experience (conservatism) (240), aggression-hostility (241) and 'sensation seeking' (242) may also be associated with migraine and/or T-TH.

Hence, it was hypothesised that individuals with an insecure attachment style would be more likely than secure individuals to (i) suffer from migraine or T-TH; and (ii) develop a headache during a stressful laboratory task. We expected that these relationships would be independent of neuroticism.

4.2 Method

4.2.1 Procedures

Where detailed descriptions have already been provided, these will not be repeated here.

Participants

Group #1: Whole sample (Table 2.1, p.33)

Experimental design

See Section 2.2, p.35

4.2.2 Measures

Attachment style was measured by the *Close Relationships Questionnaire* available at http://www.authentichappiness.sas.upenn.edu. This test was uploaded in 2005 and is the same instrument as the *Experiences in Close Relationships-Revised (ECR-R)* (456), modified for online scoring. Participants were either currently in a romantic relationship or had been in one in the past. Each of the 36 items described feelings generally experienced in intimate relationships and participants rated their agreement with each item on a 7-point Likert scale (1= *Strongly Disagree*; 7= *Strongly Agree*). For each person, the scores for all items within each scale were averaged, yielding a category measure – Secure, Preoccupied, Dismissing or Fearful – and two continuous measures: attachment-related *anxiety* (the extent to which people feel insecure about the availability and responsiveness of romantic partners) and attachment-related *avoidance* (the extent to which people are

uncomfortable about depending on others). The ECR-R demonstrates excellent stability (internal consistencies and test-retest reliability coefficients above .90) as well as good convergence and discriminant validity (456; 457).

Personality traits were measured by the NEO-PI-R (458) (Section 2.4.2.1, p.43). Demographic information (age, gender) was collected when participants completed the assessment instruments.

4.2.3 Statistical approach

Preliminary data screening indicated that many of the variables were not normally distributed. Nevertheless, differences among groups were investigated in analyses of variance using untransformed data, as violations of the normality assumption generally do not influence the outcome greatly (459). Questionnaire scores were compared among headache groups (migraine, T-TH, controls) in one-way analyses of variance. Electrically-evoked pain was investigated in Group x Phase (preliminary, final) x Trial (the first 30s shock series, the 2s shock series, the second 30s shock series) analyses of variance. The multivariate solution (Wilks' Lambda) was used for factors with more than two levels. Headache, nausea and distress ratings during the preliminary and post-stressor experimental phases were investigated in similar analyses. Changes in headache and nausea during mental arithmetic were investigated in Group x Block (before arithmetic, and after each subsequent 5-minute block of arithmetic) analyses of variance. Effects of Preoccupied versus Secure Attachment on ratings of electrically-evoked pain, headache, nausea and distress were investigated in a similar series of analyses. Small numbers within the Dismissing and Fearful categories precluded separate analysis of these attachment categories.

The association between continuous questionnaire measures (attachment anxiety, attachment avoidance, Neuroticism, Extraversion, Openness, Agreeableness and Conscientiousness) and mean headache, nausea, pain and distress ratings before and after mental arithmetic was explored in correlation analyses. In addition, whether attachment anxiety predicted headache and pain ratings independently of neuroticism was investigated in hierarchical regression analyses. In these analyses, neuroticism was entered in the first step and attachment anxiety in the second step. Attachment avoidance was not included in these analyses because preliminary analyses indicated no relationship between this attachment style and headache or pain ratings.

Results are presented as the mean ± standard error, and $p<0.05$ was considered to be statistically significant.

4.3 Results

4.3.1 Headache categories

The assessed personality traits and attachment styles were similar in the migraine, T-TH and control groups (Table 4.1 and Table 4.2). Headache and nausea ratings were similar in the migraine, T-TH and control groups during the pre- and post-stressor phases of the experiment (Table 4.2), but increased significantly during stressful mental arithmetic (main effect for Block: for headache F (4, 80) = 40.3, p<0.001; for nausea, F (1, 82) = 167.55, p < .001). During the arithmetic task, moderate or severe headache developed in 43 participants (50%). Another 30 participants (35%) reported mild increases in headache, whereas headache was minimal or decreased in 13 participants (15%) (8 migraine, 2 T-TH, 3 controls). The proportion of participants who developed a moderate or severe headache was similar in the three headache groups (40% with a history of migraine, 54% with T-TH and 65% of controls).

Table 4.1 Migraine, T-TH and controls: numbers in each attachment category

	Migraine	T-TH	Controls	TOTAL
Secure	28	25	16	69
Preoccupied	12	6	5	23
Dismissing	4	3	1	8
Fearful	5	1	0	6

Note: Of the 20 who completed only the first testing session, 13 were classified Secure, 5 Preoccupied, 2 Dismissing and 2 Fearful.

The mental arithmetic task was rated as moderately or extremely stressful by most participants (a mean rating of 4.5 on a 0-7 scale) whereas pain-related distress before and after the task was rated as "mild" (a mean rating of 2.1 on a 0-10 scale). Pain ratings to the electrical stimuli, pain-related distress and task stressfulness ratings were similar in the migraine, T-TH and control groups (Table 4.2).

4.3.2 Attachment insecurity

Both attachment anxiety and neuroticism were associated with pain, headache and pain-related distress before and after but not during stressful mental arithmetic (Table 4.3). Attachment anxiety increased in proportion to neuroticism (r = 0.378, p < .01) and decreased in proportion to conscientiousness (r = -0.206, p <.05). In contrast, attachment avoidance was unrelated any of the personality traits or to symptom or distress ratings at any stage of the experiment. In hierarchical regression analyses, attachment anxiety

predicted pain intensity and pain-related distress before and after stressful mental arithmetic independently of neuroticism (Table 4.4). Neuroticism was associated with headache both before and after the mental arithmetic task, but attachment anxiety did not account for any additional variance.

Table 4.2 Migraine, T-TH and controls: Means, standard deviations and range regarding attachment anxiety, attachment avoidance, headache, pain, nausea and pain-related distress.

	Migraine			T–TH			Headache–free controls		
Dependent variable	**Mean**	**SD**	**Range**	**Mean**	**SD**	**Range**	**Mean**	**SD**	**Range**
Attachment anxiety	3.28	1.12	1.7 –5.4	2.96	0.96	1.2–4.6	3.43	1.03	1.9–5.4
Attachment avoidance	2.94	0.97	1.3 –5.3	2.91	1.05	1.4–5.6	2.74	0.75	1.6–3.9
Neuroticism	96.92	26.06	55–157	95.04	20.75	46–153	98.17	15.79	66–132
Extraversion	115.78	20.34	75–151	119.74	14.18	92–151	118.39	16.75	87–143
Openness	128.67	19.29	94–162	126.00	20.18	83–166	124.89	19.84	83–167
Agreeableness	118.39	19.82	67–157	119.04	19.42	60–149	121.50	19.42	82–159
Conscientiousness	114.97	14.70	87–144	113.74	19.63	73–151	114.61	24.28	61–145
Headache before task	1.34	1.23	0 –6.9	0.94	0.93	0 –4.2	1.04	1.62	0 –3.1
Headache during task	3.08	1.96	0.1–8.2	2.99	2.13	0.2 –8.3	3.06	1.73	0 –6.5
Headache following task	1.82	1.62	0 –7	1.26	1.31	0 –5.3	1.34	1.78	0 –6.2
Pain before task	3.07	1.46	1 –7.4	2.64	1.22	1.1–5.7	3.27	1.25	1.6–6.3
Pain after task	2.64	1.60	0 – 8.9	2.11	1.00	0.8–4.1	2.74	1.45	1.2–6.3
Nausea before task	0.62	1.33	0–5.8	0.31	0.65	0–2.5	0.27	0.76	0–3.3
Nausea during task	3.07	1.87	0–6.3	2.97	1.95	0–7.5	3.25	1.97	0–6.7
Nausea after task	0.82	1.68	0–6.6	0.80	1.52	0–5.3	0.44	0.94	0–3.3
Distress before task	2.24	1.83	0–6.3	1.98	1.55	0–4.7	2.81	2.15	0–8
Distress after task	1.63	1.66	0–6.3	1.44	1.47	0–5.7	1.93	2.04	0–7
Rated stressfulness of task	4.67	1.15	0–7	4.41	1.26	2–7	4.50	1.62	0–7

Table 4.3 Pearson correlations between attachment dimensions, personality traits, headache, pain, distress, nausea and task stressfulness

Trait	Headache before task	Headache during task	Headache after task	Pain before task	Pain after task	Pain distress before task	Pain distress after task	Nausea before task	Nausea during task	Nausea after task	Perceived task stress
Attachment anxiety	**.258***	–.011	**.275****	**.265***	**.308****	**.310****	**.297****	.040	.023	–.028	.117
Attachment avoidance	–.099	–.093	.110	.092	.138	.117	.116	.078	–.128	–.031	.013
Neuroticism	**.248***	.169	**.241***	.108	.151	**.277***	**.240***	.177	.168	**.218***	.149
Extraversion	.009	.139	–.130	.169	.093	.108	–.083	–.077	.121	–.100	.195
Openness	–.108	–.187	–.068	–.162	–.162	–.157	**–.220***	.022	**–.229***	–.138	.043
Agreeableness	–.013	.080	–.008	.045	.033	.121	.014	–.005	.140	–.029	.096
Conscientiousness	.009	–.077	.052	.076	.129	–.064	.141	–.078	–.066	–.042	–.154

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).

Table 4.4 Hierarchical multiple regression models predicting headache and pain ratings from neuroticism and attachment anxiety

	Model 1		Model 2			
	Neuroticism (N)		Neuroticism (N) + Attachment Anxiety (AA)			
	R^2	β (N)	R^2	R^2 change	β (N)	β (AA)
Before stress						
Headache	.062*	.248*	.086*	.024	.188	.166
Pain intensity	.012	.108	.069	.058*	.009	.260*
Pain distress	.077*	.277*	.123**	.046*	.189	.232*
After stress						
Headache	.058*	.241*	.084*	.025	.175	.173
Pain intensity	.023	.151	.084*	.061*	.057	.266*
Pain distress	.057*	.240*	.102*	.044*	.153	.227*

* $p < 0.05$; ** $p < 0.01$

Participants with a preoccupied attachment style reported greater headache and electrically-evoked pain than those with a secure attachment style during the pre- and post-stressor phases of the experiment (main effect for Category: for headache, $F(1, 79) = 8.62$, $p<0.01$; for pain ratings, $F(1, 81) = 13.5$, $p<0.001$) (Figure 4.1 and Figure 4.2). These effects were maintained after controlling for neuroticism in analyses of covariance (main effect for Category: for headache, $F(1, 73) = 6.44$, $p<0.05$; for electrically-evoked pain, $F(1, 75) = 8.90$, $p<0.05$). Similarly, pain-related distress before and after the task was greater in participants with a preoccupied than secure attachment style ($F(1, 81) = 4.57$, $p<.05$) (Figure 4.3). However, this effect decreased after controlling for neuroticism (main effect for Category, $F(1, 75) = 2.13$, not significant). In contrast to these differences before and after the task, increases in headache *during* stressful mental arithmetic were similar in preoccupied and securely attached participants (Figure 4.1).

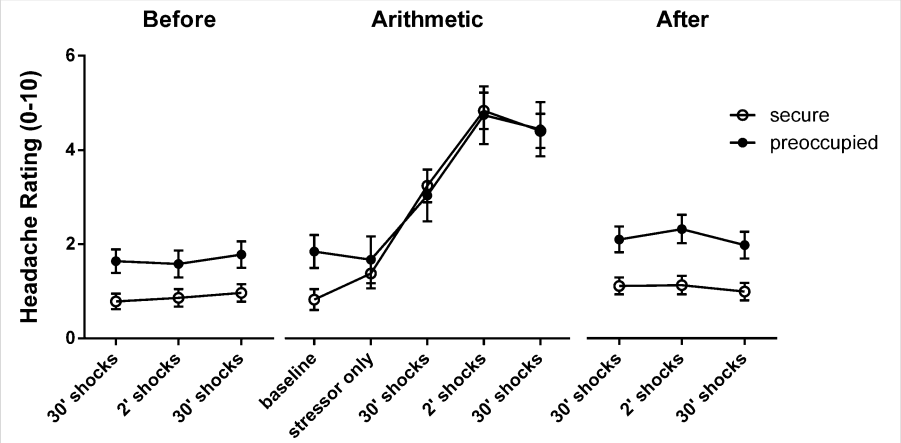


Figure 4.1 Headache ratings (± S.E.) before, during and after stressful mental arithmetic in 57 securely attached participants and 23 preoccupied participants. Headache ratings were greater in preoccupied than securely attached participants before and after arithmetic.

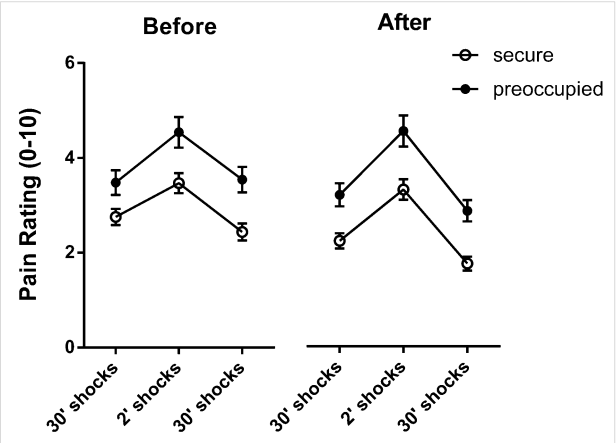


Figure 4.2 Electrically-evoked pain (± S.E.) before, during and after stressful mental arithmetic in 57 securely attached participants and 23 preoccupied participants. Pain ratings were greater in preoccupied than securely attached participants before and after arithmetic.

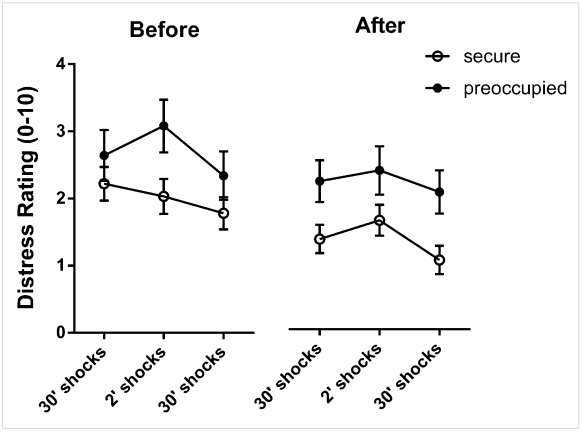


Figure 4.3 Pain-related distress ratings (± S.E.) before, during and after stressful mental arithmetic in 57 securely attached participants and 23 preoccupied participants. Distress ratings were greater in preoccupied than securely attached participants before and after arithmetic.

4.4 Discussion

The aim of this study was to investigate whether the participant's attachment style (secure, insecure) or dimensional score (anxiety or avoidance) was associated with episodic migraine or T-TH and with experimental pain and headache ratings during a headache provocation procedure: (a) before and after a stressful task; and (b) during an unpredictable and uncontrollable mental arithmetic stressor. We also investigated whether the relationship between attachment style and headache was independent of neuroticism.

4.4.1 Differences among headache groups

Our study failed to replicate findings of previous studies (243; 244), in that neither categorical nor continuous measures of attachment anxiety and attachment avoidance, nor Five Factor Model personality traits differed significantly among the migraine, T-TH and control groups. Also, contrary to previous studies (460; 461), migraine and T-TH participants were no more likely than controls to develop a stress-related headache.

With only 22 participants in the control group, our study may have lacked sufficient power to detect differences in attachment style or personality traits among the headache groups. Our findings may also reflect the age and composition of our sample. For example, the mean age of our episodic migraine sample was 25 years compared with a mean age of 36.6 ± 8.8 years for chronic sufferers in a previous clinical study (244). Savi and colleagues (243) combined results for episodic and chronic migraineurs whereas our sample did not include participants with chronic migraine. We also excluded participants with depression or other Axis 1 disorders and those on medication of any kind, whereas participants in previous studies were drawn from headache clinics which also treated depression (243; 244). These disparities might explain why our findings differed from those in clinical studies (340).

Further, in relation to attachment category membership, our sample differed from large-scale population samples, where 59% of adults were classified as secure, 11% as anxious ambivalent and 25% as avoidant, leaving 4.5% 'unclassified'(462). In contrast, in our sample, 65% of participants were classified as secure, 22% of participants had a preoccupied (anxious ambivalent) attachment style and only 8% were dismissing (avoidant). Since attachment avoidance may be particularly under-represented in psychology undergraduate samples (463), our results may generalise only to equivalent university populations.

4.4.2 Attachment styles and stress-induced headache

Compared with secure attachment, those with a preoccupied attachment style and those who scored high on the dimension of attachment anxiety reported heightened pain intensity, pain-related distress and headache. The association between attachment style and pain appeared to be specific, as there was no association with nausea and only partial overlap with neuroticism. The association between attachment anxiety scores and pain intensity and distress was present both before and after the arithmetic task. Similarly, the effect for headache was present before and after but not during the arithmetic stressor.

Why might this be so? Attachment anxiety is elicited most readily in the context of social punishment. This might have featured more strongly before and after than during the stressful task, as there was no opportunity for social interaction during the task itself. In addition, the active support provided before and after the task may have helped secure individuals to cope with pain (464), as their confidence, communication abilities and interpersonal skills enable them to appraise, solicit and utilise appropriate support in difficult situations (465; 466). Although both secure and preoccupied individuals solicit help equally in stressful situations, the help-seeking behaviour of secure individuals is instrumental, dependent on context, the degree of personal help and the emotional neutrality of the task (466). In contrast, help-seeking in preoccupied individuals is directed more toward attaining emotional support (467). Preoccupied individuals reported greater pain-distress than secure individuals, suggesting heightened stress appraisal and/or help-seeking behaviour (468).

The type of support provided by the experimenter may also have functioned to increase pain ratings in preoccupied individuals. Preoccupied individuals show greater attentional bias towards threatening stimuli than secure individuals (469-471) whereas effective support deflects attention away from the sensory/affective qualities of pain (472).

Notwithstanding verbal encouragement, the experimenter asked participants to rate pain, headache, nausea and pain-related distress every three minutes before and after the task, thereby drawing attention to their pain. Paradoxically, this may have augmented pain perception, particularly in preoccupied individuals.

Added to this, the participant's relationship with the support provider – a stranger – may have affected the degree of perceived support (465). Attachment is essentially a relational rather than trait-like construct, and in the ECR-R is measured in relation to a particular individual with whom the person is intimate. The social bonding system is believed to "borrow" the pain system to signal when important relationships are threatened (126). For example, functional imaging studies show increased activity in the insula and dorsal anterior cingulate cortex (ACC) during situations of social threat or reduced social support (473; 474), whereas attenuated ACC activity generally requires the physical or emotional presence or availability (475-477) of a *significant* other. Thus, the higher pain/headache reports in preoccupied individuals before and after the arithmetic task may have resulted from higher stress appraisals in combination with increased pain signalling in the context of pain-focusing interactions from a stranger perceived as unsupportive.

Alternatively, attentional factors may have contributed to the observed differences, irrespective of the presence or absence of experimenter support. Unless attention is *actively* directed elsewhere, painful stimuli will take precedence over competing painless stimuli (478). Before and after the task, the external environment offered relatively few distractions to the incoming pain stimuli. In contrast, the stressful task itself, including its failure manipulations (479), may have functioned to distract attention away from the immediate pain experience. Research by James and Hardardottir supports such a possibility; in an *undistracted* condition, high trait-anxious participants reported lower pain tolerance to a cold pressor task than low trait-anxious participants, but higher pain tolerance during a *distracted* condition (480). It may be that preoccupied individuals are less able to utilise internal distractions from pain than secure individuals, but this is a topic for future research.

In relation to the task itself, we note that our modifications to the arithmetic task, already a recognised stressful procedure in headache research (460; 461), may have "overshot the mark" in terms of stress induction. Even normally headache-free participants developed a headache in response to the uncontrollable, time-pressured arithmetic task when the allostatic load was increased by the sound of a crying baby, electric shocks to the forehead, loud, unpleasant beeping and an ambiguous failure manipulation (481). The

active coping approaches favoured by secure individuals to reduce their stress levels (467) would have been rendered ineffective in this unpredictable and uncontrollable context. However, in this case we might have expected a higher headache report during the stressful task in secure than preoccupied individuals, particularly when they were anxious (482) and unable to access support. Since our stressor was impersonal and unlikely to activate attachment-related cognitions (451; 467; 483), further research using an interpersonal context, e.g., simulated social exclusion (473) or inclusion of a significant other (441) would be interesting. A research design that compares stress-induced headache during active or passive support versus no social support could also help to tease out these competing explanations.

4.5 Conclusions

This study appears to be the first to assess the components of attachment insecurity (anxiety and avoidance) in relation to headache diagnostic category in a non-clinical sample of episodic headache sufferers during headache provocation. Although insecure attachment, especially a preoccupied style, was similar in migraine, T-TH and control groups, it was associated with headache, pain ratings and pain-related distress before and after a cognitive stressor. Our findings suggest that attachment anxiety may contribute to headache, pain, and pain-related distress during a mildly painful procedure when a potential support person is present, attention is being drawn to one's pain, and distractions are unavailable.

Clinical implications

Clinical implications are twofold. First, since attachment anxiety impacts on the patient-physician relationship (468), an understanding of patient attachment style may optimise treatment effectiveness. For example, patients who are most adaptive are those who have strong internal beliefs, strong beliefs in the powers of others such as health professionals and weak beliefs in chance (484) – beliefs more characteristic of securely than insecurely attached persons (485). Patients with poor self-efficacy or low perceived control over their pain – such as insecurely attached persons – are less likely to adhere to a self-management program (486). Actively directing anxiously attached headache sufferers away from the sensory and affective aspects of their headache and towards headache self-efficacy may optimise treatment.

Second, attachment anxiety may contribute to headache onset or maintenance via the quality and type of communications between the headache sufferer and their partner (63; 445). If so, a dyadic, attachment-based psychotherapy approach such as Emotionally Focused Therapy (487; 488) may help in the management of intractable headache and associated distress. To the extent that the headache is associated with attachment anxiety in the context of a distressed relationship, a psycho-educational approach with the couple could identify how responses to complaints of pain may either facilitate or attenuate headache and pain-related distress.

SECTION 3: PROXIMAL INFLUENCES IN HEADACHE

Chapter Five

5

Somatic and neurophysiological responding in headache

5.1 Introduction

The physiological changes accompanying both stress and headache have been extensively researched. Prolonged autonomic responses to, or insufficient recovery from, a stressor may trigger headache both in migraine and T-TH (28; 33). If prolonged, the autonomic or neuroendocrine responses activated to restore homeostasis after a stressful event may interact reciprocally via the trigeminovascular and other systems, involving the intra- and extracranial vasculature and perivascular spaces. Persistence or fatigue of these processes may result in an excess of inflammatory substances implicated in trigeminal sensitization or the exhaustion of pain modulation processes. Certainly, autonomic hyperactivity seems clearly associated with headache activity in other headache syndromes (489). The presence of migraine symptoms such as nausea and vomiting in the prodromal phase and during attacks suggests autonomic imbalance in migraineurs (490), which may interact with pain control centres in the brainstem, e.g. with the baroreceptor reflex (491). However, individuals differ markedly in their psychophysiological responses to standard stress exposures (492). Research is also contradictory in relation to the psychophysiological responding of migraine and T-TH to experimental stressors or the role of autonomic nervous subsystems in the genesis of the pain component of headache (297; 493). Thus, nausea has been shown to potentiate headache (210), as may anxiety and distress (494). Therefore, the purpose of this part of the study was to investigate the temporal relationship between autonomic changes and headache induced by a laboratory stressor in individuals who acquired a stress headache. Those with a history of episodic migraine and tension-type headache (T-TH) were also investigated to determine whether autonomic activation to stress differs between migraine and T-TH compared with healthy controls.

Psychophysiological reactivity was assessed as changes in systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse rate (PR), temporal pulse amplitude (TPA), nociceptive blink reflex (nBR) responses, nausea, cortisol, distress and anxiety before, during and after the task.

5.1.1 Cardiovascular reactivity

The cardiovascular system has become perhaps the most widely studied physiological system in behavioural medicine (495). Nevertheless, data are inconsistent or even contradictory regarding cardiovascular reactivity in migraine and T-TH, the relation of

cardiovascular responses to the pain component of headache and to stressors in headache-prone subjects during stress (297; 493; 496-501).

In 1913, Janeway (502) noted that migraine was common in patients with hypertension. Some subsequent studies reported a positive association (379; 503-505), arising possibly from a direct relationship between hypertension and the rennin-angiotensin system (506-508). However, other studies reported no association (509) or a negative association, e.g. lower SBP levels in migraine patients than controls (47; 510; 511). Diastolic *hypo*tension was also observed in many migraine patients before, during and after a migraine attack (512) – perhaps reflecting the inverse relationship between blood pressure levels and sensitivity to painful stimuli (513) and the mediating role of baroreceptors in this relationship (513-516). In a comprehensive review and summary, Hamed (517) stated that migraine and DBP are generally positively correlated, whereas migraine and SBP are negatively correlated. However, the direction of causation is unclear. Nor does this line of research clarify whether abnormal BP responses occur in migraine and T-TH during or following stress.

A second and hotly debated (e.g.518; 519; 520) area of research relates to the role of cardiovascular responses in the genesis of migraine pain. In Wolff's two-stage vascular theory (131), migraine aura was attributed to a reduction in cerebral and extracranial blood flow (vasoconstriction) and migraine pain to compensatory distension of the cephalic arteries. More recent 'neurogenic' theories attribute migraine pain to chemical activation of meningeal perivascular fibres (88), which lead to (i) peripheral sensitization of these nociceptors to intracranial mechanical stimulation, (ii) central sensitization of second-order trigeminovascular nerves may further sensitize peripheral nociceptors (521). Thus, vasoconstriction-dilatation is implicated in migraine pain, albeit occurring later in the migraine sequence than Wolff proposed (97).

A third line of research has specifically examined cardiovascular abnormalities in migraineurs during stress. Wolff's 'weak link' theory (cited by 522) postulated a functional relationship between stress and vasomotor activity in the temporal artery. From this theory, (i) migraine susceptibility should increase when environmental stress exacerbates the organic vulnerability of the cephalic vasomotor system, (ii) migraineurs should differ from others specifically with regard to their temporal artery blood volume pulse and (iii) these differences should be limited to stress situations. In this respect, various differences have been reported between headache groups and/or non-headache

controls during some stressful conditions (523-529). Sympathetic hypofunction has also been reported in migraine compared with T-TH or controls (530-532), with a recent study concluding that autonomous cardiovascular control is disturbed in episodic and chronic migraine, resulting in enhanced vascular reactivity, whereas cardiac regulation remains largely unchanged (496).

Although such findings point to chronic dysregulation of the vasomotor system of migraineurs relative to non-headache controls, other studies (525; 533-537) have failed to reflect the specific differences between migraine and nonmigraine subjects suggested by the weak-link theory. Similar cardiovascular responses to mental stressors were reported in all headache groups (490; 501), albeit smaller pulse amplitudes of the temporal artery in migraine than controls during a real-life stressor (501). Also contrary to the weak-link theory was a study showing that during stress, heart rate decreased in migraineurs and controls, whereas T-TH patients maintained higher heart rate (490). In another study, cardiovascular sympathetic hypofunction (e.g. reduced heart rate and blood pressure reactivity) was detected in *both* T-TH and migraine (537). In attempting to resolve these contradictions, some studies reported that differences occurred primarily during post-stress adaptation. Thus, Feuerstein reported delayed recovery in migraineurs (538). However, finger BP recovery was delayed after stress and stress-induced pain was associated with less vasoconstriction in T-TH during recovery (490; 527).

Heightened temporal pulse amplitude (TPA) was reported during headache in around one third of migraine subjects, suggesting dilatation as the source of pain (77). TPA was greater in migraineurs than other groups in response to mental arithmetic (538). During the stress period as compared with the non-stress period, stronger blood volume pulse change values were reported in migraine than control subjects, without physiological changes in other physiological response systems (EMG, heart rate) (525; 529). Greater extracranial vasoconstriction was reported in migraine patients during relaxation and recovery from stress, whereas vasoconstriction in T-TH in response to stress did not differ from that of controls (526). However, others report no enhanced temporal artery vasoconstriction in response to stress in migraineurs compared with T-TH (539), nor stress-related peripheral vasoconstriction in migraineurs with regard to digital pulse amplitude (539; 540) or finger temperature (540; 541). These postulated differences were however not always limited to stress responses within the cardiovascular system (540; 542; 543), or to stressful situations in general (536; 540; 544). Overall therefore, research bearing on Wolff's weak-link theory is suggestive but inconclusive.

In the present study it was hypothesised that increased stress would be accompanied by headache which in turn would be accompanied by increases in SBP, DBP, pulse rate and TPA. Such changes would greater in migraineurs than either controls or T-TH participants.

> ***Hypothesis 1.*** *Stress-headache will be accompanied by increased SBP, DBP, pulse rate and TPA and these would be greater in migraine than T-TH participants.*

5.1.2 Cortisol reactivity

Cortisol is a primary homeostatic regulator of the human inflammatory response to injury (545). Pain is itself a stressor (207), and inflamed tissues (e.g. from neurogenic inflammation) produce cytokines which begin a series of activities to repair the tissues, including the release of cortisol – the hallmark of the biological stress response (126). The cytokines activate the HPA axis which produces corticotropin releasing hormone (CRH) which releases adrenocorticotrophic hormone (ACTH) which in turn releases cortisol, which is needed to produce and maintain the glucose levels required during the stress response. The prolonged stress associated with any pain condition can result in higher metabolism of cortisol, expressed as a reduction in cortisol concentration (hypocortisolism). In turn, cortisol deficiency can mean the insufficient inhibition of pro-inflammatory mediators, such as prostaglandins and inflammatory cytokines (546) – aspects of the neurogenic inflammation component of headache. Persistence or fatigue of these responses may alter the brainstem excitation-inhibition balance, increasing trigeminal activation and cortical hyperarousal.

However, results are inconclusive for cortisol changes in relation to stress. The majority of cross-sectional and observational studies have shown no difference between migraine and control groups in baseline serum cortisol levels either during or between migraine attacks (547). However, given that baseline cortisol levels do not exert an anti-inflammatory effect on several pro- and anti-inflammatory mediators of the human immune inflammatory response (545), this finding is not particularly instructive. In a four-day prospective study measuring headache, perceived stress, salivary cortisol and heart rate, only perceived stress was associated with headache (17). Nevertheless, in studies where cortisol levels were repeatedly assessed over a very short time period (e.g. 15-30-minute intervals), the maximum delta increase of serum cortisol and the cortisol peak were significantly higher in migraine patients than in controls (548; 549). That is, headache sufferers may display exaggerated short-term stress-related alterations in cortisol activity over the course of a stressful event (17). In migraineurs, pain recovery correlated negatively with cortisol

change. T-TH patients maintained cortisol secretion during a low-grade cognitive stressor as opposed to the normal circadian decrease seen in controls and migraineurs, but no association was found in T-TH patients between pain and cortisol (543).

In considering the effects of cortisol concentrations on pain, however, and as demonstrated by Yeager (545), there is no dose-response relationship in cortisol regulation of inflammation – depending on concentration and time, cortisol effects can be both pro-*and* anti-inflammatory. Acutely, cortisol has anti-inflammatory effects following a systemic inflammatory stimulus (which would include headache). Normal diurnal concentrations of cortisol (and other glucocorticoids) support the activity of defence mechanisms in a permissive manner, while higher stress-induced concentrations act acutely to suppress inflammation and prevent tissue injury from an excessive or prolonged inflammatory response. However, as cortisol concentrations increase to those associated with systemic stress, a bi-phasic relationship is observed. Peak pro-inflammatory effects of cortisol were observed at the intermediate cortisol concentrations typically observed during major systemic stress (~30-50 μg/dl) – an effect not observed during low (5-10 μg/dl), 'normal' (15-20 μg/dl) or high (70-80 μg/dl) cortisol concentrations (545).

Furthermore, a time interval can increase pro-inflammatory responses: an initial cortisol concentration that acts acutely to suppress systemic inflammation also exerts a delayed (time-dependent) preparatory effect that is stimulatory, augmenting the inflammatory response to a subsequent delayed stimulus. (For extended discussion and supporting evidence see Yeager (545)). That is, chronic stress (or frequent headaches) may exert a delayed effect, augmenting the inflammatory response. Thus, chronic stress (or frequent headaches) may exert a delayed effect, augmenting the inflammatory response and engendering a delayed-type hypersensitivity reaction to acute stress.

An hypothesis that stress-headache results when cortisol levels act on the pain-producing mechanisms of headache by insufficiently inhibiting headache-related pro-inflammatory mediators was investigated by examining cortisol levels during stress-headache. It was further investigated whether cortisol levels differentiate between headache sufferers and controls and between migraine and T-TH.

> ***Hypothesis 2:*** *Cortisol levels during the task will be in the stress-associated range and discriminate between those with vs those without a stress-headache. Cortisol levels will also discriminate between migraine, T-TH and controls.*

5.1.3 Trigeminal excitation/sensitization

Activation of pain-coding trigeminovascular afferents and sensitization of brainstem trigeminal nuclei play a significant role in primary headaches (550). Many cranial nerves have general somatic afferent fibres which terminate in the trigeminal spinal nucleus regardless of the nerve they follow in the head (110). Thus, measurement of activity at brainstem level offers a way of ascertaining neuronal activity in deeper cranial structures. The spinal trigeminal nucleus is also important on the sensory side of many cranial reflex pathways: abnormal central interpretation of normal sensory input in the trigeminal sensory system (551) can trigger perivascular release of vasoactive substances causing sensitization of trigeminal afferents, vasodilatation and migraine pain (97).

At brainstem level, sensitization can be measured non-invasively by the blink reflex (BR), a physiological, protective trigeminofacial reflex aimed at facilitating eyelid closure in response to a threatening and potentially harmful stimulus (552). Early BR technology stimulated the deeper Aβ fibres in addition to the nociceptive-specific Aδ fibres. A later development, the nociceptive Blink Reflex (nBR) elicits the BR by means of a special concentric electrode with high current density at low current intensities, which limits depolarization to the superficial layer of the dermis containing Aδ fibres. It is thus considered a more sensitive marker than the BR for the functional state of the trigeminal nociceptive system (317; 320), and is used to test for the role of peripheral and central sensitization in migraine and T-TH (320; 321).

The classical BR has three components: an early, ipsilateral, pontine R1, with an onset latency of 11 ms, and two bilateral medullary components, the R2 and R3. The R2, with an onset latency of 33 ms, is probably mediated by inter-neurons in the caudal part of the spinal trigeminal nucleus while the R3, possibly part of the startle reaction (314), has an onset latency of 84ms (310; 311). The R2 reflex offers a way of assessing the excitability of the brainstem reticular formation and cortico-reticular drive (552) and early BR studies suggested that excitability of the trigeminal nuclei is increased in migraineurs relative to controls (309). In contrast to the BR, the nBR measures only the R2 reflex (315; 317).

The R2 provides a measure of habituation, the response decrement resulting from repeated stimulation (553), which is considered the eventual outcome of the opposing forces of excitation (facilitation/sensitization) and inhibition (554). If inhibitory processes fail or excitation is excessive, then habituation should be reduced. Incapacity to

progressively reduce pain-related responses under repetitive stimulation (555) may favour mechanisms of central sensitisation (107).

Facilitation of trigeminal nociception is indicated in migraine, predominantly on the headache side (320). Various studies using the BR have suggested that migraineurs show increased excitability of the trigeminal nuclei, in particular the *trigeminal nucleus caudalis,* TNC (e.g. 4; 556; 557). Lack of habituation of the nociceptive blink reflex (nBR) during stimulus repetition, despite an initial normal or low response amplitude, is a functional, possibly genetically determined, hallmark of the migrainous brain between attacks (4; 558). Sensitization of the trigeminal system is more marked on the symptomatic side of patients with unilateral pain, probably as a consequence of the recurrent activation of the trigeminal pain pathway on the affected side (559).

The R2 latency. Onset latencies of R2 depend on stimulus intensity (560), although not for current intensities higher than 2 mA (317). Using the R2 latency, deficient R2 habituation during stimulus repetition was reported in migraineurs (561; 562), although normal R2 habituation was also reported in migraineurs during an attack, which was considered to reflect ictal sensitization of trigeminal second order neurons (563). Further studies identified that habituation was reduced interictally in migraine patients (321), specifically in the prodromal period (564). Some investigators have reported longer mean onset R2 latencies in migraineurs than controls (565), while others reported no latency differences between migraine, T-TH and controls (556) at least during the interictal period (566). In contrast, Kaube and colleagues observed shortened R2 onset latencies during an acute migraine attack on the headache rather than the non-headache side, when compared with the headache-free interval. Drug treatment (parallel to pain relief) also increased the onset latencies (41). Shorter R2 latencies were also observed in migraine patients with frequent attacks compared with healthy controls (567). Changes in R2 latency are considered to result from abnormal synaptic transmission in the brainstem (566) and acute migraine attacks to involve temporary sensitisation of central trigeminal neurons (317).

R2 Area Under the Curve. The R2 AUC increases during a migraine attack, particularly on the affected side (41) and is reduced interictally in migraineurs compared with healthy controls, suggesting interictal hypo-excitability of spinal interneurons (321). In support of this, reduced interictal habituation (measured as the percentage AUC decrease in 10 consecutive blocks of 5 average rectified responses) was found in migraine-without-aura patients and in volunteers with a family history of migraine, compared to those without such history (40). Also, compared with healthy controls, chronic T-TH

patients had significantly lower normalized R2 AUC values on the left (stimulated) side (568). A slight increase of R2 (and R3) recovery in migraine patients following a preconditioning stimulus was attributed to trigeminal hyperexcitability persisting after the last attack (563); this stimulation of trigeminal nociceptors continues during the interictal period (569). R2 recovery was found to be significantly increased on both sides in both episodic and chronic migraine compared with controls (566). Changes in the R2 response area are believed to reflect impairment in central inhibitory mechanisms (552), particularly dysfunction of diffuse noxious inhibitory control (DNIC) mechanisms (570).

> ***Hypothesis 3.*** *If stress headache is the result of the failure of pain inhibitory processes, then the stress-headache group and migraine v T-TH should display more frequent R2 blinks, shorter R2 latencies and increased R2 AUC than those without headache.*

5.2 Method

5.2.1 Procedures

Where detailed descriptions have already been provided, these will not be repeated here.

Participants

Group #2: Experimental subsample (Table 2.3, p.34).

Apparatus and experimental procedures

See Section 2.2, p.35 and Figure 5.1 below.

5.2.2 Measures

The measures have been described in more detail earlier in the thesis. The specific measures used are as follows:

1. Headache and nausea self-report – 10-point VAS ratings taken during the experiment (Section 2.4.1.1, p. 42).
2. Blood pressure and pulse rate – (Section 2.3.1, p.39)
3. Temporal pulse amplitude – (Section 2.3.2, p.39)
4. Salivary cortisol – (Section 2.3.3, p.40)
5. Nociceptive blink reflexes – (Section 2.3.4, p.40)

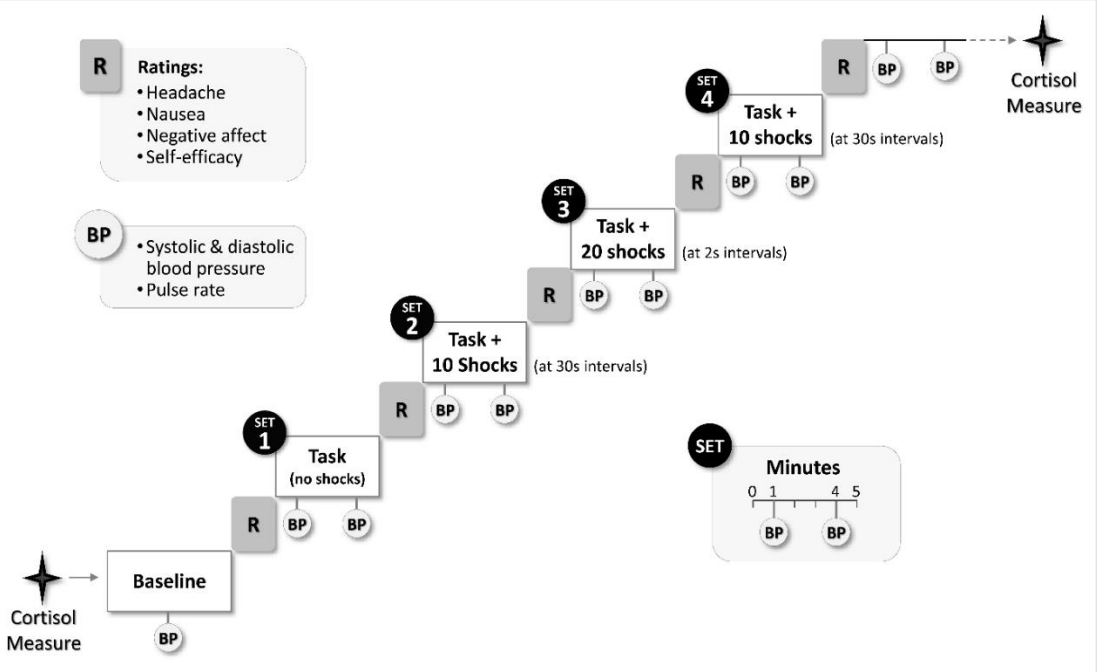


Figure 5.1 Sequence of procedures and measurement points during the stressful arithmetic task

5.2.3 Data analysis

Since previous research has indicated differences between migraine and T-TH, and between migraine/T-TH and controls, a series of planned contrasts compared headache sufferers with controls, and migraine with T-TH, in relation to the dependent variables. Repeated measures ANOVAs were used to investigate specific interactions between each headache category planned contrast at selected time points within the experiment for headache and nausea during and immediately following each consecutive shock set: in phases 1 and 3, the relation of each planned contrast was investigated for each block of stimuli: Pain-related distress during the shocks was rated at three points in Phase 1: after Set 1 (trials 1-10), Set 2 (Trials 1-20) and Set 3 (Trials 1-10). Pain measures were taken at each of four points – the sum of ratings for the first five trials in Set 1, the second five trials in Set 1, the first five trials in Set 3 and the second five trials in Set 3 (Sets 1 an 3 each consisted of 30s ISI shocks and pain ratings were taken immediately after each shock).

ANOVA was employed as it is fairly robust to violations of normality and permits investigation of interactions among factors. Significant multivariate effects were investigated in univariate analyses of variance with Greenhouse-Geisser corrections for violation of the sphericity assumption, followed by examination of simple main effects.

Repeated measures ANOVAs were used also to investigate differences between those who acquired a mild headache (rating < 4) during the stressful maths task (Phase 2 of

experiment) and those who developed a moderate or intense headache (rating > 4). Seven participants who already reported a headache at the outset of the task were excluded from this analysis. Significant interactions were investigated by computing t-tests between groups at each time point during the stressful task. Insufficient sample sizes precluded separate analyses on those within each headache category who acquired a stress headache.

Finally, repeated measures ANOVAs were used across the course of the experiment to investigate headache and the physiological variables shown in Table 5.1.

Table 5.1 Measures for each physiological variable

Variable	Measures
Vascular measures	*Percentage pulse amplitude changes from baseline *Systolic and diastolic blood pressure readings taken at Minutes 1 and 4 throughout the three phases of the experiment *Pulse rate readings at Minutes 1 and 4 throughout the three phases of the experiment.
Cortisol levels	4 measures: Upon entry, and at end of each phase (1–3) of experiment
Nociceptive blink reflex (nBR)	*Number of R2 blinks within the R2 window (27 –87 ms) *R2 latency (distance within the R2 window from stimulus onset to beginning of blink); *R2 Area Under the Curve (average amplitude of R2 reflex response within R2 window);

Analyses were run using IBM SPSS version 24. All tests of statistical significance were two-tailed. Results are presented as the mean ± standard error and $p < .05$ was considered statistically significant.

For blink reflex measures, the electromyograph waveform was filtered to remove 50 Hz electrical noise and frequencies below 10 Hz. For each sweep, 150 ms of the post-stimulus period were collected and filtered off-line. In each phase, ten responses were rectified and averaged for each of the two 30s ISI blocks, and 20 responses for each 2s ISI block. Three aspects of the R2 reflex were quantified: (i) the number of R2 reflex blinks (a measure of response strength); (ii) response latency – distance from the stimulus point to reflex response (a measure of response speed); (iii) the R2 area under the rectified curve – the response area between 27 and 87 ms after stimulus onset (the R2 window) (560). The R2 AUC provides a measure of the global EMG activity generated during the R2 reflex. As the distractions during each of the 30s ISI blocks could potentially interfere with habituation processes, habituation was assessed by changes across the 20 stimuli in the 2s ISI. Detailed procedures for calculation are described in Appendix D, p.306.

5.2.4 Stress-headache as the failure of pain-inhibitory processes

An hypothesis that stress headache results from the failure of pain-inhibitory processes was investigated in two ways:

1. Pain ratings to the electrical stimuli were compared at different time points. An increase in pain ratings during the pre-stressor phase of the experiment would indicate whether habituation occurred differentially in migraineurs compared with controls and T-TH. To determine the effect of the stressful task *per se* on headache (rather than the shocks administered during the baseline phase measures), seven participants who reported a headache level ≥ 4 were excluded from analysis. The remaining participants formed two groups by summing headache ratings across Phase 2 of the experiment (the mental arithmetic task), assigning those with a headache rating >4 into the stress-headache group and those with a rating <4 into the headache-free group.
2. R2 reflex responses were compared across the three planned contrasts (stress-headache vs low/no headache, headache sufferers v controls, migraine v T-TH) to assess the relative effects of repetitive stimulation in the sets of 30-s ISI and 2-s ISI shocks in each group. In accord with previous research, failure of inhibitory processes would be accompanied by more frequent R2 reflex blinks, shorter R2 latencies and/or increased R2 AUC in the stress-headache (v headache-free), headache sufferers (v controls) and migraine (v T-TH groups).

5.3 Results

HEADACHE IS PROVOKED BY A STRESSFUL COGNITIVE TASK

5.3.1 Headache: all participants

As shown in Table 5.2, headache increased in all participants during the stressful task (F (1,84) = 87.9, p<.001), and decreased post-task (F (1,84) = 53.8, p <.001).

Table 5.2 All participants and headache in each experimental phase: Means, standard errors and effects

Experimental Phase	Mean	SE		
Baseline (Phase 1)	1.14	0.13		
Stressful task (Phase 2)	3.07	0.21		
Post-task (Phase 3)	1.54	0.17		
All effects	***F***	***df***	***p***	***η2***
Phase	63.4	(1.44, 120.9)[G]	**<.001**	0.43
Level 1 v Level2	87.9	(1,84)	**<.001**	0.51
Level 2 v Level 3	53.8	(1,84)	**<.001**	0.39

[G] = Greenhouse Geisser correction

5.3.2 Experimentally-provoked headache ("stress-headache")

For comparison purposes, a stress-headache group (53% of participants) with headache ratings ≥4 during the stressful task was formed. As shown in Table 5.3, headache ratings in this group were also significantly higher pre- and post-task than in the mild headache group (F(1.56, 129.5) = 38.64, p <.001, Greenhouse Geisser correction).

Table 5.3 Headache in migraine, T-TH and controls across the three phases of the experiment; means, standard errors, all effects

	No/low headache		Stress headache	
Phase of experiment	**Mean**	**SE**	**Mean**	**SE**
2	0.73	0.19	1.50	0.18
Stressful task (Phase 2)	1.34	0.17	4.62	0.16
Post-task (Phase 3)	0.85	0.23	2.16	0.22

	Stress headache v no/low headache			
All effects	*F*	*df*	*p*	*η2*
Phase:	84.69	(1.56, 129.5)[G]	**<.001**	0.51
Between group:	73.40	(1,83)	**<.001**	0.47
Phase*Group	38.64	(1.56, 129.5)[G]	**<.001**	0.32
Level 1 v Level 2	65.72	(1,83)	**<.001**	0.44
Level 2 v Level 3	30.10	(1,83)	**<.001**	0.27

Since other symptom measures were also higher in Phase 1, repeated measures ANOVAs were utilised to determine whether baseline symptom measures predicted headache in Phase 2. As shown in Table 5.4, headache during the stressful task (stage 2 of the experiment) was predicted by higher headache, nausea, distress and pain ratings in Phase 1.

Table 5.4 Baseline (Phase 1) ratings of headache, nausea, distress and pain in relation to the development of stress-headache in Phase 2 Ratings were taken during or immediately after each 30-second interstimulus interval (30-sec ISI) or 2-second interstimulus interval (2sec ISI) shock series

	No/low headache		Stress-headache	
Symptom	**Mean**	**SE**	**Mean**	**SE**
Headache				
Before Set 1	.60	.186	.934	.191
Set 1 30s ISI shocks	.525	.154	1.079	.158
Set 2 2s ISI shocks	.750	.176	.895	.181
Set 3 30s ISI shocks	.675	.155	1.145	.159
Nausea				
Before Set 1	.125	.130	.605	.133
Set 1 30s ISI shocks	.050	.156	.658	.161
Set 2 2s ISI shocks	.125	.166	.658	.170
Set 3 30s ISI shocks	.213	.186	.842	.191
Distress				
Before Set 1	.850	.218	1.079	.224
Set 1 30s ISI shocks	1.825	.303	2.895	.311
Set 2 2s ISI shocks	1.625	.289	2.868	.297
Set 3 30s ISI shocks	1.338	.257	2.408	.264
Pain				
Set 1 (30s) Trials 1-5	2.768	.205	3.295	.210
Set 1 (30s) Trials 6-10	2.430	.188	3.261	.193
Set 2 (2s ISI shocks)	2.704	.177	3.535	.181
Set 3 (30s) Trials 1-5	2.518	.193	3.245	.198
Set 3 (30s) Trials 6-10	2.210	.193	3.039	.198

Group and interaction effects	***F***	***df***	***p***	***η2***
Headache				
Group main effect	4.215	(1,76)	**.044**	.053
Time*Group	.968 [G]	(2,165)	.388	.013
Nausea				
Group main effect	7.709	(1,76)	**.007**	.092
Time*Group	.294 [G]	(2,158)	.754	.004
Distress				
Group main effect	9.333	(1,76)	**.003**	.109
Time*Group	2.566 [G]	(2,166)	.075	.033
Pain (30s ISI shocks)				
Group main effect,	8.408	(1,76)	**.005**	.100
Time*Group	1.039 [G]	(2,162)	.350	.013
Pain (Shock sets 1,2 and 3)				
Group main effect	10.778	(1,76)	**.002**	.124
Time*Group	1.031 [G]	(1,106)	.337	.013

[G] = Greenhouse Geisser correction

5.3.3 Headache in migraine, T-TH and controls

As shown in Table 5.5, headache levels in all three phases were similar in migraine, T-TH and control groups.

Table 5.5 Headache in migraine, T-TH and controls across the three phases of the experiment: Means, standard errors and effects

Experimental Phase	Migraine		T-TH		Controls		Headache sufferers	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Baseline (Phase 1)	1.34	0.18	0.95	0.21	1.02	0.27	1.18	0.15
Stressful task (Phase 2)	3.08	0.33	3.00	0.39	3.13	0.43	3.06	0.25
Post-task (Phase 3)	1.86	0.25	1.29	0.29	1.30	0.35	1.62	0.20

All effects	Migraine v T-TH				Headache sufferers v controls			
	F	*df*	*p*	*ŋ2*	*F*	*df*	*p*	*ŋ2*
Phase	44.58	(1.48,94.5) [G]	**<.001**	0.41	50.70	(1.44, 119.5) [G]	**<.001**	0.38
Between Group	1.19	(1, 64)	0.280	0.02	0.18	(1, 83)	0.677	0.00
Phase*Group	0.70	(1.48,94.5) [G]	0.459	0.01	0.43	(1.44,119.5) [G]	0.585	0.01
Level 1 v Level2	0.40	(1,64)	0.528	0.01	0.23	(1,83)	0.633	0.00
Level 2 v Level 3	1.07	(1,64)	0.304	0.02	0.64	(1,83)	0.425	0.01

[G] = Greenhouse Geisser correction

CARDIOVASCULAR RESPONSES IN STRESS-HEADACHE, MIGRAINE, T-TH & CONTROLS

5.3.4 Cardiovascular responses across experiment

Blood pressure and pulse rate were measured across all phases of the experiment and TPA was measured before and during the stressful task.

5.3.4.1 Cardiovascular measures: all participants

In all participants, as shown in Figure 5.2 & Table 5.6, blood pressure and pulse rate were elevated during the stressful task compared with baseline or post-task phases; **SBP** ($F(1,88) = 52.68$, $p < .001$), **DBP** ($F(1,88) = 82.44$, $p < .001$), **pulse rate** ($F(1,86) = 20.47$, $p < .001$). Post-task declines occurred in SBP ($F(2,88) = 52.57$, $p < .001$), DBP ($F(1,88) = 37.82$, $p < .001$) and pulse rate ($F(1,86) = 29.06$, $p < .001$), although by the end of the experiment DBP was still above baseline levels ($F(1,88) = 19.7$, $p < .001$).

Temporal pulse amplitude (TPA) also increased overall 16.45% from the baseline measure taken ~1 minute before the task to the fourth minute of the task ($F(1, 74) = 23.4$, $p < .001$). By 22 minutes into the stressful task however, TPA had declined to a non-significant 7.3% above the baseline measure (Table 5.7).

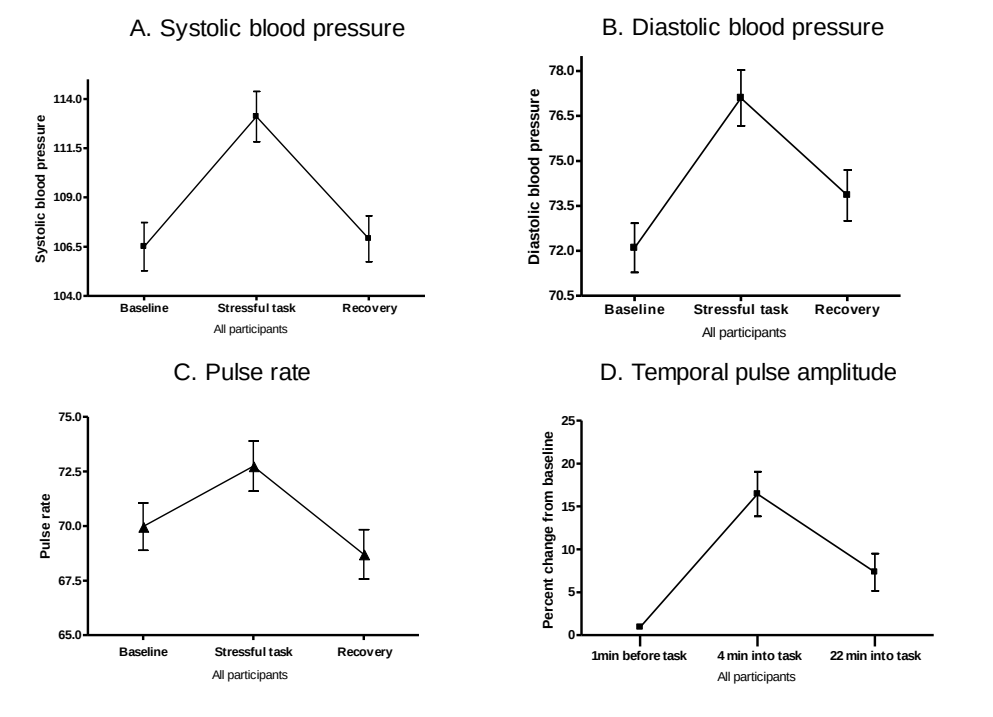


Figure 5.2 Increases (±SEM) in systolic and diastolic blood pressure, pulse rate and temporal pulse amplitude (TPA) across the three phases of the experiment. Differences between baseline and phase 2 measures are significant in all cases, differences between baseline and recovery phases are significant in the case of DBP, while differences across the stressful task are significant in the case of TPA.

Table 5.6 All participants: Blood pressure and pulse rate across experiment: means and standard errors, all effects

	SBP		DBP		Pulse rate	
Phase of experiment	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**
Baseline (Phase 1)	106.55	1.23	72.09	0.82	69.97	1.08
Stressful task (Phase 2)	113.11	1.28	77.08	0.93	72.74	1.15
Post-task (Phase 3)	106.94	1.17	73.86	0.86	68.71	1.13

	All participants			
Main and interaction effects	**F**	**df**	***p***	**η_p^2**
Systolic Blood Pressure				
Phase	44.0	(2,178)	**<.001**	0.33
Contrasts				
Level 1 v Level 2	52.68	(1,88)	**<.001**	0.37
Level 2 v Level 3	52.57	(1,88)	**<.001**	0.37
Diastolic Blood Pressure				
Phase	52.26	(1.8,155.8)[G]	**<.001**	0.37
Contrasts				
Level 1 v Level 2	82.44	(1,88)	**<.001**	0.48
Level 2 v Level 3	37.82	(1,88)	**<.001**	0.30
Pulse rate				
Phase	20.38	(1.8,153.3)[G]	**<.001**	0.19
Contrasts				
Level 1 v Level 2	20.47	(1,86)	**<.001**	0.19
Level 2 v Level 3	29.06	(1,86)	**<.001**	0.25

Table 5.7 All participants: Temporal pulse amplitude during stressful task: means, standard errors and effects

Time of testing	**Mean**	**SE**
~1min prior to task (baseline)	0.92	0.07
During Stressful Task		
At start of task (~4 min)	1.02	0.07
At end of task (~22 min)	0.95	0.07
Mean PA during task	0.98	0.07
Percent change from baseline to 4 min into task	16.45	2.59
Percent change from baseline to 22 min into task	7.33	2.17

Main and interaction effects	***F***	***df***	***p***	***η2***
Phase (all participants)	11.24	(1.6,120.1)[G]	**<.001**	0.13
Percent change from baseline to 4 min into task	23.4	(1,74)	**<.001**	0.24
Percent change from baseline to 22 min into task	0.029	(1,74)	.866	0.00

[G] = Greenhouse Geisser correction

5.3.4.2 Stress headache: cardiovascular responses

During the task, SBP, DBP, pulse rate and TPA rose equally in those with and those without stress-headache and also declined equally post-task (Figure 5.3, Table 5.8 and Table 5.9).

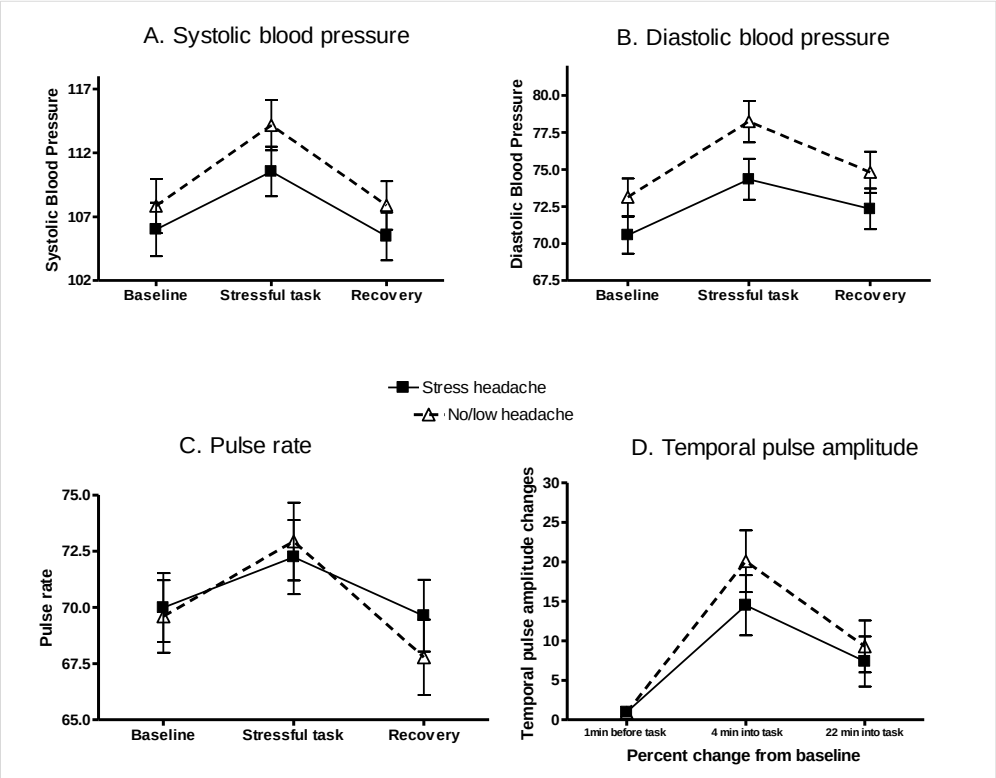


Figure 5.3 Means and standard errors for SBP, DBP, pulse rate and temporal pulse amplitude percent changes in those with vs without a stress headache.

Table 5.8 Stress headache: Blood pressure, pulse rate across experiment: means and standard errors, effects

	No/low headache		Stress headache	
Phase of experiment	**Mean**	**SE**	**Mean**	**SE**
Systolic Blood Pressure				
Baseline (Phase 1)	107.26	1.85	105.95	1.74
Stressful task (Phase 2)	113.44	1.86	111.57	1.75
Post-task (Phase 3)	107.10	1.74	106.48	1.64
Diastolic Blood Pressure				
Baseline (Phase 1)	107.26	1.85	105.95	1.74
Stressful task (Phase 2)	113.44	1.86	111.57	1.75
Post-task (Phase 3)	107.10	1.74	106.48	1.64
Pulse rate				
Baseline (Phase 1)	69.60	1.61	69.99	1.53
Stressful task (Phase 2)	72.93	1.73	72.24	1.65
Post-task (Phase 3)	67.78	1.68	69.63	1.60

Table 5.8 (continued)

Main and interaction effects	Stress headache v low/no headache			
	F	***df***	***p***	***ηp2***
Systolic Blood Pressure				
Phase	51.7	(3.8,314.8)[G]	0.269	0.02
Contrasts				
Level 1 v Level 2	35.85	(1,87)	**<.001**	0.29
Level 2 v Level 3	36.55	(1,87)	**<.001**	0.30
Group (main effect)	0.28	(1,83)	.595	0.00
Phase*Group	0.45	(2,166)	.638	0.00
Contrasts				
Level 1 v Level 2	0.15	(1,83)	.699	0.00
Level 2 v Level 3	0.81	(1,83)	.370	0.01
Diastolic Blood Pressure				
Phase	48.09	(1.8,152.4)[G]	**<.001**	0.37
Contrasts				
Level 1 v Level 2	77.54	(1,83)	**<.001**	0.48
Level 2 v Level 3	33.80	(1,83)	**<.001**	0.29
Group (main effect)	1.02	(1,83)	.315	0.01
Phase*Group	1.03	(1.8,152.4)[G]	.355	0.01
Contrasts				
Level 1 v Level 2	0.61	(1,83)	.437	0.01
Level 2 v Level 3	1.90	(1,83)	.172	0.02
Pulse rate				
Phase	19.29	(1.8,147.4)[G]	**<.001**	0.19
Contrasts				
Level 1 v Level 2	20.91	(1,82)	**<.001**	0.20
Level 2 v Level 3	27.30	(1,82)	**<.001**	0.25
Group (main effect)	0.06	(1,82)	.814	0.00
Phase*Group	1.94	(1.8,147.4)[G]	.152	0.02
Contrasts				
Level 1 v Level 2	0.78	(1,82)	.381	0.01
Level 2 v Level 3	2.90	(1,82)	.092	0.03

[G] = Greenhouse Geisser correction

Table 5.9 Stress headache: Temporal pulse amplitude during stressful task: means, standard errors, all effects

	No/low headache (n = 39)		Stress headache (n = 42)	
Time of testing	**Mean**	**SE**	**Mean**	**SE**
Baseline (≈1 min prior to task)	0.89	0.11	0.97	0.11
During stressful task				
At start of task	1.01	0.11	1.05	0.10
At end of task	0.93	0.10	0.99	0.10
Mean PA during task	0.97	0.10	1.02	0.10
Percent change from baseline to 4 min into task	20.08	3.91	14.49	3.80
Percent change from baseline to 22 min into task	9.29	3.27	7.39	3.18

	Stress headache vs no/low headache			
Main and Interaction Effects	***F***	***df***	***p***	η_p^2
Baseline (≈1min prior to task)	0.26	(1,68)	.611	0.00
During stressful task				
At start of task	0.07	(1,68)	.797	0.00
At end of task	0.19	(1,68)	.668	0.00
Mean PA during task	0.12	(1,68)	.731	0.00
Percent change from baseline to 4 min into task	1.05	(1,68)	.309	0.02
Percent change from baseline to 22 min into task	0.17	(1,68)	.678	0.00
Time*Group	0.84	(1,68)	.364	0.01

5.3.4.3 Migraine, T-TH and controls: cardiovascular responses

In repeated measures ANOVA, SBP, DBP and pulse rates were similar in migraine, T-TH and controls. However, and contrary to predictions, percentage TPA changes were *lower* in headache sufferers than controls between 4 and 22 minutes of the stressful task ($F(1,73) = 6.35$, $p < .01$.) (phase*group interaction, $F(1,73) = 4.0$, $p < .05$). Results are diagrammed in Figure 5.4 (left-hand column). Table 5.10 and Table 5.11.

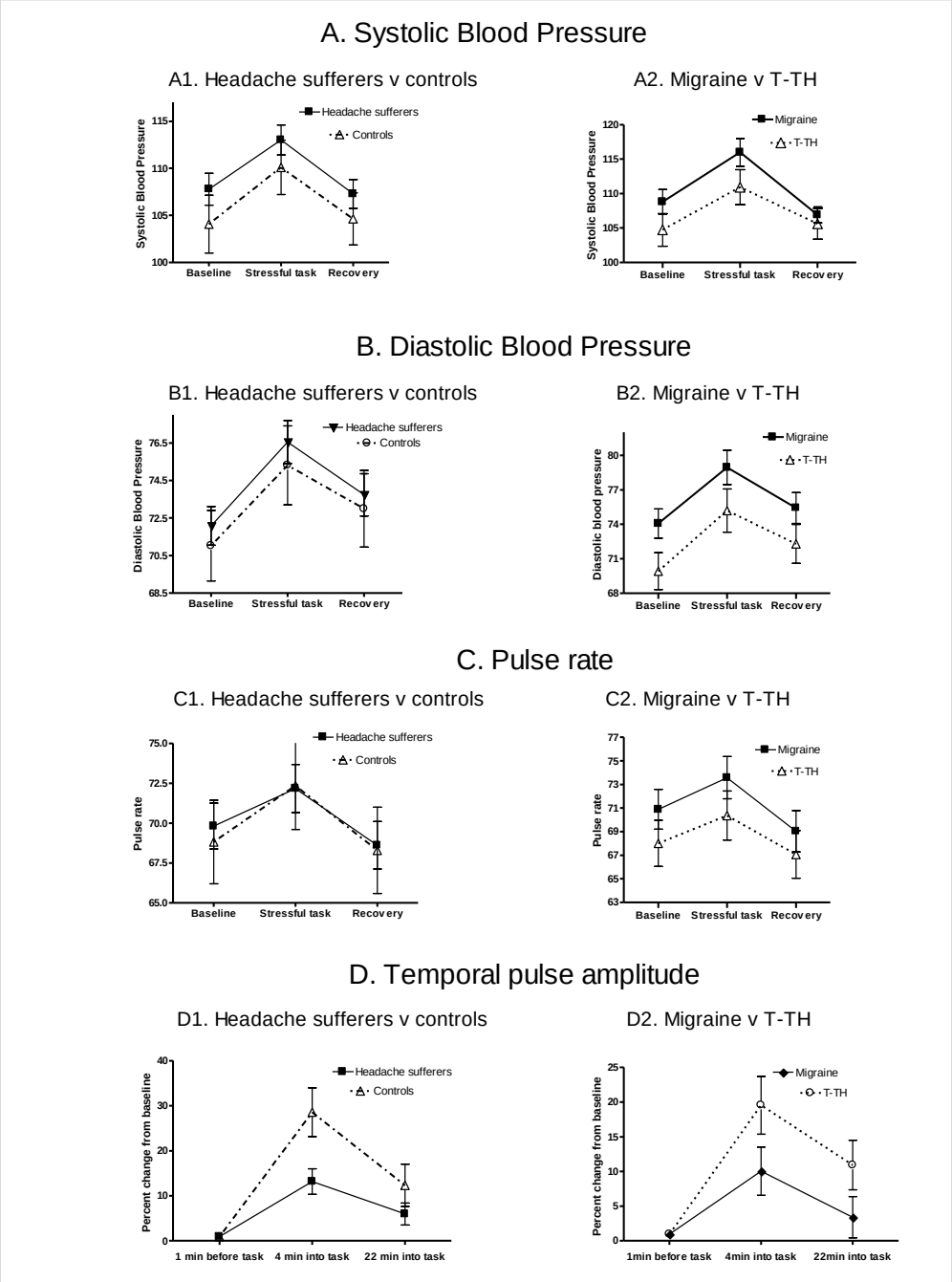


Figure 5.4 Vasomotor changes across experiment. (A1) SBP in headache sufferers vs controls, (A2) SBP in migraine v T-TH, (B1) DBP in headache sufferers v controls, (B2) DBP in migraine v T-TH, (C1) Pulse rate in headache sufferers v controls., (C2) Pulse rate in migraine v T-TH; (D1) Temporal pulse amplitude percentage changes in headache suffers v controls, (D2) TPA percentage changes in migraine v T-TH.

