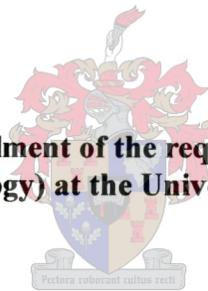


Psychological and endocrine indicators of stress:
health and management implications

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**Thesis presented in partial fulfillment of the requirements for the Master's Degree
in Science (Physiology) at the University of Stellenbosch.**



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Declaration

I, the undersigned, hereby declare that the work contained in this assignment is my own original work and has not previously in its entirety or in part been submitted at any university for a degree.

Abstract

Introduction: This is a multidisciplinary investigation of stress in working males. The physiological aspect of the stress response is focused primarily on the hypothalamic-pituitary-adrenal axis; the health outcomes focus on cardiovascular risk and the psychological aspect focuses on both personality and state.

Aims: To assess psychological and physiological measures of stress and determine if they are associated. To assess the effect of massage as a relaxation intervention on these measures.

Abstract:

Section 1

This study consisted of 16 working, stressed males. Certain measures of allostatic load were determined, on 2 occasions 1 week apart with appropriate control (serum cortisol, dehydroepiandrosterone-sulphate (DHEAs), total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein) as well as perceived stress levels (State Anxiety, Profile of Mood (POMS), Job Satisfaction (JS), Symptoms of Stress (SYMP)). Measurements of personality (Trait Anxiety and Hardiness, with subscores Commitment, Control and Challenge) and anthropometric measurements were obtained. Repeatability was assessed and then data was averaged. Correlation analysis was done between baseline physiological and psychological parameters. (All r values reported in this abstract have $P < 0.05$, unless otherwise stated).

Section 2

11 of the 16 subjects then had 1 week of intensive massage (5 x 1hr each), after which a 3rd measurement was taken.

Findings:

Section 1

Certain personalities had differing perceptions of stress (Commitment correlated positively with Vigour, $r = 0.59$; and negatively with Fatigue and POMS, $r = -0.51$ and $r = -0.54$ respectively). Certain personalities influenced JS (Commitment correlated positively to JS, $r = 0.55$; Trait Anxiety correlated negatively to JS, $r = -0.54$). Certain personalities manifested stress physiologically (Control correlated negatively with Cortisol/DHEAs, $r = -0.53$). Increased perception of stress also resulted in an increased likelihood of experiencing physiological symptoms of stress (e.g. State Anxiety correlated with SYMP, $r = 0.50$). In contrast, lower perceived stress was associated with increased job satisfaction (POMS correlated with JS, $r = -0.64$; $P < 0.01$) and those who experienced more JS had decreased risk of cardiovascular disease (CVD) (JS correlated negatively to LDL, $r = -0.53$). Physiological measures of CVD were also higher in subjects with antropometrically evaluated risk profiles.

Section 2

Baseline variability of various parameters ranged form moderate to high (CV 4.4% to 73%). The intervention had no significant measured effect. 45% of subjects increased state-related stress. These subjects had had significant lower scores for Commitment ($P < 0.05$).

Conclusion:

Section 1

Certain personality types are associated with decreased perception of stress, decreased stress symptomology and improved endocrine markers of allostatic load. Certain personality dispositions are associated with improved job satisfaction and decreased risk of CVD. These characteristics include e.g. high commitment, low anxiety and a sense of control i.e. all inherent predispositions. To improve sensitivity to intervention, 3 baseline samples should be considered in future studies.

Section2

Contrary to what was hypothesized, massage had no effect. This is possibly due to the large daily variations in these variables and outside influences, which are necessarily a part of real-life as opposed to laboratory studies. Possibly 1 week of intensive relaxation therapy is insufficient and longer-term, lifestyle changing intervention is recommended for future studies.

Samevatting

Inleiding: Hierdie studie is 'n multi-dissiplinêre ondersoek na stres in werkende mans. Die fisiologiese aspek van die stresrespons fokus primêr op die hipotalamo-pituitêre-adrenale as, terwyl die gesondheidsuitkomst op die kardiovaskulêre risiko, en die psigologiese aspek op beide persoonlikheid en status fokus.

Doel: Om psigiese en fisiologiese parameters van stress te bepaal, en om vas te stel of hulle met mekaar korreleer. Om die effek van massering, as ontspanningsterapie, op hierdie parameters te bepaal.

Afdeling 1

Sestien gespanne, werkende mans het aan hierdie studie deelgeneem. Sekere parameters van allostadiese lading (serum kortisol, dehidroepiandrosteron-sulfaat (DHEAs), totale cholesterol, lae digtheid- (LDL) en hoë digtheid lipoproteïene (HDL) is twee maal bepaal, met 'n tussenpose van een week, met gepaste kontrole. Terselfdertyd is subjektiewe ervaring van stres (Toestand Angs, Profiel van Gemoedstemming (POMS), Werksbevrediging (JS), Simptome van Stres (SYMP)), metings van persoonlikheid (Trekangs en Hardiness, i.e. Gebondenheid, Beheer en Uitdaging) en antropometriese metings ook verkry. Herhaalbaarheid is getoets en daarna is die gemiddelde van hierdie twee basislyn bepalinge gebruik. Korrelasie analises is gedoen tussen basislyn fisiologiese en psigiese parameters. (Alle r-waardes gerapporteer in hierdie samevatting het $P < 0.05$, behalwe waar anders aangedui.)

Afdeling 2

Elf van die sestien proefpersone het 1 week van intensiewe masseerterapie (5 x 1 uur elk) ondergaan, waarna 'n derde meting geneem is.

Resultate:

Afdeling 1

Sekere persoonlikhede het verskillende ervarings van stres getoon (Toegewydheid het positief gekorreleer met lewenslus, $r = 0.59$; en negatief met uitputting en POMS, $r = -0.51$ en $r = -0.54$ onderskeidelik). Sekere persoonlikhede het werksbevrediging (JS) beïnvloed (Toegewydheid het positief gekorreleer met JS, $r = 0.55$; Trait anxiety het negatief gekorreleer met JS, $r = -0.54$). Sekere persoonlikhede het ook fisiologiese geneigdheid tot stres getoon (Beheer het negatief gekorreleer met C/DHEAs, $r = -0.53$). Verhoogde ervaring van stres het 'n verhoogde waarskynlikheid vir ervaring van fisiologiese simptome van stres tot gevolg gehad (bv. Toestand Angs het positief gekorreleer met SYMP, $r = 0.50$). In teenstelling, is laer ervaring van stres geassosieer met verhoogde werksbevrediging (POMS het positief gekorreleer met JS, $r = -0.64$; $P < 0.01$). Dië persone wat hoer werksbevrediging ervaar het, het 'n laer risiko om kardiovaskulêre siektes (CVD) op te doen (JS het negatief gekorreleer met LDL, $r = -0.53$). Fisiologiese mates van CVD was ook hoër in proefpersone met antropometries geëvalueerde risiko profiele.

Afdeling 2

Die mate van variasie in die basislyn fisiologiese bepalinge het gewissel van gemiddeld tot hoog (KV 4.4 % tot 73 %). Die ingreep het geen meetbare effek getoon nie. 45 % van proefpersone het verhoogde status-verwante stres gerapporteer. Hierdie proefpersone het betekenisvol laer waardes vir Toewyding gehad ($P < 0.05$).

Gevolgtrekking:

Afdeling 1

Sekere persoonlikheidstipes word geassosieer met verlaagde ervaring van stres, verlaagde voorkoms van simptome van stres en verbeterde endokriene merkers van allostadiese lading.

Sekere persoonlikheidstrekke word geassosieer met verhoogde werksbevrediging en verlaagde risiko vir CVD. Hierdie karaktertrekke sluit hoë toegewydheid, lae angstigheid en die vermoë om beheer uit te oefen in, d.i. alle inherente karaktertrekke. Drie basislyn metings behoort in die toekoms oorweeg te word, om die sensitiwiteit vir die ingreep te verbeter.

Afdeling 2

Teenoorgesteld aan die hipotese, het massering geen effek getoon nie. Dit kan moontlik as gevolg van die groot daaglike variasie in hierdie veranderlikes wees, asook buite-invloede, wat noodwendig 'n deel van regte-lewe studies is, in teenstelling met laboratoriumstudies. Een week van intensiewe ontspanningsterapie kon ook moontlik onvoldoende gewees het. Daarom word langer-termyn, leefstyl-veranderende ingrepe aanbeveel.

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Abbreviations

ACTH – Adenocorticotrophic hormone
ADHD – Attention Deficient Hyperactivity Disorder
BMI – Body mass index
bpm – beats per minute
CBG - Corticosteroid-binding globulin
CFS – Chronic fatigue syndrome
CNS – Central Nervous System
CRF – Corticotrophic releasing factor
CV – coefficient of variation
CVD – Cardiovascular disease
DHEA - Dehydroepiandrosterone
DHEAs – Dehydroepiandrosterone sulphate
ECG – Electrocardiogram
EEG - Electroencephalogram
GR – Glucocorticoid receptor
HDL – High-density lipoprotein
HPA – Hypothalamic-pituitary-adrenocortical
HR – Heart rate
HRR – Heart rate reactivity
JSS – Job Satisfaction Survey
LDL – Low-density lipoprotein
LPL – Lipoprotein lipase
ME – Myalgic encephalomyelitis
MR - Mineralcorticoid receptors
POMS – Profile of Mood State
PVN - Paraventricular nucleus
SD – Standard deviation
SES - Socioeconomic-status
STAI – State Trait Anxiety Index
SNS – Sympathetic Nervous System

TG - Triglyceride

TM – Transcendental meditation

TABLES

Table 1: Normal ranges for serum DHEAs, for men age 15-49 (the age of this study's subject population), as cited from ⁹² pg 554.....	35
Table 2: Inclusion and exclusion criteria	54
Table 3: Subject characteristics	63
Table 4: DHEAs range of subjects and normal healthy range for males in the specified age groups.	64
Table 5: Lipid profile	65
Table 6: Subject characteristics grouped according to BMI	65
Table 7: Subject characteristics grouped according to WHR	66
Table 8: Results adjusted for age and grouped for BMI.....	66
Table 9: Results adjusted for age and grouped for WHR	67
Table 10: Stress-related psychological characteristics analysed using three different questionnaires	67
Table 11: Personality scores, i.e. Trait Anxiety and Hardiness are listed as Mean \pm SD.	69
Table 12: Correlation results between personality variables.....	70
Table 13: Coefficient of variation for lipid profile	78
Table 14: Coefficient of variation for the state-related psychological assessments	78
Table 15: Hormonal and lipid baseline and post-massage results	79
Table 16: State-related Baseline and post-massage results	80
Table 17: Change from baseline to post-massage	81
Table 18: Subject characteristics grouped according to State Anxiety response.....	83
Table 19: Subject characteristics grouped according to State Anxiety response.....	84

FIGURES

Figure 1: The Optimal Zone of Functioning	15
Figure 2: Neuroendocrine components of sympathetic-adrenal medullary system and catecholamines pathways.....	21
Figure 3: Pathway of HPA axis	22
Figure 4: Pathway of cortisol and corticosterone synthesis in the adrenal cortex ⁴⁹ pg 85.....	26
Figure 5: Pathway of cortisol and DHEA synthesis in the adrenal cortex ⁴⁹ pg 85.	35
Figure 6: Four types of allostatic load. Figure drawn by Dr. Firdaus Dhabhar, The Rockefeller University, New York. (Reprinted from ¹³¹).....	47
Figure 8: Baseline cortisol concentrations with the lower and upper limit of the normal healthy range.....	63
Figure 9: The association between age and DHEAs in 16 male working individuals	64
Figure 10: POMS score, viewed with subscores: Tension-Anxiety, Fatigue and Vigour.....	68
Figure 12: Job Satisfaction score, viewed with subscores: Contingent rewards. Operating conditions, co-workers, Nature of work, Communication.....	68
Figure 13: The association between Commitment and Vigour in 16 male working individuals .	70
Figure 14: The association between Commitment and Fatigue in 16 male working individuals.	71
Figure 15: The association between Commitment and POMS in 16 male working individuals .	71
Figure 16: The association between Commitment and Job Satisfaction in 16 male working individuals.....	72
Figure 17: The association between Trait Anxiety and Job Satisfaction in 16 male working individuals.....	72
Figure 18: The association between Trait Anxiety and Symptoms of Stress in 16 male working individuals.....	73

Figure 19: The association between Control and Cortisol/DHEAs in 16 male working	73
Figure 20: The association between POMS and Job Satisfaction in 16 male working individuals	75
Figure 21: The association between POMS and Symptoms of stress in 16 male working individuals	75
Figure 22: The association between State Anxiety and Symptoms of Stress in 16 male working individuals	76
Figure 23: The association between Job Satisfaction and LDL concentrations in 16 male working individuals	76
Figure 24: Baseline and post-massage cortisol concentrations	79
Figure 25: Baseline and post-massage cortisol/DHEAs ratio	80
Figure 26: Baseline and post-massage State Anxiety scores	81
Figure 27: Change in State Anxiety across Baseline to post-massage, relative to change in cortisol	82
Figure 28: Change in State Anxiety across Baseline to Post massage, relative to change in DHEAs	82
Figure 29: Change in State Anxiety across Baseline to Post massage, relative to changes in cortisol/DHEAs ratio	83

TABLE OF CONTENTS

Introduction	12
1 LITERATURE REVIEW	14
1.1 Work stress	14
1.2 Psychology of stress	16
1.3 Physiology of stress	20
1.4 Physiological Reactivity	23
1.5 Cortisol	26
1.5.1 Metabolic effects	27
1.5.2 Feedback mechanisms	28
1.5.3 Physiological integration	29
1.5.4 Psycho-physiological research	30
1.5.5 Cortisol and habituation	31
1.5.6 Cortisol and chronic stress	33
1.5.7 Effect of stress management interventions	34
1.6 Dehydroepiandrosterone	35
1.7 Stress and health	38
1.8 Cholesterol	41
1.9 Fat distribution	42
1.10 Obesity	44
1.11 Integration	44
1.12 Stress and Allostatic load	45
1.13 Massage and stress	50
1.14 Synthesis	53
2 METHODOLOGY	54
2.1 Research aims	54
2.2 Participants	54
2.3 Protocol	55
2.4 Psychological Questionnaires	56

2.5	Massage technique.....	58
2.6	Blood sampling procedure.....	59
2.7	Serum DHEAs, cortisol and cholesterol.....	59
2.8	Fat distribution measures.....	60
2.9	Obesity measures.....	60
2.10	Heart rate reactivity.....	61
2.11	Statistical Evaluation.....	61
3	RESULTS.....	63
3.1	Baseline study.....	63
3.1.1	Subject characteristics: Physiology.....	63
3.1.2	Group comparisons: Physiological results.....	65
3.1.3	Subject characteristics: Psychology.....	67
3.1.4	Group comparisons: Psychological results.....	69
3.1.5	Trait-related relationships.....	69
3.1.6	State-related relationships.....	74
3.2	Intervention study.....	78
3.2.1	Hormonal, lipid and psychological variability.....	78
3.2.2	Effects of the massage.....	79
4	DISCUSSION.....	85
4.1	Baseline study.....	85
4.1.1	The effects of moderate stress on health-related physiological parameters.....	86
4.1.2	Trait-related relationships.....	89
4.1.3	State-related relationships.....	92
4.2	Intervention study.....	93
4.2.1	Effects of the massage.....	97
4.2.2	Conclusion.....	100
4.3	Implications for future research.....	101

Introduction

The fact that psychological stress and physiology are linked, was first extensively explored in 1956, by Selye ¹. It was proposed that physiological manifestation of stress or anxiety are triggered by the sympathetic nervous system and can be measured on a continuum, as reflected by the level of sympathetic nervous system arousal ¹. Benson *et al.* defined relaxation as the opposite of arousal (or anxiety) and as a process resulting in a decrease in sympathetic nervous system activity ². Relaxation has been referred to as a state at the lower end of the continuum of arousal.

The idea that cumulative levels of stress may have deleterious effects on health and longevity has long intrigued investigators. This dates back to the important, early work on homeostasis, by Cannon ³, to the above mentioned work by Selye on stress ¹ and the work of Ader on psychoneuroimmunology ⁴. All these authors were instrumental in highlighting the pathological consequences of excessive physiological arousal. More recently, specific diseases that can be initiated or amplified by stress, such as cancer, diabetes and heart disease have been elucidated ⁵.

Dramatic stressful life events exact their toll, and the many events of daily life that elevate activities of physiological stress-response systems, can cause some measure of “wear and tear”. The concept of “wear and tear” is also referred to as “allostatic load” and represents the cumulative physiological toll ⁶.

There have been many recent changes in the nature of work in Western industrial societies. Increasing deregulation, downsizing of companies, increasing job insecurity, the ever-present spectre of long-term unemployment and the impact of technology have changed the character of the work and the workplace ⁷. Many of these changes are potentially threatening to workers and might be expected to have an impact on health. Attempts to reduce stress in the workplace can effectively enhance physical and psychological health ⁸.

The concepts introduced in the introduction above will be elaborated on in the literature review, which will also form the basis from which the multidisciplinary study for this thesis was designed.

1 LITERATURE REVIEW

1.1 Work stress

For most employed individuals, work represents a time commitment exceeded by no other single activity. This time should be satisfying, should respect health, and should contribute to individuals' overall quality of life. However, this is not the case for millions of workers. For many people work contributes to anxiety, frustration and conflict (anecdotal evidence). Rather than providing satisfaction, it is often a source of dissatisfaction; rather than contributing to health, it serves as a catalyst for physical and mental health problems; and rather than adding to quality of life, it detracts from it. The potential negative physiological, psychological, behavioural, and social consequences of excessive stress are many and varied. The cost of stress, reflected by reduced quality of life, poorer health, and less than optimal productivity, coupled with the increasing prevalence of stress in the workplace today, has prompted an increasing number of organizations to seek ways to prevent or reduce employee stress⁹. Indeed, surveys reveal that a growing number of companies are interested in establishing stress management programmes¹⁰.

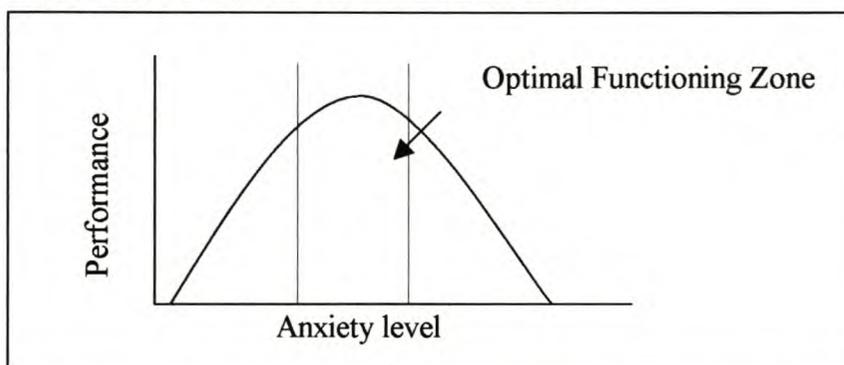
Work stress has been found as an emerging occupational hazard¹¹. When stress is perceived, the brain responds by preparing the body for defensive action. The nervous system is aroused and hormones, this response (also referred to as the "fight or flight" response) is important because it helps the body to prepare to defend against threatening situations. Short-lived or infrequent episodes of stress pose little risk. But when stressful situations go unresolved the body is kept in a constant state of activation, increasing the rate of "wear and tear" on biological systems. Ultimately, fatigue or damage results, and the ability of the body to repair and defend itself can become seriously compromised. As a result, the risk of disease escalates (to be discussed in detail in section 1.7 and 1.11).

The early signs of job stress are usually easy to recognize often presenting themselves in the form of physiological symptoms e.g. sweaty palms, gastro-intestinal tract disorders, breathing difficulties or irregular heart beats. But the effects of job stress on chronic diseases are more difficult to identify because chronic diseases take a long time to

develop and can be influenced by many factors other than stress. Nonetheless, evidence is rapidly accumulating to suggest that stress plays an important role in several types of chronic health problems - especially cardiovascular disease (to be discussed in section 1.7 – 1.11) musculoskeletal disorders, hormonal disorders (to be discussed in section 1.5 - 1.6) and psychological disorders. For example, high job demands have been shown to predict psychiatric related disorders¹². Health care expenditures are nearly 50% greater for workers who report high levels of stress¹³.

Work related stress is inherent to the occupational environment and include stressors such as time pressure, workload, financial and commuting stress. The concept of job stress should not be confused with challenge. Challenge can energize one psychologically and physically, and motivates employees to learn new skills and master their jobs. When a challenge is met, one feels relaxed and satisfied. Thus, when managed, challenge is an important ingredient for healthy and productive work. This “optimal zone of functioning” is often cited in sports psychology literature^{14,15}. This model contends that each individual has an optimal zone of anxiety associated with enhanced performance. This model helps to conceptualise the functionally optimal zone and effects anxiety has upon individual performance. This model illustrates how heightened anxiety levels over and above one’s optimal zone are detrimental to one’s performance.

Figure 1: The Optimal Zone of Functioning



Because of the relationship illustrated in the ascending portion of the curve in the above figure, some employers assume that stressful working conditions are necessary and companies must turn up the pressure on workers to remain productive and profitable in

today's economy. If employers choose to ignore the descending portion of the curve, they can be accused of setting aside health concerns. Research findings challenge this belief that excessive stress is productive. Studies show that stress management programmes in the work setting actually reduce absenteeism¹⁶, decrease use of health services¹⁷ and reduce burnout scores¹⁸. A very recent study, of so-called "healthy" organizations suggest that policies benefiting worker health also benefit the "bottom line"¹⁹. Company expectations of stress management and other health promotion programmes include enhanced employee productivity, reduced absenteeism and turnover and lower medical care/disability costs.