Table 5.10 Migraine, T-TH, controls: Blood pressure and pulse rate across experiment: means, standard errors, effects

	Migraine		T-TH		Controls		Headache sufferers	
Phase of experiment	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**
Systolic Blood Pressure								
Baseline (Phase 1)	108.80	1.87	105.69	2.22	104.53	2.48	107.22	1.42
Stressful task (Phase 2)	115.99	1.99	111.71	2.37	110.31	2.57	114.02	1.47
Post-task (Phase 3)	109.01	1.77	106.47	2.11	104.67	2.34	107.69	1.34
Diastolic Blood Pressure								
Baseline (Phase 1)	74.06	1.26	70.30	1.50	71.01	1.65	72.45	0.95
Stressful task (Phase 2)	78.95	1.48	75.63	1.76	75.84	1.88	77.49	1.08
Post-task (Phase 3)	75.42	1.33	72.67	1.59	72.80	1.74	74.20	1.00
Pulse rate								
Baseline (Phase 1)	70.89	1.69	68.00	1.96	70.13	2.16	69.92	1.26
Stressful task (Phase 2)	73.58	1.80	70.36	2.08	73.55	2.30	72.47	1.34
Post-task (Phase 3)	69.03	1.75	67.08	2.02	69.18	2.25	68.56	1.31

	Migraine v T-TH				Headache sufferers v controls			
Main and interaction effects	***F***	***df***	***p***	***ηp2***	***F***	***df***	***p***	***ηp2***
Systolic Blood Pressure								
Phase	29.44	(1.6,108.5)[G]	**<.001**	0.30	30.22	(1.6,138.1)[G]	**<.001**	0.26
Contrasts								
Level 1 v Level 2	36.73	(1, 68)	**<.001**	0.35	35.85	(1,87)	**<.001**	0.29
Level 2 v Level 3	33.59	(1, 68)	**<.001**	0.33	36.55	(1,87)	**<.001**	0.30
Group (main effect)	1.50	(1,68)	.225	0.02	1.42	(1,87)	.237	0.02
Phase*Group	0.43	(1.6,108.5)[G]	.605	0.01	0.17	(1.6,138.1)[G]	.798	0.00
Contrasts								
Level 1 v Level 2	0.29	(1, 68)	.591	0.00	0.24	(1,87)	.626	0.00
Level 2 v Level 3	0.69	(1, 68)	.409	0.01	0.13	(1,87)	.724	0.00
Diastolic Blood Pressure								
Phase	38.62	(1.7,114.6)[G]	**<.001**	0.36	37.56	(1.8,154)[G]	**<.001**	0.30
Contrasts								
Level 1 v Level 2	59.53	(1,68)	**<.001**	0.47	59.38	(1,87)	**<.001**	0.41
Level 2 v Level 3	26.16	(1,68)	**<.001**	0.28	26.76	(1,87)	**<.001**	0.24
Group (main effect)	2.67	(1,68)	.107	0.04	0.61	(1,87)	.438	0.01
Phase*Group	0.37	(1.7,114.6)[G]	.655	0.01	0.03	(1.8,154)[G]	.961	0.00
Contrasts								
Level 1 v Level 2	0.11	(1,68)	.737	0.00	0.03	(1,87)	.867	0.00
Level 2 v Level 3	0.20	(1,68)	.658	0.00	0.04	(1,87)	.838	0.00
Pulse rate								
Phase	13.49	(1.7,114.8)[G]	**<.001**	0.17	16.40	(1.8,151.4)[G]	**<.001**	0.16
Contrasts								
Level 1 v Level 2	13.63	(1,66)	**<.001**	0.17	17.84	(1,85)	**<.001**	0.17
Level 2 v Level 3	18.94	(1,66)	**<.001**	0.22	22.95	(1,85)	**<.001**	0.21
Group (main effect)	1.13	(1,66)	.291	0.02	0.07	(1,85)	.794	0.00
Phase*Group	0.37	(1.7,114.8)[G]	.662	0.01	0.17	(1.8,151.4)[G]	.818	0.00
Contrasts								
Level 1 v Level 2	0.06	(1,66)	.807	0.00	0.38	(1,85)	.538	0.00
Level 2 v Level 3	0.50	(1,66)	.483	0.01	0.07	(1,85)	.793	0.00

[G] = Greenhouse Geisser correction

Table 5.11 Temporal pulse amplitude during stressful task in migraine, T-TH, controls: means, standard errors and effects

	Migraine (*n*=36)		T-TH (*n*=23)		Controls (*n*=20)		Headache sufferers (*n*=66)	
Time of Testing	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**
~1min prior to task (baseline)	0.95	0.11	0.93	0.13	0.88	0.16	0.93	0.08
During Stressful Task:								
At start of task (~4 min)	0.99	0.10	1.05	0.12	1.11	0.15	1.00	0.08
At end of task (~22 min)	0.93	0.09	1.00	0.11	0.98	0.14	0.94	0.08
Mean PA during task	0.96	0.09	1.02	0.11	1.04	0.15	0.97	0.08
Percent change from baseline to 4 min into task	10.04	3.47	19.55	4.16	28.55	5.42	13.17	2.82
Percent change from baseline to 22 min into task	3.40	2.97	10.92	3.57	12.33	4.69	5.97	2.44

	Migraine v T-TH				Headache sufferers v controls			
Effects	***F***	***df***	***p***	***ŋ2***	***F***	***df***	***p***	***ŋ2***
Phase (all participants)	12.07	(1,59)	**<.001**	0.17	26.94	(1,73)	**<.001**	0.27
~1min prior to task (baseline)	0.01	(1,59)	0.906	0.00	0.08	(1,73)	0.776	0.00
Group effects (during stressful task)	0.01	(1,59)	0.906	0.00	0.08	(1,73)	0.776	0.00
At start of task (~4 min)	0.14	(1,59)	0.714	0.00	0.42	(1,73)	0.519	0.01
At end of task (~22 min)	0.23	(1,59)	0.632	0.00	0.06	(1,73)	0.805	0.00
Mean PA during task	0.18	(1,59)	0.672	0.00	0.21	(1,73)	0.651	0.00
Percent change from baseline to 4 min into task	3.08	(1,59)	0.084	0.05	6.35	(1,73)	**0.014**	0.08
Percent change from baseline to 22 min into task	2.62	(1,59)	0.111	0.04	1.45	(1,73)	0.233	0.02
Phase*Group	0.21	(1,59)	0.652	0.00	4.00	(1,73)	**0.049**	0.05

CORTISOL CHANGES IN STRESS-HEADACHE, MIGRAINE, T-TH & CONTROLS

5.3.5 Cortisol changes across experiment

Preliminary analyses revealed no relationship between cortisol levels and perceived task stressfulness, attachment anxiety, attachment avoidance or the modified *Ways of Coping Questionnaire* (WCQ-R) completed by participants 10 minutes after the end of the stressful task. Nor were there differences by time of testing during the semester (beginning vs end).

Absolute values of cortisol in μg/dl are shown in Figure 5.5 & Table 5.12. F ratios were computed using logarithmic transformations to offset the wide variation in results and create a normal distribution.

5.3.5.1 All participants: cortisol changes

As shown in Figure 5.5 and Table 5.12, cortisol levels declined in all participants from the point of entry to the end of the experiment (F (2.6, 202.1) = 5.19, p = .003, Greenhouse -Geisser correction), with a significant decrease from point of entry to the end of phase 1 (F (1,77)=6.05, p <.01). Consistent with normal diurnal cortisol variations (571), time of testing was also significant, F (1,76) = 5.02, p <.05), in that afternoon-tested participants showed the greatest declines in cortisol levels across the task, F (2.3, 102.1) = 4.95, p <.01, Greenhouse-Geisser correction).

In a supplementary analysis, levels of cortisol were computed, as per Yeager (545): low (5-10 μg/dl); normal (15-20 μg/dl), stress-associated (30-50 μg/dl), and high (>60 μg/dl). Frequencies at each testing point for cortisol are shown in the bar-charts in Figure 5.6. During the stressful task, cortisol levels were predominantly in the 'low' range rather than the 'stress-associated' range[3], possibly reflecting a cortisol 'fatiguing' process (572).

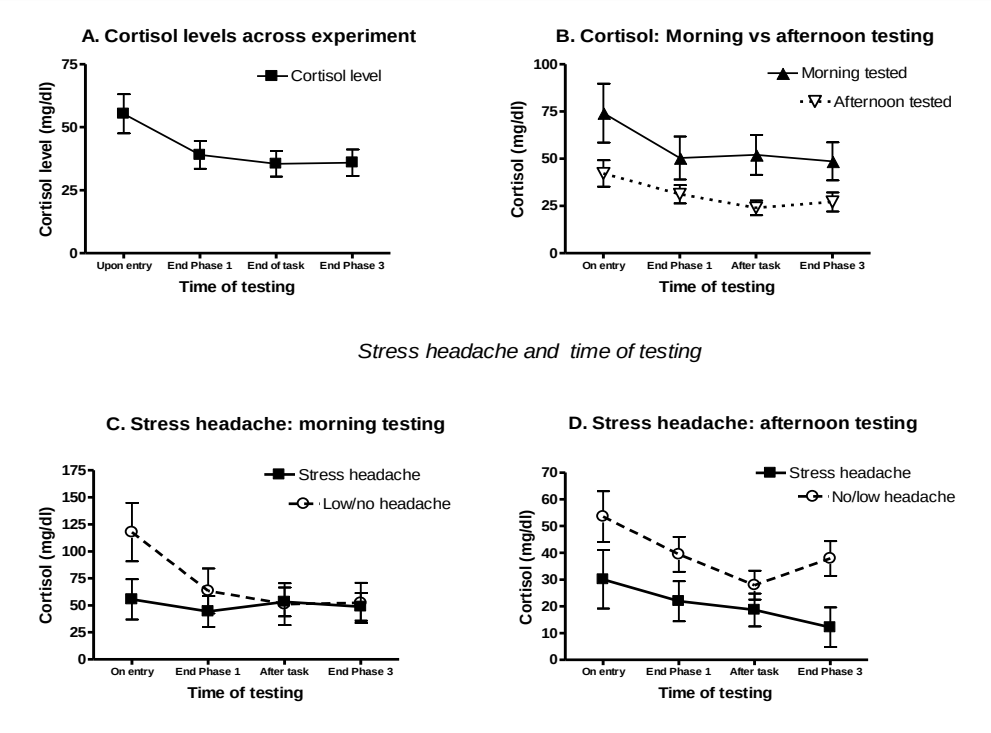


Figure 5.5 Absolute cortisol levels in μg/dl across experiment for (A) all participants, (B) cortisol levels in participants tested in the morning compared with the afternoon, (C) morning -tested participants who acquired a stress headache v those who did not, (D) afternoon tested participants who acquired a stress headache v those who did not.

[3] Kruskal Wallis testing indicated that there were no differences in cortisol levels in either morning- or afternoon-tested groups at any of the four testing points between those with and without stress headache.

Table 5.12 All participants: Cortisol measures across experiment: Means, standard errors, all effects

Time of cortisol test	Mean	SE
Morning Tested		
T1 (end Phase 1):	74.19	15.59
T2 (end Phase 1):	50.37	11.38
T3 (end Phase 2):	52.02	10.52
T4 (end Phase 3):	48.64	10.09
Afternoon Tested		
T1 (entry):	42.20	7.02
T2 (end Phase 1):	31.19	4.83
T3 (end Phase 2):	23.97	3.91
T4 (end Phase 3):	27.11	5.05

Effects (log transformed)	*F*	*df*	*p*	*ŋ2*
All participants				
Phase	5.19	(2.6, 202.1) [G]	**0.003**	0.06
T1 v T2	6.05	(1, 77)	**0.016**	0.07
T2 v T3	0.13	(1, 77)	0.719	0.00
T3 v T4	0.57	(1, 77)	0.451	0.01
Time of testing	5.02	(1, 76)	**0.028**	0.06
Morning Tested				
Phase	1.41	(3, 93) [G]	0.244	0.04
T1 v T2	2.30	(1, 31)	0.140	0.07
T2 v T3	0.74	(1, 31)	0.395	0.02
T3 v T4	0.99	(1, 31)	0.328	0.03
Afternoon Tested				
Phase	4.95	(2.3, 102.1) [G]	**0.007**	0.10
T1 v T2	3.85	(1, 45)	0.056	0.08
T2 v T3	2.95	(1, 45)	0.093	0.06
T3 v T4	0.00	(1, 45)	0.953	0.00

[G] = Greenhouse Geisser correction

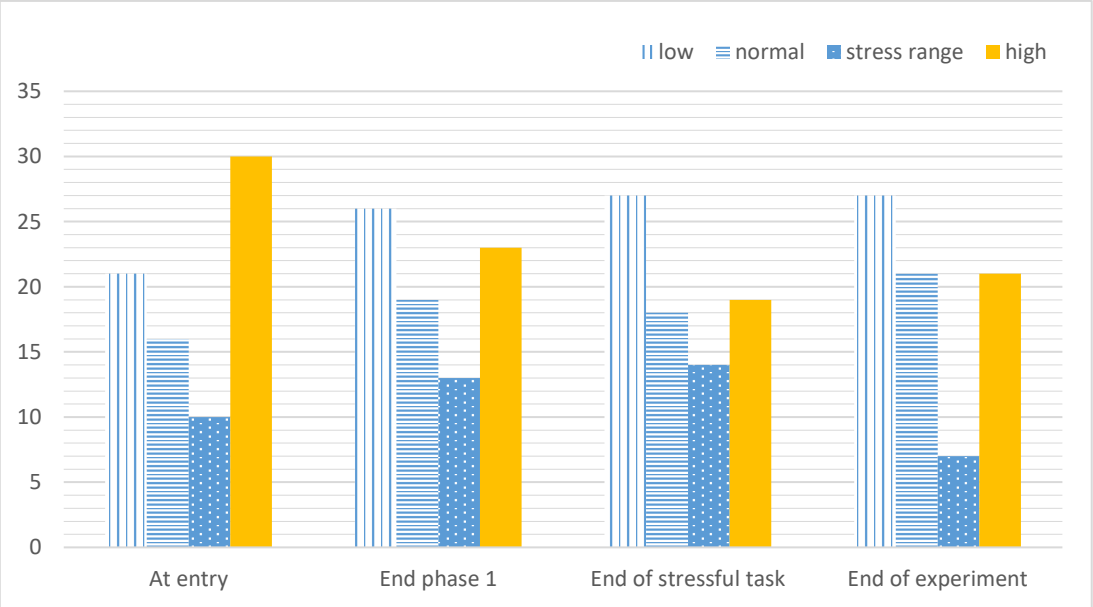


Figure 5.6 Frequency of low, normal, 'stress-associated' and high levels of cortisol at each testing point.

5.3.5.2 Stress-headache and cortisol

As shown in Table 5.13, cortisol levels declined overall more in the stress-headache than the no/low headache group ($F(1,71) = 6.11$, $p < .01$), especially from entry to the end of phase 1 ($F(1,73) = 6.22$, $p < .05$). Time of testing was significant ($F(1,71) = 7.48$, $p < .01$), in that these group differences occurred only in those tested in the afternoon (($F(1,42) = 4.49$, $p < .05$), the main cortisol decline again from entry to the end of phase 1 ($F(1,42) = 4.14$, $p < .05$). As diagrammed in Fig 5.5 the pattern of responses between morning and afternoon-tested groups differed, with cortisol levels in the stress-headache group continuing to decline post-task relative to those without headache ($F(2.3, 96.8) = 5.46$, $p < .01$, Greenhouse Geisser correction).

In a multiple regression analysis in which stress-headache was the dependent variable, and cortisol levels (both absolute levels and changes from the previous testing-point) were entered as independent variables, cortisol accounted for 13.2% of the variance in headache. Cortisol level at the end of the stressful task was an independent predictor of headache ($\beta = .524$, $p = .013$).

Table 5.13 Stress-headache and cortisol levels across experiment: means, standard errors, all effects

	No/low headache (n = 39)		Stress headache (n = 42)	
Time of testing	**Mean**	**SE**	**Mean**	**SE**
Morning tested				
T1 (at entry)	117.822	27.09	55.45	18.69
T2 (end Phase 1)	63.360	20.85	44.36	14.39
T3 (end Phase 2)	51.150	19.42	53.23	13.40
T4 (end Phase 3)	52.320	18.52	48.63	12.78
Afternoon tested				
T1 (at entry)	53.51	9.50	30.09	10.90
T2 (end Phase 1)	39.41	6.51	21.90	7.46
T3 (end Phase 2)	27.93	5.37	18.68	6.16
T4 (end Phase 3)	37.89	6.47	12.17	7.42

Table 5.13 (continued)

	Stress headache vs no/low headache			
Main and Interaction Effects	***F***	***df***	***p***	η_p^2
All participants				
Group	6.11	(1, 71)	**0.016**	0.08
Phase	5.50	(2.6, 191.8) [G]	**0.002**	0.07
T1 v T2	6.22	(1, 73)	**0.015**	0.08
T2 v T3	0.28	(1, 73)	0.598	0.00
T3 v T4	0.30	(1, 73)	0.587	0.00
Phase*Group	1.01	(2.6, 191.8) [G]	0.383	0.01
T1 v T2	0.01	(1, 73)	0.937	0.00
T2 v T3	3.37	(1, 73)	0.071	0.04
T3 v T4	1.31	(1, 73)	0.256	0.02
Time of testing	7.48	(1, 71)	**0.008**	0.10
Phase*Time of testing	0.43	(2.6, 187) [G]	0.705	0.01
Phase*Group*Time of testing	0.12	(2.6, 187) [G]	0.337	0.02
Morning tested				
Group	2.31	(1,29)	0.139	0.07
Phase	1.80	(3, 87)	0.153	0.06
T1 v T2	2.72	(1, 29)	0.110	0.09
T2 v T3	0.23	(1, 29)	0.634	0.01
T3 v T4	0.44	(1, 29)	0.512	0.01
Phase*Group	1.15	(3, 87)	0.336	0.04
T1 v T2	0.30	(1, 29)	0.591	0.01
T2 v T3	1.09	(1, 29)	0.304	0.04
T3 v T4	0.04	(1, 29)	0.834	0.00
Afternoon tested				
Group	4.49	(1, 42)	**0.040**	0.10
Phase	5.46	(2.3,96.8) [G]	**0.004**	0.12
T1 v T2	4.14	(1, 42)	**0.048**	0.09
T2 v T3	2.91	(1, 42)	0.095	0.06
T3 v T4	0.05	(1, 42)	0.818	0.00
Phase*Group	0.44	(2.3,96.8) [G]	0.671	0.01
T1 v T2	0.35	(1, 42)	0.559	0.01
T2 v T3	1.04	(1, 42)	0.313	0.02
T3 v T4	1.47	(1, 42)	0.233	0.03

[G] = Greenhouse Geisser correction

5.3.5.3 Cortisol in migraine, T-TH and controls

Headache sufferers v controls. Overall, cortisol levels were similar in headache sufferers and controls, although effects differed by time of testing {F (1,74) = 4.87, p = .030), as did the pattern of results across the experiment in the afternoon-tested group (F (2.2, 98.1) = 3.24, p <.05, Greenhouse-Geisser correction). In the afternoon-tested group, cortisol levels had declined by the end of the stressful task, particularly in controls (F (1,44) =5.40, p <.05) (Figure 5.7 (B) and Table 5.14).

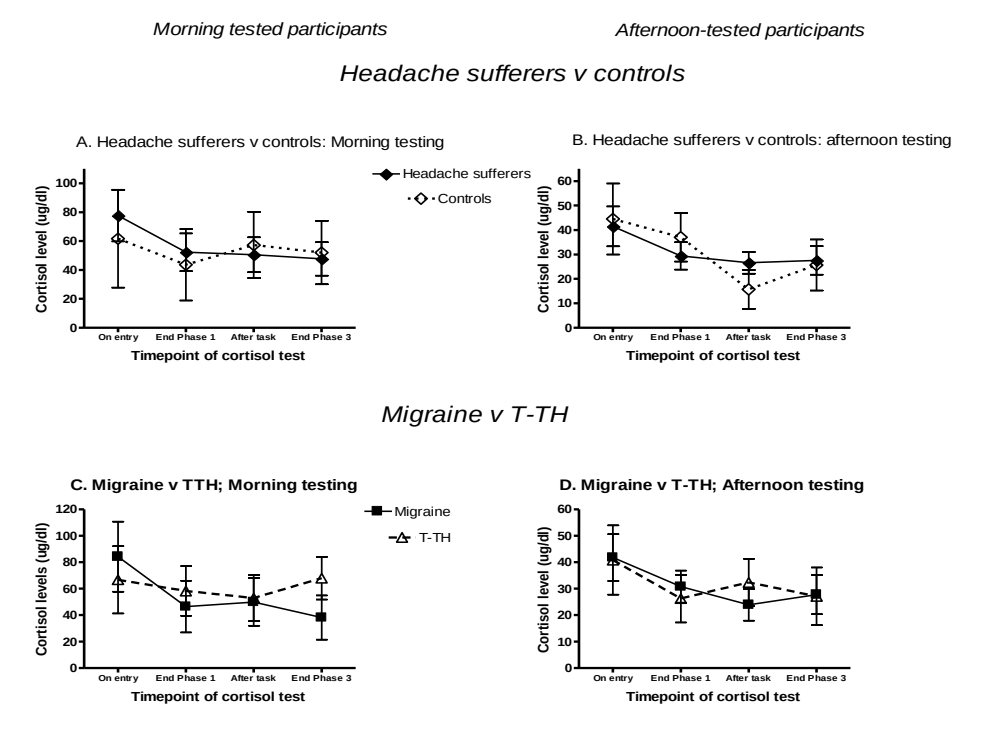


Figure 5.7 Cortisol levels (µg/dl) in morning (A) and afternoon tested (B) participants, comparing headache sufferers v controls (C) and migraine v T-TH (D).

Migraine v T-TH. Cortisol levels were similar in morning-tested migraine and T-TH groups, but in afternoon-tested participants, the pattern of cortisol response differed across each phase of the experiment (F(2,66.8)=3.64, p<.05), declining especially from entry to the end of phase 1 (F(1,33) = 4.74, p <.05). During the stressful task, migraine cortisol levels declined while T-TH increased (F (1,33) = 7.48, p<.01). From Kruskal-Wallis computations, mean T-TH at the end of the experiment was in the stress-associated range (32 µg/dl) whereas the migraine mean at the same point was in the 'normal' range (20 µg/dl) (545). This suggests greater stress reactivity in T-TH than migraine participants.

Table 5.14 Cortisol levels across experiment in migraine, T-TH, controls: means, standard errors, all effects

Time of Testing	Migraine (*n*=37)		T-TH (*n*=23)		Controls (*n*=18)		Headache sufferers (*n*=60)	
	Mean	**SE**	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**
Morning tested								
T1 (at entry)	84.28	26.49	66.74	25.52	61.63	33.78	77.70	17.87
T2 (end Phase 1)	46.42	19.51	58.26	18.80	43.55	24.70	52.28	13.07
T3 (end Phase 2)	49.99	18.04	52.88	17.38	57.29	22.83	50.54	12.08
T4 (end Phase 3)	38.15	16.71	67.90	16.10	52.00	21.91	47.69	11.60
Afternoon tested								
T1 (at entry)	41.77	8.84	40.85	13.06	44.51	14.52	41.48	8.14
T2 (end Phase 1)	30.79	6.07	26.26	8.97	37.01	9.94	29.37	5.57
T3 (end Phase 2)	23.91	6.02	32.38	8.90	15.68	7.96	26.57	4.46
T4 (end Phase 3)	27.77	7.39	27.11	10.92	25.65	10.44	27.56	5.85

Main and interaction effects	Migraine v T-TH				Headache sufferers v controls			
	F	***df***	***p***	***ŋ2***	***F***	***df***	***p***	***ŋ2***
All participants								
Group	0.85	(1, 58)	0.361	0.01	0.54	(1, 74)	0.467	0.01
Phase	3.52	(2.5,152.9)[G]	**0.022**	0.06	2.65	(2.6, 199.6)[G]	0.057	0.03
T1 v T2	5.02	(1, 60)	**0.029**	0.08	3.00	(1, 76)	0.088	0.04
T2 v T3	0.03	(1, 60)	0.864	0.00	0.20	(1, 76)	0.659	0.00
T3 v T4	0.58	(1, 60)	0.448	0.01	0.09	(1, 76)	0.763	0.00
Phase*Group	0.52	(2.5,152.9)[G]	0.641	0.01	0.33	(2.6, 199.6)[G]	0.777	0.00
T1 v T2	0.03	(1, 60)	0.854	0.00	0.38	(1, 76)	0.538	0.01
T2 v T3	1.07	(1, 60)	0.304	0.02	0.07	(1, 76)	0.795	0.00
T3 v T4	0.07	(1, 60)	0.792	0.00	0.38	(1, 76)	0.539	0.00
Time of testing	3.14	(1, 58)	0.082	0.05	4.87	(1, 74)	**0.030**	0.06
Phase*Time of testing	0.35	(2.5, 145.9)[G]	0.757	0.01	1.35	(2.6, 191.7)[G]	0.261	0.02
Phase*Group*Time of testing	1.11	(2.5, 145.9)[G]	0.340	0.02	0.74	(2.6, 191.7)[G]	0.510	0.01
Morning tested								
Group	2.44	(1, 25)	0.131	0.09	0.95	(1, 30)	0.338	0.03
Phase	0.88	(3,75)	0.457	0.03	1.02	(3,90)	0.387	0.03
T1 v T2	1.77	(1, 25)	0.195	0.07	1.57	(1, 30)	0.220	0.05
T2 v T3	0.24	(1, 25)	0.629	0.01	1.57	(1, 30)	0.220	0.05
T3 v T4	0.08	(1, 25)	0.775	0.00	1.35	(1, 30)	0.254	0.04
Phase*Group	0.54	(3,75)	0.658	0.02	0.34	(3,90)	0.795	0.01
T1 v T2	0.94	(1, 25)	0.341	0.04	0.00	(1, 30)	0.972	0.00
T2 v T3	0.32	(1, 25)	0.575	0.01	0.92	(1, 30)	0.344	0.03
T3 v T4	0.41	(1, 25)	0.527	0.02	0.38	(1, 30)	0.540	0.01
Morning tested								
Group	0.02	(1, 33)	0.901	0.00	0.01	(1, 44)	0.928	0.00
Phase	3.64	(2,66.8) [G]	**0.031**	0.10	3.24	(2.2,98.1)[G]	**0.038**	0.07
T1 v T2	4.74	(1,33)	**0.037**	0.13	1.41	(1, 44)	0.242	0.03
T2 v T3	0.07	(1,33)	0.793	0.00	5.40	(1, 44)	**0.025**	0.11
T3 v T4	1.51	(1,33)	0.228	0.04	0.53	(1, 44)	0.471	0.01
Phase*Group	0.97	(2,66.8) [G]	0.387	0.03	0.77	(2.2,98.1)[G]	0.478	0.02
T1 v T2	0.75	(1,33)	0.392	0.02	0.86	(1, 44)	0.358	0.02
T2 v T3	7.48	(1,33)	**0.010**	0.18	2.56	(1, 44)	0.117	0.05
T3 v T4	1.70	(1,33)	0.201	0.05	2.23	(1, 44)	0.143	0.05

[G] = Greenhouse Geisser correction

STRESS-HEADACHE AS FAILURE OF PAIN INHIBITORY PROCESSES?

5.3.6 Stress-headache and pain ratings during Phase 1

In further analyses, to identify whether stress-headache was attributable to the failure of pain inhibitory processes that resulted in sensitization during Phase 1, increases in pain and pain-related distress across the two sets of 30-s ISI shocks during the 15-20 minutes of Phase 1 were compared between those who did and those who did not develop headache. Each of the two 30-s ISI sets was divided into two blocks consisting of trials 1-5 and trials 6-10 respectively. Pain ratings to the 2-second ISI shock series in Phase 1 were excluded from this analysis since a 2-second ISI interval does not permit habituation to occur (573).

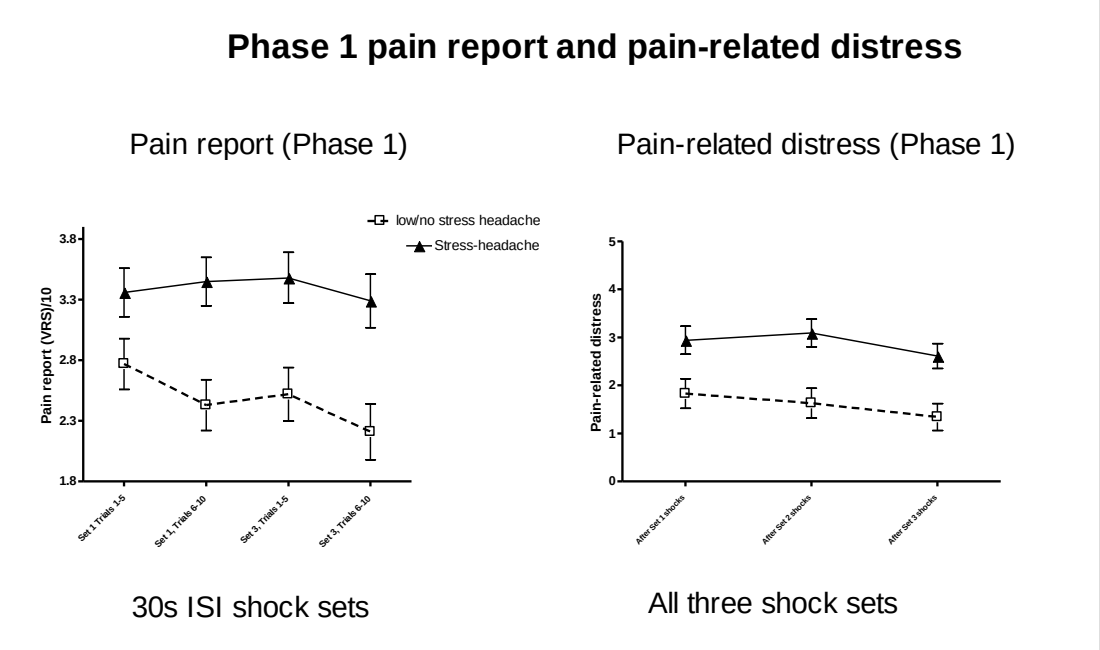


Figure 5.8 Changes in pain report and pain-related distress over Phase 1 of experiment in stress-headache vs headache-free participants. Each 30s ISI set was further divided into two blocks of 5 trials each.

This hypothesis was not supported. Although the means of the groups differed significantly in pain ratings across the four blocks of the two Phase 1 30-s ISI shock sets, $F(1,76) = 8.4$, $p = .005$), there was a downward linear trend, $F(1,76) = 8.6$, $p = .004$ for both groups (Figure 5.8). Ratings of pain-related distress likewise showed a linear decline, $F(1,76) = 8.6$, $p = .004$, across the two sets of 30-s ISI shocks in Phase 1 for both groups. Therefore, sensitization as assessed by this method cannot be said to have occurred in either those with or those without stress-headache.

5.3.7 Number of R2 reflex blinks

The average number of R2 blinks was computed for each block of 10 trials of the 30-second ISI and for each block of 20 trials of the 2-second ISI.

5.3.7.1 All participants: Number of R2 Reflex Blinks

As shown in Table 5.15 and Figure 5.9(1), in all participants, the number of blinks to the 30sISI shocks decreased during the stressful task (F (1,106) = 39.88, p <.001), especially in the second block of shocks (F (2,105) =26.78, p <.001). Post task, the number of blinks increased (F (1,106), = 6.32, p <.01), especially in the first block of shocks (F (1,106) = 9.96, p <.01).

In contrast, the number of blinks to the 2-second ISI shocks *increased* during the stressful task (F (1,106) = 22.97, p <.001), then declined during the post-test phase (F (1,106) = 46.63, p<.001).

Table 5.15 All participants: Number of R2 reflex blinks across experiment: Means, standard errors, all effects

Shock Set	Trials	Mean	SE
30 second ISI shocks (10 trial blocks)			
1.1	1–10	7.07	0.38
1.2	1–10	7.01	0.37
2.1	1–10	6.31	0.38
2.2	1–10	5.51	0.36
3.1	1–10	6.78	0.37
3.2	1–10	6.00	0.37
2 second ISI shocks (20 trial blocks)			
1	1–20	7.50	0.63
2	1–20	9.33	0.66
3	1–20	6.09	0.58

Effects and contrasts	*F*	*df*	*p*	*ŋ2*
30 second ISI shocks (10 trial blocks)				
Phase (main effect)	21.40	(2, 105)	**<.001**	0.29
Block (main effect)	26.78	(2, 105)	**<.001**	0.20
Phase*Block	7.39	(2, 105)	**0.001**	0.12
Contrasts				
Phase				
Level 1 v Level 2	39.88	(1, 106)	**<.001**	0.27
Level 2 v Level 3	6.32	(1, 106)	**0.013**	0.06
Phase*Block				
Level 1 v Level 2	9.96	(1, 106)	**0.002**	0.09
Level 2 v Level 3	0.01	(1, 106)	0.941	0.00

2 second ISI shocks (20 trial blocks)				
Phase (main effect)	30.82	(1.8,192.9)[G]	**<.001**	0.23
Contrasts				
Phase				
Level 1 v Level 2	22.97	(1, 106)	**<.001**	0.18
Level 2 v Level 3	46.63	(1, 106)	**<.001**	0.31

ISI = Interstimulus Interval.
Note: In the 30s shock sets, the first number represents the phase, the second the block.

5.3.7.2 Number of R2 reflex blinks and stress-headache

In both types of shocks, those with stress-headache had a similar number of blinks to those without, decreasing to the 30sISI shocks during the stressful task, while increasing to the 2sISI shocks (Table 5.16). These patterns are diagrammed in Figure 5.9 (2).

5.3.7.3 Number of R2 reflex blinks in migraine, T-TH, controls

Headache sufferers v controls. The number of R2 reflex blinks was similar in both groups. These patterns are diagrammed in Fig 5.8 (3) and means and SEs are shown in Table 5.16.

Migraine v T-TH. Migraine and T-TH had a similar number of blinks to both 30sISI and 2sISI shocks, decreasing during the stressful task to the 30sISI shocks, ($F(1,83) = 25.64$, $p < .001$), especially from first to second block of 30s shocks ($F(1,83= 19.55$, $p < .001$), while increasing to the 2sISI shocks ($F(1,83) = 23.79$, $p<.001$) – see Table 5.16. These patterns are illustrated in Figure 5.9(4).

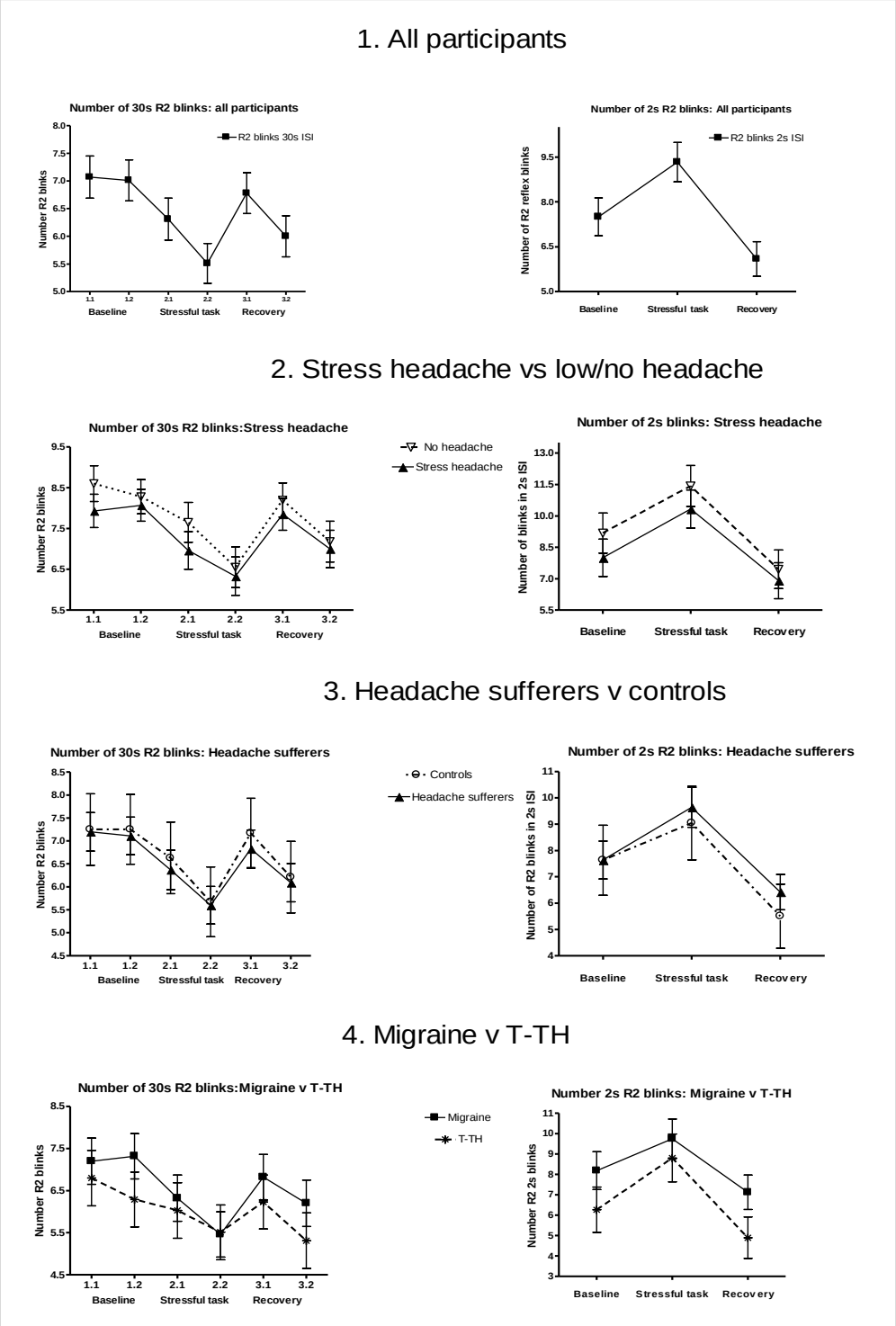


Figure 5.9 Number of R2 reflex blinks in 30s and 2s ISI. (1) all participants, (2) stress headache (3) headache sufferers v controls, (4) migraine v T-TH.

Table 5.16 Number of R2 reflex blinks across experiment in migraine, T-TH, controls, those with stress-headache: means, standard errors, all effects

Shock Set	Trials	Migraine (*n*=40)		T-TH (*n*=26)		Controls (*n*=19)		Headache sufferers (*n*=66)		No/low headache (*n*=39)		Stress Headache (*n*=36)	
		Mean	**SE**	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**
30 second ISI shocks (10 trial blocks)													
1.1	1-10	7.20	0.55	6.80	0.66	7.25	0.78	7.20	0.42	8.60	0.44	7.93	0.41
1.2	1-10	7.32	0.54	6.29	0.65	7.25	0.76	7.11	0.41	8.28	0.42	8.07	0.39
2.1	1-10	6.32	0.55	6.03	0.66	6.63	0.78	6.37	0.43	7.65	0.49	6.96	0.46
2.2	1-10	5.46	0.54	5.51	0.65	5.67	0.76	5.60	0.41	6.55	0.50	6.33	0.47
3.1	1-10	6.82	0.54	6.23	0.64	7.17	0.76	6.83	0.41	8.20	0.42	7.85	0.39
3.2	1-10	6.20	0.55	5.31	0.66	6.21	0.78	6.09	0.42	7.18	0.50	7.00	0.46
2 second ISI shocks (20 trial blocks)													
1	1-20	8.18	0.93	6.26	1.11	7.63	1.33	7.64	0.72	9.18	0.96	8.00	0.89
2	1-20	9.74	0.97	8.80	1.17	9.04	1.40	9.64	0.76	11.43	0.98	10.33	0.91
3	1-20	7.12	0.85	4.89	1.02	5.50	1.22	6.42	0.67	7.45	0.92	6.91	0.86

Note: 1.1 refers to Set 1 Block 1; 1.2 = Set 1, Block 2, etc.

	Migraine v T-TH				Headache sufferers v controls				Stress headache v no/low headache			
Main and interaction effects	***F***	***df***	***p***	***ŋ2***	***F***	***df***	***p***	***ŋ2***	***F***	***df***	***p***	***ŋ2***
30 second ISI shocks (10 trial blocks)												
Main effects												
Group	0.44	(1,83)	0.510	0.01	0.04	(1,103)	0.843	0.00	0.49	(1,84)	0.488	0.01
Phase	15.29	(2, 82)	**<.001**	0.27	14.41	(2, 102)	**<.001**	0.22	20.94	(2, 83)	**<.001**	0.34
Block	19.55	(2, 82)	**<.001**	0.19	20.87	(1,102)	**<.001**	0.17	30.41	(2, 83)	**<.001**	0.27
Interaction effects												
Phase*Group	1.18	(2, 82)	0.314	0.03	0.06	(2, 102)	0.942	0.00	0.19	(2, 83)	0.828	0.00
Block*Group	0.61	(2, 82)	0.437	0.01	0.18	(2, 102)	0.674	0.00	2.56	(2, 83)	0.113	0.03
Phase*Block	3.00	(2, 82)	0.055	0.07	6.38	(2, 102)	**0.002**	0.11	6.26	(2, 83)	**0.003**	0.13
Phase*Block*Group	1.81	(2, 82)	0.170	0.04	0.21	(2, 102)	0.812	0.00	0.16	(2, 83)	0.852	0.00
Contrasts												
Phase												
Level 1 v Level 2	25.64	(1,83)	**<.001**	0.24	27.24	(1, 103)	**<.001**	0.21	40.20	(1,84)	**<.001**	0.32
Level 2 v Level 3	1.86	(1,83)	0.176	0.02	4.79	(1, 103)	**0.031**	0.04	11.24	(1,84)	**0.001**	0.12

	Migraine v T-TH				Headache sufferers v controls				Stress headache v no/low headache			
Main and interaction effects	***F***	***df***	***p***	***ŋ2***	***F***	***df***	***p***	***ŋ2***	***F***	***df***	***p***	***ŋ2***
Phase*Block												
Level 1 v Level 2	3.66	(1,83)	0.059	0.04	8.48	(1, 103)	0.004	0.08	7.86	(1,84)	**0.006**	0.09
Level 2 v Level 3	0.08	(1,83)	0.777	0.00	0.00	(1, 103)	0.968	0.00	0.06	(1,84)	0.814	0.00
Phase*Group												
Level 1 v Level 2	2.00	(1,83)	0.161	0.02	0.02	(1, 103)	0.886	0.00	0.00	(1,84)	0.960	0.00
Level 2 v Level 3	1.86	(1,83)	0.176	0.02	0.02	(1, 103)	0.876	0.00	0.23	(1,84)	0.634	0.00
Phase *Group*Block												
Level 1 v Level 2	3.66	(1,83)	0.059	0.04	0.25	(1, 103)	0.620	0.00	0.00	(1,84)	0.979	0.00
Level 2 v Level 3	1.29	(1,83)	0.259	0.02	0.00	(1, 103)	0.968	0.00	0.23	(1,84)	0.629	0.00
2 second ISI shocks (20 trial blocks)												
Main effects												
Group	1.64	(1,83)	0.203	0.02	0.14	(1,103)	0.712	0.00	0.63	(1,84)	0.429	0.01
Phase	24.90	(1.8,152.1) [G]	**<.001**	0.23	22.76	(1.8,187.4) [G]	**<.001**	0.18	31.22	(1.8,151.4) [G]	**<.001**	0.27
Interaction effects												
Phase*Group	1.04G	(1.8, 152.1) [G]	.350	.01	.42 [G]	(1.8, 187.4) [G]	.640	.00	0.27	(1.8,151.4) [G]	0.739	.00
Contrasts												
Phase												
Level 1 v Level 2	23.79	(1, 83)	**<.001**	0.22	13.54	(1, 103)	**<.001**	0.12	25.96	(1, 84)	**<.001**	0.24
Level 2 v Level 3	37.56	(1, 83)	**<.001**	0.31	34.62	(1, 103)	**<.001**	0.25	46.36	(1, 84)	**<.001**	0.36
Phase*Group												
Level 1 v Level 2	1.37	(1, 83)	0.246	0.02	0.39	(1, 103)	0.531	0.00	0.01	(1, 84)	0.933	0.00
Level 2 v Level 3	1.47	(1, 83)	0.228	0.02	0.08	(1, 103)	0.782	0.00	0.27	(1, 84)	0.606	0.00

ISI = Interstimulus interval

[G] = Greenhouse Geisser correction

5.3.8 R2 Blink Reflex latencies across experiment

To allow for the small number of blinks in some participants, R2 latencies were averaged for each block of 10 trials in the 30s ISI and each block of 20 trials in the 2-s ISI.

5.3.8.1 All participants: R2 latencies

As shown in Table 5.17, R2 reflex latencies to the 30sISI shocks differed by phase (F (2,75) = 3.84, p <.05), declining significantly post-task (F (1,76) = 7.51, p<.01). They also differed by block, declining from first to second block of shocks (F (1,76) = 12.03, p <.01). In contrast, 2sISI shocks were similar across all three phases of the experiment, Fig 5.10 (1).

Table 5.17 All participants: R2 blink reflex latencies across experiment: means, standard errors, all effects

Shock Set	Trials	Mean	SE
30 second ISI shocks (10 trial blocks)			
1.1	1–10	44.49	0.68
1.2	1–10	42.67	0.62
2.1	1–10	44.75	0.72
2.2	1–10	43.67	0.64
3.1	1–10	43.41	0.59
3.2	1–10	42.38	0.60
2 second ISI shocks (20 trial blocks)			
1	1–20	40.89	0.69
2	1–20	40.72	0.64
3	1–20	39.55	0.60

Effects and contrasts	*F*	*df*	*p*	*ŋ2*
30 second ISI shocks (10 trial blocks)				
Phase (main effect)	3.84	(2,75) [G]	**.026**	0.09
Block (main effect)	12.03	(1,76)	**.001**	0.14
Phase*Block	0.58	(2,75)	.561	0.21
Contrasts				
Phase				
Level 1 v Level 2	1.37	(1,76)	.246	0.02
Level 2 v Level 3	7.51	(1,76)	**.008**	0.09
Phase*Block				
Level 1 v Level 2	0.85	(1,76)	.361	0.01
Level 2 v Level 3	0.01	(1,76)	.931	0.00
2 second ISI shocks (20 trial blocks)				
Phase (main effect)	2.76	(2,81)	.069	0.06
Contrasts				
Phase				
Level 1 v Level 2	0.07	(1, 82)	.799	0.00
Level 2 v Level 3	3.53	(1, 82)	.064	0.04

Note: 1.1 refers to Set 1, block 1; 1.2 to Set 1, block 2, etc
[G] = Greenhouse Geisser correction; ISI = Interstimulus Interval

5.3.8.2 Stress headache and R2 blink reflex latencies

R2 latencies were longer in those with than without stress-headache in phases 1 and 2 (baseline and stressful task) ($F(2,71) = 3.67$, $p < .05$). Post-task, latencies also differed between the groups, increasing in the stress-headache group to the 30sISI shocks ($F(1,72) = 6.93$, $p = .01$) and the 2sISI shocks ($F(1,77) = 5.29$, $p < .05$), while reducing in those with low/no headache (Figure 5.10(2), Table 5.18).

5.3.8.3 *R2 blink reflex latencies in migraine, T-TH and controls*

Headache sufferers v controls. Latencies were similar in headache sufferers and controls. However, latencies varied according to the phase of the experiment ($F(1,75) = 9.45$, $p < .01$), reducing post-task to both the 30sISI shocks, $F(1,75) = 5.43$, $p < .05$ and 2sISI shocks, $F(1,81) = 5.68$, $p < .05$. (Figure 5.10(3), Table 5.18).

Migraine v T-TH. Latencies varied between migraine and T-TH according to both phase and block (phase*group*block $F(1,58) = 10.21$, $p < .01$). In migraineurs, latencies decreased from first to second block of 30sISI shocks in phase 1, while increasing in T-TH during the second block of the stressful task. Post-task, latencies increased in T-TH in the first block of 30sISI shocks, then decreased relative to migraineurs ($F(1,58) = 5.25$, $p < .01$). For the 2sISI shocks latencies were similar in migraine and T-TH. (Figure 5.10(4), Table 5.18.)

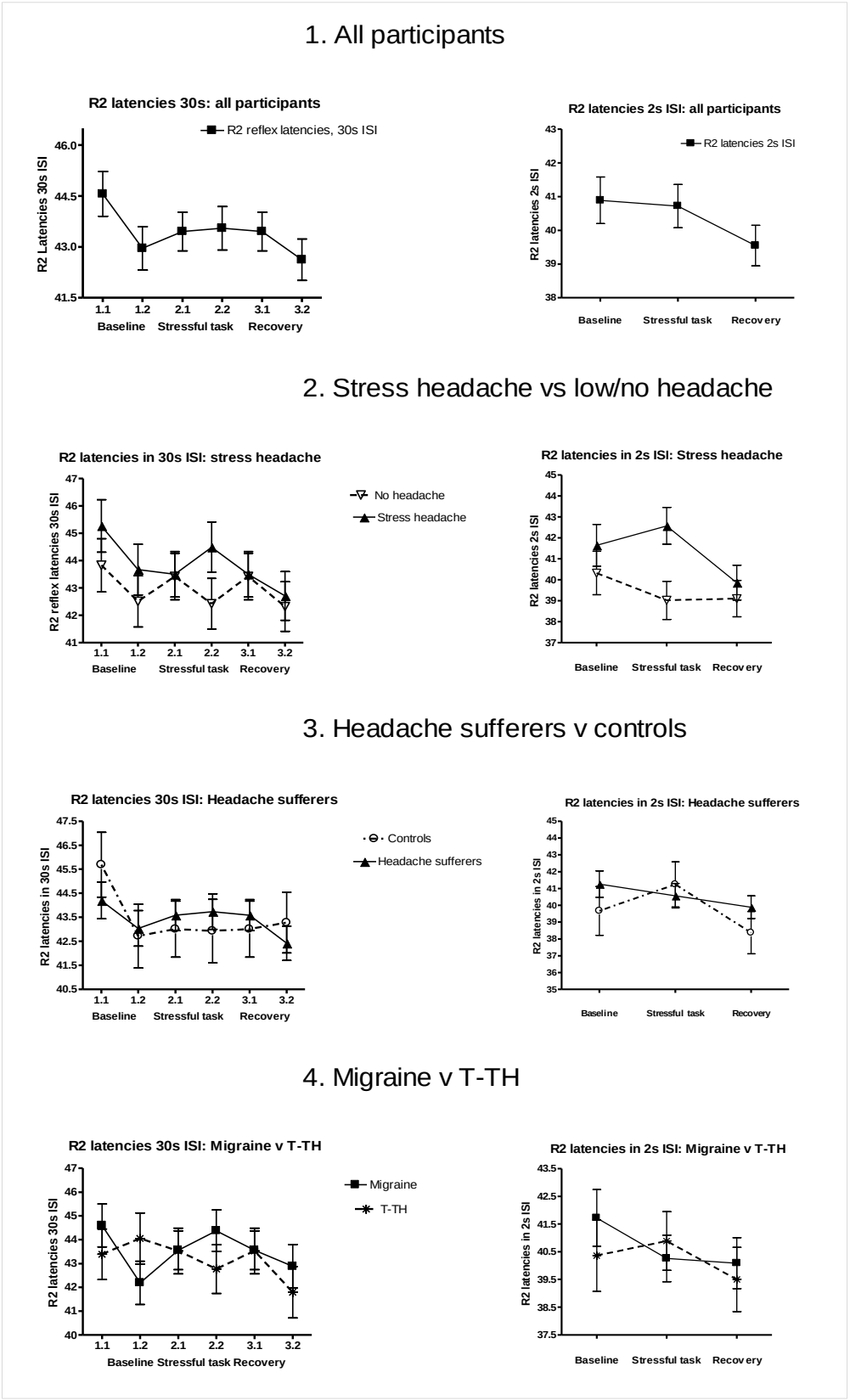


Figure 5.10 R2 nociceptive blink reflex latencies (means ± SE). (1) whole group, (2) those with vs without stress headache, (3) headache sufferers v controls, (4) migraine v T-TH.

Table 5.18 R2 blink reflex latencies across experiment in migraine, T-TH, controls, those with stress-headache: means, standard errors, all effects

Shock Set	Trials	Migraine (*n*=40)		T-TH (*n*=26)		Controls (*n*=19)		Headache sufferers (*n*=66)		No/low headache (*n*=39)		Stress Headache (*n*=36)	
		Mean	**SE**	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**
30 second ISI shocks (10 trial blocks)													
1.1	1-10	44.50	0.92	43.35	1.09	45.68	1.41	44.13	0.78	43.81	1.00	45.18	1.00
1.2	1-10	41.79	0.84	43.59	1.00	42.90	1.30	42.60	0.72	42.16	0.90	43.44	0.90
2.1	1-10	44.48	0.98	44.90	1.16	44.81	1.49	44.73	0.82	43.62	1.04	46.01	1.04
2.2	1-10	44.33	0.89	42.66	1.06	43.65	1.33	43.67	0.74	42.35	0.92	44.84	0.92
3.1	1-10	43.46	0.84	43.40	0.99	43.18	1.22	43.48	0.67	43.33	0.87	43.50	0.87
3.2	1-10	42.64	0.92	41.92	1.09	42.58	1.25	42.33	0.69	42.42	0.88	42.11	0.88
2 second ISI shocks (20 trial blocks)													
1	1-20	41.72	1.02	40.36	1.29	39.67	1.45	41.26	0.79	40.32	1.04	41.64	1.00
2	1-20	40.26	0.84	40.89	1.06	41.24	1.34	40.57	0.73	39.02	0.91	42.57	0.88
3	1-20	40.09	0.92	39.50	1.16	38.38	1.26	39.89	0.68	39.10	0.87	39.86	0.83

Main and interaction effects	Migraine v T-TH				Headache sufferers v controls				Stress headache v no/low headache			
	F	***df***	***p***	***η2***	***F***	***df***	***p***	***η2***	***F***	***df***	***p***	***η2***
30 second ISI shocks (10 trial blocks)												
Main effects												
Group	0.04	(1, 58)	0.833	0.00	0.07	(1, 75)	0.796	0.00	1.41	(1, 72)	0.239	0.02
Phase	2.58	(2,57)	0.085	0.08	3.10	(2,74)	0.051	0.08	4.37	(2.71)	**0.016**	0.11
Block	8.35	(1,58)	**0.005**	0.13	9.45	(1, 75)	**0.003**	0.11	12.00	(1,72)	**0.001**	0.14
Interaction effects												
Phase*Group	0.39	(2,57)	0.682	0.01	0.40	(2,74)	0.670	0.01	3.67	(2.71)	**0.032**	0.09
Block*Group	0.01	(1,58)	0.936	0.00	0.09	(1, 75)	0.770	0.00	0.04	(1,72)	0.846	0.00
Phase*Block	0.01	(2,57)	0.995	0.00	1.00	(2,74)	0.371	0.03	0.25	(1,71)	0.781	0.01
Phase*Block*Group	5.08	(2,57)	**0.009**	0.15	0.49	(2,74)	0.618	0.01	0.99	(2,71)	0.906	0.00
Contrasts												
Phase												
Level 1 v Level 2	1.83	(1, 58)	0.181	0.03	0.37	(1, 75)	0.542	0.00	1.01	(1, 72)	0.318	0.01
Level 2 v Level 3	5.25	(1, 58)	**0.026**	0.08	5.43	(1, 75)	**0.022**	0.07	8.18	(1, 72)	**0.006**	0.10
Phase*Block												
Level 1 v Level 2	0.00	(1, 58)	0.957	0.00	1.20	(1, 75)	0.276	0.02	0.33	(1, 72)	0.567	0.00
Level 2 v Level 3	0.00	(1, 58)	0.958	0.00	0.09	(1, 75)	0.771	0.00	0.01	(1, 72)	0.917	0.00

Main and interaction effects	Migraine v T-TH				Headache sufferers v controls				Stress headache v no/low headache			
	F	*df*	*p*	*η2*	*F*	*df*	*p*	*η2*	*F*	*df*	*p*	*η2*
Phase*Group												
Level 1 v Level 2	0.68	(1, 58)	0.414	0.01	0.50	(1, 75)	0.484	0.01	1.02	(1, 72)	0.315	0.01
Level 2 v Level 3	0.05	(1, 58)	0.828	0.00	0.00	(1, 75)	0.962	0.00	6.93	(1, 72)	**0.010**	0.09
Phase *Group*Block												
Level 1 v Level 2	10.21	(1, 58)	**0.002**	0.15	0.36	(1, 75)	0.549	0.00	0.01	(1, 72)	0.904	0.00
Level 2 v Level 3	0.96	(1, 58)	0.332	0.02	0.17	(1, 75)	0.681	0.00	0.19	(1, 72)	0.662	0.00
2 second ISI shocks (20 trial blocks)												
Main effects												
Group	0.13	(1,63)	0.721	0.00	0.41	(1,81)	0.522	0.01	3.02	(1,77)	0.086	0.04
Phase	1.36	(2, 62)	0.265	0.04	3.08	(2, 80)	0.051	0.07	3.86	(2, 76)	**0.025**	0.09
Interaction effects												
Phase*Group	0.92	(2, 62)	0.405	0.03	1.38	(2, 80)	0.258	0.03	2.70	(2, 76)	0.074	0.07
Contrasts												
Phase												
Level 1 v Level 2	0.38	(1, 63)	0.542	0.01	0.31	(1, 81)	0.577	0.00	0.08	(1, 77)	0.785	0.00
Level 2 v Level 3	1.31	(1, 63)	0.258	0.02	5.68	(1, 81)	**0.019**	0.07	4.75	(1, 77)	**0.032**	0.06
Phase*Group												
Level 1 v Level 2	0.47	(1, 42)	0.497	0.01	2.05	(1, 81)	0.156	0.02	2.59	(1, 77)	0.112	0.03
Level 2 v Level 3	2.07	(1, 42)	0.157	0.05	2.15	(1, 81)	0.147	0.03	5.29	(1, 77)	**0.024**	0.06

Note: 1.1 refers to Set 1, block 1; 1.2 to Set 1, block 2, etc.
ISI = Interstimulus Interval

5.3.9 R2 Area Under the Curve (AUC)

The area under the curve (R2 AUC, the response area) in volts*seconds was computed to evaluate the global EMG activity generated during the R2 reflex.

5.3.9.1 All participants: R2AUC

In a main effect for phase, (F (2,84) = 24.84, p <.001), AUC to the 30s ISI shocks declined from baseline to stressful task (F(1,85) = 38.30, p <.001). There was also a main effect for block (F (2,84) = 6.69, p<.01), whereby AUC declined from first to second block, particularly during the stressful task (phase*block interaction, F(1,85) = 13.91, p <.001). For the 2sISI shocks, there was again a main effect for phase (F (2,84) = 13.23, p <.001) with a significant post-task decline from stressful task to post-task (F(1,83) = 16.98, p <.001). Figure 5.11(1). Table 5.19.

Table 5.19 All participants: R2 AUC across experiment: means, standard errors, all effects

Shock Set	Trials	Mean	SE
30 second ISI shocks (10 trial blocks)			
1.1	1–10	0.00092	0.00009
1.2	1–10	0.00091	0.00009
2.1	1–10	0.00073	0.00008
2.2	1–10	0.00058	0.00007
3.1	1–10	0.00070	0.00008
3.2	1–10	0.00061	0.00007
2 second ISI shocks (20 trial blocks)			
1	1–20	0.00033	0.00005
2	1–20	0.00034	0.00006
3	1–20	0.00019	0.00003

Effects and contrasts	*F*	*df*	*p*	*η2*
30 second ISI shocks (10 trial blocks)				
Phase (main effect)	24.84	(2, 84)	**<.001**	0.37
Block (main effect)	14.05	(2, 84)	**<.001**	0.14
Phase*Block	6.89	(2, 84)	**0.002**	0.14
Contrasts				
Phase				
Level 1 v Level 2	38.30	(1, 85)	**<.001**	0.31
Level 2 v Level 3	0.00	(1, 85)	0.985	0.00
Phase*Block				
Level 1 v Level 2	13.91	(1, 85)	**< .001**	0.14
Level 2 v Level 3	3.69	(1, 85)	0.058	0.04
2 second ISI shocks (20 trial blocks)				
Phase (main effect)	13.23	(2, 84)	**<.001**	0.24
Contrasts				
Phase				
Level 1 v Level 2	0.05	(1, 85)	0.816	0.00
Level 2 v Level 3	16.98	(1, 85)	**< .001**	0.17

Note: 1.1 refers to Set 1, block 1; 1.2 to Set 1, block 2, etc.
ISI = Interstimulus Interval

5.3.9.2 Stress headache and R2AUC

As shown in Figure 5.11(2), there was a significant phase*group*block interaction for the 30sISI shocks, $F(1,81) = 4.0$, $p<.05$, in which AUC declined in the low/no headache group from first to second blocks of phase 1, while AUC in the stress-headache group declined markedly from first to second block of the stressful task ($F(1,81) = 11.23$, $p =.001$) and increased during the first post-task block. The groups were similar for the 2sISI shocks, with AUC declines from stressful task to post-task ($F(1,80) = 15.97$, $p <.001$). (Fig 5.11 (2), Table 5.20).

5.3.9.3 R2AUC in migraine, T-TH, controls

Headache sufferers v controls. In both groups, R2AUC declined from first to second block of 30sISI shocks in phase 1 and 2 (phase*block ($F(2,83)=4.87$, $p <.01$), and increased in the first post-task block, $F (1,84) = 9.69$, $p <.01$). Groups were similar in the 2sISI shocks (Fig 5.11 (3), Table 5.20).

Migraine v T-TH. Two-way interactions indicated that the pattern of responses to the 30sISI shocks differed overall between migraine and T-TH. Differences were most evident post-task ($F(1,65) = 5.15$, $p <.05$), where AUC rose in migraineurs while declining in T-TH. AUC also rose from first to second block of the 30sISI shocks in migraineurs, while declining in T-TH. (block*group ($F(2,64) = 4.48$, $p <.05$; phase*block ($F(2,64) = 4.73$, $p <.01$). These results suggest that R2AUC was lower in T-TH than migraine.

R2AUC to the 2sISI shocks were similar in migraine and T-TH (Fig 5.11(4), Table 5.20).

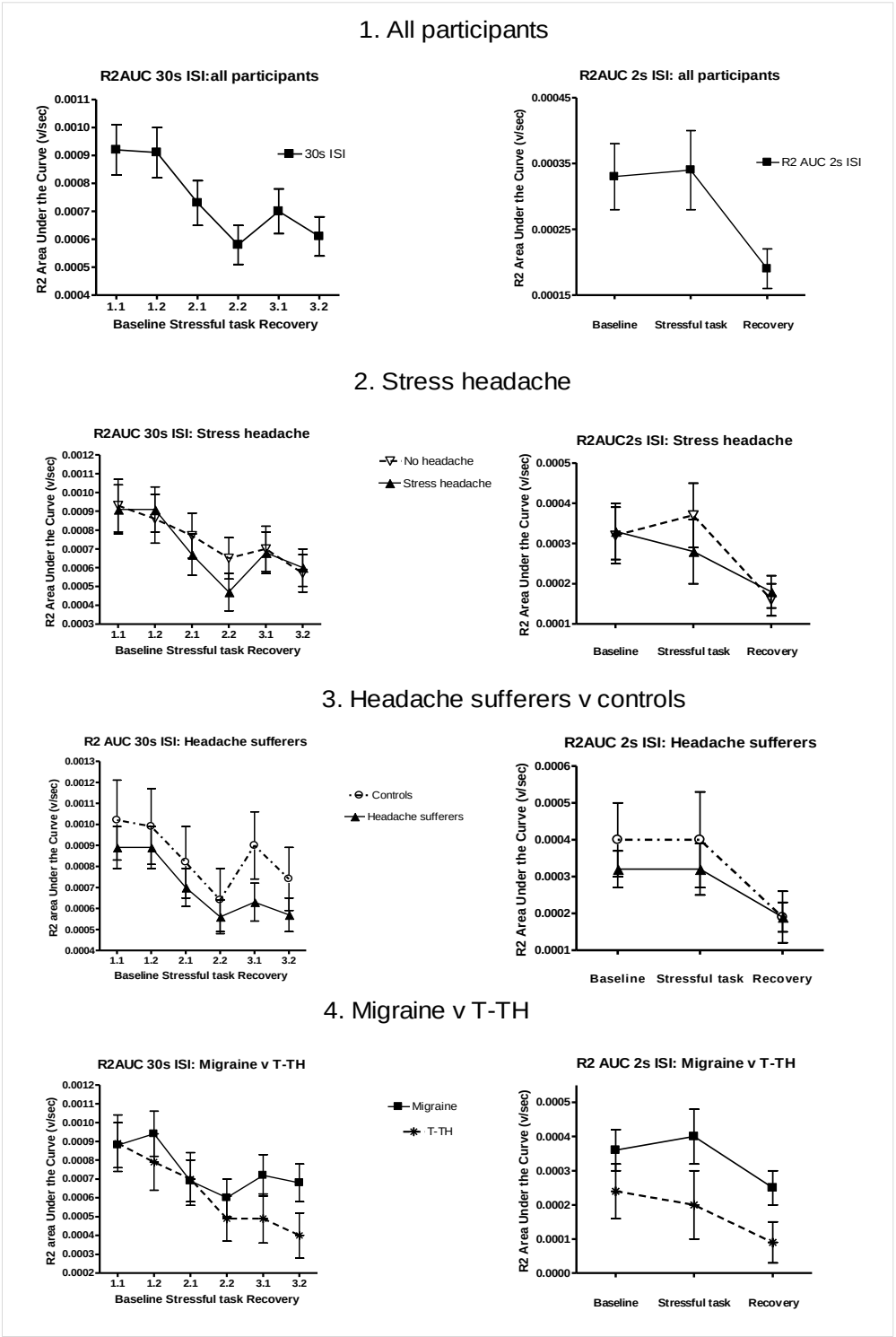


Figure 5.11 R2 Area Under the Curve (Means ± SE). (1) All participants, (2) Stress headache, (3) Headache sufferers v controls, (4) Migraine v T-TH.

Table 5.20 R2 AUC across experiment in migraine, T-TH, controls, stress-headache: means, standard errors, all effects

Shock Set	Trials	Migraine (*n*=40)		T-TH (*n*=26)		Controls (*n*=19)		Headache sufferers (*n*=66)		No/low headache (*n*=39)		Stress Headache (*n*=36)	
		Mean	**SE**	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**
30 second ISI shocks (10 trial blocks)													
1.1	1-10	0.00088	0.00012	0.00089	0.00015	0.00102	0.00019	0.00089	0.00010	0.00093	0.00014	0.00091	0.00013
1.2	1-10	0.00094	0.00012	0.00079	0.00015	0.00099	0.00018	0.00089	0.00010	0.00086	0.00013	0.00091	0.00012
2.1	1-10	0.00069	0.00011	0.00070	0.00014	0.00082	0.00017	0.00070	0.00009	0.00077	0.00012	0.00067	0.00011
2.2	1-10	0.00060	0.00010	0.00049	0.00012	0.00064	0.00015	0.00056	0.00008	0.00065	0.00011	0.00047	0.00010
3.1	1-10	0.00072	0.00011	0.00049	0.00013	0.00090	0.00016	0.00063	0.00009	0.00070	0.00012	0.00068	0.00011
3.2	1-10	0.00068	0.00010	0.00040	0.00012	0.00074	0.00015	0.00057	0.00008	0.00057	0.00010	0.00060	0.00010
2 second ISI shocks (20 trial blocks)													
1	1-20	0.00036	0.00006	0.00024	0.00008	0.00040	0.00010	0.00032	0.00005	0.00032	0.00007	0.00033	0.00007
2	1-20	0.00040	0.00008	0.00020	0.00010	0.00040	0.00013	0.00032	0.00007	0.00037	0.00008	0.00028	0.00008
3	1-20	0.00025	0.00005	0.00009	0.00006	0.00019	0.00007	0.00019	0.00004	0.00016	0.00004	0.00018	0.00004

	Migraine v T-TH				Headache sufferers v controls				Stress headache v no/low headache			
Main and interaction effects	***F***	***df***	***p***	***ŋ2***	***F***	***df***	***p***	***ŋ2***	***F***	***df***	***p***	***ŋ2***
30 second ISI shocks (10 trial blocks)												
Main effects												
Group	0.60	(1,65)	0.442	0.01	0.63	(1,84)	0.430	0.01	0.08	(1,81)	0.784	0.00
Phase	20.12	(2, 64)	**< .001**	0.39	15.95	(2, 83)	**<.001**	0.28	24.15	(2, 80)	**<.001**	0.38
Block	9.22	(2, 64)	**0.003**	0.12	13.82	(2, 83)	**<.001**	0.14	28.48	(2, 80)	**<.001**	0.26
Interaction effects												
Phase*Group	2.88	(2, 64)	0.064	0.08	1.00	(2, 83)	0.371	0.02	2.05	(2, 80)	0.136	0.05
Phase*Block	4.73	(2, 64)	**0.012**	0.13	4.87	(2, 83)	**0.010**	0.11	5.55	(2, 80)	**0.006**	0.12
Block*Group	4.48	(2, 64)	**0.038**	0.06	1.05	(2, 83)	0.307	0.01	0.27	(2, 80)	0.607	0.00
Phase*Block*Group	0.75	(2, 64)	0.476	0.02	0.50	(2, 83)	0.609	0.01	2.59	(2, 80)	0.081	0.06
Contrasts												
Phase												
Level 1 v Level 2	27.61	(1, 65)	**< .001**	0.30	27.56	(1, 84)	**< .001**	0.25	37.41	(1, 81)	**< .001**	0.32
Level 2 v Level 3	1.05	(1, 65)	0.310	0.02	0.45	(1, 84)	0.503	0.01	0.01	(1, 81)	0.918	0.00
Phase*Block												

	Migraine v T-TH				Headache sufferers v controls				Stress headache v no/low headache			
Main and interaction effects	***F***	***df***	***p***	***ŋ2***	***F***	***df***	***p***	***ŋ2***	***F***	***df***	***p***	***ŋ2***
Level 1 v Level 2	8.78	(1, 65)	**0.004**	0.12	9.69	(1, 84)	**0.003**	0.10	11.23	(1, 81)	**0.001**	0.12
Level 2 v Level 3	5.09	(1, 65)	**0.027**	0.07	1.30	(1, 84)	0.257	0.02	2.19	(1, 81)	0.143	0.03
Phase*Group												
Level 1 v Level 2	0.05	(1, 65)	0.822	0.00	0.01	(1, 84)	0.923	0.00	3.08	(1, 81)	0.083	0.04
Level 2 v Level 3	5.15	(1, 65)	**0.027**	0.07	1.66	(1, 84)	0.201	0.02	3.01	(1, 81)	0.086	0.04
Phase *Group*Block												
Level 1 v Level 2	0.22	(1, 65)	0.643	0.00	0.00	(1, 84)	0.971	0.00	3.71	(1, 81)	0.058	0.04
Level 2 v Level 3	0.58	(1, 65)	0.448	0.01	0.80	(1, 84)	0.372	0.01	4.00	(1, 81)	**0.049**	0.05
2 second ISI shocks (20 trial blocks)												
Main effects												
Group	2.95	(1, 66)	0.090	0.04	0.25	(1, 84)	0.615	0.00	0.06	(1, 80)	.805	0.00
Phase	8.95	(2, 65)	**<.001**	0.22	12.21	(2, 83)	**<.001**	0.23	13.73	(2, 79)	**<.001**	0.26
Interaction effects												
Phase*Group	0.78	(2, 65)	0.464	0.02	0.71	(2, 83)	0.495	0.02	1.64	(2, 79)	.201	0.04
Contrasts												
Phase												
Level 1 v Level 2	0.00	(1, 66)	0.959	0.00	0.04	(1, 84)	0.847	0.00	0.00	(1, 80)	.997	0.00
Level 2 v Level 3	12.31	(1, 66)	**0.001**	0.16	15.43	(1, 84)	**< .001**	0.16	15.97	(1, 80)	**< .001**	0.17
Phase*Group												
Level 1 v Level 2	1.51	(1, 66)	0.224	0.02	0.00	(1, 84)	0.998	0.00	3.08	(1, 80)	.083	0.04
Level 2 v Level 3	0.25	(1, 66)	0.621	0.00	0.84	(1, 84)	0.362	0.01	2.29	(1, 80)	.134	0.03

Note: 1.1 refers to Set 1, block 1; 1.2 to Set 1, block 2, etc.
ISI = Interstimulus interval

5.4 Discussion

The aim of this paper was to examine the relationship between: symptom measures, cardiovascular activity, cortisol and nociceptive-specific blink reflexes to headache during a stressful laboratory task in episodic migraine and T-TH compared with controls. Headache ≥ 4 on a 10-point VAS scale was reported during the task by 53% of participants (the 'stress-headache' group), 67% of whom were in the control group. Headaches were not formally diagnosed but were relatively short-lasting and associated with nausea in some participants. 'Stress-headaches' may be akin to T-TH (574).