Stress management programmes can be implemented into companies in a straightforward and inexpensive manner without disrupting production schedules or creating upheavals in the organization's structure or function. This can be evaluated for efficiency in the short term. Although projections of such benefits of health promotion programmes are often uncritically accepted. Scientific studies that have assessed employee behaviour (absenteeism and productivity) pre and post stress management intervention have not always been that all that promising²⁰. Further critical scientific research is required in this field of workplace stress management, the manifestations of stress in the working environment, optimal management strategies and effective measurement tools.

1.2 Psychology of stress

Initially the stress response was viewed as an unvarying reflex¹. A major shift was introduced when Mason²¹ noted that animals produced large glucocorticoid responses when exposed to novel experiences, but that future exposures resulted in progressively diminished reactions. Mason argued that the physiological responses, and the stressfulness of a stimulus, could not be purely reflexive but instead are modified by experience, the nature of the environment, and the challenge itself. Therefore, the stressfulness of an event is not a simple property of the stimulus but results from cognitive and emotional reactions by the organism to the stimulus²².

The term “stress” refers to the psychological state which derives from the person’s appraisal²³ of the success with which he or she can adjust to the demands of the environment²⁴. The difference between stress and anxiety appears to be that anxiety is the tendency to perceive stressful situations as potentially threatening, whereas stress is perceived as challenging or demanding but not necessarily dangerous. Stress is not a dimension of the physical or psychosocial environments; it cannot be defined simply in terms of workload or the occurrence of events determined by consensus to be stressful. Equally it cannot be defined in terms of the responses that are sometime consequences of stress, such as physiological mobilization or performance dysfunction. Stress resides in the person’s perception of the balance between the demands and their ability to cope with those demands. The absolute level of demands is therefore not the important factor in determining the experience of stress at work. What is important is the disparity that exists between the person’s perception of those demands and their ability to cope with them.

Lovullo²² has defined stress as the subjective feeling that is produced by events that are perceived as overwhelming and beyond one’s control. Events that typically elicit stress are called stressors and are present in the environment. Not all people respond to stressors in the same way, however. Differences between people in how they react to the same environmental stressor highlight the fact that stress itself is not “out there” in the environment. Instead, stress lies in the transaction between the individual and the stressor, the individual’s unique perception, interaction with and reaction to the stressor.

Personality characteristics (also referred to as personality “traits”) represent cognitive, affective, or behavioural tendencies on the part of a person that are relatively stable across time and context. They refer to enduring characteristics that help to define a person’s identity and help to distinguish one person from another. Personality characteristics make up one class of psychological variables that are relevant to this study. Personality may play a role in the interaction between a stressor and the individual, as it is likely that certain personality types are more likely to perceive particular stressors

as more stressful than others. Hence, personality processors modulate the interaction between a particular event (stressor) and the stressfulness experienced by the individual.

In addition to the more stable personality attributes, people also experience a variety of transient psychological states e.g. fear, fatigue and depression. These “states” may last only a few seconds, or they might persist for months or more. Regardless of duration, they are less stable and less enduring than are personality characteristics, which can remain relatively unchanged for very long periods of time ²⁵. Hence, personality characteristics remain relatively constant, whereas the acute “state” comes and goes more readily.

A number of studies have investigated personality characteristics, and their associated perceptions, evaluations, and emotions and the effect these may have on long-term health as reviewed elsewhere ²⁶. Scheier and Bridges ²⁶ review the literature on the effects of hostility and anger, emotional suppression, depression, fatalism, and pessimism and the effect these may have on coronary heart disease, cancer, and acquired immunodeficiency syndrome. The review locates persuasive evidence linking certain personality traits to the specific health outcomes, for example the evidence linking hostility and anger to a variety of heart disease outcomes, or evidence linking emotional suppression to breast cancer.

Introduced by Kobasa *et al.* ²⁷, the term Hardiness is considered a personality characteristic consisting of the interrelated traits of Commitment, Control and Challenge. Hardiness is considered as the measure of a tendency to engage/participate in the stressful event as opposed to alienating oneself from it. It is not simply enduring the stress but rather the ability to cultivate one's way under difficult conditions. Highly committed individuals find it easy to involve themselves actively in whatever they are doing or experiencing, being generally curious about and interested in activities, things and people. They tend to involve themselves fully in life and find their experiences interesting and meaningful. Individuals with a high sense of control believe and act as if they can influence the events taking place around them through their responses (mental,

verbal, physical). They tend to believe and act as if they can influence the course of events, within reasonable limits. Challenge describes the expectation that life will change and that the process of change, rather than stability, is the normative mode of life. Individuals high in Challenge regard changes as important stimuli to personal development and opportunities for personal growth.

Hardiness has been shown to have a buffering effect on illness²⁷⁻²⁹. The hardy personality appears to be useful in coping with stressful events. People who exhibit hardiness perceive changes as natural, meaningful, and even interesting despite their stressfulness and, in that sense, hold stress in perspective. They can take decisive action to find out more about the changes, to incorporate them into an ongoing life plan, and to learn from their occurrence whatever may be of value for the future. In these ways, hardy individuals transform stressful events into less stressful forms. This process protects health because the environmental stresses and the mental preoccupation associated with them are decreased in intensity and duration. As the events become less stressful, they have a diminished potential to debilitate, and hence health may be preserved.

In contrast, people low in hardiness tend to find themselves and the environment boring, meaningless and threatening. They feel powerless in the face of overwhelming forces, believing that life is best when it involves no changes. As such they have no real conviction that development is either possible or important, and are passive in their interactions with the environment. When stressful events occur, such individuals will have little basis for optimistic cognitive appraisal or decisive actions that could transform the events. Individuals low in hardiness have been shown to engage in maladaptive coping strategies, such as cognitive and behavioural avoidance or denial (e.g. pretending the stressful event did not occur or eating, or drinking). As their personalities provide little or no buffer, the stressful events are left free to have a debilitating effect on health.

Anxiety is an emotion associated with the fight or flight response. Anxiety is defined as “a sense of apprehension, and the anticipation of physical harm”²². Trait anxiety is also a measure of personality predisposition and reflects individual differences in the reaction

intensities during anxiety-provoking situations. The general assumption is that those who are high in trait anxiety are more susceptible to stress i.e. are more vulnerable to stress, than those who are low in trait anxiety. It is proposed that individuals with different trait anxiety differ in terms of what stimuli are processed³⁰. Individuals high in trait anxiety tend to worry more than those low in trait anxiety³¹.

In summary, a stressor may exist in the environment but stress itself is internally perceived. Different personality types perceive the same stressor differently. Although the links between personality and health are being extensively researched, the precise linkages between personality traits and psychological states and their influence on the health status of the individual have yet to be determined.

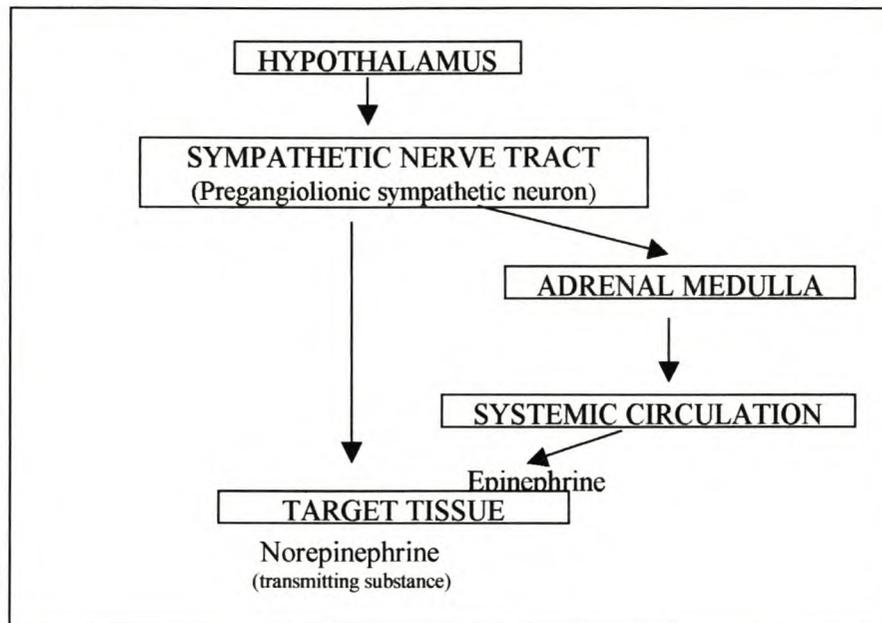
1.3 Physiology of stress

Interest in the physiological response to the experience of stress can be traced back through the early pioneering work of Cannon³ and Selye¹, and has tended to focus on the activity in two neuroendocrine systems: the sympathetic-adrenal medullary system and the hypothalamic-pituitary-adrenocortical (HPA) system. The adrenal glands, and their associated hormones, have thus been central to discussion of stress physiology and psycho-physiological theory. Particular interest has been expressed in the behavioural and physiological functions of the catecholamines, epinephrine and norepinephrine, and glucocorticoids.

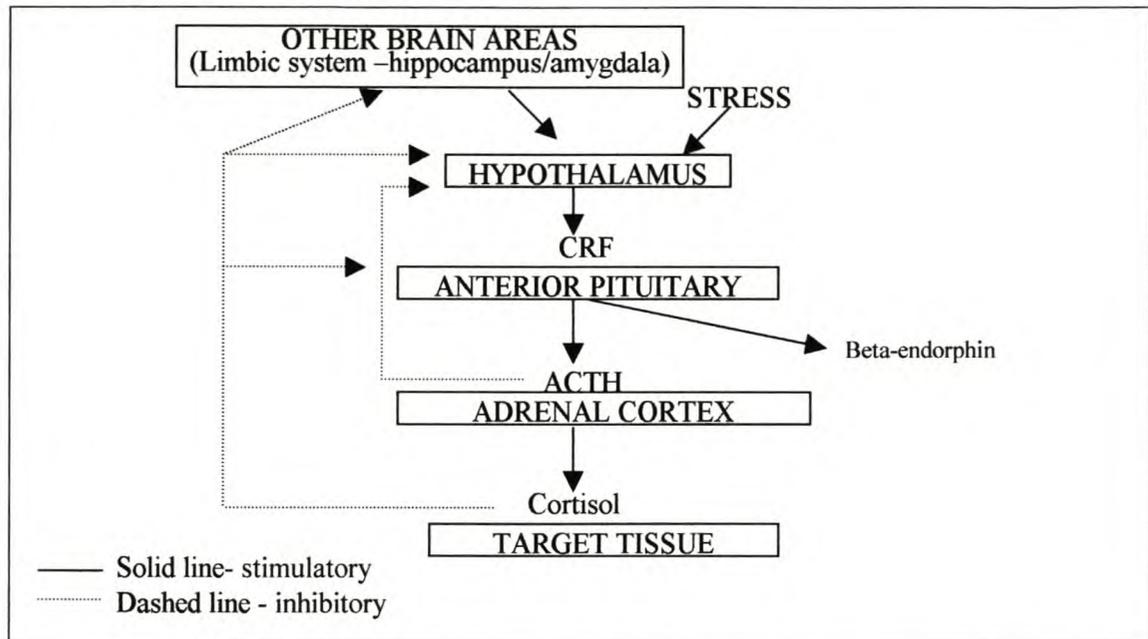
The main effects of epinephrine are the mobilization of the glucose as a source of energy, and an increase in heart rate and cardiac output. Norepinephrine, by contrast, is a more potent vasoconstrictor, and is particularly important in the maintenance of blood pressure through changes in peripheral resistance. Increased blood pressure may serve, in turn, to decrease heart rate. Both hormones accelerate the rate and increase the depth of respiration, and both affect smooth muscles. The behavioural function of the sympathetic-adrenal medullary system, and the catecholamines, was first explored by Cannon³. The evidence accumulated since the early studies suggests that increased

activity in this system prepares the body for “fight” or “flight”, and thus facilitates rapid powerful and sustained coping.

Figure 2: Neuroendocrine components of sympathetic-adrenal medullary system and catecholamines pathways.



Cortisol's secretion is regulated by three primary structures: the pituitary gland, the hypothalamus, and the hippocampus. The positive signal for the secretion of cortisol begins at the paraventricular nucleus (PVN) of the hypothalamus. The PVN has a high concentration of specialized neurons that produce the neuropeptide known as corticotrophin releasing factor (CRF). These CRF neurons project to the median eminence of the hypothalamus, where their axonal processes form specialized junctions with the portal capillaries of the pituitary stalk³². The portal vein carries CRF to the anterior pituitary (adenohypophysis), where corticotroph cells produce the complex protein, pro-opiomelanocortin. Corticotrophin releasing factor (CRF) cleaves this protein into adrenocorticotrophic hormone (ACTH) and the opion agonist, beta-endorphin, and the two are released in identical quantities into the systemic circulation³³. Each pulse of ACTH circulates to the adrenal cortex where it causes an increased rate of cortisol synthesis, resulting in a pulse of cortisol being released into the bloodstream (See Figure 3 below).

Figure 3: Pathway of HPA axis

Cortisol is secreted as periodic pulses regulated by the frequency and amplitude of ACTH pulses arising from the pituitary. Cortisol has a pronounced diurnal pattern, with a peak beginning just prior to awakening, a nadir in the late evening and early morning, and additional rises during the day related to meal times. Cortisol's diurnal cycle is tied to the sleep-wake cycle rather than to the light-dark cycle³⁴. The implication of this diurnal rhythm is that plasma values during sleep can be as much as 18 times less than that of awakening. This 18-fold variation dictates that the diurnal cycle must be taken into account and the sampling time of day must be controlled when testing subjects. The average 8 a.m. plasma concentration of cortisol in adult humans is 13 $\mu\text{g}/\text{dl}$ equivalent to 358 nmol/l with a secretion rate of 15 mg/day .

Cortisol secretion is regulated by negative feedback at the pituitary, hypothalamus, and hippocampus³⁵ (see dashed line in Figure 3). These sites each have different feedback dynamics, resulting in highly sensitive regulation. At the pituitary, the rate of pro-opiomelanocortin synthesis is rapidly slowed at the cell nucleus. At the hypothalamus, CRF gene expression is inhibited by mechanisms sensitive to cortisol concentration and its rate of change. The result is a modulation in the rate at which the pituitary secreted ACTH pulses. The negative feedback relationship changes over the day. Adrenal cortex sensitivity is highest in the morning, and the feedback sensitivity of the system is lowest

at that time ³⁶. These are the dynamics that may account for the greatly increased rate of cortisol secretion in the early morning, accounting for the circadian rhythm cortisol presents.

Cortisol has two states – one serving normal metabolic and diurnal functions (*permissive function*), and one coming into play in times of stress. The HPA axis, under normal conditions, produces sufficient quantities of glucocorticoid to allow normal tissue regulation ³⁷. During stress high levels of cortisol are produced to exert regulatory control over stress-related processes that would otherwise prove injurious. For example, an immune response can be fatal unless regulated by stress levels of glucocorticoids secreted during infection. Under severe stress, the maximal rate of cortisol secretion is 300-400 mg/day.

1.4 Physiological Reactivity

Physiological reactivity can be illustrated via the manner in which one's cardiovascular system reacts to a stress (psychological or physiological). Cardiovascular reactivity is a joint function of the sympathetic and parasympathetic nervous influences. People who tend to respond to stress with relatively large heart rate and blood pressure increases, appear to have elevated levels of sympathetic outflow from the brainstem cardiovascular control centres ³⁸.

Physiological reactivity refers to sudden shifts (generally elevations) in physiological activity in response to specific stimuli. Short-term elevations are time limited. Reactivity focuses on acute changes in functioning as opposed to the assessment of resting levels of a variable. The cumulative effects of repeated elevations can result in considerable exposure to elevated levels of physiological activity. Chronic exposure to repeated elevations in the physiological system have been proposed to impact heavily on homeostasis and health ⁶. Lovallo ²² hypothesized specifically that exaggerated cardiovascular response tendencies may have negative health outcomes, due to the fact that the sympathetic nervous system *and* accompanying endocrine reactions can exert damaging effects on the body when responses are frequent and of large magnitude.

Individuals differ considerably in their extent of physiological responses to stressful situations or events. Manuck and Garland (1980)³⁹ found that individuals who had higher heart rate elevation (termed Heart Rate Reactivity, HRR) in response to a cognitively challenging task had similarly large responses to the same task and to a different cognitive task when retested 13 months later. Other studies confirm that individual differences in tendency to interpret stimuli as requiring a greater or lesser degree of physiologic reactivity, appear to be relatively stable characteristics⁴⁰, may therefore be considered trait-like qualities, somewhat like a personality trait.

HRR is also stable across different types of tasks, such as a cold pressor and reaction time tests conducted 2 weeks to 13 months apart⁴¹ and across public speaking and mental arithmetic tasks tested 3 weeks apart⁴². These observations reinforce its trait-like qualities. This stability over time and across situations provides a basis for considering reactivity tendencies as capable of affecting health. The idea that persistently large cardiovascular responses may themselves be a disease risk (e.g. coronary artery disease or hypertension) is known as the “cardiovascular reactivity hypothesis”²². This hypothesis is based on findings suggesting that exaggerated stress-induced cardiovascular reactivity may independently play a role in the pathogenesis of hypertension and coronary heart disease^{43,44}.

Whether or not HRR is purely physiological or influenced by psychological aspects still remains debatable. Lovallo^{41,45} compared high and low HR reactive individuals in two stress tasks (aversion or rewarded i.e. threat or monetary rewards as motivation). The high HRR group had the largest heart rate changes in response to the task, regardless of the nature of the incentive. This data support the idea that cardiovascular reactivity may identify individuals likely to show exaggerated autonomic responses to a variety of situations. The cardiovascular reactivity groups did not differ in their perceptions or evaluations of the tasks, however. Overall, subjects in the threat avoidance group rated that task as much more aversive than the other subjects rated the rewarded task. Within each study, the high HR reactors did not report feeling more activated or distressed than their less reactive counterparts during either task. Because the heart rate response groups

did not have different subjective experiences, one can suspect that their cardiovascular response differences did not result from differences in how they evaluated the tasks and formed emotional reactions. Instead, it appears that the HR response differences were based on reactive differences in the physiological system itself.

In a similar study, the same researchers ⁴⁶, compared cortisol and norepinephrine response in high and low HR reactive men during two versions of the same two stress challenges (aversion versus rewarded versions). They found that the low HR reactors showed little or no change in either cortisol and norepinephrine to either task. The high HR reactors produced significant cortisol rises to the aversion task, but not the rewarded tasks, indicating greater global sympathetic activation in the former. Therefore, the tendency to produce large sympathetically mediated cardiac responses appears to be tied to cortisol activation only under conditions evoking negative emotions. Sgoutas-Emch *et al.* ⁴² have similarly shown that high HR reactors produced larger cortisol responses to mental arithmetic stress. One can conclude from these findings that there exists a relationship between high HRR and HPA axis response to stressful stimuli.

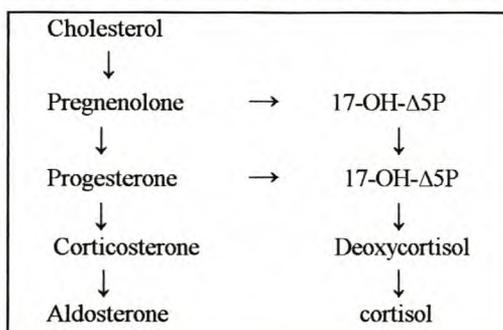
In summary, high and low HR reactors appear to psychologically experience challenging events in the same way, suggesting that they are not differentially reactive because of differences in evaluations of the situation or the resulting emotions. Secondly, the tendency for high HR reactors to be accompanied by large cortisol responses under stressful situations suggests that individual differences in stress reactivity are organized at a level above the separate output pathways for autonomic and endocrine outflow, possibly the limbic system. Lovallo hypothesized that the hypothalamus is the structure most capable of producing this integrated response pattern ²². This line of reasoning led to the proposal that people with different HRR have differences in the hypothalamic amplification of signals arriving from evaluative and emotion-producing centres in the brain. The presumed amplification difference may therefore result in consistent individual differences in integrated autonomic and endocrine outflow, accounting for the differences between subjects in both heart rate and cortisol responses ²².

Evidence is slowly accumulating to suggest that exaggerated cardiovascular reactivity may play a predictive role in future cardiovascular disease ²². For example, high cardiovascular reactors have been shown to be more likely to have hypertensive parents ⁴⁷. A review, ⁴³ of the literature pertaining to physiological reactivity and cardiovascular disease (CVD) concluded that although there is promising evidence to suggest that physiological reactivity plays a role in CVD, it should not be regarded as yet, as a “risk factor” for CVD.

1.5 Cortisol

Cortisol is the primary hormone secreted by the zona fasciculata of the adrenal cortex. All human steroid hormones (including the likes of cortisol and DHEA) are derived from cholesterol. The cells of steroidogenic tissue of the adrenal cortex can synthesize cholesterol *de novo* from acetate, mobilize intracellular cholesterol ester pools, or import lipoprotein cholesterol from plasma. About 80% of the cholesterol is usually provided by circulating plasma lipoproteins. Adrenal tissue *in vitro* utilizes low-density lipoprotein (LDL) cholesterol via a specific receptor-mediated pathway. Adrenal glands of animals other than rat and mouse, do not have specific binding sites for high-density lipoprotein (HDL), and most species apparently do not use HDL cholesterol for adrenal steroid biosynthesis ⁴⁸. There are two principle glucocorticoids, cortisol (found in humans and other species) and corticosterone (produced in rats, mice, and others) (See Figure 4 for synthesis pathways).