Cardiovascular responses. In all participants, the task elicited increases in systolic and diastolic blood pressure, pulse rate and TPA, indicating increased sympathetic-adrenomedullary activation (525). These responses decreased in the post-task phase.

Salivary cortisol levels decreased across the experiment, particularly from entry to the end of phase 1 (baseline), and – consistent with diurnal variations (571) – particularly in those participants tested in the afternoon.

Trigeminal nociception. During the stressful task, the number of blinks decreased to the 30sISI shocks while increasing to the 2sISI shocks. Post-task, the opposite effect occurred, i.e. the number of blinks increased to the 30sSI shocks. Mechanisms that drove this change in reactivity across the three phases of the experiment are unknown. However, a potential explanation is that stress-evoked inhibitory influences suppressed blinks to intermittent electrical stimuli during the stressful task. If so, these influences were not strong enough to counter facilitatory influences associated with temporal summation to the 2sISI shocks.

R2 latencies. If as Kimura (552) suggests, decreasing R2 latencies reflect enhanced trigeminal excitability, then for all participants, excitability decreased slightly during the task (R2 latencies lengthened relative to phase 1), then increased significantly post-task (latencies were again shorter). This is consistent with findings that R2 latencies in healthy adults increase during a task (575) – a change not necessarily related to arousal as "there is no direct relation between the specific systems activated to perform the task and the neural connections of the blink reflex" (575, p.61). The task may also distract attention from the stimulation (576).

R2AUC to the 30sISI shocks declined from first to second block in phase 1 and more so in phase 3. According to the dual process theory (554), R2AUC represents the balance between facilitation and habituation. Facilitation, if present, accounts for the initial transitory increase in response amplitude; it is detectable as a higher first block absolute amplitude value. Habituation (decreases in amplitude and duration after repeated stimulation) accounts for the delayed response decrement during the course of a task or session (575). Since nBR activity decreased overall across the experiment, yet headache report increased, it may be speculated that inhibitory influences on the blink reflex were responsible for the nBR decrease. That is, the systematic decrease of amplitudes during the task suggests that habituation – or at least a decrease in activation (575) – occurred, reflecting the operation of central inhibitory controls (552).

Stress-headache

As headache usually subsided a few minutes after the stressful task, the 'stress-headaches' resembled tension-type rather than migraine headache.

i) *Cardiovascular responses* including TPA were similar in those with and without stress-headache.

   Under some conditions, arterial distension is a pain-producing mechanism, i.e. pain intensity is positively correlated with an increase in temporal blood volume (527; 538). This most likely requires perivascular inflammation, as distension of scalp arteries during everyday activities such as exercise does not evoke pain. During attacks of migraine headache, antidromic activation of trigeminal perivascular nociceptors may induce "sterile vascular inflammation" that subsequently develops into a source of pain, its degree depending on context, duration and course of the primary stimulus or insult (88; 577). Since pain report to electrical stimuli prior to the task was significantly greater ($p < .01$) in those who later developed stress-headache, the absence of a temporal artery-pain relationship in these individuals may reflect activation of the baroreceptor reflex during the task (a homeostatic process that helps to maintain blood pressure) (517). (When this reflex is activated, there is an inverse relationship between blood pressure and pain sensitivity in normotensive individuals (513; 578).)

ii) *Salivary cortisol* levels were lower in those with than without stress-headache, and cortisol level at the end of the stressful task was an independent predictor of headache during the task.

* In morning-tested participants, both groups were in the high range upon entry, the mean for those who did *not* develop stress-headache being exceptionally high (117.82 ± 27.09 ug/dl). Mean cortisol before the task (i.e. at the end of phase 1) was still high in the group who did not develop stress-headache, and cortisol is considered to have protective effects at this level (545). In contrast, by the end of phase 1, cortisol levels in those who developed stress-headache had declined to the intermediate range – ~30-50 ug/dl – the level at which peak pro-inflammatory effects of cortisol are typically observed during systemic stress (545). Cortisol remained at approximately this level in both groups during and following the task. Thus, protective levels of cortisol in the morning-tested stress-headache group had already declined prior to the stressful task.

* In the afternoon-tested participants without headache, cortisol levels on entry were in the intermediate/'stress-associated' (anti-inflammatory) range, but in the 'normal' range for those with stress-headache and, by the end of the experiment, in the low range. Thus, the anti-inflammatory and anti-nociceptive effects of cortisol may have been lacking in the afternoon-tested stress-headache group during and following the test.

Consistent with this interpretation, those without stress-headache also reported much lower 'perceived stress' levels during the task than those with stress-headache ($p<.001$) as well as lower pain and pain-distress reports before and after the task. Relevant to this, Schoonman reported that only perceived stress and not cortisol was associated with headache (17).

Nevertheless, further research should examine whether chronic stress in some participants may have biased these results, since in individuals with chronic stress exposure, cortisol exerts a delayed (time dependent) stimulatory effect (545), i.e. one in which the pro-inflammatory effects of cortisol are potentiated. A biological measure of chronic stress such as scalp hair cortisol, which provides a cumulative measure of free cortisol in the blood over a period of several weeks or even months (579) could be used to assess this possibility.

iii) *Nausea.* Consistent with research showing that nausea potentiates headache (210), those with stress-headache had high levels of nausea before and during the task, suggesting autonomic disturbance in these participants.

iv) *Trigeminal nociception in those with stress-headache (vs those with low/no headache).*

* The number and patterning of R2 blinks were similar in those with and without stress-headache. However,

* *R2 latencies* to the 30sISI shocks increased during the stressful task in those with stress-headache, especially during the last block. Post-task, latencies decreased in those with stress-headache, while increasing in those without. Thus, trigeminal excitability was reduced during the task in the stress-headache group, but increased thereafter (552), while the opposite effect was seen in those with low/no stress-headache.

* *R2AUC* decreased to the 30sISI shocks during the task in the stress-headache group, rising sharply during the first post-task block. This suggests habituation or decreased activation during the task followed by post-task facilitation – a reduced threshold (580) – in the stress-headache group.

As participants were not asked to rate pain to the electrical stimuli during the math task, it is uncertain whether there was increased sensitivity to trigeminal input in those with stress-headache (i.e. central processing of afferent trigeminal input). The higher distress ratings in those with stress-headache may have disrupted inhibitory controls on trigeminal nociceptive activity at brainstem level, increasing headache.

Taken together, no one defining physiological variable differentiated those with and without stress headache. Nevertheless, from the above we may postulate that (i) autonomic disturbance may impede supra-spinal pain inhibition or activate pain facilitatory mechanisms (552; 581), and/or (ii) cortisol secretion occurs in concentrations which reduce its anti-inflammatory (or increase its pro-inflammatory) properties. The resulting increased nociceptive input to the spinal cord may over-ride effective pain modulation (552), perhaps contributing to a negative feedforward cascade (192) in which headache persists beyond the stressful event.

Migraine, T-TH and controls

Cardiovascular changes In line with research showing similarities of autonomic arousal including BP in T-TH and controls (533; 582), SBP and pulse rate changes across the experiment were similar in migraine, T-TH and controls across the experiment. Thus, results did not support hypotheses of greater sympathetic cardiovascular activation in those with a migraine history or research showing higher cardiovascular *stress* responses in T-TH than migraine (490; 527; 528).

Temporal pulse amplitude (TPA). Furthermore, and also contrary to previous research (e.g. 77), controls rather than headache sufferers had higher TPA changes early in the stressful task, perhaps indicating sympathetic *hypo*function (CF 528) in headache sufferers during stress or a greater role for peripheral than central factors in controls during stress.

The finding of reduced TPA in headache sufferers compared with controls questions the role of vasodilatation as a primary factor in headache pain. Instead an impaired recovery process from stress has been proposed in headache sufferers (583), perhaps the result of an imbalance of autonomic control (584**).** Price & Tursky (585) reported salient differences between migraineurs and non-migraineurs in the second half of the measurement period, when sustained activation was associated with habituation failure (553). Likewise, Feuerstein (538) reported greater temporal artery dilatation in migraineurs than either T-TH or combined migraine-TTH during the first and second minute of each six-minute post-stress adaptation period. The 50 minute latency period between maximum psycho-physiologic response and maximum mean headache ratings (525) may make it difficult to detect such differences in the present study. Future research should measure post-stress adaptation for a longer period to ascertain differences in cardiovascular responses to stress between migraine/nonmigraine individuals.

Cortisol responsiveness During the stressful task, cortisol levels declined in controls compared with headache sufferers, particularly in afternoon-tested participants, but increased in T-TH relative to migraine. Mean cortisol levels at the end of the experiment were in the stress-associated range in T-TH (32μg/dl), whereas the migraine mean was in the normal range (20μg/dl). This result is consistent with Leistad's (543) findings of greater stress reactivity in T-TH than migraine.

Trigeminal nociception. Results for nociceptive blink reflex measures showed the following:

1. The *number of R2 reflex blinks* to the 30sISI shocks decreased during the stressful task in all headache groups, especially from the first to second block of shocks in migraine v T-TH, while increasing to the 2s ISI shocks. This decreasing sensitivity to the 30sISI shocks during the stressful task suggests the operation of central inhibitory factors (552).

2. *R2 latencies* to the 30sISI shocks decreased in migraineurs relative to T-TH from the first to second block of phase 1 (indicating increased excitability) but increased from the first to second block of the stressful task (decreased excitability). Meanwhile, in the T-TH group, latencies decreased during the task and post-task declines were particularly marked, suggesting greater blink reflex excitability in T-TH than migraine.

3. *R2AUC* increased in migraineurs relative to T-TH from the first to second block of 30sISI shocks in phase 1 and again in phase 3. As explained above, the initial transitory increase in response amplitude in migraine compared with T-TH suggests facilitation effects in migraineurs, the delayed response decrement during the course of the task suggests habituation (or at least reduced activation) and the post-task spike in response amplitude in migraineurs suggests post-task facilitation (554), i.e. a reduced nociceptive blink reflex threshold, which may make for delayed recovery from painful stimulation in migraineurs.

Alternatively, under certain circumstances, psychological stress factors (e.g. NA, self-efficacy) may exacerbate or even over-ride neurophysiological factors. For example, higher heart rate is correlated with both arousal and emotion (527; 538); personality factors such as neuroticism predict blunted cardiovascular (and cortisol) stress reactivity (586; 587) and anxious attachment is associated with greater pain sensitivity (446). Thus, Lehrer (527) further commented that her T-TH patients were generally more sensitive and reactive to pain and verbalized differently in describing pain. Likewise, Feuerstein (538) called for investigation of the potential role of emotion in differential physiological reactivity to stress. In the next chapter, therefore, we examine psychological influences on stress-headache.

5.5 Conclusions

Taken together, these findings suggest that an imbalance of autonomic control, ineffective pain-inhibition and the loss of the anti-inflammatory and antinociceptive effects of cortisol may contribute to stress-headache. Delays in recovery following stressor exposure may also be salient in determining differential responsivity to a stressor. However, there was no strong correlate of headache intensity, so no definitive physiological biomarker for stress-headache was identified. That is, physiological changes of themselves did not offer information as to who did or did not acquire a stress headache, and it was unclear whether these changes reflected individual differences in responding to psychological stress or physiological changes associated with headache. The next chapter will therefore investigate psychological responses to stress as these may pertain to headache.

Chapter Six

6

Negative affect and self-efficacy in headache

Published as: “Psychological generators of stress-headaches”

PAPER 2 – PSYCHOLOGICAL GENERATORS OF STRESS-HEADACHES

Manuscript Details

Published Title:

Psychological generators of stress-headaches

Authors:

Juanita K. M. Berry, B.A. (Hons) [a]; Peter D Drummond, PhD [a]

Author affiliations:

[a] School of Psychology, Murdoch University, Perth, Western Australia, Australia

Reference:

Berry J.K.M., Drummond P.D. Psychological generators of stress-headaches. *Journal of Behavioural Medicine*, (2018) 41(1):109–121, https://doi.org/10.1007/s10865-017-9872-9.

Key words:

psychological stress, negative affect, migraine, tension-type headache, efficacy expectancies

Abstract

Psychological stress triggers headaches, but how this happens is unclear. To explore this, 38 migraine sufferers, 28 with tension-type headache (T-TH) and 20 controls rated nausea, NA, task-expectancies and headache at 5-minute intervals during an aversive 20-minute mental arithmetic task with a fixed failure rate. Blood pressure and pulse rate were measured every 3 minutes and salivary cortisol was sampled before and after the task. Multiple regression analysis indicated that irritation, anxiety and the absence of sluggishness (i.e., alertness) independently predicted increases in headache intensity during the task ($p<.001$), but increases in headache were unrelated to changes in cardiovascular activity or cortisol. Changes that preceded headache onset were explored in repeated measures ANOVAs, comparing those who developed headache with those who did not. In general, nausea, NA and self-efficacy expectancies were higher in participants who went on to develop headache than in those who remained headache-free ($p<.05$ to $p<.001$). Together, these findings suggest that headache developed when participants overextended themselves during a stressful task, adopting an information processing style which impeded emotional adjustment to changing situational demands. Learning to modify perceptions of threat, and adopting a more flexible, less outcome-dependent processing style, might help to prevent headache from spiralling upward.

6.1 Introduction

Migraine is defined as episodic headache lasting 4 to 24 hours, commonly unilateral, accompanied by gastrointestinal disturbances and hypersensitivity to light and sound (7). In migraine with aura, headache is preceded by focal neurological symptoms. Migraine affects some 18% of females and 6% of males (47). In contrast to migraine, tension-type headache (T-TH) is a featureless headache in which the pain is bilateral with a pressing, tightening quality (7).

Since both migraine and T-TH are significant sources of disability and suffering (5) and, as psychosocial factors are more amenable to control than physiological factors (51), investigation of initiating psychosocial factors is important. Both stress and NA have been implicated as significant headache precipitants that exacerbate the painful component of migraine and T-TH (27; 28; 30-33; 588). Tension, irritability, annoyance, depression and fatigue increase during the migraine prodromal period (27; 224). However, it is not altogether clear how stress leads to headache or whether this involves a specific form of negative affect (NA) (589), as NA encompasses a broad range of moods (228).

NA arises from subcortical emotional activity as a sense of immediate unpleasantness related to threat; the resultant feelings can subsequently be modified by visceral activity (142; 148) or by neurocognitive processes such as expectancies or reappraisal (212; 213). Thus, NA could increase headache intensity by exacerbating the affective response to pain, disrupting inhibitory pain control by altering functional activity in brain regions that modulate pain (126; 210; 246). Specifically, negative moods such as anxiety, discouragement and irritation/anger may increase pain perception (590; 591), thereby triggering headache (294; 588). In addition, the discomfort associated with headache could evoke recuperative 'sickness behaviors' (287) linked with nausea and affective states such as sluggishness and confusion (592). Consequently, a reciprocal relationship between NA and headache (593; 594), possibly involving feedback loops (595), might influence headache onset and cessation (596).

Neurocognitive processes might also influence the pain-negative affect connection (142); expectancies influence neural activation in pain-inhibitory areas, while reappraisal influences pain perception by altering threat appraisal and anxiety (212). Reappraisal could also influence NA in specific directions: anxiety may accompany moderate success-expectancy, whereas irritation accompanies low success-expectancy and discouragement the expectancy of failure (288). Self-efficacy, the conviction that one can produce the

behavior required to achieve a particular outcome in a specific situational context (597), can moderate both headache (176) and the impact of stressful events on headache (257), although how this occurs is unclear.

Our aim was to identify the antecedents of stress-headache using a biopsychosocial approach (Figure 6.1). Developed from pain processing (288) and other perceptual processing models (289), this model postulates that stress-headache results from interactions in a specific context between distal *tonic processes (*e.g., headache history and attachment anxiety) (598) and proximal *phasic responses* such as the emotional-physiological responses evoked by a stressful stimulus. Thus, we aimed to investigate the roles in headache onset and intensity of nausea, pain-related NA (anxiety, irritation and discouragement), 'stress-related' NA (sluggishness, confusion and tension) (126; 228), self-efficacy reappraisals and physiological responses (changes in cardiovascular activity and cortisol) (1; 33; 77; 490; 501; 543). Since perceived control may trigger reappraisal processes that alter the pain experience (272), increasingly non-contingent failure feedback was provided as a stressful task progressed. We expected that as efficacy expectations fell, NA and stress-headache would increase, and that migraine and T-TH sufferers would show higher stress responses and lower self-efficacy than controls.

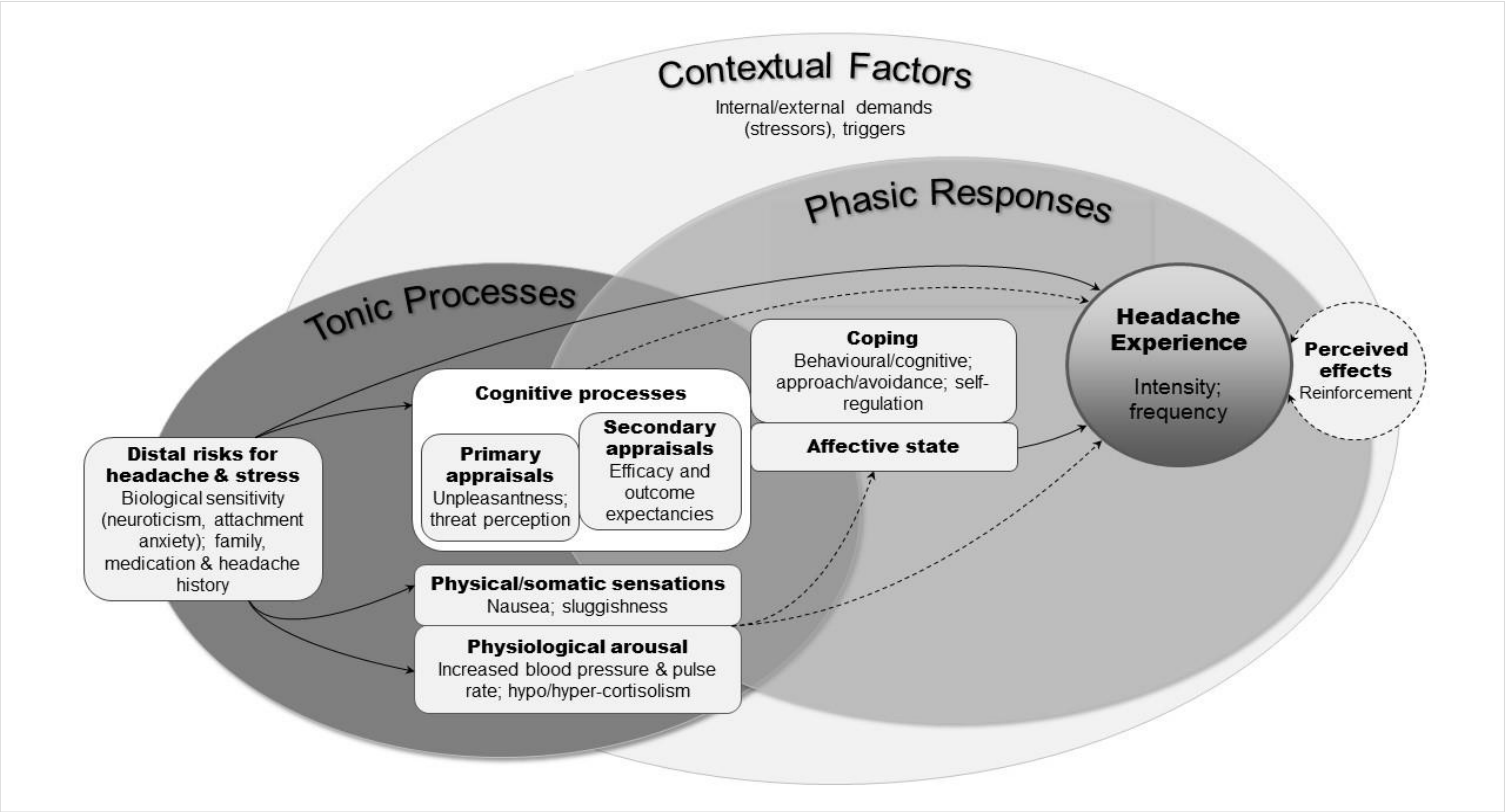


Figure 6.1 A biopsychosocial model of stress-headache adapted from perceptual and pain processing models. The model posits that in a given context, stress-headache results from interactions between distal, tonic processes including headache history, personality or attachment anxiety, and proximal, phasic responses including the physical–emotional responses to a stressful stimulus. Inter-relationships between physical sensations, secondary appraisals, physiological arousal and negative affective states were examined in this paper. Arrows indicate links but do not necessarily imply direction.

6.2 Method

6.2.1 Procedures

Where detailed descriptions have already been provided, these will not be repeated here.

Participants

Group #2: Experimental subsample (Table 2.3, p.34).

Apparatus and experimental procedures

See Section 2.2, p.35.

6.2.2 Measures

6.2.2.1 Self-reports

Self-reported headache, nausea, NA and task self-efficacy – 10-point VAS ratings taken during the experiment (Section 2.4.1.1, p.42 and Section 2.4.1.2, p.43).

6.2.2.2 Cardiovascular activity

See Section 2.3.1, p.39 and Figure 6.2 below.

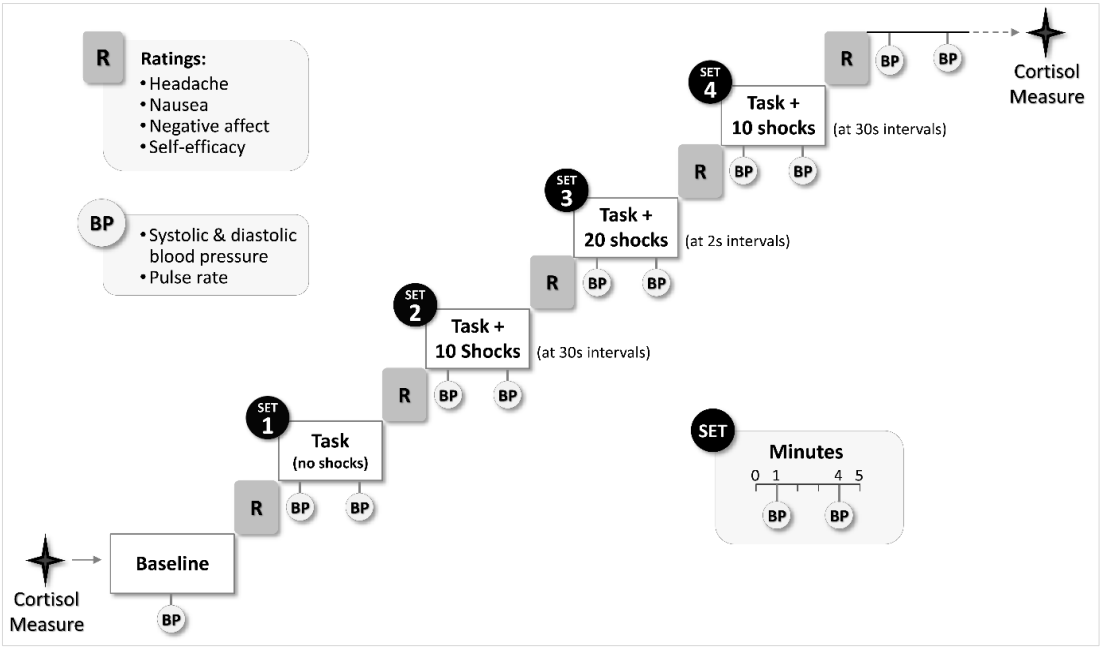


Figure 6.2 Sequence of procedures and measurement points during the stressful arithmetic task

6.2.2.3 Salivary Cortisol

Salivary cortisol was measured before and 10 minutes after the task when participants were seated quietly. The participant chewed for 10 seconds on small cotton, citric-acid-free dental rolls (599), which were transferred to labelled test tubes and frozen at -40°C until the saliva was assayed. A standard assay kit and procedure was employed (600), and the same batch of assay solution was used for all samples. A logarithmic transformation corrected wide variability in cortisol levels. (See also Section 2.3.3, p.40).

6.2.3 Data analysis

Initially, changes from baseline in headache intensity during the task were plotted against task stressfulness and changes from baseline in pain-related negative affects (anxiety, irritation, discouragement), stress-related affective states (sluggishness, confusion, tension), efficacy expectancies, nausea, systolic/diastolic blood pressure, pulse rate and salivary cortisol. Multiple regression analysis determined which subset of dependent variables best predicted increases in headache intensity, where increases were calculated as the difference between ratings of headache intensity during the task minus intensity at baseline.

The next set of analyses aimed to investigate which of the predictor variables were associated with headache onset at each 5-minute measurement point during the task. Headache onset was defined as the point at which headache ratings were first equal to or greater than 3 on the 10 cm visual analogue scale (corresponding to mild headache; ratings below this indicated that headache was minimal). Those with headache at baseline (n=7) were excluded from this analysis. Of the remaining participants, Group 1 (n=23) showed no change in headache ratings throughout the task; Group 2 (n=13) had headache onset in Set 1; Group 3 (n=21) onset in Set 2; and Group 4 (n=19) showed onset in Set 3. As headache began in Set 4 in only three participants, this last group was excluded from analysis.

Since previous research has indicated differences between migraine and T-TH, and between migraine and controls, a series of planned contrasts compared migraineurs with controls, and migraine with T-TH, in relation to the dependent variables. In particular, multivariate differences for arrays of related dependent variables (cardiovascular changes, pain-related NA and stress-related affective states) and univariate differences for nausea and efficacy expectancies were investigated in Group (planned contrast) x Set (before arithmetic and after each subsequent 5-min block of arithmetic with repeated contrasts between consecutive sets) analyses of variance. Although ratings of NA and task-self-efficacy were skewed, clustering at the lower end of the continuum, ANOVA

was employed as it is reasonably robust to violations of normality and permits investigation of interactions among factors. Significant multivariate effects were investigated in univariate analyses of variance with Greenhouse-Geisser corrections for violation of the sphericity assumption, followed by examination of simple main effects.

Analyses were run using IBM SPSS version 24. All tests of statistical significance were two-tailed. Results are presented as the mean ± standard error and $p<.05$ was considered statistically significant.

6.3 Results

Of the final sample of 72 females and 14 males, 38 met diagnostic criteria for episodic migraine, 28 for episodic T-TH and 20 formed a control group (6 or fewer headaches per year, with an average duration of less than 2 hours) (Table 2.3, p.34). As might be expected, nausea was associated more frequently with migraine than T-TH or the mild headaches reported by controls. In addition, the frequency and duration of headache episodes were greater in the migraine than T-TH group. All other demographic variables were similar in all three groups.

6.3.1 Stress-induced headache

Headache and nausea increased in parallel during the stressful task. Changes in headache intensity across the task were associated with increases in nausea, anxiety, confusion, discouragement, irritation and perceived task stressfulness but were unrelated to cardiovascular or cortisol responses. In a multiple regression analysis, irritation, anxiety and the absence of sluggishness (i.e., alertness) were significant independent predictors of increases in headache intensity across the task, $R^2 = .576$ ($p<.001$) (Table 6.1).

Table 6.1 Predictors of change in headache intensity across the stressful task

Changes across task	Mean	SD	Correlation with headache intensity	Beta weight	Significance
Headache intensity	2.08	2.03			
Nausea	1.69	1.91	.339**	.110	.416
Anxiety	1.50	1.85	.467**	.352	.033
Confusion	1.32	1.99	.386**	−.013	.939
Discouragement	1.63	2.01	.216*	−.139	.265
Irritation	3.05	1.94	.526**	.565	.000
Sluggishness	2.15	1.64	−.039	−.375	.004
Tension	1.51	1.59	−.007	−.040	.773
Self-efficacy	1.73	1.83	−.055	−.127	.270

Changes across task	Mean	SD	Correlation with headache intensity	Beta weight	Significance
Systolic blood pressure	5.97	7.75	−.161	−.139	.184
Diastolic blood pressure	3.89	5.70	.013	.065	.522
Pulse rate	1.70	8.84	−.024	.073	.425
Cortisol	−.05	.44	.210	.083	.361
Perceived task stress	4.46	1.40	.430**	.118	.245

[a] Changes in cortisol were unrelated to changes in headache intensity both in participants who completed the experiment in the morning and in those who completed the experiment in the afternoon
* Correlation is significant at the .05 level (2-tailed); ** Correlation is significant at the .01 level (2-tailed)

To clarify relationships between changes in headache and NA, each dependent variable was investigated in relation to time of headache onset. Findings are presented in Figure 6.3 – Figure 6.5, and tests of statistical significance are summarised in Table 6.2. The main points are listed below:

Cardiovascular responses peaked in the first arithmetic set (Figure 6.3) but were unrelated to headache onset in any of the first three sets.

Nausea, NA and self-efficacy expectancies generally were higher in participants who went on to develop headache in the next set of arithmetic than in those who remained headache-free; nausea and NA began to increase 10-15 minutes before headache onset in participants who developed headache later in the task (Figure 6.3 – Figure 6.5).

NA sometimes declined following headache onset, but remained higher in those with than without stress-headache (Figure 6.4, Figure 6.5).

Self-efficacy expectancies were higher in those with stress-headache following headache onset, but this difference was not maintained over the course of the experiment; in particular, self-efficacy peaked towards the end of the task in those without stress-headache (Figure 6.5).

Headache categories (migraine, T-TH, controls)

The proportion of participants who developed a moderate or severe headache was similar in the three headache categories (40% of the migraine group, 54% of the T-TH group and 65% of controls). Of the 13 participants whose headache was minimal or decreased across the course of the task, 8 had a migraine history (22.7% of the migraine group), 2 (7%) a T-TH history and 3 (15%) were controls.

Self-efficacy expectancies were lower in migraineurs than controls during the experiment, particularly in Set 1 (Figure 6.6, Table 6.3).

No other main effects were statistically significant. However, in repeated measures ANOVAs, controls showed greater initial increases (and faster declines) in tension, confusion and irritation than migraineurs (Figure 6.6, Table 6.4). Similarly, by set 3, irritation and sluggishness were greater in migraine sufferers than in those with T-TH (Figure 6.6, Table 6.5).

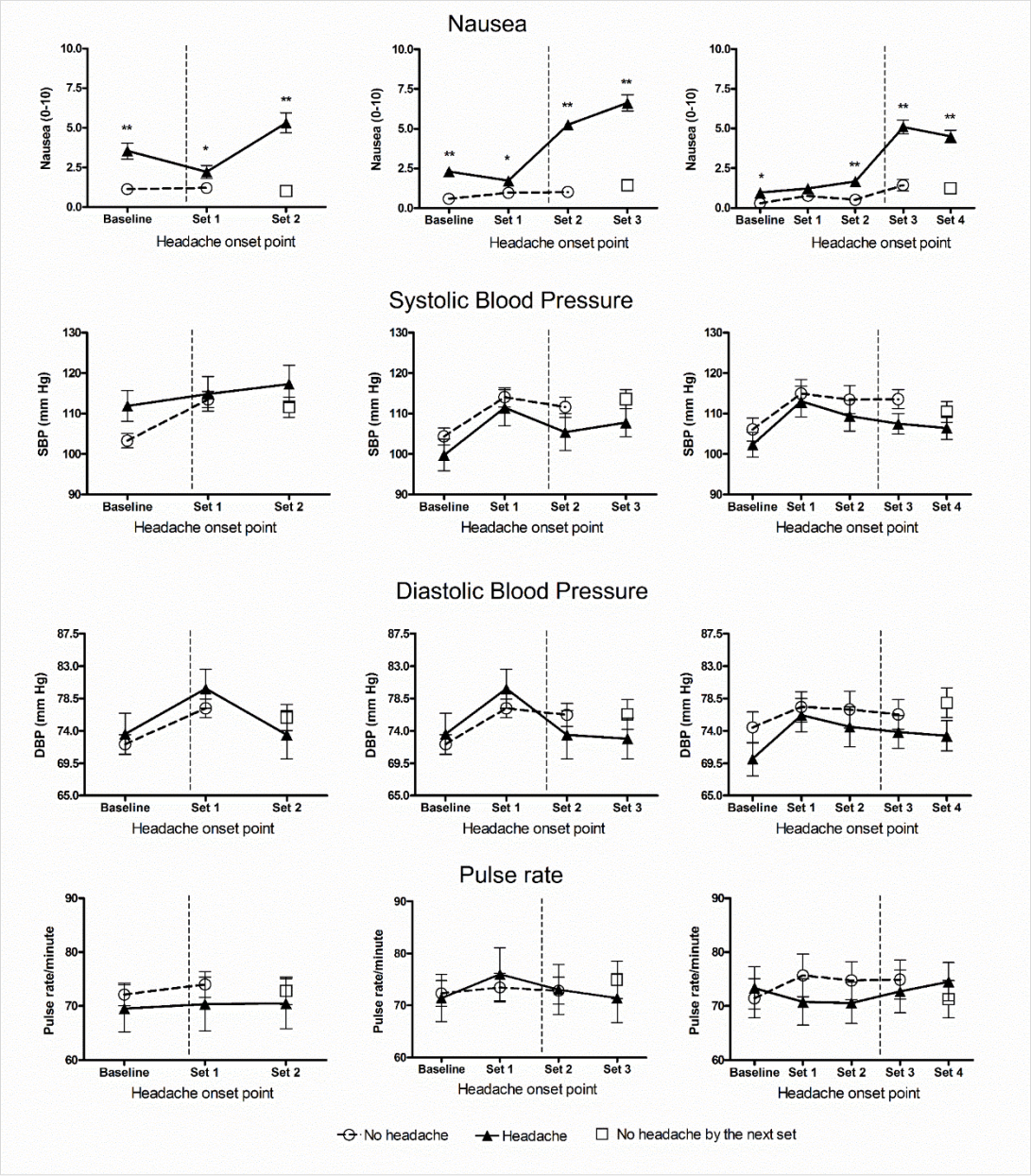


Figure 6.3 Ratings (±SE) of nausea and cardiovascular responses in relation to headache onset during stressful mental arithmetic in 13 participants whose headache started in Set 1, 21 whose headache started in Set 2, and 19 whose headache started in Set 3. (As headache began in Set 4 for only 3 participants, this group was not included in the analysis.) The *vertical dotted line* refers to headache onset point. The *asterisk* denotes significant differences between those with no headache and those with headache. As these exploratory analyses do not control for Type 1 errors, they should be interpreted with caution. *Note*: a subset of participants who developed headache in Set 1 entered the experimental phase with nausea resulting from baseline experimentation.

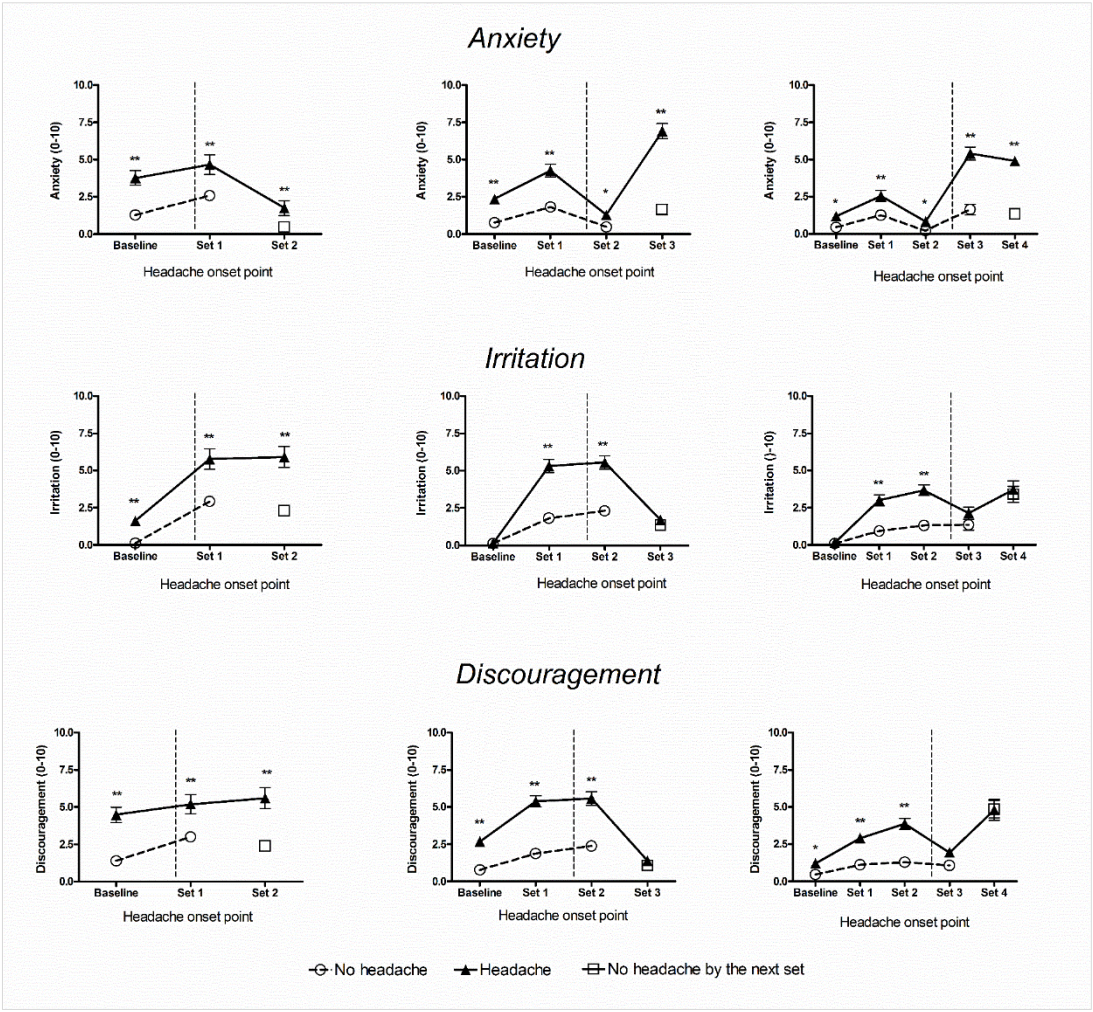


Figure 6.4 Ratings (±SE) of pain affects of anxiety, irritation and discouragement before and during stressful mental arithmetic in 13 participants whose headache started in Set 1, 21 whose headache started in Set 2 and 19 whose headache started in Set 3. The *vertical dotted line* refers to headache onset point. The *asterisk* denotes significant differences between those with no headache and those with headache. As these exploratory analyses do not control for Type 1 errors, they should be interpreted with caution.

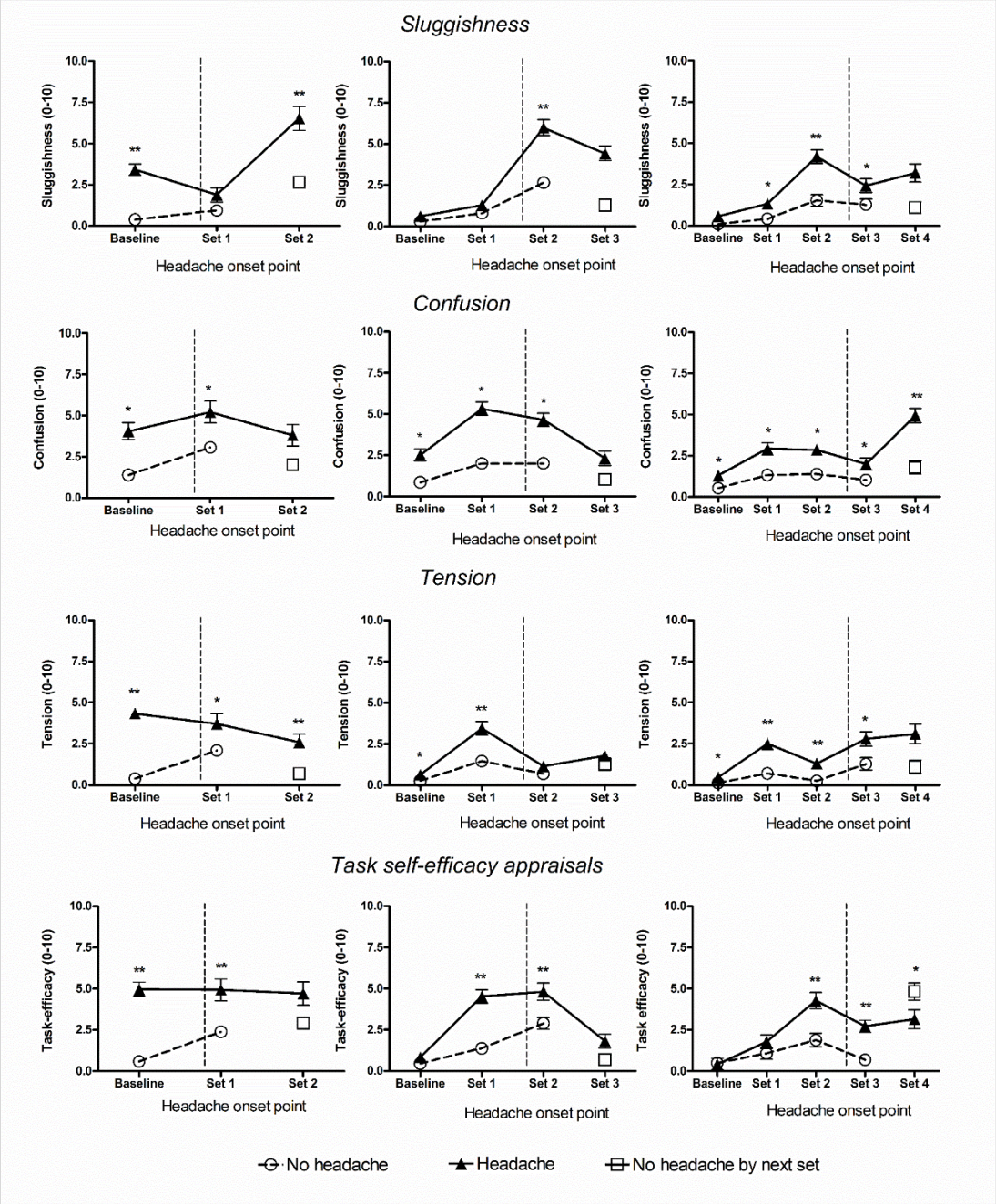


Figure 6.5 Ratings (±SE) of self-efficacy, confusion, sluggishness and tension before and during stressful mental arithmetic in 13 participants whose headache started in Set 1, 21 whose headache started in Set 2, and 19 whose headache started in Set 3. The vertical dotted line refers to headache onset point. The *asterisk* denotes significant differences between those with no headache and those with headache. As these exploratory analyses do not control for Type 1 errors, they should be interpreted with caution. *Note*: a subset of participants who developed headache in Set 1 entered the experimental phase with sluggishness resulting from baseline experimentation.

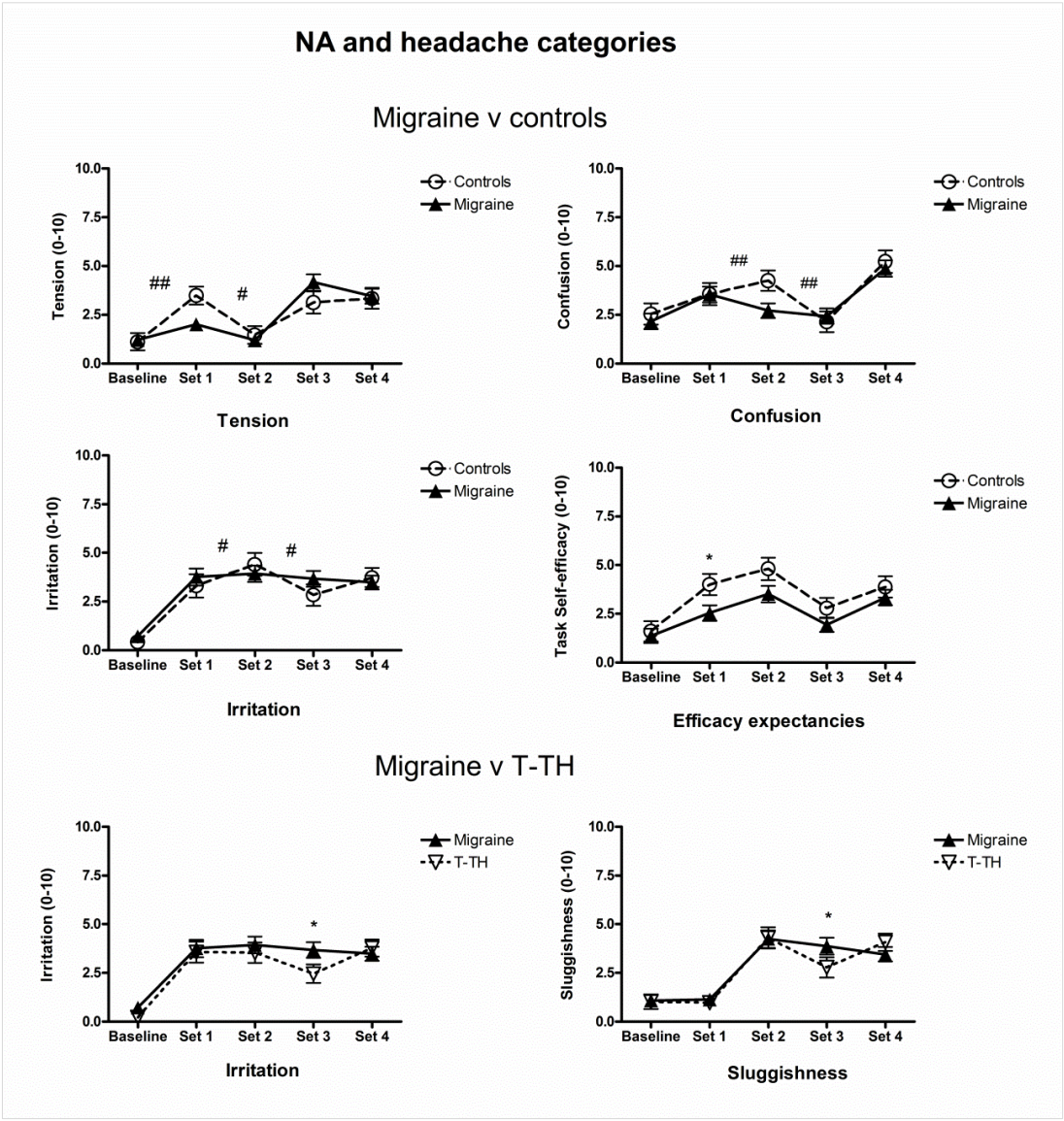


Figure 6.6 Significant negative affect differences across the experiment in migraine versus controls, and migraine versus T-TH. The hash # and ## refers to significant group × time differences between consecutive time points #$p < .05$; ##$p < .01$, *asterisks* to significant differences between groups, *$p < .05$; **$p < .01$. As these exploratory analyses do not control for Type 1 errors, they should be interpreted with caution.

Table 6.2 Effects for Group (stress-headache) and group*time interactions for each independent variable for participants whose headache began in Set 1, 2 or 3

	Set 1		Set 2		Set 3	
	Group	**Group*time**	**Group**	**Group*time**	**Group**	**Group*time**
Nausea						
	F (1,77)=19.3, p<.001, ηp2=.20	F(1,77)=6.7, p=.011, ηp2=.08	F (1,64)= 81.6, p<.001, ηp2=.56	F(1.7,110.6)=20.8, p<.001, ηp2=.25	F (1,43) = 50.5, p <.001, ηp2=.54	F(3,129)=14.6 , p<.001, ηp2=.25
Pain-related NAs						
Multivariate	F(3,75)= 10.8, p<.001, ηp2=.30	F(3,75)=4.7, p=.004, ηp2=.16	F(6,252)=52.7, p<.001, ηp2=.56	F(6,252)=10.7, p<.001, ηp2=.20	F(3,41)=16.9, p<.001, ηp2=.55	F(9,35)=3.9, p=.002, ηp2=.50
Anxiety	F(1,77)=16.1, p<.001, ηp2=.17	F(1,77)=0.5, p=.467, ηp2=.01	F (1,64) = 26.2, p<.001, ηp2=.29	F(2,128)=.6.4, p<.002, ηp2=.09	F(1,43) =50.4, p<.001, ηp2=.54	F(2.3,100.9)=13.5, p<.001, ηp2=.24
Irritation	F(1,77)=31.5, p<.001, ηp2=.29	F(1,77)=9.8, p=.087, ηp2=.04	F(1,64)= 52.2, p<.001, ηp2=.45	F(2,128)=25.5, p<.001, ηp2=.29	F(1,43)=22.7, p<.001, ηp2=.35	F(3,129)=8.0, p<.001, ηp2=.16
Discouragement	F(1,77)=24.4, p<.001, ηp2=.24	F(1,77)=1.9, p=.173, ηp2=.02	F(1,64)=64.1, p<.001, ηp2=.50	F(2,128)=5.0, p=.008, ηp2=.07	F (1,43) = 26.9, p<.001, ηp2=.38	F(3,129)=6.3, p=.001, ηp2=.13
Stress-related NAs						
Multivariate	F(3,75)=6.4, p=.001, ηp2=.20	F(3,75)=8.6, p<=.001, ηp2=.26	F(3,62)=17.7, p<.001, ηp2=.46	F(6,59)=5.2, p<.001, ηp2=.35	F(3,41)=11.9, p<.001, ηp2=.47	F(9,35)=2.0, p=.063, ηp2=.34
Sluggishness	F(1,77)=30.9, p<.001, ηp2=.29	F(1.77)=17.8, p<.001, ηp2=.19	F(1,64)= 28.8, p <.001, ηp2=.31	F(1.3,85.8)=17.2, p<.001, ηp2=.21	F(1,43) = 30.9, p <.001, ηp2=.42	F(2.2, 93.5)=5.0, p=.007, ηp2=.10
Confusion	F(1,77)=19.7, p<.001, ηp2=.20	F(1.77)=0.6, p=.369, ηp2=.01	F(1,64)=54.1, p< .001, ηp2=.46	F(2,128)=4.3, p=.015, ηp2=.06	F(1,43)=15.5, p<.001, ηp2=.26	F(3.,129)=1.2, p=.316, ηp2=.03
Tension	F(1,77)=42.2, p<.001, ηp2=.35	F(1,77)=13.8, p<.001, ηp2=.15	F(1,64) = 14.0, p< .001, ηp2= .18	F(1.7,109.7)=6.8, p=.003, ηp2=.10	F(1,43) =25.5, p<.001, ηp2=.37	F(2.1,88.8)=2.5, p=.086, ηp2=.06

	Set 1		Set 2		Set 3	
	Group	**Group*time**	**Group**	**Group*time**	**Group**	**Group*time**
Self-efficacy						
	F (1,77)=47.4, p<.001, ηp2=.38	F(1,77)=7.4, p=.008, ηp2=.09	F(1,64)=21.4, p<.001, ηp2=.25	F(2,128)=12.3, p<.001, ηp2=.16	F(1,43)=10.1, p=.003, ηp2=.19	F(3.129)=7.6, p=.001, ηp2=.15
Cardio-vascular						
Multivariate	F(3,35)=1.0, p=.384, ηp2=.08	F(3,35)=1.5, p=.228, ηp2=.11	F(3,28)=1.02, p=.398, ηp2=1.0	F(6,24)=0.5, p=.818, ηp2=.10	F(3,20)=0.4, p=.764, ηp2=.06	F(9,14)=1.5, p=.228, ηp2=.50
SBP	F (1,37)=1.7, p=.196, ηp2=.05	F(1,37)=3.5, p=.069, ηp2=.09	F(1,30) =1.0, p=.337, ηp2=.03	F(2,60)=0.4, p=.702, ηp2=.01	F(1,22)=1.1, p=.301, ηp2=.05	F(3,66)=.0.3, p=.814, ηp2=.01
DBP	F (1, 37) =0.6, p=.452, ηp2=.02	F(1,37)=0.2, p=.680, ηp2=.00	F(1,30) =0.3, p=.867, ηp2=.00	F(2,60)=0.6, p=.573, ηp2=.02	F(1,22)=1.0 =.339, ηp2=.04	F(3,66)=.0.4, p=.788, ηp2=.02
Pulse rate	F (1,37)=0.6, p=.448 ηp2=.02	F(1,37)=0.1, p=.713, ηp2=.00	F(1,30) =.00, p=.974, ηp2=.00	F(1.6,48)=0.3, p=.698, ηp2=.01	F(1,22)=.0.2, p=.632, ηp2=.01	F(2.3,49.7)=1.1, p=.342, ηp2=.05

Table 6.3 Rating changes (±SE) in nausea and negative affect in relation to headache category (migraine, T-TH, controls)

		Controls		Migraine		T-TH	
		Mean	**SE**	**Mean**	**SE**	**Mean**	**SE**
Nausea	Baseline	2.37	0.46	1.52	0.34	1.72	0.41
	Set 1	1.60	0.42	1.76	0.31	1.28	0.32
	Set 2	3.28	0.54	2.86	0.39	2.90	0.50
	Set 3	4.79	0.65	4.67	0.47	4.83	0.59
	Set 4	4.98	0.58	4.51	0.42	4.33	0.54
Anxiety	Baseline	2.50	0.52	1.92	0.38	1.73	0.40
	Set 1	3.66	0.55	2.97	0.40	3.12	0.49
	Set 2	1.39	0.39	0.92	0.28	0.99	0.33
	Set 3	5.26	0.65	4.76	0.47	5.12	0.60
	Set 4	5.30	0.61	4.66	0.44	4.44	0.55
Confusion	Baseline	2.55	0.55	2.17	0.40	1.75	0.43
	Set 1	3.57	0.57	3.54	0.41	3.72	0.49
	Set 2	4.25	0.53	2.72	0.38	3.42	0.46
	Set 3	2.14	0.53	2.43	0.38	1.99	0.43
	Set 4	5.23	0.58	4.88	0.42	4.38	0.55
Discouragement	Baseline	2.41	0.52	2.14	0.38	1.93	0.45
	Set 1	3.57	0.54	3.61	0.39	3.47	0.49
	Set 2	4.30	0.57	3.85	0.42	3.79	0.52
	Set 3	2.47	0.47	2.79	0.34	2.42	0.44
	Set 4	5.40	0.62	5.25	0.45	4.72	0.52

		Controls		Migraine		T-TH	
		Mean	**SE**	**Mean**	**SE**	**Mean**	**SE**
Irritation	Baseline	0.42	0.29	0.73	0.21	0.23	0.23
	Set 1	3.32	0.60	3.77	0.43	3.57	0.53
	Set 2	4.42	0.58	3.93	0.42	3.54	0.52
	Set 3	2.85	0.55	3.68	0.40	2.46	0.48
	Set 4	3.73	0.49	3.48	0.35	3.78	0.43
Sluggishness	Baseline	0.92	0.39	1.09	0.28	1.02	0.38
	Set 1	1.93	0.43	1.13	0.31	0.97	0.32
	Set 2	4.48	0.61	4.24	0.44	4.30	0.55
	Set 3	3.02	0.56	3.87	0.41	2.78	0.52
	Set 4	4.09	0.52	3.46	0.38	4.08	0.45
Tension	Baseline	1.12	0.44	1.21	0.32	1.26	0.40
	Set 1	3.49	0.46	2.02	0.34	2.61	0.44
	Set 2	1.47	0.46	1.20	0.33	1.12	0.35
	Set 3	3.13	0.57	4.17	0.41	3.08	0.54
	Set 4	3.34	0.53	3.45	0.39	3.98	0.46
Self-efficacy	Baseline	1.60	0.52	1.37	0.37	1.27	0.43
	Set 1	4.00	0.55	2.54	0.40	2.56	0.47
	Set 2	4.81	0.58	3.52	0.42	3.95	0.49
	Set 3	2.80	0.51	1.94	0.37	1.87	0.41
	Set 4	3.88	0.54	3.33	0.39	3.96	0.49

Table 6.4 F-ratios for significant group*time interactions across headache categories and consecutive sets of mental arithmetic

Variables	Main and interaction effects		Migraine v controls				Migraine v T-TH			
			F	df	p	η_p^2	F	df	p	η_p^2
Nausea	Group		0.40	(1,56)	.527	.01	0.01	(1,62)	.921	.00
	Group*time	Baseline – Set 1	4.94	(1,56)	**.030**	.08	2.07	(1,62)	.156	.03
		Set 1-Set 2	0.78	(1,56)	.380	.01	0.61	(1,62)	.439	.01
		Set 2-Set 3	0.32	(1,56)	.574	.01	0.05	(1,62)	.827	.00
		Set 3-Set 4	0.73	(1,56)	.398	.01	0.54	(1,62)	.465	.01
Anxiety	Group		1.16	(1,56)	.287	.02	0.00	(1,62)	.944	.00
	Group*time	Baseline – Set 1	0.04	(1,56)	.844	.00	0.52	(1,62)	.474	.01
		Set 1-Set 2	0.12	(1,56)	.732	.00	0.03	(1,62)	.869	.00
		Set 2-Set 3	0.00	(1,56)	.980	.00	0.15	(1,62)	.702	.00
		Set 3-Set 4	0.10	(1,56)	.754	.00	2.14	(1,62)	.149	.03
Confusion	Group		0.57	(1,56)	.453	.01	0.04	(1,62)	.848	.00
	Group*time	Baseline – Set 1	0.26	(1,56)	.611	.00	1.04	(1,62)	.312	.02
		Set 1-Set 2	7.66	(1,56)	**.008**	.12	0.96	(1,62)	.331	.02
		Set 2-Set 3	7.37	(1,56)	**.009**	.12	3.79	(1,62)	.056	.06
		Set 3-Set 4	0.64	(1,56)	.425	.01	0.00	(1,62)	.944	.00
Discouragement -	Group		0.05	(1,56)	.832	.00	0.33	(1,62)	.566	.01
	Group*time	Baseline – Set 1	0.26	(1,56)	.611	.00	0.02	(1,62)	.900	.00
		Set 1-Set 2	1.05	(1,56)	.310	.02	0.03	(1,62)	.858	.00
		Set 2-Set 3	1.84	(1,56)	.181	.03	0.42	(1,62)	.521	.01
		Set 3-Set 4	0.27	(1,56)	.609	.00	0.04	(1,62)	.847	.00

Variables	Main and interaction effects		Migraine v controls				Migraine v T-TH			
			F	df	p	η_p^2	F	df	p	η_p^2
Irritation	Group		.16	(1,56)	.690	.00	1.01	(1,62)	.319	.02
	Group*time	Baseline – Set 1	0.04	(1,56)	.839	.00	0.18	(1,62)	.673	.00
		Set 1-Set 2	4.61	(1,56)	**.036**	.08	0.17	(1,62)	.682	.00
		Set 2-Set 3	5.42	(1,56)	**.024**	.09	3.00	(1,62)	.088	.05
		Set 3-Set 4	1.60	(1,56)	.211	.03	4.28	(1,62)	**.043**	.06
Sluggishness	Group		.13	(1,56)	.723	.00	.11	(1,62)	.739	.00
	Group*time	Baseline – Set 1	3.07	(1,56)	.085	.05	0.04	(1,62)	.844	.00
		Set 1-Set 2	0.46	(1,56)	.499	.01	0.09	(1,62)	.766	.00
		Set 2-Set 3	3.69	(1,56)	.060	.06	4.94	(1,62)	**.030**	.07
		Set 3-Set 4	2.05	(1,56)	.158	.04	3.78	(1,62)	.056	.06
Tension	Group		.07	(1,56)	.789	.00	.00	(1,62)	.997	.00
	Group*time	Baseline – Set 1	7.04	(1,56)	**.010**	.11	1.15	(1,62)	.288	.02
		Set 1-Set 2	4.41	(1,56)	**.040**	.07	2.00	(1,62)	.163	.03
		Set 2-Set 3	3.68	(1,56)	.060	.06	2.32	(1,62)	.133	.04
		Set 3-Set 4	0.74	(1,56)	.394	.01	2.97	(1,62)	.090	.05
Self-efficacy	Group		4.77	(1,56)	**.033**	.08	.23	(1,62)	.632	.00
	Group*time	Baseline – Set 1	3.31	(1,56)	.074	.06	0.04	(1,62)	.843	.00
		Set 1-Set 2	0.06	(1,56)	.802	.00	0.44	(1,62)	.510	.01
		Set 2-Set 3	0.28	(1,56)	.597	.01	0.63	(1,62)	.430	.01
		Set 3-Set 4	0.11	(1,56)	.746	.00	0.68	(1,62)	.412	.01

Table 6.5 Multivariate and univariate F ratios for group and group*time interactions for each planned contrast

		Planned contrast 1 Migraine v controls		*Planned contrast 2* Migraine v T-TH	
		Group	**Group*Time**	**Group**	**Group*Time**
Nausea		F(1, 56)=0.4, p=.527, η_p^2=.01	F(2.6, 146.5)=0.8, p=.502, η_p^2=.01 [a]	F(1, 62)=.01, p=.921, η_p^2=.00	F(2.7, 166.7)= .43, p=.712, η_p^2=.01
Pain-related NAs	Multivariate	F(3, 54)=.1.83, p=.152, η_p^2=.09	F(12, 45)=1.25, p=.279, η_p^2=.25	F(3, 60)=1.2, p=.322, η_p^2=.06	F(12, 51)=1.04, p=.426, η_p^2=.20
	Anxiety	F(1, 56)=1.2, p=.287, η_p^2=02	F(2.8,155.6)=.04, p=.987, η_p^2=.00	F(1, 62)=.01, p=.944, η_p^2=.00	F(2.4, 148.1)=.34, p=.749, η_p^2=.01
	Irritation	F(1, 56)=0.2, p=.690, η_p^2=.00	F(2.2, 125.3)=1.0, p=.366, η_p^2=.02 [b,c]	F(1, 62)=1.01, p=.319, η_p^2=.02	F(2.7, 164.9)=1.3, p=.276, η_p^2=.02 [d]
	Discouragement	F(1, 56)=.05, p=.832, η_p^2=.00	F(2.6, 144.9)=.29,p=.805, η_p^2=.01	F(1, 62)=.33, p=.566, η_p^2=.01	F(2.6, 162.4)=0.2, p=.910, η_p^2=.00
Openness	Multivariate	F(3, 54)=.26, p=.852, η_p^2=.01	F(12, 45)=1.8, p=.076, η_p^2=.33	F(3, 60)=.18, p=.912, η_p^2=.01	F(12, 51)=1.25, p=.278, η_p^2=.23
	Sluggishness	F(1, 56)=0.1, p=.723, η_p^2=.00	F(2.4, 134.7)=1.3,p=.271, η_p^2=.02	F(1, 62)=.11, p=.739, η_p^2=.00	F(2.7, 166.8)=1.6, p=.206, η_p^2=.02 [c]
	Confusion	F(1, 56)=0.6, p=.453, η_p^2=.01	F(3.3, 184.9)=2.04, p=.104, η_p^2=04 [b,c]	F(1, 62)=.04, p=.848, η_p^2=.00	F(3, 189.1)=1.4, p=.242, η_p^2=.02 [c]
	Tension	F(1, 56)=0.1, p=.789, η_p^2=.00	F(2.7, 154)=2.67, p=.104, η_p^2=.05 [a,b]	F(1, 62)=.00, p=.997, η_p^2=.00	F(2.9, 181.3)=2.0, p=.120, η_p^2=.03
Self-efficacy		**F(1, 56)=4.8, p=.033, ηp2=.08**	F (3.2, 179.6)=0.7, p=.546, η_p^2=.01	F(1, 62)=.23, p=.632, η_p^2=.00	F(2.9, 176.9)=0.4, p=.750, η_p^2=.01

		Planned contrast 1 **Migraine v controls**		***Planned contrast 2*** **Migraine v T-TH**	
		Group	**Group*Time**	**Group**	**Group*Time**
Cardiovascular	Multivariate	F(3, 27)=0.7, p=.545, η_p^2=.07	F(12, 18)=0.8, p=.659, η_p^2=.34	F(3, 26)=0.5, p=.648, η_p^2=.06	F(12, 17)=0.6, p=.774, η_p^2=.31
	SBP	F(1, 29)=1.2, p=.284, η_p^2=.04	F(4, 116)=1.0, p=.429, η_p^2=.03	F(1, 28)=0.0, p=.966, η_p^2=.00	F(3.1, 88)=0.2, p=.881, η_p^2=.01
	DBP	F(1, 29)=1.8, p=.195, η_p^2=.06	F(2.3, 65.7) =0.9, p=.410, η_p^2=.03	F(1, 28)=0.7, p=421, $\eta_p^2$2=.023	F(2.2, 61.1)=0.4, p=.685, η_p^2=.01
	Pulse rate	F(1, 29)=0.0, p=.967, η_p^2=.00	F(3.1, 90)=0.3, p=.860, η_p^2=.01	F(1, 28)=0.02, p=.874, η_p^2=.00	F(4, 112)=1.1, p=.367, η_p^2=.04

[a] = repeated measures contrasts between baseline and Set 1
[b] = repeated measures contrast between Set 1 and Set 2
[c] = repeated measures contrast between Set 2 and Set 3
[d] = repeated measures contrast between Set 3 and Set 4

6.4 Discussion

The primary aim of this study was to identify the psychosocial antecedents of stress-induced headache. Nausea and NA rose during the stressful task, and headache intensity was linked with heightened irritation, anxiety and alertness rather than a headache predisposition. However, cardiovascular activity and cortisol levels were unrelated to headache onset.

We expected that stress-headache onset would be associated with increases in NA, nausea, cardiovascular activity and cortisol levels, and with reductions in self-efficacy. Our key finding was identifying an increase in nausea, pain-related NA and stress-related NA before headache onset. This implies but does not dictate a causal relationship as, for example, the stressor might have triggered neurobiological or psychological responses that manifested first as nausea and NA and then as headache. Once the headache began, nausea and NA generally continued to rise, remaining higher in those with than without stress-headache. A reciprocal relationship may thus have existed between nausea, NA and headache. The two-way relationship between nausea and headache has been noted before (210; 601).

Unexpectedly, headache onset was preceded by higher rather than lower efficacy expectancies. One explanation is that low initial expectancies minimised discouragement and associated symptomatology. Consistent with this, patterns of expectancies differed markedly between those with and without stress-headache. Those acquiring a stress-headache had higher initial expectancies which dropped sharply mid-way through the task, in association with increases in NA. Individuals who perceive a high degree of control generally persist in the face of failure (272). In the present study, participants who acquired a stress-headache apparently remained confident of success until the task was well underway, perhaps only belatedly realising its uncontrollability. In contrast, those remaining headache-free showed a 'wait-and-see' pattern, their lower initial efficacy expectancies gradually rising to a high point at task end. This increase in expectancies may have corresponded with reappraising the task as a challenge rather than a threat.

These contrasting patterns also suggest different information processing styles. The assimilative-accommodative processing distinction is central to explaining how cognitive processing regulates affective states and thus how self-efficacy can moderate the impact of stressful events on headache. The hallmark of the top-down, assimilative style is active persistence – trying harder – in the face of failure and best suits knowledge-based tasks

with clear 'correct' answers. Failure leads eventually to discouragement and giving-up (602-604). This style fits the pattern of our stress-headache participants. In contrast, those who remained headache-free displayed a pattern consistent with bottom-up accommodative processing. This style of 'flexible readjustment' permits realignment of expectancies to match situational demands, minimizing dysphoria and pain (605), and suits a time-pressured, unpredictable-uncontrollable task (606) such as ours.

We expected that changes in physiological arousal would be associated with headache, particularly in migraine and T-TH sufferers, because negative appraisals and threats may promote withdrawal of parasympathetic tone and a reciprocal excitation of sympathetic tone (148). However, cortisol and cardiovascular changes were unrelated to stress-headache acquisition or headache category (see also 607). Thus, our results offer little support for the idea that stress-headache is a direct response to a general increase in physiological arousal, or that a primary autonomic abnormality increases vulnerability to episodic headaches. Nonetheless, autonomic dysregulation in stress-headache cannot be discounted entirely because headache was not examined in relation to disturbances in intracranial or extracranial vascular reactivity (77; 524) or to other physiological indices of headache. Furthermore, parasympathetic processes were not measured in our study (148).

Counter-intuitively, stress-headache developed in 65% of our controls but in only 40% of the migraine group. Self-efficacy ratings were higher in controls than migraineurs, perhaps because such individuals are generally less sensitive to pain and less reactive to stressful events than migraineurs (608). However, the adoption of an assimilative information processing style by controls may have impeded adjustment to situational demands and possibly increased headache risk (605). In contrast, the prior headache experiences of migraine sufferers may have resulted in more accurate appraisals of the headache potential of the task, which they attempted to minimise by utilising energy-conserving accommodative processing rather than the analytic processing associated with (chronic) migraine headache (609). In this way, our stressful task may have tapped into psychosocial factors that trigger headache in most people.