Figure 4: Pathway of cortisol and corticosterone synthesis in the adrenal cortex ⁴⁹ pg 85.



Cortisol is transported in the blood. In blood, about 3-5% of the total cortisol is the unbound, biologically active fraction, while the remainder is bound to the proteins

albumin and transcortin (also called corticosteroid-binding globulin or CBG). The unbound, biologically active form of cortisol fraction passes through the parotid gland into the saliva and also through the kidney into the urine; cortisol crosses the blood-brain barrier, allowing it to reach all parts of the central nervous system (CNS), and enters the cerebrospinal fluid via the choroids plexus to reach important regulatory sites on the amygdala, hippocampus, and hypothalamus. It also reaches the anterior pituitary via the systemic circulation. The adrenal steroids have receptors in every nucleated cell type in the body. Cortisol crosses the cell membrane to combine with its receptor in the cytoplasm. This receptor complex enters the cell nucleus, where its primary action is to induce or inhibit expressions of a wide range of regulatory genes ⁴⁸.

It is said that 4% of the cortisol in the blood of healthy men and women is free to affect target tissue, with the balance being bound to transport proteins, primarily CBG ⁵⁰, samples of this particular study were taken at rest at 8 a.m.. However, CBG binding characteristic are not static and the ratio of free to bound cortisol is not constant. Cortisol and CBG display roughly synchronous circadian rhythms ⁵¹, but cortisol varies by 200% and CBG only by 25% of their minimum values.

1.5.1 Metabolic effects

Cortisol is a key regulator of glucose metabolism. The effects of cortisol and corticosterone are very similar, although cortisol is more potent, based on several criteria of receptor action ³⁴. Glucocorticoids cause shifts in carbohydrate metabolism throughout the body that increase circulating energy substrates at the cost of stored energy (gluconeogenesis); they also increase cardiovascular tone, alter cognition, and inhibit growth, the immune response and inflammatory responses, and reproduction ³⁷. These changes are central to successful adaptation to acute physical stress, as they increase readily available energy and supportive metabolism and defer energetically costly anabolism until less stressful times. The notorious fragility of an organism with adrenocortical insufficiency in adapting to stress testifies to the importance of glucocorticoids. For example rats deprived of their adrenal glands are not viable for long, but under careful maintenance they show greatly reduced motor activity, inability to

undertake sustained exercise, poor temperature regulation, deficient food intake, and impaired circulation⁵². Also, the immune function can be exaggerated, resulting in autoimmune disorders. Centrally mediated changes include altered sensory processors and impaired learning and memory. Humans suffering from adrenal insufficiency (Addison's disease) show these same changes and report altered sensory perception and altered moods, feelings of paranoia, and other delusions.

1.5.2 Feedback mechanisms

The hippocampus is the highest site of negative feedback for glucocorticoid regulation and is considered the primary point of negative feedback regulation of cortisol during normal activity and periods of stress as it has more corticosteroid receptors than any other region³⁵, (refer to Figure 3).

Receptors for the adrenal steroid hormones in mammals such as the rat are identified as the mineralocorticoid receptors (MR, or type-I receptor) and the glucocorticoid receptors (GR, or type-II receptor)⁵³. Both GR and MR are present in the hippocampus. The GR has a single steroid-binding domain that is specific to glucocorticoids. The MR has a binding domain with an affinity for aldosterone and glucocorticoids. As a result, glucocorticoids alone bind to the GR while both substances bind to the MR. The presence of two receptor types with varying affinities for corticosterone (high affinity (MR) and low affinity (GR)) suggests a graded regulation of negative feedback over a wide range of concentrations. GR and MR have a 10-20 fold difference in binding affinities.

The two receptor regulation of varying affinity for the ligand has led some workers to postulate that MRs regulate diurnal variations and normal metabolic secretion of the glucocorticoids and the GRs regulate their stress-related secretion³⁶. During the permissive period (normal daily diurnal glucocorticoid concentrations) the high affinity MR are occupied, resulting in impairing hippocampal outflow and hence inhibiting CRF production⁵⁴. Hence the negative feedback control is highly sensitive and cortisol concentrations are kept low. During acute stress states, MR's and the low-affinity GR's

become occupied ⁵³. Cortisol secreted in response to acute stress does not appear to have an inhibitory effect on subsequent activity in the HPA axis ³⁶. The result being that cortisol concentrations are able to peak during acute stress states. This does, however, have a cost associated with it, as the long term effect results in impairment and possible loss of hippocampal neurons ⁵⁵. The loss of cells in a critical feedback site such as the hippocampus may leave the system less able to regulate cortisol output diurnally in response to normal metabolic demands, resulting in chronically high concentrations of cortisol and hence increased hippocampal vulnerability to further stress-related neuron loss, paving the way for systemic and cognitive consequences. These and related findings have led to the formulation of the glucocorticoid cascade hypothesis ⁵⁶.

The two-receptor system regulating ACTH secretion does, however, allow for flexibility in the adrenocortical system, allowing the concentrations to be very low as well as to rise quite high for brief periods of time. Because of the nature of short duration of most stress responses and their emergency nature, it may be desirable for the system to be able to produce large quantities of cortisol unrestricted by negative feedback. This fluctuating activity would not be possible with only a single receptor system unless the feedback control was much looser than what it has been shown to be ³⁶.

1.5.3 Physiological integration

It has been shown that gender and the phases of the menstrual cycle exert important effects on HPA responsiveness to psychosocial stress in healthy subjects ⁵⁷. Hence, it has been suggested that changes in free cortisol may partly be explained by gonadal steroid estradiol influences on CBG concentrations. Cortisol responsivity varies with menstrual phase, and the use of oral contraceptives elevate basal plasma cortisol concentrations ⁵⁸. The result being that measurement of cortisol in females through the phases of the menstrual cycle is quite complex. There is added benefit to rather investigate male subjects, i.e. no interference from the use of oral contraceptives and the different phases of the menstrual cycle. Also, men have been shown to have a stronger hypothalamic drive to stressful stimulation than women ⁵⁹, placing them more at risk of stress-related

disorders. Men also show enhanced salivary cortisol responses to a public speaking and mental arithmetic task in many studies⁶⁰⁻⁶².

Cortisol concentration has been found to be unrelated to age, weight, smoking status, sleep duration, time of waking, and alcohol consumption the night prior to sampling⁵⁸. Cortisol concentration does not change with age⁶³, although it has been suggested that the adrenal secretion of cortisol is maintained during aging at the expense of Δ 5-steroids, such as DHEA⁶⁴.

1.5.4 *Psycho-physiological research*

Methods of measuring physiological cortisol include: plasma, salivary, nocturnal (10 p.m. – 8 a.m.) cortisol/creatinine, 24h urinary and 24h urinary cortisol/creatinine⁶⁵. In terms of the influence one's psychological state has had on cortisol concentrations, physiological measures of cortisol have been found to correspond to psychologically based perceptions of daily stress⁶⁶, perceived stress scores⁶⁷ and changes in state anxiety⁶⁸. Cummins and Gevirtz showed that intensity of stress was a significant but modest predictor of daily cortisol measured by nocturnal (10 p.m. – 8 a.m.) urine samples⁶⁹. Although others studies have failed to demonstrate an association between basal cortisol and state-related stress measures^{70,71}.

Mood has also been shown to have an affect on cortisol concentrations. Negative mood has been shown to correlate positively with cortisol concentrations^{71,72}. Van Eck *et al.* showed that negative mood was a stronger predictor of cortisol level than were stressful events⁷¹. The negative mood related secretion of cortisol appears to be dependent at least in part on stimulation by the amygdala of the HPA axis⁷³. The amygdala (implicated in emotion related processes including negative mood such as disgust, fear or anger)^{34,73} plays a significant role in the HPA function⁷⁴. The connection between the amygdala and the hypothalamus takes the form of a multisynaptic pathway from the central nucleus of the amygdala, via the stria terminalis, to the bed nucleus of the stria terminalis and then to the lateral hypothalamus-perifornical region and to the PVN of the

hypothalamus. The set of connections just described, accounts for a chain of events by which cortical events, including environmental and endogenous stimuli in conjunction with evaluative processes, can result in the beginnings of an emotional response and its accompanying hormonal output. The cortical amygdaloid circuit is very likely to be a critical link in the emotional experience and the physiological response to that emotional event. It is also probable that the hippocampus participates in this process by assisting in the activation of stored memories. The hippocampus and the amygdala influence the HPA axis via the PVN.

Anxiety and distress is also associated with elevated cortisol concentrations in chronically distressed patients having endured hostage trauma⁷⁵ and psychiatric patients with major depressive illness⁷⁶. Even healthy younger individuals who experience more anxiety and distress have higher baseline cortisol concentrations than the concentrations in the individual who do not have these traits⁷⁷⁻⁷⁹. Also, individuals who repress anxiety have higher baseline cortisol concentrations than those individuals who experience low concentrations of anxiety⁷⁸.

1.5.5 *Cortisol and habituation*

In the previous three paragraphs baseline cortisol measures and the extent at which they have been shown to correlate with psychological state have been discussed. In this section the response to acute stress will be discussed. Berger *et al.*⁸⁰ showed that there exists a broad spectrum of cortisol responses among healthy young males to a variety of acute stress tests, with a continuum between complete reactors to non-reactors. They showed that the cortisol response did not correlate with the subjective judgment of stress. The magnitude of increased cortisol secretion associated with stressful events has been shown to be associated with whether the event was still ongoing and on how frequently a similar kind of event had previously occurred. Also, events that were reported to be recurrent had a smaller effect on cortisol than more novel events⁷¹. These findings suggest that habituation in cortisol response to stressful stimuli can occur.

Kirschbaum *et al.*⁶² distinguished high cortisol responders from low cortisol responders to experimental stress tests in healthy male individuals. The high cortisol responders lacked adaptation, and showed reduced habituation of the adrenocortical stress responses to repeated exposure to acute stress. Trait related psychological variables were able to predict the sub-groups of cortisol responses: high responders viewed themselves as less attractive, had less self-esteem, and were more depressed⁶². It is noteworthy that Epel *et al.*⁸¹ found that lean women did not habituate (showed lack of adaptation) to repeated stress in relation to their cortisol reactivity. Although even the authors could not explain this finding, this link between physical profile and stress reactivity illustrates that more multidisciplinary studies are important to foster an understanding of such associations.

A study by Curtis *et al.*⁸² provides additional evidence for the lack of adrenal cortical activation during confrontation with a chronically stressful stimulus. He studied phobic patients during the course of their treatment and when confronted with the phobic object (exaggerated exposure or “flooding”). Despite the very large increase in the anxiety measured by self-ratings or as observed by the investigators, plasma cortisol failed to show any increase during the “flooding” sessions. The session started at 7 p.m., which is a time of rather low cortisol secretion, but a time that, if sufficiently distressed by a novel event (in this case surgery), is capable of showing profound increases in cortisol⁸³. The lack of response at this time in the phobic patients indicates the possibility of suppression and/or adaptation to a chronically distressing stimulus. It appears as though the HPA axis demonstrates relative flexibility in the components of the control of the system. Munck *et al.*³⁷ put forward a hypothesis that stress-induced increases in glucocorticoid concentrations protect not against the source of the stress itself but rather against the body’s normal reactions to stress, preventing those reactions from overshooting themselves and threatening homeostasis. A continually responsive HPA axis even under conditions of chronic stress has been proposed to be important for survival⁸⁴. The difficulty in describing the regulatory changes that occur to the HPA axis under stress conditions is because it generally is very difficult to quantify the amount of stress being experienced, the fact that different forms of psychological stress exist and that different individuals react to and perceive stress differently.

These findings in human subjects suggest that there is adaptation to chronic stress, and that re-exposure to the now familiar stimulus, the chronic stressor, fails to lead to increased adrenocortical activity, which in some ways parallels the results obtained in the individuals exposed to chronic work stress of Caplan *et al.*. The habituation theory contradicts the glucocorticoid cascade hypothesis (mentioned earlier), which describes chronic exposure to stress resulting in hippocampal damage and escalating cortisol concentrations. Possibly the discrepancy between these two theories lies in the chronicity and degree of exposure or the intensity of the stress.

1.5.6 *Cortisol and chronic stress*

Caplan *et al.*⁸⁵ compared plasma cortisol measured at twice daily with subjects' reports of workload and job strain. They demonstrated that high workload employees showed lower than normal morning cortisol values and did not show the expected decrease in cortisol from morning to afternoon. Low workload employees showed the expected circadian rhythm. One can hypothesize from these results that stress could lower mean cortisol by either exhausting the adrenal output or by suppressing its reactivity to chronic stress. An alternative hypothesis one can make from these results is that the stress experienced by high workload simply altered the circadian rhythm of cortisol. Other researchers have suggested that stress may interfere with the circadian rhythm of cortisol. Loriaux and Cutler⁸⁶ pg 178, state "stress blunts the normal circadian cortisol rhythm by increasing secretion nocturnally when it is normally low". Factors that could cause an altered circadian rhythm may be specific to some high workload individuals, examples include: work load patterns/activities beyond the normal working hours i.e. late nights or early mornings, resulting in disturbed sleep-wake patterns. Disturbed sleep-wake patterns have been found to be associated with altered diurnal rhythms of cortisol⁸⁷. These results do suggest that rather than seeing a persistent elevation of cortisol during chronic exposure to a potentially stressful stimulus, certain individuals may actually suppress below baseline, a result which has been reported by Mason *et al.* for monkeys⁸⁸.

In summary, investigations that have examined the influence of various psychological stressors on endocrine secretion in human studies have produced conflicting results. Differences exist in the sampling method and intervals of these studies and the pulsatile nature of hormonal release is showed not always to be taken into account. One should always bear in mind that some studies on stress and cortisol assess the acute response whereas others assess the effect of chronic stress on the HPA axis.

The neurological literature suggests that over exposure to stress (chronic stress) results in impairment of the negative feedback mechanism and the resultant escalating cortisol concentrations. Although persistently elevated cortisol during chronic stress studies has not been consistently reported, in order to explain this pattern, researchers have hypothesized that habituation may occur, or that disturbed sleep wake patterns associated with chronic work stress may play an influential role.

1.5.7 Effect of stress management interventions

Efforts to reduce stress by improving psychosocial competence of managers have been shown to reduce cortisol concentrations⁸⁹. The intervention took place over a period of 1 year and the subjects underwent a 2-hour bi-weekly training session for that period. Also, stress reduction technique of transcendental meditation (TM) has reduced basal cortisol concentrations and cortisol responsiveness to stress significantly after 4 months of practice in healthy males⁹⁰. These are the only two stress management studies that I am aware of that look at cortisol specifically. Most stress reduction programmes assess the physiological effectiveness through blood pressure, symptom checklist, muscle tension, pulse rate⁸. Although one stress management study (in the work setting) has assessed catecholamine concentrations⁹¹. After reviewing the literature, I am of the opinion, that from a physiological perspective, most stress management programmes haven't sufficiently or accurately assessed the impact of the stress management on the physiological system, as blood pressure, pulse rate and muscle tension are insufficient indicators of physiological relaxation. No study has assessed the effects of occupational based stress management on chronic physiological indicators of stress.

1.6 Dehydroepiandrosterone

Dehydroepiandrosterone (DHEA) is by far the major steroid product of the adrenal cortex in humans and all its production can be traced to the adrenal cortex⁶⁴. Ninety nine percent of DHEA is sulphated before secretion and circulates primarily in its sulphated form (DHEAs), and the concentration of free DHEA is less than 1% of the total DHEA⁴⁸.

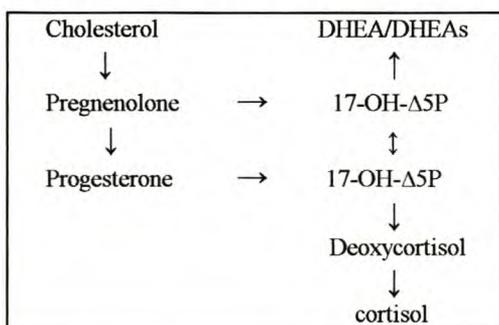
Peak serum DHEA and DHEAs concentrations occur at age 25 years, and they decrease thereafter⁹². After the second decade they decline about 20% for every decade, diminishing 90-95% by age 85-90 years. DHEAs concentrations do not exhibit any form of circadian rhythm because DHEA has a long circulating half-life⁴⁸.

Table 1: Normal ranges for serum DHEAs, for men age 15-49 (the age of this study's subject population), as cited from⁹² pg 554.

	Age range (yr)	Concentration range (ng/ml)	Concentration range (nmol/l)
Men	15-39	1500-5500	3841-14084
	40-49	1000-4000	2561 - 10244

Although DHEA and cortisol can both be derived from the same precursor, 17-hydroxypregnenolone (17-OH- Δ 5P), the plasma concentrations of DHEA decline with age (as stated previously), whereas cortisol concentrations remain relatively unchanged⁵⁸. The precise mechanisms which control the relative rates of 17-OH- Δ 5P conversion to DHEA and to cortisol remain to be established. Glucocorticoid receptors are present in virtually every tissue and organ in the body and mediate wide ranging effects (as described previously). All tissues studied to date contain steroid sulphatases which rapidly convert DHEAs to DHEA⁴⁸. DHEA is a functional antagonist of cortisol^{93,94}. Generally, low DHEA is considered deleterious, as is chronically high cortisol⁹⁵.

Figure 5: Pathway of cortisol and DHEA synthesis in the adrenal cortex⁴⁹ pg 85.



Androgens typically raise serum LDL cholesterol concentrations and reduce serum HDL cholesterol concentrations ⁹⁶. These changes are believed to account at least in part for the increased risk of atherosclerosis and CVD in men treated with anabolic steroids. DHEA does not, however, have the same atherogenic properties as other androgens. Cholesterol biosynthesis has been shown to be inhibited after DHEA treatment ^{97,98}. DHEA administration did not affect serum HDL cholesterol concentrations ⁹⁹. DHEA administration in healthy male volunteers dramatically reduces low-density lipoprotein (LDL) concentration and body fat ⁹⁹. These findings support the evidence of DHEA playing a protective role in arteriosclerotic processes. The reducing effect that DHEA has on serum LDL cholesterol concentrations (referred to before) in the absence of an effect on serum high-density lipoprotein (HDL) cholesterol, contrasts markedly with the effects of other androgens on lipids. Therefore, DHEA is more analogous to an oestrogen effect in this regard ⁹⁶. It has been proposed in the literature that DHEA has played a protective role against CVD ¹⁰⁰, but the clinical significance of DHEA in CVD remains uncertain. DHEA may achieve this protective effect through its depleting effect on mevalonate, a precursor in the cholesterol synthesis pathway ¹⁰¹.

On the topic of DHEA and cholesterol it is relevant to note at this point, that DHEAs concentration have been found to correlate negatively with the total cholesterol concentrations in chronic fatigue patients ¹⁰² and in obese women ¹⁰³. Symptoms associated with fatigue are sometimes sufficiently severe that they warrant being diagnosed as a discrete disorder (chronic fatigue syndrome (CFS) or myalgic encephalomyelitis (ME)). General fatigue and fatigability (onset of symptoms after exertion) have been found to be associated with high levels of psychological distress in the workplace ¹⁰⁴. Also, DHEA concentrations in chronic fatigue patients have been shown to be significantly lower than healthy matched controls ¹⁰².

Perceived stress scores have been found to correlate negatively to DHEAs concentrations ¹⁰⁵, suggesting an association between perceived stress and lower DHEAs concentrations. As mentioned before, the opposite is true for cortisol. Some studies that used both physiological measures explain the results as a ratio. The cortisol/DHEAs ratio

has been found to be increased during the chronic stress of serious long-term illness¹⁰⁶ and in acutely ill patients¹⁰⁷.

Figure 5 shows the recognised shift in pregnenolone metabolism away from DHEA production to that of the glucocorticoids (i.e. cortisol). The precise mechanisms involved in this dissociation of adrenal androgen and cortisol production have not been identified, and both extra-adrenal and intra-adrenal factors have been implicated. The physiological relevance of changes in cortisol/DHEAs ratio is clarified by the recent evidence that DHEA has antiglucocorticoid effects in several systems¹⁰⁸. DHEA and its sulphate (DHEAs) have also been found to have effects on cognition, metabolism, and the immune system^{109, 110}. DHEA has been shown to alleviate amnesia and enhance long-term memory retention in mice¹¹¹, which is opposite to the effects cortisol has on cognition (to be discussed in section 1.7). The cortisol/DHEAs ratio, as opposed to cortisol or DHEA concentrations assessed individually, is thought to be the best way to assess adrenal steroid immunomodulatory function⁴⁹.

However, the cortisol/DHEA ratio is not always influenced by changes in both hormones in opposite directions. A change in one individual hormone without a change in the corresponding hormone in the opposite direction is also seen. For example, there have been reports of a dissociation of cortisol and DHEA during stress, i.e. pre-operative cortisol increased by 61%, while DHEA remained constant¹¹². DHEAs and cortisol in obese women have been found to be positively associated¹⁰³. Maccario *et al.*¹⁰³, speculated that the conversion of DHEAs into testosterone and the subsequent positive effect on ACTH-dependant cortisol response could, in turn, also account for the positive correlation between DHEAs and cortisol secretion.

DHEAs's antiglucocorticoid effects can explain the following beneficial effects of DHEA: anti-stress, anti-diabetic, anti-obesity, anti-aging, boosting immune system, protecting brain neurons and thereby improving memory¹⁰⁸. The antiglucocorticoid properties of DHEA suggest that DHEA blocks the potentially deleterious effects of

stress-induced cortisol release. A stress reduction programme in healthy middle-aged army officers has been shown to increase DHEA concentrations ¹¹³. Also, Glaser *et al.* showed that men over 45 and women of all age groups who are experienced practitioners of transcendental meditation (TM), have serum DHEAs concentrations that are higher than those found in healthy, normal, non-meditating population ¹¹⁴.

The literature reveals that cortisol/DHEAs ratio may be a better indicator of stress related metabolic shifts, and hence both cortisol and DHEA should be measured when assessing the effectiveness of any form of stress management intervention on the physiological and endocrinological system. No stress management intervention study has assessed the effect thereof on cortisol/DHEAs ratio.

1.7 Stress and health

Many clinical researchers agree that stress is an important factor in disease ⁵, and aging ⁵⁶. Stress and other emotional responses are components of complex interactions of genetic, physiological, behavioural and environmental factors. These authors suggest that together that chronic activation of the stress response affects the body's ability to remain healthy and to resist disease. The specific physiological systems in stress and emotion appear to exert powerful influences on the nervous, endocrine, and immune systems and therefore have important implications for the initiation or progression of certain diseases such as cancer, CVD and other illnesses ⁵, and aging ⁵⁶. For this review I will focus specifically on the proposed mechanism related to cognitive function deficits and to CVD.

Sapolsky *et al.* ⁵⁶, suggest that in the aging process and chronic stress situations, down regulation of the corticosteroid receptors occurs, and consequently a resistance of the HPA axis to the negative feedback actions of the glucocorticoids arises. This hypothesis (discussed previously), the glucocorticoid cascade hypothesis results in escalating glucocorticoid concentrations. The predominantly catabolic responses to acute emergency, excessive exposure to this specific steroid (as seen during prolonged stress or in pathological, Cushingoid states) can cause elevated glucose in blood and urine,

excessive food intake, loss of bone density and muscle mass, shrinkage of the thymus and lymph nodes, and impaired immune function. Because of this immune suppressive effect of cortisol, a sustained alteration in the regulation of the HPA axis function with chronically increased cortisol concentrations, may predispose individuals to many illnesses e.g. steroid induced diabetes and hypertension.

Administered corticosteroids have detrimental effects on cognitive function ¹¹⁵. Human clinical research supports a hippocampal link between cortisol and cognition. Psychological changes occur in this state of excess cortisol, including mood swings and depression ¹¹⁶. Certain psychological disorders characterized by elevated cortisol concentrations, exhibit cognitive deficits, i.e. cortisol-related cognitive deficits and loss of hippocampal volume have been observed in Cushing's disease, depression, normal aging, and Alzheimer's disease ¹¹⁷⁻¹²⁰. All these situations show increased serum cortisol concentrations and the associated cognitive deficits are e.g. impaired spatial memory and impaired declarative memory. The degree of cortisol-related cognitive decline has been shown to be related to the hippocampal atrophy ^{121,122}. Excessive cortisol appears to have a damaging effect on the hippocampus and thus indirectly affects memory and cognition.

Other researchers have reported a relationship between cognitive deficits, loss of hippocampal volume, and presumed severe HPA activation due to childhood physical and sexual abuse or traumatic wartime stress ¹²³⁻¹²⁵. The effect of cortisol on cognition is not limited to prolonged exposure. In an experimental situation stress-induced increases in salivary glucocorticoid have been shown to have a detrimental effect on declarative memory ^{126, 127}, on memory retrieval ¹²⁸, as well as on overall task performance ¹²⁹. These experimental stress environments included a water maze spatial task with rats, psychosocial laboratory tests, public speaking tests and mentally challenging flight scenarios done on pilots.

McEwen ¹¹⁵ have attempted to explain this association between the cortisol, the hippocampus and cognitive deficits. As mentioned before, the hippocampus is a key limbic system structure, important for the establishment of memories ¹³⁰. In the brain,

actions of cortisol and epinephrine released during stressful situations include promoting retention of memories of emotionally charged events, both positive and negative, and thereby helping the individual to avoid potentially dangerous situations in the future. Yet, over-activity of the HPA axis (chronic stress) or chronic treatment with glucocorticoids promotes reorganization of nerve cells and their connections, together with excess excitatory neurotransmitters. This promotes reduced neuronal excitability, neuronal atrophy, and, in extreme cases, death of brain cells, particularly in the hippocampus^{55,131,132}. The result being that overactivity of the HPA axis results in memory loss. This is clearly witnessed in PTSD, where the stress-related memories are erased from recollection. Erasing very stressful memories serves a protective function. Hence, the effect of moderate and severe cortisol concentrations on cognition both serve as survival functions, the one promoting memory retention and the other promoting memory loss, both promoting survival in the relevant situations.

Psychological factors are increasingly being recognised as important contributors to the onset and course of CVD. Tennant and McLean¹³³ recently reviewed the current literature on the impact of stress on CVD. The evidence reviewed revealed that personalities with high scores in anxiety, depression and distress were at risk for CVD. Life-event stress and anxiety are risk factors for both hypertension and myocardial ischemia¹³⁴⁻¹³⁷. Relevant to life-event stress and anxiety, elevated cortisol concentrations have also been associated with greater incidence of atherosclerosis¹³⁸.

A large proportion of the literature relating stress to CVD has investigated work-related stress. Although many aspects of one's work environment relative to the development of CVD have been studied, much interest has focused on models of inherent "tension" at work. One such model has been the "job strain" model, defined by Karasek *et al.*¹³⁹ as high demand but low decision latitude jobs. In one prospective study starting in 1928, male workers were tested and followed and retested after 6 years. Job strain was associated with a 4-fold increase in the risk of cardiovascular system-related death. Subsequent studies have supported the relationship between job strain and CVD risk^{140,141} but other studies have failed to find an association^{142,143}.

More recently, research has begun to focus on other forms of work-related stress. For example, one model views work stress as the outcome of high work demands and low reward¹⁴⁴. This model was able to predict cardiac events^{142,144} and has been correlated with the progression of carotid arteriosclerosis¹⁴⁵. Low job control has been shown to predict future cardiac events¹⁴⁶. Also, psychosocial work factors have been found to be significantly associated with CVD risk factors (hypertension, hyperlipidaemia, overweight, smoking and alcohol consumption)¹⁴⁷. The prevalence of hyperlipidaemia for example, was found to increase when high levels of psychological demands were combined with low social support at work for men, and with low decision latitude for women. Taken together, these studies suggest an association between work stress and CVD risk.

In this section thus far I have discussed the mechanisms of cortisol induced effects specifically pertaining to cognition and CVD as separate problems. However, there are also situations in which cortisol is linked to both CVD and brain-related disorders. Stressful life events are risk factors for depression¹⁴⁸ and depressive illness is characterised by significantly higher basal cortisol concentrations⁷⁶. A recent study showed that depressed people had a 3-4 times greater risk of fatal coronary heart events¹⁴⁹, possibly as a result of the associated hypercortisolism.

1.8 Cholesterol

The relationship between stress, cholesterol and CVD is quite complex. Not all blood cholesterol has the same atherogenic potential. Elevated plasma total cholesterol is considered a risk factor for CVD¹⁵⁰. Total cholesterol is thought to be less predictive of developing CVD than any of the other lipoprotein sub-fractions. The prevalence of CVD appears to increase with increasing concentrations of LDL cholesterol and decrease with increasing HDL cholesterol¹⁵¹. In addition, it has been shown that the relationship between HDL/total cholesterol and coronary risk factors is as strong or stronger than the relationship of LDL or HDL cholesterol alone. The Framingham study¹⁵² and Williams

*et al.*¹⁵³ showed that the HDL/total cholesterol ratio was one of the most powerful predictors of risk of developing coronary heart disease.

Emotional arousal induced through public speaking has been shown to increase triglyceride concentrations¹⁵⁴. A number of investigators have found during times of high stress (final medical examinations) cholesterol concentrations are appreciably higher than at other times (regular academic term time)^{155,156}. Francis⁶⁸ showed that peak period of stress are followed closely (approximately 10 days) with significant elevations in total cholesterol concentrations and significant decreases in the ratio of HDL/total cholesterol. Dimsdale and Herd¹⁵⁷ reviewed 60 such studies which assess plasma lipid concentrations under short-term emotional arousal. The studies reviewed span a remarkable breadth of stressful situations from viewing disturbing films to taking an examination or participating in military courses. Free fatty acid concentrations were almost invariably elevated in the context of a stressful event and most of the studies reviewed found that cholesterol increased from 8 to 65% above baseline under stressful conditions. Cortisol has been found to be associated with cholesterol concentrations in individuals with type A behaviour¹⁵⁸, suggesting that increases in cholesterol in the stressed Type A personality may be as a result of the increases in basal cortisol concentrations. These authors postulated that because cholesterol is a precursor to cortisol, elevated cholesterol may cause an elevation in cortisol concentrations. It is also thought that the mechanisms by which glucocorticoids produce insulin insensitivity, could lead to hypercholesterolaemia¹³⁸.

1.9 Fat distribution

The waist to hip ratio (WHR) measures fat distribution, with population norms having already been established¹⁵⁹. A high WHR has been proven to an approximate measurement for an excess of intra-abdominal fat¹⁶⁰. People with high WHR measurements can be said to have a “central” fat distribution, while people with low WHR measurements can be said to have a “peripheral” fat distribution. The clearest examples of the association between cortisol secretion and central fat in humans are seen

in people with Cushing's syndrome ¹⁶¹. It is reported that 79 – 97% of the cases of Cushing's syndrome presented show distinctive signs of centripetal obesity ⁴⁸.

WHR is a convenient method of assessing body fat distribution because it requires less equipment and less training and is cheaper than more sophisticated methods. Ratios of above 0.95 for men and 0.86 for women place the individual at significantly increased health risk of disease ¹⁵⁹.

Low socioeconomic-status (SES) is associated with financial strain, job insecurity and general increased stress. WHR is increased at the lower end of the SES gradient, in Swedish males ¹⁶². WHR is also increased with decreasing job grade, as observed in the Whitehall studies ¹⁶³. Might it be that increased stress associated with low SES explains the association with increased WHR?

Certain findings have supported the hypothesis that stress induced cortisol secretion may also contribute to central fat ¹⁶⁴⁻¹⁶⁶. Epel *et al.* ⁸¹ found that central fat distribution is related to greater vulnerability to stress and cortisol reactivity. A greater cortisol reactivity to challenge is also found in women with central fat distribution ^{167, 168}. Lipoprotein lipase (LPL) is a fat storing enzyme and *in vitro*, cortisol increases LPL activity in fat tissue. But, cortisol has an especially exaggerated effect on the visceral fat tissue LPL activity ¹⁶⁹. Hence, this could explain how cortisol appears to stimulate metabolic pathways that support triglyceride accumulation in visceral adipocytes. On this topic it is also noteworthy that specifically high density of GR's has been found in intra-abdominal fat tissue ¹⁷⁰.

Other researchers, ¹⁷¹ and ¹⁷² have found abnormal HPA axis responsiveness (non-suppression of cortisol after dexamethasone) among overweight men and women with greater central fat than peripheral fat. This finding confirms an association between HPA axis dysregulation and abdominal obesity in otherwise healthy individuals. As previously described (section 1.5.2) the HPA axis is regulated by feedback inhibition created by MR and GR in the hippocampus. The density and function of these receptors have been reported to be dependent on the prevailing activity of the axis, with repeated or chronic

activation leading to down-regulation of the receptors^{84,56,173}. This could be expressed as elevated responses to stimuli along the HPA axis as described above in the case of abdominal obesity, hence, explaining the association between abdominal obesity and stress. WHR was also found to be negatively correlated with serum DHEA concentration in obese women¹⁷⁴, suggesting that the antiglucocorticoid effects of DHEA may protect against abdominal obesity. On this topic of stress and abdominal obesity, it is relevant that adults with central fat distribution have greater cardiovascular reactivity to acute stress^{175,176} relative to those low in WHR.

Central fat distribution poses increased metabolic risks as it is associated with a predisposition towards CVD, stroke and diabetes^{177,178}. Although WHR with obesity appears to be more closely associated with diabetes than CVD, high WHR without obesity appears to be more closely associated with CVD than diabetes¹⁷⁸.

1.10 Obesity

Obesity, estimated for example by body-mass-index (BMI), is used to assess weight relative to height. In general, the assumption is that the higher the index, the more the body fat. Obesity-related health risks begin in the BMI range of 25-30 kg/m²¹⁵⁹. A high BMI is associated with a number of diseases including hypertension, hypercholesterolaemia, diabetes and CVD¹⁷⁹. It has been shown, however, that WHR is a stronger risk factor than BMI for stroke¹⁸⁰. An association between job strain and BMI has been observed¹⁸¹.

1.11 Integration

As summarised by McEwen and Seeman¹⁸² cortisol and epinephrine help mobilize and replenish energy in acute stress; yet they can promote central fat deposition, insulin resistance, hypertension, and cardiovascular disease when the body does not burn off the energy it obtains from food and stores it instead as fat. Specifically, repeated HPA axis activation in response to stress accelerates progression towards Type II diabetes, including abdominal obesity, arteriosclerosis, and hypertension¹³⁸. Clearly, interventions that could prevent the above described syndrome, or cluster of phenomena, now called

Metabolic Syndrome X¹⁸³, could benefit many people. Spence *et al.*¹⁸⁴ reviewed the intervention programmes used to treat hypertensive patients. The interventions that were included in the review covered the conventional drug and weight loss programmes as well as psychological interventions e.g. behavioural cognitive approaches, and other forms of stress management approaches. Spence concluded that in patients with hypertension, the contribution of stress should be considered, and for hypertensive patients in whom stress appears to be an important issue, stress management should be considered as an intervention.

1.12 Stress and Allostatic load

The literature on stress is highly disjointed and it lacks scientific consensus regarding the most effective means of measuring stress. The researchers who first coined the term “allostatic load” and who determined the parameters contained within this concept¹⁸⁵, assisted in integrating a number of otherwise disjointed research fields. Allostatic load is a general term referring to a chronic physiological state. Allostatic load is relevant to this literature review, as this broad term integrates the physiological indicators of stress mentioned thus far. Allostatic load is derived from the term *allostatis*. *Allostasis*, as defined by Sterling and Eyer, is the ability to achieve stability, through change¹⁸⁵. *Allostasis* is critical to survival of an organism by promoting adaptation to an environment or simply re-establishment of a new homeostasis. Through *allostasis*, the autonomic nervous system, the HPA axis, and the cardiovascular, metabolic, and immune systems protect the body by responding to the internal and external challenges. *Allostasis* is achieved by the actions of mediators, such as catecholamines and glucocorticoids. *Allostasis* emphasizes the dynamics of internal physiological systems, stressing that healthy functioning requires ongoing adjustments of the internal physiological environment. Physiological systems exhibit fluctuating levels of activity as they respond and adapt to the environment. This dynamic conceptualisation of internal physiological regulation contrasts with the earlier view of optimal functioning that emphasized the importance of maintaining constancy of the internal environment (*homeostasis*) as a hallmark of healthy functioning. In contrast, *allostasis* emphasises the physiological imperative that “an organism must be able to vary all the parameters of its internal environment and match them appropriately to environmental demands”¹⁸⁵. The concept

of optimal operating ranges of physiological systems has replaced the earlier emphasis on optimal homeostatic set points. The emphasis is on much broader boundaries of operation. Allostatic systems enable an organism to respond to its physical state (e.g. awake, sleep, standing, exercising) and to cope with, for example noise, crowding, isolation, hunger, extremes of temperature, physical danger, psychosocial stress, and microbial and parasitic infections.

“Allostatic load” refers to the view that a multisystem physiological toll is exacted on the body through cumulative attempts at adaptation. Hormones associated with stress and allostatic load can protect the body in the short term and promote adaptation, but in the long term excessive allostatic load causes changes in the body that lead to disease. A broader view of stress is that it is not just the dramatic stressful events that exact their toll, but rather the many events of daily life that elevate activities of physiological systems to cause some measure of “wear and tear”. “Allostatic load,” has been suggested to reflect not only the impact of life experiences but also of genetic load because genetic predisposition can alter susceptibility to the consequences of the load. Individual habits, such as diet, exercise, and substance abuse, and developmental experiences that set life-long patterns of behaviour and physiological reactivity also influence allostatic load ¹³¹. For each physiological system, there are both short-term adaptive actions (allostasis) that are protective and long-term effects that can be damaging (allostatic load).

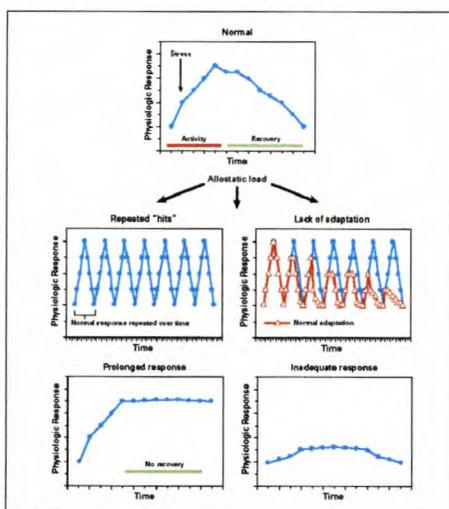
Allostatic load can hence be defined as “An excessive level, over weeks, months, and years, of mediators of allostasis, resulting either from too much release of the mediator or from the inefficient operation of the allostatic systems, that produce the mediators and fail to shut off their release when not needed” ¹⁸⁶.

The body responds to the external and internal environment by producing hormonal and neurotransmitter mediators that set in motion physiological responses of cells and tissues throughout the body, leading to a coordination of physiological responses to the current circumstances. No matter what the “stressor”, the body responds to challenge by turning on an allostatic response, thus initiating a complex pathway for adaptation and coping,

and then shutting off this response when the challenge has passed. The primary allostatic responses involve the sympathetic nervous system and HPA axis as previously described in section 1.3.

The *top panel* in Figure 6, (see below) illustrates the normal allostatic response, in which a response is initiated by a stressor, sustained for an appropriate interval, and then turned off. The remaining panels illustrate four conditions that lead to allostatic load: (1) repeated "hits" from multiple novel stressors, (2) lack of adaptation, (3) prolonged response due to delayed shut down, and (4) inadequate response leading to compensatory hyperactivity of other mediators (e.g., inadequate secretion of glucocorticoid, resulting in increased concentrations of cytokines that are normally counterregulated by glucocorticoids).

Figure 6: Four types of allostatic load. Figure drawn by Dr. Firdaus Dhabhar, The Rockefeller University, New York. (Reprinted from ¹³¹)



Quantifying allostatic load, a major challenge, has been attempted with the use of measures of metabolic and cardiovascular pathophysiology. Recently, eight physiological measurements were taken at regular intervals in the MacArthur Studies of Successful Aging ⁶, between 1988 and 1991. These were used to calculate 10 indicators of increased activity of allostatic systems. 4030 men and women meeting the age criteria (70-79) were screened according to physical and cognitive functioning. 1313 subjects met the relative "high functioning" criteria i.e. not physically or mentally impaired, making up the study

population. Allostatic load was estimated by determining the number of measures for which a person had values in the highest quartile of the study population, from among the following: systolic blood pressure, overnight urinary cortisol and catecholamine excretion, the WHR measurement, the glycosylated hemoglobin value, and the ratio of serum HDL to the total serum cholesterol concentration; and the number of the following for which the person had values in the lowest quartile: serum concentration of DHEAs and serum concentration of HDL cholesterol. In cross-sectional analyses of baseline data, subjects with higher levels of physical and mental functioning had lower allostatic-load scores and a lower incidence of cardiovascular disease, hypertension, and diabetes. These researchers concluded that their comprehensive multicomponent measure of allostatic load (including measures of HDL and total cholesterol concentrations as well as other CVD related measures) more strongly predicts incidence of CVD than any individual risk factor. During the three years of follow-up (1988 to 1991), people with higher allostatic load scores at baseline, were more likely to have cardiovascular disease that included incidents and were significantly more likely to have declines in cognitive and physical functioning ¹⁸⁷. Among women in this group, 198 subjects were followed up 2.5 years later. Increased cortisol secretion was able to predict a decline in memory; similarly declines in cortisol were associated with improvements in memory ¹⁸⁷. The results were confirmed in another follow-up study 7 years later, (1988 to 1996) showing that higher baseline allostatic load scores predicted significantly increased risks for incident CVD as well as increased risks for decline in physical and cognitive functioning *and for mortality* ¹⁸⁸.

The following parameters and values are used as measurements of allostatic load:

1. Systolic and diastolic blood pressure, indices of cardiovascular activity (≥ 148 mm Hg; ≥ 83 mm Hg respectively).
2. WHR, an index of more chronic levels of metabolism and adipose tissue deposition, thought to be influenced by increased glucocorticoid activity (≥ 0.94).
3. Serum HDL and total cholesterol, related to the development of atherosclerosis-increased risks being seen with higher levels in the case of total cholesterol and lower levels in the case of HDL (total cholesterol/HDL ratio ≥ 5.9 ; HDL ≤ 1.45 mmol/l).