Consistent with this interpretation, NA increased rapidly in controls but then subsided whereas, in migraineurs, NA increased as the task progressed and persisted at high levels. Ultimately, the "driven", "perfectionistic" characteristics of migraineurs (131) may lead them to "expend too much energy in an effort to overcome external obstacles" resulting in "fatigue... (and) high risk for headache" (610 p.94). 'Overactivity' can increase pain (611), whereas a mindful, detached mindset can reduce it (612). Future research could identify the

extent to which these outcomes are stressor- rather than setting-specific, apply to chronic headache sufferers and/or represent a learned coping response. Use of a stressor optimally requiring an assimilative style may be instructive, as would specific indicators of the tendency to over-extend oneself during task performance.

This study was the first to explore inter-relationships between stress-induced headache and psychological (NA, expectancies, reappraisal), somatic (nausea) and physiological (cardiovascular, cortisol) responses during an unpredictable and uncontrollable 'daily hassles' simulation. Findings were consistent with our biopsychosocial model of headache, but should be interpreted cautiously. To minimise the type 1 error rate, significant multivariate effects were investigated in univariate analyses incorporating planned contrasts between groups and across time, followed by contrasts between groups at each time point to clarify significant main effects and interactions. However, as this approach resulted in a large number of statistical tests, our findings require replication. In addition, bias induced by the choice of stressor and the use primarily of a university student sample may lessen the generalizability of our results to clinical populations or chronic headache sufferers. Since the task itself increased NA, our paradigm did not permit definitive conclusions about the impact of headache on NA. Further, we did not collect reports of positive affect, so our assessment of stress – the collapse of positive emotions (45) – did not capture this dimension. Since positive emotions hasten return to homeostasis, they could reduce headache and autonomic arousal. Future research should assess these possibilities. Our groups were matched for age, gender and education, but headache frequency and duration were greater in the migraine than the T-TH group. Whether these variables influence responses to stress independently of headache diagnosis requires further study.

In conclusion, our findings suggest that stress-headache developed when participants misappraised their ability to master a stressful task, over-extending themselves by trying to manage it. Thus, stress-headache may develop when adjustment to changing environmental demands is poor. Learning to modify perceptions of threat, and adopting a more flexible, less outcome-dependent processing style, might help to reduce or prevent stress-related headache.

Chapter Seven

7

Appraisal, personality and headache

Overview

Background. Headache has been consistently linked with exaggerated primary appraisals of harm and with secondary appraisals of inadequate coping abilities. Personality traits have likewise been consistently linked with stress appraisals that increase headache risk.

Methods. Multiple regression analyses and regression-based path analysis were used to test hypotheses that the high negative affect (NA) preceding stress-headache resulted from:

i. heightened threat appraisals which increase stressor exposure, and
ii. greater stressor reactivity (less use of problem- and emotion-management, greater use of avoidance, reduced pain and task self-efficacy).

Five factor model (FFM) personality traits and an anxious or avoidant attachment style were expected to moderate headache-related NA.

Results. Discouragement and tension predicted headache intensity and mediated the effect of threat appraisals and stressor reactivity on headache. Problem avoidance, high outcome expectancies and pain-control belief predicted headache, and these aspects of secondary appraisal were variously moderated by high agreeableness, high neuroticism, low openness, low extraversion and high conscientiousness.

Conclusions. Discouragement, tension and anxiety predict headache and are elicited by stressor exposure (the likelihood of a subjective stress or threat appraisal) and stressor reactivity (high outcome expectancies, avoidant coping and low pain self-efficacy (belief in one's ability to decrease pain).

7.1 Introduction

In Chapter 3, neuroticism and aspects of extraversion and conscientiousness were found to predict headache during the stressful task. However, the particular *processes* by which these traits and their facets may induce headache during stress require elucidation. Also, as described in chapter 6, high NA and high-yet-inflexible expectations preceded headache. Migraineurs also had higher and more sustained NA over the course of a stressful task than T-TH or controls. But what is the source of this NA? Subtle cognitive dysfunctions, including dysfunctional prospective memory, have been reported in migraine-without-aura patients (613; 614). Since the experience of stress is fundamentally one of disrupted affective processing, occurring when top-down controls can no longer keep the spontaneous behavioural and emotional dictates of more primitive brain control systems in check (126), stress-related cognitive disruption may underlie or exacerbate headache-related NA in headache patients. But how may such cognitive disruption be assessed *in situ*?

In Lazarus' cognitive theory of stress and the emotions, an event can only be stressful if appraised as such (615). The stress process is initiated by *primary appraisals*, pre-cognitive 'affective computations' arising from subcortical emotional command centres as a sense of immediate unpleasantness (126). An event is assessed as to whether it constitutes a threat (of harm or loss), is benign-positive, e.g. a challenge, or is irrelevant (159). Signals of punishment, direct injury, a block to important goals, the unfamiliar or pain can stimulate a threat appraisal and associated NA (167).

Health is compromised when situations are habitually appraised as stressful or a threat (185). In a study of air traffic controllers, minor illnesses and psychological distress were independently predicted both by objective stressors (weather conditions, congestion) and subjective stress (616). Threat/stress appraisals may be greater in in headache-prone individuals. Headache patients were more likely to interpret minor occurrences as major distressing situations (194). Although many factors mediate this relationship (617), headache-prone individuals can become increasingly risk-averse, over-estimating the likelihood of a stressor's capacity for disruption (184; 344; 618-620), i.e. stressor exposure. In a vicious cycle, appraisals of threat increase subjective stress, in turn increasing the likelihood of subsequent threat appraisals (stressor exposure) (184) and headache risk (620).

Stressor exposure can be measured by self-reports of the stressfulness and threat posed by an event (621). It was hypothesised that stressor exposure would be greater in those who developed a stress-headache and in headache sufferers compared with controls.

Secondary appraisals may further (or not) the stress process. These 'cognitive computations' (143) arise from the interaction of the various emotion systems with cortically-based self-representation systems (126; 143). Assessment is made of (i) one's coping resources and options, (ii) one's personal degree of control and who is deemed accountable, and (iii) outcome expectancies. These jointly determine emotional/somatic reactivity to the stressor (159). Depending on the appraisal, headache-relevant NA may be elevated or reduced (166). Thus, a stressor perceived as outside one's control is associated with increased NA and subjective stress, decreased active coping (232; 269; 270), increased autonomic arousal (256), and physiological changes such as norepinephrine (NE) depletion and increased serotonin (5-HT) sensitization (225; 264; 622-626).

When pain is the stressor, pain self-efficacy appraisals further determine reactivity (597), likewise influencing NA and autonomic arousal, as well as pain tolerance, anticipated and experienced pain intensity and pain unpleasantness (256; 625-629) – although general affective processing and affective pain processing may not correspond in a one-to-one fashion (250). Pain self-efficacy appraisals predict treatment outcome and distinguish headache sufferers from controls (176; 597; 630-634).

7.1.1 Measures

Thus, the following aspects of stressor reactivity were measured:

1. **Coping options** – estimates of one's capacity to cope with the stressor by:
    a) *Problem engagement* – taking action to change the situation, to remove or eliminate stressors or reduce their intensity, in order to make them more congruent with one's goals. It is associated with reduced NA (635-637), and has been linked positively to extraversion (638), agreeableness and conscientiousness (636; 639).
    b) *Emotion management* – adjusting to the situation and diminishing its emotional impact, should the circumstances remain inconsistent with one's goals. It "involves a strong internal focus … adjusting oneself, so that one can accept, function in and adapt to undesirable circumstances, whether these adjustments be through changing one's goals, reinterpreting the meaning and implications of the situation, seeking comfort and support from others, or through other means" (163,p.1365). Emotion-management may serve as a buffer in the face of stress, reducing anxiety and other negative emotions. It correlates negatively with distress, perceived stress and

negative affectivity, and positively with indicators of adaptation, including positive affectivity, self-esteem and quality of emotional support (163; 640).

c) *Problem/emotion avoidance* – attempts to minimise, deny or ignore the existence of the stressor or the need to deal with it (159; 641). Problem avoidance is associated with the prospective generation of both chronic and acute life stressors (642) and, depending on the stressor and level of distress (643), with neuroticism, low trait conscientiousness, greater pain report and somatic distress (344; 420; 636; 638; 644). Its association with neuroticism may derive from the fact that high-N scorers are less able to regulate NA during stress, catastrophically magnifying negative symptoms and thereby their encoding and recall (405; 408). The converse may be true for individuals high in positive affectivity (extraversion), and indeed, extraversion (and high-conscientiousness) predicted more problem solving and cognitive restructuring (645) compared with low-scorers on these dispositions.

2. **Pain self-efficacy** – Estimates of the individual's capacity to cope with the stressor of pain, specifically belief in one's ability to:

   a) *Control pain* – Pain-control belief is a significant predictor of health outcomes in patients with chronic pain (646; 647). Physiologically, perceived pain control influences levels of catecholamines and endogenous opioids which, in turn, affect pain report (597). Psychologically, a sense of uncontrollability over pain augments perception of pain intensity, demoralization, and negative emotional reactions to nociceptive stimulation (648). Therefore, doubts about pain control are associated with increased pain, psychological distress, and avoidance of painful activities (256; 649; 650).

   b) *Decrease pain* – Although research specific to pain-decrease belief is limited, stronger beliefs may be associated with a psychological rather than a biomedical perspective on pain, such as the value of relaxation in pain management (651).

3. **Outcome expectancies**– Higher outcome expectancies were predictive of headache (Chapter 6), perhaps resulting in use of the 'assimilative' processing style associated with migraine (606; 609). Expectancies can determine feelings: discouragement relates to a failure expectancy, irritation to a low expectancy of success, anxiety to moderate success expectancy (288). It was expected that higher outcome

expectancies would predict headache and possibly discouragement if the person believed themselves to have the ability to succeed, but nonetheless were failing.

Identifying the precise role of appraisal processes in headache may increase the efficacy of headache treatment programs since, unlike physiological reactivity, stress appraisal processes constitute a relatively modifiable component of the stress process.

7.1.2 Personality traits as moderators of appraisal processes

In stressor exposure and reactivity, personality may play a significant role (184), via cognitive biases in the information processing of valenced stimuli. The trait of neuroticism (negative affectivity) for example may be associated with headache because high scorers are more likely to appraise demanding situations as threatening (652), to then encounter stressful situations (185) and to have difficulties regulating NA during stress (181). The converse may be true for individuals high in positive affectivity (extraversion) (645). Similarly, perfectionism is associated with chronic headache (620) which may relate to indices of negative affectivity in university students (653). Individuals scoring high in neuroticism are particularly sensitive to the minor irritations of daily life and exhibit a tendency to dwell upon and magnify mistakes and shortcomings. This may in turn make them more likely to experience a significant amount of distress (654), increasing headache vulnerability. Johnson (655) for example argued that the 'high negative affect' indicative of trait neuroticism was uniquely related to 'diseases of a tension-type, such as high blood pressure, migraine or neck pain'.

By influencing NA and/or the propensity to assess a situation as a threat, personality traits may influence harm/loss appraisals and thus the high NA leading to headache.

Personality traits may also mediate risk appraisals by increasing the tendency to repress NA. For example, air traffic controllers who claimed not to feel stress were nevertheless showing signs of arousal (616), and may have been what is termed 'repressors' in the literature (low trait anxiety coupled with high defensiveness). These individuals disengage from stressful information by means of selective attention, ignoring or denial of their emotional response (656), i.e. avoidance. Similarly, a lack of 'enthusiasm for new experiences' – an aspect of the trait of openness (406) – was predictive of headache in clinical populations (240; 360).

Low-extraversion may increase the frequency, intensity or duration of the autonomic stress response (657; 658), whereas neuroticism, low-openness or low-agreeableness may be associated with blunted cardiovascular or cortisol reactivity during a mental stressor (418; 586). These somatic responses may themselves increase appraisals of harm or risk.

Furthermore, in conjunction with high harm avoidance, low self-directedness (which is characteristic of impulsivity) (406) may increase stressor exposure, NA and headache (344). Impulsive individuals for example may fail to implement positive health behaviours (400), to monitor known and idiosyncratic headache triggers (589) or to engage in positive and routine self-care – such as maintaining a healthy diet, abstaining from smoking, excessive alcohol intake, illicit drug use or abuse of headache medications (420; 589; 659-661).

Therefore, it was expected that anxious attachment or personality traits which heighten (or fail to dampen) NA would be associated with headache via increased stressor exposure – i.e. neuroticism, low-openness (conservatism), low-conscientiousness (impulsivity).

On the basis of previous research, it was also expected that problem avoidance would be greater in individuals scoring high in neuroticism but low in conscientiousness, that problem engagement would be greater in those scoring high in extraversion, and emotion management greater in those scoring high in openness.

7.1.3 Research paradigm

Since NA can precipitate headache, the present research adopted the paradigm of *biopsychosocial synergism* (424), within which multiple and interacting variables would be involved in the link between headache and NA. Distal factors such as individual differences in stable personality traits and attachment-based styles of relating (424) were expected to interact with proximal factors such as stress appraisal processes, temporary emotional states or psychophysiological reactivity. Jointly, these factors may create broad mood states which influence cognitive-emotional processing during stress (181) and thus headache activity. Attachment style may also impact stressor exposure by altering emotion regulatory capacities and relationship skills (especially with attachment-relevant stressors), influencing baseline levels of NA (449; 662). Following on from the work of Bolger and Zuckerman (185) on personality in the stress process, the following conceptual model was developed, as illustrated in Figure 7.1.

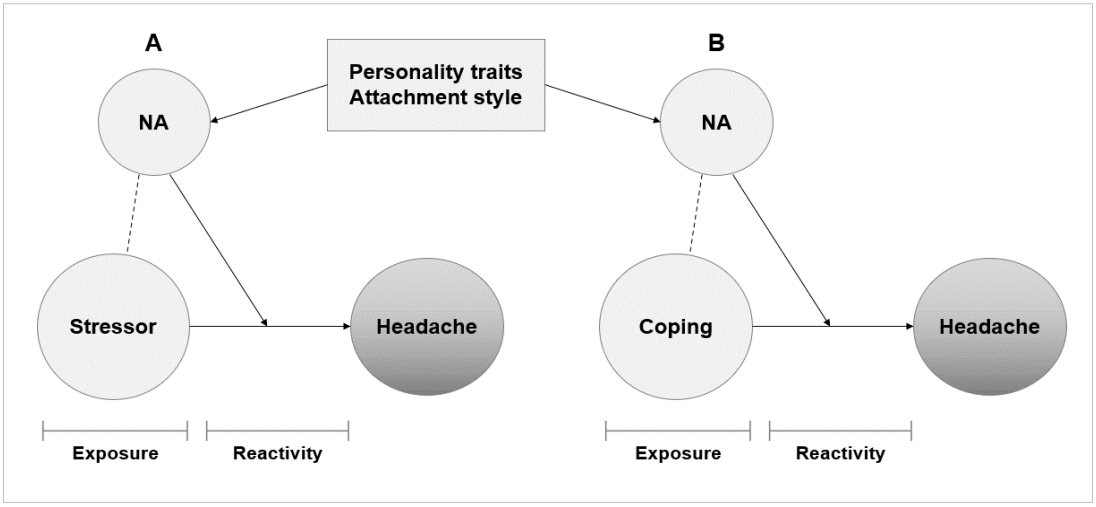


Figure 7.1 General framework linking stressor exposure and reactivity to NA, personality and attachment style. After Bolger & Zuckerman (185). (A) Primary appraisal (exposure to stressors) and secondary appraisal (stressor reactivity); (B) components of stressor reactivity: coping choice and coping effectiveness. Dotted lines indicate a mediating relationship, solid lines a moderating relationship. Therefore, in (A) NA mediates stressor exposure and moderates stressor reactivity. In (B), NA mediates coping choice and moderates coping effectiveness. Personality and attachment style may moderate NA.

7.2 Method

7.2.1 Procedures

Where detailed descriptions have already been provided, these will not be repeated here.

Participants

Group #2: Experimental subsample (Table 2.3, p.34).

Apparatus and experimental procedures

See Section 2.2, p.35.

7.2.2 Measures

The measures have been described in more detail earlier in the thesis. The specific measures used are as follows:

1. Personality assessment: NEO-PI-R (323) Section 2.4.2.1, p.43.
2. Self-rated headache, nausea and affect during the laboratory stressor. These 10-point VAS scales are described in Section 2.4.1.1, p.42. As NA preceded headache, a score for each affect was computed as the average of the first two blocks of the arithmetic task.

3. Outcome expectancies. At the beginning of each math set, participants were asked to "please rate your ability to avoid mistakes for the remainder of the task" "How well do you think you will go in the test?" scored on a 0-10 Scale, where 0 = no ability, 10 = complete ability. Outcome expectancy was the average score for the first and second math sets.
4. Stress coping in the laboratory stressor was assessed using the *Ways of Coping Questionnaire, WCQ-R* (Adapted version), Section 2.4.2.3, p.44.
5. Pain coping: *Coping Styles Questionnaire – Revised* (CSQ-R)(329) (Section 2.4.2.4, p.45).
6. Stressor exposure: Measure #1: Subjective stress appraisals.
7. Stressor exposure: Measure #2: Task threat vs challenge

7.2.2.1 Stressor exposure: Measure #1: Subjective stress appraisals

The four stressor appraisal questions in the *Ways of Coping Questionnaire* (WCQ-R)(663) were modified as follows. The changes are italicised.

1. *Perceived Controllability:* How much control did you feel that you had over *your results in this test*? (1 = none at all, 7 = total control).
2. *Felt arousal* or emotional impact: Did it affect you in a minor way or did you feel that this *test affected you more than that?* (1 = hardly at all, 7 = affected me greatly).
3. *Perceived importance* of stressor: Was *doing well in the test* important to you? (1 = not at all, 7 = extremely important).
4. *Subjective stressfulness:* "How stressful did you find this *testing experience* to be?"

In a Principal Components Analysis, these four stressor appraisal questions yielded a two-factor solution with varimax rotation, shown in Table 7.1. Consistent with Lazarus (664), these stressor exposure factors were termed "Subjective stress" and "Controllability" and the relationship of each with headache intensity was computed separately.

Table 7.1 Component matrix for four primary appraisal dimensions of the modified WCQ-R (Extraction method: Principal component analysis, Varimax with Kaiser normalization).

	Arithmetic stressor	
Dimension	**Factor 1 (Subjective stress)**	**Factor 2 (Uncontrollability)**
Stressor uncontrollability		.949
Stressor importance	.709	.310
Stressor impact	.808	–.195
Subjective stress	.823	–.137

7.2.2.2 Stressor exposure: Measure #2: Task threat vs challenge

As an additional check on the validity of the primary appraisal measures, the extent to which participants viewed the task as a threat or a challenge was assessed by means of the following open-ended question immediately following the stressful task, the answer to which was written down: "Please consider what was the worst aspect of this test for you? And what do you believe motivated you in the maths test that you have just completed, i.e. what was at stake for you in doing well, or at least in not doing badly?" To ensure that participants gave more than one-word answers to this question, the experimenter added two probe questions as needed: "Could you comment a little more about that?" and "Can you give me a specific example of what you mean?" These answers were added to the form.

Three raters independently scored these answers as either 1 = challenge appraisal, or 2 = threat appraisal. Threat appraisals consisted of expressed feelings of humiliation or embarrassment, threats to self-image or competence ("Didn't want to look stupid"; "tried to save face"; "Didn't want anyone to see how useless I am at maths").

A challenge appraisal was scored if the participant expressed or anticipated pride in succeeding or persisting at the task despite obstacles: "I just wanted to get it right – a challenge"; "A sense of pride – I've always been quite good at maths"; "To achieve a sense of fulfilment- if I could do well in the maths test given the situation with the pain and the noise"; "To see if I could try and work out which type of baby cry it was".

Of the responses obtained to the question, 57% of participants appraised the task as a challenge, 43% as a threat. Kappa inter-rater reliability coefficient = 0.978.

7.2.2.3 Measuring stressor reactivity

A modified WCQ-R was scored as per Folkman & Lazarus' factor analysis of a community sample (663). (See Appendix C, p.305)

1. Problem engagement: confrontive coping and planful problem solving subscales.
2. Emotion management: distancing, self-controlling, support-seeking, accepting responsibility and positive reappraisal subscales.
3. Avoidant coping: 'escape-avoidance' subscale.
4. Pain-control and pain-decrease belief were separately assessed on a seven point VAS scale, (*Coping Styles Questionnaire*) (329), Section 2.4.2.4 (page 45). Zero = no

control/can't decrease it at all, 3 = some control/can decrease it somewhat, and 6 = complete control/can decrease it completely.

5. Outcome expectancy and self-efficacy changes. Following two practice questions, participants rated their 'ability to avoid mistakes for the remainder of the task', on a ten-point VAS rating scale. Zero corresponded to 'none' and 10 to 'totally'. Outcome expectancy was the sum of the first two efficacy measures in the arithmetic task (measured prior to the task and head shocks). Task self-efficacy *changes* consisted of outcome expectancies minus the efficacy ratings for the three arithmetic sets.

7.2.3 Data analysis

Since previous research indicates coping differences between migraine, T-TH and controls, two planned contrasts compared outcomes in (i) headache sufferers v controls and (ii) migraine v T-TH. (iii) Comparisons were also made between those who did and did not acquire a stress headache. These differences were investigated in Group (planned contrast) multivariate analyses of variance. Although ratings were skewed, clustering in the lower end of the continuum, analysis of variance was employed to investigate these relationships as it is fairly robust to violations of normality.

Preliminary analyses included t-tests, chi-square tests, bivariate correlation analyses and analyses of covariance to investigate group (planned contrast) differences on various measures including catastrophizing, active coping, coping flexibility, pain self-efficacy, headache frequency, age of onset, gender and age. The association between mean headache intensity during the arithmetic task and each of the stress/pain coping methods reported during the laboratory stressor was explored with Pearson's correlation coefficient. Bivariate correlational relationships were examined for possible covariates.

Hierarchical multiple regressions were performed to determine how much variance was accounted for by NA in the relationship between stressor reactivity and headache. The dependent variable was mean headache ratings across the task. Independent variables were personality traits, insecure attachment style and either stressor exposure (perceived stressfulness, uncontrollability, threat v challenge), or stressor reactivity (problem engagement, emotion management, problem avoidance, pain-control belief, pain-decrease belief, outcome expectancy, decline in self-esteem). These variables were entered at the first step, the six NA at the second step (Model A). Analyses were then

repeated with all NA at the first step, stressor exposure/reactivity, personality and attachment at the second step (Model B).

The moderating roles of personality traits or attachment status were further explored using Hayes' macro for regression-based path analysis (665), Models 8, 58 or 59 – diagrammed in Figure 7.2. In assessing the role of the moderator, W = moderator, X = predictor variable, and the X*W relationship is the indicator of significance.

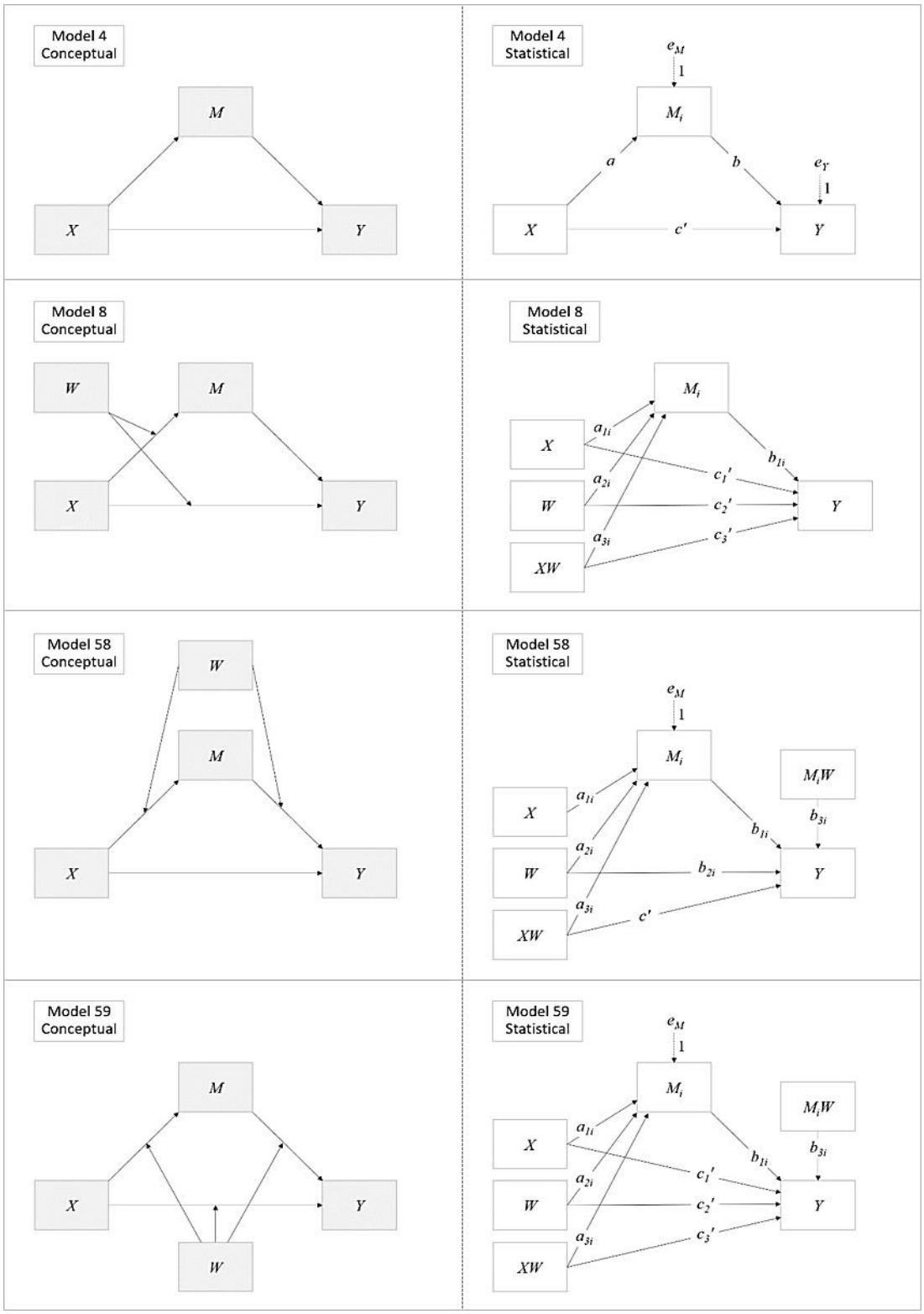


Figure 7.2 A simple mediation model (Model 4), and conditional process models (Models 8, 58, 59) in conceptual (left) and statistical (right) forms. From Hayes (665) All tests of statistical significance were two-tailed. Results are presented as the mean ± standard error, and $p < 0.05$ was considered to be statistically significant. X = predictor variable, Y = outcome variable (headache), M = mediator, W = moderating variable.

HYPOTHESIS 1: STRESSOR EXPOSURE PREDICTS HEADACHE THROUGH INCREASED NA, MODERATED BY PERSONALITY TRAITS.

7.3 Hypothesis 1 results

7.3.1 Stressor exposure and headache intensity: migraine, T-TH and controls

As Table 7.2 shows, headache sufferers were more likely than controls to appraise the task as a threat rather than a challenge, whereas appraisals of 'stressfulness' and 'uncontrollability' were similar between migraine, T-TH and controls.

Table 7.2 Primary appraisals of the stressful task in migraine, T-TH and controls.

	Controls		Headache		Migraine		T-TH	
	Mean	**SE**	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**
F1: Stressfulness	0.21	0.21	0.05	0.12	0.08	0.14	–0.04	0.17
F2: Uncontrollability	0.12	0.21	–0.04	0.12	–0.08	0.16	0.08	0.19
Threat v challenge	1.18	0.10	1.51	0.06	1.48	0.08	1.50	0.09

Appraisals WCQ-R (Adapted)	**Headache sufferers v controls**				**Migraine v T-TH**			
	F	***df***	***p***	***ŋ2***	***F***	***df***	***p***	***ŋ2***
Factor 1: Perceived stressfulness	0.82	(1, 88)	0.366	0.01	0.28	(1, 69)	0.596	0.00
Factor 2: Uncontrollability	0.42	(1, 88)	0.518	0.00	0.45	(1, 69)	0.502	0.01
Threat (v challenge)	7.66	(1, 89)	0.007	0.08	0.04	(1, 70)	0.845	0.00

7.3.2 Stressor exposure and stress-headache intensity

Table 7.3 Comparison of primary appraisals between those with and without stress headache

Primary appraisals (Adapted WCQ-R)	**Low/no stress headache**		**Stress-headache**		**Effects**			
	Mean	**SE**	**Mean**	**SE**	***F***	***df***	***p***	***ŋ2***
F1: Stressfulness	–0.439	0.147	0.406	0.138	17.578	(1, 83)	**<.001**	0.175
F2: Uncontrollability	0.119	0.161	–0.062	0.152	0.671	(1, 83)	0.415	0.008
Threat v challenge	1.700	0.143	1.867	0.135	0.722	(1, 83)	0.398	0.009

As shown in Table 7.3, subjective stress appraisals (stressor exposure) were greater in those with than without stress-headache ($p < .001$). However, threat appraisals and perceived stressor (un)controllability did not discriminate between those with and without stress-headache.

7.3.3 Does NA mediate the relationship between stressor exposure and headache intensity?

As shown in Table 7.4, correlation analysis indicated that subjective stress appraisals were related to threat appraisals ($p < .05$) and all six NA ($p < .01$), particularly discouragement ($r = 0.586$) and anxiety ($r = 0.457$). Threat appraisals were related to confusion, discouragement, sluggishness and tension ($p < .05$).

Table 7.4 Pearson correlations between primary appraisals and NA during the four sets of the arithmetic task

	Subjective stress	(Un)controllability	Threat/challenge
Factor 1: Subjective stress (Perceived stressfulness)	–		
Factor 2: Uncontrollability	0.000	–	
Threat (v challenge)	0.238*	–0.013	–
Anxiety	0.457**	–0.166	0.186
Confusion	0.550**	–0.159	0.248*
Discouragement	0.586**	–0.197	0.260*
Irritation	0.539**	–0.164	0.206
Sluggishness	0.513**	–0.136	0.230*
Tension	0.399**	–0.173	0.269*

Note: Two tailed test. Significance: *p<.05, **p<.01

Hierarchical multiple regression analyses were then conducted in order to determine whether stressor exposure predicted headache intensity once all NA were controlled for. At the first step, stressor exposure (primary appraisals of stressfulness, uncontrollability and threat), insecure attachment style (anxious and avoidant), and FFM personality factors were entered, and accounted for 38% of the variance in headache intensity during the laboratory stressor ($p<.0001$). Specifically, subjective stress ($\beta=0.520$, $p<.001$) predicted headache intensity (Model 1A in Table 7.5). Entering the six NA at the second step (Model 2A in Table 7.5) accounted for 49% of variance ($p < .0001$) in headache intensity. In particular, discouragement ($\beta=0.526$, $p = .007$) and tension ($\beta=0.168$, $p = 0.030$) independently predicted headache intensity.

By contrast, entering stressor exposure, personality and attachment status variables second (Model 2B in Table 7.5) accounted for virtually all of the variance that these variables shared with the six NA (1.7% of the shared total of 87%, $p < .0001$). Together these analyses indicate that the association between discouragement, tension and headache almost completely accounted for the relationship between subjective stress appraisals and headache intensity during the laboratory stressor.

Table 7.5 Hierarchical multiple regression: Predicting headache intensity from stressor exposure, attachment and personality .

	Model 1A	Model 1B	Model 2
R^2	0.380 ***	0.853***	0.870***
R^2 change			
Model 1A or 1B to Model 2	0.490***	0.017	
Beta weights in each model			
Perceived stressfulness	**0.520*** **		–0.029
Perceived uncontrollability	–0.040		0.012
Challenge or threat appraisal	0.063		–0.018
Attachment anxiety	–0.149		–0.048
Attachment avoidance	0.050		0.005
Neuroticism	0.098		0.062
Extraversion	0.137		–0.006
Openness	–0.160		–0.020
Agreeableness	0.122		–0.081
Conscientiousness	0.007		0.054
Anxiety		0.142	0.126
Confusion		0.023	0.028
Discouragement		**0.418***	**0.526***
Irritation		**0.268***	0.193
Sluggishness		0.002	0.017
Tension		**0.172***	**0.168***

Note: [a] R^2 = 0.870 (full regression model), p<.0001, *p<.05, **p<.01, ***p<.001.

7.3.4 Moderating effects of personality traits on NA associated with stressor exposure

Table 7.6 shows Pearson correlations between the distal factors of personality and attachment style and each NA.

Table 7.6 Pearson correlations between personality traits, attachment status and NA during the stressful task

	Anxious	Confused	Discouraged	Irritated	Sluggish	Tense
Attachment anxiety	0.112	0.000	–0.007	–0.067	0.097	0.187*
Attachment avoidance	–0.074	–0.075	–0.093	–0.103	–0.086	–0.031
Neuroticism	0.236	0.213*	0.134	0.006	0.064	0.297**
Extraversion	0.200*	0.107	0.170	0.076	0.046	0.253**
Openness	–0.172	–0.054	–0.116	–0.109	–0.193*	–0.208*
Agreeableness	0.196*	0.223*	0.235*	0.156	0.124	0.093
Conscientiousness	–0.152	–0.208*	–0.169	–0.054	–0.134	–0.231**

To determine the extent to which each personality trait moderated headache-related NA, conditional process analyses (665), Model 58 (Figure 7.2), investigated their relationships with NA and headache. As shown in Table 7.7, the higher the level of agreeableness, the greater the degree of discouragement (p =.011) – although the lower the level of tension (as indicated by indirect effects in which boot values were entirely above zero). Conservatism (low-openness) also moderated the effects of subjective stress on headache via a direct association with increased tension (p <.001) and an indirect association with heightened discouragement.

Table 7.7 Conditional indirect effects of agreeableness and openness as moderators of discouragement and tension in the relationship between subjective stress and headache (Model 59).

		M_1 Discouragement				M_2 Tension			
AGREEABLENESS (A)[a]									
$M*W_{Agreeableness}$		F (1,74) = 0.00, p = .994				F (1,74) = 0.57, p = .453			
	Trait score	***Coeff***	***SE***	***p***		***Coeff***	***SE***	***p***	
Constant		0.345	1.310	.793		1.000	1.110	.367	
Effect of X on M		1.320	1.270	.304		1.720	1.073	.113	
Effect of W on M		0.028	0.011	**.011**		0.006	0.009	.495	
X*W		0.000	0.010	.968		–0.008	0.009	.353	
		Effect	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***
Indirect effects of X on Y	Low A	0.910	.182	.504	1.232	0.251	.123	.045	.518
	Medium A	0.916	.142	.661	1.223	0.171	.077	.020	.325
	High A	0.920	.177	.651	1.353	0.115	.091	–.079	.283
OPENNESS (O)[b]									
$M*W_{Openness}$		F (1,77) = 0.495, p = .484				F (1,77) = 2.97, p = .089			
	Trait score	***Coeff***	***SE***	***p***		***Coeff***	***SE***	***p***	
Constant		3.745	1.437	.011		3.300	1.150	.005	
Effect of X on M		2.240	1.255	.078		2.390	1.000	**.019**	
Effect of W on M		–0.001	0.011	.960		–0.013	0.009	.163	
Conditional effects of X on M at values of W	Low O	–	–	–		1.070	0.280	**<.001**	
	Medium O	–	–	–		0.760	0.170	**<.001**	
	High O	–	–	–		0.520	0.196	**.010**	
		Effect	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***
Indirect effects of X on Y	Low O	1.040	.243	.515	1.478	0.330	.174	.067	.745
	Medium O	0.892	.143	.624	1.184	0.163	.083	.018	.339
	High O	0.782	.176	.525	1.238	0.074	.081	–.077	.245

[a] *Agreeableness score values:* Low (16th percentile) = 103.48; Medium (50th percentile) = 128; High (84th percentile) =147; [b] *Openness score values:* Low (16th percentile) = 102.12; Medium (50th percentile) = 121; High (84th percentile) =136

Abbreviations: A = Agreeableness, O = Openness, W = moderating variable, X = antecedent variable (subjective stress), Y = consequent variable (headache intensity), M = mediating variable, a = relationship between antecedent variable and M, c = direct relationship between X and Y, b = relationship between M and Y (see also Figure 7.2).

Note: Interactions are significant when confidence intervals are entirely above or below zero (shaded boot value areas indicate that the interaction is significant).

HYPOTHESIS 2: STRESSOR REACTIVITY INCREASES THE NA ASSOCIATED WITH HEADACHE, MODERATED BY PERSONALITY TRAITS.

7.4 Hypothesis 2 results

7.4.1 Stressor reactivity in migraine, T-TH, controls

As shown in Table 7.8, stressor reactivity was similar in migraine, T-TH and controls. However, appraised ability to decrease pain was greater in T-TH than migraine participants (p =.008).

Table 7.8 Aspects of stressor reactivity: means and standard errors, all effects

Secondary appraisals (stressor reactivity)	Migraine		T-TH		Controls	
	Mean	SE	Mean	SE	Mean	SE
Problem engagement	1.042	0.082	1.051	0.095	1.095	0.106
Emotion management	0.965	0.070	0.935	0.082	0.940	0.097
Problem avoidance	0.662	0.099	0.756	0.116	0.754	0.126
Ability to control pain	3.368	0.173	3.875	0.201	3.714	0.236
Ability to decrease pain	3.053	0.141	3.643	0.164	3.429	0.216
Outcome expectancy	3.034	0.345	3.123	0.402	4.074	0.483
Self-efficacy changes	2.638	0.250	2.902	0.291	3.252	0.338

	Headache sufferers v controls				Migraine v T-TH			
	F	*df*	*p*	*ŋ2*	*F*	*df*	*p*	*ŋ2*
Multivariate analysis								
Stressor reactivity	0.730	(7,77)	0.647	0.062	1.58	(7,58)	0.159	0.160
Univariate analyses								
Problem engagement	0.213	(1, 83)	0.645	0.003	0.005	(1, 64)	0.943	0.000
Emotion management	0.001	(1, 83)	0.975	0.000	0.079	(1, 64)	0.780	0.001
Problem avoidance	0.194	(1, 83)	0.661	0.002	0.378	(1, 64)	0.541	0.006
Ability to control pain	0.345	(1, 83)	0.558	0.004	3.644	(1, 64)	0.061	0.054
Ability to decrease pain	0.427	(1, 83)	0.515	0.005	7.438	(1, 64)	**0.008**	0.104
Outcome expectancy	2.925	(1, 83)	0.091	0.034	0.028	(1, 64)	0.867	0.000
Self-efficacy changes	1.663	(1,83)	0.201	0.020	0.471	(1,64)	0.495	0.007

7.4.2 Stressor reactivity and stress-headache

Overall, as shown in Table 7.9, stressor reactivity was greater in those with than without stress-headache (p <.001), viz. greater problem avoidance (p = .001), higher outcome expectancy (p <.001) and lower pain-decrease belief (p = .009).

Table 7.9 Stress-headache and aspects of stressor reactivity: means, standard errors, all effects

Secondary appraisals (stressor reactivity)	Low/no stress headache		Stress-Headache		Effects			
	Mean	SE	Mean	SE	*F*	*df*	*p*	*η2*
					Multivariate analysis			
					10.173	(7,77)	**<.001**	0.480
					Univariate analyses			
Problem engagement	1.069	0.08	1.039	0.07	0.081	(1, 83)	.777	0.001
Emotion management	0.942	0.07	0.944	0.07	0.001	(1, 83)	.977	0.000
Problem avoidance	0.496	0.09	0.893	0.08	11.380	(1, 83)	**.001**	0.121
Ability to control pain	3.700	0.17	3.500	0.16	0.729	(1, 83)	.396	0.009
Ability to decrease pain	3.600	0.15	3.044	0.14	7.184	(1, 83)	**.009**	0.080
Outcome expectancy	1.804	0.27	4.739	0.25	63.677	(1, 83)	**<.001**	0.434
Self-efficacy changes	2.774	0.247	2.962	0.233	0.307	(1,83)	0.581	0.004

7.4.3 Does NA mediate the relationship between stressor reactivity and headache intensity?

As Table 7.10 shows, coping styles were intercorrelated (p <.01) as were pain-decrease and pain-control beliefs (p <.01). Pain-control belief also correlated with problem engagement and emotion management but was unrelated to NA, whereas pain-decrease belief correlated inversely with confusion but was uncorrelated with any coping style. Thus, separate assessment of these aspects of pain self-efficacy is indicated. Outcome expectancy was correlated with problem avoidance (p <.01) and with all NA (p <.01).

Table 7.10 Pearson correlations between aspects of stressor reactivity and each negative affect

	Problem engage-ment	Emotion manage-ment	Problem avoidance	Pain control belief	Pain decrease belief	Outcome expectancy	Self-efficacy change
Problem engagement	-	**0.502****	**0.321****	0.168	0.072	–0.024	**0.220***
Emotion management	**0.502****	-	**0.451****	**0.278****	0.126	–0.017	0.022
Problem Avoidance	**0.321****	**0.451****	-	0.203	–0.015	**0.412****	**0.218***
Pain control belief	0.168	**0.278****	0.203	-	**0.427****	–0.002	0.096
Pain decrease belief	0.072	0.126	–0.015	**0.427****	-	–0.165	–0.015
Outcome expectancy	–0.024	–0.017	**0.412****	–0.002	–0.165	-	0.155
Self-efficacy change	**0.220***	0.022	**0.218***	0.096	–0.015	0.155	-

	Problem engage-ment	Emotion manage-ment	Problem avoidance	Pain control belief	Pain decrease belief	Outcome expectancy	Self-efficacy change
Anxiety	0.138	0.193	**0.440****	–0.005	–0.047	**0.603****	**0.421****
Confusion	0.039	0.064	**0.414****	–0.097	**–0.233***	**0.712****	0.184
Discouragement	0.014	0.126	**0.446****	–0.110	–0.191	**0.704****	0.130
Irritation	–0.004	0.080	**0.430****	–0.052	–0.072	**0.647****	0.001
Sluggishness	0.123	**0.219***	**0.541****	–0.071	–0.137	**0.616****	**0.269***
Tension	0.081	0.182	**0.473****	0.077	–0.004	**0.674****	**0.324****

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).

Hierarchical multiple regression analysis was conducted to assess whether stressor reactivity (problem engagement, emotion management, problem avoidance, pain-control, pain-decrease, outcome expectancy, self-efficacy changes), insecure attachment style (anxious and avoidant) and FFM personality traits predicted headache intensity during the cognitive task, after controlling for the influence of anxiety, confusion, discouragement, irritation, sluggishness and tension (each NA was averaged across the first two blocks of the arithmetic task).

At the first step, stressor reactivity, personality traits and insecure attachment jointly accounted for 66.6% of the variance in headache intensity during the laboratory stressor ($p<.0001$). In particular, outcome expectancy ($\beta= .603$, $p<.001$) and avoidant coping ($\beta= 0.266$, $p<.01$), predicted headache intensity (Model 1A in Table 7.11). Entering the six NA at the second step (Model 2 in Table 7.11) accounted for 23.9% of variance ($p <.001$) in headache intensity. Anxiety ($\beta= 0.229$, $p <.05$), discouragement ($\beta= 0.376$, $p <.05$), irritation ($\beta= 0.305$, $p =.05$), avoidant coping ($\beta= 0.121$, $p <.05$), ability to decrease pain ($\beta= –0.140$, $p <.05$), outcome expectancy ($\beta= 0.142$, $p <.05$) and agreeableness ($\beta= –0.104$, $p <.05$) independently predicted headache intensity at this step.

By contrast, entering NA measures first (Model 1B), and all stressor-reactivity measures, attachment style and personality factors second (Model 2 in Table 7.11) accounted for almost all of the variance in headache intensity (85.3% of the shared total of 90.5%, $p <.0001$). Together these analyses indicate that the association between NA (primarily anxiety, discouragement, irritation) and headache intensity during the cognitive stressor almost completely accounted for the relationship between stressor reactivity measures and headache.

Table 7.11 Predicting headache intensity from stressor reactivity, NA, attachment and personality: in multiple regression analyses.

	Model 1A	Model 1B	Model 2
R^2	**0.666*** **	**0.853*** **	**0.905*** **
R^2 change			
Model 1A or 1B to Model 2	**0.239*** **	**0.052** **	
Beta weights in each model			
Problem engagement	–0.038		–0.042
Emotion management	0.086		–0.016
Avoidance	**0.266** **		**0.121***
Ability to control pain	–0.132		0.022
Ability to decrease pain	–0.066		**–0.140***
Outcome expectancy	**0.603*** **		**0.142***
Self-efficacy change	–0.017		–0.032
Attachment anxiety	–0.021		–0.024
Attachment avoidance	0.004		–0.020
Neuroticism	0.072		0.026
Extraversion	0.027		–0.039
Openness	–0.095		0.003
Agreeableness	–0.008		**–0.104***
Conscientiousness	–0.002		0.009
Anxiety		0.142	**0.229** **
Confusion		0.023	–0.104
Discouragement		**0.418***	**0.376***
Irritation		**0.268***	**0.305***
Sluggishness		0.002	–0.065
Tension		**0.172***	0.123

*= p<.05, ** = p<.01, ***= p<.001

7.4.4 Moderating effects of personality traits on NA and headache intensity

Agreeableness was an independent predictor of headache intensity (Table 7.11). In regression-based path analysis, Model 59 (665) (see Figure 7.2), the moderating role of this trait on the established mediators of anxiety (M_1), irritation (M_2), discouragement (M_3) was examined.

Of the three coping options, higher levels of agreeableness moderated the relationship between *problem avoidance* and headache (medium, p <.01; high, p < .05), specifically because more agreeable individuals were also more anxious and discouraged (Table 7.12 and Table 7.13). The higher levels of anxiety, irritation and discouragement in more

agreeable individuals ($p<.05$) were associated also with higher outcome expectancy and reduced pain self-efficacy (pain-decrease belief), thereby increasing headache vulnerability.

Other FFM traits. Conditional process analyses for the other FFM personality traits are shown in Supplementary Data Table 7.14 – Table 7.21 (pages 190 – 197). These indicate that high neuroticism ($p<.05$), openness ($p<.05$), low-conscientiousness (impulsivity) ($p<.05$) moderated the relationship between stressor reactivity and headache by increasing pain-decrease belief. However, neuroticism ($p <.05$), introversion ($p <.05$), conservatism ($p <.05$) and conscientiousness ($p <.01$) also moderated the relationship between stressor reactivity and headache by increasing avoidant coping, since all were associated with greater discouragement early in the stressful task.

Table 7.12 The relationship between three potential coping options during the laboratory stressor and headache intensity, as moderated by FFM agreeableness

		Problem Engagement (X_1)			Emotion Management (X_2)			Avoidance (X_3)		
AGREEABLENESS (A) [a]										
X*Agreeableness		F (1,71) = 0.055, p = .816			F (1,71) = 1.224, p = .272			F (1,71) = 0.163, p = .688		
Anxiety*A		F (1,71) = 0.363, p = .549			F (1,71) = 0.549, p = .461			F (1,73) = 0.284, p = .596		
Irritation*A		F (1,71) = 0.776, p = .381			F (1,71) = 0.785, p = .378			F (1,73) = 0.823, p = .367		
Discouragement * A		F (1,71) = 0.492, p = .485			F (1,71) = 0.420, p = .519			F (1,73) = 0.745, p = .2391		
	Trait score	***Coefficient***	***SE***	***p***	***Coefficient***	***SE***	***p***	***Coefficient***	***SE***	***p***
Conditional direct effects of X on Y (Y= headache)	Low A	–.140	.242	.566	–.017	.020	.384	.354	.278	.207
	Medium A	–.088	.214	.683	.002	.017	.888	.441	.171	**.012**
	High A	–.044	.334	.895	.019	.026	.467	.514	.247	**.041**
		Effect	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***
Conditional indirect effects of X on Y, mediated by anxiety	Low A	.192	.275	–.312	.767	.021	.024	–.020	.075	.287	.271	–.208	.842
	Medium A	.241	.186	–.146	.585	.021	.015	–.006	.052	.273	.142	.033	.583
	High A	.260	.218	–.198	.678	.019	.016	–.010	.052	.246	.177	–.081	.620
Conditional indirect effects of X on Y, mediated by irritation	Low A	.007	.191	–.347	.491	.000	.014	–.025	.034	–.022	.249	–.600	.470
	Medium A	.032	.137	–.225	.356	.011	.013	–.008	.044	.135	.183	–.192	.566
	High A	.053	.308	–.449	.850	.030	.027	–.009	.098	.338	.294	–.029	1.119
Conditional indirect effects of X on Y, mediated by discouragement	Low A	.032	.621	–1.436	1.092	.003	.041	–.091	.080	.710	.558	–.538	1.731
	Medium A	.295	.390	–.581	1.000	.046	.031	–.010	.111	.914	.333	.262	1.549
	High A	.445	.428	–.422	1.271	.071	.045	–.006	.170	.990	.427	.059	1.746

[a] *Agreeableness score values:* Low (16th percentile) = 102.12; Medium (50th percentile) = 121; High (84th percentile) = 136.88

Abbreviations: X = antecedent variable, Y = outcome variable (headache), A = agreeableness

Note: Interactions are significant when confidence intervals are entirely above or below zero (shaded boot value areas indicate that the indirect interaction is significant).

Table 7.13 The relationship between pain control beliefs, pain decrease beliefs, outcome expectancy and headache intensity, as moderated by FFM agreeableness

		Pain control belief (X_1)			Pain decrease belief (X_2)			Outcome expectancy(X_3)		
AGREEABLENESS (A) [a]										
X*Agreeableness		F (1,72) = 1.114, p = .295			F (1,72) = 1.055, p = .308			F (1,72) = 0.963, p = .330		
Discouragement*A		F (1,72) = 0.048, p = .827			F (1,72) = 0.018, p = .894			F (1,72) = 0.197, p = .658		
Anxiety*A		F (1,72) = 1.994, p = . 168			F (1,72) = 2.320, p = .132			F (1,72) = 0.571, p = .452		
Irritation * A		F (1,72) = 1.602, p = .210			F (1,72) = 1.780, p = .186			F (1,72) = 0.045, p = .833		
	Trait score	***Coefficient***	***SE***	***p***	***Coefficient***	***SE***	***p***	***Coefficient***	***SE***	***p***
Conditional direct effects of X on Y (Y= headache)	Low A	.067	.115	.563	–.148	.130	.259	.259	.082	**.002**
	Medium A	–.019	.083	.820	–.254	.091	**.007**	.203	.052	**.000**
	High A	–.094	.111	.401	–.348	.136	**.013**	.153	.068	**.027**
		Effect	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***
Conditional indirect effects of X on Y, mediated by anxiety	Low A	–.072	.075	–.263	.019	–.057	.075	–.227	.070	.110	.060	.020	.254
	Medium A	–.023	.048	–.137	.059	–.044	.051	–.158	.044	.100	.039	.034	.185
	High A	.015	.067	–.145	.129	–.034	.071	–.218	.071	.091	.045	.010	.187
Conditional indirect effects of X on Y, mediated by irritation	Low A	.030	.114	–.137	.333	–.003	.123	–.292	.225	.061	.114	–.154	.304
	Medium A	–.017	.044	–.132	.046	–.041	.075	–.234	.073	.106	.074	.002	.288
	High A	.021	.126	–.357	.178	.001	.193	–.495	.296	.141	.103	.020	.420
Conditional indirect effects of X on Y, mediated by discouragement	Low A	–.386	.286	–1.101	.002	–.365	.248	–.902	.043	.285	.144	–.002	.582
	Medium A	–.153	.141	–.476	.075	–.200	.132	–.503	.008	.268	.097	.019	.410
	High A	–.022	.114	–.267	.191	–.093	.120	–.371	.102	.252	.121	–.086	.383

[a] *Agreeableness score values:* Low (16th percentile) = 102.12; Medium (50th percentile) = 121; High (84th percentile) = 136.88

Abbreviations: X = antecedent variable, Y = outcome variable (headache), A = agreeableness

Note: Interactions are significant when confidence intervals are entirely above or below zero (shaded boot value areas indicate that the interaction is significant).

7.5 Discussion

These studies aimed to assess whether headache-related NA arises from stress-related disruptions in affective information processing, specifically negative primary and secondary appraisal processes which increase stressor exposure (the tendency to make primary stress/harm appraisals) and/or stressor reactivity – the emotional and somatic responses to a stressor. Stressor exposure was believed to increase headache-related NA when a situation was appraised as stressful or as a threat. Stressor reactivity was expected to increase NA when problem engagement or emotion management was low, problem avoidance high, belief in one's capacity to control or decrease pain was low and (from Chapter 6) outcome expectancy was high. By influencing the strength of the emotional response through cognitive biases related to valenced stimuli, the personality traits of neuroticism, agreeableness, conscientiousness, introversion and conservatism were expected to moderate headache intensity.

Stressor exposure. Consistent with previous research (e.g. 184), headache sufferers were more likely than controls to make a threat appraisal of the cognitive task. Those who developed stress-headache appraised the stressor as highly stressful but not as a threat *per se*. This relationship was mediated by discouragement and tension and moderated by agreeableness, since agreeableness was associated with higher levels of discouragement.

Discouragement and tension may have mediated the relationship between exposure and headache at a neurophysiological level, since increased distress may reduce the nociceptive threshold at the synapse (666) or disrupt inhibitory controls (Chapter 5). At a cognitive level, agreeableness is associated with more co-operative behaviour and more socially adaptive modes of conflict resolution (392-394), suggesting that high scorers in this dimension are more conscious of the needs and reactions of others. Their very concern for others' opinions of them may have predisposed them to discouragement/depression in the face of failure feedback (288; 667), contributing also to response conflict (323) (see below) which increases stress sensitivity (668).

Stressor reactivity. Stressor reactivity is a multifaceted construct, but only three of its hypothesised (psychological) components predicted headache intensity – high outcome expectancy ($p < .05$) and problem avoidance ($p < .05$) were positive predictors, pain-decrease (but not pain-control) belief ($p < .05$) was a negative predictor. Apart from pain-decrease belief, these relationships were mediated by anxiety, discouragement and irritation and, as predicted, were moderated by personality traits which either exaggerated NA (neuroticism,

introversion, conservatism), or else demanded persistence in the face of failure (agreeableness and conscientiousness).

As the strongest predictors of headache, high outcome expectancy and avoidant coping were also highly associated with the six NA ($r < .01$). High outcome expectancy may have set in motion the analytic, assimilative processing style of "tenacious goal pursuit", associated with migraine headache (606; 609) (Chapter 6). These participants appear to have set themselves a success goal – and goals are important determinants of behaviour. For example, individuals are more likely to endure a task despite pain for important goals (669). However, the (unexpectedly) insoluble nature of the task meant that high outcome expectancy was followed by a sharp decline in efficacy expectancies mid-way through the task (Figure 6.5), likely when its insoluble nature became evident. At this point, headache or vacillation (668) – or both – may have reduced the capacity of these participants to modify self-expectations or 'change tack', i.e. switch to the more flexible accommodative processing style. The fact that high outcome expectancies were associated with high conscientiousness ($p < .001$) is consistent with this observation.

Furthermore, at the point where self-efficacy declined and headache peaked (shown in Figure 6.4 and Figure 6.5), the desire to give up (avoid) was most likely to have emerged. Avoidant coping predicted headache and was associated with all six NA ($r < .01$). Avoidance goals are more likely to lead to conflicts in goal pursuit (670) and have capacity to cause distress, especially when self-regulation is failing (671). At that point, neither problem-engagement nor emotion-management were able to "save the day", since during headache (and stress),'primitive' brain structures may be activated, compromising pre-frontal-cortically-based cognitive processes and strategies (672; 673). This may explain why, contrary to predictions based on previous research (163; 635-637; 640), neither problem engagement nor emotion management coping was related to headache intensity during the stressful task. Effective behaviour also requires consistency in motivation (668). Hence participants with initially high outcome expectancy and confidence would have been most susceptible to approach-avoidance conflict as headache increased. Coactivated approach and avoidance motives can be detrimental to effective self-regulation (668) and such response conflict may cause vacillation and increase pain sensitivity (674).

Belief in one's ability to decrease pain was a further aspect of stressor reactivity which related to headache, albeit inversely. This relationship was not mediated by NA since pain-decrease belief was (negatively) associated only with confusion ($p < .05$). However,

confusion is characteristic of the disrupted affective information processing that occurs during stress (126). By reducing confusion, pain-decrease belief may buffer such disruption. Pain-decrease belief may also be associated with a psychological rather than a biomedical view of headache and practical methods for reducing stress, such as relaxation (651), although coping methods associated with high or low pain-decrease belief await research.

Contrary to predictions based on previous research (256; 597; 646-650), pain control belief was unrelated either to headache or to NA. Pain-"control" may even be something of an oxymoron, since control refers to the process of activating or de-activating effector responses that stabilize a regulated variable, either by reversing a perturbation that has already occurred or by minimising an impending perturbation (666). As such, 'control' is unlikely in the case of pain or existing NA and may only result in 'struggle', which by decreasing acceptance can paradoxically increase pain sensitivity (276; 675-679). Interestingly, pain-control belief in this study was indirectly associated with extraversion ("positive affectivity") and reduced discouragement. Extraversion is associated with subjective self-confidence, challenge/determination rather than stress appraisals and general but unspecified evaluation of task difficulty, with the result that extraverts frequently attempt to solve problems irrespective of their actual ability (163; 640; 680). Belief in one's ability to 'control' pain may thus reflect hope rather than a realistic appraisal of one's capacity to manage pain, especially if NA is high.

Taken together, the NA associated with stress-related disruptions in affective processing may elicit headache. Such disruptions may also be associated with unrealistic and rigid outcome expectancies, leading to conflict between avoidance and approach goals which increases pain sensitivity. Task and pain self-efficacy decline. Discouragement, anxiety and irritation increase, despite which the headache-prone individual pushes themselves past their own limits.

Study limitations

The exploratory nature of some of these analyses limits their generalizability to other stressors or other populations. Although theoretically derived, the concept of appraisals is, by definition, fluid, hence definitive psychometric measures of either stressor exposure or stressor reactivity are largely absent in the literature. Furthermore, only psychological aspects of stressor reactivity were assessed in this study. Further research is required to determine the applicability of these constructs to other populations.

7.6 Conclusions

Results of the present study support the essential role of the emotional system in the pain component of headache. Primary subjective stress appraisals and secondary appraisals which increase stressor reactivity are associated with increased anxiety, discouragement, irritation and tension which predict headache. Aspects of stressor reactivity that predict headache include avoidance, reduced belief in one's ability to decrease (not control) pain and high outcome expectancies. These aspects of reactivity may be most evident during an unpredictable and uncontrollable task in which an approach-avoidance conflict is set up. The resulting vacillation and reduced self-regulatory capacities may contribute to the high NA and reduced self-efficacy preceding headache.

Personality traits which were associated with stronger NA (high neuroticism, low extraversion, low openness) or tendencies to persist beyond what might be considered reasonable (high-agreeableness, high-conscientiousness), moderated the relationships between stressor exposure, stressor reactivity and headache. This occurred because these traits were associated with the increased discouragement, anxiety/tension and/or irritation and/or reduced self-efficacy associated with headache.

Supplementary Data

Table 7.14 The relationship between three potential coping options during the laboratory stressor and headache intensity, as moderated by FFM neuroticism

		Problem Engagement (X_1)			Emotion Management (X_2)			Avoidance (X_3)		
NEUROTICISM (N)[a]										
X*Neuroticism		F (1,71) = 0.517, p = .474			F (1,71) = 1.763, p = .188			F (1,71) = 0.037, p = .848		
Anxiety*N		F (1,71) = 1.322, p = .254			F (1,71) = 0.889, p = .349			F (1,71) = 1.262, p = .265		
Irritation*N		F (1,71) = 0.313, p = .578			F (1,71) = 0.155, p = .695			F (1,71) = 0.106, p = .746		
Discouragement *N		F (1,71) = 0.112, p = .739			F (1,71) = 0.023, p = .637			F (1,71) = 0.145, p = .705		
	Trait score	***Coefficient***	***SE***	***p***	***Coefficient***	***SE***	***p***	***Coefficient***	***SE***	***p***
Conditional direct effects of X on Y (Y= headache)	Low N	–.234	.334	.487	.025	.024	.304	.418	.293	.157
	Medium N	–.070	.205	.734	.002	.016	.907	.384	.189	**.046**
	High N	.099	.281	.724	–.022	.023	.353	.348	.228	.133
		Effect	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***
Conditional indirect effects of X on Y, mediated by anxiety	Low N	.087	.242	–.340	.650	–.008	.016	–.038	.026	.224	.290	–.327	.842
	Medium N	.134	.141	–.158	.410	.016	.012	–.004	.041	.240	.136	.026	.563
	High N	.101	.177	–.291	.469	.024	.023	–.016	.075	.140	.259	–.334	.736
Conditional indirect effects of X on Y, mediated by irritation	Low N	.186	.361	–.314	1.126	.004	.019	–.031	.049	.163	.232	–.252	.685
	Medium N	.090	.210	–.308	.555	.012	.015	–.011	.048	.328	.222	–.087	.790
	High N	–.079	.366	–.883	.552	.023	.025	–.020	.077	.540	.365	–.162	1.297
Conditional indirect effects of X on Y, mediated by discouragement	Low N	.172	.429	–.613	1.146	.001	.032	–.064	.071	.316	.412	–.389	1.276
	Medium N	.113	.316	–.606	.691	.024	.022	–.015	.074	.613	.308	.142	1.340
	High N	.034	.568	–1.418	.836	.056	.037	–.010	.133	.984	.532	.257	2.332

[a] *Neuroticism score values:* Low (16th percentile) = 74; medium (50th percentile) = 95; high (84th percentile) = 116.64

Abbreviations: X = antecedent variable, Y = outcome variable (headache), N = neuroticism

Note: Interactions are significant when confidence intervals are entirely above or below zero (shaded boot value areas indicate that the interaction is significant).

Table 7.15 The relationship between beliefs regarding pain control & pain-decrease ability, outcome expectancy and headache intensity, as moderated by FFM neuroticism

		Pain control (X_4)				Pain decrease (X_5)				Outcome expectancy (X_6)			
NEUROTICISM (N)[a]													
X*Neuroticism		F (1,72) = 1.286, p = .261				F (1,72) = 0.844, p = .361				F(1,72) = 15.922, p < **.001**			
Anxiety*N		F (1,72) = 1.053, p = .308				F (1,72) = 0.209, p = .649				F (1,72) = 2.202, p = .142			
Irritation*N		F (1,72) = 0.425, p = .517				F (1,72) = 1.397, p = .241				F (1,72) = 0.010, p = .920			
Discouragement *N		F (1,72) = 0.032, p = .858				F (1,72) = 0.091, p = .763				F (1,72) = 0.450, p = .505			
	Trait score	***Coefficient***	***SE***	***p***		***Coefficient***	***SE***	***p***		***Coefficient***	***SE***	***p***	
Conditional direct effects of X on Y (Y= headache)	Low N	.053	.121	.666		–.183	.135	.178		.036	.064	.576	
	Medium N	–.029	.086	.737		–.271	.095	**.006**		.245	.050	**<.001**	
	High N	–.111	.104	.286		–.358	.134	**.009**		.455	.081	**<.001**	
		Effect	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***
Conditional indirect effects of X on Y, mediated by anxiety	Low N	–.104	.100	–.345	.041	–.120	.091	–.353	.001	.117	.073	.007	.289
	Medium N	–.031	.047	–.147	.042	–.034	.046	–.132	.054	.108	.040	.039	.193
	High N	.007	.040	–.099	.077	.027	.064	–.078	.190	.071	.055	–.037	.183
Conditional indirect effects of X on Y, mediated by irritation	Low N	–.116	.146	–.462	.116	–.170	.181	–.551	.180	.135	.128	–.040	.446
	Medium N	–.065	.080	–.253	.067	–.103	.104	–.344	.065	.166	.092	.021	.381
	High N	.031	.101	–.157	.250	.100	.164	–.259	.423	.200	.118	–.050	.423
Conditional indirect effects of X on Y, mediated by discouragement	Low N	–.237	.197	–.713	.054	–.309	.262	–.935	.043	.174	.148	–.122	.468
	Medium N	–.137	.127	–.439	.056	–.152	.127	–.462	.020	.145	.098	–.070	.327
	High N	–.022	.160	–.311	.346	–.029	.144	–.376	.207	.102	.140	–.165	.393

[a] *Neuroticism score values:* Low (16th percentile) = 74; medium (50th percentile) = 95; high (84th percentile) = 116.64

Abbreviations: X = antecedent variable, Y = outcome variable (headache), N = neuroticism

Note: Interactions are significant when confidence intervals are entirely above or below zero (shaded boot value areas indicate that the interaction is significant).

Table 7.16 The relationship between three potential coping options during the laboratory stressor and headache intensity, as moderated by FFM extraversion

		Problem Engagement (X_1)				Emotion Management (X_2)				Avoidance (X_3)			
EXTRAVERSION (E)[a]													
X*Extraversion		F (1,71) = 0.467, p = .497				F (1,71) = 0.369, p = 545.				F (1,71) = 0.350, p = .556			
Anxiety*E		F (1,71) = 0.160, p = .691				F (1,71) = 0.360, p = .551				F (1,71) = 0.328, p = .568			
Irritation*E		F (1,71) = 0.638, p = .427				F (1,71) = 0.898, p = .346				F (1,71) = 1.985, p = .163			
Discouragement *E		F (1,71) = 0.294, p = .589				F (1,71) = 0.360, p = .346				F (1,71) = 0.458, p = .501			
	Trait score	***Coefficient***	***SE***	***p***		***Coefficient***	***SE***	***p***		***Coefficient***	***SE***	***p***	
Conditional direct effects of X on Y (Y= headache)	Low E	.116	.362	.749		–.017	.031	.578		.668	.321	**.041**	
	Medium E	–.073	.201	.717		–.004	.017	.824		.534	.185	**.005**	
	High E	–.237	.293	.422		.008	.022	.728		.419	.238	.082	
		Effect	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***
Conditional indirect effects of X on Y, mediated by anxiety	Low E	.256	.277	–.198	.883	.033	.029	–.008	.104	1.170	.294	.255	–.106
	Medium E	.218	.191	–.127	.602	.020	.015	–.006	.052	1.072	.283	.152	.019
	High E	.186	.233	–.329	.601	.011	.016	–.022	.041	.934	.247	.196	–.196
Conditional indirect effects of X on Y, mediated by irritation	Low E	.080	.296	–.503	.742	.030	.043	–.054	.120	.090	.500	–1.188	.872
	Medium E	.060	.183	–.285	.466	.020	.017	–.008	.058	.382	.214	–.065	.784
	High E	–.012	.359	–.789	.721	–.014	.029	–.078	.043	.429	.309	–.085	1.121
Conditional indirect effects of X on Y, mediated by discouragement	Low E	.280	.601	–.837	1.704	.074	.056	.000	.219	1.109	.660	.230	2.849
	Medium E	.137	.297	–.584	.641	.026	.022	–.013	.072	.691	.289	.244	1.385
	High E	.048	.338	–.803	.589	–.001	.024	–.062	.037	.411	.361	–.151	1.253

[a] *Extraversion score values:* Low (16th percentile) = 99.24; medium (50th percentile) = 119; high (84th percentile) = 136

Abbreviations: X = antecedent variable, Y = outcome variable (headache), E = extraversion

Note: Interactions are significant when confidence intervals are entirely above or below zero (shaded boot value areas indicate that the interaction is significant).

Table 7.17 The relationship between beliefs in pain-control, pain-decrease ability, outcome expectancy and headache intensity, as moderated by FFM extraversion

		Pain control (X_4)				Pain decrease (X_5)				Outcome expectancy (X_6)			
EXTRAVERSION (E)[a]													
X*Extraversion		F (1,72) = 0.047, p = .830				F (1,72) = 0.124, p = 725.				F (1,72) = 0.000, p = .996			
Anxiety*E		F (1,72) = 0.211, p = .647				F (1,72) = 0.647, p = .424				F (1,72) = 0.205, p = .652			
Irritation*E		F (1,71) = 1.070, p = .304				F (1,72) = 0.499, p = .482				F (1,72) = 0.678, p = .413			
Discouragement *E		F (1,71) = 0.465, p = .497				F (1,72) = 0.197, p = .658				F (1,72) = 0.211, p = .647			
	Trait score	***Coefficient***	***SE***	***p***		***Coefficient***	***SE***	***p***		***Coefficient***	***SE***	***p***	
Conditional direct effects of X on Y (Y= headache)	Low E	–.010	.108	.926		–.303	.144	**.039**		.203	.083	**.017**	
	Medium E	–.028	.094	.766		–.261	.097	**.009**		.203	.056	**<.001**	
	High E	–.043	.129	.742		–.226	.145	.124		.202	.095	**.038**	
		Effect	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***
Conditional indirect effects of X on Y, mediated by anxiety	Low E	–.019	.056	–.147	.074	–.025	.100	–.251	.156	.097	.066	–.017	.244
	Medium E	–.056	.050	–.170	.027	–.063	.057	–.186	.042	.108	.044	.029	.200
	High E	–.076	.088	–.317	.032	–.077	.075	–.249	.047	.110	.056	.023	.249
Conditional indirect effects of X on Y, mediated by irritation	Low E	.005	.057	–.112	.118	.046	.128	–.186	.323	.086	.093	–.118	.266
	Medium E	–.090	.079	–.261	.046	–.111	.114	–.380	.082	.191	.081	.036	.358
	High E	–.244	.178	–.655	.049	–.310	.246	–.916	.059	.307	.147	.045	.640
Conditional indirect effects of X on Y, mediated by discouragement	Low E	–.062	.142	–.409	.166	–.054	.195	–.594	.184	.183	.132	–.083	.449
	Medium E	–.170	.111	–.445	–.012	–.120	.112	–.399	.028	.179	.096	–.040	.349
	High E	–.197	.189	–.648	.087	–.129	.201	–.580	.230	.154	.180	–.245	.469

[a] *Extraversion score values:* Low (16th percentile) = 99.24; medium (50th percentile) = 119; high (84th percentile) = 136

Abbreviations: X = antecedent variable, Y = outcome variable (headache), E = extraversion

Note: Interactions are significant when confidence intervals are entirely above or below zero (shaded boot value areas indicate significant interactions).

Table 7.18 The relationship between three potential coping options during the laboratory stressor and headache intensity, as moderated by FFM openness

		Problem Engagement (X_1)				Emotion Management (X_2)				Avoidance (X_3)			
OPENNESS (O)[a]													
X*Openness		F (1,71) = 0.272, p = .604				F (1,71) = 0.612, p = .436				F (1,71) = 0.360, p = .550			
Anxiety*O		F (1,71) = 0.007, p = .932				F (1,71) = 0.017, p = .897				F (1,71) = 0.093, p = .761			
Irritation*O		F (1,71) = 0.494, p = .484				F (1,71) = 0.564, p = .455				F (1,71) = 0.013, p = .909			
Discouragement *O		F (1,71) = 0.002, p = .965				F (1,71) = 0.017, p = .897				F (1,71) = 0.075, p = .785			
	Trait score	***Coefficient***		***SE***	***p***	***Coefficient***		***SE***	***p***	***Coefficient***		***SE***	***p***
Conditional direct effects of X on Y (Y= headache)	Low O	.074		.351	.834	.018		.030	.557	.526		.307	.090
	Medium O	–.093		.207	.656	–.002		.016	.888	.387		.183	**.038**
	High O	–.222		.348	.526	–.018		.025	.485	.279		.247	.264
		Effect	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***
Conditional indirect effects of X on Y, mediated by anxiety	Low O	.438	.418	–.273	1.405	.036	.035	–.021	.120	.258	.302	–.315	.937
	Medium O	.167	.142	–.104	.455	.018	.012	–.003	.043	.255	.149	–.006	.580
	High O	–.060	.173	–.507	.192	.003	.013	–.024	.030	.235	.177	–.036	.653
Conditional indirect effects of X on Y, mediated by irritation	Low O	.404	.611	–.295	2.004	.047	.053	–.021	.183	.454	.560	–.651	1.581
	Medium O	.034	.164	–.281	.418	.012	.013	–.008	.044	.282	.199	–.109	.692
	High O	–.092	.223	–.578	.373	–.001	.015	–.028	.038	.167	.230	–.156	.742
Conditional indirect effects of X on Y, mediated by discouragement	Low O	.688	.716	–.442	2.354	.071	.061	–.027	.214	1.143	.682	.007	2.704
	Medium O	.113	.294	–.566	.636	.030	.022	–.011	.076	.788	.299	.289	1.469
	High O	–.347	.508	–1.488	.537	–.005	.033	–.073	.061	.549	.357	–.005	1.384

[a] *Openness score values:* Low (16th percentile) = 103.48; medium (50th percentile) = 128; high (84th percentile) = 147

Abbreviations: X = antecedent variable, Y = outcome variable (headache), O = openness

Note: Interactions are significant when confidence intervals are entirely above or below zero (shaded boot value areas indicate that the interaction is significant).

Table 7.19 Pain control belief, pain decrease belief and outcome expectancy as moderated by the trait of openness

		Pain control (X_4)				Pain decrease (X_5)				Outcome expectancy (X_6)			
OPENNESS (O)[a]													
X*Openness		F (1,72) = 0.001, p = .978				F (1,72) = 0.313, p = .577				F (1,72) = 0.578, p = .450			
Anxiety*O		F (1,72) = 0.013, p = .909				F (1,72) = 0.139, p = .710				F (1,72) = 0.163, p = .687			
Irritation*O		F (1,72) = 0.404, p = .527				F (1,72) = 0.005, p = .944				F (1,72) = 0.167, p = .684			
Discouragement *O		F (1,72) = 0.001, p = .973				F (1,72) = 0.327, p = .569				F (1,72) = 0.029, p = .864			
	Trait score	***Coefficient***	***SE***		***p***	***Coefficient***	***SE***		***p***	***Coefficient***	***SE***		***p***
Conditional direct effects of X on Y (Y= headache)	Low O	–.045	.167		.788	–.152	.189		.425	.262	.101		**.011**
	Medium O	–.049	.088		.584	–.238	.096		**.015**	.188	.054		**.001**
	High O	–.051	.116		.662	–.304	.143		**.037**	.131	.102		.201
		Effect	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***
Conditional indirect effects of X on Y, mediated by anxiety	Low O	.033	.096	–.143	.254	–.078	.106	–.312	.121	.082	.079	–.037	.267
	Medium O	–.016	.049	–.137	.062	–.052	.053	–.168	.046	.097	.038	.026	.173
	High O	–.056	.068	–.242	.017	–.023	.065	–.179	.082	.105	.057	–.004	.219
Conditional indirect effects of X on Y, mediated by irritation	Low O	.153	.227	–.177	.670	–.207	.279	–.865	.211	.157	.131	–.001	.499
	Medium O	–.019	.062	–.154	.106	–.090	.097	–.312	.082	.154	.087	.025	.359
	High O	–.078	.112	–.332	.138	.004	.158	–.332	.330	.143	.124	–.050	.436
Conditional indirect effects of X on Y, mediated by discouragement	Low O	.101	.251	–.405	.649	–.326	.335	–.995	.357	.178	.145	–.197	.380
	Medium O	–.093	.116	–.354	.108	–.157	.112	–.415	.018	.224	.103	–.053	.359
	High O	–.243	.176	–.669	.021	–.069	.129	–.364	.145	.262	.146	–.116	.476

[a] *Openness score values:* Low (16th percentile) = 103.48; medium (50th percentile) = 128; high (84th percentile) = 147

Abbreviations: X = antecedent variable, Y = outcome variable (headache), O = openness

Note: Interactions are significant when confidence intervals are entirely above or below zero (shaded boot value areas indicate that the interaction is significant).

Table 7.20 The relationship between three potential coping options during the laboratory stressor and headache intensity, as moderated by FFM conscientiousness

		Problem Engagement (X_1)				Emotion Management (X_2)				Avoidance (X_3)			
CONSCIENTIOUSNESS (C)[a]													
X*Conscientiousness		F (1,71) = 0.595, p = 0.443				F (1,71) = 0.617, p = .435				F (1,71) = 2.387, p = .127			
Anxiety*C		F (1,71) = 1.801, p = 0.184				F (1,71) = 1.775, p = .187				F (1,71) = 1.643, p = .204			
Irritation*C		F (1,71) = 0.366, p = 0.547				F (1,71) = 0.169, p = .693				F (1,71) = 0.662, p = .419			
Discouragement* C		F (1,71) = 0.040, p = 0.843				F (1,71) = 0.006, p = .941				F (1,71 = 0.048, p = 0.828			
	Trait score	***Coefficient***	***SE***		***p***	***Coefficient***	***SE***		***p***	***Coefficient***	***SE***		***p***
Conditional direct effects of X on Y (Y= headache)	Low C	.138	.296		.642	–.010	.021		.630	.357	.197		.075
	Medium C	–.023	.203		.911	.001	.016		.928	.598	.187		**.002**
	High C	–.148	.255		.564	.011	.020		.606	.785	.257		**.003**
		Effect	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***
Conditional indirect effects of X on Y, mediated by anxiety	Low C	.243	.241	–.277	.693	.017	.019	–.011	.062	.162	.181	–.209	.525
	Medium C	.176	.161	–.159	.488	.018	.014	–.006	.048	.283	.156	.022	.635
	High C	.018	.182	–.310	.441	.015	.021	–.024	.062	.383	.225	.021	.888
Conditional indirect effects of X on Y, mediated by irritation	Low C	.074	.292	–.556	.640	.017	.021	–.016	.066	.348	.281	–.296	.898
	Medium C	.035	.165	–.316	.392	.010	.013	–.009	.045	.218	.202	–.139	.675
	High C	.015	.204	–.321	.525	.005	.017	–.023	.051	.105	.313	–.431	.864
Conditional indirect effects of X on Y, mediated by discouragement	Low C	.263	.497	–.965	1.048	.038	.036	–.013	.127	.767	.406	.224	1.832
	Medium C	.126	.324	–.640	.677	.024	.023	–.018	.074	.896	.323	.294	1.565
	High C	.009	.398	–.900	.786	.013	.028	–.039	.076	1.003	.483	.058	1.935

[a] *Conscientiousness score values:* Low (16th percentile) = 98; Medium (50th percentile) = 116; High (84th percentile) = 130

Abbreviations: X = antecedent variable, Y = outcome variable (headache), C = conscientiousness

Note: Interactions are significant when confidence intervals are entirely above or below zero (shaded boot value areas indicate that the interaction is significant).

Table 7.21 The relationship between pain-control and pain-decrease beliefs, outcome expectancy and headache intensity, as moderated by FFM conscientiousness

		Pain control (X_4)				Pain decrease (X_5)				Outcome expectancy (X_6)			
CONSCIENTIOUSNESS (C)[a]													
X*Conscientiousness		F (1,72) = 4.354, p = **0.040**				F (1,72) = 0.627, p = .431				F (1,72) = 14.894, p < **.001**			
Anxiety*C		F (1,72) = 2.103, p = 0.151				F (1,72) = 2.226, p = .140				F (1,72) = 0.076, p = .783			
Irritation*C		F (1,72) = 0.850, p = 0.360				F (1,72) = 0.600, p = .441				F (1,72) = 1.106, p = .297			
Discouragement* C		F (1,72) = 0.278, p = 0.600				F (1,72) = 0.123, p = .726				F (1,72) = 4.889, p = **0.030**			
	Trait score	***Coefficient***	***SE***		***p***	***Coefficient***	***SE***		***p***	***Coefficient***	***SE***		***p***
Conditional effects of Discouragement (M3) on Conscientiousness	Low C									.009	.145		.949
	Medium C									.260	.132		.053
	High C									.464	.183		**.013**
Conditional direct effects of X on Y (Y= headache)	Low C	–.150	.105		.156	–.295	.118		**.015**	.437	.080		**<.001**
	Medium C	.007	.086		.938	–.229	.096		**.020**	.237	.051		**<.001**
	High C	.135	.113		.235	–.176	.125		.166	.073	.060		.224
		Effect	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***	***Effect***	***Boot SE***	***Boot LLCI***	***Boot ULCI***
Conditional indirect effects of X on Y, mediated by anxiety	Low C	–.029	.053	–.162	.055	–.029	.063	–.162	.107	.133	.050	.019	.218
	Medium C	–.031	.047	–.141	.047	–.059	.057	–.185	.046	.129	.042	.045	.209
	High C	–.027	.081	–.206	.115	–.090	.090	–.290	.069	.124	.058	.017	.247
Conditional indirect effects of X on Y, mediated by irritation	Low C	–.059	.099	–.274	.125	–.031	.149	–.401	.203	.228	.100	–.038	.376
	Medium C	–.035	.064	–.196	.059	–.081	.098	–.324	.063	.130	.084	–.006	.327
	High C	–.018	.091	–.252	.121	–.096	.139	–.456	.104	.066	.128	–.099	.409
Conditional indirect effects of X on Y, mediated by discouragement	Low C	–.149	.157	–.565	.056	–.118	.171	–.582	.078	.008	.128	–.210	.327
	Medium C	–.142	.123	–.418	.054	–.170	.133	–.500	.017	.193	.103	–.045	.366
	High C	–.130	.183	–.557	.178	–.219	.215	–.740	.100	.305	.165	–.085	.574

[a] *Conscientiousness score values:* Low (16th percentile) = 98; Medium (50th percentile) = 116; High (84th percentile) = 130

Abbreviations: X = antecedent variable, Y = outcome variable (headache), C = conscientiousness

Note: Interactions are significant when confidence intervals are entirely above or below zero (shaded boot value areas indicate that the interaction is significant).

Chapter Eight

8

Coping choice, effectiveness and headache

Overview

Objective. To determine the contribution of headache coping to headache-related NA in episodic migraine and T-TH sufferers during experimentally-provoked headache.

Background. Prior research has indicated that non-adaptive coping characterises headache sufferers and that high negative affect (NA) precedes headache onset. However, it is unclear whether threat-based coping tactics contribute to or result from headache and the relative role of response-focused and antecedent-focused coping in increasing headache intensity.

Methods. Stress and pain coping and NA in participants with episodic migraine or T-TH were assessed following a cognitive laboratory task.

Results. Anxiety mediated the effects of coping on headache, increasing the use of the threat-based coping methods of wishful thinking, self-criticism, pain catastrophizing and praying/hoping. These predicted headache and further increased anxiety. The response-focused method of ignoring-pain-sensations was greater in those without stress-headache, but reappraisal and (behavioural) suppression were similar between migraine, T-TH and controls.

Conclusions. By focusing attention on the affective qualities of pain, threat-based coping methods contribute to the anxiety associated with headache. Results are attributed to the context-specific nature of coping and the response conflict engendered by the task itself.

8.1 Introduction

Failing to cope adequately with pain and stress may influence headache frequency and intensity more than the stressor itself (169; 187; 194; 196; 681-683). Hence, if ineffective, the specific coping methods chosen to regulate oneself and manage a task may, in addition to stressor exposure and reactivity, constitute a further source of headache-related NA. In a stepwise process, the individual first detects whether regulation is needed, selects an option suited to the context, stimulus strength and one's personal resources, and finally translates a general strategy into situation-specific 'tactics' (171). Such tactics differentially activate the neurocognitive pain perceptual processes of attention, expectancy and reappraisal (212). Ineffective pain regulation – the conscious increase or decrease of pain affect (684) – may occur when regulatory strategies and coping tactics either fail to regulate when it would be good to do so, or 'misregulate', i.e. have adverse outcomes (171).

Tactics can be driven by attentional control or by volitional cognitive change (685). Effective *attention control* tactics deflect attention away from pain and activate areas of the dorsolateral prefrontal cortex involved in the top-down modulation of pain (686). Ineffective tactics either focus on pain or attempt to suppress it (169). Effective *volitional cognitive control* tactics consciously alter pain appraisals and/or expectancies (166), changing the intensity of pain by changing its meaning (687). They alter the emotional valence of pain and involve activation of the (right) lateral prefrontal cortical areas (688; 689), areas which are critically involved in broad aspects of executive behavioural control (690).

One factor influencing coping selection is the appraised threat/stress level. Higher threat appraisals increase the likelihood that coping tactics will be selected from the threat system rather than the drive (goal achievement) or self-soothing systems (167). Imbalance between these systems can increase NA and ongoing NA can itself become a source of threat (168). As shown in Figure 8.1, threat-based coping occurs along two continua – active-inhibitory and social-nonsocial (167). Active threat-based coping includes self-criticism and pain catastrophising – an exaggerated negative orientation toward pain stimuli and pain experience (691) which includes elements of rumination (excessive focus on pain sensations), magnification (exaggerating the threat value of pain sensations) and helplessness (perceiving oneself as unable to cope with pain symptoms) (691). Focusing on pain increases both its intensity and unpleasantness (262). Hence, catastrophising heightens pain severity and reduces pain tolerance (276; 691), including in headache (692). In thermal pain, pain-related catastrophising increased temporal summation and reduced

habituation (693). Migraineurs are more likely than controls to catastrophise, ruminate on the negative effect of their headache, criticise themselves or blame others (170; 193; 297; 694-697).

'Fear-avoidant' (inhibitory) coping also arises from the threat system, and is characterized by suppressive thoughts, increased nonverbal complaint and decreased ability to search for social support (279). Wishful thinking, substance misuse, displacing or forcefully inhibiting negative feelings ('emotional suppression') are common examples of dysfunctional fear-avoidant coping in response to a stressor (663). By paradoxically increasing the salience of unwanted stimuli, such as NA and pain, 'fear-avoidant' tactics may increase threat and hence pain sensitivity (419; 698). Thus, individuals using anger suppression reported greater pain sensitivity and intensity than those adopting anger expression (699-702). Wishful thinking, praying or hoping (703), worrying and attending to the negative effect of one's headaches (694), rumination and self-blame (193) as well as other blame (170) were associated with more frequent headaches.

Thus, the higher and more sustained NA in migraineurs than T-TH and those with than without stress headache (Chapter 6) may relate to their use of coping tactics which by increasing threat, increase headache-related NA.

Taxonomy of threat-based coping strategies

These occur in two key domains: 1) Active-inhibitory and 2) Social-nonsocial.

- *Active, non-social* – defensive, persecutory and displacement aggression, flight, active avoidance and safety seeking, e.g. pain catastrophizing.
- *Inhibitory, non-social* – freezing, fainting, passive avoidance, cutting off, camouflaging and concealing, e.g. wishful thinking, praying/hoping.
- *Active social* – ritualised (symbolic) threat, distress calling, seeking protection or reassurance from others, e.g. support-seeking, venting.
- *Inhibitory social* – submission and appeasement, e.g. suppression, self-blame/criticism.

Figure 8.1 A taxonomy of threat-based coping strategies

However, the unique nature of pain as a stressor (207) means that coping with pain and coping with stress may not be conceptually equivalent. Specifically, the use of threat-based inhibitory strategies may result from rather than cause headache-related NA. The persisting pain, focal neurological symptoms, headache-related disability and repeated goal disruption accompanying headache can be expected both to increase NA and to reduce coping options, especially those involving volitional cognitive change. Thus, the

more severe the headache, the less likely were children to use behavioural and cognitive distraction techniques or information seeking (672). Additionally, the experience of recurrent and uncontrollable headache may result, over time, in learned helplessness and consequent passivity (268; 704; 705), since during any perceived-uncontrollable stressor, including recurrent headache, goals shift into emotion management and the avoidance of negative consequences (159).

In the presence of headache therefore, antecedent-focused tactics (those applied early in the emotion trajectory before emotion is generated) may be reduced. Conversely, response-focused tactics – those applied *after* emotion has been generated – such as behavioural suppression (the ongoing inhibition of outward signs of emotion) or venting (the outward expression of emotion) are more likely to be activated. The result may be a failure to downregulate NA (706). Examples of antecedent-focused strategies are situation management (akin to problem-focused coping), redirecting attention, or the volitional cognitive control strategies of detachment (the deliberate cognitive distancing from a stimulus in order to observe one's thoughts, including those about pain) and reappraisal (thinking of a stressor in a way that reduces its emotional valence) (684).

That reappraisal is more effective than suppression in downregulating NA has been widely demonstrated (684; 707-709). Reappraisal also reduced cardiovascular inflammatory risk whereas suppression increased such risk (710). In electromyographic studies, *distraction* was shown to act very early (within 300ms) in the emotion-generative process, downregulating amygdala arousal and activating cortical areas involved in the top-down modulation of pain (686; 711; 712). In functional MRI studies, *detachment* was associated with reduced subjective distress, attenuated subjective and physiological measures of anticipatory anxiety for pain and reduced reactivity to receipt of pain itself (688).

Since the high NA associated with headache makes overlap between threat-based and response-focused strategies almost inevitable (713), the present study assessed whether more intense headache was associated with an increased likelihood of response-focused coping such as suppression or venting, and/or a reduced likelihood of volitional cognitive control strategies such as problem-focused coping, detachment or reappraisal.

In sum, it was hypothesised that:

1. Threat-based coping strategies would be associated with higher NA and would be greater in headache sufferers than controls and in those with than without stress-headache.
2. Headache or a headache history would be associated with increased use of response-focused strategies and/or reduced use of antecedent-focused volitional control strategies.

8.2 Method

8.2.1 Procedures

Where detailed descriptions have already been provided, these will not be repeated here.

Participants

Participants were those in the experimental sub-sample (n = 86), Table 2.3, p.34.

Experimental design and procedures

Described in Sections 2.2, p.35.

8.2.2 Measures

1. Stress coping was assessed using the modified *Ways of Coping Questionnaire, WCQ-R,* described in Section 2.4.2.3, p.44.
2. Pain coping: *Coping Styles Questionnaire – Revised (CSQ-R)(329)* (Section 2.4.2.4, p.45)
3. NEO personality inventory (Section 2.4.2.1, p.43)

8.2.3 Data analysis

Since previous research indicates coping differences between migraine, T-TH and controls, two planned contrasts compared outcomes in (i) headache sufferers v controls and (ii) migraine v T-TH. A third group comprised those who acquired v did not acquire a stress headache. Differences were investigated in Group (planned contrast) multivariate analyses of variance. Although ratings were skewed, clustering in the lower end of the continuum, analysis of variance was employed to investigate these relationships as it is fairly robust to violations of normality.

Preliminary analyses included t-tests, chi-square tests, bivariate correlation analyses and analyses of covariance to investigate group (planned contrast) differences on various

measures including catastrophizing, active coping, coping flexibility, pain self-efficacy, headache frequency, age of onset, gender and age. The association between mean headache intensity during the arithmetic task and each of the stress/pain coping methods reported during the laboratory stressor was explored with Pearson's correlation coefficient. Bivariate correlational relationships were examined for possible covariates.

Hierarchical multiple regression analyses were performed to determine whether NA mediated the relationship between stress-induced headache (mean headache ratings across the arithmetic task), stress coping tactics (problem-focused coping, wishful thinking, detachment, venting, reappraisal, self-criticism, suppression and attention deployment), pain coping tactics (pain-distraction, pain-reinterpretation, pain-catastrophising, ignoring-pain-sensations, praying/hoping and coping self-statements), FFM personality traits and attachment style. These were entered at the first step, all NA at the second step. This analysis was repeated with all NA at the first step, stressor exposure, personality and attachment at the second step.

All tests of statistical significance were two-tailed. Results are presented as the mean ± standard error, and $p < 0.05$ was considered to be statistically significant.

8.3 Results

Exploratory hierarchical regression analyses indicated that coping strategies during the laboratory stressor were unrelated to age, gender, education level, migraine family history, aura, phono- or photo-sensitivity. Hence these variables were not included in subsequent analyses.

THREAT-BASED COPING AND HEADACHE INTENSITY

In multivariate analyses, the threat-based pain coping strategies of praying/hoping and pain catastrophising, and the stress coping strategies of wishful thinking and self-criticism were compared for each planned contrast.

8.3.1 Threat-based coping strategies in migraine, T-TH, controls

In multivariate analyses of variance, threat-based coping strategies were similar in migraine, T-TH and control groups (Table 8.1).

Table 8.1 Threat-based coping in migraine, T-TH and controls: Means, standard errors, effects

	Migraine		T-TH		Controls	
Coping tactic	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**
Praying and hoping	8.21	0.96	9.76	1.16	11.41	1.41
Wishful thinking	0.74	0.11	0.86	0.14	0.74	0.15
Self-criticism	1.17	0.15	1.14	0.18	0.82	0.20
Pain catastrophising	11.05	1.01	8.35	1.22	8.59	1.42

	Headache sufferers v controls				Migraine v T-TH			
	F	**df**	***p***	**η_p^2**	**F**	**df**	***p***	**η_p^2**
Multivariate analysis								
Threat-based coping	1.79	(4,85)	0.138	0.08	2.23	(4,66)	0.075	0.12
Univariate analyses								
Praying and hoping	2.45	(1, 88)	0.121	0.03	1.05	(1, 69)	0.308	0.02
Wishful thinking	0.05	(1, 88)	0.831	0.00	0.48	(1, 69)	0.493	0.01
Self-criticism	2.26	(1, 88)	0.137	0.03	0.02	(1, 69)	0.901	0.00
Pain catastrophising	0.86	(1,88)	0.356	0.01	2.92	(1,69)	0.092	0.04

8.3.2 Threat-based coping strategies in stress-headache

Threat-based strategies were greater in those with than without stress-headache (p <.001), viz. praying/hoping (p <.05), pain catastrophising (p <.01), wishful thinking (p <.001) and self-criticism (p<.001) (Table 8.2).

Table 8.2 Threat-based coping in those with vs without stress-headache: means, standard errors, effects

	Low/no headache		Stress-headache		Stress-headache vs low/no headache			
Coping tactic	**Mean**	**SE**	**Mean**	**SE**	**F**	**df**	***p***	**η_p^2**
Multivariate analysis								
Threat-based coping					8.23	(4,80)	**<.001**	0.29
Univariate analyses								
Praying and hoping	7.48	1.04	10.78	0.98	5.36	(1, 83)	**0.023**	0.06
Wishful thinking	0.43	0.10	1.02	0.10	18.27	(1, 83)	**<.001**	0.18
Self-criticism	0.68	0.14	1.40	0.13	15.00	(1, 83)	**<.001**	0.15
Pain catastrophising	7.03	0.94	11.67	0.88	12.99	(1,83)	**0.001**	0.14

ANTECEDENT AND RESPONSE-FOCUSED COPING IN HEADACHE INTENSITY

8.3.3 Antecedent-focused coping in migraine, T-TH, controls

Antecedent-focused strategies of pain distraction, pain reinterpretation, problem-focused coping, detachment, reappraisal and attention deployment were similar in migraine, T-TH and controls (Table 8.3).

Table 8.3 Antecedent-focused coping strategies in migraine, T-TH and controls: means and standard errors, effects.

	Migraine		T-TH		Controls	
Pain coping	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**
Pain distraction	22.10	1.61	26.34	1.93	21.50	2.18
Pain reinterpretation	9.05	1.11	9.48	1.33	8.27	1.46
Problem focused coping	1.17	0.09	1.24	0.10	1.30	0.11
Detachment	0.79	0.07	0.89	0.09	0.82	0.10
Reappraisal	0.85	0.10	0.67	0.12	0.68	0.13
Attention deployment	1.17	0.22	1.31	0.26	1.77	0.30

	Headache sufferers v controls				Migraine v T-TH			
	F	**df**	***p***	**η_p^2**	**F**	**df**	***p***	**η_p^2**
Multivariate analysis								
Antecedent-focused coping	1.42	(6,83)	0.217	0.09	1.64	(6,64)	0.151	0.13
Univariate analyses								
Pain distraction	1.01	(1, 88)	0.318	0.01	2.86	(1, 69)	0.095	0.04
Pain reinterpretation	0.17	(1, 88)	0.685	0.00	0.06	(1, 69)	0.802	0.00
Problem focused coping	0.93	(1, 88)	0.338	0.01	0.31	(1, 69)	0.577	0.00
Detachment	0.00	(1, 88)	0.979	0.00	0.78	(1, 69)	0.381	0.01
Reappraisal	0.24	(1, 88)	0.623	0.00	1.36	(1, 69)	0.247	0.02
Attention deployment	3.06	(1, 88)	0.084	0.03	0.17	(1, 69)	0.677	0.00

8.3.4 Antecedent-focused coping and stress-headache

Antecedent-focused strategies – both attentional control and volitional cognitive control – were similar in those with and without stress-headache (Table 8.4).

Table 8.4 Antecedent-focused coping in those with and without stress headache: means, standard errors, effects

	Low/no headache		Stress-headache		Stress-headache vs low/no headache			
Coping tactic	**Mean**	**SE**	**Mean**	**SE**	**F**	**df**	***p***	**η_p^2**
Multivariate analysis								
Antecedent-focused coping					1.15	(6,78)	.342	0.08
Univariate analyses								
Pain Distraction	21.65	1.64	24.40	1.55	1.49	(1 ,83)	0.226	0.02
Pain Reinterpretation	9.35	1.09	8.38	1.03	0.42	(1 ,83)	0.519	0.01
Problem focused coping	1.21	0.08	1.17	0.08	0.13	(1 ,83)	0.720	0.00
Detachment	0.72	0.08	0.88	0.07	2.53	(1 ,83)	0.116	0.03
Reappraisal	0.67	0.09	0.73	0.09	0.25	(1 ,83)	0.621	0.00
Attention deployment	1.15	0.22	1.51	0.21	1.38	(1 ,83)	0.244	0.02

8.3.5 Response-focused coping in migraine, T-TH, controls

The response-focused coping strategies of ignoring pain sensations, coping self-statements, venting and behavioural suppression were similar in migraine, T-TH and controls (Table 8.5).

Table 8.5 Response-focused coping strategies in migraine, T-TH and controls: means and standard errors, effects

	Migraine		T-TH		Controls	
Pain coping	**Mean**	**SE**	**Mean**	**SE**	**Mean**	**SE**
Ignoring pain sensations	13.38	0.86	14.14	1.04	13.77	1.25
Coping self-statements	14.57	0.65	14.72	0.78	14.50	0.89
Venting	0.32	0.07	0.43	0.09	0.48	0.11
Behavioural suppression	1.42	0.10	1.37	0.12	1.51	0.14

	Headache sufferers v controls				Migraine v T-TH			
	F	**df**	***p***	**η_p^2**	**F**	**df**	***p***	**η_p^2**
Multivariate analysis								
Response-focused coping	0.47	(4,85)	.759	0.02	0.35	(4,66)	.842	0.02
Univariate analyses								
Ignoring pain sensations	0.04	(1, 88)	0.850	0.00	0.31	(1, 69)	0.578	0.00
Coping self-statements	0.00	(1, 88)	0.977	0.00	0.02	(1, 69)	0.880	0.00
Venting	1.28	(1, 88)	0.261	0.01	0.89	(1, 69)	0.350	0.01
Behavioural suppression	0.94	(1, 88)	0.334	0.01	0.08	(1, 69)	0.772	0.00

8.3.6 Response-focused coping and stress-headache

The tactic of *ignoring pain sensations* was more prevalent in those with low/no headache ($p < .05$) than those who developed stress-headache (Table 8.6).

Table 8.6 Response-focused coping in those with and without stress-headache: means, standard errors, effects

	Low/no headache		Stress-headache		Stress-headache vs low/no headache			
Coping tactic	**Mean**	**SE**	**Mean**	**SE**	**F**	**df**	***p***	η_p^2
Multivariate analysis								
Response-focused coping					2.06	(4,80)	0.094	0.09
Univariate analyses								
Ignoring sensations	15.15	0.91	12.04	0.86	6.14	(1, 83)	**0.015**	0.07
Coping self-statements	14.95	0.67	14.09	0.63	0.87	(1, 83)	0.355	0.01
Venting	0.32	0.08	0.41	0.07	0.72	(1, 83)	0.397	0.01
Behavioural suppression	1.48	0.10	1.29	0.10	1.62	(1, 83)	0.207	0.02

DOES NA MEDIATE THE RELATIONSHIP BETWEEN COPING AND STRESS-HEADACHE?

8.3.7 Correlations between NA, headache intensity and coping tactics

As shown in Table 8.7 and Table 8.8, catastrophising, praying/hoping, wishful thinking, detachment, venting, self-criticism and attention deployment correlated with headache intensity ($p,.05$ to $p<.01$). Catastrophising and wishful thinking correlated with all NA and with pain distress at the end of phase 1 of the experiment., self-criticism with all NA during the task, venting with all NA but confusion. Praying/hoping correlated with anxiety, confusion and pain distress.

Table 8.7 Pearson correlations between each pain and stress coping tactic and NA

	Headache	Anxious	Confused	Discouraged	Irritated	Sluggish	Tense	Pain distress
Distract from pain	0.084	0.077	0.073	0.044	0.050	0.048	0.126	–0.021
Reinterpret pain	–0.019	–0.022	–0.050	–0.006	0.023	0.055	0.103	–0.105
Catastrophise about pain	0.403**	**0.339****	**0.375****	**0.309****	**0.348****	**0.319****	**0.427****	**0.352****
Ignore sensations	–0.207	–0.185	**–0.224***	–0.155	–0.186	–0.176	–0.106	–0.145
Pray/Hope	0.249*	**0.275***	**0.245***	0.155	0.172	0.163	0.172	0.272*
Coping self–statements	–0.049	–0.111	–0.132	–0.071	–0.056	–0.134	–0.039	–0.191
Focus on problem	–0.011	0.014	–0.047	0.068	0.082	0.165	0.081	0.020
Wishful Thinking	0.568**	**0.494****	**0.496****	**0.499****	**0.515****	**0.524****	**0.529****	**0.376****
Detach	0.222*	0.164	0.172	0.182	0.202	**0.268***	**0.301****	0.196
Vent	0.282**	**0.284****	0.184	**0.285****	**0.233***	**0.287****	**0.308****	0.113
Reappraise	0.140	0.092	0.049	0.167	0.182	0.203	**0.220***	0.154
Criticise self	0.433**	**0.391****	**0.416****	**0.355****	**0.331****	**0.265***	**0.321****	0.067
Suppress	–0.085	–0.037	–0.067	–0.048	–0.041	–0.029	–0.082	–0.125
Deploy attention	0.252*	0.194	0.160	0.198	0.213	**0.271***	**0.296****	**0.261***

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).

Table 8.8 Pearson correlations between headache intensity, and pain and stress coping strategies reported immediately after the task

	Distract from pain	Reinterpret pain	Catastro–phise	Ignore pain Sensations	Pray/ Hope	Coping self–statements	Focus on problem	Wishful Thinking	Detach	Vent	Reappraise	Criticise self	Suppress	Deploy attention
Headache intensity	0.084	–0.019	**0.403****	–0.207	**0.249***	–0.049	–0.011	**0.568****	**0.222***	**0.282****	0.140	**0.433****	–0.085	**0.252***
Distract from pain	–	**0.364****	0.143	0.063	**0.230***	**0.385****	0.207	0.068	**0.240***	**0.273****	0.187	0.134	**0.208***	**0.313****
Reinterpret pain	**0.364****	–	–0.088	**0.382****	–0.063	**0.405****	**.410****	0.165	**0.418****	0.195	**0.345****	–0.010	**0.445****	**0.282****
Catastrophise	0.143	–0.088	–	**–0.255****	**0.423****	–0.128	0.017	**0.342****	**0.211***	0.164	0.091	**0.250***	–0.075	0.089
Ignore sensations	0.063	**0.382****	**–0.255****	–	**–0.270****	**0.428****	0.186	0.005	0.113	0.100	**0.267***	–0.135	**0.237***	–0.114
Pray/Hope	**0.230***	–0.063	**0.423****	**–0.270****	–	–0.033	–0.016	**0.296****	**0.266***	**0.311****	0.028	0.037	–0.046	**0.285****
Coping self–statements	**0.385****	**0.405****	–0.128	**0.428****	–0.033	–	0.114	0.114	**0.310****	0.129	**0.259***	0.039	**0.211***	0.164
Focus on problem	0.207	**0.410****	0.017	0.186	–0.016	0.114	–	0.108	**0.338****	**0.288****	**0.409****	0.038	**0.447****	**0.322****
Wishful Thinking	0.068	0.165	**0.342****	0.005	**0.296****	0.114	0.108	–	**0.489****	**0.331****	**0.344****	**0.328****	–0.068	**0.273****
Detach	**0.240***	**0.418****	**0.211***	0.113	**0.266***	**0.310****	**0.338****	**0.489****	–	**0.396****	**0.570****	0.172	**0.490****	**0.546****
Vent	**0.273****	0.195	0.164	0.100	**0.311****	0.129	**0.288****	**0.331****	**0.396****	–	**0.466****	**0.275****	0.206	**0.426****
Reappraise	0.187	**0.345****	0.091	**0.267***	0.028	**0.259***	**0.409****	**0.344****	**0.570****	**0.466****	–	0.040	**0.401****	**0.355****
Criticise self	0.134	–0.010	**0.250***	–0.135	0.037	0.039	0.038	**0.328****	0.172	**0.275****	0.040	–	–0.083	0.134
Suppress	**0.208***	**0.445****	–0.075	**0.237***	–0.046	**0.211***	**0.447****	–0.068	**0.490****	0.206	**0.401****	–0.083	–	**0.253***
Deploy attention	**0.313****	**0.282****	0.089	–0.114	**0.285****	0.164	**0.322****	**0.273****	**0.546****	**0.426****	**0.355****	0.134	**0.253***	–

* Correlation is significant at the 0.05 level (2-tailed).

** Correlation is significant at the 0.01 level (2-tailed).

Hierarchical multiple regression analyses were conducted to assess whether pain and stress coping strategies, attachment style and FFM personality traits predicted headache intensity during the cognitive task, after controlling for the influence of anxiety, confusion, discouragement, irritation, sluggishness and tension (each NA was averaged across the four sets of the arithmetic task).

In the first analysis (Model A), a significant regression equation was found at Step 1 ($F(21,59) = 3.61$, $p < .0001$) with an R^2 of 0.562. That is, 56.2% of the variance in headache intensity was predicted by pain and stress coping tactics, insecure attachment and FFM personality traits. Wishful thinking ($\beta = 0.612$, $p < .001$) was the most significant predictor at this step, with trait-conscientiousness second ($\beta = 0.231$, $p < .05$). At Step 2, with an R^2 of 0.917, all NA jointly predicted a further 35.5% of the variance (F change $(6,21) = 37.954$, $p < .0001$). Wishful thinking ($\beta = 0.612$, $p < .0001$) and conscientiousness ($\beta = 0.231$, $p < .05$) were significant predictors at this step.

To determine the mediating role of NA, in a repeated analysis (Model B), all NA measures were entered in step 1 and pain and stress coping tactics, attachment style and personality factors in step 2. As shown in the "B" model in Table 8.9**,** all NA jointly predicted 87.6% of the variance at step 1 ($F(6,21) = 87.145$, $p < .0001$), but at step 2, with an R^2 of 0.875, the R^2 change of 4.1% was not significant. These analyses indicate that NA accounted for nearly all the variance in headache intensity. Anxiety ($\beta = 0.491$, $p < .0001$) was the only independent predictor of headache intensity at this point.

Table 8.9 Hierarchical regression analyses: Predicting headache intensity from NA, stress and pain coping strategies, insecure attachment and personality traits

	Model 1A	Model 1B	Model 2
R^2	**0.562*** **	**0.876*** **	**0.917*** **
R^2 **change**			
Model 1A or 1B to Model 2	**0.355*** **	**0.041**	
Beta weights in each model			
Problem-focused coping	–0.040		–0.065
Wishful thinking	**0.612*** **		0.123
Detachment	–0.201		–0.052
Venting	0.132		–0.011
Reappraisal	–0.043		0.065
Self-criticism	0.210		0.035
Suppression	0.192		–0.027
Attention deployment	0.060		0.063
Pain distraction	0.117		0.061
Pain reinterpretation	–0.109		–0.017
Pain catastrophising	0.217		0.090
Ignoring pain sensations	–0.115		–0.043
Praying/hoping	–0.173		–0.028
Coping self-statements	–0.049		0.076
Attachment anxiety	0.014		–0.033
Attachment avoidance	0.035		0.019
Neuroticism	0.017		0.039
Extraversion	0.124		–0.032
Openness	–0.148		–0.005
Agreeableness	0.020		–0.096
Conscientiousness	**0.231***		0.098
Anxiety		**0.566*** **	**0.491*** **
Confusion		0.148	0.219
Discouragement		0.183	0.221
Irritation		0.097	–0.038
Sluggishness		–0.103	0.033
Tension		0.104	–0.037

Note: * = p<.05, ** = p <.01, *** = p <.001

8.4 Discussion

These studies aimed to assess the role of specific coping tactics in upregulating (or failing to downregulate) headache-related NA. It was expected that threat-based coping methods would increase headache-related NA, and that headache would be associated with greater use of response-focused and less use of antecedent-focused coping.

8.4.1 Threat-based coping and headache

Threat-based coping predicted headache and was driven by anxiety. Although similar between migraine, T-TH and controls, the threat-based tactics of praying/hoping, self-criticism, pain catastrophising and especially wishful thinking were greater ($p < .05$ to $p < .001$) in those who developed headache during the cognitive task compared with those who did not. That 67% of controls developed headache may account for the null results in the comparison between headache sufferers and controls.

Anxiety disrupts amygdala-prefrontal circuitry, with reciprocal interactions occurring between anxiety, headache and threat-based coping. Anxious individuals show increased attentional capture by cues signalling danger and are more likely to interpret emotionally ambiguous stimuli in a threat-related manner (229). Deficient recruitment of prefrontal control mechanisms and amygdaloid hyper-responsivity to threat potentially alter associative, attentional and interpretative processes that sustain a threat-related processing bias. In turn, anxiety strengthens the activation of threat-related representations by augmenting the output from threat-evaluation processes and so making the selection of threat-related interpretations more likely (714).

Thus, since pain and emotion increase when attention is paid to them and painful stimuli can be experienced as less intense during distraction conditions (253; 715-717), anxiety can increase pain by compromising attentional and interpretative processes. Paradoxically, attempts to suppress pain awareness function to increase pain, since in the absence of focused attention (718), pain stimuli take precedence over non-pain stimuli (627). Also, in experientially avoidant tactics such as wishful thinking and praying/hoping, the signal value of pain is increased (698; 719; 720), hence increasing pain intensity (678). Efforts to avoid or suppress the emotion-eliciting aspects of noxious stimuli similarly focus attention on these stimuli, increasing their threat value (276; 419; 675; 678; 719; 721). In a vicious cycle, this can engender Pavlovian fear-conditioning, provoking

physiological and behavioural fear responses to headache symptoms (including headache-related NA) in a similar manner to intrinsically threat-related stimuli (722; 723).

Therefore, for a coping tactic to reduce NA, the individual's attention must be *actively* directed elsewhere and the distractor must have sufficient potency to compete for attentional resources (416; 724-726). Furthermore, attention must be redirected away from the affective component of pain towards its sensory aspects ('sensory monitoring'). Participants instructed to attend to objective, sensory aspects of cold pressor pain reported less distress than those distracted by interesting slides during immersion in the icy water (253; 727). Likewise, in effective hypnotic pain modulation (the technique of "focused analgesia") (228), attention is actively focused on the painful area receiving stimulation, while emotion-generating images, thoughts and self-statements are simultaneously redirected towards their sensory/external components via the generation of an 'obstructive hallucination', e.g. imagining the painful area as numb and warm (251; 728). To the extent that attentional capacities are reduced in migraineurs (729), dissociating the sensory from the affective aspects of pain may be difficult. Skills in the "metacognition of attention" – such as monitoring one's attentional performance – may improve selective attending during stress (730). Such approaches may functionally address the imbalance of amygdala-prefrontal activity associated with anxiety, downregulating the amygdala response to threat-related cues and/or upregulating prefrontal control mechanisms (229).

Non-evaluative acceptance of pain is also important, as an inflexible agenda of pain control is likely to induce "struggle", increasing pain intensity (276). Thus, the negative cognitions associated with pain-catastrophizing increase the focus on pain and NA, increasing pain perception by predisposing to threatening interpretations of ambiguous stimuli (169; 260-263). Pain catastrophising has also been shown to increase temporal summation at the synapse, reducing capacity for pain modulation (693). Similarly, by focusing attention on supposed self-deficits, self-criticism can engender dysphoria and hopelessness, increasing the probability of headache (302; 731-733).

8.4.2 Response-focused tactics and headache

This hypothesis received limited support, in that the response-focused tactic of *ignoring pain sensations* was related to less intense headache. This may be because it was unrelated to anxiety, and perhaps also because, by definition, it consists of sensory monitoring (see above), although this requires further research. Both antecedent-focused coping and response-focused coping strategies were similar in migraine, T-TH and controls.

The classic suppression-reappraisal distinction noted elsewhere (708; 709; 734) was also unsupported. However, the nature of the stressor may partially account for these results. During an unpredictable, time-pressured task with pain and non-contingent failure feedback, reappraisal – with its emphasis on controlling the personal meaning that the event has for the individual – is unlikely to be a workable option (171). Neither time nor opportunity were available for cognitively re-evaluating – or detaching from– this rapidly changing task. Suppression, with its emphasis on controlling one's behavioural responses to events, may at such times be one's best – or only – coping option, particularly if emotion intensity is high (735) or the stressor cannot be controlled (736). Secondly, in this study, suppression appears to have functioned as a proactive coping method; its correlations with NA were non-significant (and tended to be negative), and it was strongly correlated with proactive pain coping (pain-distraction, reinterpreting pain, ignoring sensations, coping self-statements) and the antecedent-focused methods of problem-solving, reappraisal, detachment and attention deployment. Thus, the antecedent – response-focused distinction between suppression and reappraisal in this study was largely negated. In addition, Gilbert (737) makes a case for suppression as a *social* coping method, which evolved – along with self-blame – in hostile-dominant relationship contexts (discussion below). If so, suppression may function differently in the nonsocial context of this cognitive task.

8.4.3 Response conflict and coping with headache

Furthermore, the adoption of goal-relevant volitional cognitive control strategies which upregulate prefrontal control mechanisms (and potentially reduce amygdala hyperactivation) was effectively "punished" in this task. Goals are important determinants of behaviour and individuals are more likely to endure a task despite pain for important goals (669). Stress also arises when important goals are threatened (641). As explained in chapter 7, participants with high outcome expectancy faced a response conflict upon finding that goal achievement was thwarted by noncontingent failure feedback and impeded task progress. Normally, in stressful and painful situations, avoidance (e.g. of frustration) is a primary way of regulating behaviour (644), but a strong desire to succeed may conflict with the wish to avoid defeat. This coactivation of approach and avoidance motives is problematic (670), resulting in goal conflict and vacillation in behaviour (668). In a vicious cycle, attentional processes are compromised (263), lower mood and persisting high levels of frustration interfere with task completion, triggering the use of self-regulatory resources (193; 668; 670; 738). Distress increases, especially when self-regulation is failing (671). By compromising effective self-regulation, such response conflicts can intensify pain (668; 739).

Such response conflict is not uncommon in situations which are novel, (740) difficult (741) or contradictory (668), and may be more common in those with pain than pain-free controls (739). In the absence of response conflict, it is noteworthy that 'dissociated imagery' (e.g. imagining a pleasant scene, akin to wishful thinking), successfully reduced pain unpleasantness (742) or self-reported discomfort (713). Perhaps wishful thinking upregulates headache-related NA only in situations of response conflict? Particularly if such response conflict is associated with learned helplessness? And perhaps antecedent-focused coping is efficacious only in the absence of such conflict? Further research could assess these possibilities.

Thus, context may be more pertinent than tactic or timing in determining whether failure to regulate or misregulation leads to NA, including in tactics which are threat-based. For example, passive pain coping – an avoidant set of cognitions and behaviours in which the sufferer relinquishes control and depends on others – is generally associated with greater pain report than active coping (efforts to function despite pain) (743). However, it can be efficacious for headache sufferers in the early stages of a stressor, when response options are yet to be formulated (159; 744).

This concept of response conflict is not new to the migraine literature. As Price pointed out, the stressor of pain frequently occurs in a context which is threatening for reasons other than the pain itself (288). This includes interpersonal conflict. Thus, some 98% of emotion regulation episodes involve adaptations to significant others (161; 706; 745; 746). In his study of 1200 migraineurs, Sacks described how 'situational' migraine may arise in hostile-dominant relationship contexts characterised by 'malignant emotional binds', where active coping is precluded (426). In such contexts, it may be more adaptive to attend to the power and threat of others while monitoring one's own behaviour for its threat-safeness (167). There may be little one can do to alter the behaviour of the dominant person, especially if one is trapped with him or her. Here, the inhibitory social behaviours of appeasement and submission (suppression and self-criticism/blame) may offer a means of self-protection, enabling the individual to 'make safe' and elicit care (167). In conflict situations, although associated with dysphoria and headache, self-criticism/self-blame as a defensive/safety or appeasement behaviour can reduce arousal (747) and calm self and dominant others (748). As indicated above, in social situations of humiliation and entrapment, suppression may be one's best option for dealing with depression and the increased pain sensitivity associated with interpersonal distress (748). Further research on the role of suppression and self-blame in response to a *social* stressor is indicated.

These ‘damage control’ coping responses may also assist in bodily regulation; the dorsal-vagal branch of the parasympathetic nervous system is activated, bodily systems shut down, metabolic demands reduce and the pain threshold increases (148). Where active coping is precluded, the ‘fold into helplessness’ accompanying a migraine attack may itself be a protective reflex (749) Over time, these safety-seeking social strategies become linked into intimate self-self and self-other relationships (167). This ecological perspective is consistent with studies showing a greater incidence in migraineurs than non-migraineurs of anxious attachment, PTSD and a child maltreatment history (750-753). Hence, there may be strong contextually-based reasons why migraineurs adopt ‘fear avoidant’ tactics, fail to use social support or to regulate distress at all (426). It may even be the case that the response conflict evoked in our research design – where individuals over-extended themselves in a context which consistently thwarted goal progress – was of a kind likely to lead to a ‘learned helplessness’ response{Overmier, 2002 #978}(268). Perhaps then the deciding factor in stress-related headache is whether or not response conflict leads to this constellation of behavioural responses.

Thus ultimately, consistent with the transactional model (615), contextual factors including various forms of response conflict may be the *sine qua non* in determining the relationship between coping choice, coping efficacy and headache-related NA. Further research on the relationship of coping and headache within different (relationship) contexts, especially those evoking a learned helplessness response, is recommended.

8.4.4 Clinical implications

Literature and research in Acceptance and Commitment Therapy (ACT) (675) and mindfulness-based cognitive therapy (MBCT) promotes pain/emotional acceptance as an antidote to internal or response conflict (276; 754). This approach eschews the idea of coping in favour of acceptance, since a coping emphasis may encourage, or at least permit, a somewhat inflexible agenda of pain control, promoting an unproductive struggle against one’s current reality (276). Thus, pain acceptance was shown to be a key mechanism underlying improvement in pain outcome during an MBCT intervention for headache pain (755). In addition, given the central role of anxiety in the selection of headache coping tactics, methods which downregulate the amygdala response to potentially threat-related cues and upregulate prefrontal control mechanisms can be usefully taught, using extinction and reinstatement approaches (723).

In facilitating acceptance, headache treatment programs should aim to develop skills and awareness of:

1. The components of effective coping – i.e. of methods which increase pain self-efficacy, decrease stressor uncontrollability and reduce the likelihood of learned helplessness responses.
2. Sensory monitoring and redirecting emotion-eliciting stimuli toward their sensory/external components
3. Skills in the "metacognition of attention', such as (i) identifying beliefs about self, others and the environment which underlie one's adoption of certain coping tactics; (ii) monitoring one's attentional performance, even in situations where external cues about its functioning are not yet present, (iii) developing selective attending skills which enable dissociation of sensory and emotional aspects of a stimulus.
4. Distress tolerance through self-compassionate observation and acknowledgement of external (e.g. others' behaviour and motivations) and internal (one's own reactions and thoughts) aspects of the context (756).
5. Emotional competence/intelligence in identifying one's own and others' emotions, activating self-soothing behaviours in the 'safeness' domain (737) and increasing the range of non-submissive coping strategies (757; 758).

Limitations of this study

The generalizability of these coping results is limited by reliance on a predominantly undergraduate population, since university students have a relatively consistent level of education, are familiar with testing situations and may view the task more as a 'challenge' than a threat. The WCQ-R may also limit the assessment of coping, since although widely used, it pre-dates the acceptance-based coping and emotion processing research literatures (276; 734). Nor are self-soothing behaviours canvassed sufficiently. Also, although the measure was chosen for its adaptability to a particular stressor (663; 759), parity of scoring between original and adapted versions is difficult to achieve and these differences may have biased the results.

Furthermore, in replicating the 4:1 migraine gender ratio, our sample was composed primarily of women, and at least some coping strategies may be gender-specific (760).

8.5 Conclusions

There is a bidirectional relationship between headache and coping, and this relationship is mediated by anxiety. By increasing the attention paid to pain and NA, threat-based coping tactics are associated with more intense headache, which further upregulates anxiety. Headache itself was associated not with the response-focused method of suppression, but with less use of *ignoring pain sensations*. Coping is compromised in situations where approach and avoidance motives are coactivated, and the NA thus generated, especially when combined with learned helplessness responses, may increase headache vulnerability. Coping optimally with the experience of headache involves a focus on decreasing rather than controlling pain, increasing skills in the metacognition of attention and restructuring thinking away from threat-based appraisals.

SECTION 4: CONCLUSION

Chapter Nine

9

General discussion and conclusions

9.1 Aims and description

From the point of view of homeostatic regulation, the neurovascular condition of migraine – and to a lesser extent T-TH – is a conundrum. Following stress, normal homeostatic mechanisms could be expected to return autonomic stress responses to baseline. However, anomalous responses to a stressor have been described, particularly in migraine, and placed under the rubric of "stress sensitivity". These include alterations in normal homeostatic mechanisms during stress (e.g. abnormal autonomic function), failure to habituate to repeated stressors of the same kind (558), failure to shut down the stress response in a normal manner (596) and altered or ineffective responses to stress that lead to compensatory increased responses, e.g. over-active threat appraisals (184) or alterations in brainstem processing that lead to central sensitisation (111). Nevertheless, there is relatively little knowledge of the activity and reciprocal relationships between biological and psychological aspects of the multilevel stress response as these pertain to headache activity during a stressful episode. Thus, in an experimental study using a biopsychosocial model, the aim of this thesis was to investigate whether and how each component of the psychobiological stress process may induce headache in those with episodic migraine and T-TH during headache provoked by a stressful cognitive task. Since stress is a commonly reported precipitant of headache, and more amenable to modification than physiological stress responses, results of this study were expected to inform headache treatment and management and to potentially offer information on other disorders similarly impacted by stress.

Following the recommendations of Koolhaas and colleagues (761), an established cognitive stressor, a stressful arithmetic task (33), was modified to be both unpredictable (non-contingent failure feedback) and uncontrollable (time pressured, loud background noises, head shocks). Participants rated the stressfulness of the task at a mean level of 4.5 on a 7-point scale.

In a three-phase experiment before, during and after the task, participants rated headache, nausea, pain and pain distress or negative affect (NA) on a ten-point VAS scale immediately following the administration of 2 milliamp head shocks over the supraorbital nerve on the forehead. Ten shocks were administered at 30 second intervals, 20 shocks at 2 second intervals and a further 10 shocks at 30s intervals. In the 25-minute arithmetic task, in the second phase of the experiment, participants continued to receive the sequence of head shocks while completing four sets of addition and subtraction exercises. Each arithmetic set was time pressured and at increasing levels of difficulty. Meanwhile, an

audio recording of a crying baby was played in the background at steadily increasing volume. Blood pressure was taken at approximately 3-minute intervals. Following each arithmetic set, the participant rated headache, nausea, pain, anxiety, confusion, discouragement, irritation, sluggishness, tension and self-efficacy. Cortisol was measured at four points during the task – at entry, and at the end of each phase of the experiment. Trigeminal nociception during the experiment was measured via nociceptive blink reflex recordings, using a sequence of 10 shocks at 30s intervals, 20 shocks at 2s intervals and a further 10 shocks at 30s intervals within each phase of the experiment. In order to take these measurements, participants were placed in a Faraday cage, a room lined with metal sheets to screen out electrical noise.

A week prior to testing, participants completed a headache questionnaire and a headache diagnostic category was assigned according to I.H.S. criteria (7). Participants also completed the NEO-PI-R (323), *Ways of Coping Questionnaire – Revised (WCQ-R)* (663), (Pain) *Coping Styles Questionnaire* (329) and *Close Relationships Questionnaire* (attachment styles) (434).

Immediately following the stressful task, participants filled out a modified version of the WCQ-R (663). Participants were asked to rate four dimensions of the task – task stressfulness, controllability, impact and importance on a 7-point scale. A further 36 questions tapped participant coping strategies during the task on a four-point scale (‘not used at all’ to ‘used a lot’).

9.2 Stress, allostasis, allostatic load and headache

The ambiguity of the term “stress” (see Section 1.1.1) confuses adaptive changes to a current or anticipated stressor (e.g. release of catecholamines to increase heart rate and blood pressure) with the maladaptive changes which lead to wear-and-tear on the organism (e.g. elevated and prolonged heart rate contributing to heart attack). Thus, the use of the terms ‘allostasis’ – achieving stability through change – and ‘allostatic load’ – the cost to the organism of such changes – offer greater precision when considering the relationship between different aspects of the stress response and headache.

With the onset of a stressor, adaptive processes usually come into play that may be measurable in psychophysiological stress responses (e.g. circulating glucocorticoids, changing appraisals). Effector responses often impact numerous bodily parameters at the same time. When conditions are stable and predictable, individuals learn to make anticipatory responses that allow adaptations to avoid physiological dysregulation.

Initially arbitrary cues become, by virtue of prior association, conditioned to elicit corrective responses. Disturbances are appropriately balanced by a counter-regulatory response. In allostasis, a response is initiated by a stressor, sustained for an appropriate interval and then turned off.

A specific injury initiating a large nociceptive barrage either activates cortico-striatal circuitry into a response that copes with the injury and aids recovery or a response that diminishes the cortico-striatal threshold. When a stressor is protracted, frequent or prolonged, the usual regulatory mechanisms become ineffective in handling the reactions to a stressor, increasing allostatic load. Normally responsive allostasis – i.e. the efficient turning on and shutting down of responses – is disrupted by a constellation of internal states of dysregulation. The afferent signal is functionally amplified, enhancing the gain for inducing learning, which in turn imprints novel neocortical anatomical and functional memory traces (666). Effector loops may over-respond in magnitude or duration, remain active even if the initiating disturbance is no longer present, and/or become un-coordinated, competing concurrently with other effectors. (291). Persistence of these dysregulated responses can lead to compensatory increased responses to other mediators, with long-term alterations in normal homeostatic mechanisms, such as autonomic function and brainstem processing. Although regulation will eventually settle at a balance point, prolonged elevation of the regulated variable is inefficient and metabolically costly beyond what is normally required, leading to disease (291). In a maladaptive feedforward cascade, increasing allostatic load progressively damages brain and body systems (192).

In chronic pain conditions, for example, the human brain undergoes extensive reorganization – peripheral reorganization of afferent signalling, changing sensitivity for nociceptors and molecular changes at the level of the spinal cord which generally give rise to central sensitization (111). Capacity to activate central opioid neurotransmission is reduced (762). There is a lowered mesolimbic threshold for the conscious perception of pain and increased activity in the medial prefrontal cortex and amygdala. In multiple animal models there is evidence of the critical role of the amygdala, where its properties seem to modulate even spinal cord central sensitization processes (763) and influence prefrontal activity (764). This renders the pain more distressing (209). These limbic brain properties are the primary determinant that explain almost all of the variance of the outcome parameter for the transition to chronic pain (666). Persistence of negative moods becomes a maladaptive process, at least partially maintained by neuropathological mechanisms (666). Such changes have been documented in chronic daily headache as well as chronic migraine (192).

9.3 Study findings 1: Allostatic load and stress-headache

In what follows, using the framework of allostatic load, we will examine the sequence of psychophysiological responses to the laboratory stressor in episodic migraine and T-TH participants and those who developed headache during the stressful task – 67% of whom were controls. As diagrammed in Figure 9.1, the stages of the stress response were considered as: stressor–appraisals–coping–psychophysiological stress responses–strain, where strain may be considered equivalent to allostatic load.

After McEwen (765), four conditions lead to allostatic load:

- Type 1: Repeated "hits" from multiple stressors,
- Type 2: Lack of adaptation to a stressor,
- Type 3: Prolonged response due to delayed shut down,
- Type 4: Inadequate response that leads to compensatory hyperactivity of other mediators.

9.3.1 Primary stressor appraisals/stressor exposure

Factor analysis of the four task dimensions rated during the modified WCQ-R (140) yielded two factors – subjective stressfulness and stressor controllability. Only 'subjective stressfulness' ("how stressed-out am I?") related to headache. If the answer effectively was "very", the person felt discouraged and tense. This may relate to Panksepp's explanation that the experience of stress arises when top-down cognitive functions that regulate affective processing are disrupted, since these act as a brake on the emotional turmoil engendered by stressful situations (126).

After Bolger (185), subjective stress appraisals were considered to measure *stressor exposure*, the *likelihood* of appraising a situation as stressful or a threat. Subjective stress and appraisals are likely to compound, increasing the chances of further such appraisals (766). Continuous appraisals of situations as being threatening (767), whether during daily hassles or major life events (768) can result in Type 1 allostatic load (214) – a greater number of "hits" (765).

High neuroticism (N) can further add to allostatic load, since high-N scorers experience greater threat perception and anxiety (300; 344; 350; 365; 644; 652; 769) and are more susceptible to experiencing NA and frustration during daily hassles than low-scorers on this trait (184). Exaggerated harm appraisals are thought to confer stress

vulnerability during threat (407) and high scorers experience high levels of subjective stress and low feelings of control each time they encounter acute stress (770; 771). However, over time the HPA axis and autonomic reactivity become downregulated as a result of allostatic load (60; 586; 765). Thus, primary stress appraisals may increase headache vulnerability, especially in individuals scoring high in neuroticism.

9.3.2 Discouragement and tension

In multiple regression analyses, discouragement and tension accounted for 87% of the variance in the relationship between subjective stress appraisals and headache. NA was greater in those who developed headache during the task than those whose headache was mild. The heightened NA of those who developed a headache fits with the third of McEwen's criteria for allostatic load – that of "prolonged response". Furthermore, and as discussed below, the high NA as one arm of the stress response may have interacted with the other arm of the stress response (physiological and autonomic responses), potentiating these responses.

Agreeableness moderated the relationship between subjective stress appraisals and headache, by reducing the level of discouragement associated with this appraisal. This is consistent with findings of lower headache severity in more agreeable individuals, since agreeable individuals are less often engaged in interpersonal conflict and anxiety-producing life events (185; 194; 201; 392-394; 772).

High openness to experience (O) reduced the degree of tension associated with a subjective stress appraisal, thus potentially reducing allostatic load. Since high-O individuals tend on a motivational and cognitive level to explore new experiences (773), they may have been more likely to appraise the (novel) task as a challenge rather than as a threat, thereby reducing subjective stress and NA (160; 774). Also, since high-O scorers are characteristically emotionally expressive (323), the frequent affect ratings during the task may have suited these individuals.

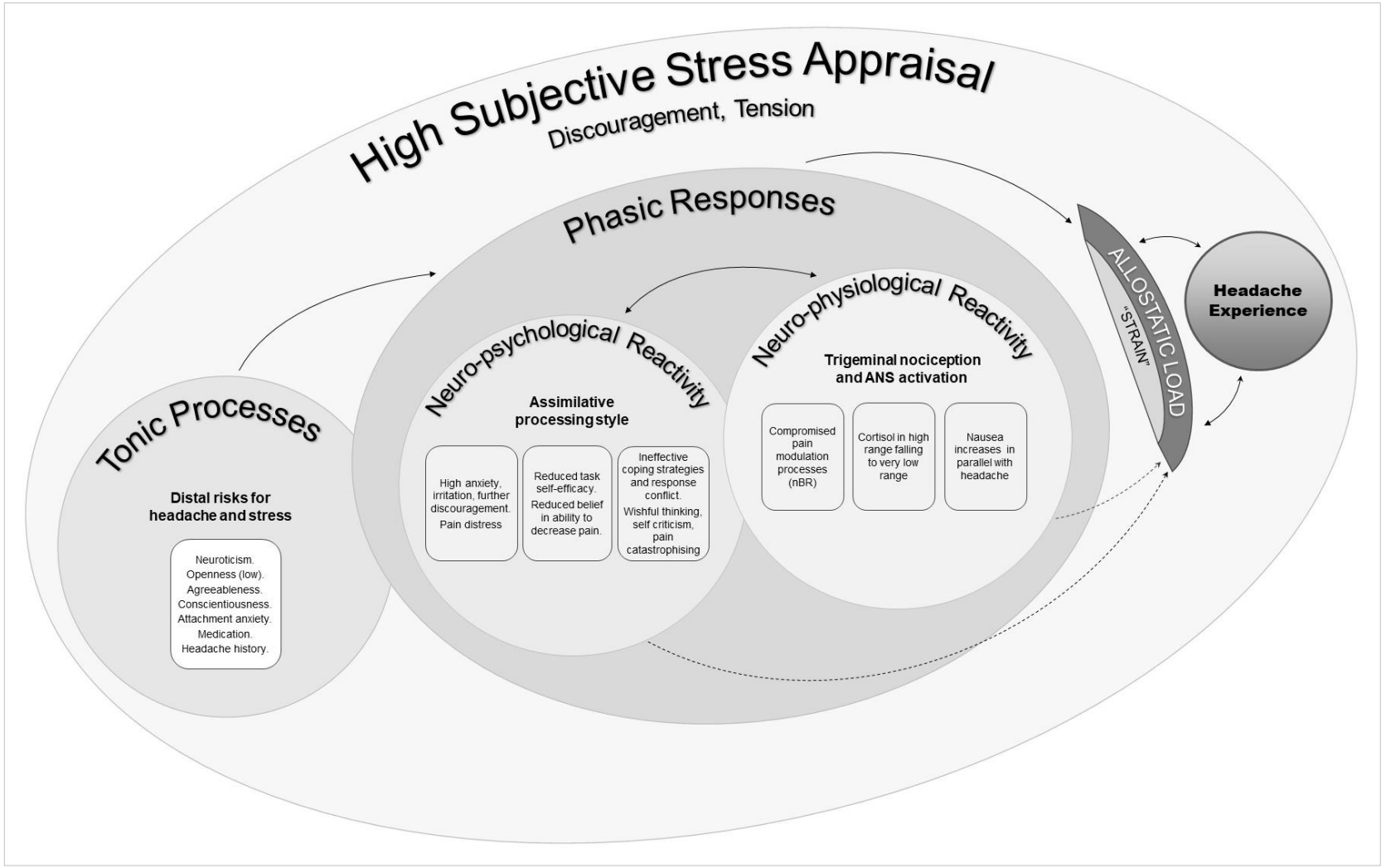


Figure 9.1 Cascade of effects increasing allostatic load and thus increasing vulnerability to stress-headache.

9.3.3 Secondary appraisals/stressor reactivity

Stressor reactivity arises from secondary appraisals of one's coping options and expected efficacy in relation to both stress and pain. Problem avoidance and low belief in one's ability to decrease pain ("pain-decrease" belief) were lower in those with than without headache. Participants who developed headache had higher pain report, pain distress, NA and self-efficacy expectancies than those with no-or-low headache. Higher secondary stress appraisals influenced both neuropsychological and neurophysiological reactivity and may increase allostatic load, since the cumulative effect of stress reactions impedes a return to 'normal' levels.

9.3.3.1 Neuropsychological responses #1: Reduced task self-efficacy

The assimilative-accommodative processing distinction is central to explaining how cognitive processing regulates affective states and thus how self-efficacy can moderate the impact of stressful events on headache. The hallmark of the top-down assimilative style is active persistence – trying harder – in the face of failure. Its style of "tenacious goal pursuit" best suits knowledge-based tasks with clear 'correct' answers and is associated with greater pain sensitivity (606) and migraine headache (609). Its opposite, accommodative processing, is a bottom-up style which permits flexible adaptation to changing task demands (606). Thus, of the reactivity measures, high outcome expectancy was the strongest predictor of headache, possibly because such expectancies set in motion the analytic, assimilative processing style. These participants appear to have set themselves a success goal – and goals are important determinants of behaviour. For example, individuals are more likely to endure a task despite pain to achieve important goals (669). The sharp decline in self-efficacy expectancies mid-way through the task suggests that although these participants' confidence had waned, they could neither modify self-expectations nor 'change tack', e.g. switch to the more flexible accommodative processing style. Lack of adaptation to a stressor is an example of Type 2 allostatic load. The association of high outcome expectancies with conscientiousness – a trait characterised by a desire to do things well and to follow a plan rather than act spontaneously (323) – is consistent with this observation.

9.3.3.2 Neuropsychological responses #2: Pain self-efficacy beliefs

Stress-headache was associated with lowered confidence in being able to reduce pain. Most research has involved belief in being able to control rather than reduce pain, but

although these beliefs are correlated, pain-control belief *per se* was unrelated to headache. Physiologically, perceived pain control influences levels of catecholamines and endogenous opioids which in turn affect pain report (597). Psychologically, a sense of uncontrollability over pain augments perception of pain intensity, demoralisation, and negative emotional reactions to nociceptive stimulation (648). Therefore, doubts about pain control are associated with increased pain, psychological distress and avoidance of painful activities (256; 649). Pain-decrease belief may assist the sufferer because it encourages active pain management, e.g. though relaxation (651). Its reduction may result in avoidance, whereby an adequate response is not turned on in the first place (Type 2 allostatic load) and both avoidance and low pain-decrease belief predicted stress-headache.

9.3.3.3 Neuropsychological responses #3: Pain affects: discouragement, anxiety, irritation

In multiple regression analyses, discouragement, anxiety and irritation – the triumvirate of pain affects (228) – accounted for 90% of the variance in the relationship between stressor reactivity and headache.

From a behaviour selection perspective, nociception, pain and negative moods are viewed on a single continuum of aversion (666). Below-threshold nociception is constant, frequently in the absence of pain perception (666), since even the most common behavioural repertoires require nociception to avoid injury. The function therefore of acute pain and NA is to signal the failure of the nociceptive machinery designed to avoid injury – a signal that aversion has failed or is about to.

Since pain unpleasantness must be considered part of the brain's emotional repertoire, the emotional limbic circuitry, especially the dorsal stratum, is part of the process for transferring nociception into conscious pain. Many of the regions associated with pain processing are also associated with emotions, attention and stress (775-780), so that pain threshold and magnitude can be readily modulated by mood and attention (781), expectations (212) or simple changes in instructions (782).

Once pain is present, its salience draws attention, interferes with other thought processes and imposes a state of negative mood (666). When evoked, pain gives rise to new peripheral and spinal cord nociceptive learning/sensitisation (783; 784) and emotional learning, mediated through descending pathways (785), that is potentiated by the salience and perceived value of the aversive event. The output in turn modulates striatal-cortical loops to control behavioural repertoires (666). As such, once the conscious perception of

pain occurs, the behavioural repertoire following pain is shifted into minimizing injury or retracting away from the environment that has the potential for injury.

Therefore, just as pain motivates the avoidance of further bodily injury and promotes behaviours that enhance healing (666), anxiety can be viewed as an emotional state, sustained by sympathetic arousal that promotes behaviours that diminish anticipated danger within one's immediate physical space. Anxiety (and tension) arise from the subcortical *FEAR* system, an aversive state of worry, fear, uneasiness or apprehension, which accompanies an uncertain, existential threat (166). Anxiety results from being unable to predict, control or obtain desired outcomes (786), and influences pain intensity (229; 787) and sensitivity (Section 1.5.1).

At a peripheral level, anxiety and other NA might provoke headache by instigating adrenal release, changing blood lipid levels, infusing sugar into the blood stream, increasing heart rate, respiration, muscle tension and blood flow through pain-sensitized vessels. At a central level, NA may activate the amygdala, septo-limbic system, PAG and paraventricular hypothalamic nucleus, which in turn activates a series of events in the superior salivatory nucleus (SSN) and trigeminovascular system (111), the substrate of primary headache (97). Any one or combination of these processes may contribute to a headache attack.

Thus, anxiety can trigger headache (788), to the point where reduced anxiety was a stronger predictor of lower headache impact after 6 months than changes in headache frequency or changes in medication (634). Likewise, the myofascial nociceptive input associated with tension may cause pain by reducing neck/shoulder muscle micro-circulation (789), sensitizing myofascial trigger points in the neck and shoulders (790) or activating intrafusal fibres within the muscle spindle that detect stretch (791). In such ways, anxiety and tension can trigger learned behavioural responses which aim to avoid pain and stress but which ultimately evoke headache.