4. Blood plasma concentrations of glycosylated hemoglobin, an integrated measure of glucose metabolism over several days time ($\geq 7.1\%$).
5. Serum DHEAs, a functional HPA axis antagonist ($\leq 2.5 \mu\text{mol/l}$).
6. Overnight urinary cortisol excretion, an integrated measure of 12 hr HPA axis activity ($\geq 25.7 \text{ mg/gram of creatine}$).
7. Overnight urinary norepinephrine and epinephrine excretion concentrations, integrated indices of 12 hr Sympathetic Nervous System activity ($\geq 48 \text{ mg per gram of creatine}$; and $\geq 5 \text{ mg/gram of creatine}$).

The MacArthur studies' initial values for allostatic load were determined by summing across indices of subjects' status with respect to 10 components of allostatic load (see below). For each of the 10 indicators, subjects were classified into quartiles based on the distribution of scores¹⁸⁷. The decision to use distributions in the cohort was based on the fact that analyses of relationships between allostatic load and health outcomes were based on longitudinal data. Allostatic load was measured by summing the number of parameters for which the subject fell into the "highest" risk quartile (i.e., top quartile for all parameters except HDL cholesterol and DHEAs for which membership in the lowest quartile corresponds to highest risk). Several alternative criteria for calculating allostatic load were also examined. One such alternative using a stricter criterion was based on a sum of the number of parameters for which the subject fell into the top (or bottom) 10% of the distribution (i.e., the group at highest "risk"). Another measure of allostatic load was also based on averaging z-scores for each of the parameters. In each case, analyses yielded essentially the same results as the measure based on the quartile criteria, though the latter showed the strongest effects. These concurrent results suggest that the disease risks associated with allostatic load arise from being, relatively higher on various measures of physiologic regulation rather than only at the most extreme levels.

The 10 components were equally weighted because the component loadings on the relevant factors have been shown to be virtually the same⁶. The measure of allostatic load assesses what are largely modest deviations from optimal physiological levels. The population from which the values of allostatic load were derived was a cohort of non-hospitalised individuals, functioning adequately in daily life. However, given that this is a

new concept and few researchers have actively used it, and no-one has actively questioned it, it is likely that some of the components of allostatic load may change with time and a greater understanding of stress indicators

1.13 Massage and stress

Beard and Wood give the definition of massage ascribed to by most practitioners today: “massage is the term used to designate certain manipulations of the soft tissues of the body; these manipulations are most effectively performed with the hands, and are administered for the purpose of producing effects on the nervous system, the muscular system as well as the effects on the local and general circulation of the blood and lymph”¹⁸⁹. Therapeutic massage has also been described as the manipulation of the soft tissue of the body areas to bring about generalised improvements in health¹⁹⁰.

A number of studies have reported on the subjective effects of massage on muscle relaxation and psychological state. Four of these studies were studies with patient populations as subjects. In a study of evaluating the use of massage on the well-being of cancer patients, it has been reported that patients found massage to be beneficial in assisting relaxation and reducing physical and emotional symptoms¹⁹¹. Another study on patients in a palliative care setting, reported that the patients considered massage to be beneficial in reducing anxiety, tension, pain and depression, although this was not a controlled study¹⁹². Similarly, Fraser and Kerr reported that patients perceived back massage as relaxing¹⁹³. Massage has also been found to enhance feelings of psychological well-being by reducing tension, depression, anger, fatigue, anxiety, and confusion¹⁹⁴. Little empirical data exists as to the tranquilizing and mental health effects of massage although there have been many testimonials of the relaxing effects. Relaxation appears to be the most important benefit of massage¹⁹⁵. These studies that have attempted to examine the effects of back massage, have largely been based on qualitative observations and subjective reports. Research into massage therapy is increasing yet the number of studies documenting objective physiological changes following therapeutic massage still remains limited.

Field ¹⁹⁶ reviews the physiological and therapeutic effects of massage on very specific groups of people such as those with Attention Deficient Hyperactivity Disorder (ADHD), depression etc.. Massage has been shown to decrease anxiety in individuals with Post-Traumatic Stress Disorder ¹⁹⁷, when compared with the control group. Massage of these subjects also significantly decreased the salivary cortisol concentrations. Massage has also been shown to improve the mood of depressed individuals, as the massage intervention caused a shift in the EEG activation from right frontal activation (normally associated with sad affect) to left frontal EEG activation (normally associated with happy affect) or at least to symmetry (midway between sad and happy affect) following the 20-minute massage ¹⁹⁸. Massage has also been shown to improve concentration ability and decrease fidgeting in adolescents with ADHD ¹⁹⁹. In this particular study, the massage therapy group compared with the relaxation therapy group, showed significantly less fidgeting following the session. After the therapy was applied for 10 consecutive school days, the massage therapy group spent significantly more time on tasks and were less hyperactive in the classroom as assessed by the Conners Scale, by the teacher who was unaware of the group assignment.

The immediate psychological effects of massage as discussed in the previous two paragraphs, can therefore be significant. Massage has also been shown to produce positive mood enhancement (measured directly after the massage) ¹⁹⁴ in healthy students, but no study has looked at the longer-term effects of massage on mood. State anxiety has typically been shown to decrease directly after a massage ²⁰⁰⁻²⁰², but again the longer term effect of massage on anxiety has not been reported in relatively healthy individuals. Certain of these studies have not included a control group ^{192,204}, while others have ^{193,197,200-202}, in the form of relaxation in massage chair, or video viewing, or being in a room for equivalent time or reading in a room. These findings confirm that massage does have immediate relaxatory effects. The question that still remains unanswered, is how long this effect lasts. If the goal is to impact on health, long-term physiological and psychological effects are important.

Link ²⁰³ compared the effectiveness of three stress management treatments namely, massage, restricted environmental stimulation (flotation), and stress management training on physiological and psychological measures of stress. Although each group showed significant reductions in physical and emotional symptoms of stress, the massage appeared to be the most effective stress management technique as it altered the largest number of stress symptoms.

On-site massage is a form of massage that is specifically directed at working individuals. On-site massage was developed in the 1980's by a US therapist David Palmer, as a practical method of easing employee tension in the work place. Used initially by Apple Computers Co., today it is widely used in the USA. Virgin, Sony and ATandT are among thousands of companies who have seen productivity levels rise since providing this service for their workforce (anecdotal evidence). On-site massage is performed through the clothes on a specifically designed chair. Each session lasts approximately 15-20 minutes and is aimed at the corporate environment where time is crucial. The initial aim is to relax the client, to then de-stress and relieve general muscular tension, and then to rejuvenate and revitalize, sending the client back to work fresh and energized.

The *Touch Research Institute* in Florida has published a study in the peer-reviewed scientific literature on the benefits of On-Site Massage ²⁰⁰ and the results are as follows:

1. Enhanced alertness (decreased EEG Alpha and Beta Waves and increased delta activity)
2. Increased mathematical ability (mathematical problems completed in significantly less time and with significantly fewer errors after massage)
3. Decreased anxiety and job stress levels

Only two other scientific studies exist that investigated the effects of massage on people in the working environment. Together, their results showed that on-site massage decreased anxiety, decreased job stress and reduced systolic and diastolic blood pressure

202,204

Monotonous work, high perceived work load and time pressure have been shown to be associated with musculoskeletal symptoms ²⁰⁵, hence massage is a very appropriate intervention in the workplace setting, as it addresses that associated musculoskeletal tension at the same time as increasing relaxation.

1.14 Synthesis

This literature elucidates the detrimental effects of long-term stress on health. The HPA axis plays a central role in this process. Cortisol, reflecting HPA activity and DHEA, an HPA axis antagonist, are integral components in the stress response. The HPA axis is inseparably intertwined with psychological components such as perception of stress or coping strategies due to anatomical and functional links with the limbic system. Hence a multi-disciplinary, psycho-physiological approach should be adopted when studying stress. The physiological mechanisms of the HPA axis response are complex. Chronic stress can result in permanent structural changes in the brain and have other detrimental health outcomes e.g. CVD risk, cognitive decline, abdominal obesity, Metabolic Syndrome X etc. Stress and its effects on the body is of physiological relevance.

As the global population grows, and as competition for limited resources increases, the experience of stress increases. This experience of stress is very well illustrated in the workplace. The healthy workforce is a vital component of every country's success. Stress reduction programmes applied in the workplace occur relatively frequently in countries like USA and UK, and have been shown to effectively improve psychological and physiological health. Massage has been shown to reduce the immediate experience of anxiety. The effect of massage as a chronic stress-reduction technique has not been assessed.

2 METHODOLOGY

2.1 *Research aims*

- To assess the effects of chronic “psychological” stress on selected stress-related endocrine and cardiovascular variables.
- To determine if psychological parameters of stress (perceptions and personality) correlate with physiological indicators of stress.
- To determine if a specific relaxation intervention (massage) has any effect on the psychological or physiological markers of stress.

2.2 *Participants*

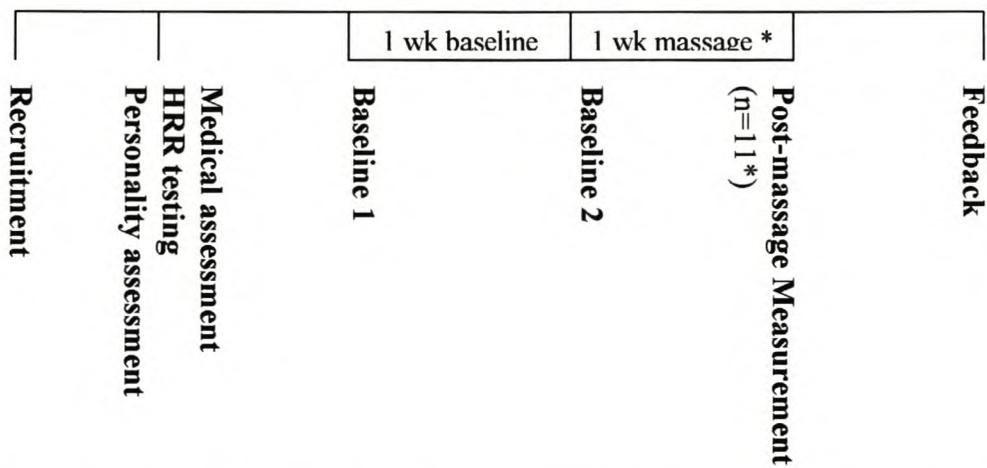
Subjects were recruited by placement of flyers on bulletin boards in community and office buildings and via word of mouth. Twenty-two working male individuals volunteered. Subjects were in a variety of occupations within different organisations (as opposed to a single occupation). The inclusion and exclusion criteria are listed in Table 2. Potential confounding variables for the hormone concentrations and psycho/physiological measurements were identified as: disease, medication, exercise levels, previous exposure to stress management interventions, their degree of exposure (intensity) and chronicity of stress (duration). See Appendix 3 to view the questionnaire devised as part of the screening process. Six volunteers were excluded on the basis of the exclusion criteria.

Table 2: Inclusion and exclusion criteria

INCLUSION CRITERIA	EXCLUSION CRITERIA
Need to be classified as “healthy” individuals i.e. no history of pathological or psychological disorders, also have passed ECG in heavy medical check (done in the last 3 years). An ECG was offered to those who hadn’t had one.	Highly trained people - to prevent interference by the effect of chronic exercise stress. Regular training or exercise regimes will also exclude a person from this study.
On no current medication	If had a professional massage in the last 2 months
Male between the age of 24-45.	If currently practising formal relaxation techniques e.g. yoga, tai chi, meditation, progressive relaxation etc.
Not exercising more than two hours per week	
Been working in a particular position for a minimum of 2 years	
Experiencing moderate or severe stress over the past 2 years.	

2.3 Protocol

The study was found to be ethically acceptable by the Medical Research Council, Tygerberg, in June 2001. The study was performed on 16 apparently “healthy” men aged 24-42. The protocol was repeated four times, with four subjects participating each time, occurring within a four month period. The procedure occurred in the following sequence of events:



Medical assessment Consisted of: an electrocardiogram (ECG) and physical medical assessment, resting HR and blood pressure assessment (See information sheet and the consent for prior, Appendix 2 and 4, which was read and signed prior to participating).

HRR testing: see section 2.10 for details.

Personality assessment: consisted of the trait related assessments, i.e. Hardiness scale and Trait Anxiety Inventory, see section 2.4 for details.

Baseline 1, 2 and Post-massage measurement: consisted of Psychological state related questionnaires, namely the State Anxiety Inventory, the POMS and the JSS, see section 2.4 for details. Physiological measures of stress included serum cortisol, DHEAs, cholesterol, LDL, HDL and TG concentrations, see sections 2.6 and 2.7 for details.

1 wk of massage: see section 2.5 and Appendix 1 for details.

Feedback: All subjects were given feedback.

* 5 individuals, who volunteered were unable to participate in the intervention, but were still interested in remaining in the study for the baseline evaluation.

2.4 Psychological Questionnaires

Trait questionnaires (Hardiness and Trait Anxiety) were completed at a single time point, the State questionnaires were completed at the 2 baseline time points, as well as at the 3rd post-massage time point. See Appendix 5-10 for questionnaires. Please note, the questionnaires in the appendices are presented for review, but are copyrighted, and should be treated as such. It is important to note that when administering the questionnaires the experimenter refrained from answering any questions regarding expected outcome of results. In response to any questions the experimenter instructed the subjects to just answer the questionnaires according to how they honestly feel.

- **Hardiness Scale:** On the basis of existential personality theory, Kobasa²⁰⁶ proposed Hardiness as a global personality construct which moderates stress-health relationships. Hardiness was conceived as consisting of three components all inextricably intertwined and therefore not mutually exclusive: *Commitment* (as opposed to alienation) captures the hardy person's curiosity about and sense of the meaningfulness of life. *Control* (as contrasted with powerlessness) summarises the belief in one's ability to influence the course of events. *Challenge* (as opposed to threat) characterises the expectation that it is normal for life to change, and for development to be stimulated thereby. For the purposes of this study the revised Hardiness scale, the 12-item scale was used²⁰⁶. For clarification, some studies use the Personal Views Survey (PVS, Hardiness Institute, Inc., 1985) to assess Hardiness. This is a 50-item scale, which was considered too elaborate for the subjects to complete considering they had other questionnaires to complete.

- **State-Trait Anxiety Inventory (STAI):** The trait version of the STAI refers to relatively stable individual differences in anxiety-proneness (i.e. tendency to perceive stressful situations as dangerous and threatening). The state version of the STAI²⁰⁷ measures anxiety level of the respondent at the time of administration. The STAI has demonstrated reliability (internal consistency alpha's ranged from 0.90 to 0.94) and validity (increases under conditions of experimentally induced stressors)²⁰⁷. State anxiety has typically been shown to decrease following a massage²⁰⁰⁻²⁰² as well as in

response to occupational stress-management in 21 studies, as reviewed in ⁸. Examination of these studies revealed that the net reduction in anxiety was on average a score of about 5.00, whereas among control groups, the average net reduction in anxiety score was less than 1.00.

- Profile of Mood States (POMS): The POMS ²⁰⁸ is a 65-item self-report inventory with several subscales tapping various mood states (Tension-Anxiety, Depression, Anger, Vigour, Fatigue, and Confusion) and generating a Total Mood Disturbance Score. The POMS is particularly suited to assessing changes in distress, with a 1-week time frame embedded in the directions (“How have you been feeling during the past week?”). Only the score from the Tension-Anxiety, Vigour and Fatigue subscales will be used in the present investigation, as these are appropriate subscales to reflect a “stressed” state. Tension-Anxiety is descriptive of heightened musculoskeletal tension. Fatigue represents a mood of weariness, inertia and low energy level. Vigour describes a mood of vigorousness and high energy (Vigour is summed negatively for POMS total score).

- Job Satisfaction Survey (JSS): The JSS ²⁰⁹ is a 36 item self-report inventory with 9 facets (*Pay, Promotion, Supervision, Benefits, Contingent Rewards, Operating Procedures, Co-workers, Nature of Work and Communication*). The internal consistency alpha’s for the subscales ranged from .60 for the Co-workers subscale, to .91 for the total scale. The validity correlations ranged from .61 for Co-workers to .80 for Supervision. Only the score from the Contingent Rewards, Operating Procedures, Co-workers, Nature of Work and Communication subscales will be used in the present investigation, 5 of the possible 9 subscales. *Contingent Rewards*, refers to the satisfaction with rewards (not necessarily monetary) given for good performance, *Operating Conditions* refers to satisfaction with the rules and procedures of the workplace. Satisfaction with *Co-workers* is related to one’s relationships with colleagues. *Nature of Work* refers to satisfaction with type of work done. *Communication* refers to satisfaction with communication within the organization. The other subscales present in the JSS are very dependent on the

structure from which the individual comes (the participants came from differing organizations), hence they were not included.

- Symptoms of Stress: The questionnaire used to assess the stress symptoms was a combination of 3 different questionnaires assessing somatic symptoms²¹⁰⁻²¹². Each of these 3 questionnaires was based on research assessing stress symptoms. I combined these questionnaires to get a more in-depth assessment of stress symptoms. I selected a rating scale, as opposed to a positive/negative response, to increase the likelihood that subtle changes in stress symptoms would be detected. The symptoms questionnaire was designed to indicate the degree of stress-related symptoms experienced by the individual. The test-retest correlations for each of the three selected questionnaires (mentioned above) were high for all the “somatic stress” subscales, all r values > 0.77 ($P < 0.001$), promising stability for my merged scale. The merged Stress Symptom questionnaire was been tested on 17 working male individuals prior to commencement of the study. All 17 individuals were between the ages of 24 and 42. The questionnaire was completed at two time points, 1 week apart and was shown to be satisfactorily stable ($r = 0.76$; $P < 0.01$). This merged Symptoms of Stress questionnaire consisted of a list of 21 different stress-related symptoms. On the questionnaire, participants are instructed to rate themselves on each symptom using a four-point rating scale of distress, with “never” being scored as 1 and a score of 4 representing “often or continuously” i.e. extreme distress.

2.5 *Massage technique*

The massage therapy was administered by the investigator to ensure consistency of technique. The investigator had completed a 14-week Bioenergy Massage course, taught by a certified massage therapist, aromatherapist and reflexologist. The massage therapy was done once a day for a week (Monday to Friday) at convenient times for the subjects. The subjects still had full work obligations and the massage was done outside their working times. The massages were done in a warm, quiet room, with the doors shut and curtains drawn. In short, the massage was applied to the legs, back, neck and shoulders

and combined deep tissue techniques with more relaxing massage strokes. See Appendix 1 for the full description of the technique used.

2.6 Blood sampling procedure

All resting blood samples were taken on a Monday morning between 7:30 a.m. and 9 a.m., after an overnight fast. Each subject was re-tested at the same time within these bounds for visits 2 and 3. All blood sampling was done after completing the psychological State related questionnaires. Cortisol concentrations are frequently measured in the early hours of the morning as an easy-to-assess index of the adrenocortical status: “Adhering to laboratory routine and the assumption that circadian peak concentrations are observed at this time, blood or saliva is usually sampled between 8 a.m. and 9 a.m. for analysis of total and free cortisol”^{63,213}.

Whole blood samples were collected by venepuncture of an antecubital vein. The blood samples were always taken by a trained phlebotomist giving attention to standard “universal safety precautions,” and careful handling. Blood was collected into 6 ml SST (gel) Vacutainer tubes (BD Vacutainer Systems, Plymouth, UK) and allowed to clot at room temperature for 15 minutes. The samples were then centrifuged at 3000 rpm for 10 minutes at 4 °C, after which the serum was decanted into eppendorf tubes and frozen at -80 °C until subsequent batch analysis (to exclude day-to-day assay variation).

2.7 Serum DHEAs, cortisol and cholesterol

Frozen serum samples were analysed by qualified medical technologists, using standard automated laboratory procedures, for total serum concentration of cortisol (Access B module 81600, Beckman/Coulter, Fullerton, CA) and DHEAs (Immulite I, Diagnostics Products, Los Angeles, CA). Serum determinants for cortisol using the above mentioned are for total cortisol which includes both the biologically active, unbound fraction and the bound fraction.

The full lipid profile analysis includes determination of serum concentrations of: total cholesterol, triglycerides (TG), low-density lipoproteins (LDL) and high-density

lipoproteins (HDL). The total cholesterol concentrations of the serum samples were determined with Technicon RA systems from Bayer Prod. no. T01-1970-85. HDL was prepared with Technicon RA systems from Bayer. Prod.. no. T01-2801-56. The TG concentrations were determined with Technicon RA systems from Bayer Prod. no T01-2426-85. The controls used were:

1. Bayer TEST point Assayed chemistry control 1 Prod no. T03-1220-62
2. Bayer TEST point Assayed chemistry control 2 Prod.no.T03-1221-62

All determinations were done on a Technicon RA1000 auto-analyser from Technicon Instruments Corporation, Tarry Town, New York. LDL cholesterol was determined by the Friedewald formula ²¹⁴: $LDL\ cholesterol\ (mmol/l) = Total\ cholesterol - (TG/2.2 + HDL)$

2.8 Fat distribution measures

Waist circumference was measured twice at the midpoint between the upper iliac crest and lower costal margin in the midaxillary line. Hip circumference was measured twice at the maximum width of the buttocks. The circumferences were measured with the subjects standing and to the nearest 0.5 cm. One observer performed all the measurements. The waist-hip ratio (WHR) was calculated as the mean waist circumference divided by the mean hip circumference for a particular subject. WHR was classified as high if the individual's WHR was greater than 0.95. If it was smaller than, or equal to 0.95, the individual was classified as having a low WHR. This classification split for fat distribution is in accordance with previous research ¹⁵⁹.

2.9 Obesity measures

The BMI (Body Mass Index) was calculated as weight divided by height (kg/m^2). The subjects wore only light shorts and shirt when they were weighed. Body height without shoes was measured to the nearest 0.5 cm. BMI was used to categorise subjects as lean to average (≤ 25) or overweight (> 25) on the basis of the estimated division of BMI for overweight ^{151,159}.

2.10 Heart rate reactivity

Heart rate reactivity (HRR) classification was done on the basis of observing the change in heart rate from baseline to the 10-second peak during the first minute after exposure of the hand to cold water immersion. Depending on the degree of heart rate change, individuals were classified as having either high or low HRR. The subjects lay quietly for 15 minutes (an adaptation period). During this time each subject was fitted with a beat-to-beat Polar heart rate monitor, consisting of an elasticised electrode belt, which incorporated a Polar Coded Transmitter S810 (Polar Electro Oy, Kempele, Finland) and a Polar Coded Interface watch S810 (Polar Electro Oy, Kempele, Finland) which was worn on the subject's wrist. The "ribbed" electrodes were made moist with water, to ensure good conduction and the transmitter was positioned centrally, directly below the xiphisternum. The belt was attached tight enough to minimise movement of the electrodes but did not cause any discomfort. The 15-minute adaptation period was followed by a 5-minute baseline and then a 1-minute cold pressor test consisting of immersion of the right hand up to the wrist in ice water (+4 °C). The 5-minute baseline heart rate was the average for the whole 5-minute period. The change in heart rate from baseline was taken as the average of the highest continuous 10-seconds of response during immersion. In accordance with previous studies, if the baseline to peak heart rate was greater than 19 bpm (beats per minute) the individual was classified as high HRR, and below 19 bpm, low HRR ⁴¹.

An individual's HRR is a stable measure which doesn't change over time (as described in section 1.4), it is not expected to change with the intervention and hence was only assessed once at baseline 1, with a view to grouping individuals according to their HRR results. The same is the case for the stable personality questionnaires that were only assessed once at baseline. The "state" questionnaires detect more subtle changes in mood and psychological state and hence were utilised at baseline 1, 2 and post-massage.

2.11 Statistical Evaluation

Data were collected and entered into Microsoft Excel Spreadsheets. Statistical analysis was performed using Statistica (version 6). Baseline data was averaged. Results were calculated as the mean \pm the SD (standard deviation). P-values were reported as either

0.05 or 0.01. If a P value of <0.05 was given it meant the P value fell between 0.01 and 0.05. Due to the fact that this study consisted of a small number of subjects ($n=16$), the possibility of an erroneous significance (Type I error) must not be disregarded.

After the subjects were divided into 2 groups according to either BMI, WHR or HRR classification, group comparisons were made. The results were analysed using parametric statistics (t-test) for BMI. If the distribution of data was not normal, the non-parametric Mann Whitney U test was used to assess significance and these P values were used. The main reason for doing this was usually because of a small sample size. Pearson's correlations were used to assess association between various parameters at baseline. Parametric paired t-tests were used to assess effect of intervention. Due to the fact that this study consisted of a small number of subjects ($n=16$), the possibility of an erroneous significance (Type I error) must not be disregarded.

Coefficients of variation (CV) of the group for various parameters (variability between subjects) were calculated as the standard deviation divided by the mean, expressed as a percentage. To calculate a CV for the individuals for repeatability (variability within subjects) an average CV was calculated by taking the average of the CV values for each individual²¹⁵. This CV value was calculated over the 2 baseline time points.

3 RESULTS

3.1 Baseline study

3.1.1 Subject characteristics: Physiology

For the 16 subjects mean \pm SD for age, weight, BMI and WHR are displayed in Table 3. Eight of the sixteen men had BMI (kg/m^2) ≥ 25 (50%), and eight < 25 (50%). Five of the 16 men had WHR > 0.95 (31%) and thirteen men had WHR ≤ 0.95 (69%).

Table 3: Subject characteristics

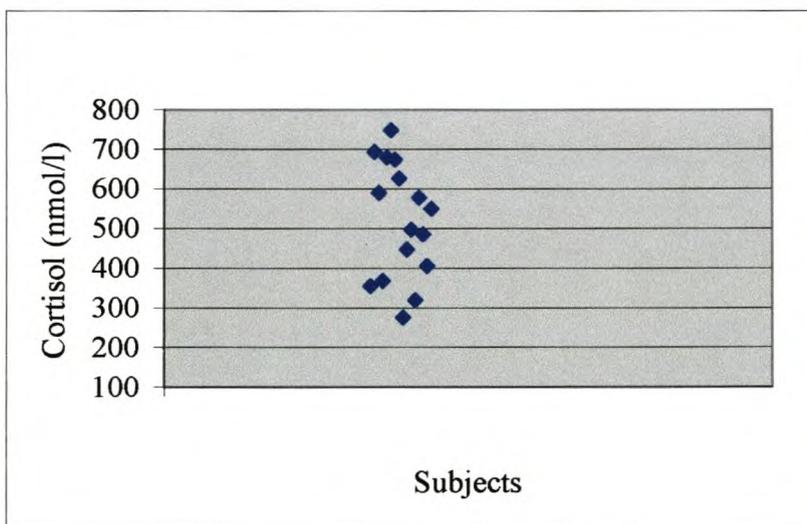
Characteristics	Baseline	Healthy Normal range
Age (yr)	31 \pm 5.3	
Weight (kg)	81.6 \pm 10.7	
BMI (kg/m^2)	25.3 \pm 3.6	21-25 *
WHR	0.945 \pm 0.056	< 1.0 **

* 151

**159

The mean cortisol concentration for the group at baseline was 518 \pm 147 (nmol/l). Thirteen of the 16 subjects were within the normal range recommended for cortisol of 200 – 650 (nmol/l) (National Health Laboratory Service (NHLS) South Africa) and 3 subjects were elevated above this range (refer to Figure 7).

Figure 7: Baseline cortisol concentrations with the lower and upper limit of the normal healthy range



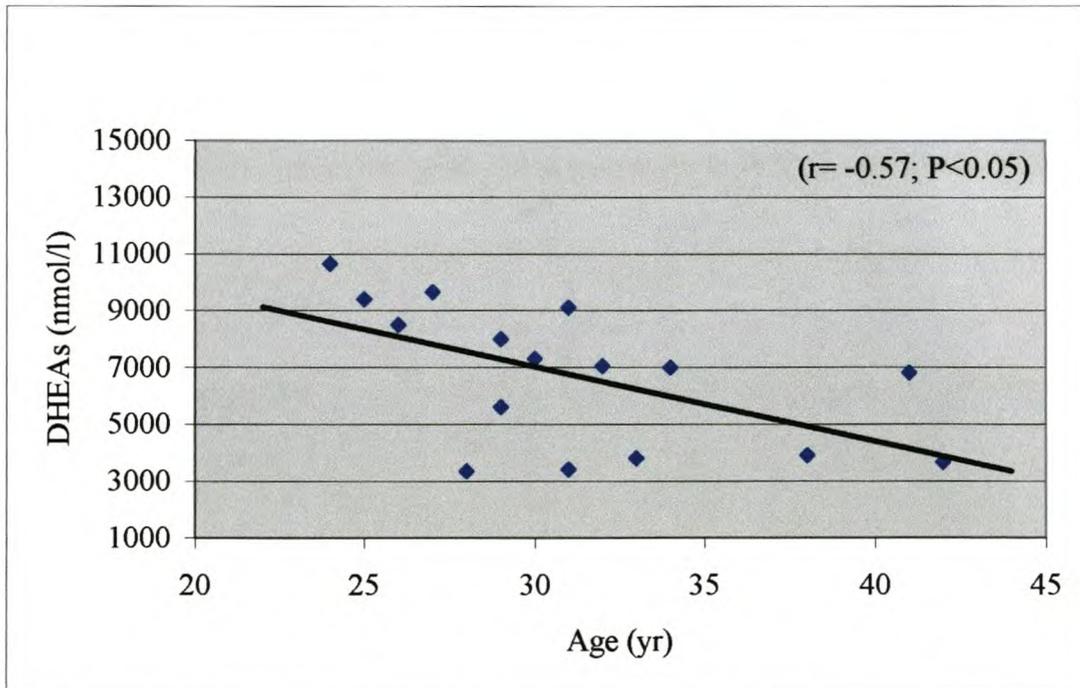
The whole group's baseline DHEAs concentrations fell within the normal range for the age and gender of the subjects ⁹², (refer to Table 4). DHEAs decreases with age hence two categories of normal ranges are given for different ages. DHEAs normal ranges also differ between males and females. Since age is a factor known to influence DHEAs concentrations, I correlated baseline DHEAs concentration with age and found the expected negative linear correlation, see Figure 8. I also found a significant negative correlation between age and cortisol concentration ($r = -0.52$; $P < 0.05$).

Table 4: DHEAs range of subjects and normal healthy range for males in the specified age groups.

Age group and number of subjects in that category	Mean \pm SD	Minimum and maximum of subjects in the category	Normal healthy range*
15-39 yr (n= 14)	6907 \pm 2508	3350 - 10650	3841 - 14084
40-49 yr (n= 2)	5225 \pm 2227	3650 - 6800	2561 - 10244

* ⁹²

Figure 8: The association between age and DHEAs in 16 male working individuals



Footnote: Pearson's correlation coefficient (r); linear regression line indicated.

Data of the lipid profiles are given in Table 5. There were 7 subjects whose average baseline cholesterol concentrations were above the recommended value (Medical

Research Council, Tygerberg South Africa) and of these 7 individuals 3 had elevated LDL cholesterol. Three subjects had lower than recommended HDL/Total Cholesterol ratios. Of these 3, only 2 also had elevated LDL. LDL concentrations correlated positively with age ($r= 0.65$; $P<0.01$).

Table 5: Lipid profile

Variable	Mean \pm SD of baseline (averaged)	Normal healthy range*
Cholesterol (mmol/l)	5.09 \pm 1.0	< 5.2
LDL (mmol/l)	3.29 \pm 0.84	< 3.8
HDL/Total Cholesterol (%)	26.3 \pm 6.5	> 20
Triglyceride (mmol/l)	1.13 \pm 0.71	<2.0

* Medical Research Council, Tygerberg South Africa

3.1.2 Group comparisons: Physiological results

Two variables that have significance for health are BMI and WHR (refer to methodology section 2.8, 2.9 and 2.10). Therefore I grouped subjects according to these variables. No significant differences were found between overweight subjects ($n=8$) and those subjects within the normal healthy weight range ($n=8$) as classified by BMI, except for their WHR and HDL cholesterol (refer to Table 6). Subjects with normal weight had significantly higher HDL cholesterol ($P<0.05$).

Table 6: Subject characteristics grouped according to BMI

Variable	Normal weight (BMI <25)	Overweight (BMI \geq 25)	P value *
Age (yrs)	29.5 \pm 3.30	33.00 \pm 6.57	NS
WHR	0.92 \pm 0.04	0.97 \pm 0.06	$P< 0.05$
Total Cholesterol (mmol/l)	4.86 \pm 0.67	5.33 \pm 1.24	NS
LDL (mmol/l)	3.08 \pm 0.62	3.50 \pm 1.01	NS
HDL (mmol/l)	1.39 \pm 0.19	1.18 \pm 0.10	$P< 0.05$
Cortisol (nmol/l)	569.5 \pm 150.3	465.9 \pm 132.3	NS
DHEAs (nmol/l)	7044 \pm 2572	6350 \pm 2492	NS
Cortisol/DHEAs	0.095 \pm 0.048	0.077 \pm 0.013	NS

* Statistical analysis: unpaired t-test

Abbreviations: NS: not significant, $P\geq 0.05$

When subjects were divided into two groups according to high WHR ($n=5$) and low WHR ($n=11$), significant differences were found for several variables (refer to Table 7).

High WHR were found to have significantly higher Total Cholesterol, LDL and TG concentrations and lower HDL/Total Cholesterol, expressed as a percentage.

Table 7: Subject characteristics grouped according to WHR

Variable	Peripheral fat (WHR < 1)	Central fat (WHR ≥ 1)	P value *
Age (yr)	30.00 ± 2.49	34.00 ± 8.80	NS
BMI (kg/m ²)	23.71 ± 2.02	28.73 ± 3.95	P<0.05
Cholesterol (mmol/l)	4.67 ± 0.71	6.01 ± 0.98	P<0.05
LDL (mmol/l)	2.97 ± 0.61	4.00 ± 0.89	P<0.05
HDL (mmol/l)	1.33 ± 0.18	1.19 ± 0.16	NS
HDL/Tot.Cholesterol (%)	28.9 ± 5.0	20.6 ± 6.0	P<0.05
Triglyceride (mmol/l)	0.84 ± 0.34	1.79 ± 0.90	P<0.05
Cortisol (nmol/l)	529.9 ± 134.1	490.9 ± 186.1	NS
DHEAs (nmol/l)	6614 ± 2272	6880 ± 3157	NS
Cortisol/DHEAs	0.091 ± 0.041	0.075 ± 0.011	NS

* Statistical analysis: Mann Whitney U test

Abbreviations: NS: not significant, P≥0.05

WHR and BMI were significantly related to age. Hence, one must keep in mind the effect that age may have had on these results. Correlations indicated that only 3 other variables were related to age. A significant positive correlation was found between age and LDL ($r = 0.65$; $P < 0.01$) and the significant negative correlation found between age and cortisol and DHEAs (mentioned previously). There was no correlation between age and Cortisol/DHEAs ($r = 0.04$; $P > 0.05$). The comparison between the 2 groups in Table 6 and Table 7 were reanalysed by ANCOVA co-varying for age. The adjusted means appear in Table 8 and Table 9.

Table 8: Results adjusted for age and grouped for BMI

Variable	Normal weight (BMI < 25)	Overweight (BMI ≥ 25)	P value *
Subjects (n)	8	8	
LDL (mmol/l)	3.26 ± 0.54	3.32 ± 0.54	NS
Cortisol (nmol/l)	548.1 ± 103.4	487.3 ± 103.4	NS
DHEAs (nmol/l)	6569 ± 1721	6824 ± 1721	NS
Cortisol/DHEAs	0.097 ± 0.028	0.075 ± 0.028	NS

* Statistical analysis: unpaired t-test

Abbreviations: NS: not significant, P≥0.05

Table 9: Results adjusted for age and grouped for WHR

Variable	Peripheral fat (WHR < 1)	Central fat (WHR ≥1)	P value *
Subjects (n)	11	5	
LDL (mmol/l)	3.07 ± 0.39	3.78 ± 0.60	P<0.05
Cortisol (nmol/l)	511.2 ± 89.7	531.9 ± 136.5	NS
DHEAs (nmol/l)	6224 ± 1374.8	7737 ± 2093	NS
Cortisol/DHEAs	0.092 ± 0.024	0.072 ± 0.037	NS

* Statistical analysis: Mann Whitney U test

Abbreviations: NS: not significant, P≥0.05

Subjects were also grouped according to HRR but no test could be done on the two groups as 2 subjects made up the high HRR group. No significant differences were found with ranking HRR increase value with Spearman's Rank correlation with the physiological parameters.

3.1.3 Subject characteristics: Psychology

The stress related psychological characteristics are presented in Table 10. All the subjects' State Anxiety scores fell within the "normal range" as given by Spielberger *et al.*²⁰⁷ for healthy adult males. There were, however, 5 subjects whose Trait Anxiety scores fell above this range. Another good measure of stress is the Tension-Anxiety subscale of the POMS²⁰⁸. For the Tension-Anxiety score, 3 of our subjects were below the normal range and 2 subjects above it²⁰⁸. Other state-related factors assessed by the POMS are illustrated in Figure 9, and those assessed with Job Satisfaction are presented in Figure 10.

Table 10: Stress-related psychological characteristics analysed using three different questionnaires

Characteristic	Score Baseline	Normal range*
Trait Anxiety	39.38 ± 10.2	25.70 – 44.08
State Anxiety	37.31 ± 7.76	25.32 – 46.12
Tension-Anxiety †	12.34 ± 6.23	6.10 – 19.70

* Min (mean – SD) to max (mean + SD) of large population in healthy males^{207, 208},

† subscale of POMS

Figure 9: POMS score, viewed with subscores: Tension-Anxiety, Fatigue and Vigour

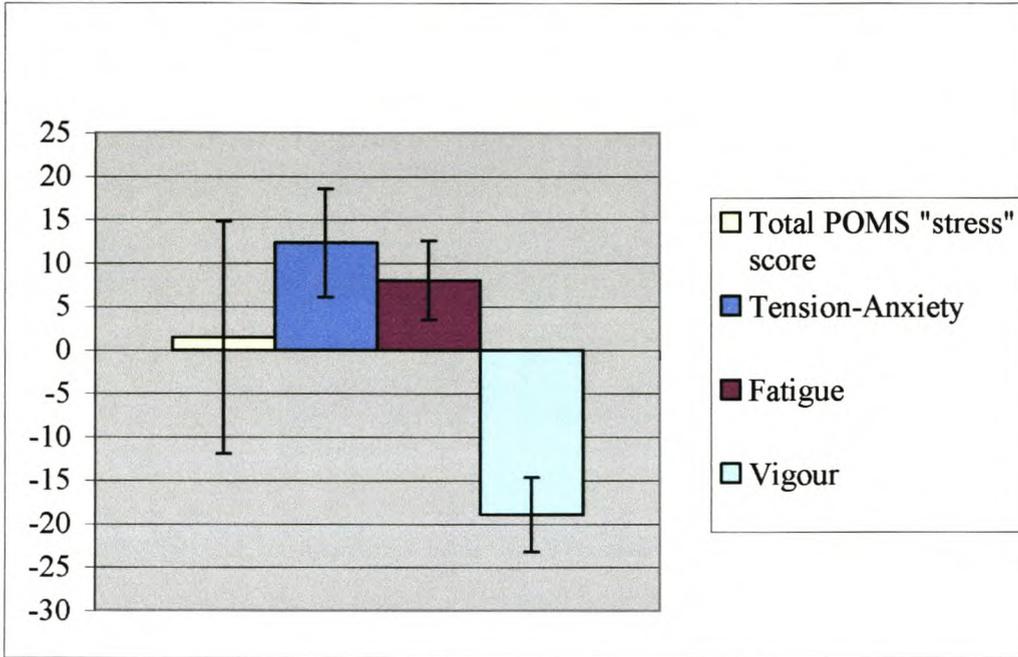
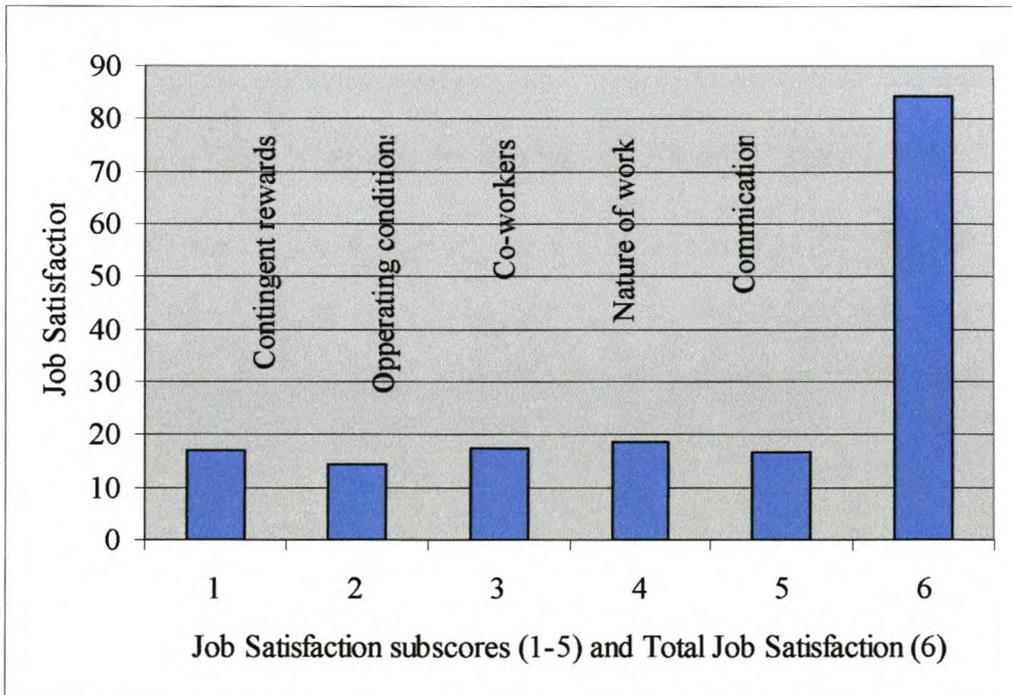


Figure 10: Job Satisfaction score, viewed with subscores: Contingent rewards, Operating conditions, co-workers, Nature of work, Communication



3.1.4 Group comparisons: Psychological results

When subjects were divided into two groups according to BMI and WHR (high BMI (n=8) and normal BMI (n=8) and high WHR (n=5) and low WHR (n=11) no significant differences were found for any of the psychological variables. No significant differences were found with ranking HRR increase value with Spearman's Rank correlation with the any of the psychological parameters.

3.1.5 Trait-related relationships

Personality predisposition refers to a characteristic that is relatively stable over time. The personality characteristics of the subjects in this study are given in Table 11. The personality scores listed in Table 11 were correlated with psychological and physiological parameters. This took place in three logical steps, firstly correlating personality with personality scores (step 1), secondly correlating personality with state-related scores (step 2), and thirdly, correlating personality with physiological results (step 3). Personality variables were selected to be our independent variables and hence are displayed on the x-axes.

Table 11: Personality scores, i.e. Trait Anxiety and Hardiness are listed as Mean \pm SD.