Similarly, in a behaviour selection framework, depression/discouragement can be conceptualized more globally as an abstract cognition of perceived or anticipated danger. that results in withdrawal, self-isolation, reduced physical activity and diminished motivated behaviour (666). These NA arise from deactivation of the subcortical *SEEKING* circuit when circumstances are ambiguous and important goals are thwarted (126). Endogenous opioid production declines (286), as occurs also when self-efficacy is reduced (256), while chronic pain is associated with a reduced capacity to activate central opioid neurotransmission (762). The resulting feelings of sadness, despair, emptiness or loss of interest or pleasure in activities that constitute depression and discouragement may result from an expectancy of failure (288)

or the realization that one can make no progress at all towards a goal (641), but can also be explained as a way of protecting oneself in an adverse environment by reducing one's engagement with it. From this perspective, pain and headache can function to encourage social withdrawal and isolation. This view is supported by the association of depression with headache attacks (274; 733; 792; 793), and the capacity of stress to trigger headache (302; 794). Migraine and depression also have a shared etiology (348). Thus, depression, especially in headache-prone individuals, is likely to increase the frequency of behaviours that constrain one's personal space. Thus, when stress impedes usual top-down control processes, impacting emotional processing capacities and one's general sense of efficacy, the resulting discouragement and headache are likely to increase the likelihood of social withdrawal (285; 795). Furthermore, as pointed out by a number of clinicians, this association can be functional in hostile-dominant interpersonal contexts where active coping is precluded and the 'fold into immobility' associated with headache is potentially protective (167; 426; 749).

Less is known about how anger, or its milder version irritation, may inhibit behaviour, but one explanation may lie in the association of anger with headache (588) and disease outcome generally (796; 797). It is possible for example that the presence of headache may function to limit aggression, as with the 'anger-in' response associated with headache (793), protecting the well-being of the individual or others with whom the individual identifies, even in relation to a perceived wrong (798; 799).

Therefore, just as nociception and pain protect against bodily injury by limiting behaviour, negative moods can function to minimize exposure to danger and promote survival by also inhibiting behaviour (666). It also seems plausible that pain and negative moods which increase pain perception (anxiety, discouragement, irritation), or affective states which influence motivation (sluggishness, tension, confusion) may induce recuperative 'sickness behaviours' until headache subsides.

Anxiously attached individuals may however exaggerate and sustain headache-related NA, over-emphasising their sense of helplessness and vulnerability because signs of weakness and neediness can sometimes elicit attachment figures' attention and care (800). Unlike secure and avoidant people, who tend to view negative emotions as goal-incongruent states that should either be managed effectively or suppressed, anxiously attached individuals attend to internal indicators of distress (801). This includes hypervigilant attention to the physiological aspects of emotional states, heightened recall of threat-related experiences and rumination on real and potential threats (432). In the present study, attachment anxiety but not attachment avoidance was associated with pain,

pain-related distress and headache before and after, but not during mental arithmetic. This finding was attributed in part to the fact that the task itself was attachment-irrelevant (i.e. having no direct implications for one's relationships), and unlike the first and third phases of the experiment, involved no interaction with the experimenter. The stressful task itself may also have functioned to deflect attention away from pain (416). Research using an attachment-relevant stressor is recommended to further determine the relationships between anxious attachment and headache.

However, in the stress-headache (and migraine) participants in this study, NA continued past the end of the task. Persisting NA can exacerbate threat (168), potentially perpetuating headache as well as nausea. NA which is prolonged even after the stressor is over is an example of Type 3 allostatic load.

9.3.3.4 Neuropsychological responses #4: Response conflict

Since stress may only arise when important life goals are threatened (162), positive coping strategies are directed at ensuring that goal achievement is furthered (or at least not blocked). Avoidant coping was a predictor of stress-headache possibly because in this context, regulating one's behaviour through avoidance led to conflicts in goal pursuit (670). Avoidance goals may also create distress, especially when self-regulation is failing (671). Allostatic load is increased because individuals are attempting to control or reverse a perturbation that has already occurred. 'Control' of pain is not possible at this point and will result only in internal struggle (670): one can only learn strategies for decreasing it – such as sensory monitoring (262). Moreover, such reactions themselves, rather than settling the organism back into equilibrium, further perturb it. Thus, the threat-based, experientially avoidant coping strategies of wishful thinking and praying/hoping, pain catastrophising or self-criticism which predicted headache intensity are likely only to intensify headache-related NA (719).

Furthermore, when coactivated with approach motives, especially in the context of high outcome expectancy, the resulting approach-avoidance conflict produces marked vacillation as well as ineffectiveness in goal pursuit (670). This increases NA and triggers the use of self-regulatory resources (668). The end-result could be increased pain sensitivity and headache. These responses may be considered examples of Type 4 allostatic load – inadequate responses that lead to compensatory hyperactivity of other mediators.

Avoidant coping is moderated by personality. Since individuals high in neuroticism tend to magnify risks and anticipate adverse outcomes relative to gains, they are inclined

towards ‘harm avoidance’, the tendency to eschew ‘risky’ decisions in favour of ‘safe’ ones in a risk-taking decision-making situation (344; 802). Low- agreeableness and low-conscientiousness were also related to avoidant coping. Conscientiousness was also inversely related to pain catastrophising, and thus indirectly to headache intensity. Given the aforementioned characteristics of conscientious individuals, the negative association between conscientiousness and avoidant coping, pain catastrophising and stress-headache is unsurprising.

9.3.3.5 Neuropsychological responses #5: Increased threat-based coping

Anxiety was found to mediate the relationship between pain/stress threat-based coping tactics and headache. The threat-based tactics of wishful thinking, pain catastrophising, self-criticism and praying/hoping all predicted headache intensity during the stressful task. Anxiety is thought to disrupt the balance between amygdala-prefrontal circuitry, potentially leading to altered associative, attentional and interpretative processes that sustain a threat-related processing bias in individuals. In a reciprocal relationship, anxiety may strengthen the activation of threat-related representations by augmenting the output from the threat-appraisal processes and so making the selection of threat-related interpretations – and anxiety – more likely (714). At the same time, this imbalance may downregulate prefrontal control mechanisms, increasing the likelihood of response-focused coping and decreasing antecedent-focused coping. Thus, NA downregulation does not occur. In this way, poor coping during stress-headache increases the chances of Type 1 allostatic load (greater number of “hits”).

9.3.3.6 Neurophysiological responses #1: Nausea

Defined as ‘an unpleasant sensation of a protective mechanism elicited by the interaction of inherent factors and changeable psychological states’(803), nausea is considered to function as a protective mechanism, warning the organism to avoid potential toxic ingestion (804). Individuals are proposed to each have a dynamic threshold for nausea, which depends on the interaction of inherent factors (age, gender, race) and more changeable psychological factors – anxiety, expectation, anticipation and adaptation (803). Physiological responses that accompany nausea include an increase in SNS activity, a decrease in PNS activity, an increase of abnormal dysrhythmic gastric activity and an increase in plasma vasopressin. This autonomic outflow during nausea is likely modulated by the central nervous system (CNS). Nausea has been shown to increase headache and scalp tenderness, thus adding to the pain burden (805).

In this study, once the headache began, nausea and NA generally continued to rise, remaining higher in those with than without stress-headache. Both nausea ratings at the end of phase 1 of the experiment, and nausea ratings during the task predicted stress-headache. A reciprocal relationship may thus have existed between nausea, negative affect and headache. The two-way relationship between nausea and headache has been noted before (210; 806). A relationship between nausea and NA is also suggested by functional magnetic imaging (fMRI) research showing that activity in the medial prefrontal cortex and the pregenual anterior cingulate cortex, areas of the brain involved in higher cognitive function and emotion, correlate positively with an increase in heart rate during nausea. In addition, bursts of cardiovagal modulation precede transition to a higher level of nausea, perhaps by prompting interoceptive re-evaluation by the individual which culminates in higher nausea ratings (807). This research suggests the importance of cognitive and emotional centres in modulating the parasympathetic to sympathetic shift associated with nausea (808; 809). Thus, nausea adds to headache via Type 3 allostatic load – prolonged response.

9.3.3.7 Neurophysiological response #2: Cortisol levels

Cortisol levels differentiated between those with and without stress-headache, being particularly low in afternoon-tested stress-headache participants. Glucocorticoids are critical for energy mobilization and distribution in multiple organ systems and are needed to assure energy availability even in the absence of stress. There is also a marked diurnal rhythm of HPA axis activation, with peak levels corresponding to the waking phase (810). Diurnal glucocorticoids may play an important part in regulating energy homeostasis during daily activities (811).

Stress responses may be considered a 'special case' of HPA axis drive, boosting energy when it is needed for adaptive responses (812). Higher levels of glucocorticoids activate the glucocorticoid receptor (GR) which is thought to mediate glucocorticoid effects on mobilization of energy stores (liver, fat and muscle), inflammation and neural function (among others) (813). Given that stress levels of glucocorticoids are read primarily by the GR, this receptor is generally assumed to subserve the bulk of feedback regulation (814). Since inappropriate or prolonged HPA axis activation is energetically costly and linked with numerous physiological and psychological disease states (812), proper control of the stress response is of critical importance. The fact that cortisol secretions in the afternoon-tested stress-headache group declined from relatively low levels at entry to extremely low levels at the conclusion of the experiment suggests not only the unavailability of energy reserves for these individuals, but deficient control of the

stress response (812). Since appropriate levels of gluco-corticoids have anti-inflammatory and anti-nociceptive effects, headache may result from glucocorticoid withdrawal and reduced HPA activation when acute stress ends (282). Hypocortisolism can be viewed as Type 4 allostatic load, characterised as a lack of normal response of a generally hypoactive system – which occurs also in fibromyalgia and other chronic pain syndromes (214). Low HPA axis responsiveness may result in increased activity of other systems, such as the immune system, with corresponding implications for health (214; 815).

9.3.3.8 Neurophysiological responses #3: Nociceptive blink reflexes

Under normal circumstances, habituation – reduced responsiveness to repetitive stimuli – occurs as part of the homeostatic counter-response to a stressor (555). Since incapacity to progressively reduce pain-related responses to repetitive stimuli may favour mechanisms of central sensitisation (111), habituation deficiency is considered a functional hallmark of the migrainous brain between attacks (558). In nociceptive blink reflex (nBR) studies, longer recovery times (566), longer R2 latencies (816) and greater R2 area-under-the-curve measures (817) are reported in migraineurs.

In those with stress-headache, longer R2 latencies to the 30s ISI shocks, particularly during the latter half of the stressful task were observed. These were considered to indicate reduced trigeminal excitability during the task, indicating the operation of inhibitory controls. R2 area-under-the-curve (a measure of global nociceptive activity) was also greater, especially post-task, suggesting increased activation (a reduced threshold) in this group. That these participants also reported greater pain and pain distress before the task suggests an imbalance in excitatory (e.g. arousal) and inhibitory responses to this stressor, with resultant weaker inhibition of nociceptive input to the synapse (566). This may be considered an example of Type 2 allostatic load – lack of adaptation to a stressor.

In combination, these psychophysiological responses increased allostatic load, and thus stress headache. In sum, during stress, both limbs of the stress response – NA and physiological arousal – may, by different mechanisms, disrupt inhibitory pain control. The sum of multiple aspects of pain processing can increase headache intensity by exacerbating the affective response to pain, possibly altering functional connectivity between cortico-thalamic pain modulating circuitry (246), the periaqueductal gray (247), amygdala and visceroceptive cortex (248).

9.4 Study findings 2: Allostatic responses in low/no headache

Figure 9.2 shows the sequence of events by which allostatic responses are turned off without contributing to allostatic load. Low subjective threat/stress appraisals are associated with low levels of discouragement and tension (positive affect was not assessed in this study). Modest outcome expectancies ensure that task self-efficacy remains stable, precluding the adoption of 'learned helplessness' behaviours in favour of a flexible 'accommodative processing' style which permits ready adaptation to changing task demands. The individual maintains belief in their ability to reduce pain. This combination of effects reduces the likelihood of response conflict from the coactivation of approach and avoidance motives, thereby avoiding vacillation, distress and the triggering of regulatory resources. This in turn means lower levels of anxiety, irritation and discouragement.

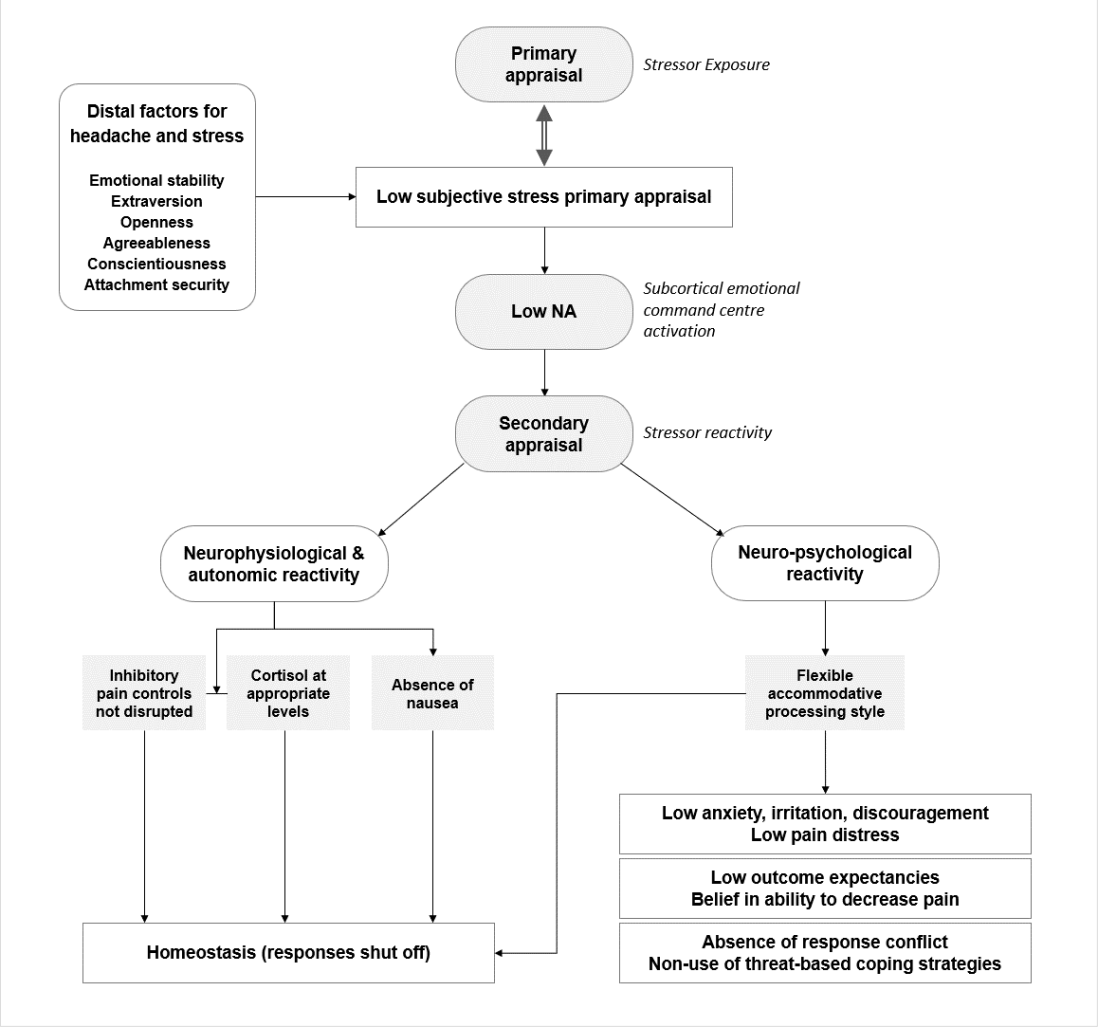


Figure 9.2 Pathways to homeostasis in those who did not develop a headache during the stressful task

Reduced anxiety also means less use of the threat-based coping tactics of wishful thinking, self-criticism, pain catastrophising and praying/hoping which would otherwise further increase threat and impede the use of volitional cognitive control coping methods. This combination of responses reduces the affective response to pain, possibly by maintaining balance in amygdala-prefrontal circuitry, i.e. downregulating amygdaloid hyperactivation and upregulating prefrontal control mechanisms, further increasing the individual's perceived control. At the neurophysiological level, low levels of nausea, adequate cortisol response and low trigeminal activation help reduce the pain distress which otherwise has capacity to disrupt inhibitory controls, potentially inducing head pain. The nett effect is that homeostatic balance is restored and any headache quickly dissipates.

9.5 Study findings 3: Allostatic load in episodic migraine, T-TH & controls

The cephalic response of migraine is regarded as pre-emptive rather than reactive (200). Initial sensory information in one area of the body (e.g. nausea, high NA) operates as an early signal of an event that could potentially perturb a perhaps critical variable elsewhere in the body. Corrective effectors are activated, i.e. occur pre-emptively before the criterion value is perturbed. This is evident perhaps in the increased irritability and tension characteristic of the migraine prodrome. However, post-attack, these responses do not readily shut off, terminating only through sleep or emesis (596). For such reasons, migraine has been described as an example of allostatic load (192). As many of the T-TH participants were at the lower end of the migraine spectrum (so-called 'probable migraine'), additional exploratory comparisons between migraineurs and controls were performed to better identify migraine-specific factors (see Supplementary Table 9.2, page 243). Table 9.1 outlines the psychophysiological responses in episodic migraine and T-TH participants in this study compared with controls as these may pertain to types of allostatic load.

Table 9.1 Variables associated with allostatic load in episodic migraine, T-TH and controls

Variable	Comparative psychophysiological responses in migraine, T-TH and controls	Type of allostatic load for migraine group
Primary appraisal	Greater threat appraisals in migraine than T-TH associated with discouragement, confusion, sluggishness and tension	Type 1
Affects	Migraineurs show slower post-task declines in tension, confusion and irritation than controls #	Type 3
Pain report before task	Similar in all three groups	–
Pain distress before task	Similar in all three groups	–
Outcome expectancy	Lower in migraine than controls #	–
Self-efficacy changes	Lower in migraine than controls #	–

Variable	Comparative psychophysiological responses in migraine, T-TH and controls	Type of allostatic load for migraine group
Pain-control belief	Similar in all three groups	–
Pain decrease belief	Lower in migraine than T-TH	Possible Type 2
Pain coping strategies	Similar in all three groups	–
Stress coping strategies *(problem engagement, emotion management, avoidant)*	Similar in all three groups	–
Nausea	Similar in all three groups	–
Cortisol	Similar in all three groups	–
Blood pressure & pulse rate	Similar in all three groups	–
Temporal pulse amplitude	Higher in controls than headache sufferers	–
Number of R2 reflex blinks	Similar in all three groups	–
R2 latencies	Longer in migraine than T-TH in phase 1, shorter in phase 2 and phase 3, longer than T-TH at end of experiment	Type 3
R2 Area-under-the-curve	Greater post-task AUC in migraine than T-TH (i.e. reduced threshold)	Type 3

See also Supplementary Table 9.2, page 243

Rather than a subjective stress appraisal, migraineurs were more likely than T-TH or controls to make a 'threat' appraisal – "this might hurt me" – which was associated with discouragement, confusion, sluggishness and tension. In controls, NA increased rapidly during the stressful task but subsided quickly whereas, in migraineurs, NA increased as the task progressed and persisted at high levels. Nausea also was greater and more sustained in migraineurs than T-TH. Self-efficacy ratings were higher in controls than migraineurs, perhaps because such individuals are generally less sensitive to pain and less reactive to stressful events than migraineurs (28).

This table illustrates however that relatively few indices distinguished migraine from T-TH or controls in this experiment. Only 40% of migraineurs reached a 'critical point' in which allostatic load led to stress-headache, despite their increased vulnerability via greater threat appraisals, higher and more prolonged NA and higher post-task R2 AUC (indicating greater post-task excitability). Thus, other effects apparently were able to offset or counteract this vulnerability. One such effect is lower outcome expectancy, which predisposed towards the use of an accommodative processing approach, and reduced NA. However, the extent to which attentional processes may underlie this information processing style was not assessed in this study, and these have been identified as a source of vulnerability (albeit a remediable one) in migraineurs (729).

T-TH also showed evidence of being more stress-sensitive than migraineurs, as for example when post-task cortisol levels increased in T-TH to the 'stress associated' level, while remaining in the 'normal' range in migraineurs. In blink reflex measures, T-TH

showed greater blink reflex excitability as evidenced by reduced latencies during and following the task, but smaller post-task R2 area-under-the-curve, suggesting faster recovery from painful stimuli. This may be linked to the greater belief in T-TH sufferers of a capacity to reduce pain. Further research can help determine the relative role of these and other variables in reducing allostatic load in headache sufferers.

9.6 Clinical implications

Ultimately, consistent with Lazarus' theory of stress and the emotions (160), stress relates to headache through emotion-eliciting appraisals which are inherently relational, i.e. they reflect an evaluation of what the stimulus circumstances imply for the person's future well-being in relation to that person's specific configuration of needs, goals, resources, abilities and predispositions. Appraisals, coping and thus headache are influenced by personality traits, attachment anxiety and context. For example, migraine is more prevalent in those raised in hostile, invalidating or abusive environments (751-753), where active coping is precluded, the sufferer is frequently in a 'malignant emotional bind' (426) and submission and self-criticism are tools of survival (748). Neuroticism and agreeableness may exacerbate these conflicts. Short-term, these responses may assist in bodily regulation (167) because the dorsal-vagal branch of the parasympathetic nervous system is activated, bodily systems shut down, metabolic demands decrease and the pain threshold increases (148). The 'fold into helplessness' accompanying a migraine attack may itself be a protective reflex (426; 749). However, long term, such learned helplessness responses may increase the level of allostatic load and dysregulation to the point where some individuals transition to chronic daily headache (818).

Psychosocial interventions for headache thus include cognitive techniques such as CBT or ACT to enable modification of stress/threat appraisal processes. Individuals are taught through hypnosis or mindfulness training to enter the state of flow (819) which is antithetical to stress. Behavioural interventions could include teaching active coping skills and appropriate assertiveness, including their application in interpersonal situations where the sufferer is being dominated or put-down (167). Skills in distress tolerance (756) and the 'metacognition of attention' (730) could further assist sufferers to increase their ability to self-soothe during stressful situations, to monitor their attentional performance and to develop selective attending skills which would enable the dissociation and active redirection of sensory and emotional aspects of noxious stimuli.

9.7 Strengths and limitations of this study

This study is one of a very few which examines each component of the stress process as it relates to experimentally-provoked headache. It also is one of few which investigates interactions between provoked headache and stress appraisal processes, headache-related NA, expectancies, reappraisal, and autonomic/physiological (nausea, cardiovascular, cortisol) responses during an unpredictable and uncontrollable 'daily hassles' simulation in episodic migraine, T-TH and controls. Attachment status and Five Factor Model personality traits were also examined in relation to headache.

Findings were consistent with our biopsychosocial model of headache but should be interpreted cautiously. To minimize the type 1 error rate, significant multivariate effects were investigated in univariate analyses incorporating planned contrasts between groups and across time, followed by contrasts between groups at each time point to clarify significant main effects and interactions. However, as this approach resulted in a large number of statistical tests, our findings require replication. The small sample sizes represent a significant limitation which has already been discussed (section 3.5, page 65, *Study Limitations*). In addition, bias induced by the choice of stressor and the use primarily of a university student sample may lessen the generalizability of our results to clinical populations or chronic headache sufferers. Since the task itself increased NA, our paradigm did not permit definitive conclusions about the impact of headache on NA. Further, we did not collect reports of positive affect, so our assessment of stress – the collapse of positive emotions (45) – did not capture this dimension. Since positive emotions hasten return to homeostasis, they could reduce headache and autonomic arousal. Future research should assess these possibilities. Our groups were matched for age, gender and education, but headache frequency and duration were greater in the migraine than the T-TH group. Whether these variables influence responses to stress independently of headache diagnosis requires further study.

Other limitations of this study were that depression and anxiety were controlled for only through participant selection, with reliance on patient self-disclosure rather than psychometric testing for depression/anxiety. It is possible therefore that our sample included individuals with undiagnosed mood disorders. Furthermore, migraine with and without aura were grouped together, nor were separate computations made for gender.

9.8 Directions for future research

Many areas for future research can be identified, the results of which would have extended the findings of this study. These include:

1. *The influence of positive emotions on headache.* The present study examined only the relationship of NA and headache. Since stress involves the collapse of positive and negative emotions (45), and the pre-eminence of the limbic system in the pain response (666), examining how positive emotions and humour may reduce pain and hasten the return to homeostasis could be of clinical value.
2. *The moderating role of personality traits on physiological stress responses.* Previous research has identified a relationship between various personality traits, cardiovascular and cortisol responses during stress (418). This could extend the findings of the present study as to how personality moderates the aspects of the stress process which result in headache.
3. *Attachment anxiety processes in headache.* The present study used only an attachment-irrelevant stressor. Use of an attachment-relevant stressor within a social context which was both supportive and non-supportive could help determine the relationship of context to headache. In addition, the relationship of headache to processes associated with anxious-attachment, such as exaggerated threat appraisals, beliefs about one's ability to handle distress and attributions of threat-related events to uncontrollable causes or global personal inadequacies (432) could be ascertained.
4. *Headache coping.* The present study examined only threat-based coping in headache. Additional measures tapping the relationship to headache of the drive and particularly the self-soothing domains (167) would be of clinical value.
5. In assessing the disruption to cognitive processing of affective information during stress, the present study explored the relationship of headache to NA, outcome expectancy and manipulated changes in task self-efficacy during stress. Research designs which systematically manipulate these variables and the use of analytic rather than accommodative processing styles could further assess their relationship to headache.
6. The present study inferred that response conflict of an approach-avoidance nature may lie behind the adoption of specific threat-based coping strategies. Further research which also used avoidance-avoidance and approach-approach response conflict could clarify and extend these findings.

7. The mediating roles of NA in the relationship between primary and secondary appraisals and headache were explored in this study. However, the mediating roles of pain beliefs and perceived stressor-controllability may also be significant in appraisal and coping processes in headache and could be investigated further.
8. Effective pain management methods require the development of attentional capacities which may be compromised in migraineurs (729), but which may be developed by skills-based programs in the "meta-cognition of attention" (730). Assessment of the efficacy of such programs in helping migraineurs cope with the pain component of headache would be of clinical value.
9. An analysis of the key 'decision points' relating to headache coping in terms of their failure to regulate or to mis-regulate headache-related NA in different contexts and particularly with different regulatory goals (171) would clarify how and when specific headache coping methods may be effective or otherwise.

9.9 Conclusions

In sum, the present findings suggest that headache results when stressor-induced psychological and neurophysiological responses increase allostatic load past a critical point. Anxiety, discouragement, tension and irritation mediated the relationship between primary and secondary stress appraisals, coping and headache intensity during the stressful task. Behavioural coping responses, especially those related to learned helplessness, may increase allostatic load. FFM personality traits and attachment anxiety influenced headache intensity by moderating negative moods.

Learning to modify stress and threat appraisals, revise unrealistically high self-expectations, dissociate sensory and affective aspects of pain and adopt coping styles which accept rather than struggle against pain may reduce vulnerability to stress-induced headache.

Supplementary data

Table 9.2 Analyses of variance, migraine v controls: means and standard errors, significant effects (see also Table 9.1, page 237)

	Migraine		Controls	
	Mean	**SE**	**Mean**	**SE**
Tension across task	2.71	0.207	2.85	0.286
Confusion across task	3.391	0.324	3.795	0.446
Irritation (set 3)	3.676	0.402	2.845	0.554
Outcome expectancy	2.54	0.235	3.42	0.324
Task self-efficacy (changes across task)	2.836	0.232	3.871	0.320
	F	**df**	**p**	**η^2**
Tension	3.028	(2.2, 123)[G]	0.047	0.051
Confusion	2.922	(2.5, 139)[G]	0.046	0.050
Irritation (set 3)	5.416	(1, 56)	0.024	0.088
Outcome expectancy	5.18	(1, 56)	0.027	0.085
Task self-efficacy (changes across task)	6.835	(1,56)	0.011	0.109

[G] = Greenhouse Geisser correction

References

1. Drummond P, Passchier J. 2006. Psychological mechanisms in migraine, pp. 385-392. In *The Headaches (3rd Edition)*, ed. J Olesen, P Goadsby, N Ramadan, P Tfelt Hansen, K Welch. Philadelphia: Lippincott Williams & Wilkins.
2. Gerber W, Kropp P, Schoenen J. 1996. Born to be wild oder doch gelern? Neue verhaltensmedizinische Erkenntnisse zur Athopathogenese der Migrane [Born to be wild or learned behaviour? New data from behavioural medicine on the etiopathogenesis of migraine]. *Verhaltenstherapie* 6:210-20
3. Aurora S, Kulthia A, Barrodale P. 2011. Mechanism of chronic migraine. *Curr Pain Headache Rep.* 15:57-63
4. de Tommaso M, Ambrosini A, Brighina F, Coppola G, Perrotta A, et al. 2014. Altered processing of sensory stimuli in patients with migraine. *Nat Rev Neurol* 10:144–55
5. Lipton R, Stewart W, Diamond S, Diamond M, Reed M. 2001. Prevalence and burden of migraine in the United States: Data from the American Migraine Study II. *Headache* 41:646-57
6. Stovner L, Hagen K, Jensen R, Katsarava Z, Lipton RB, et al. 2007. The global burden of headache: A documentation of headache prevalence and disability worldwide. *Cephalalgia* 27:193-210
7. Headache Classification Committee of the International Headache S. 2013. The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia* 33:629-808
8. Cuvellier JC. 2019. Pediatric vs. Adult Prodrome and Postdrome: A Window on Migraine Pathophysiology? *Front Neurol* 10:199
9. Dodick DW. 2018. A Phase-by-Phase Review of Migraine Pathophysiology. *Headache* 58 Suppl 1:4-16
10. Goadsby P, Lipton R, Ferrari M. 2002. Migraine - current understanding and treatment. *N Engl J Med* 346:257-70
11. Dorn LD, Burgess ES, Friedman TC, Dubbert B, Gold PW, Chrousos GP. 1997. The longitudinal course of psychopathology in Cushing's syndrome after correction of hypercortisolism. *J Clin Endocrinol Metab* 82:912-9
12. Rasmussen B, Jensen R, Schroll M, Olesen J. 1991. Epidemiology of headache in a general population - a prevalence study. *J Clin Epidemiol* 44:1147-57
13. Blau J. 1990. Common headaches: Type, duration, frequency and implications. *Headache* 30:701-4

14. Martin PR, Lae L, Reece J. 2007. Stress as a trigger for headaches: Relationship between exposure and sensitivity. *Anxiety, Stress Coping* 20:393-407

15. Martin PR, MacLeod C. 2009. Behavioral management of headache triggers: Avoidance of triggers is an inadequate strategy. *Clin Psychol Rev* 29:483-95

16. Robbins L. 1994. Precipitating factors in migraine: A retrospective review of 494 patients. *Headache* 34:214-6

17. Schoonman G, Evers D, Ballieux B, Geus E, de Kloet E, et al. 2007. Is stress a trigger factor for migraine? *Psychoneuroendocrinology* 32:532-8

18. Bank J, Marton S. 2000. Hungarian migraine epidemiology. *Headache* 40:164-9

19. Fukui PT, Goncalves TR, Strabelli CG, Lucchino NM, Matos FC, et al. 2008. Trigger factors in migraine patients. *Arq Neuropsiquiatr* 66:494-9

20. Osterhaus S, Passchier J. 1992. The optimal length of headache recording in juvenile migraine patients. *Cephalalgia* 12:297-9

21. Al-Shimmery E. 2010. Precipitating and Relieving Factors of Migraine Headache in 200 Iraqi Kurdish Patients. *Oman Med J.* 25:212–7

22. Tunis MM, Wolff HG. 1953. Studies on headache: Long-term observations of the reactivity of the cranial arteries in subjects with vascular headache of the migraine type. *AMA Arch Neurol Psychiatry* 70:551-7

23. Feuerstein M, Bortolussi L, Houle M, Labbe E. 1983. Stress, temporal artery activity, and pain in migraine headache: A prospective analysis. *Headache* 23:296-304

24. Kohler T, Haimerl C. 1990. Daily stress as a trigger of migraine attacks: results of thirteen single-subject studies. *J Consult Clin Psychol* 58:870-2

25. Mosley T, Penzien D, Johnson C, Brantley P, Wittrock D, Andrew, ME, Payne T. 1991. Time series analysis of stress and headache. *Cephalalgia* 11:306-7

26. Henryk-Gutt R, Rees W. 1973. Psychological aspects of migraine. *J Psychosom Res* 17:141-53

27. Houtveen JH, Sorbi MJ. 2013. Prodromal functioning of migraine patients relative to their interictal state--an ecological momentary assessment study. *PLoS One* 8:e72827

28. Cathcart S, Petkov J, Winefield AH, Lushington K, Rolan P. 2010. Central mechanisms of stress-induced headache. *Cephalalgia* 30:285-95

29. Martin P, Nathan P, Milech D, Van Keppel M. 1988. The relationship between headaches and mood. *Behav Res Ther* 26:353-6

30. Martin PR, Theunissen C. 1993. The role of life event stress, coping and social support in chronic headaches. *Headache* 33:301-6

31. Schramm S, Moebus S, Lehmann N, Galli U, Obermann M, et al. 2015. The association between stress and headache: A longitudinal population-based study. *Cephalalgia* 35:853-63

32. Spierings EL, Sorbi M, Maassen GH, Honkoop PC. 1997. Psychophysical precedents of migraine in relation to the time of onset of the headache: the migraine time line. *Headache* 37:217-20

33. Stronks DL, Tulen JH, Verheij R, Boomsma F, Fekkes D, et al. 1998. Serotonergic, catecholaminergic, and cardiovascular reactions to mental stress in female migraine patients. A controlled study. *Headache* 38:270-80

34. Schoenen J. 1996. Deficient habituation of evoked cortical potentials in migraine: a link between brain biology, behavior and trigeminovascular activation? *Biomed Pharmacother* 50:71-8

35. Schoenen J, Ambrosini A, Sandor P, De Noordhout A. 2003. Evoked potentials and transcranial magnetic stimulation in migraine: published data and viewpoint of their pathophysiologic significance. *Clin Neurophysiol* 114:955-72

36. Main A, Vlakonikolis I, Dowson A. 2000. The wavelength of light causing photophobia in migraine and tension-type headache between attacks. *Headache* 40:194-9

37. Vijayan N, Gould S, Watson C. 1980. Exposure to sun and precipitation of migraine. *Headache* 20:42-3

38. Bjork M, Stovner LJ, Hagen K, Sand T. 2011. What initiates a migraine attack? Conclusions from four longitudinal studies of quantitative EEG and steady-state visual-evoked potentials in migraineurs. *Acta Neurologica Scandinavica. Supplementum*:56-63

39. Katsavara Z, Giffin N, Diener H, Kaube H. 2003. Abnormal habituation of 'nociceptive' blink reflex in migraine - evidence for increased excitability of trigeminal nociception. *Cephalalgia* 23:814 - 9

40. Di Clemente L, Coppola G, Magis D, Fumal A, De Pasqua V, et al. 2007. Interictal habituation deficit of the nociceptive blink reflex: an endophenotypic marker for presymptomatic migraine? *Brain* 130:765-70

41. Kaube H, Katasavara Z, Przywara S, Drepper J, Ellrich J, Diener H. 2002. Acute migraine headache. Possible sensitization of neurons in the spinal trigeminal nucleus? *Neurology* 58:1234-8

42. Welch K, D'Andrea T, Barkley G, Ramadan M. 1990. The concept of migraine as a state of central neuronal hyper-excitability. *Neurol Clinics* 8:817-28

43. Levy D, Strassman AM, Burstein R. 2009. A critical view on the role of migraine triggers in the genesis of migraine pain. *Headache* 49:953-7

44. Steptoe A. 1997. Stress and disease. In *Cambridge Handbook of Psychology, Health and Medicine (pp 174-177)* ed. A. Baum, S. Newman, J. Weinman, R. West, C McManus. Cambridge, U.K.: Cambridge University Press.

45. Zautra A. 2003. *Emotions, stress and health*. Oxford: Oxford University Press.

46. Vingerhoets A. 2004. Stress (Chapter 5, pp. 113-140). In *Health Psychology*, ed. A Kaptein, J Weinman. Oxford: Blackwell.

47. Breslau N, Rasmussen BK. 2001. The impact of migraine: Epidemiology, risk factors, and co-morbidities. *Neurology* 56:S4-12

48. Koopmans G, Lamers L. 2000. Chronic conditions, psychological distress and the use of psychoactive medications. *J Psychosom Res*:115-23

49. Holroyd K. 2004. Recurrent Headache Disorders. In *Psychosocial Aspects of Pain: A Handbook for Health Care Providers*, ed. R Dworkin, W Breitbart, 27. Seattle, WA: IASP Press.

50. Martelletti P, Birbeck GL, Katsarava Z, Jensen RH, Stovner LJ, Steiner TJ. 2013. The Global Burden of Disease survey 2010, Lifting The Burden and thinking outside-the-box on headache disorders. *J Headache Pain* 14:13

51. Hemper K. 2008. *Headache in Adolescents: Prevention and Complementary Therapies*. http://www.medscape.com/viewprogram/17068?src=rss

52. Ferrari M. 2008. Migraine Genetics: A Fascinating Journey Towards Improved Migraine Therapy. *Headache* 48:697-700

53. Rains J, Penzien D, McCrory D, Gray R. 2005. Behavioral headache treatment: history, review of the empirical literature, and methodological critique. *Headache* 45 Suppl 2:S92-109

54. Lee HJ, Lee JH, Cho EY, Kim SM, Yoon S. 2019. Efficacy of psychological treatment for headache disorder: A systematic review and meta-analysis. *J Headache Pain* 20

55. Andrasik F, Grazzi L, Sansone E, D'Amico D, Raggi A, Grignani E. 2018. Non-pharmacological Approaches for Headaches in Young Age: An Updated Review. *Front Neurol* 9:1009

56. Charles AC, Flippen C, al e. 2007. Memantine for prevention of migraine: a retrospective study of 60 cases *J Headache Pain* 8:248-50

57. Chopra R, Robert T, al e. 2012. Non-pharmacological and pharmacological prevention of episodic migraine and chronic daily headache. *West Virginia Med J* 108:88-91

58. Raggi A, Grignani E, Leonardi M, Andrasik F, Sansone E, et al. 2018. Behavioral Approaches for Primary Headaches: Recent Advances. *Headache* 58:913-25

59. Lovallo W. 2005. *Stress & Health: Biological and psychological interactions, 2nd ed* Thousand Oaks, California: Sage Publications.

60. McEwen BS. 1998. Stress, adaptation, and disease. Allostasis and allostatic load. *Ann N Y Acad Sci* 840:33-44

61. Onder H, Hamamci M, Alpua M, Ulusoy EK. 2019. Comorbid fibromyalgia in migraine patients: clinical significance and impact on daily life. *Neurol Res*

62. Dubin AE, Patapoutian A. 2010. Nociceptors: the sensors of the pain pathway. *J Clin Invest* 120:3760-72

63. Koslowska K. 2009. Attachment relationships shape pain-signaling behaviour. *J Pain* 10:1020-8

64. Chapman C. 2005. Psychological Aspects of Pain: A Consciousness Studies Perspective. In *The Neurological Basis of Pain*, ed. M Pappagallo: McGraw-Hill.

65. Melzack R. 1999. From the gate to the neuromatrix. *Pain* Suppl 6:6

66. Van Hees J, Gybels J. 1981. C nociceptor activity in human nerve during painful and nonpainful skin stimulation. *J Neurol, Neurosurg Psychiat* 44:600-7

67. Adriaensen H, Gybels J, Handwerker H, Van Hees J. 1984. Nociceptor discharges and sensations dur to prolonged noxious mechanical stimulation: A paradox. *Hum Neurobiol* 3:53-8

68. Cervero F, Gilbert R, Hammond R, Tanner J. 1993. Development of secondary hyperalgesia following non-painful thermal stimulation of the skin: A psychophysical study in man. *Pain* 54:181-9

69. Nakamura Y, Chapman C. 2002. Measuring pain: An introspective look at introspection. *Conscious Cogn.* 11:582-92

70. Lacroix-Fralish ML, Mogil JS. 2009. Progress in genetic studies of pain and analgesia. *Annu Rev Pharmacol Toxicol* 49:97-121

71. Foulkes T, Wood JN. 2008. Pain genes. *PLoS Genet* 4:e1000086

72. Liu-Chen L-Y, Han D, Moskowitz M. 1983. Pia arachnoid contains substance P originating from trigeminal neurons. *Neuroscience* 9:803-8

73. Edvinsson L, McCulloch J, Uddman R. 1981. Substance P: immunohistochemical localization and effect upon cat pial arteries in vitro and in situ. *J. Physiol. (Land.)* 318:251-8

74. Uddman R, Edvinsson L, Hara H. 1989. Axonal tracing of autonomic nerve fibers to the superficial temporal artery in the rat. *Cell Tissue Res.* 256:559-65

75. Ulrich-Lai Y, Flores C, Harding-Rose C, Goodis H, Hargreaves K. 2001. Capsaicin-evoked release of immunoreactive calcitonin gene-related peptide from rat trigeminal ganglion: Evidence for intraganglionic neurotransmission. *Pain* 91:219-26

76. Moskowitz M, Macfarlane R. 1993. Neurovascular and molecular mechanisms in migraine headaches. *Cerebrovasc Brain Metab Rev* 5:159-77

77. Drummond PD. 1982. Extracranial and cardiovascular reactivity in migrainous subjects. *J Psychosom Res* 26:317-31

78. Olesen J. 1991. Clinical and pathophysiological observations in migraine and tension-type headache explained by integration of vascular, supraspinal and myofascial inputs. *Pain* 46:125-32

79. Blake P, Burstein R. 2019. Emerging evidence of occipital nerve compression in unremitting head and neck pain. *J Headache Pain* 20

80. Messlinger K, Dostrovsky J, Strassman A. 2006. Anatomy and physiology of head pain. In *The Headaches, 3rd edn*, ed. J Olesen, P Goadsby, N Ramadan, P Tfelt-Hansen, W KMA:95–109. Philadelphia: Lippincott Williams & Wilkins.

81. Mendell L. 1966. Physiological properties of unmyelinated fiber projection to the spinal cord. *Exp Neurol.* 16:316–32

82. Tommerdahl M, Delemos K, Favorov O, Metz C, Vierck C, Jr., Whitsel B. 1998. Response of anterior parietal cortex to different modes of same- site skin stimulation. *J Neurophysiol* 80:3272–83

83. Selby G, Lance J. 1960. Observations on 500 cases of migraine and allied vascular headache. *J Neurol Neurosurg Psychiatry* 23:23 - 32

84. Hoheisel U, Mense S. 1989. Long-term changes in discharge behaviour of cat dorsral horn neurones following noxious stimulation of deep tissues. *Pain* 36:239-47

85. Dubner R. 1991. Basic mechanisms of pain associated with deep tissues. *Can J Physiol Pharmacol* 69:607-9

86. Dubner R. 1992. Hyperalgesia and expanded receptive fields. *Pain* 48:3-4

87. Strassman A, Raymond S, Burstein R. 1996. Sensitization of meningeal sensory neurons and the origin of headaches. *Nature* 384:560 - 4

88. Burstein R, Yamamura H, Malick A, Strassman A. 1998. Chemical stimulation of the intracranial dura induces enhanced responses to facial stimulation in brain stem trigeminal neurons. *J Neurophysiol* 79:964-82

89. Woolf CJ. 1996. Windup and central sensitization are not equivalent [editorial]. *Pain* 66:105-8

90. Wadiche JI, Amara SG, Kavanaugh MP. 1995. Ion fluxes associated with excitatory amino acid transport. *Neuron* 15:721–8

91. Kawamoto K, Matsuda H. 2004. Nerve growth factor and wound healing. In *Progress in Brain Research*, ed. A Luigi, C Laura, Volume 146:369-84: Elsevier.

92. Doubell T, Mannion R, Woolf C. 1999. The dorsal horn: State-dependent sensory processing, plasticity and the generation of pain. In *Textbook of Pain (4th ed)*, ed. P Wall, R Melzack:165-81. NY: Churchill Livingstone.

93. Nieus T, Sola E, Mapelli J, Saftenku E, Rossi P, D'Angelo E. 2006. LTP Regulates Burst Initiation and Frequency at Mossy Fiber–Granule Cell Synapses of Rat Cerebellum: Experimental Observations and Theoretical Predictions. *J Neurophysiol* 95:686-99

94. Drummond P, Knudsen L. 2011. Central pain modulation and scalp tenderness in frequent episodic Tension-Type Headache. *Headache* 51:375-83

95. Klein J, Tendi E, Dib-Hajj S, Fields R, Waxman S. 2003. Patterned Electrical Activity Modulates Sodium Channel Expression in Sensory Neurons. *J Neurosci Res* 74:192–8

96. Waxman S, Dib-Hajj S, Cummins T, Black J. 2000. Sodium channels and their genes: dynamic expression in the normal nervous system, dysregulation in disease states (1). *Brain Res Rev* 886:5–14

97. Goadsby P. 2005. Migraine Pathophysiology. *Headache* 45:S14-S24

98. Damasio A. 2000. *The feeling of what happens : body and emotion in the making of consciousness*. NY: Harcourt.

99. Jassar H, Nascimento TD, Kaciroti N, DosSantos MF, Danciu T, et al. 2019. Impact of chronic migraine attacks and their severity on the endogenous μ-opioid neurotransmission in the limbic system. *NeuroImage: Clinical* 23

100. Angus-Leppan H, Lambert G, Michalicek J. 1997. Convergence of occipital nerve and superior sagittal sinus input in the cervical spinal cord of the cat. *Cephalalgia* 17:625-30

101. Edmeads J. 1988. The cervical spine and headache. *Neurology* 38:1874–8

102. Goadsby P, Knight YE, Hoskin KL. 1997. Stimulation of the greater occipital nerve increases metabolic activity in the trigeminal nucleus caudalis and cervical dorsal horn of the cat. *Pain* 73:23-8

103. Turkdogan D, Cagirici S, Soylemez D, Sur H, Bilge C, Turk U. 2006. Characteristic and overlapping features of migraine and tension-type headache. *Headache* 46:461-8

104. Goadsby P, Lipton R, Ferrari M. 2002. Migraine: current understanding and management. *N Engl J Med* 346:257-70

105. Cao Y, Aurora S, Vikingstad EM, Patel SC, Welch KMA. 1999. Functional MRI of the red nucleus and occipital cortex during visual stimulation of subjects with migraine. *Cephalalgia* 19:462-3

106. Raskin N, Hosobuschi Y, Lamb S. 1987. Headache may arise from perturbation of the brain. *Headache* 27:416-20

107. Burstein R, Yarnitsky D, Good-Aryeh I, Ransil B, Bajwa Z. 2000. An association between migraine and cutaneous allodynia. *Ann Neurol* 47:614-24

108. Knight Y, Bartsch T, Kaube H, Goadsby P. 2002. P/Q-type calcium channel blockade in the periaqueductal gray facilitates trigeminal nociception: A functional genetic link for migraine? *J Neurosci* 22:RC213

109. Knight Y, Goadsby P. 2001. The periaqueductal gray matter modulates trigeminovascular input: A role in migraine? *Neuroscience* 106:793-800

110. Snell R. 2010. *Clinical Neuroanatomy for Medical Students, 7th Ed* Lippincott Williams & Wilkins.

111. Burstein R, Jakubowski M. 2005. Unitary hypothesis for multiple triggers of the pain and strain of migraine. *J Compar Neurology* 493:9-14

112. Suzuki R, Morcuende S, Webber M, Hunt S, Dickenson A. 2002. Superficial NK1-expressing neurons control spinal excitability through activation of descending pathways. *Nat Neurosci* 5:1319–26

113. Kerr F, Olafson R. 1961. Trigeminal and cervical volleys. *Arch Neurol* 5:69-76

114. Fields H. 2000. Pain modulation: Expectation, opioid analgesia, and virtual pain. *Prog Brain Res* 122:245-53

115. Porreca F, Ossipov M, Gebhart G. 2002. Chronic pain and medullary descending facilitation. *Trends Neurosci* 25:319-25

116. Fields H, Basbaum A. 1999. Central nervous system mechanisms of pain modulation. In *Textbook of pain*, ed. P Wall, R Melzack:309-29. Hong Kong: Churchill Livingstone.

117. Jessell T, Kelly D. 1991. Pain and analgesia. In *Principles of Neural Science*, ed. E Kandel, J Schwartz, T Jessell:385–99. London: Prentice Hall.

118. Baliki M, Geha P, Apkarian A. 2009. Parsing pain perception between nociceptive representation and magnitude estimation. *J Neurophysiol* 101:875–87

119. Piovesan E, Kowacs P, Oshinsky M. 2003. Convergence of cervical and trigeminal sensory afferents. *Curr Pain Headache Rep.* 7:377-83

120. Treede R, Kenshalo D, Gracely R, Jones A. 1999. The cortical representation of pain. *Pain* 79:105-11

121. Rainville P, Duncan G, Price D, Carrier B, Bushnell M. 1997. Pain affect encoded in human anterior cingulate but not somatosensory cortex. *Science* 277:968 - 71

122. Standring S, ed. 2005. *Gray's Anatomy: The anatomical basis of clinical practice*. London: Elsevier Churchill Livingstone.

123. Cannon W. 1832. *Wisdom of the Body*. USA: W.W. Norton & Co.

124. Selye H. 1976. *Stress in health and disease*. Reading, MA: Butterworth.

125. De la Torre B. 1994. Psychoendocrinologic mechanisms of live stress. *Stress Medicine* 10:107-14

126. Panksepp J. 1998. *Affective Neuroscience: The Foundations of Human and Animal Emotions*. Oxford University Press.

127. Suchecki D, Nelson DY, Van Oers H, Levine S. 1995. Activation and inhibition of the hypothalamic-pituitary-adrenal axis of the neonatal rat: Effects of maternal deprivation. *Psychoneuroendocrinology* 20:169-82

128. Michelson D, Licinio J, Gold P. 1995. Mediation of the stress response by the hypothalamic-pituitary-adrenal axis. In *Neurobiological and clinical Consequences of Stress: From Normal Adaptation to PTSD.*, ed. DSCAYD M.J. Friedman:235-8. Philadelphia: Lippincott-Raven Pubs.

129. Panksepp J. 1996. Affective neuroscience: A paradigm to study the animate circuits for human emotions. In *Emotions: Interdisciplinary perspectives*, ed. R Kavanaugh, B. Zimmerberg, & S. Fein. Mahwah, N.J.: Lawrence Erlbaum.

130. Cooper SJ. 2008. From Claude Bernard to Walter Cannon. Emergence of the concept of homeostasis. *Appetite* 51:419-27

131. Wolff H. 1963. *Headache and other head pain (2nd ed)*. NY: Oxford University Press.

132. Torpy D, Chrousos G. 1997. General Adaptation Syndrome: An overview. In *Endocrinology of critical disease*, ed. K Ober. New Jersey: Humana Press.

133. Sterling P, Eyer J. 1988. Allostasis: A new paradigm to explain arousal pathology. In *Handbook of life stress, cognition, and health*, ed. S Fisher, J Reason:629–49. NY: Wiley.

134. Koolhaas JM, Bartolomucci A, Buwalda B, de Boer S, Flügge G, et al. 2011. Stress revisited: A critical evaluation of the stress concept. *Neuroscience and Biobehavioral Reviews* 35:1291–301

135. Scheurink A, Ammar A, Benthem B, van D, Sodersten P. 1999. Exercise and the regulation of energy intact. *Int. J. Obes. Relat. Metab. Disord.* 23:51-6

136. Garcia A, Marti O, Valies A, Dal-Zotto S, Armario A. 2000. Recovery of the hypothalamic-pituitary-adrenal response to stress. Effect of stress intensity, stress duration and previous stress exposure. *Neuroendocrinology* 72:114-25

137. Romero L, Dickens M, Cyr N. 2009. The reactive scope model: a new model integrating homeostasis, allostasis and stress. *Horm. Behav.* 55:375-89

138. Amat J, Barat M, Paul E, Bland S, Watkins L, Maier S. 2005. Medial prefrontal cortex determines how stressor controllability affects behaviour and dorsal raphe nucleus. *Nat Neurosci* 8:365-71

139. Sotres-Bayon F, Quirk G. 2010. Prefrontal control of fear: more than just extinction. *Curr Opin Neurobiol* 20:231-5

140. Folkman S, Lazarus RS. 1985. If it changes it must be a process: study of emotion and coping during three stages of a college examination. *J Pers Soc Psychol* 48:150-70

141. Zautra A. 2003. *Emotions, stress, and health*. Oxford: Oxford University Press.

142. Siegel D. 2012. *Pocket Guide to Interpersonal Neurobiology: An integrative handbook of the mind*. NY: WW Norton.

143. LeDoux J. 1996. *The Emotional Brain: The Mysterious Underpinnings of Emotional Life*. NY: Simon and Schuster.

144. Damasio A. 2003. *Looking for Spinoza: Joy, Sorrow, and the Feeling Brain*. U.S.A.: Harcourt.

145. Damasio A. 1999. *The Feeling of What Happens: Body and Emotion in the Making of Consciousness*. NY: Harcourt.

146. Welch KM, Nagesh V, Aurora SK, Gelman N. 2001. Periaqueductal gray matter dysfunction in migraine: cause or the burden of illness? *Headache* 41:629-37

147. LeDoux J. 1993. Emotional networks in the brain. In *Handbook of Emotions (pp. 109-118)*, ed. M Lewis, J Havilands. NY: Guildford Press.

148. Porges S. 2011. *The Polyvagal Theory: Neurophysiological foundations of emotions, attachment, communication and self-regulation*. NY: W.W. Norton & Co.

149. Candor M, Ahmed S, Koob G, Le Moal M, Stinus L. 1992. Corticotropin-releasing factor induces a place aversion independent of its neuroendocrine role. *Brain Res* 597:304-9

150. Dunn A, Berridge C. 1990. Physiological and behavioral responses to corticotrophin-releasing factor administration: Is CRF a mediator of anxiety or stress responses? *Brain Res. Revs.* 15:71-100

151. Kalin N, Takahashi L. 1990. Fear-motivated behaviour induced by prior shock experience is mediated by corticotropin-releasing hormone systems. *Brain Res* 509:80-1

152. Krasnegor N, Lyon G, Goldman-Rakic S, eds. 1997. *Development of the prefrontal cortex*. Baltimore: Paul H. Bookes.

153. Quaade F, Vaernet K, Larsson S. 1974. Stereotaxic stimulation and electrocoagulation of the lateral hypothalamus in obese humans. *Acta Neurochir.* 30:111-7

154. Heath R. 1963. Electrical self-stimulation of the brain in man. *Am. J. Psychiat.* 120:571-7

155. Wise R. 1982. Neuroleptics and operant behavior:The anhedonia hypothesis. *Behav. Brain Sci.* 5:39-88

156. Blackburn JR, Pfaus JG, Phillips AG. 1992. Dopamine functions in appetitive and defensive behaviours. *Prog Neurobiol* 39:247-79

157. Salamone JD. 1994. The involvement of nucleus accumbens dopamine in appetitive and aversive motivation. *Behav Brain Res* 61:117-33

158. Holmes T, Rahe R. 1967. The Social Readjustment Rating Scale. *J Psychosom Res* 11:213-8

159. Lazarus R, Folkman S. 1984. *Stress, appraisal and coping*. NY: Springer.

160. Lazarus RS. 1993. From psychological stress to the emotions: a history of changing outlooks. *Annu Rev Psychol* 44:1-21

161. Folkman S, Lazarus RS, Dunkel-Schetter C, DeLongis A, Gruen RJ. 1986. Dynamics of a stressful encounter: cognitive appraisal, coping, and encounter outcomes. *J Pers Soc Psychol* 50:992-1003

162. Lazarus RS. 1991. *Emotion and Adaptation*. NY: Oxford Press.

163. Smith C, Kirby L. 2009. Putting appraisal in context: Toward a relational model of appraisal and emotion. *Cogn Emotion* 23:1352 -72

164. Bennett P, Lowe R, Honey K. 2003. Brief report. *Cogn Emotion* 17:511-20

165. Oatley K, Kelter D, Jenkins JM. 2006. *Understanding Emotions*. Malden, MA: Blackwell Publishing.

166. Lazarus RS. 1991. Progress on a cognitive-motivational-relational theory of emotion. *The American psychologist* 46:819-34

167. Gilbert P. 2005. Compassion and cruelty, A biopsychosocial approach. In *Compassion: Conceptualisations, research and use in psychotherapy*, ed. P Gilbert:9-74. East Sussex: Routledge.

168. Wagner D, Heatherton T. 2014. Emotion and self-regulation failure. In *Handbook of Emotion Regulation*, ed. J Gross:p. 613. NY: Guilford.

169. Lake AE. 2009. Headache as a Stressor: Dysfunctional versus Adaptive Coping Styles. *Headache* 49:1369-77

170. Massey EK, Garnefski N, Gebhardt WA, van der Leeden R. 2011. A daily diary study on the independent and interactive effects of headache and self-regulatory factors on daily affect among adolescents. *Br J Health Psychol* 16:288-99

171. Gross JJ. 2015. Emotion Regulation: Current Status and Future Prospects. *Psychol Inquiry* 26:1-26

172. American-Psychological-Association. nd. *Personality*. https://www.apa.org/topics/personality/

173. Winter D, Barenbaum N. 1999. History of modern personality theory and research, pp. 3-27. In *Handbook of Personality Theory and Research* ed. L Pervin, O John. NY: Guilford.

174. Mischel W, Shoda Y. 1994. Personality psychology has two goals: Must it be two fields? *Psych Inquiry* 5:156-8

175. Heath R, Saliba M, Mahmassani O, Major S, Khoury B. 2008. Locus of control moderates the relationship between headache pain and depression. *J Headache Pain* 9:301-8

176. French DJ, Holroyd KA, Pinell C, Malinoski PT, O'Donnell F, Hill KR. 2000. Perceived self-efficacy and headache-related disability. *Headache* 40:647-56

177. Mahdavi A, Nikmanesh E, AghaeI M, Kamran F, Tavakoli Z, Seddigh F. 2015. Predicting the level of job satisfaction based on hardiness and its components among nurses with tension headache. *J Med Life* 8:93-6

178. Scheier MF, Carver CS. 1987. Dispositional optimism and physical well-being: the influence of generalized outcome expectancies on health. *J Pers* 55:169-210

179. Block J. 1995. A contrarian view of the Five-Factor approach to personality description. *Psychol Bull* 117:187-215

180. Briggs S. 1989. The Optimal Level of Measurement for Personality Constructs. In *Personality Psychology*, ed. D Buss, N Cantor. NY: Springer.

181. Rusting C. 1998. Personality, mood, and cognitive processing of emotional information: three conceptual frameworks. *Psych Bull* 124:165-96

182. Watson L, Clark I, Tellegen A. 1988. Development and validation of brief measures of positive and negative affect: The PANAS scales. *J. Person. Soc. Psych.* 54:1063-70

183. Salovey P, Mayer J, Goldman S, Turvey C, TP P. 1995. Emotional attention, clarity and repair: Exploring emotional intelligence using the meta-mood scale. In *Emotion, disclosure and health*, ed. J Pennebaker:125-54. Washington, DC: American Psychological Association.

184. Bolger N, Schilling EA. 1991. Personality and the problems of everyday life: the role of neuroticism in exposure and reactivity to daily stressors. *J Pers* 59:355-86

185. Bolger N, Zuckerman A. 1995. A framework for studying personality in the stress process. *J Pers Soc Psych* 69:890-902

186. Thoits P. 2010. Stress and health. *J Health Soc Behav* 51:S41-S53

187. Spierings E, Sorbi M, Haimowitz B, Tellegen B. 1996. Changes in daily hassles, mood, and sleep in the 2 days before a migraine headache. *Clin J Pain* 12:38-42

188. Selekler H, Sengun E, Altun N. 2010. Sleep Quality and Depression in Episodic and Chronic Migraine Sufferers. *Noropsikiyatri Arsivi* 47:196-200

189. Ginty AT, Phillips AC, Higgs S, Heaney JL, Carroll D. 2012. Disordered eating behaviour is associated with blunted cortisol and cardiovascular reactions to acute psychological stress. *Psychoneuroendocrinology* 37:715-24

190. Wade J, Hart R. 2002. Attention and the Stages of Pain Processing. *Pain Medicine* 3:30-8

191. Wade J, Price D, eds. 2000. *Nonpathological factors in chronic pain: Implications for assessment and treatment*. Washington DC: American Psychological Association.

192. Borsook D, Maleki NB, R, Becerra L, McEwen B. 2012. Understanding migraine through the lens of maladaptive stress responses: a model disease of allostatic load. *Neuron* 73:219-34

193. Massey EK, Garnefski N, Gebhardt WA. 2009. Goal frustration, coping and well-being in the context of adolescent headache: a self-regulation approach. *Eur J Pain* 13:977-84

194. De Benedittis G, Lorenzetti A. 1992. The role of stressful life events in the persistence of primary headache: major events vs. daily hassles. *Pain* 51:35-42

195. Massey EK, Garnefski N, Gebhardt WA, van der Leeden R. 2009. Daily frustration, cognitive coping and coping efficacy in adolescent headache: a daily diary study. *Headache* 49:1198-205

196. Fernandez E, Sheffield J. 1996. Relative contributions of life events versus daily hassles to the frequency and intensity of headaches. *Headache* 36:595-602

197. Evans G, Cohen S. 1987. Environmental stress. In *Handbook of Environmental Psychology*, ed. D Sokols, I Altman, 1. NY: John Wiley & Sons.

198. Kanner AD, Coyne JC, Schaefer C, Lazarus RS. 1981. Comparison of two modes of stress measurement: Daily hassles and uplifts versus major life events. *J. Behav. Med.* 4:1-39

199. DeLongis A, Holtzman S. 2005. Coping in context: the role of stress, social support, and personality in coping. *J Personality* 73:1633-56

200. Borsook D, Maleki NB, R. 2015. Migraine (Chapter 42). In *Neurobiology of Brain Disorders* ed. M Zigmond, L Rowlands, J Coyle:693-708: Academic press.

201. De Benedittis G, Lorenzetti A, Pieri A. 1990. The role of stressful life events in the onset of chronic primary headache. *Pain* 40:65-75

202. Swindle RE, Moos RH. 1992. Life domains in stressors, coping and adjustment. In *Person Environment Psychology: Models and Perspectives, pp. 1-33*, ed. W.B. Walsh, R. Price, K.B.Crack. Mahawah, NJ: Erlbaum.

203. Craig K, Brown K, Baum A. 2008. Environmental Factors in the Etiology of Anxiety. In *Neuropsychopharmacology: The Fifth Generation of Progress*, ed. ACo Neuropsychopharmacology. Brentwood, TN.

204. Glass DC, Singer JE. 1972. *Urban Stress*. New York: Academic Press.

205. Foa EB, Zinbarg R, Rothbaum BO. 1992. Uncontrollability and Unpredictability in Post-Traumatic Stress Disorder: An Animal Model. *Psychol Bull* 112:218-38

206. Grillon C. 2008. Models and mechanisms of anxiety: evidence from startle studies. *Psychopharmacology* 199:421-37

207. Melzack PD. 1999. Pain and Stress: A new perspective. In *Psychosocial Factors in Pain: Critical perspectives, pp 89-106*, ed. RJ Gatchel, DC Turk. NY: Guilford Press.

208. Korff M, Jensen M, Karoly P. 2000. Assessing global pain severity by self-report in clinical and health services research. *Spine (Phila Pa 1976)* 25:3140–51

209. Apkarian AV, Bushnell MC, Treede RD, Zubieta JK. 2005. Human brain mechanisms of pain perception and regulation in health and disease. *Eur J Pain* 9:463-84

210. Drummond PD, Granston A. 2005. Painful stimulation of the temple induces nausea, headache and extracranial vasodilation in migraine sufferers. *Cephalalgia* 25:16-22

211. Marshall G, Zimbardo P. 1979. Affective consequences of inadequately explained physiological arousal. *J Pers Soc Psychol* 37:970-88

212. Wiech K, Ploner M, Tracey I. 2008. Neurocognitive aspects of pain perception. *Trends in cognitive sciences* 12:306-13

213. Leventhal H, Brissette I, Leventhal E. 2003. The common-sense model of self-regulation of health and illness. In *The self-regulation of health and illness behaviour, pp 42-65*, ed. L Cameron, H Leventhal: Routledge.

214. Heim C, Ehlert U, Hellhammer DH. 2000. The potential role of hypocortisolism in the pathophysiology of stress-related bodily disorders. *Psychoneuroendocrinology* 25:1-35

215. Goadsby PJ, Holland PR, Martins-Oliveira M, Hoffmann J, Schankin C, Akerman S. 2017. Pathophysiology of Migraine: A Disorder of Sensory Processing. *Physiol Rev* 97:553-622

216. Chapman C, Gavrin J. 1999. Suffering the contributions of persisting pain. *Lancet* 353:2233-7

217. Willis W, Westlund KN. 1997. Neuroanatomy of the Pain System and of the Pathways That Modulate Pain. *J Clin Neurophysiol* 14:2-31

218. Bandler R, Shipley M. 1994. Columnar organization in the midbrain periaqueductal gray: Modules for emotional expression. *Trends Neurosci* 17:379-89

219. Bolles R, Fanselow M. 1980. A perceptual-defensive-recuperative model of fear and pain. *Behav Brain Sci* 3:291-301

220. Basbaum A, Fields H. 1984. Endogenous pain control systems: Brainstem spinal pathways and endorphin circuitry. *Ann Rev Neurosci* 7:309-38

221. Fields H, Basbaum A. 1999. Central nervous system mechanisms of pain modulation. In *Textbook of Pain, 4th ed*, ed. P Wall, R Melzack:309-29. Hong Kong: Churchill Livingstone.

222. Hutchinson R, Renfrew J. 1978. Functional parallels between the neural and environmental antecedents of aggression. *Neurosci Biobehav Rev* 2:33-58

223. Bang A. 2015. *Your jaw may be to blame for your migraine headaches* https://health.clevelandclinic.org/your-jaw-may-be-to-blame-for-your-migraine-headaches/

224. Spierings EL, Ranke AH, Honkoop PC. 2001. Precipitating and aggravating factors of migraine versus tension-type headache. *Headache* 41:554-8

225. Weiss J, Goodman P, Losito B, Corrigan S, Charry J, Bailery W. 1981. Behavioral depression produced by an uncontrollable stressor: Relationship to norepinephrine, dopamine, and serotonin levels in various regions of the rat brain. *Brain Res Rev* 3:167-205

226. Roy M, Peretz I, Rainville P. 2008. Emotional valence contributes to music-induced analgesia. *Pain* 134:140-7

227. Shaygan M, Boger A, Kroner-Herwig B. 2017. Valence and Arousal Value of Visual Stimuli and Their Role in the Mitigation of Chronic Pain: What Is the Power of Pictures? *J Pain* 18:124-31

228. Fernandez E. 2002. *Anxiety, depression and anger in pain: research findings and clinical options*. Dallas, Texas: Advanced Psychological Resrouces.

229. Bishop SJ. 2007. Neurocognitive mechanisms of anxiety: an integrative account. *Trends in cognitive sciences* 11:307-16

230. Rosenzweig MR. 1996. Reciprocal relations between psychology and neuroscience. *Int J Psychol* 31:4871-

231. Romano JM, Turner JA. 1985. Chronic pain and depression: does the evidence support a relationship? *Psychol Bull* 97:18-34

232. Overmier JB, Seligman ME. 1967. Effects of inescapable shock upon subsequent escape and avoidance responding. *J Comp Physiol Psychol* 63:28-33

233. Haefeli M, Elfering A. 2006. Pain assessment. *Eur Spine J* 15:S17-S24

234. Vingerhoets A. 2004. Stress. In *Health Psychol*, ed. AJW Kaptein:113-40. Oxford: B.P.S. Blackwell.

235. Breslau N, Andreski P. 1995. Migraine, personality, and psychiatric comorbidity. *Headache* 35:382-6

236. Breslau N, Chilcoat HD, Andreski P. 1996. Further evidence on the link between migraine and neuroticism. *Neurology* 47:663-7

237. Barnes G. 1975. Extraversion and pain. *Brit J Soc Clin Psychol* 14:303-8

238. Lynn R, Eysenck H. 1961. Tolerance for pain, extraversion and neuroticism. *Percept Mot Skills* 12:161-2

239. Petrie A, Collins W, Solomon P. 1960. The tolerance for pain and for sensory deprivation. *Am J Psychol* 73:80-90

240. Mateos V, Garcia-Monco JC, Gomez-Beldarrain M, Armengol-Bertolin S, Larios C. 2011. [Personality factors, degree of disability and therapeutic management of patients with migraine visiting a neurology unit for the first time (Psicomig study)]. *Rev Neurol* 52:131-8

241. Cao M, Zhang S, Wang K, Wang YH, Wang W. 2002. Personality traits in migraine and tension-type headaches: A five-factor model study. *Psychopathology* 35:254-8

242. Wang G, Ding X, Wang W, Wang Y. 1999. Personality and response to repeated visual stimulation in migraine and tension-type headaches. *Cephalalgia* 19:718-24

243. Savi L, Buccheri R, Tambornini A, De Martino P, Albasi C, Pinessi L. 2005. Attachment styles and headache. *J Headache Pain* 6:254-7

244. Rossi P, Di Lorenzo G, Malpezzi M, Di Lorenzo C, Cesarino F, et al. 2005. Depressive symptoms and insecure attachment as predictors of disability in a clinical population of patients with episodic and chronic migraine. *Headache* 45:561-70

245. Cahill CM, Cook C, Pickens S. 2014. Migraine and reward system-or is it aversive? *Curr Pain Headache Rep* 18:410

246. Noseda R, Kainz V, Borsook D, Burstein R. 2014. Neurochemical pathways that converge on thalamic trigeminovascular neurons: potential substrate for modulation of migraine by sleep, food intake, stress and anxiety. *PLoS One* 9:e103929

247. Li Z, Liu M, Lan L, Zeng F, Makris N, et al. 2016. Altered periaqueductal gray resting state functional connectivity in migraine and the modulation effect of treatment. *Sci Rep* 6

248. Hadjikhani N, Ward N, Boshyan J, Napadow V, Maeda Y, et al. 2013. The missing link: enhanced functional connectivity between amygdala and visceroceptive cortex in migraine. *Cephalalgia* 33:1264-8

249. Wei HL, Chen J, Chen Y, Yu Y, Zhou G, et al. 2019. Impaired functional connectivity of limbic system in migraine without aura. *Brain Imaging Behav*

250. Rainville P. 2004. Pain and emotions. In *Psychological methods of pain control: Basic science and clinical perspectives*, ed. D Price, M Bushnell:117-41. Seattle: IASP Press.