Personality Variable	Mean \pm SD of baseline (averaged)	Absolute minimum and maximum values*
Trait Anxiety	39.38 \pm 10.17	20 to 88
Hardiness	6.38 \pm 3.42	-18 to 18
H - Control	1.81 \pm 1.56	-6 to 6
H - Commitment	2.50 \pm 1.93	-6 to 6
H - Challenge	2.06 \pm 1.88	-6 to 6

H- subscales for Hardiness follow

* for the tests

STEP 1: Trait vs Trait

The personality variables of Trait Anxiety and Hardiness showed a relatively weak negative association with each other. No specific Hardiness subscale was more greatly associated with Trait Anxiety (Commitment, $r = -0.56$ and Challenge, $r = -0.56$), but Control was unassociated (NS) with Trait Anxiety, indicating their independence from each other as trait factors (refer to Table 12).

Table 12: Correlation results between personality variables

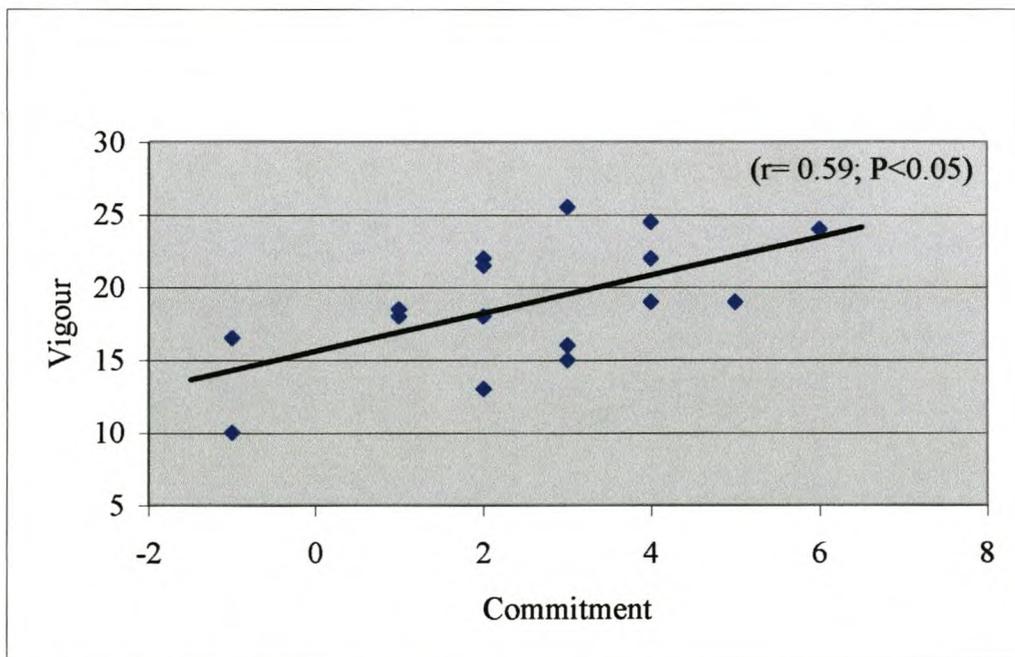
	Person's coefficient	P value
Trait Anxiety vs Hardiness	r= -0.54	P<0.05
Trait Anxiety vs Control	r= 0.46	NS
Trait Anxiety vs Commitment	r= -0.56	P<0.05
Trait Anxiety vs Challenge	r= -0.56	P<0.05

Abbreviation: NS: not significant, $P \geq 0.05$

STEP 2: Trait vs State

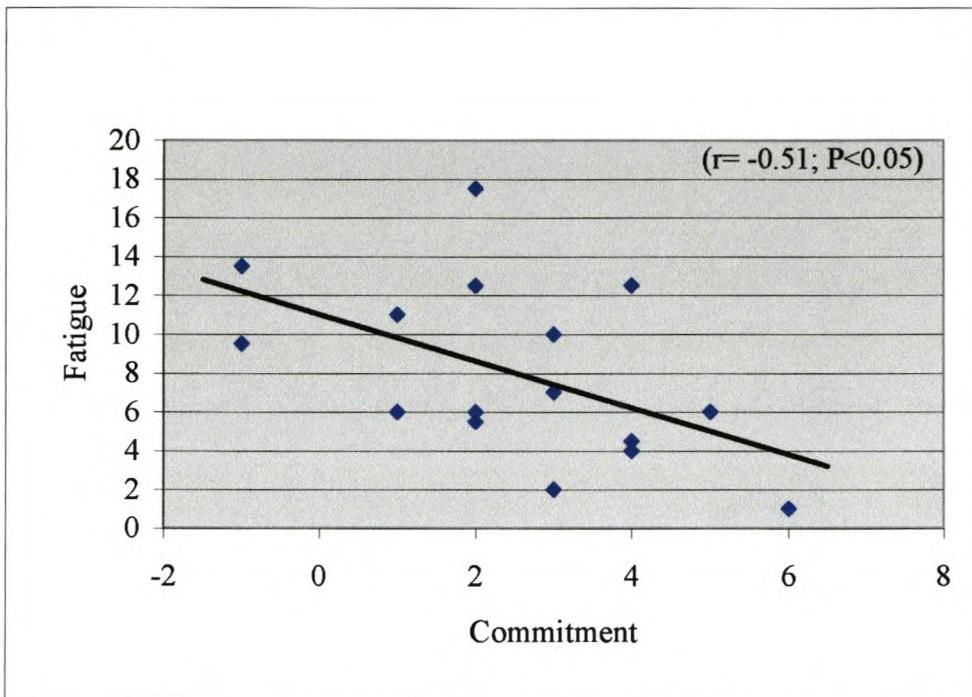
From Figure 11, Figure 12 and Figure 13 it can be seen that Commitment scores (personality-related score) correlated positively with Vigour and negatively with Fatigue and total POMS (state-related scores). Commitment scores correlated positively with Job Satisfaction and Trait Anxiety correlated negatively with Job Satisfaction (refer to Figure 14 and Figure 15). Commitment and Trait Anxiety scores also correlated negatively with one another ($r = -0.56$; $P < 0.05$).

Figure 11: The association between Commitment and Vigour in 16 male working individuals



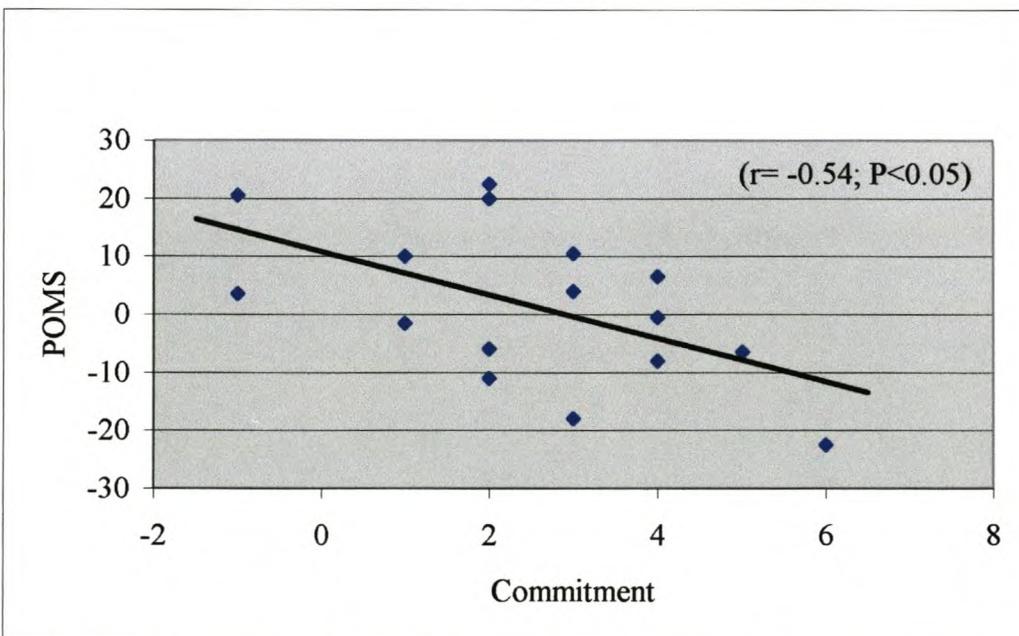
Footnote: Pearson's correlation coefficient (r); linear regression line indicated.

Figure 12: The association between Commitment and Fatigue in 16 male working individuals



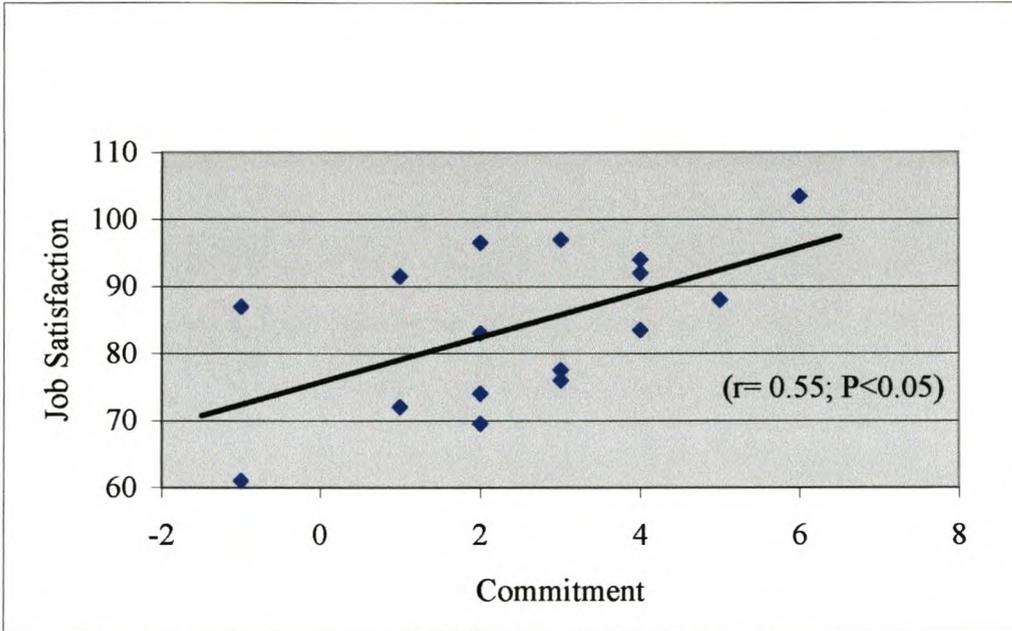
Footnote: Pearson's correlation coefficient (r); linear regression line indicated.

Figure 13: The association between Commitment and POMS in 16 male working individuals



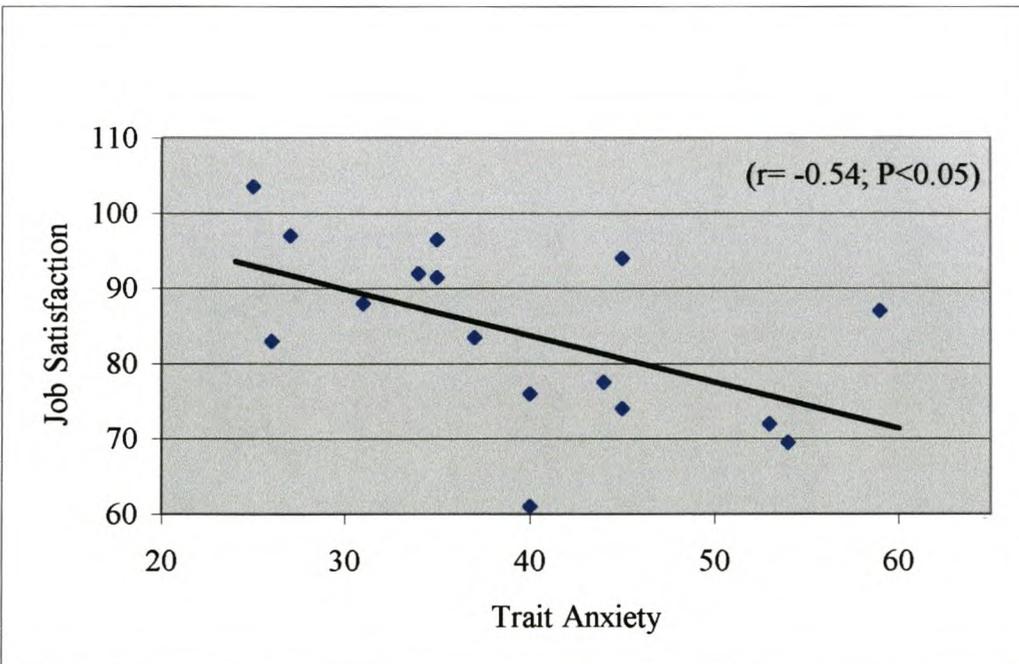
Footnote: Pearson's correlation coefficient (r); linear regression line indicated.

Figure 14: The association between Commitment and Job Satisfaction in 16 male working individuals



Footnote: Pearson's correlation coefficient (r); linear regression line indicated.

Figure 15: The association between Trait Anxiety and Job Satisfaction in 16 male working individuals

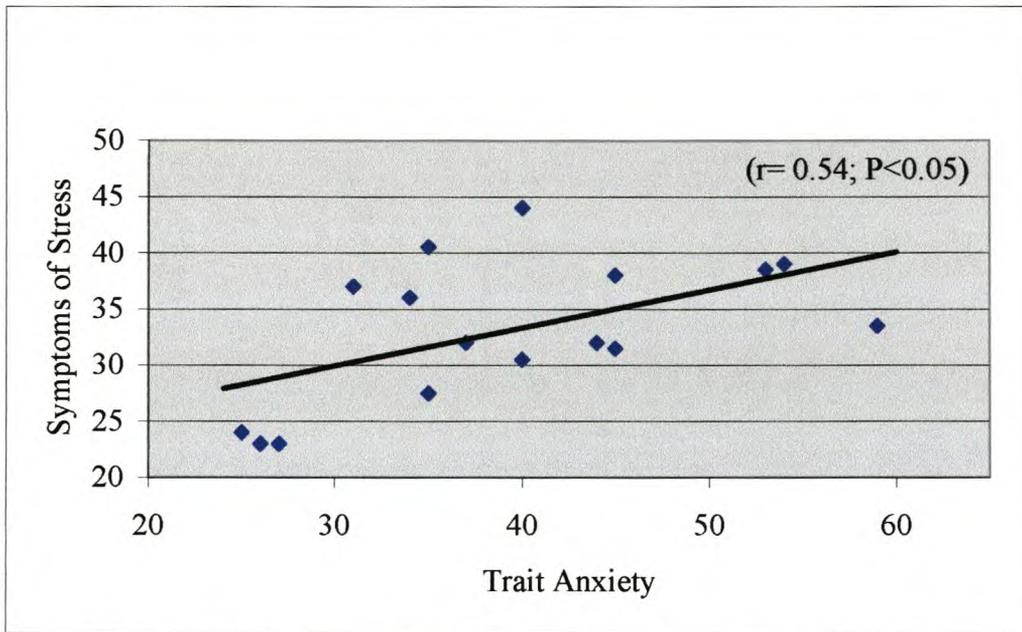


Footnote: Pearson's correlation coefficient (r); linear regression line indicated.

STEP 3: Trait vs Physiology

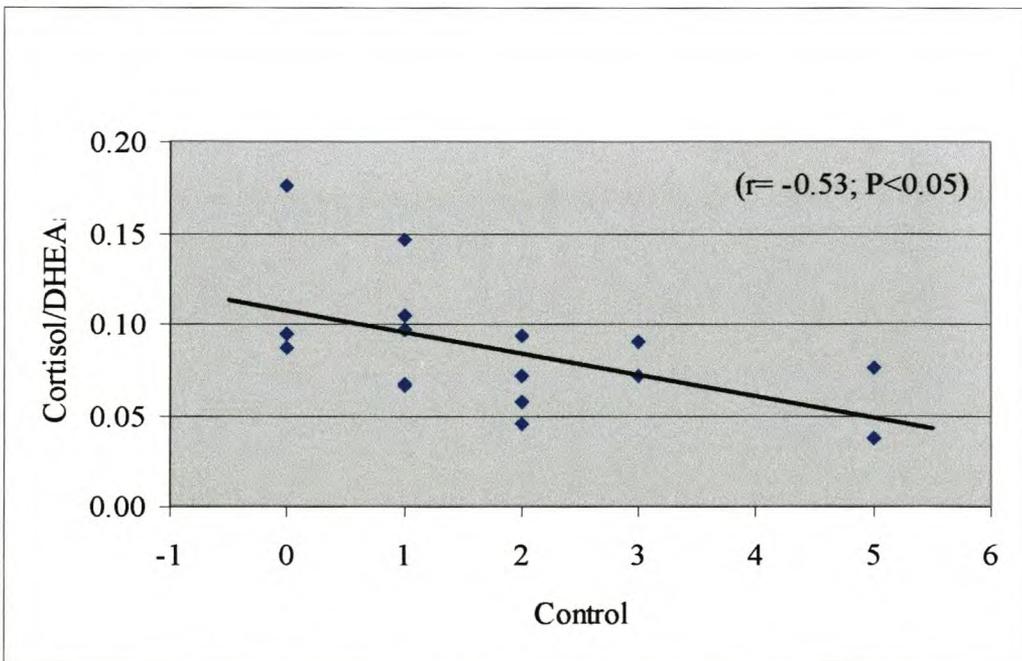
Trait Anxiety correlated positively with Symptoms of Stress (refer to Figure 16). The personality trait of Control correlated negatively with cortisol/DHEAs ratio (refer to Figure 17), but no other physiological variable was associated with personality scores.

Figure 16: The association between Trait Anxiety and Symptoms of Stress in 16 male working individuals



Footnote: Pearson’s correlation coefficient (r); linear regression line indicated.

Figure 17: The association between Control and Cortisol/DHEAs in 16 male working Individuals



Footnote: Spearman’s Ranked correlation coefficient (r); linear regression line indicated.

In summary, personality was assessed by two scales, one which included 3 subscales. The two main scales and the subscales were correlated, firstly with each other, secondly with state-related results and thirdly with physiological results. Although there were some associations between the 5 personality scores, none were greater than $r=-0.56$. Relating personality scores to state-related psychological scores, the best association was found between Trait Anxiety and State Anxiety ($r= 0.78$; $P<0.05$). From a physiological perspective, Trait Anxiety was associated with symptoms of stress and the personality factor of Control was inversely associated with hormonal markers of stress. The high level of inter-relatedness of various personality factors precluded the use of multiple regression analysis.

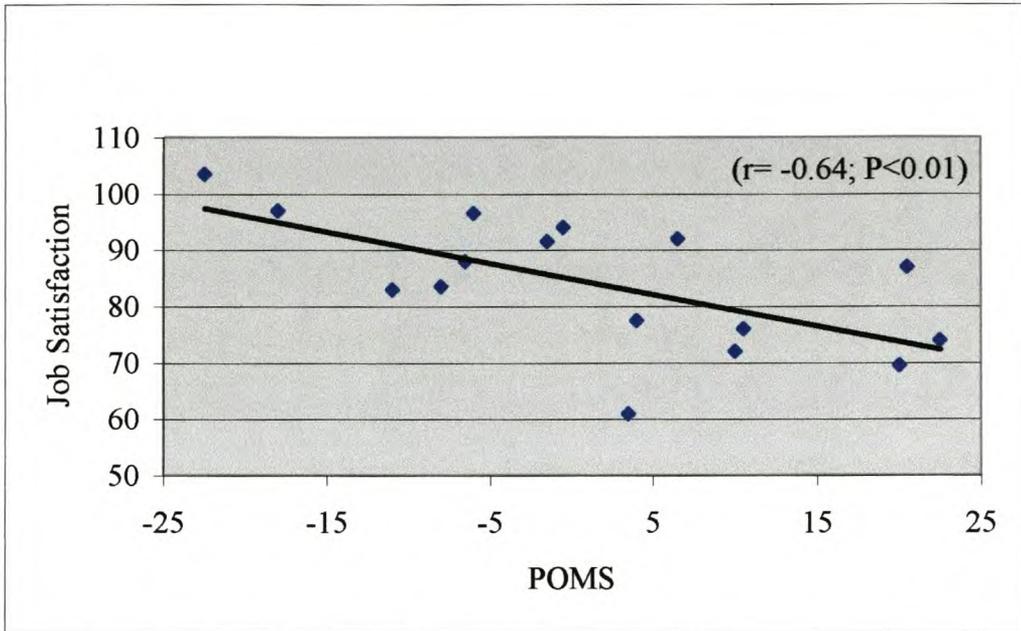
3.1.6 State-related relationships

One's state differs from personality predispositions (trait-related) since it is less stable over time, whereas personality predispositions are relatively stable over time. The same logical process for locating correlations between personality and other variables was also used to check for correlations between state-related and other results. Firstly, I checked for correlation between the state scores themselves (step 1). Then possible associations between state scores and physiological variables were assessed (step 2). For these correlations, state-related scores were selected to be the independent variables and hence were displayed on the x-axis.

STEP 1: State vs State

POMS and State Anxiety scores were highly significantly associated with each other ($r= 0.81$; $P<0.01$). The subscores of Tension-Anxiety and Fatigue were highly associated ($r=0.87$; $P<0.01$) but Tension-Anxiety was not as strongly associated with Vigour ($r= -0.54$; $P<0.05$). POMS correlated negatively with Job Satisfaction (refer to Figure 18), as did State Anxiety ($r= -0.56$; $P<0.05$). It is noteworthy that all three subscores of POMS (Tension-Anxiety, Fatigue and Vigour) also correlated individually with Job Satisfaction ($r= -0.51$; $r= -0.62$; $r= 0.60$ respectively, all $P<0.05$).