251. Rainville P, Bushnell M, Duncan G. 2000. Brain imaging studies of hypnosis and hypnotic modulation of pain affect. *International society of Hypnosis Newsletter* 22:17-8

252. Harvard-Health-Publishing. nd. *The pain-anxiety-depression connection.* https://www.health.harvard.edu/healthbeat/the-pain-anxiety-depression-connection

253. Leventhal H, Everhart D. 1980. Emotion, pain and physical illness. In *Emotions and psychopathology (pp. 263-299)*, ed. C Izard. NY: Plenum.

254. Lazarus RS. 1992. Coping with the stress of illness. *WHO Reg Publ Eur Ser* 44:11-31

255. Beecher HK. 1956. Relationship of significance of wound to pain experienced. *J Am Med Assoc* 161:1609-13

256. Bandura A, Cioffi D, Taylor CB, Brouillard ME. 1988. Perceived self-efficacy in coping with cognitive stressors and opioid activation. *J Pers Soc Psychol* 55:479-88

257. Marlowe N. 1998. Self-efficacy moderates the impact of stressful events on headache. *Headache* 38:662-7

258. Hirsch MS, Liebert RM. 1998. The physical and psychological experience of pain: the effects of labeling and cold pressor temperature on three pain measures in college women. *Pain* 77:41-8

259. Carver C. 2001. Depression, Hopelessness, Optimism and Health. In *International Encyclopedia of the Social and Behavioural Sciences*, ed. N Smelser, P Baltes. Oxford: Pergamon.

260. Bantick SJ, Wise RG, Ploghaus A, Clare S, Smith SM, Tracey I. 2002. Imaging how attention modulates pain in humans using functional MRI. *Brain* 125:310-9

261. Watson D, Pennebaker JW. 1989. Health complaints, stress, and distress: exploring the central role of negative affectivity. *Psychol Rev* 96:234-54

262. Miron D, Duncan GH, Bushnell MC. 1989. Effects of attention on the intensity and unpleasantness of thermal pain. *Pain* 39:345-52

263. Chajut E, Algom D. 2003. Selective attention improves under stress: implications for theories of social cognition. *J Pers Soc Psychol* 85:231-48

264. Watkins LR, Maier SF. 2005. Immune regulation of central nervous system functions: from sickness responses to pathological pain. *J Intern Med* 257:139-55

265. Schiaffino KM, Revenson TA. 1995. Why Me - the Persistence of Negative Appraisals over the Course of Illness. *J Appl Soc Psychol* 25:601-18

266. Bandura A. 1997. *The exercise of control*. NY: WH Freeman & Co.

267. Maddux J. 2005. Self-efficacy: The power of believing you can. In *Handbook of positive psychology (pp. 227-287)*, ed. C Snyder, S Lopez. NY: Oxford University Press.

268. Maier SF, Watkins LR. 2005. Stressor controllability and learned helplessness: the roles of the dorsal raphe nucleus, serotonin, and corticotropin-releasing factor. *Neurosci Biobehav Rev* 29:829-41

269. Overmier JB. 2002. On learned helplessness. *Integr Physiol Behav Sci* 37:4-8

270. Ajzen I. 2002. Perceived behavioral control, self-efficacy, locus of control, and the theory of planned behavior. *J Appl Soc Psychol* 32:665-83

271. Russo A, Santangelo G, Tessitore A, Silvestro M, Trojsi F, et al. 2019. Coping Strategies in Migraine without Aura: A Cross-Sectional Study. *Behavioural neurology* 2019:5808610

272. Arntz A, Schmidt A, eds. 1989. *Perceived control and the experience of pain*: John Wiley & Sons.

273. McCaul KD, Monson N, Maki RH. 1992. Does distraction reduce pain-produced distress among college students? *Health Psychol* 11:210-7

274. Drummond P, Holroyd K. 2000. Psychological modulation of pain. In *The Headaches*, ed. J Olesen, P Tfelt-Hansen, K Welsh:217-21. Philadelphia: Lippincott, Williams and Wilkins.

275. Evers AW, Kraaimaat FW, Geenen R, Bijlsma JW. 1998. Psychosocial predictors of functional change in recently diagnosed rheumatoid arthritis patients. *Behav Res Ther* 36:179-93

276. McCracken LM, Eccleston C. 2006. A comparison of the relative utility of coping and acceptance-based measures in a sample of chronic pain sufferers. *Eur J Pain* 10:23-9

277. Leeuw M, Goossens ME, Linton SJ, Crombez G, Boersma K, Vlaeyen JW. 2007. The fear-avoidance model of musculoskeletal pain: current state of scientific evidence. *J Behav Med* 30:77-94

278. Zale E, Ditre J. 2015. Pain-related fear, disability and the fear-avoidance model of chronic pain. *Curr Opin Psychol* 5:24-30

279. Wieser T, Walliser U, Womastek I, Kress HG. 2012. Dysfunctional coping in headache: avoidance and endurance is not associated with chronic forms of headache. *Eur J Pain* 16:268-77

280. Ruscheweyh R, Pereira D, Hasenbring MI, Straube A. 2019. Pain-related avoidance and endurance behaviour in migraine: an observational study. *The Journal of Headache and Pain* 20:9

281. Kozlowska K. 2009. Attachment relationships shape pain-signaling behavior. *J Pain* 10:1020-8

282. McEwen B, Kalia M. 2010. The role of corticosteroids and stress in chronic pain conditions. *Metabolism* 59:S9-S15

283. Lipton R, Buse D, Hall C, Tennen H, Defreitas T, et al. 2014. Reduction in perceived stress as a migraine trigger: testing the "let-down headache" hypothesis. *Neurology* 82:1395–401

284. Sapolsky R. 1994. *Why zebras do not get ulcers: A guide to stress, stress related disease and coping*. NY: W.H. Freeman.

285. Bussone G, Grazzi L. 2013. Understanding the relationship between pain and emotion in idiopathic headaches. *Neurol Sci* 34 Suppl 1:S29-31

286. Frew A. 2005. *The influence of discouragement, anxiety and anger on pain: an examination of the role of endogenous opioids*. PhD. Murdoch University

287. Montagna P, Pierangeli G, Cortelli P. 2010. The primary headaches as a reflection of genetic darwinian adaptive behavioral responses. *Headache* 50:273-89

288. Price D. 1999. *Psychological mechanisms of pain and analgesia.* Seattle: IASP Press.

289. Witkiewitz K, Marlatt GA. 2007. Modeling the complexity of post-treatment drinking: it's a rocky road to relapse. *Clin Psychol Rev* 27:724-38

290. Boyer B, Paharia M. 2008. *Comprehensive Handbook of Clinical Health Psychology*. John Wiley & Sons, Inc. .

291. Ramsay D, Woods S. 2014. Clarifying the Roles of Homeostasis and Allostasis in Physiological Regulation. *Psychol Rev* 12:225-47

292. Bieri P. 1987. Pain: a case study for the mind-body problem. *Acta Neurochirurgica Supplementum* 38:157-64

293. Koolhaas JM, Bartolomucci A, Buwalda B, de Boer S, Flügge G, et al. 2011. Stress revisited: A critical evaluation of the stress concept. *Neurosci Biobehav Rev* 35:1291–301

294. Martin PR, Teoh HJ. 1999. Effects of visual stimuli and a stressor on head pain. *Headache* 39:705-15

295. Cohen J. 1988. *Statistical power analysis for the behavioral sciences (rev. ed.)*. NY: Academic Press.

296. Ukestad LK, Wittrock DA. 1996. Pain perception and coping in female tension headache sufferers and headache-free controls. *Health Psychol* 15:65-8

297. Hassinger H, Semenchuk E, O'Brien W. 1999. Appraisal and coping responses to pain and stress in migraine headache sufferers. *J Behav Med* 22:327-40

298. Field B, Swarm R. c2008. *Chronic pain*. Cambridge, Mass: Hogrefe.

299. Breslau N, Lipton RB, Stewart WF, Schultz LR, Welch KM. 2003. Comorbidity of migraine and depression: investigating potential etiology and prognosis. *Neurology* 60:1308-12

300. Breslau N, Merikangas K, Bowden CL. 1994. Comorbidity of migraine and major affective disorders. *Neurology* 44:S17-22

301. Pompili M, Di Cosimo D, Innamorati M, Lester D, Tatarelli R, Martelletti P. 2009. Psychiatric comorbidity in patients with chronic daily headache and migraine: a selective overview including personality traits and suicide risk. *J Headache Pain* 10:283-90

302. Holroyd K, Stensland M, Lipchik G, Kimberly R, Hill M, et al. 2001. Psychosocial Correlates and Impact of Chronic Tension-type Headaches. *Headache* 40:3-16

303. Mongini F, Rota E, Evangelista A, Ciccone G, Milani C, et al. 2009. Personality profiles and subjective perception of pain in head pain patients. *Pain* 144:125-9

304. Blumenfeld A, Schim J, Brower J. 2010. Pure tension-type headache versus tension-type headache in the migraineur. *Curr Pain Headache Rep* 14:465-9

305. Bigal M, Krymchantowski M, Lipton R. 2009. Barriers to Satisfactory Migraine Outcomes. What have we learned, where do we stand? *Headache* 49:1028-41

306. Schaffer A. November 7 2006. *Migraine headaches: can electricity block migraines? It may come as a shock*. http://www.nytimes.com/2006/11/07/health/07migr.html?pagewanted=2&_r=0&ex=1163566800;

307. Kaube H, Katsarava Z, Kaufer T, Diener H, Ellrich J. 2000. A new method to increase nociception specificity of the human blink reflex. *Clin Neurophysiol* 111:413-6

308. Kirschbaum C, Hellhammer DH. 2000. Salivary cortisol. In *Encyclopedia of Stress (pp. 379–383)* ed. G Fink. San Diego: Academic Press.

309. Atekin B, Yaltkaya K, Ozkaynak S, Oguz Y. 2001. Recovery cycle of the blink reflex and exteroceptive suppression of temporalis muscle activity in migraine and tension-type headache. *Headache* 41:142-9

310. Hopf H. 1994. Topodiagnostic value of brain stem reflexes. *Muscle Nerve* 17:475-84

311. Hopf H. 2002. Trigeminal reflexes. *Movement Dis* 17:S20-S2

312. Ellrich J. 2000. Brain stem reflexes: Probing human trigeminal nociception. *News Physiol Sci* 15:94-7

313. Vallis-Sole J, Vila N, Obach V, Alvarez R, Gonzalez L, Chamorro A. 1996. Brain stem reflexes in patients with Wallenberg's syndrome: correlation with clinical and magnetic resonance imaging (MRI) findings. *Muscle Nerve* 19:1093-9

314. Ellrich J, Katsavara Z, Przywara S, Kaube H. 2001. Is the R3 component of the human blink reflex nociceptive in origin? *Pain* 92:389-95

315. Katsarava Z, Ellrich J, Diener H, Kaube H. 2002. Optimized stimulation and recording parameters of human ‘‘nociception specific’’ blink reflex recordings. *Clin Neurophysiol* 113:1932-6

316. de Tommaso M, Santostasi R, Devitofrancesco V, Franco G, Vecchio E, et al. 2011. A comparative study of cortical responses evoked by transcutaneous electrical vs CO(2) laser stimulation. *Clin Neurophysiol* 122:2482-7

317. Kaube H, Katsarava Z, Kaufer T, Diener H-C, Ellrich J. 2000. A new method to increase nociception specificity of the human blink reflex. *Clin Neurophysiol* 111:413-6

318. Katsarava Z, Ellrich J, Diener H, Kaube H. 2002. Optimized stimulation and recording parameters of human 'nociception specific' blink reflex recordings. *Clinical Neurophysiology* 113:1932-6

319. Katsavara Z, Frings M, Kaube H, Diener H, Limmroth V. 2002. Selective damage of trigeminal Adelta fibres in Raeder's syndromer following dissection of the ICA detected by a nociceptive blink reflex. *Cephalalgia* 22:151-3

320. Katsavara Z, Lehnerdt G, Duda B, Ellrich J, Diener H, Kaube H. 2002. Sensitization of trigeminal nociception specific for migraine but not pain of sinusitis. *Neurology* 59:1450-3

321. Katsavara Z, Giffin N, Diener HC, H. K. 2003. Abnormal habituation of 'nociceptive' blink reflex in migraine - evidence for increased excitability of trigeminal nociception. *Cephalalgia* 23:814-9

322. Price DD, McGrath PA, Rafii A, Buckingham B. 1983. The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. *Pain* 17:45-56

323. Costa P, McCrae R. 1985. *The NEO Personality Inventory Manual*. Odessa, FL: Psychological Assessment Resources.

324. Brennan K, Clark C, Shaver P. 1998. Self-report measurement of adult attachment: an integrative overview. In *Attachment Theory and Close Relationships* ed. J Simpson, W Rholes:46–76. NY: Guilford.

325. George C, Kaplan N, Main M. 1985. *The Adult Attachment Interview*. http://www.psychology.sunysb.edu/attachment/measures/content/aai_interview.pdf

326. Shaver P, Mikulincer M. 2004. What do self-report attachment measures assess? In *Adult attachment: Theory, research, and clinical implications (pp. 17-54),* ed. W Rholes, J Simpson. NY: Guilford.

327. Cook S, Heppner P. 1997. A psychometric study of three coping measures. *Educ Psych Measurement* 57:906-23

328. Tunks E, Bellissimo A. 1988. Coping with the coping concept: a brief comment. *Pain* 34:171-4

329. Rosenstiel AK, Keefe FJ. 1983. The use of coping strategies in chronic low back pain patients: relationship to patient characteristics and current adjustment. *Pain* 17:33-44

330. Tuttle DH, Shutty MS, Degood DE. 1991. Empirical Dimensions of Coping in Chronic Pain Patients - a Factorial Analysis. *Rehabil Psychol* 36:179-88

331. Widiger TA, Costa PT, Jr. 1994. Personality and personality disorders. *J Abnorm Psychol* 103:78-91

332. Mischel W. 1968. *Personality and assessment*. Wiley.

333. Sperling M. 1952. A psychoanalytic study of migraine and psychogenic headache. *Psychoanal Rev* 331:152-63

334. Wolff H. 1937. Personality factors and reactions of subjects with migraine. *Arch Neurol Psychiatry* 37:895

335. Friedman A, von Storch T, Merritt H. 1954. Migraine and tension headache: a clinical study of 2000 cases. *Neurology* 4:773-88

336. Martin J, Rome H, Swenson W. 1967. Muscle contraction headache: a psychiatric review. *Res Clin Stud Headache* 1:184-204

337. Hathaway SR, McKinley J. 1940. *The MMPI Manual*. NY: Psychological Corporation.

338. Schiele B, Baker A, Hathaway S. 1943. The Minnesota multiphasic personality inventory. *Lancet* 63:292–7

339. Boz C, Velioglu S, Ozmenoglu M, Sayar K, Alioglu Z, et al. 2004. Temperament and character profiles of patients with tension-type headache and migraine. *Psychiat Clin Neurosci* 58:536-43

340. Rasmussen B. 1982. Migraine and tension-type headache in a general population: Psychosocial factors. *Int J Epidemiol* 21:1138-43

341. Rasmussen B, Jensen R, Olesen J. 1992. Impact of headache on sickness absence and utilisation of mdedical services: A Danish population study. *J Epidemiol Community Health* 46:443-46

342. Phillips J, Gatchel R. 2000. Extraversion-Introversion and chronic pain. In *Personality characteristics of patients with pain*, ed. R Gatchel, J Weisberg. Washington DC: American Psychological Association.

343. Silberstein SD, Lipton RB, Breslau N. 1995. Migraine: association with personality characteristics and psychopathology. *Cephalalgia* 15:358-69; discussion 36

344. Naylor B, Boag S, Gustin SM. 2017. New evidence for a pain personality? A critical review of the last 120 years of pain and personality. *Scand J Pain* 17:58-67

345. Talarowska M, Zboralski K, Chamielec M, Gałecki P. 2011. The MMPI-2 neurotic triad subscales and depression levels after pharmacological treatment in patients with depressive disorders - clinical study. *Psychiatria Danubina* 23:347-54

346. Lipton RB, Silberstein SD. 1994. Why study the comorbidity of migraine? *Neurology* 44:S4-5

347. Breslau N, Schultz LR, Stewart WF, Lipton RB, Lucia VC, Welch KM. 2000. Headache and major depression: is the association specific to migraine? *Neurology* 54:308-13

348. Stam A, de Vries B, Janssens A, Vanmolkot K, Aulchenko V, et al. 2010. Shared genetic factors in migraine and depression: Evidence from a genetic isolate. *Neurology* 74:288–94

349. Arena J, Blanchard E, Andrasik F, Applebaum K. 1986. Obsessions and compulsions in three kinds of headache sufferers: Analysis of the Maudsley questionnaire. *Behav Res Ther* 24:127-32

350. Merikangas K, Stevens D, Angst J. 1993. Headache and personality: results of a community sample of young adults. *J Psychiatr Res* 27:187-96

351. Brandt J, Celentano D, Stewart W, Linet M, Folstein M. 1990. Personality and emotional disorder in a community sample of migraine headache sufferers. *Amer J Psychiat* 147:303-8

352. Eysenck H. 1960. Levels of personality, constitutional facors and social influence: an experimental approach. *Int J Soc Psychiat* 6:12-24

353. Eysenck H. 1967. *The Biological Basis of Personality*. Springfield, IL: Thomas.

354. Eysenck H, Eysenck S. 1975. *Manual of the Eysenck Personality Questionnaire*. San Diego: Educational and Industrial Testing Service.

355. Eysenck H, Eysenck S. 1991. *Eysenck Personality Questionnaire - Revised (EPQ - R)*. Hodder & Stoughton.

356. Contrada R, Coups E. 2003. Personality and self-regulation in health and disease: Toward a integrative perspective. In *The self-regulation of health and illness behaviour*, ed. L Cameron, H Leventhal: Routledge.

357. Smith T, Williams P. 1992. Personality and health: Advantages and limitations of the five factor model. *J Pers* 60:395-423

358. Lecic-Tosevski D, Vukovic O, Stepanovic J. 2011. Stress and personality. *Psychiatriki* 22:290-7

359. Matthews KA. 1982. Psychological perspectives on the type A behavior pattern. *Psychol Bull* 91:293-323

360. Sotodehasl N, Amirahmadi E, Ghorbani R, Masoudian N, Samaei A. 2019. Association between personality traits and migraine headache. *Koomesh* 21:46-51

361. Saunders E, Nazir R, Kamali M, Ryan K, Evans S, Langenecker S. 2014. Gender differences, clinical correlates and longitudinal outcome of bipolar disorder with co-morbid migraine. *J Clin Psychiatry* 75:512–9

362. Shulman B. 1993. Psychiatric approach to the patient hospitalized for headache. Headache Quarterly, 4(1), 63-67. *Headache Quart* 4:63-7

363. Siegel S, Carneiro R, Buslei R, Brabant G, Buchfelder M, Kreitschmann-Andermahr I. 2013. The role of personality factors in the development of headache in patients with pituitary adenomas. *Exp Clin Endocrinol Diabetes* 121 - OP8_47

364. Magyar M, Gonda X, Pap D, Edes A, Galambos A, et al. 2017. Decreased Openness to Experience Is Associated with Migraine-Type Headaches in Subjects with Lifetime Depression. *Front Neurol* 8:270

365. Kim S, Kim H, Cho J, Kwon M, Chang Y, et al. 2016. Direct and Indirect Effects of Five Factor Personality and Gender on Depressive Symptoms Mediated by Perceived Stress. *PLoS One* 11

366. Suls J, Green P, Hillis S. 1998. Emotional reactivity to everyday problems, affective inertia, and neuroticism. *Pers Soc Psychol Bull* 24:127–36

367. Suls J, Rittenhouse J. 1987. Personality and Physical Health: An Introduction. *J Personality* 55:155-67

368. Magnus K, Diener E, Fujita F, Pavot W. 1993. Extraversion and neuroticism as predictors of objective life events: a longitudinal analysis. *J Pers Soc Psychol* 65:1046-53

369. Ashina S, Bendtsen L, Buse D, Lyngberg A, Lipton R, Jensen R. 2017. Neuroticism, depression and pain perception in migraine and tension-type headache. *Acta Neurol Scand* 136:470-6.

370. Garramone F, Baiano C, Russo A, D'Iorio A, Tedeschi G, et al. 2020. Personality profile and depression in migraine: a meta-analysis. *Neurol Sci* 41:543-54

371. Aaseth K, Grande R, Leiknes K, Benth J, Lundqvist C, Russell M. 2011. Personality traits and psychological distress in persons with chronic tension-type headache. The Akershus study of chronic headache. *Acta Neurol Scand* 124:375–82

372. Andrasik F, Blanchard EB, Arena JG, Teders SJ, Teevan RC, Rodichok LD. 1982. Psychological functioning in headache sufferers. *Psychosom Med* 44:171-82

373. Zuckerman M. 2002. Zuckerman-Kuhlman Personality Questionnaire (ZKPQ): an alternative five-factorial model (Chapter 16). In *Big Five Assessment*, ed. B De Raad, M Perugini:377-96: Hogrefe & Huber.

374. Saklofske D, Eysenck H. 1994. Extraversion-introversion. In *Encyclopedica of Human Behavior*, ed. V Ramachandran:321-32. San Diego: Academic Press.

375. Eysenck H. 1973. *On Extroversion*. Crosby Lockwood.

376. Barnes G. 1975. Extraversion and pain. *British Journal of Social & Clinical Psychology* 14:303-8

377. Schalling D. 2008. Tolerance for experimentally induced pain as related to personality. *Scandinavian Journal of Psychology* 12:271-81

378. Schwarzer R, Leppin A. 1991. Social support and health: A theoretical and empirical overview. *Journal of Social and Personal Relationships* 8:99-127

379. Ziegler D, Paolo A. 1995. Headache symptoms and psychological profile of headache-prone individuals. A comparison of clinic patients and controls. *Arch Neurol* 52:602-6

380. Moffatt A, Swash M, Scott D. 1972. Effect of tyramine in migraine; a double-blind study *J Neurol Neurosurg Psychiatry* 35 496-9

381. Philips HC, Jahanshahi M. 1985. The effects of persistent pain: The chronic headache sufferer. *Pain* 21:163-76

382. Omdal R, Waterloo K, Koldingsnes W, Husby G, Mellgren SI. 2001. Somatic and psychological features of headache in systemic lupus erythematosus. *J Rheumatol* 28:772-9

383. Hollister P. 2006. E/I Extravert or introvert, How we get and direct our energy. *The People Process, http://thepeopleprocess.com/articles/extravert-or-introvert.php*

384. Winter AC, Hoffmann W, Meisinger C, Evers S, Vennemann M, et al. 2011. Association between lifestyle factors and headache. *J Headache Pain* 12:147-55

385. Hershey AD. 2010. Lifestyles of the young and migrainous. *BMC neurology* 75:680-1

386. Breslau N, Andreski P. 1995. Migraine, Personality and Psychiatric Comorbidity. *Headache* 35:382-6

387. Nyklicek I, Vingerhoets AJJM, Denollet JKL. 2002. Emotional (non)-expression and health: Data, questions, and challenges. *Psychol Health* 17:517-28

388. Berry D, Pennebaker JW. 1993. Nonverbal and verbal emotional expression and health. *Psychother Psychosom* 59:11-9

389. Pennebaker JW. 1985. Traumatic experience and psychosomatic disease: Exploring the roles of behavioural inhibition, obsession and confiding. *Canadian Psychol* 26:82-95

390. Cole SW, Kemeny ME, Fahey JL, Zack JA, Naliboff BD. 2003. Psychological risk factors for HIV pathogenesis: mediation by the autonomic nervous system. *Biol Psychiatry* 54:1444-56

391. Tedeschi RG, Calhoun LG. 1996. The Posttraumatic Growth Inventory: measuring the positive legacy of trauma. *J Trauma Stress* 9:455-71

392. Moskowitz D. 1994. Cross-situational generality and the interpersonal circumplex. *J Pers Soc Psychol* 66:921–33

393. Graziano W, Jensen-Campbell L, Hair E. 1996. Perceiving interpersonal conflict and reacting to it: The case for agreeableness. *J Pers Soci Psychol* 70:820–35

394. Jensen-Campbell L, Graziano W. 2001. Agreeableness as a moderator of interpersonal conflict *J Personality* 69:323–62

395. Martin PR, Seneviratne HM. 1997. Effects of food deprivation and a stressor on head pain: 1. *Health Psychol* 16:310-8

396. Liossi C. 2011. Time-course of attentional bias for threat-related cues in patients with chronic daily headache–tension type: Evidence for the role of anger. *Eur J Pain* 15:92-8

397. Mollet GA, Harrison DW. 2006. Emotion and pain: a functional cerebral systems integration. *Neuropsychology Review* 16:99-121

398. Nicholson R, Buenevar L, Ong J, Gramling S. 2003 Differences in anger expression between individuals with and without headache after controlling for depression and anxiety *Headache* 43:651 - 63

399. Cooper WD, Glover DR, Hormbrey JM, Kimber GR. 1989. Headache and blood pressure: evidence of a close relationship. *J Hum Hypertens* 3:41-4

400. Booth-Kewley S, Vickers RR, Jr. 1994. Associations between major domains of personality and health behavior. *J Pers* 62:281-98

401. Christensen AJ, Smith TW. 1995. Personality and patient adherence: correlates of the five-factor model in renal dialysis. *J Behav Med* 18:305-13

402. Vedel A. 2016. Big Five personality group differences across academic majors: A systematic review. *Pers Indiv Diff* 92:1-10

403. Digman JM. 1997. Higher-order factors of the big five. *J Pers Social Psychol* 73:1246-56

404. Hirsh J, Deyoung G, Peterson J. 2009. Metatraits of the Big Five differentially predict engagement and restraint of behavior. *J Pers* 77:1085-102

405. Larsen RJ. 1992. Neuroticism and selective encoding and recall of symptoms: evidence from a combined concurrent-retrospective study. *J Pers Soc Psychol* 62:480-8

406. Costa P, McCrae R. 1987. Personality assessment in psychosomatic medicine: Value of a trait taxonomy. In *Advances in psychosomatic medicine: Vol. 17. Research paradigms in psychosomatic medicine*, ed. GAW Fava, T.N., 17:pp. 71-82. Basel, Switzerland: Karger.

407. Schneider T. 2004. The role of Neuroticism on psychological and physiological stress responses. *J Exper Soc Psychol* 40:795-804

408. Costa P, McCrae R. 1987. Neuroticism, somatic complaints, and disease: is the bark worse than the bite? *J Pers* 55:299-316

409. Feldman PJ, Cohen S, Doyle WJ, Skoner DP, Gwaltney JM, Jr. 1999. The impact of personality on the reporting of unfounded symptoms and illness. *J Pers Soc Psychol* 77:370-8

410. Shostak BB, Peterson RA. 1990. Effects of Anxiety Sensitivity on Emotional Response to a Stress Task. *Behaviour Research and Therapy* 28:513-21

411. Keogh E, Cochrane M. 2002. Anxiety sensitivity, cognitive biases, and the experience of pain. *J Pain* 3:320-9

412. Norton PJ, Asmundson GJ. 2004. Anxiety sensitivity, fear, and avoidance behavior in headache pain. *Pain* 111:218-23

413. DeYoung C. 2015. Cybernetic Big Five Theory. *J Res Personality* 56:33-58

414. Gray J, McNaughton N. 2000. *The neuropsychology of anxiety: An enquiry into the function of the septo-hippocampal system*. NY: Oxford University Press.

415. Hirsh J, Inzlicht M. 2008. The devil you know: Neuroticism predicts neural response to uncertainty. *Psychol Science* 19:962-7

416. Hodes RL, Howland EW, Lightfoot N, Cleeland CS. 1990. The effects of distraction on responses to cold pressor pain. *Pain* 41:109-14

417. Richards A, French C, Johnson W, Naparstek J, Williams J. 1992. Effects of mood manipulation and anxiety on performance of an emotional Stroop task. *Brit J Psychol* 83:479-91

418. Jonassainta C, Why Y, Bishop G, Tong E, Diong S, et al. 2009. The effects of Neuroticism and Extraversion on cardiovascular reactivity during a mental and an emotional stress task. *Int J Psychophysiol* 74:274-9

419. Salkovskis PM, Campbell P. 1994. Thought suppression induces intrusion in naturally occurring negative intrusive thoughts. *Behav Res Ther* 32:1-8

420. Ode S, Robinson M. 2007. Agreeableness and the Self-Regulation of Negative Affect: Findings Involving the Neuroticism/Somatic Distress Relationship. *Pers Individ Dif* 43:2137–48

421. Canli T, Zhao Z, Whitfield S, Gotlik I, Gabrieli J. 2002. Amygdala response to happy faces as a function of extraversion. *Science* 296:2191

422. Hemphill J. 2003. Interpreting the magnitudes of correlation coefficients. *Amer Psychol* 58:78-9

423. Richard F, Bond C, Stokes-Zoota J. 2003. One hundred years of social psychology quantitatively described. *Rev Gen Psychol* 7:331-63

424. Jorgensen R, Johnson B, Kolodziej M, Schreer G. 1996. Elevated blood pressure and personality: A meta-analytic review. *Psych Bull* 120:293-320

425. Marcussen R, Wolff H. 1949. A formulation of the dynamics of the migraine attack. *Psychosom Med* 11:251-6

426. Sacks O. 1992. *Migraine, 2nd ed (Revised and Expanded)*. Vintage Books.

427. Bowlby J. 1973. *Attachment and loss. Separation: anxiety and anger*. NY: Basic Books.

428. Bowlby J. 1979. *The making and breaking of affectional bonds*. London: Tavistock.

429. Bowlby J. 1969/1982. *Attachment and loss. Attachment.* NY Basic Books.

430. Bowlby J. 1980. *Attachment and Loss. Loss*. NY: Basic Books.

431. Mukilincer M, Florian V. 1998. The relationship between adult attachment styles and emotional and cognitive reactions to stressful events, pp 143-65. In *Attachment theory and close relationships*, ed. J Simpson, S Rholes. NY: Guilford.

432. Mukilincer M, Shaver P. 2007. *Attachment in adulthood: structure, dynamics and change*. NY: Guilford.

433. Hazan C, Shaver P. 1987. Romantic love conceptualized as an attachment process. *J Pers Soc Psychol* 52:511-24

434. Bartholomew K, Horowitz L. 1991. Attachment styles among young adults: a test of a four category model *J Pers Soc Psychol* 61:226–44

435. Griffin D, Bartholomew K. 1994. The metaphysics of measurement: the case of adult attachment in advances in personal relationships, pp.17-52. In *Attachment processes in adulthood*, ed. K Bartholomew, D Perlman. London: Jessica Kingsley.

436. Fraley R, Shaver P. 2000. Adult romantic attachment: theoretical developments, emerging controversies and unanswered questions. *Rev Gen Psychol* 4:132-54

437. Anderson D, Hines R. 1994. Attachment and pain. In *Psychosocial vulnerability to chronic pain*, ed. R Grzesiak, D Ciccone:17-152. NY: Springer.

438. Meredith P, Ownsworth T, Strong J. 2008. A review of the evidence linking adult attachment theory and chronic pain: presenting a conceptual model. *Clin Psychol Rev* 28:407–29

439. Andrews N, Meredith P, Strong J. 2011. Adult attachment and reports of pain in experimetally-induced pain. *Eur J Pain* 15:523-30

440. Meredith P, Strong J, Feeney J. 2006. The relationship of adult attachment to emotion, catastrophizing, control, threshold and tolerance, in experimentally-induced pain. *Pain* 120:44–52

441. Wilson C, Ruben M. 2011. A pain in her arm: romantic attachment orientations and the tourniquet task. *Pers Relationship* 18:242–65

442. Rowe A, Carnelley K, Harwood J, Micklewright D, Russouw L, et al. 2012. The effect of attachment orientation priming on pain sensitivity in pain-free individuals. *J Soc Pers Relat*

443. Mukilincer M, Shaver P. 2003. The attachment behavioral system in adulthood: activation, psychodynamics and interpersonal processes, pp 53-152. In *Advances in experimental social psychology*, ed. M Zanna. NY: Academic Press.

444. Mukilincer M. 1999. Adult attachment style and affect regulation: strategic variation in self-appraisals. *J Pers Soc Psychol* 75:420-35

445. Mikhail S, henderson P, Tasca G. 1994. An interpersonally based model of chronic pain: an application of attachment theory. *Clin Psychol Rev* 14:1-16

446. MacDonald G, Kingsbury R. 2006. Does physical pain augment anxious attachment? . *J Soc Pers Relat* 23:291–304

447. McWilliams L, Asmundson G. 2007. The relationship of adult attachment dimensions to pain-related fear, hypervigilance and catastrophizing. *Pain* 127:27-34

448. Ognibene T, Collins N. 1998. Adult attachment styles, perceived social support and coping strategies. *J Soc Pers Relat* 15:323-45

449. Anders, S, Tucker J. 2000. Ault attachment style, interpersoal commuication competence and social support. *Pers Relationship* 7:379-89

450. Schore A. 2003. *Affect dysregulation and disorders of the self*. WW Norton.

451. Schore A. 1994. *Affect regulation and the origin of the self: the neurobiology of emotional development*. Lawrence Erlbaum, New Jersey.

452. Henry É. 2011. Céphalées chroniques quotidiennes d'origine migraineuse et abus médicamenteux: le rôle central du cortex orbitofrontal. *Doulers* 12:272

453. Lev R, Granovsky Y, Yarnitsky D. 2013. Enhanced pain expectation in migraine: EEG-based evidence for impaired prefrontal function. *Headache* 53:1054–70

454. Pine D, Cohen P, Brook J. 1996. The association between major depression and headache: results of a longitudinal epidemiologic study in youth. *Child Adolesc Psychopharmacol* 6:153-64

455. Merikangas K, Risch N, Merkikangas J, Weissman M, Kidd K. 1988. Migraine and depression: association and familial transmission. *J Psychiatr Res* 22:119-29

456. Fraley RC, Waller NG, Brennan KA. 2000. An item-response theory analysis of self-report measures of adult attachment. *J Pers Soc Psychol* 78:350-65

457. Sibley C, Liu J. 2004. Short-term temporal stability and factor structure of the revised experiences in close relationships (ECR-R) measure of adult attachment. *Pers Indiv Differences* 36:969-75

458. Costa PJ, McCrae R. 1985. *The NEO Personality Inventory manual*. Odessa, FL: Psychological Assessment Resources.

459. Tabachnik B, Fidell L. 2000. *Using Multivariate Statistics (4th ed)*. Allyn & Bacon.

460. Cathcart S, Petkov J, Winefield A, Lushington K, Rolan P. 2010. Central mechanisms of stress-induced headache. *Cephalalgia* 30:285-95

461. Stronks D, Tulen JH, Verheij R, Boomsma F, Fekkes D, et al. 1998. Serotonergic, Catecholaminergic, and Cardiovascular Reactions to Mental Stress in Female Migraine Patients. A Controlled Study. *Headache* 38:270-80

462. Mickelson K, Kessler K, Shaver P. 1997. Adult attachment in a nationally representative sample. *J Pers Soc Psychol* 71:1092-106

463. Hazan C, Shaver PR. 1990. Love and Work, An Attachment-Theoretical Perspective. *J Pers Soc Psychol* 59:270-80

464. Brown J, Sheffield D, Leary M, Robinson M. 2003. Social Support and Experimental Pain. *Psychosom Med* 65:276-83

465. Bartholomew K, Cobb R, Poole J. 1997. Adult attachment patterns and social support processes, pp. 359-377. In *Sourcebook of social support and personality*, ed. G Pierce, B Lakey, I Sarason, B Sarason. NY: Plenum Press.

466. Mukilincer M, Florian V. 1995. Appraisal of and coping with a real-life stressful stiatuion: the contribution of attachment styles. *Pers Soc Psychol Bull* 21:400 -14

467. Tzafrir A, Nadler A, Friedland N. 1996. Attachment styles, self esteem and help-seeking as a function of help's instrumentality. *J Pers Soc Psychol* 21:318-26

468. Kolb L. 1982. Attachment behavior and pain complaints. *Psychosomatics* 23:413-25

469. Dewitte M, De Houwer J, Koster EH, Buysse A. 2007. What's in a name? Attachment-related attentional bias. *Emotion (Washington, D.C.)* 7:535-45

470. Vrticka P, Andersson F, Grandjean D, Sander D, Vuilleumier P. 2008. Individual attachment style modulates human amygdala and striatum activation during social appraisal. *PLoS One* 3:e2868

471. Vrticka P, Vuilleumier P. 2012. Neuroscience of human social interactions and adult attachment style. *Front Hum Neurosci* 6:212

472. Boston A, Sharpe L. 2005. The role of threat-expectancy in acute pain: effects on attentional bias, coping strategy effectiveness and response to pain. *Pain* 119:168-75

473. Eisenberger N. 2011. Why rejection hurts: What social neuroscience has revealed about the brain's response to social rejection. In *The Handbook of Social Neuroscience*, ed. J Decety, J Cacioppo:(p. 586-98). NY: Oxford University Press.

474. Eisenberger N, Jarco J, Lieberman N, Naliboff B. 2006. An experimental study of shared sensitivity to physical pain and social rejection. *Pain* 126:132-8

475. Master S, Eisenberger N, Taylor S, Naliboff B, Shirinyan D, Lieberman N. 2009. A picture's words: Partner photographs reduce experimentally-induced pain. *Psychol Sci* 20:1216-318

476. Gump BB, Polk DE, Kamarck T, Shiffman S. 2001. Partner interactions are associated with reduced blood pressure in the natural environment: Ambulatory monitoring evidence from a healthy, multiethnic adult sample. *Psychosom Med* 63:423-33

477. Seltzer LJ, Ziegler TE, Pollak SD. 2010 Social vocalizations can release oxytocin in humans. *Proc R Soc Lond [Biol]* 277:2661-6

478. Eccleston C. 1995. Chronic pain and distraction: An experimental investigation into the role of sustained and shifting attention in the processing of chronic persistent pain. *Behav Res Ther* 33:391-405

479. Arntz A, Dreesen L, De Jong P. 1994. The influence of anxiety on pain: Attentional and attributional mediators. *Pain* 56:307-14

480. James J, Hardardottir D. 2002. Influence of attention focus and trait anxiety on tolerance of acute pain. *Brit J Health Psych* 7:149 -62

481. McEwen B. 1998. Stress, adaptation, and disease. Allostasis and allostatic load. *Ann Ny Acad Sci* 840:33-44

482. Simpson J, Rholes S, Nelligan J. 1992. Support seeking and support giving within couples in an anxiety-provoking situation: The role of attachment styles. *J Pers Soc Psychol* 62:434-46

483. Schore A. 2003a. *Affect Regulation and the Repair of the Self*. WW Norton.

484. Cohen S, Rodriguez M. 1995. Pathways linking affective disturbances and physical disorders. *Health Psychol* 14:374 - 80

485. Ciechanowski P, Sullivan M, Jensen M, J R, Summers H. 2003. The relationship of attachment style to depression, catastrophizing and health care utilization in patients with chronic pain *Pain* 104:627-37

486. Williams DA, Keefe FJ. 1991. Pain beliefs and the use of cognitive-behavioral coping strategies. *Pain* 46:185-90

487. Greenberg L, Johnson S. 1988. *Emotionally Focused Therapy for Couples*. NY: Guilford Press.

488. Johnson S, Hunsley J, Greenberg L, Schindler D. 1999. Emotionally Focused Couples Therapy: Status and Challenges. *Clin Psychol: Sci Pract* 6:67-79

489. Goadsby PJ. 2002. Pathophysiology of cluster headache: a trigeminal autonomic cephalgia. *Lancet Neurol* 1:251-7

490. Leistad RB, Sand T, Nilsen KB, Westgaard RH, Stovner LJ. 2007. Cardiovascular responses to cognitive stress in patients with migraine and tension-type headache. *BMC Neurol* 7:23

491. Dworkin BR, Elbert T, Rau H, Birbaumer N, Pauli P, et al. 1994. Central effects of baroreceptor activation in humans: attenuation of skeletal reflexes and pain perception. *Proc Natl Acad Sci U S A* 91:6329-33

492. Carroll D. 1992. *Health Pyschology: Stress, Behaviour and Disease*. London: The Palmer Press.

493. Shechter A, Stewart WF, Silberstein SD, Lipton RB. 2002. Migraine and autonomic nervous system function: a population-based, case-control study. *Neurology* 58:422-7

494. Kalser R, Kengeter J, Chaykin N, Cohn D, Silberstein S. 2019. Psychological factors and headache. In *Neurology Medlink*

495. Burg M, Pickering T. 2011. The Cardiovascular System, chapter 3. In *The Handbook of Stress Science: Biology, Psychology, and Health*, ed. R Contrada, A Baum. NY: Springer.

496. Mamontov OV, Babayan L, Amelin AV, Giniatullin R, Kamshilin AA. 2016. Autonomous control of cardiovascular reactivity in patients with episodic and chronic forms of migraine. *J Headache Pain* 17:52

497. Drummond PD. 1985. Vascular-Responses in Headache-Prone Subjects during Stress. *Biological Psychology* 21:11-25

498. Holm J, Lamberty K, McSherry W, Davis P. 1997. The stress response in headache sufferers: Physiological and psychological reactivity. *Headache* 37:221-7

499. Martin PR, Todd J, Reece J. 2005. Effects of noise and a stressor on head pain. *Headache* 45:1353-64

500. Passchier J, Goudswaard P, Orlebeke J, Verhage F. 1990. Are migraine and achievement motivation related? A psychophysiological study of responses to real-life achievement stress in young headache sufferers. *Funct Neurol* 5:135-43

501. Passchier J, van der Helm-Hylkema H, Orlebeke JF. 1984. Psychophysiological characteristics of migraine and tension headache patients. Differential effects of sex and pain state. *Headache* 24:131-9

502. Janeway T. 1913. A clinical study of hypertensive cardiovascular disease. *Arch Intern Med* 12:755-98

503. Featherstone HJ. 1985. Medical Diagnoses and Problems in Individuals with Recurrent Idiopathic Headaches. *Headache* 25:136-40

504. Baldrati A, Bini L, D'Alessandro R, Cortelli P, de Capoa D, et al. 1985. Analysis of outcome predictors of migraine towards chronicity. *Cephalalgia* 5 Suppl 2:195-9

505. Cirillo M, Stellato D, Lombardi C, De Santo NG, Covelli V. 1999. Headache and cardiovascular risk factors: positive association with hypertension. *Headache* 39:409-16

506. Paterna S, Di Pasquale P, D'Angelo A, Seidita G, Tuttolomondo A, et al. 2000. Angiotensin-converting enzyme gene deletion polymorphism determines an increase in frequency of migraine attacks in patients suffering from migraine without aura. *Eur Neurol* 43:133-6

507. Schrader H, Stovner L, Helde G, Sand T, Bovim G. 2001. Prophylactic treatment of migraine with angiotensin converting enzyme inhibitor (lisinopril): randomised, placebo controlled, crossover study. *BMJ* 322:19-22

508. Sliwka U, Harscher S, Diehl RR, van Schayck R, Niesen WD, Weiller C. 2001. Spontaneous oscillations in cerebral blood flow velocity give evidence of different autonomic dysfunctions in various types of headache. *Headache* 41:157-63

509. Chen TC, Leviton A, Edelstein S, Ellenberg JH. 1987. Migraine and Other Diseases in Women of Reproductive Age - the Influence of Smoking on Observed Associations. *Arch Neurol-Chicago* 44:1024-8

510. Wiehe M, Fuchs SC, Moreira LB, Moraes RS, Fuchs FD. 2002. Migraine is more frequent in individuals with optimal and normal blood pressure: a population-based study. *J Hypertens* 20:1303-6

511. Hagen K, Stovner LJ, Vatten L, Holmen J, Zwart JA, Bovim G. 2002. Blood pressure and risk of headache: a prospective study of 22 685 adults in Norway. *J Neurol Neurosur Ps* 72:463-6

512. Secil Y, Unde C, Beckmann YY, Bozkaya YT, Ozerkan F, Basoglu M. 2010. Blood pressure changes in migraine patients before, during and after migraine attacks. *Pain practice : the official journal of World Institute of Pain* 10:222-7

513. Bruehl S, Chung OY, Ward P, Johnson B, McCubbin JA. 2002. The relationship between resting blood pressure and acute pain sensitivity in healthy normotensives and chronic back pain sufferers: the effects of opioid blockade. *Pain* 100:191-201

514. Ghione S. 1996. Hypertension-associated hypalgesia. Evidence in experimental animals and humans, pathophysiological mechanisms, and potential clinical consequences. *Hypertension* 28:494-504

515. Schobel HP, Ringkamp M, Behrmann A, Forster C, Schmieder RE, Handwerker HO. 1996. Hemodynamic and sympathetic nerve responses to painful stimuli in normotensive and borderline hypertensive subjects. *Pain* 66:117-24

516. al'Absi M, Petersen K, Wittmers L. 2000. Blood pressure but not parental history for hypertension predicts pain perception in women. *Pain* 88:61-8

517. Hamed S. nd. *Blood pressure changes in patients with migraine: Evidences, controversial views and potential mechanisms of comorbidity*.

518. Shevel E. 2011. The extracranial vascular theory of migraine--a great story confirmed by the facts. *Headache* 51:409-17

519. Shevel E. 2011. The extracranial vascular theory of migraine: an artificial controversy. *J Neural Transm (Vienna)* 118:525-30

520. Ray B, Wolff H. 1940. Experimental studies on headache. Pain-sensitive structures of the head and their significance in headache. *Arch Surg* 41:813-56

521. Jorum E, Orstavik K, Schmidt R, Namer B, Carr RW, et al. 2007. Catecholamine-induced excitation of nociceptors in sympathetically maintained pain. *Pain* 127:296-301

522. Adams HE, Feuerstein M, Fowler JL. 1980. Migraine headache: review of parameters, etiology, and intervention. *Psychol Bull* 87:217-37

523. Arena JG, Blanchard EB, Andrasik F, Appelbaum K, Myers PE. 1985. Psychophysiological comparisons of three kinds of headache subjects during and between headache states: analysis of post-stress adaptation periods. *J Psychosom Res* 29:427-41

524. McCaffrey RJ, Goetsch VL, Robinson J, Isaac W. 1986. Differential responsivity of the vasomotor response system to a "novel" stressor. *Headache* 26:240-2

525. Gannon LR, Haynes SN, Cuevas J, Chavez R. 1987. Psychophysiological correlates of induced headaches. *J Behav Med* 10:411-23

526. Haynes SN, Gannon LR, Bank J, Shelton D, Goodwin J. 1990. Cephalic blood flow correlates of induced headaches. *J Behav Med* 13:467-80

527. Lehrer PM, Murphy AI. 1991. Stress reactivity and perception of pain among tension headache sufferers. *Behav Res Ther* 29:61-9

528. Pogacnik T, Sega S, Mesec A, Kiauta T. 1993. Autonomic function testing in patients with tension-type headache. *Headache* 33:63-8

529. Rojahn J, Gerhards F. 1986. Subjective stress sensitivity and physiological responses to an aversive auditory stimulus in migraine and control subjects. *J Behav Med* 9:203-12

530. Havanka-Kanniainen H. 1986. Cardiovascular reflex responses during migraine attack. *Headache* 26:442-6

531. Havanka-Kanniainen H, Tolonen U, Myllyla VV. 1986. Autonomic dysfunction in adult migraineurs. *Headache* 26:425-30

532. Havanka-Kanniainen H, Tolonen U, Myllyla VV. 1988. Autonomic dysfunction in migraine: a survey of 188 patients. *Headache* 28:465-70

533. Anderson CD, Stoyva JM, Vaughn LJ. 1982. A test of delayed recovery following stressful stimulation in four psychosomatic disorders. *J Psychosom Res* 26:571-80

534. Andrasik F, Blanchard EB, Arena JG, Saunders NL, Barron KD. 1982. Psychophysiology of Recurrent Headache - Methodological Issues and New Empirical-Findings. *Behavior Therapy* 13:407-29

535. Cohen RA, Williamson DA, Monguillot JE, Hutchinson PC, Gottlieb J, Waters WF. 1983. Psychophysiological response patterns in vascular and muscle-contraction headaches. *J Behav Med* 6:93-107

536. Philips HC, Hunter MS. 1982. A psychophysiological investigation of tension headache. *Headache* 22:173-9

537. Mikamo K, Takeshima T, Takahashi K. 1989. Cardiovascular sympathetic hypofunction in muscle contraction headache and migraine. *Headache* 29:86-9

538. Feuerstein M, Bortolussi L, Houle M, Labbe E. 1983. Stress, temporal artery activity, and pain in migraine headache: a prospective analysis. *Headache* 23:296-304

539. Feuerstein M, Bush C, Corbisiero R. 1982. Stress and chronic headache: a psychophysiological analysis of mechanisms. *J Psychosom Res* 26:167-82

540. Cohen MJ, Rickles WH, McArthur DL. 1978. Evidence for physiological response stereotypy in migraine headache. *Psychosom Med* 40:344-54

541. Anderson CD, Franks RD. 1981. Migraine and tension headache: is there a physiological difference? *Headache* 21:63-71

542. Pritchard DW, Wood MM. 1983. EMG levels in the occipitofrontalis muscles under an experimental stress condition. *Biofeedback Self Regul* 8:165-75

543. Leistad RB, Stovner LJ, White LR, Nilsen KB, Westgaard RH, Sand T. 2007. Noradrenaline and cortisol changes in response to low-grade cognitive stress differ in migraine and tension-type headache. *J Headache Pain* 8:157-66

544. Morley S, Hunter M. 1983. Temporal artery pulse amplitude wave shapes in migraineurs: a methodological investigation. *J Psychosom Res* 27:485-92

545. Yeager MP, Pioli PA, Guyre PM. 2011. Cortisol exerts bi-phasic regulation of inflammation in humans. *Dose Response* 9:332-47

546. Geiss A, Varadi E, Steinbach K, Bauer H, Anton F. 1997. Psychoneuroimmunological correlates of persisting sciatic pain in patients who underwent discectomy *Neuroscience Letters* 237:65-8

547. Lippi G, Mattiuzzi C. 2017. Cortisol and migraine: A systematic literature review. *Agri* 29:95-9

548. Peres MF, Sanchez del Rio M, Seabra ML, Tufik S, Abucham J, et al. 2001. Hypothalamic involvement in chronic migraine. *J Neurol Neurosurg Psychiatry* 71:747-51

549. Rainero I, Ferrero M, Rubino E, Valfre W, Pellegrino M, et al. 2006. Endocrine function is altered in chronic migraine patients with medication-overuse. *Headache* 46:597-603

550. Akerman S, Holland PR, Goadsby PJ. 2011. Diencephalic and brainstem mechanisms in migraine. *Nature reviews. Neuroscience* 12:570-84

551. May A, Goadsby PJ. 1999. The trigeminovascular system in humans: pathophysiologic implications for primary headache syndromes of the neural influences on the cerebral circulation. *J Cereb Blood Flow Metab* 19:115-27

552. Kimura J. 2001. Studies of the facial nerve and the blink reflex. In *Electrodiagnosis in diseases of nerve and muscle: Principles and practice (4th ed)*, ed. J Kimura:409-38. NY: Oxford University Press.

553. Harris J. 1943. Habituatory response decrement in the intact organism. *Psych Bull* 40:385–422

554. Groves PM, Thompson RF. 1970. Habituation: a dual-process theory. *Psychol Rev* 77:419-50

555. Valeriani M, de Tommaso M, Restuccia D, Le Pera D, Guido M, et al. 2003. Reduced habituation to experimental pain in migraine patients: a CO(2) laser evoked potential study. *Pain* 105:57-64

556. Sand T, Zwart JA. 1994. The blink reflex in chronic tension-type headache, migraine, and cervicogenic headache. *Cephalalgia* 14:447-50; discussion 394-5

557. de Tommaso M, Guido M, Libro G, Sciruicchio V, Puca F. 2000. The three responses of the blink reflex in adult and juvenile migraine. *Acta Neurologica Belgica* 100:96-102

558. Coppola G, Pierelli F, Schoenen J. 2009. Habituation and migraine. *Neurobiol Learn Mem* 92:249-59

559. Sandrini G, Tassorelli C, Cecchini A, Alfonsi E, Nappi G. 2002. Effects of nimesulide on nitric oxide-induced hyperalgesia in humans – a neurophysiological study. *Eur J Pharmacol* 450:259–62

560. Ellrich J, Treede R. 1998. Characterization of blink reflex interneurons by activation of diffuse noxious inhibitory controls in man. *Brain Res* 803:161–8

561. Schoenen J. 1998. Cortical electrophysiology in migraine and possible pathogenetic implications. *Clin Neurosci* 5:10-7

562. Schoenen J, Wang W, Albert A, Delwaide PJ. 1995. Potentiation instead of habituation characterizes visual evoked potentials in migraine patients between attacks. *Eur J Neurol* 2:115-22

563. de Tommaso M, Murasecco D, Libro G, Guido M, Sciruicchio V, et al. 2002. Modulation of trigeminal reflex excitability in migraine: effects of attention and habituation on the blink reflex. *Int J Psychophysiol* 44:239-49

564. De Marinis M, Pujia A, Natale L, D'Arcangelo E, Accornero N. 2003. Decreased habituation of the R2 component of the blink reflex in migraine patients. *Clin Neurophysiol* 114:889-93

565. Bank J, Bense E, Kiraly C. 1992. The blink reflex in migraine. *Cephalalgia* 12:289-92

566. Polat B, Aysal F, Ozturk M, Mutluay B, Altunkaynak Y, et al. 2018. Blink Reflex in Episodic and Chronic Migraine. *Noro Psikiyatr Ars* 55:146-51

567. Welch KM. 2003. Contemporary concepts of migraine pathogenesis. *Neurology* 61:S2-8

568. Peddireddy A, Wang K, Svensson P, Arendt-Nielsen L. 2009. Blink reflexes in chronic tension-type headache patients and healthy controls. *Clin Neurophysiol* 120:1711-6

569. Ambrosini A, Schoenen J. 2003. The electrophysiology of migraine. *Curr Opin Neurol* 16:327-31

570. de Tommaso M, Losito L, Difruscolo O, Libro G, Guido M, Livrea P. 2005. Changes in cortical processing of pain in chronic migraine. *Headache* 45:1208-18

571. Dijckmans B, Tortosa-Martínez J, Caus N, González-Caballero G, Martínez-Pelegrin B, et al. 2017. Does the diurnal cycle of cortisol explain the relationship between physical performance and cognitive function in older adults? *Eur Rev Aging Phys Act* 14:6-

572. Payne J. 2004. A Neuroendocrine-Based Regulatory Fatigue Model. *Biol Res Nursing* 6:141-50

573. Ellrich J, Bromm B, Hopf HC. 1997. Pain-evoked blink reflex. *Muscle Nerve* 20:265-70

574. Tepper S. April, 2003. *Abstracts and Citations: Comment following Lipton, RB et al, p. 423*. https://headachejournal.onlinelibrary.wiley.com/doi/pdf/10.1046/j.1526-4610.2003.03085_1.x

575. Boelhouwer AJ, Brunia CH. 1977. Blink reflexes and the state of arousal. *J Neurol, Neurosurg, Psychiat* 40:58-63

576. Gregoric M. 1973. Habituation of the blink reflex (role of selective attention), pp. 673-677. In *New Developments in Electromyography and Clinical Neurophysiology*, ed. J Desmedt, 3. Basel: Karger.

577. DiSabato DJ, Quan N, Godbout JP. 2016. Neuroinflammation: the devil is in the details. *J Neurochem* 139 Suppl 2:136-53

578. D'Antono B, Ditto B, Sita A, Miller SB. 2000. Cardiopulmonary baroreflex stimulation and blood pressure-related hypoalgesia. *Biol Psychol* 53:217-31

579. Russell E, Koren G, Rieder M, Van Uum S. 2012. Hair cortisol as a biological marker of chronic stress: Current status, future directions and unanswered questions. *Psychoneuroendocrinology* 37:589-601

580. Woolf CJ. 2011. Central sensitization: implications for the diagnosis and treatment of pain. *Pain* 152:S2-15

581. Cruccu G, Iannetti GD, Marx JJ, Thoemke F, Truini A, et al. 2005. Brainstem reflex circuits revisited. *Brain* 128:386-94

582. Malmo RB, Shagass C. 1949. Physiologic study of symptom mechanisms in psychiatric patients under stress. *Psychosom Med* 11:25-9

583. Sternbach R. 1966. *Principles of Psychophysiology: An introductory text and readings*. NY: Academic Press.

584. Kuritzky A. 1987. Autonomic nervous system imbalance in migraineurs. *Cephalalgia* 7 Suppl 6:539-41

585. Price K, Tursky B. 1975. The effect of varying stimulus parameters on judgments of nociceptive electrical stimulation. *Psychophysiology* 12:663-6

586. Bibbey A, Carroll D, Roseboom TJ, Phillips AC, de Rooij SR. 2013. Personality and physiological reactions to acute psychological stress. *Int J Psychophysiol* 90:28-36

587. Bibbey A, Ginty AT, Brindle RC, Phillips AC, Carroll D. 2016. Blunted cardiac stress reactors exhibit relatively high levels of behavioural impulsivity. *Physiol Behav* 159:40-4

588. Martin PR, Nathan PR, Milech D, van Keppel M. 1988. The relationship between headaches and mood. *Behav Res Ther* 26:353-6

589. Martin PR. 2016. Stress and Primary Headache: Review of the Research and Clinical Management. *Curr Pain Headache Rep* 20:45

590. Frew AK, Drummond PD. 2007. Negative affect, pain and sex: the role of endogenous opioids. *Pain* 132 Suppl 1:S77-85

591. Frew AK, Drummond PD. 2008. Stress-evoked opioid release inhibits pain in major depressive disorder. *Pain* 139:284-92

592. Smith AP. 2016. Acute tension-type headaches are associated with impaired cognitive function and more negative mood. *Frontiers in Neurology* 7

593. Karlson CW, Litzenburg CC, Sampilo ML, Rapoff MA, Connelly M, et al. 2013. Relationship between daily mood and migraine in children. *Headache* 53:1624-34

594. Massey EK, Garnefski N, Gebhardt WA, van der Leeden R. 2009. Daily frustration, cognitive coping and coping efficacy in adolescent headache: a daily diary study. *Headache* 49:1198-205

595. Noseda R, Constandil L, Bourgeais L, Chalus M, Villanueva L. 2010. Changes of meningeal excitability mediated by corticotrigeminal networks: a link for the endogenous modulation of migraine pain. *J Neurosci* 30:14420-9

596. Villanueva L. 2012. How does migraine attack stop? *Headache* 52:188

597. Bandura A, O'Leary A, Taylor CB, Gauthier J, Gossard D. 1987. Perceived self-efficacy and pain control: opioid and nonopioid mechanisms. *J Pers Soc Psychol* 53:563-71

598. Berry JK, Drummond PD. 2014. Does attachment anxiety increase vulnerability to headache? *J Psychosom Res* 76:113-20

599. Shirtcliff EA, Granger DA, Schwartz E, Curran MJ. 2001. Use of salivary biomarkers in biobehavioral research: cotton-based sample collection methods can interfere with salivary immunoassay results. *Psychoneuroendocrinology* 26:165-73

600. Kalman BA, Grahn RE. 2004. Measuring salivary cortisol in the behavioral neuroscience laboratory. *J Undergrad Neurosci Educ* 2:A41-9

601. Drummond PD, Granston A. 2004. Facial pain increases nausea and headache during motion sickness in migraine sufferers. *Brain* 127:526-34

602. de Ridder D, Kuijer R. 2006. Managing immediate needs in the pursuit of health goals: The role of coping in self-regulation. In *Self-regulation in health behavior (Chapter 7)*, ed. D de Ridder, J de Wit. Chichester, England: John Wiley & Sons.

603. Fiedler K. 2000. Towards an integrative account of affect and cognition phenomena using the BIAS computer algorithm. In *Feeling and thinking: The role of affect and social cognition (pp 163-185)*, ed. J Forgas. Mahwah NJ: Erlbaum.

604. Fiedler K. 2001. Affective influences on social information processing. In *The Handbook of Affect and Social Cognition (pp 163-185)*, ed. J Forgas. Mahwah, NJ: Erlbaum.

605. Viana M, Nappi G. 2014. Chronobiological correlates of headache: three decades on. *Funct Neurol* 29:213-4

606. Brandtstadter J, Renner G. 1990. Tenacious goal pursuit and flexible goal adjustment: explication and age-related analysis of assimilative and accommodative strategies of coping. *Psychol Aging* 5:58-67

607. Schoonan G, Evers D, Ballieux B, Geus E, de Kloet E, et al. 2007. Is stress a trigger factor for migraine? *Psychoneuroendocrinology* 32:532-8

608. Cathcart S, Bhullar N, Immink M, Della Vedova C, Hayball J. 2012. Pain sensitivity mediates the relationship between stress and headache intensity in chronic tension-type headache. *Pain Res Manag* 17:377-80

609. Di Sabato F, Buonfiglio M, Mandillo S. 2013. Analytic information processing style in migraineurs. *Neurol Sci* 34:1145-50

610. Harrigan JA, Kues JR, Ricks DF, Smith R. 1984. Moods that predict coming migraine headaches. *Pain* 20:385-96

611. Andrews N, Strong J, Meredith P. 2015. Overactivity in chronic pain: Is it a valid construct? *Pain*

612. Fox SD, Flynn E, Allen RH. 2011. Mindfulness meditation for women with chronic pelvic pain: a pilot study. *J Reprod Med* 56:158-62

613. Santangelo G, Russo A, Trojano L, Falco F, Marcuccio L, et al. 2016. Cognitive dysfunctions and psychological symptoms in migraine without aura: a cross-sectional study. *J Headache Pain* 17:76

614. Santangelo G, Russo A, Tessitore A, Garramone F, Silvestro M, et al. 2018. Prospective memory is dysfunctional in migraine without aura. *Cephalalgia* 38:1825-32

615. Lazarus R, Launier R. 1978. Stress-related transactions between person and environment. In *Perspectives in Interactional Psychology*, ed. L Pervin:287-327. NY: Springer.

616. Repetti R. 1993. Short-term effects of occupational stressors on daily mood and health complaints. *Health Psychology* 12:125-31

617. Hamilton-Webb A, Naylor R, Manning L, Conway J. 2019. 'Living on the edge': using cognitive filters to appraise experience of environmental risk. *J Risk Res* 22:303-19

618. Grimley DM, Williams CD, Miree LL, Baichoo S, Greene S, Hook EW. 2000. Stages of readiness for changing multiple risk behaviors among incarcerated male adolescents. *Am J Health Behav* 24:361-9

619. Demski C, Capstick S, Pidgeon N, Sponsato R, Spence A. 2016. Experience of extreme weather affects climate change mitigation and adaptation responses. *Climatic Change* 140:149-64

620. Bottos S, Dewey D. 2004. Perfectionists' appraisal of daily hassles and chronic headache. *Headache* 44:772-9

621. Wethington E, Almeida D, Brown G, Frank E, Kessler R. 2001. The assessment of stressor exposure. In *Assessment in Behavioral medicine*, ed. A Vingerhoets, 5: Brunner Routledge.

622. Scharff L, Turk DC, Marcus DA. 1995. The relationship of locus of control and psychosocial-behavioral response in chronic headache. *Headache* 35:527-33

623. Hudzynski L, Levenson H. 1985. Biofeedback behavioral treatment of headache with locus of control pain analysis: A 20-month retrospective study. *Headache* 25:380-6

624. Martin NJ, Holroyd KA, Penzien DB. 1990. The headache-specific locus of control scale: adaptation to recurrent headaches. *Headache* 30:729-34

625. Marlowe N. 1998. Stressful events, appraisal, coping and recurrent headache. *J Clin Psychol* 54:247-56

626. Martin NJ, Holroyd KA, Rokicki LA. 1993. The Headache Self-Efficacy Scale: adaptation to recurrent headaches. *Headache* 33:244-8

627. Eccleston C, Crombez G. 1999. Pain demands attention: a cognitive-affective model of the interruptive function of pain. *Psychol Bull* 125:356-66

628. Müller M. 2012. Will it hurt less if I believe I can control it? Influence of actual and perceived control on perceived pain intensity in healthy male individuals: a randomized controlled study. *J Behav Med* 35:529-37

629. Vancleef L, Peters M. 2011. The influence of perceived control and self-efficacy on the sensory evaluation of experimentally induced pain. *J Behav Therap Exper Psych* 42:511-17

630. Anderson K, Dowds B, Pelletz R, Edwards W, Peeters-Asdourian C. 1995. Development and initial validation of a scale to measure self-efficacy beliefs in patients with chronic pain. *Pain* 63:77-84

631. Maizels M. 2005. Why should physicians care about behavioral research? *Headache* 45:411-3

632. Nicholson RA, Hursey KG, Nash JM. 2005. Moderators and mediators of behavioral treatment for headache. *Headache* 45:513-9

633. Penzien DB, Rains JC, Lipchik GL, Nicholson RA, Lake AE, 3rd, Hursey KG. 2005. Future directions in behavioral headache research: applications for an evolving health care environment. *Headache* 45:526-34

634. Smith T, Nicholson R. 2006. Are changes in cognitive and emotional factors important in improving headache impact and quality of life? *Headache* 46:878

635. David J, Suls J. 1999. Coping efforts in daily life: role of big five traits and problem appraisals. *J Pers* 67:265-94

636. O'Brien TB, DeLongis A. 1996. The interactional context of problem-, emotion-, and relationship-focused coping: the role of the big five personality factors. *J Pers* 64:775-813

637. Hooker K, Frazier L, Monahan D. 1994. Personality and coping among caregivers of spouses with dementia. *Gerontologist* 34:386-92

638. McCrae R, Costa P. 1986. Personality, coping and effectiveness in an adult sample. *J Pers* 54:385–405

639. Watson D, Hubbard B. 1996. Adaptational style and dispositional structure: Coping in the context of the Five-Factor model. *J Personality* 64:737-74

640. Smith C, Lazarus R. 1990. Emotion and adaptation. In *Handbook of personality: Theory and research (pp 609-637)*, ed. L Pervin. NY: Guilford Press.

641. Lazarus RS. 1991. Cognition and motivation in emotion. *The American psychologist* 46:352-67

642. Holahan CJ, Moos RH, Holahan CK, Brennan PL, Schutte KK. 2005. Stress generation, avoidance coping, and depressive symptoms: a 10-year model. *J Consult Clin Psychol* 73:658-66

643. van Berkel H. 2009. *The Relationship Between Personality, Coping Styles and Stress, Anxiety and Depression*. Canterbury

644. Carver C, Scheier M. 1999. Stress, coping and self-regulatory processes, pp 553-575. In *Handbook of Personality: Theory and Research*, ed. L Pervin, O John. NY: Guilford.

645. Connor-Smith JK, Flachsbart C. 2007. Relations between personality and coping: A meta-analysis. *J Personal Social Psychol* 93:1080-107

646. Morone NE, Rollman BL, Moore CG, Li Q, Weiner DK. 2009. A mind-body program for older adults with chronic low back pain: results of a pilot study. *Pain Med* 10:1395-407

647. Hanley MA, Raichle K, Jensen M, Cardenas DD. 2008. Pain catastrophizing and beliefs predict changes in pain interference and psychological functioning in persons with spinal cord injury. *J Pain* 9:863-71

648. Flor H, Turk DC. 1989. Psychophysiology of chronic pain: do chronic pain patients exhibit symptom-specific psychophysiological responses? *Psychol Bull* 105:215-59

649. Dolce JJ. 1987. Self-efficacy and disability beliefs in behavioral treatment of pain. *Behav Res Ther* 25:289-99

650. Litt MD. 1988. Self-efficacy and perceived control: cognitive mediators of pain tolerance. *J Pers Soc Psychol* 54:149-60

651. Baird AJ, Haslam RA. 2013. Exploring Differences in Pain Beliefs Within and Between a Large Nonclinical (Workplace) Population and a Clinical (Chronic Low Back Pain) Population Using the Pain Beliefs Questionnaire. *Physical Therapy* 93:1615-24

652. Gallagher D. 1990. Extraversion, neuroticism and appraisal of stressful academic events. *Personality Indiv Differences* 11:1053-7

653. Minarik ML, Ahrens AH. 1996. Relations of eating behavior and symptoms of depression and anxiety to the dimensions of perfectionism among undergraduate women. *Cognitive Ther Res* 20:155-69

654. Hewitt PL, Flett GL. 1991. Perfectionism in the Self and Social Contexts - Conceptualization, Assessment, and Association with Psychopathology. *J Pers Soc Psychol* 60:456-70

655. Johnson M. 2003. The vulnerability status of neuroticism: over-reporting or genuine complaints? *Pers Indiv Differ* 35:877-87

656. Roth R, Cohen S. 1986. Approach avoidance and coping with stress. *American Psychologist* 41:813-19

657. Norris C, Larsen J, Cacioppo J. 2007. Neuroticism is associated with larger and more prolonged electrodermal responses to emotionally evocative pictures. *Psychophysiology* 44:823-6

658. Johnson E, Gentry W. 1992. Personality, elevated blood pressure, and essential hypertension: A research agenda (pp. 319-334). . In *Series in health psychology and behavioral medicine* ed. E Johnson, W Gentry, S Julius. Washington DC: Hemisphere Publishing Corp.

659. Tangney J, Baumeister R, Boone A. 2004. High self-control predicts good adjustment, less pathology, better grades, and interpersonal success. *J Personality* 72:271-322

660. Jang K, Hu S, Livesley W, Angleitner A, Riemann R, et al. 2001. Covariance structure of neuroticism and agreeableness: A twin and molecular genetic analysis of the role of the serotonin transporter gene. *J Pers Soc Psychol* 81:295–304

661. Onaya T, Ishii M, Katoh H, Shimizu S, Kasai H, et al. 2013. Predictive index for the onset of medication overuse headache in migraine patients. *Neurol Sci* 34:85

662. Shaver P, Mukilincer M. 2014. Adult attachment and emotion regulation, pp 237-250. In *Handbook of Emotion Regulation*, ed. J Gross:237-50. NY: The Guilford Press.

663. Folkman S, Lazarus R. 1985. If it changes it must be a process: Study of emotion and coping during three stages of a college examination. *J Pers Soc Psychol* 48:150-70

664. Lazarus RS. 1993. Coping theory and research: past, present, and future. *Psychosom Med* 55:234-47

665. Hayes A. 2018. *Introduction to Mediation, Moderation and Conditional Process Analysis: A regression-based approach (2nd ed)*. NY: The Guilford Press.

666. Baliki MN, Apkarian AV. 2015. Nociception, Pain, Negative Moods, and Behavior Selection. *Neuron* 87:474-91

667. Lockenhoff CE, Duberstein PR, Friedman B, Costa PT, Jr. 2011. Five-factor personality traits and subjective health among caregivers: the role of caregiver strain and self-efficacy. *Psychol Aging* 26:592-604

668. Robinson M, BM W, Meier B. 2008. Approach, avoidance, and self-regulatory conflict: An individual differences perspective. *J Exp soc Psychol* 44:65-79

669. Schrooten MGS, Wiech K, Vlaeyen JWS. 2014. When Pain Meets... Pain-Related Choice Behavior and Pain Perception in Different Goal Conflict Situations. *J Pain* 15:1166-78

670. Miller N, ed. 1944. *Experimental studies of conflict, pp 431-465*. Oxford: Ronald press.

671. Coats EJ, JanoffBulman R, Alpert N. 1996. Approach versus avoidance goals: Differences in self-evaluation and well-being. *Pers Soc Psychol B* 22:1057-67

672. Bandell-Hoekstra I, Abu-Saad H, Passchier J, Frederiks C, Feron F, Knipschild P. 2002. Coping and Quality of Life in relation to headache in Dutch schoolchildren. *Eur J Pain* 6:315-21

673. Resick P, Monson C, Chard K. 2017. *Cognitive Processing Therapy for PTSD: A comprehensive manual*. NY: Guilford.

674. Emmons R, King L, Sheldon K. 1993. Goal conflict and the self-regulation of action. In *Handbook of mental control (pp 528-551)*, ed. D Wegner, J Pennebaker. Upper Saddle River, NJ: Prentice-Hall.

675. Hayes S. 2016. Acceptance and Commitment Therapy, Relationship Frame Theory and the Third Wave of Behavioural and Cognitive Therapies. *Behav Ther* 47:869-85

676. Chiros C, O'Brien WH. 2011. Acceptance, appraisals, and coping in relation to migraine headache: an evaluation of interrelationships using daily diary methods. *J Behav Med* 34:307-20

677. Lillis J, Thomas JG, Lipton RB, Rathier L, Roth J, et al. 2019. The Association of Changes in Pain Acceptance and Headache-Related Disability. *Annals of behavioral medicine : a publication of the Society of Behavioral Medicine* 53:686-90

678. McCracken LM. 1998. Learning to live with the pain: acceptance of pain predicts adjustment in persons with chronic pain. *Pain* 74:21-7

679. Viane I, Crombez G, Eccleston C, Poppe C, Devulder J, et al. 2003. Acceptance of pain is an independent predictor of mental well-being in patients with chronic pain: empirical evidence and reappraisal. *Pain* 106:65-72

680. Burns KM, Burns NR, Ward L. 2016. Confidence-More a Personality or Ability Trait? It Depends on How It Is Measured: A Comparison of Young and Older Adults. *Front Psychol* 7:518-

681. Hahn SE, Smith CS. 1999. Daily hassles and chronic stressors: conceptual and measurement issues. *Stress Med* 15:89-101

682. Serido J, Almeida DM, Wethington E. 2004. Chronic stressors and daily hassles: unique and interactive relationships with psychological distress. *J Health Soc Behav* 45:17-33

683. Massey E, Garnefski N, Gebhardt W, Van der Leeden R. 2011. A daily diary study on the independent and interactive effects of headache and self-regulatory factors on daily affect among adolescents. *Brit J Health Psych* 16:288-99

684. Gross J. 1998. Antecedent- and response-focused emotion regulation: divergent consequences for experience, expression and physiology. *J Pers Soc Psychol* 74:224-37

685. Ochsner KN, Gross JJ. 2005. The cognitive control of emotion. *Trends in cognitive sciences* 9:242-9

686. Lorenz J, Minoshima S, Casey KL. 2003. Keeping pain out of mind: the role of the dorsolateral prefrontal cortex in pain modulation. *Brain* 126:1079-91

687. Beecher HK. 1959. Generalization from pain of various types and diverse origins. *Science* 130:267-8

688. Kalisch R, Wiech K, Critchley HD, Seymour B, O'Doherty JP, et al. 2005. Anxiety reduction through detachment: subjective, physiological, and neural effects. *J Cogn Neurosci* 17:874-83

689. Kalisch R, Wiech K, Herrmann K, Dolan RJ. 2006. Neural correlates of self-distraction from anxiety and a process model of cognitive emotion regulation. *J Cogn Neurosci* 18:1266-76

690. Tanji J, Hoshi E. 2008. Role of the lateral prefrontal cortex in executive behavioral control. *Physiol Rev* 88:37-57

691. Sullivan M, Wideman T. 2011. Pain catastrophizing and fear of movement: detection and intervention. In *Clinical Pain Management: A Practical Guide, 1st edition*, ed. M Luynch, K Craig, P Peng: Blackwell.

692. Buenaver LF, Edwards RR, Smith MT, Gramling SE, Haythornthwaite JA. 2008. Catastrophizing and pain-coping in young adults: associations with depressive symptoms and headache pain. *J Pain* 9:311-9

693. Edwards RR, Smith MT, Stonerock G, Haythornthwaite JA. 2006. Pain-related catastrophizing in healthy women is associated with greater temporal summation of and reduced habituation to thermal pain. *Clin J Pain* 22:730-7

694. Passchier J, Mourik J, Brienen J, Hunfield J. 1998. Cognitions, emotions and behavior of patients with migraine when taking medication during an attack. *Headache* 38:458-64

695. Sorbi M, Tellegen B, Dulong A. 1989. Long-term effects of training in relaxation and stress-coping in patients with migraine - A 3-year follow up. *Headache* 29:111-21

696. Materazzo F, Cathcart S, Pritchard D. 2000. Anger, depression, and coping interactions in headache activity and adjustment: a controlled study. *J Psychosom Res* 49:69-75

697. Huber D, Henrich G. 2003. Personality traits and stress sensitivity in migraine patients. *Behav Med* 29:4-13

698. Wenzlaff R, Wegner D. 2000. Thought suppression. *Ann Rev Psychol* 51:59-91

699. Burns JW, Bruehl S, Caceres C. 2004. Anger management style, blood pressure reactivity, and acute pain sensitivity: evidence for "Trait x Situation" models. *Ann Behav Med* 27:195-204

700. Burns JW, Quartana PJ, Bruehl S. 2009. Anger management style moderates effects of attention strategy during acute pain induction on physiological responses to subsequent mental stress and recovery: a comparison of chronic pain patients and healthy nonpatients. *Psychosom Med* 71:454-62

701. Quartana P, Burns J. 2007. Painful consequences of anger suppression. *Emotion (Washington, D.C.)* 7:400-14

702. Quartana P, Yoon K, Burns J. 2007. Anger suppression, ironic processes and pain. *J Behav Med* 30:455-69

703. Thorn BE, Rich MA, Boothby JL. 1999. Pain beliefs and coping attempts - Conceptual model building. *Pain Forum* 8:169-71

704. Amat J, Baratta M, Paul E, Bland S, Watkins L, Maier S. 2005. Medial prefrontal cortex determines how stressor controllability affects behavior and dorsal raphe nucleus. *Nat Neurosci* 8:365-71

705. Fernandez E, Turk DC. 1989. The utility of cognitive coping strategies for altering pain perception: a meta-analysis. *Pain* 38:123-35

706. Gross J, Richards J, John O. 2006. Emotion regulation in everyday life. In *Emotion regulation in couples and families: Pathways to dysfunction and health (pp. 13-35)*, ed. D Snyder, J Simpson, J Hughes. Wahsington, DC: American Psychological Association.

707. Goldin PR, McRae K, Ramel W, Gross JJ. 2008. The neural bases of emotion regulation: reappraisal and suppression of negative emotion. *Biol Psychiatry* 63:577-86

708. Gross JJ, John OP. 2003. Individual differences in two emotion regulation processes: implications for affect, relationships, and well-being. *J Pers Soc Psychol* 85:348-62

709. Gross JJ, Levenson RW. 1993. Emotional suppression: physiology, self-report, and expressive behavior. *J Pers Soc Psychol* 64:970-86

710. Appleton AA, Buka SL, Loucks EB, Gilman SE, Kubzansky LD. 2013. Divergent associations of adaptive and maladaptive emotion regulation strategies with inflammation. *Health Psychol* 32:748-56

711. Thiruchselvam R, Blechert J, Sheppes G, Rydstrom A, Gross JJ. 2011. The temporal dynamics of emotion regulation: an EEG study of distraction and reappraisal. *Biol Psychol* 87:84-92

712. Ferri J, Schmidt J, Hajcak G, Canli T. 2013. Neural correlates of attentional deployment within unpleasant pictures. *Neuroimage* 70:268-77

713. Hackett G, Horan J. 1980. Stress inoculation for pain: What's really going on? *J Counsel Psych* 27:107-16

714. Mathews A, Mackintosh B. 1998. A cognitive model of selective processing in anxiety. *Cogn Ther Res* 22:539-60

715. MacLeod C, Grafton B. 2014. Regulation of emotion through modification of attention. In *Handbook of Emotion Regulation*, ed. JJ Gross:p. 508. NY: Guilford.

716. Terkelsen AJ, Andersen OK, Molgaard H, Hansen J, Jensen TS. 2004. Mental stress inhibits pain perception and heart rate variability but not a nociceptive withdrawal reflex. *Acta Physiol Scand* 180:405-14

717. Quevedo AS, Coghill RC. 2007. Attentional modulation of spatial integration of pain: evidence for dynamic spatial tuning. *J Neurosci* 27:11635-40

718. Luciano J, Gonzalez S. 2007. Analysis of the efficacy of different thought suppression strategies. *Int J Psychol & Psychol Ther* 7:335-45

719. Wegner DM. 1994. Ironic processes of mental control. *Psychol Rev* 101:34-52

720. Wegner DM, Schneider DJ, Carter SR, 3rd, White TL. 1987. Paradoxical effects of thought suppression. *J Pers Soc Psychol* 53:5-13

721. Trinder H, Salkovskis PM. 1994. Personally relevant intrusions outside the laboratory: long-term suppression increases intrusion. *Behav Res Ther* 32:833-42

722. Beaver JD, Mogg K, Bradley BP. 2005. Emotional conditioning to masked stimuli and modulation of visuospatial attention. *Emotion (Washington, D.C.)* 5:67-79

723. Van Damme S, Crombez G, Hermans D, Koster EH, Eccleston C. 2006. The role of extinction and reinstatement in attentional bias to threat: a conditioning approach. *Behav Res Ther* 44:1555-63

724. Johnson MH, Breakwell G, Douglas W, Humphries S. 1998. The effects of imagery and sensory detection distractors on different measures of pain: how does distraction work? *Br J Clin Psychol* 37 (Pt 2):141-54

725. Ahles TA, Blanchard EB, Ruckdeschel JC. 1983. The multidimensional nature of cancer-related pain. *Pain* 17:277-88

726. Spence C, Bentley DE, Phillips N, McGlone FP, Jones AK. 2002. Selective attention to pain: a psychophysical investigation. *Exp Brain Res* 145:395-402

727. Leventhal H, Brown D, Shacham S, Engquist G. 1979. Effects of preparatory information about sensations, threat of pain, and attention on cold pressor distress. *J Pers Soc Psychol* 37:688-714

728. Zachariae R, Bjerring P. 1994. Laser-induced pain-related brain potentials and sensory pain ratings in high and low hypnotizable subjects during hypnotic suggestions of relaxation, dissociated imagery, focused analgesia, and placebo. *Int J Clin Exp Hypn* 42:56-80

729. Kam JW, Mickleborough MJ, Eades C, Handy TC. 2015. Migraine and attention to visual events during mind wandering. *Exp Brain Res* 233:1503-10

730. Whitmarsh S, Oostenveld R, Almeida R, Lundqvist D. 2017. Metacognition of attention during tactile discrimination. *Neuroimage* 147:121-9

731. Everson SA, Goldberg DE, Kaplan GA, Cohen RD, Pukkala E, et al. 1996. Hopelessness and risk of mortality and incidence of myocardial infarction and cancer. *Psychosom Med* 58:113-21

732. Nicholson RA, Houle TT, Rhudy JL, Norton PJ. 2007. Psychological risk factors in headache. *Headache* 47:413-26

733. Tschannen TA, Duckro PN, Margolis RB, Tomazic TJ. 1992. The relationship of anger, depression, and perceived disability among headache patients. *Headache* 32:501-3

734. Gross JJ. 1998. Antecedent- and response-focused emotion regulation: divergent consequences for experience, expression, and physiology. *J Pers Soc Psychol* 74:224-37

735. Sheppes G, Catran E, Meiran N. 2009. Reappraisal (but not distraction) is going to make you sweat: physiological evidence for self-control effort. *Int J Psychophysiol* 71:91-6

736. Troy AS, Shallcross AJ, Mauss IB. 2013. A person-by-situation approach to emotion regulation: cognitive reappraisal can either help or hurt, depending on the context. *Psychol Sci* 24:2505-14

737. Gilbert P, Irons C. 2005. Focused therapies and compassionate mind training for shame and self attacking, pp. 263-325. In *Compassion: Conceptualisations, Research and Use in Psychotherapy*, ed. P Gilbert. East Sussex: Routledge.

738. Powers W. 2004. *Making sense of behavior: The meaning of control*. New Canaan, CT: Benchmark Publications.

739. Fisher E, Keogh E, Eccleston C. 2016. Adolescents' approach-avoidance behaviour in the context of pain. *Pain* 157:370-6

740. Norman D, Shallice T. 1986. Attention to action: willed and automatic control of behaviour. In *Consciousness and self-regulation: Advances in research and theory*, ed. R Davidson, G Schwartz, D Shapiro, 4:1-18. NY: Plenum Press.

741. Muraven M, Baumeister RF. 2000. Self-regulation and depletion of limited resources: Does self-control resemble a muscle? *Psychological Bulletin* 126:247-59

742. Zachariae R, Oster H, Bjerring P. 1994. Effects of hypnotic suggestions on ultraviolet B radiation-induced erythema and skin blood flow. *Photodermatol Photoimmunol Photomed* 10:154-60

743. Brown GK, Nicassio PM. 1987. Development of a questionnaire for the assessment of active and passive coping strategies in chronic pain patients. *Pain* 31:53-64

744. Suls J, Fletcher B. 1985. The relative efficacy of avoidant and nonavoidant coping strategies: A meta-analysis. *Health Psychol* 4:249-88

745. Levenson R, Haase C, Bloch L, Holley S, Seider B. 2014. Emotion Regulation in Couples, ch 17. In *Handbook of emotion Regulation*, ed. J Gross. The Guilford Press.

746. Campos J, Walle E, Dahl, A, Main A. 2011. Reconceptualizing emotion regulation *Emotion Rev* 3:26-35

747. Forrest MS, Hokanson JE. 1975. Depression and autonomic arousal reduction accompanying self-punitive behavior. *J Abnorm Psychol* 84:346-57

748. Gilbert P. 2000. Varieties of submissive behaviour: Their evolution and role in depression. In *Subordination and Defeat: An Evolutionary Approach to Mood Disorders (pp. 3-46)*, ed. L Sloman, P Gilbert. Hillsdqale, NJ: Lawrence Erlbaum.

749. Levine P. 2010. *In an unspoken voice: How the body releases trauma and restores goodness*. Berkley, CA: North Atlantic Books.

750. Heckman CJ, Clay DL. 2005. Hardiness, history of abuse and women's health. *J Health Psychol* 10:767-77

751. Tietjen GE, Brandes JL, Peterlin BL, Eloff A, Dafer RM, et al. 2010. Childhood maltreatment and migraine (part I). Prevalence and adult revictimization: a multicenter headache clinic survey. *Headache* 50:20-31

752. Tietjen GE, Brandes JL, Peterlin BL, Eloff A, Dafer RM, et al. 2010. Childhood maltreatment and migraine (part II). Emotional abuse as a risk factor for headache chronification. *Headache* 50:32-41

753. Tietjen GE, Brandes JL, Peterlin BL, Eloff A, Dafer RM, et al. 2010. Childhood maltreatment and migraine (part III). Association with comorbid pain conditions. *Headache* 50:42-51

754. Day MA, Thorn BE, Ward LC, Rubin N, Hickman SD, et al. 2014. Mindfulness-based cognitive therapy for the treatment of headache pain: a pilot study. *Clin J Pain* 30:152-61

755. Day MA, Thorn BE. 2016. The mediating role of pain acceptance during mindfulness-based cognitive therapy for headache. *Complementary therapies in medicine* 25:51-4

756. Neacsiu A, Bohus M, Linehan M. 2014. Dialectical Behaviour Therapy: An Intervention for Emotion Dysregulation, ch 29. In *Handbook of Emotion Regulation*, ed. J Gross. NY: Guilford Press.

757. Saarni C. 1999. *The development of emotional competence*. NY: Guilford Press.

758. Saarni C. 2011. Emotional development in childhood. In *Encyclopedia on early childhood development: Emotions (pp 1-7)*, ed. R Tremblay, R Barr, Peters, RD, M Boivin. Montreal: Center of Excellence for Early Childhood Development and Strategic Knowledge Cluster on Early Child Development.

759. Cook S, Heppner P. 1997. A Psychometric Study of Three Coping Measures. *Educ Psychol Meas* 57:906 - 23

760. Fisher J. 2017. Women and Mental Health. *InPsych* 39:12-5

761. Koolhaas J, Bartolomucci A, Buwalda B, de Boer S, Flugge G, et al. 2011. Stress revisited: a critical evaluation of the stress concept. *Neurosci Biobehav Rev* 35:1291-301

762. Martikainen IK, Pecina M, Love TM, Nuechterlein EB, Cummiford CM, et al. 2013. Alterations in Endogenous Opioid Functional Measures in Chronic Back Pain. *Journal of Neuroscience* 33:14729-37

763. Li W, Neugebauer V. 2004. Block of NMDA and non-NMDA receptor activation results in reduced background and evoked activity of central amygdala neurons in a model of arthritic pain. *Pain* 110:112-22

764. Ji G, Neugebauer V. 2011. Pain-related deactivation of medial prefrontal cortical neurons involves mGluR1 and GABA(A) receptors. *J Neurophysiol* 106:2642-52

765. McEwen B. 1998. Protective and damaging effects of stress mediators. *N Engl J Med* 338:171-9

766. Britton JC, Lissek S, Grillon C, Norcross MA, Pine DS. 2011. Development of anxiety: the role of threat appraisal and fear learning. *Depression anxiety* 28:5-17

767. Baum A, Cohen L, Hall M. 1993. Control and intrusive memories as possible determinants of chronic stress. *Psychosom Med* 55:274-86

768. Scott M, Stradling S. 1994. Post traumatic stress idsorder without the trauma. *Br J Clin Psychol* 33:71-4

769. Merikangas KR. 1995. Association between psychopathology and headache syndromes. *Curr Opin Neurol* 8:248-51

770. Melamed S, Shirom A, Toker S, Berliner S, Shapira I. 2006. Burnout and risk of cardiovascular disease: evidence, possible causal paths, and promising research directions. *Psychol Bull* 132:327-53

771. Kudielka BM, Hellhammer DH, Wust S. 2009. Why do we respond so differently? Reviewing determinants of human salivary cortisol responses to challenge. *Psychoneuroendocrinology* 34:2-18

772. Leclerc J. 2006. Personality traits may predict blood pressure. In *Cardiol News*

773. DeYoung C, Peterson J, Higgins D. 2005. Sources of openness/intellect: cognitive and neuropsychological correlates of the fifth factor of personality. *J Pers* 73:825–58

774. Penley J, Tomaka J. 2002. Associations among the Big five, emotional responses and coping with acute stress. *Pers Indiv Dif* 32:1215-28

775. Phan KL, Wager T, Taylor SF, Liberzon I. 2002. Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. *Neuroimage* 16:331-48

776. Cardinal RN, Parkinson JA, Hall J, Everitt BJ. 2002. Emotion and motivation: the role of the amygdala, ventral striatum, and prefrontal cortex. *Neurosci Biobehav Rev* 26:321-52

777. Davis M, Hitchcock JM, Bowers MB, Berridge CW, Melia KR, Roth RH. 1994. Stress-induced activation of prefrontal cortex dopamine turnover: blockade by lesions of the amygdala. *Brain Res* 664:207-10

778. Gallagher M, Schoenbaum G. 1999. Functions of the amygdala and related forebrain areas in attention and cognition. *Ann N Y Acad Sci* 877:397-411

779. Han CJ, O'Tuathaigh CM, van Trigt L, Quinn JJ, Fanselow MS, et al. 2003. Trace but not delay fear conditioning requires attention and the anterior cingulate cortex. *Proc Natl Acad Sci U S A* 100:13087-92

780. Lane RD, Reiman EM, Bradley MM, Lang PJ, Ahern GL, et al. 1997. Neuroanatomical correlates of pleasant and unpleasant emotion. *Neuropsychologia* 35:1437-44

781. Bushnell MC, Ceko M, Low LA. 2013. Cognitive and emotional control of pain and its disruption in chronic pain. *Nature reviews. Neuroscience* 14:502-11

782. Baliki MN, Geha PY, Fields HL, Apkarian AV. 2010. Predicting value of pain and analgesia: nucleus accumbens response to noxious stimuli changes in the presence of chronic pain. *Neuron* 66:149-60

783. Basbaum AI, Bautista DM, Scherrer G, Julius D. 2009. Cellular and molecular mechanisms of pain. *Cell* 139:267-84

784. Ikeda H, Heinke B, Ruscheweyh R, Sandkuhler J. 2003. Synaptic plasticity in spinal lamina I projection neurons that mediate hyperalgesia. *Science* 299:1237-40

785. Vera-Portocarrero LP, Zhang ET, Ossipov MH, Xie JY, King T, et al. 2006. Descending facilitation from the rostral ventromedial medulla maintains nerve injury-induced central sensitization. *Neuroscience* 140:1311-20

786. Barlow DH. 2000. Unraveling the mysteries of anxiety and its disorders from the perspective of emotion theory. *Amer Psychol* 55:1247-63

787. Almarzooqi S, Chilcot J, McCracken L. 2017. The role of psychological flexibility in migraine headache impact and depression. *J Context Behav Sci*

788. White K, Farrell A. 2006. Anxiety and Psychosocial Stress as Predictors of Headache and Abdominal Pain in Urban Early Adolescents. *J. Pediatr. Psychol* 31: 582-96

789. Larsson R, Oberg PA, Larsson SE. 1999. Changes of trapezius muscle blood flow and electromyography in chronic neck pain due to trapezius myalgia. *Pain* 79:45-50

790. Simons DG, Mense S. 1998. Understanding and measurement of muscle tone as related to clinical muscle pain. *Pain* 75:1-17

791. Hubbard DR, Berkoff GM. 1993. Myofascial trigger points show spontaneous needle EMG activity. *Spine (Phila Pa 1976)* 18:1803-7

792. Venable VL, Carlson CR, Wilson J. 2001. The role of anger and depression in recurrent headache. *Headache* 41:21-30

793. Nicholson RA, Gramling SE, Ong JC, Buenaver L. 2003. Differences in anger expression between individuals with and without headache after controlling for depression and anxiety. *Headache* 43:651-63

794. Janke EA, Holroyd KA, Romanek K. 2004. Depression increases onset of tension-type headache following laboratory stress. *Pain* 111:230-8

795. Bussone G, Grazzi L, Panerai AE. 2012. Pain, emotion, headache. *Headache* 52 Suppl 2:98-101

796. Miller TQ, Smith TW, Turner CW, Guijarro ML, Hallet AJ. 1996. A meta-analytic review of research on hostility and physical health. *Psychol Bull* 119:322-48

797. Suinn RM. 2001. The terrible twos--anger and anxiety. Hazardous to your health. *The American psychologist* 56:27-36

798. Averill J. 2012. *Anger and aggression: An essay on emotion*. Springer.

799. Smedslund J. 1993. How shall the concept of anger be defined? *Theory Psychol* 3:5-33

800. Cassidy J, Berlin L. 1994. The insecure/ambivalent pattern of attachment: Theory and research. *Child Devel* 65:971-81

801. Cassidy J, Kobak R. 1988. Avoidance and its relationship with other defensive processes. In *Clinical implications of attachment (pp. 300-323)*, ed. J Belsky, T Nezworski. Hillsdale, NJ: Erlbaum.

802. Paulus M, Rogalsky C, Simmons A, Feinstein J, Stein M. 2003. Increased activation in the right insula during risk-taking decision making is related to harm avoidance and neuroticism. *NeuroImage* 19:1439-48

803. Stern R, Koch K, Andrews P. 2011. *Nausea: mechanisms and management*. Oxford University Press.

804. Singh P, Yoon SS, Kuo B. 2016. Nausea: a review of pathophysiology and therapeutics. *Therap Adv Gastroenterol* 9:98-112

805. Treleaven-Hassard S. 2013. *The nociceptive blink reflex in migraine : an investigation of endogenous and exogenous modulators on the trigeminal nervous system in migraine sufferers*. PhD. Murdoch University, Perth, W.A.

806. Granston A, Drummond PD. 2005. Painful stimulation of the temple during optokinetic stimulation triggers migraine-like attacks in migraine sufferers. *Cephalalgia* 25:219-24

807. LaCount LT, Barbieri R, Park K, Kim J, Brown EN, et al. 2011. Static and dynamic autonomic response with increasing nausea perception. *Aviat Space Environ Med* 82:424-33

808. Kim J, Napadow V, Kuo B, Barbieri R. 2011. A combined HRV-fMRI approach to assess cortical control of cardiovagal modulation by motion sickness. *Conference proceedings : ... Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Annual Conference* 2011:2825-8

809. Napadow V, Sheehan JD, Kim J, Lacount LT, Park K, et al. 2013. The brain circuitry underlying the temporal evolution of nausea in humans. *Cereb Cortex* 23:806-13

810. Kalsbeek A, van der Spek R, Lei J, Endert E, Buijs RM, Fliers E. 2012. Circadian rhythms in the hypothalamo-pituitary-adrenal (HPA) axis. *Mol Cell Endocrinol* 349:20-9

811. Dallman MF, la Fleur SE, Pecoraro NC, Gomez F, Houshyar H, Akana SF. 2004. Minireview: glucocorticoids--food intake, abdominal obesity, and wealthy nations in 2004. *Endocrinology* 145:2633-8

812. Herman JP, McKlveen JM, Ghosal S, Kopp B, Wulsin A, et al. 2016. Regulation of the Hypothalamic-Pituitary-Adrenocortical Stress Response. *Compr Physiol* 6:603-21

813. DeMaria EJ, Lilly MP, Gann DS. 1987. Potentiated hormonal responses in a model of traumatic injury. *J Surg Res* 43:45-51

814. Myers B, McKlveen JM, Herman JP. 2012. Neural Regulation of the Stress Response: The Many Faces of Feedback. *Cell Mol Neurobiol*

815. McEwen BS. 1998. Protective and damaging effects of stress mediators. *N Engl J Med* 338:171-9

816. Unal Z, Domac FM, Boylu E, Kocer A, Tanridag T, Us O. 2016. Blink reflex in migraine headache. *North Clin Istanb* 3:1-8

817. de Tommaso M, delussi M. 2017. Nociceptive blink reflex habituation biofeedback in migraine. *Funct Neurol* 32:123-30

818. Manack AN, Buse DC, Lipton RB. 2011. Chronic migraine: epidemiology and disease burden. *Curr Pain Headache Rep* 15:70-8

819. Csikszentmihalyi M. 2008. *Flow: The Psychology of Optimal Experience*. Harper Perennial.

APPENDICES

Appendix A Headache questionnaire based on IHS criteria

Headache History: Summary Form

Name			Age	
Address				
Phone	Email			
Medical history	Do you suffer from any chronic medical conditions? e.g. Neurological, respiratory problems, heart disease, gastric ulcer, ear problems		Yes	No
	Are you taking any medication at present?		Yes	No
	Details			
	Any psychological/psychiatric treatment at present?		Yes	No
Headache details	How frequent are your headaches?		Per month	
			Per year	
	How long does your headache last?			
	How many of your headaches are severe?			
	Please rate the average intensity of your headaches	Mild (0-3)	Moderate (4-6)	Severe (7-10)
	Of your headaches, how many are migraine?			
	Headache location?			
	Is the headache just on one side		Yes (L/R)	No
	Does the headache throb?		Yes	No
	Is the headache aggravated by physical activity, e.g. walking up steps?		Yes	No
	During the headache are you.....			
	Prone to feel nauseated?		Yes	No
	Prone to vomiting?		Yes	No
	More sensitive to sound?		Yes	No
	More sensitive to light?		Yes	No
	More sensitive to smell?		Yes	No
	Do you get a warning or aura before your headaches?		Yes	No
	Details			
	Possible triggers? (in order)			
	What treatments do you use for your headaches? (in order)			
Headache history	Does anyone in your family have migraine?		Yes	No
	Details			
	How old were you when your headaches first started?			
	Have you seen a doctor or specialist about your headaches?		Yes	No
	When? Result?			

Appendix B Data collection sheet

DATA COLLECTION SHEET

Age _____ **Gender** _____

Time of last snack/meal _____
Medication Yes/No Details: _____

_____

Migraine sufferer? _____ Side of head? _____
For females only
Date of fist day of last period _____
28 day cycle? _____If no, how many days is your cycle? _____

Date	Time	Temperature	Humidity

Systolic Pressure	Diastolic Pressure	Pulse rate

After 15 minutes relaxation, obtain 1st cortisol reading

Ratings at baseline

Headache	
Nausea	
Distress	

PREPARATION

1. Remove any makeup with makeup remover wipe
2. Press leads onto EMG electrodes and cut two to half moons.
3. Use an alcohol swab to wipe under the stimulated side eye, cheek bone and behind the ear.
4. Get participants to look straight ahead and stick one of the half electrodes under the eye, as close to the lashes as comfortably possible.
5. Stick the second half electrode towards the corner of the eye about 3 mm away from the active electrode.
6. Stick the full electrode behind the ear.
7. Feel for the supraorbital notch and cleanse the forehead area above it with a prep-pad. Rub the skin well with the prep pad. Attach a double adhesive washer to the concentric electrode and put a smear of gel on the exposed metal washer, ensuring no gel fills the centre void on the concentric electrode. Remove the adhesive cover and attach to the forehead in the area above the supra-orbital notch.
8. Connect concentric electrode to leads (red to red, black to white).
9. Connect EMG leads (under eye to VIN+, corner of eye to VIN–, behind ear to ground).
10. Attach double adhesive washers to photo-plethysmographs and attach at both temples. Cover with headband.
11. Start Acqknowledge and ensure data is clean and free from artefact.

Systolic Pressure	Diastolic Pressure	Pulse rate

BEFORE MATHS

Set CCU dial to 2mA

Concentric electrode attached to the: Left/Right

Turn stimulator trigger on for 10 shocks at 30s intervals

	Systolic	Diastolic	Pulse rate
After 1 minute			
After 4 minutes			

Readings for 10 shocks at 30s intervals

#		Rating	mA
1	C2		
2	C2		
3*	C2		
4	C2		
5	C2		
6	C2		
7	C2		
8*	C2		
9	C3		
10	C4		

Ratings during and after the 10 shocks

	During shocks	Now
Headache		
Nausea		
Distress		

***WAIT TWO MINUTES. During this period take a further set of BP readings*.**

Systolic pressure	Diastolic pressure	Pulse rate

Turn on stimulator trigger for 20 shocks at 2s intervals.

Ratings during and after the 2-second shocks

	During shocks	Now
Pain rating		
Headache		
Nausea		
Distress		

Turn stimulator trigger on for another 10 shocks at 30s intervals

#		Rating	mA
1	C2		
2	C2		
3*	C2		
4	C2		
5	C2		
6	C2		
7	C2		
8*	C2		
9	C3		
10	C4		

WAIT 2 MINUTES, during which time take a further set of BP readings.

Systolic pressure	Diastolic pressure	Pulse rate

Ratings during and after the 10 shocks

	During shocks	Now
Pain rating		
Headache		
Nausea		
Distress		

Save the Acqknowledge file ("subject name" before maths)

Obtain 2nd cortisol reading.

MATHS

Start the math practice questions

Open a new Acqknowledge file

After the practice questions, do a 2-minute baseline recording and take BP readings

Systolic	Diastolic	Pulse rate

When you are ready, start the Maths questions, start the stopwatch timer, place an event mark in the Acknowledge recording and start the tape of the baby crying.

During first five minutes

	Systolic	Diastolic	Pulse rate
After 1 minute			
After 4 minutes			

At 5 minutes: turn on stimulator trigger for the 10 shocks at 30s intervals

During second five minutes

	Systolic	Diastolic	Pulse rate
After 1 minute			
After 4 minutes			

2 minutes after 2nd set of ratings: turn on stimulator trigger for the 20 shocks at 2s intervals

During third five minutes

	Systolic	Diastolic	Pulse rate
After 1 minute			
After 4 minutes			

Immediately after 3rd set of ratings: turn on stimulator trigger for the 10 shocks at 30s intervals

During fourth five minutes

	Systolic	Diastolic	Pulse rate
After 1 minute			
After 4 minutes			

After the math program finishes, place an event mark in the Acknowledge recording, and record for another 5 minutes while the subject sits quietly

	Systolic	Diastolic	Pulse rate
After 1 minute			
After 4 minutes			

Save the Acqknowledge file ("subject name" maths)

Administer the coping scale

10 minutes after the maths finishes, collect 3rd cortisol sample.

POST MATHS

Turn stimulator trigger on for 10 shocks at 30s intervals

#		Rating	mA
1	C2		
2	C2		
3*	C2		
4	C2		
5	C2		
6	C2		
7	C2		
8*	C2		
9	C3		
10	C4		

Blood pressure readings

	Systolic	Diastolic	Pulse rate
After 1 minute			
After 4 minutes			

Ratings during and after the 10 shocks

	During shocks	Now
Pain rating		
Headache		
Nausea		
Distress		

WAIT 2 MINUTES, during which take BP readings

Systolic	Diastolic	Pulse rate

Turn on stimulator trigger for 20 shocks at 2s intervals

Ratings during and after the 2-second shocks

	During shocks	Now
Pain rating		
Headache		
Nausea		
Distress		

WAIT 2 MINUTES, during which take BP reading

Systolic	Diastolic	Pulse rate

Turn stimulator trigger on for another 10 shocks at 30s intervals

#		Rating	mA
1	C2		
2	C2		
3*	C2		
4	C2		
5	C2		
6	C2		
7	C2		
8*	C2		
9	C3		
10	C4		

	Systolic	Diastolic	Pulse rate
After 1 minute			
After 4 minutes			

Ratings during and after the 10 shocks

	During shocks	Now
Pain rating		
Headache		
Nausea		
Distress		

Save the Acqknowledge file ("subject name" post maths)

Obtain 4th cortisol reading.

Appendix C "Ways of Coping" maths test

WAYS OF COPING (Adapted) MATHS TEST

NAME: _____ **DATE:** _____

Please read each item below and indicate, by circling the appropriate category, to what extent you used this way of coping in the maths test.

How you coped	Not used	Used some-what	Used quite a bit	Used A great deal
1. Just concentrated on what I had to do next – the next step	0	1	2	3
2. I tried to analyse the problem in order to understand it better	0	1	2	3
3. Used distractions to take my mind off things	0	1	2	3
4. I felt that time would make a difference – the only thing to do was wait	0	1	2	3
5. I did something which I didn't think would work, but at least I was doing something	0	1	2	3
6. Tried to find out more about what to do	0	1	2	3
7. Criticised or lectured myself	0	1	2	3
8. Tried not to burn my bridges, but leave things open somewhat	0	1	2	3
9. Hoped a miracle would happen	0	1	2	3
10. Went along with fate; sometimes I just have bad luck	0	1	2	3
11. Went on as if nothing had happened	0	1	2	3
12. Looked for the silver lining, so to speak; tried to look on the bright side of things	0	1	2	3
13. I expressed anger to the person(s) who caused the problem	0	1	2	3
14. I told myself things that helped me to feel better	0	1	2	3
15. Tried to forget the whole thing	0	1	2	3
16. I waited to see what would happen before doing anything	0	1	2	3
17. I made a plan of action and followed it	0	1	2	3
18. I let my feelings out somehow	0	1	2	3
19. Got away from it for a while; tried to relax myself	0	1	2	3
20. I tried not to act too hastily or follow my first hunch	0	1	2	3
21. Maintained my pride and kept a stiff upper lip	0	1	2	3
22. Changed something so things would turn out all right	0	1	2	3
23. Didn't let it get to me; refused to think too much about it	0	1	2	3
24. Made light of the situation; refused to get too serious about it	0	1	2	3
25. Drew on my past experiences; I was in a similar situation before	0	1	2	3
26. I knew what had to be done, so I doubled my efforts to make things work	0	1	2	3
27. Came up with a couple of different solutions to the problem	0	1	2	3
28. Accepted it, since nothing could be done	0	1	2	3
29. I tried to keep my feelings from interfering too much	0	1	2	3
30. I daydreamed or imagined a better time or place than the one I was in	0	1	2	3
31. Wished that the situation would go away or somehow be over with	0	1	2	3
32. I prayed	0	1	2	3
33. I prepared myself for the worst	0	1	2	3
34. I thought about how a person I admire would handle this situation and used that as a model	0	1	2	3
35. I reminded myself how much worse things could be	0	1	2	3
36. I tried something entirely different from any of the above (please describe).	0	1	2	3

Appendix D Blink Reflex Quantification procedure

- Open file
- Change Time scale to 6 minutes
- Remove manual stimulus marker channel (select channel, Edit>Remove Waveform)
- Duplicate BR wave and label the duplicate BR abs (select BR; Edit>Duplicate Waveform)
- Select BR abs wave

  In some files a band stop filter was applied for between 49-51Hz (at 1000 coefficients) to remove electrical artifact.
- Transform > Digital Filters > FIR > Band Stop Filter
- Digital Filter Text Box > Window = Blackman; Low Frequency (Hz) = 49; High Frequency = 51; Number of Coefficients = 1000; √ Filter Entire Wave, OK.

  In some files a band stop filter was applied for between 99-102Hz (at 1000 coefficients) to remove electrical artifact.
- Transform > Digital Filters > FIR > Band Stop Filter
- Digital Filter Text Box > Window = Blackman; Low Frequency (Hz) = 99; High Frequency = 102; Number of Coefficients = 1000; √ Filter Entire Wave, OK.

  In some case the eyeball roll was removed by high pass filtering with a cut-off frequency of 20Hz at 400 coefficients
- Transform > Digital Filters > FIR > High Pass Filter
- Digital Filter Text Box > Window = Blackman; Cut-off Frequency (Hz) = 20; Number of Coefficients = 400; √ Filter Entire Wave, OK.

  All files that belong to the same participant were filtered the same way.
- Edit > Select All
- Ensure BR abs wave selected, Maths functions > Abs
- Select stimulus marker waveform, Maths functions > Abs
- Reset waves so that raw BR wave sits underneath abs wave
- Select stimulus marker waveform. Set functions on toolbar as Time, Delta T and Integral (CH = BR abs).
- Change Time Scale to .1 second.
- Transform>Find Peak = Positive Peak; Threshold Level = 1, Fixed; Set first cursor to = Peak + 0 ms; Set second cursor to = Peak + -60 ms; Paste measurements into journal tick; Measurement output = Save measurements as Excel Spreadsheet File tick, Ask for file name and location tick, Open spreadsheet after final peak is found tick; OK.

  A text box will pop up asking to perform ‘Find all peaks’ operation. Select ‘Yes’.

- Find Peak = Positive Peak; Threshold Level = 1, Fixed; Set first cursor to = Peak + 27 ms; Set second cursor to = Peak + 87ms; Paste measurements into journal tick; Don't Find.
- Transform>Find All Peaks. Copy the new data from Journal and paste into Excel file next to the previous data. Make sure the Times match.
- Save Excel file as participant number and condition.

Latencies

- Ensure Journal is open. Copy the empty 'Latency' data sheet from Excel. At the end of the AUC data insert the cursor and select the 'Paste' from the Edit menu. Ensure each stimulus has an event marker.
- Go to the first flag and determine latency (in the 27-87ms window). Type in latency for specific stimulus.
- Once all latencies have been determined, copy the data and paste into Excel data sheet next to AUC data. Make sure that the latency data matches the AUC data by comparing the stimulus labels.

Collating

- Each participant should have an Excel file with 3 worksheets (1 for each condition – Baseline, Maths, Post Maths). Each worksheet should have the pre marker AUC data; the post marker AUC data and the latency data.

Appendix E Computer program for data collection in the stressful task

```
                                                        36
      incr lvl   ' error rate too low so make harder
   end if
elseif tna = 2 then  'sum is 0,1,2
   if SumCAs = 2 then
      incr lvl
   elseif SumCAs = 0 then
      decr lvl
   end if
elseif tna = 3 then  'sum is 0,1,2,3
   if SUmCAs > 1 then
      incr lvl
   else
      decr lvl
   end if
elseif tna = 4 then
   if SumCAs > 2 then
      incr lvl
   elseif SumCAs < 2 then
      decr lvl
   end if
elseif tna = 5 then
   if SUmCAs > 2 then
      incr lvl
   else
      decr lvl
   end if
elseif tna = 6 then
   if SumCAs > 3 then
      incr lvl
   elseif SumCAs < 3 then
      decr lvl
   end if
elseif tna = 7 then
   if SUmCAs > 3 then
      incr lvl
   else
      decr lvl
   end if
end if
if lvl < 1 then lvl = 1
if lvl > 5 then lvl = 5
Return
Rem ################### display question ################# ??????????????
dquest:
        incr qp(lvl) ' get next ? for this level
        If qp(lvl) > 200 Then qp(lvl) = 1  ' cycles thru 1-200
dq1:
        cls
        locate 13, 36
        Print "                              "
        locate 13, 36
        GoSub debounce
        Print sum$(lvl, qp(lvl))
        GoSub status
        locP = 47
        ansl = suml(lvl, qp(lvl))
        If ansl = 0 Then ansl = 1
        Print #5, "Answer length "; ansl
        HH = 0
        cans$ = ""
        cpam$ = "D"  ' will initialize tcount to be tout(lvl)
        GoSub initialiseClock

' want to wait until either time count expires or ansl digits entered

      Do Until ((tcount = 0) Or (HH = ansl))
          If instat Then
              ans$ = inkey$ ' read keypress  : ans$ = ucase$(ans$)
              If ans$ = "|" Then
                 If pracflag = 1 Then    'short cut out of practice trials
                    tna = %nprac
                    Return
                 Else
                   GoSub saveresults
                   GoTo mlex
                 End If
              End If
              If ans$ >= "0" And ans$ <= "9" Then
                incr locP
                incr HH
                locate 13, locP
                Print ans$ ' echo
                cans$ = cans$ + ans$  ' concatenate the answer
              End If
          Else ' check the clock
                                                  Page 7
```

```
                                                        J6
' Written by David Nicholson for Juanita Miller Berry
' time is 3:15 5 May 2006
' uses the following input files
' # afmaths.txt
' # timeout.txt allows 5 time outs for each of the 5 levels
' #4 reads program parameters

' uses the following output files - #5 = int.TMP scratch file [overwrites]
' output file name is juanita.dat as #1

DefInt A-Z

Dim sum$(5, 200) ' holds the sum as an ascii string
Dim sum(5, 200) ' holds the answer as a number
Dim suml(5, 200) ' holds the length of the answer string
Dim sumptr(5)
Dim qp(5)        ' holds pointers for level cycles 1 thru 200
Dim cycles(8)    ' keeps track of last 8 answers
Dim tout(5)
Dim numqs(30)    ' says how many questions warnings apply for
Dim presact$(15) ' holds selection of display event times
Dim MOODVAS(9, 10) ' no of total VAS checks  5 pretest, 3 in maths, 1 post]
Dim lsc$(120), tmt$(120)
Dim ctype$(3)
dim last$(8)  ' for testing

VERSION$ = "6:00am wednesday 4 May 2006"

%textmode = 0
%medres = 1
%hires = 2

%xposR = 459   ' hi res graphics positions
%ypos =   116
%xposL = 159

%ytpos = 15   ' text locations only
%xtposL = 1
%xtposR =  64
%VasCalls = 5   ' number of times moodVAS is called in total
%vastimeout = 15  'seconds
%NumMoods = 9 ' no of different moods

%TooSlow = 5     ' purple   set up colors for feedback
%NormalFg = 14    ' yellow
%Correct = 2      ' green
%Incorrect = 4    ' red
%NormalBg = 0    ' black
%yellow = 14
%black = 0
%bluebg = 1  ' warning background colour
%whitefg = 7 ' warning screen char colour
%debounces = 10

' PAIN =        1
' UNPL =        2
' ANX =         3
' CONFUSED =    4
' DISCOURAGED = 5
' ANGER =       6
' SLUGGISH =    7
' LIVELY =      8
' SELFEFF=      9

%nprac = 5  ' no of practice questions

cmess = 0
cls

Rem %%%%%%%%%%%%%%%%%%%% THE REAL CODE !!  %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
mlstart:

GoSub signon
GoSub contmess
GoSub startingmessage
GoSub openoutputfile   'JUANITA.DAT
GoSub initvals
GoSub inpmaths
GoSub params
GoSub genpretest  ' general instructions
GoSub contmess
gosub runmoodvas  ' PRE TRIAL mood ratings
GoSub beginpracticemess
GoSub contmess
GoSub practice
                                                    Page 1
```

```
                                                    J6
GoSub endpracticemess     ' end of practice message
GoSub contmess
gosub realtrialsounds
GoSub runtrials   ' includes 3 VAS ratings within session
gosub runmoodvas   ' POST TRIAL mood ratings
GoSub endmessage
GoSub hiddenkey
GoSub contmess
GoSub saveresults        ' Saves to hard disk and floppy
GoSub resettime     ' asks experimenter to reset the time

mlex:
cls :locate 14, 10
Print "Program closing"
Stop

Rem ############## hidden key ##########################################
hiddenkey:
hk1:
cls:gosub debounce:locate 10,10:?"Experimenter - Press special key"
While Not instat: Wend
aa$ = input$(1)
If aa$ = "+" Then GoTo hkex
GoTo hk1
hkex:
Return

Rem ################ SIGNS ON WITH VERSION NUMBER ########################
signon:
cls
locate 10, 5
Print VERSION$
delay 1
Return

Rem ################ save results to Hard disk and floppy #################
saveresults:
Rem TO HARD DISK
ofilenm$ = "JUANITA.DAT"
cls :locate 10,10:?"Appending session data to hard disk : Juanita.dat": delay 2
Open ofilenm$ For Append As #1
GoSub WRITEFILE
cls: locate 10, 10: Print "Press a key when floppy disk ready"
ofilenm$ = "a:" + ofilenm$ ' makes into a:juanita.dat
Open ofilenm$ For Append As #1
cls :locate 10,10
?"Appending session data to floppy disk : Juanita.dat": delay 2

GoSub WRITEFILE
Return

WRITEFILE:
Print #1,Left$(SSNAME$ + "                    ", 20);
For nm = 1 To %NumMoods
for vc = 1 to %VasCalls
Print #1, using "### "; MOODVAS(nm, vc);
Next vc
Next nm
Print #1,
Close 1
Return

Rem ################## check a key value ############################
checkkey:
cls: locate 10, 10
input"press key required ";dummy$
Print "As a character "; dummy$
Print "As a value     "; Val(dummy$)
If Val(dummy$) = 99 Then GoTo ckex1
ckex1:
Return
Rem ################ sets up window for slider ######################
slider:
screen %hires,0

line (%xposL,%ypos) - (%xposR, %ypos)
line (%xposL,%ypos-1) - (%xposL, %ypos+1)
line (%xposR,%ypos-1) - (%xposR, %ypos+1)

cnt = 50
xcur = 309 '(equals a value of 50)
ycur = %ypos
GoSub redraw
cpam$ = "V"   ' will initialize tcount to be 15 to complete VAS
GoSub initialiseClock
                                                Page 2
```

```
chloop:
If instat Then   'either VAS key or return
         achar$ = UCase$(inkey$)
         If Asc(achar$) = 13 Then GoTo slidex  ' return implies an answer
             if ((achar$ = "/") and (xcur< %xposR)) then ' ensure correct keys
                oldxcur = xcur
                incr cnt
                incr xcur, 3
                GoSub redraw
             elseif ((achar$ = "Z") and (xcur > %xposL)) then
                oldxcur = xcur
                decr cnt
                decr xcur, 3
                GoSub redraw
             End If
ElseIf tcount <> 0 Then
             oldtcount = tcount
             GoSub checkclock
             If oldtcount <> tcount Then
                 locate 20, 4
                 If ((tcount > 0) And (tcount < 16)) Then Print tcount
             END IF
             If tcount <= 0 Then
                son = 1  ' flags sound on
                oldnt$ = Right$(Time$, 1)
                play0 = 0
                play5 = 1
             End If
ElseIf son = 1 Then
    GoSub noiseon
End If
GoTo chloop

slidex:
  If xcur <> 0 Then
     VASVAL = (xcur - 159) / 3
  Else
     VASVAL = 0
  End If
  MOODVAS(m, MOODP) = VASVAL
  son = 0
  Screen 0, 0
Return
Rem ################ turns noise on and off ######################
noiseon:
         nt$ = Right$(Time$, 1)
         If oldnt$ = Right$(Time$, 1) Then Return
         oldnt$ = Right$(Time$, 1)
         If play0 = 0 Then
            play5 = 0
            play0 = 1
            locate 20, 10
            Print "YOUR TIME HAS ELAPSED. PLEASE MAKE YOUR RATING IMMEDIATELY"
            If mute$ = "N" Then sound 500, 17
         ElseIf play5 = 0 Then
                play5 = 1
                play0 = 0
                locate 20, 5
         Print "                                                                                "
                If mute$ = "N" Then sound 1000, 17
         End If
Return
Rem ################### redraw ####################################
redraw:
PSet (xcur, ycur - 2)
PSet (xcur, ycur - 1)
PSet (xcur, ycur + 1)
PSet (xcur, ycur + 2)
preset(oldxcur, ycur-2)
preset(oldxcur, ycur-1)
preset(oldxcur, ycur+1)
preset(oldxcur, ycur+2)
Return
Rem ######################### graphics mode ########################
Sub graphicsmode(newmode)
cls
Screen newmode, 0
locate 8, 1
input"Change screen mode "; dummy$
cls
Screen 0, 0
Stop
Return
End Sub
```

```
                                                                    J6
Rem ######################### mood VAS 9 ratings #########################
runmoodVAS:
GoSub savetime  ' effectively stops the clock whilst mood ratings done
incr moodp
For m = 1 to %NumMoods
  GoSub genTXTmood
  GoSub MoodText   ' displays specific mood text
  GoSub slider
Next m
if dtest$ = "Y" then
  cls:?:?:?:?
  ?"Moods just rated for rating number : ";moodp
  ?
  for t = 1 to %nummoods
    ?using"#";t;
    ?using " ###";moodvas(t,moodp)
  next t
  delay 8
  cls
  end if
GoSub restoreTIME  'restores clock, as though the Mood VAS were never there
GoSub resetscreen
Return

Rem ################## general text for MOOD VAS  ####################
genTXTmood:
screen %hires,0
cls: ?:?:?
Print "  Please rate your mood RIGHT AT THIS MINUTE by moving the "
Print "  cursor left or right with the indicated arrow keys. ": Print
GoSub keytext
Return
Rem ################## Specific text for MOOD VAS ####################
MoodText:
if M = 1 then                          'HEADACHE/PAIN
  screen %hires,0
  locate %ytpos,   %xtposL+5
  Print "No headache"
  locate %ytpos,   %xtposR-4
  Print "Headache as strong as"
  locate %ytpos+1,   %xtposR-4
  Print "it could possibly get"
elseif M = 2 then                          ' UNPLEASANT/NAUSEA
  screen %hires,0
  locate %ytpos,   %xtposL+5
  Print "No nausea"
  locate %ytpos+1,   %xtposL+5
  Print "at all"
  locate %ytpos,   %xtposR-4
  Print "Nausea as strong as"
  locate %ytpos+1, %xtposR-4
  Print "it could possibly get"
elseif M = 3 then                          ' ANXIOUS
  screen %hires,0
  locate %ytpos,   %xtposL+8
  Print "Not Anxious"
  locate %ytpos+1,   %xtposL+8
  Print "at all"
  locate %ytpos,   %xtposR-4
  Print "Extremely"
  locate %ytpos+1, %xtposR-4
  Print "Anxious"
elseif M = 4 then                          ' CONFUSED
  screen %hires,0
  locate %ytpos,   %xtposL+7
  Print "Not Confused"
  locate %ytpos+1,   %xtposL+7
  Print "at all"
  locate %ytpos,   %xtposR-4
  Print "Extremely"
  locate %ytpos+1, %xtposR-4
  Print "Confused"
elseif M = 5 then                          ' DISCOURAGED
  screen %hires,0
  locate %ytpos,   %xtposL+4
  Print "Not Discouraged"
  locate %ytpos+1,   %xtposL+4
  Print "at all"
  locate %ytpos,   %xtposR-4
  Print "Extremely"
  locate %ytpos+1, %xtposR-4
  Print "Discouraged"
elseif M = 6 then                          ' ANGRY
  screen %hires,0
  locate %ytpos,   %xtposL+10
                                                    Page 4
```

```
                                                    J6
  Print "Not Annoyed"
  locate %ytpos+1,   %xtposL+10
  Print "at all"
  locate %ytpos,   %xtposR-4
  Print "Extremely"
  locate %ytpos+1, %xtposR-4
  Print "Annoyed"
elseif M = 7 then                              ' SLUGGISH
  screen %hires,0
  locate %ytpos,   %xtposL+7
  Print "Not Sluggish"
  locate %ytpos+1,   %xtposL+7
  Print "at all"
  locate %ytpos,   %xtposR-4
  Print "Extremely"
  locate %ytpos+1, %xtposR-4
  Print "Sluggish"
elseif M = 8 then                              ' LIVELY
  screen %hires,0
  locate %ytpos,   %xtposL+9
  ? "Not Lively"
  locate %ytpos+1,   %xtposL+9
  ? "at all"
  locate %ytpos,   %xtposR-4
  ? "Extremely"
  locate %ytpos+1, %xtposR-4
  ? "Lively"
else    '       M = 9                          ' SELF EFFICACY
  screen %hires,0
  cls
  Print: Print: Print
  ? "Please rate your ability to avoid mistakes for the remainder of the task"
  ? "by moving the cursor left or right with the indicated arrow keys"
  Print
  GoSub keytext
  locate %ytpos,   %xtposL+2
  Print "No ability"
  locate %ytpos+1, %xtposL+2
  Print "to prevent mistakes"
  locate %ytpos,   %xtposR-4
  Print "Complete ability"
  locate %ytpos+1, %xtposR-4
  Print "to prevent mistakes"
End if
return
Rem ################### prints instructions about the keys #############
keytext:
Print "  Press ENTER to register your rating": Print
Print "  You have 15 seconds to make your rating"
Return
Rem ################## input subject parameters ###################
params:
pms2:
cls: locate 10, 10
GoSub debounce
SSNAME$ = ""
Input "  Enter Subject name and DOB ";Ssname$:?
GoSub debounce
If SSNAME$ = "" Then GoTo pms2
lvl = 3

open "timeOUT.txt" for input as #4

input #4, sessionlength$ ' session length
for ip = 1 to 5: input #4, tout(ip) : next ip  'timeouts for each level
input #4, NVASchecks      ' number of times vas is run embedded in maths
for I = 1 to NVASchecks+1 : input #4, presact$(i): next I ' vas times
input #4, DTest$
input #4, Mute$
close 4

if DTest$ = "Y" then
  cls : for ip = 1 to 5: print using "###"; tout(ip); : next ip:?
  ?"Session length : " ;sessionlength$
  ?"# Vas checks : "  ; nvaschecks
  ?"VAS checks "
  for I = 1 to nvaschecks: ?presact$(i): next i
  ?"Backstop : "    ;presact$(nvaschecks+1)
  ?"Display test (Y/N) : "; dtest$
  ?"Mute (Y/N)         : "; mute$
  DELAY 5
end if
Return

Rem ################ read in and validate maths sums ################
                                                Page 5
```

```
inpmaths:
Open "afmaths.txt" For Input As #2
For outifl = 1 To 5
For inifl = 1 To 200
Input #2, aline$, alinen$
alinen = Val(alinen$)
Rem ?aline$, alinen$, alinen, len( alinen$ )
Rem input dummy$
Rem if dummy$ = "99" then goto mlex
sl = Len(aline$)
Rem  error checking
If Left$(aline$, 1) <> "(" Then GoTo merr
For r = 2 To sl
If Mid$(aline$, r, 1) = "+" Then GoTo nr1
Next r
GoTo merr
nr1:
ssecn = r + 1
firstn = Val(Mid$(aline$, 2, r - 2))

For r = ssecn To sl
If Mid$(aline$, r, 1) = ")" Then GoTo nr2
Next r
GoTo merr
nr2:

secn = Val(Mid$(aline$, ssecn, r - ssecn))
sm = (firstn + secn)

For r = ssecn To sl
If Mid$(aline$, r, 1) = "-" Then GoTo nr3
Next r
GoTo merr
nr3:

thirdn = Val(Mid$(aline$, r + 1, sl - r))
ans = sm - thirdn
If ans <> alinen Then GoTo merr

sum$(outifl, inifl) = aline$
sum(outifl, inifl) = alinen
suml(outifl, inifl) = Len(alinen$)

Next inifl
Next outifl

GoTo nexit
merr:
cls: locate 9, 10
   Print "File AFMATHS"
   locate 11, 10
   Print "Error maths questions line # "; ifl
   locate 12, 10
   Print: Print ans, aline$, alinen
   locate 14, 10
   Print "Program closing": delay 3
   Stop
nexit:
Close (2)
cls:  locate 10, 1: Print "Maths routines read successfully": delay 1: cls
Return
Rem ################# handles practice trials #################

practice:
cls
GoSub rscreen
tna = 0
pracflag = 1
while tna <> %nprac
   GoSub dquest
   GoSub level ' may change level based on answer
   pracflag = 0
Wend
Return

' ################## changes level according to lvl and last 8 results

' each time Ss responds this requires a decision to be made about whether
' they need to go up or down a level

level:
If tna > 7 Then  ' 8 or more
   if SumCAs < 4 then
      decr lvl   ' error rate too high so make easier
   elseif SumCAs > 4 then
```

```
                                                        36
      incr lvl   ' error rate too low so make harder
   end if
elseif tna = 2 then  'sum is 0,1,2
   if SumCAs = 2 then
      incr lvl
   elseif SumCAs = 0 then
      decr lvl
   end if
elseif tna = 3 then  'sum is 0,1,2,3
   if SUmCAs > 1 then
      incr lvl
   else
      decr lvl
   end if
elseif tna = 4 then
   if SumCAs > 2 then
      incr lvl
   elseif SumCAs < 2 then
      decr lvl
   end if
elseif tna = 5 then
   if SUmCAs > 2 then
      incr lvl
   else
      decr lvl
   end if
elseif tna = 6 then
   if SumCAs > 3 then
      incr lvl
   elseif SumCAs < 3 then
      decr lvl
   end if
elseif tna = 7 then
   if SUmCAs > 3 then
      incr lvl
   else
      decr lvl
   end if
end if
if lvl < 1 then lvl = 1
if lvl > 5 then lvl = 5
Return
Rem ##################### display question ################## ??????????????
dquest:
        incr qp(lvl) ' get next ? for this level
        If qp(lvl) > 200 Then qp(lvl) = 1  ' cycles thru 1-200
dq1:
        cls
        locate 13, 36
        Print "                          "
        locate 13, 36
        GoSub debounce
        Print sum$(lvl, qp(lvl))
        GoSub status
        locP = 47
        ansl = suml(lvl, qp(lvl))
        If ansl = 0 Then ansl = 1
        Print #5, "Answer length "; ansl
        HH = 0
        cans$ = ""
        cpam$ = "D"  ' will initialize tcount to be tout(lvl)
        GoSub initialiseClock

' want to wait until either time count expires or ansl digits entered

      Do Until ((tcount = 0) Or (HH = ansl))
          If instat Then
              ans$ = inkey$ ' read keypress  : ans$ = ucase$(ans$)
              If ans$ = "|" Then
                 If pracflag = 1 Then    'short cut out of practice trials
                    tna = %nprac
                    Return
                 Else
                   GoSub saveresults
                   GoTo mlex
                 End If
              End If
              If ans$ >= "0" And ans$ <= "9" Then
                incr locP
                incr HH
                locate 13, locP
                Print ans$ ' echo
                cans$ = cans$ + ans$  ' concatenate the answer
              End If
          Else ' check the clock
                                                Page 7
```

```
                                                    J6
            GoSub checkclock
          End If
      Loop   '  waiting for ansL digits or timeout to occur

        If tcount = 0 Then
            lastA = 0
            lst$ = "X"
            GoSub tooslowfb
        ElseIf Val(cans$) = sum(lvl, qp(lvl)) Then
                GoSub correctFB
                lastA = 1 'i.e. was correct
                lst$ = "C"
        Else
                lastA = 0
                lst$ = "X"
                GoSub incorrectFB
                        End If
dqexit:
        incr tna
        GoSub last8
         Gosub check4P  ' check for a (P)ause
        GoSub debounce
Return
Rem ################ check for a P ##############################
Check4P:
If ucase$( inkey$ ) = "P" then
   Gosub debounce
   Cls
   Locate 10,10:?"PROGRAM PAUSED"
   Paused$ = "P"
   Gosub savetime
   While Paused$ = "P"
     While not instat : wend
     If ucase$( inkey$ ) = "C" then Paused$ = "C"
      Gosub restoretime
   wend
end if  ' no P pressed so keep going
return
Rem ################ sums last8 answers ##############################
last8:
Rem this next bit keeps track of last 8 questions
incr cycleA
If cycleA > 8 Then cycleA = 1
cycles(cycleA) = lastA    ' lastA has value 0 or 1
last$(cycleA) = lst$ ' used for testing
sumcas = 0
For ci = 1 To 8: sumcas = sumcas + cycles(ci): Next ci

Return
Rem ################ debounce keys ##################################
debounce:
for j = 1 to %debounces:d$=inkey$:next j  ' rem throw away unwanted chars
Return
Rem ################ variables get initial values ###################
initvals:
Rem qp points to each of the 5 levels and range from 1-200
Rem initial level set by group a thru d in s/r params
Rem for I = 1 to 5:sumptr(I)=0:next I

out %oport,1
cycleA = 0: tna = 0
For i = 1 To 5: qp(i) = 0: Next i  ' pointer to nxt ? by level

For i = 1 To 8: cycles(i) = 0: last$(i) = " ":Next i

for i = 1 to %NumMoods :for j = 1 to %VasCalls:moodvas(i,j)=0:next j:next I
MOODP = 0
Return

Rem ################ displays status level etc ######################
status:
if DTest$ = "Y" then
  locate 6, 1
  ?"Number of VAS checks in maths task : ";nvaschecks
  for I = 1 to nvaschecks
  ?using "# ";I;:?"Vas check at : ";presact$(i)
  next I
  ?"Backstop at    : " ;presact$(nvaschecks+1)
  ?"Session Length : " ;sessionlength$
  ?"Current Time   : " ;currenttime$
  ?"Waiting on     : " ;presact$(event)
  ?"Event number   : " ;event
  ?"Actual question : "; sum$(lvl, qp(lvl))
  ?"Correct answer  : "; sum(lvl, qp(lvl))
  ?"# answer digits : "; suml(lvl,qp(lvl) )
                                                  Page 8
```

```
                                                    J6
  ?"Total answers ";
  ? using "###"; tna
  ?"Last 8 answers ";
  For ci = 1 To 8
    ? using "# "; cycles(ci);
  Next ci
  ?
  ?"              1 2 3 4 5 6 7 8 "
  ?"Sum last 8 "; sumcas
  ' display ascii depiction
  ?"              ";
  for ci = 1 to 8:?" ";:?right$(last$(ci),1);:next ci:?
  ?"cycle ptr(1-8) "; cycleA
  ?"Question # "; qp(lvl)
  ?"Level "; lvl
  ?"Timeout "; tout(lvl)
end if 'display is set to Y = yes, N = no display
Return
Rem ######################## feedback - too slow ##########################
tooslowfb:
Print #5, "TOO SLOW"
Rem color  %normalFG, %TooSlow  ' purple
Rem gosub dlplus
Rem gosub resetscreen
GoSub blanksum
Print "TOO SLOW !!"
if mute$ ="N" then sound 2200, 10
if mute$ ="N" then sound 3000, 10
if mute$ ="N" then sound 2200, 10
if mute$ ="N" then sound 3000, 10
if mute$ ="N" then sound 2200, 10
if mute$ ="N" then sound 3000, 10
if mute$ ="N" then sound 2200, 10
if mute$ ="N" then sound 3000, 10
if mute$ ="N" then sound 2200, 10
if mute$ ="N" then sound 3000, 10
if mute$ ="N" then sound 2200, 10
if mute$ ="N" then sound 3000, 10
delay 2
GoSub blanksum
Return
Rem ######################## feedback correct #############################
correctFB:
Print #5, "CORRECT"
Rem color  %normalFG, %correct   ' green
Rem gosub resetscreen
GoSub blanksum
Print "CORRECT "
if mute$ ="N" then sound 100, 3
if mute$ ="N" then sound 150, 3
if mute$ ="N" then sound 200, 3
delay 2
GoSub blanksum
Return

Rem ################ delay with noise ####################################
dlplus:
For nl = 1 To 2
if mute$ ="N" then sound 500, 10
if mute$ ="N" then sound 1000, 10
Next nl
Return

Rem ############### sets screen back to normal immediately #################
rscreen:
color %yellow, %black ' reset screen to normal page and color
cls
Return
Rem ######################## feedback incorrect ###########################
incorrectFB:
Print #5, "INCORRECT"
GoSub blanksum
Print "INCORRECT"
if mute$ ="N" then sound 2200, 10
if mute$ ="N" then sound 3000, 10
if mute$ ="N" then sound 2200, 10
if mute$ ="N" then sound 3000, 10
if mute$ ="N" then sound 2200, 10
if mute$ ="N" then sound 3000, 10
if mute$ ="N" then sound 2200, 10
if mute$ ="N" then sound 3000, 10
if mute$ ="N" then sound 2200, 10
if mute$ ="N" then sound 3000, 10
if mute$ ="N" then sound 2200, 10
if mute$ ="N" then sound 3000, 10
                                                    Page 9
```

```
                                                    J6
delay 2
GoSub blanksum
Return
Rem ######################## restores screen ################################
resetscreen:
Print #5, "RESETTING SCREEN"
cls
Rem delay 2
color %yellow, %black ' reset screen to normal page and color
cls
Return
Rem ################ general pretest instructions
genpretest:
cls
locate 3, 1
Print "   Maths questions will be presented": ?:?:?
Print "   The computer will keep track of the number of problems"
Print "   you get wrong throughout the task. "
Return

Rem ############## Initial message ########################
beginmess:
locate 23, 1
GoSub debounce
Print "   Please press any key to begin"
While Not instat: Wend
GoSub debounce
Return
Rem ############## continue message ########################
contmess:
incr cmess
locate 23, 1
GoSub debounce
Rem ?"# ";cmess;
Print "   Please press any key to continue"
While Not instat: Wend
GoSub debounce
Return
Rem ############### practice message ############################
beginpracticemess:
cls
locate 5, 1
Print "   These are practice trials "
Return
Rem ################ end practice message ######################
endpracticemess:
cls
locate 10, 1
Print "   End of practice trials": Print: Print
Print "   Please press any key to"
Print "   begin the experiment"
Print: Print
Return
Rem ########## INITIALISE CLOCK ######################## ############
initialiseClock:
' this routine waits for on exact time seconds change to be more accurate
if cpam$ = "D" then
   tcount = tout(lvl)
else
   tcount = %vastimeout
end if
oldsecs$ = Right$(Time$, 1)
inclk1:
   newsecs$ = Right$(Time$, 1 )
   If newsecs$ = oldsecs$ Then GoTo inclk1 ' no change in seconds
   oldsecs$ = newsecs$
Return
Rem ################## blank the sum area ######################
blanksum:
locate 13, 36
Print "                    "
locate 13, 36
Return
Rem ################## check the clock ##########################
checkclock:
  ' software clock
   newsecs$ = Right$(Time$, 1)
   If newsecs$ <> oldsecs$ Then
         oldsecs$ = newsecs$
         decr tcount
   End If
Return
Rem ################## starting message ############################
startingmessage:
cls
```

```
                                                    J6
locate 10, 10
Print "Maths test starting"
delay 1
cls
Return
Rem ################### open outputfile for testing #################
openoutputfile:
Open "int.tmp" For Output As #5
Return
Rem ##################  end of task message ########################
endmessage:
cls
locate 10, 1
Print "   The task is now finished": Print: Print
Print "   Please alert the experimenter that you have finished immediately"
Return
Rem ################## reset the time ##############################
resettime:
cls
locate 10, 3
?"Please enter the time including the colon as in hh:mm "
Return
Rem ################ The real trials ##############################
runtrials:
GoSub rscreen  ' set screen to normal
GoSub INITIALISEtime
GoSub getTIME
event = 1
while Not ((currentTime$ >= SessionLength$) AND (event = NvasChecks+1))
    GoSub getTIME
    if CurrentTime$ >= Presact$(event) then
       GoSub runmoodVAS
       incr event
    else
       GoSub dquest 'display the next question
       GoSub rscreen  ' set screen to normal
       GoSub level
    end if
wend
Return
Rem ############### get the current mins and secs #################
getTIME:
currentTIME$ = Right$(Time$, 5)
Return
INITIALISEtime:
Time$ = "00:00:00"
Return
savetime:
savedTIME$ = Right$(Time$, 5)
Return
restoreTIME:
Time$ = "00:" + savedTIME$
Return
Rem ########################## temporary message for testing #############
exitmess:
cls
locate 10, 10
Print "Program closing"
Stop
Return
' ###########################################################################
realtrialsounds:
if mute$ ="N" then sound 450,7
if mute$ ="N" then sound 300,7
Return
End  'of program
```

Page 11