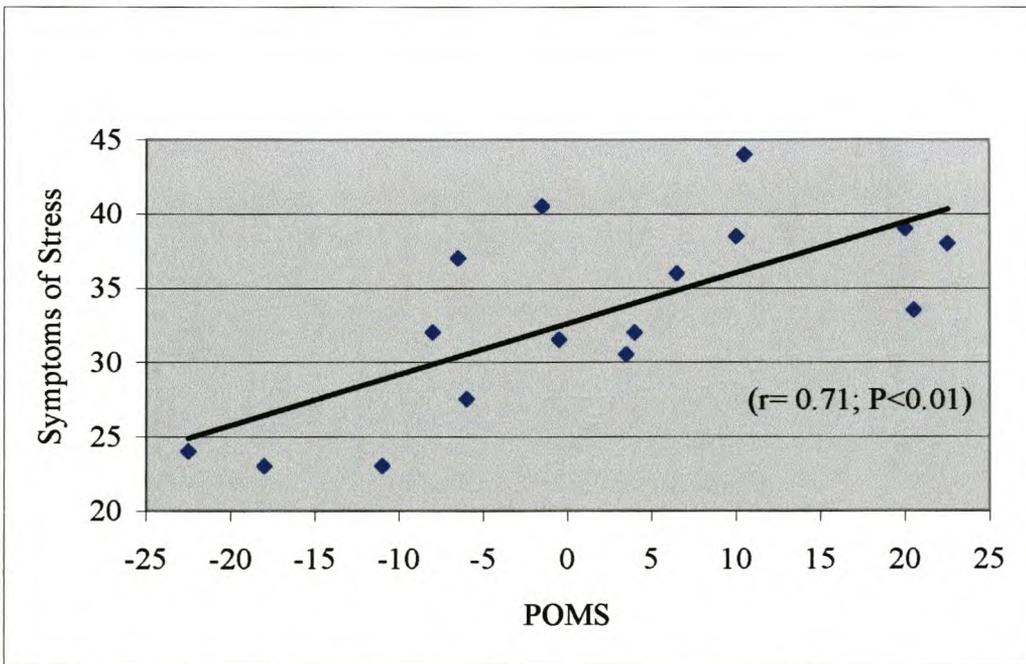
Figure 18: The association between POMS and Job Satisfaction in 16 male working individuals



Footnote: Pearson’s correlation coefficient (r); linear regression line indicated.

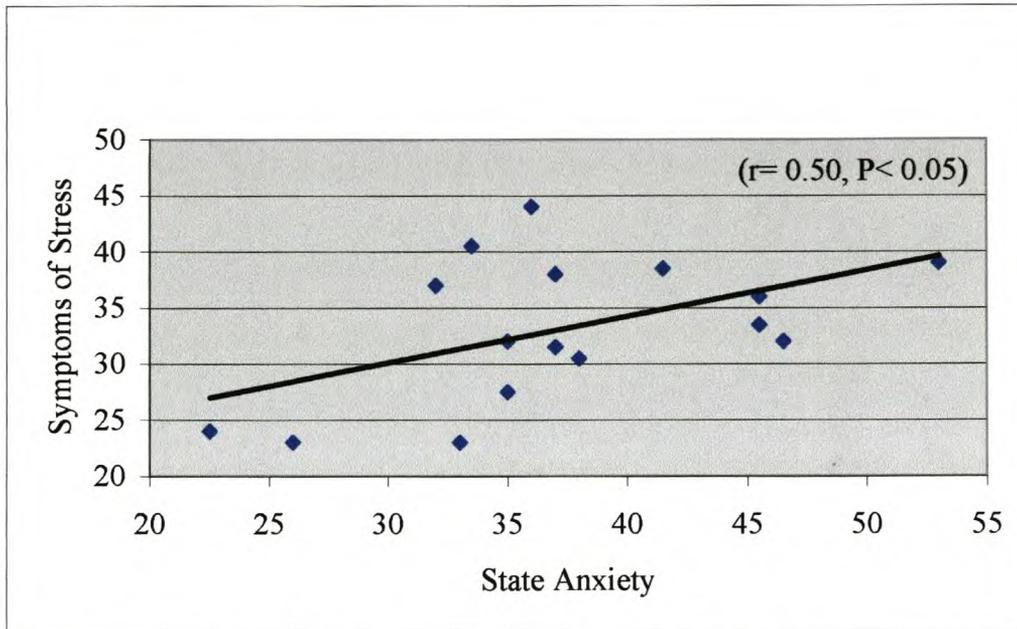
STEP 2: Both POMS and State Anxiety correlated positively with Symptoms of Stress (refer to Figure 19 and Figure 20). It is noteworthy that all three subscores of POMS (Tension-Anxiety, Fatigue and Vigour) also correlated individually with Symptoms of Stress ($r = 0.72; P < 0.01$, $r = 0.62; P < 0.05$, $r = -0.53; P < 0.05$ respectively).

Figure 19: The association between POMS and Symptoms of stress in 16 male working individuals



Footnote: Pearson’s correlation coefficient (r); linear regression line indicated.

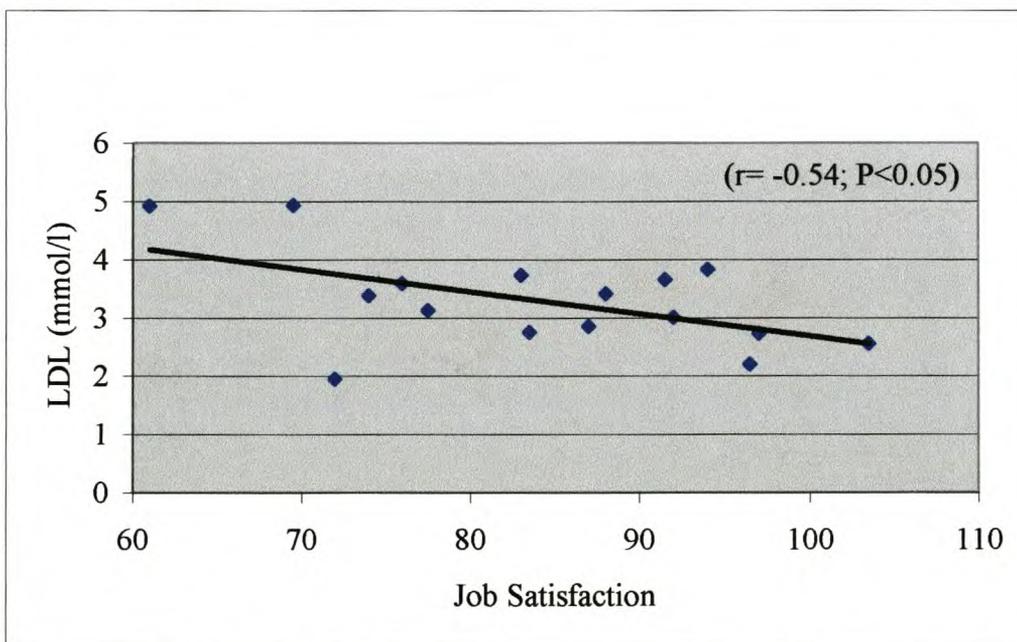
Figure 20: The association between State Anxiety and Symptoms of Stress in 16 male working individuals



Footnote: Pearson’s correlation coefficient (r); linear regression line indicated.

Job Satisfaction correlated negatively with LDL (refer to Figure 21). No other physiological variable correlated with either POMS or State Anxiety. Therefore, baseline cortisol and DHEAs concentration and cortisol/DHEAs were unrelated to psychological state-related stress.

Figure 21: The association between Job Satisfaction and LDL concentrations in 16 male working individuals



Footnote: Pearson’s correlation coefficient (r); linear regression line indicated.

As mentioned previously age correlated positively with LDL ($r= 0.65$; $P> 0.05$), therefore it is possible that the association between Job Satisfaction and LDL was influenced by age, but age did not correlate with Job Satisfaction.

In summary, stress-related “state” was assessed by two scales, POMS and State Anxiety which appeared to be highly associated ($r= 0.78$; $P<0.05$). In addition the state-related Job Satisfaction was also assessed. A stressful state adversely affected a sense of job satisfaction. State-related stress also appeared to be associated with increased stress symptoms. Job satisfaction was associated with lower LDL. The high level of interrelatedness of the various personality factors precluded the use of multiple regression analysis.

3.2 Intervention study

3.2.1 Hormonal, lipid and psychological variability

Part of the rationale for doing a baseline study with 16 subjects was to assess the week-to-week variation of the physiological and state-related psychological variables. The variability of a series of measurements performed on different subjects using the same protocol (especially at the same time of day when a circadian pattern is suspected) can be broken down into two elements: the biological variability (between-individual variability) and the random error variability (which includes both within-individual variability and method error).

The CV for cortisol for the group at baseline was 32% for time point 1 and 28% for time point 2. The CV for the individuals across the two time points was 12.7% (see methods section 2.11 for CV calculation methods). The CV for DHEAs for the group was 40% for time point 1 and 34% for time point 2. The CV for the individuals across the two time points was 7.3%. The CV for lipid profile is shown in Table 13 and the CV of the psychological assessments in Table 14.

Table 13: Coefficient of variation for lipid profile

Variable	CV of group at Baseline 1	CV of group at Baseline 2	CV of individuals across the 2 baseline time points
Total Cholesterol (mmol/l)	20%	20%	4.9%
LDL (mmol/l)	28%	25%	7.8%
HDL (mmol/l)	17%	14%	5.6%
Triglyceride (mmol/l)	73%	65%	22.7%
HDL/total cholesterol (%)	27%	23%	5.7%

Table 14: Coefficient of variation for the state-related psychological assessments

Variable	CV of group at Baseline 1	CV of group at Baseline 2	CV of individuals across the 2 baseline time points
State Anxiety	24%	24%	12.8%
Job Satisfaction	15%	14%	4.4%
POMS	55%	54%	19.9%
Vigour	20%	30%	11.7%
Tension-Anxiety	54%	52%	26.2%
Symptoms of Stress	24%	24%	12.8%

3.2.2 Effects of the massage

In order to assess the effects of the massage intervention, two techniques were employed. Firstly, the 2 baseline results were averaged and compared with the post-massage results. Secondly, the degree of change from baseline to post-massage was calculated and compared with the CV's presented in the previous section.

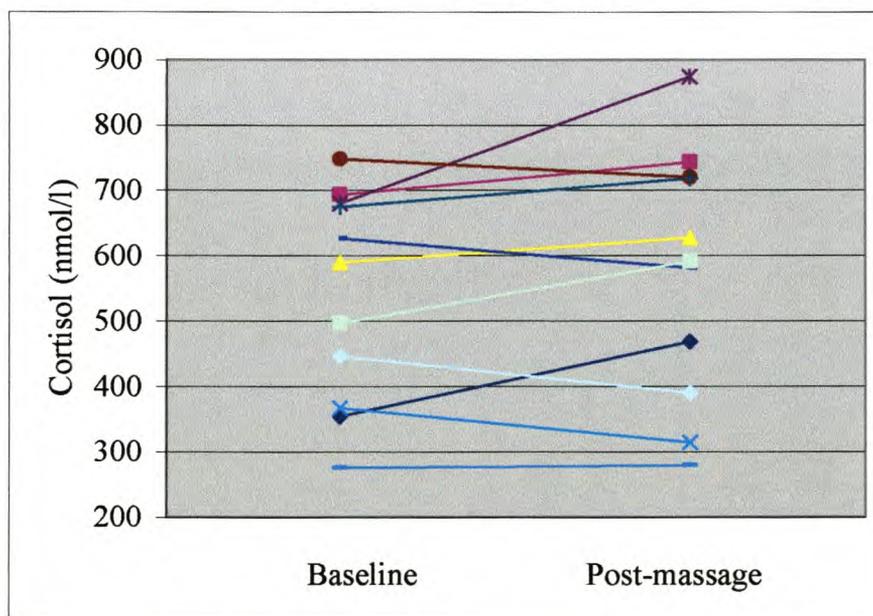
STEP 1: Comparisons of Baseline and post-massage physiological results are presented in Table 15. Post-massage cortisol was similar to the baseline average cortisol. Post-massage DHEAs was similar to the baseline average DHEAs. The individual results for cortisol are seen in Figure 22 and for the cortisol/DHEAs ratios in Figure 23.

Table 15: Hormonal and lipid baseline and post-massage results

Variable	Baseline	Post massage	P value
Cortisol (nmol/l)	518 ±161	573 ± 191	NS
DHEAs (nmol/l)	6027 ± 2572	5927 ± 2609	NS
Cortisol/DHEAs	0.098 ± 0.034	0.113 ± 0.061	NS
Total Cholesterol (mmol/l)	5.57 ± 0.79	5.62 ± 0.69	NS
LDL (mmol/l)	3.67 ± 0.71	3.83 ± 0.70	NS
HDL (mmol/l)	1.30 ± 0.22	1.30 ± 0.24	NS
Triglyceride (mmol/l)	1.35 ± 0.76	1.10 ± 0.61	NS

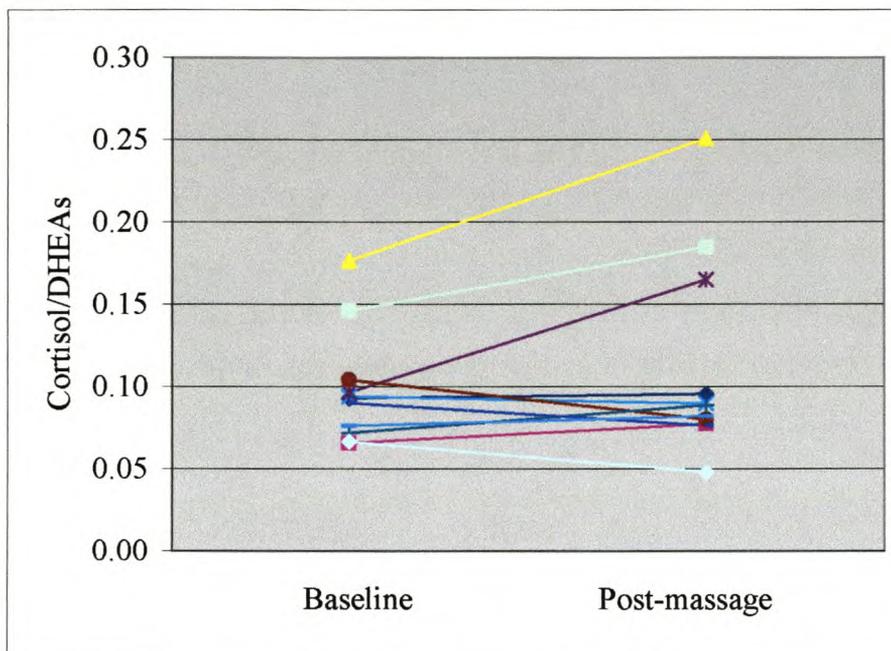
Statistical Analysis: Paired t-test

Figure 22: Baseline and post-massage cortisol concentrations



Footnote: Baseline is average of baseline 1 and baseline 2

Figure 23: Baseline and post-massage cortisol/DHEAs ratio



Footnote: Baseline is average of baseline 1 and baseline 2

Averaging the baseline results and comparing them to the post-massage results was also done for the state-related variables (see Table 16). Individual changes in State Anxiety can be seen in Figure 24.

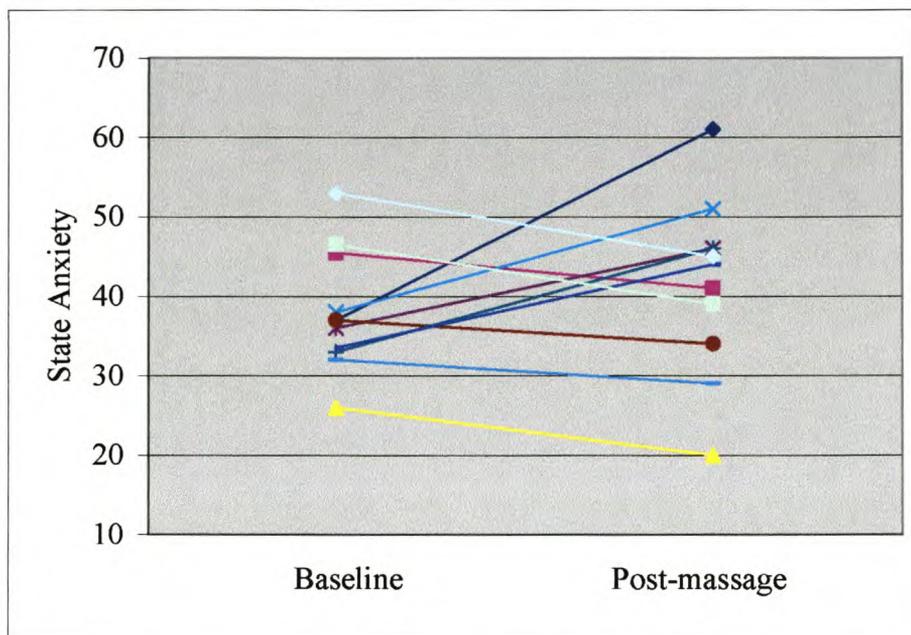
Table 16: State-related Baseline and post-massage results

	Baseline	Post message	P value
State Anxiety	37.95 ± 7.65	41.45 ± 11.00	NS
Job Satisfaction	82.14 ± 11.47	80.55 ± 10.54	NS
POMS	2.68 ± 12.24	4.09 ± 13.59	NS
P - Tension-Anxiety	13.00 ± 6.19	12.63 ± 6.52	NS
P- Fatigue	8.45 ± 4.47	9.73 ± 5.24	NS
P - Vigour	18.77 ± 3.83	18.27 ± 3.93	NS
Symptoms of Stress	34.05 ± 6.79	33.73 ± 7.10	NS

Statistical Analysis: Paired t-test

P- subscales for POMS follow

Figure 24: Baseline and post-massage State Anxiety scores



STEP 2: The range of response displayed in Table 17 indicate that for each variable some subjects declined whereas others increased. The individual changes in hormonal concentrations (cortisol, DHEAs and cortisol/DHEAs ratio) relative to State Anxiety change are displayed in Figure 25, Figure 26 and Figure 27 respectively.

Table 17: Change from baseline to post-massage

	Mean	Range of Change	Range of % change
Cortisol (nmol/l)	32.50	-56 to 193	-0.14 to 0.29
DHEAs (nmol/l)	-100.00	-1750 to 1700	-0.25 to 0.29
Cortisol/DHEAs	0.014	-0.24 to 0.074	-0.02 to 0.07
Total Cholesterol (mmol/l)	0.05	-0.49 to 0.68	-0.07 to 0.13
LDL (mmol/l)	0.16	-0.44 to 0.64	-0.44 to 0.64
HDL (mmol/l)	0.00	-0.20 to 0.13	-0.16 to 0.13
Triglyceride (mmol/l)	-0.25	-1.21 to 0.28	-0.52 to 0.36
State Anxiety	1.45	-8 to 10.5	-0.23 to 0.65
Job Satisfaction	-1.59	-9.5 to 6	-0.10 to 0.08
Symptoms of Stress	0.32	-4.5 to 4.5	-0.14 to 0.14

Figure 25: Change in State Anxiety across Baseline to post-massage, relative to change in cortisol

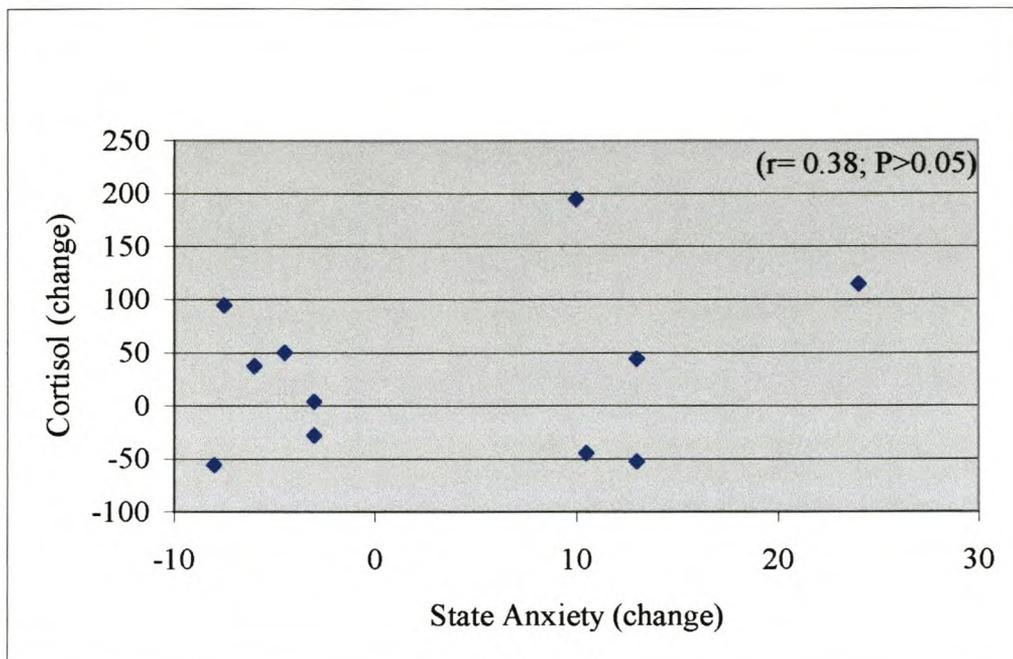


Figure 26: Change in State Anxiety across Baseline to Post massage, relative to change in DHEAs

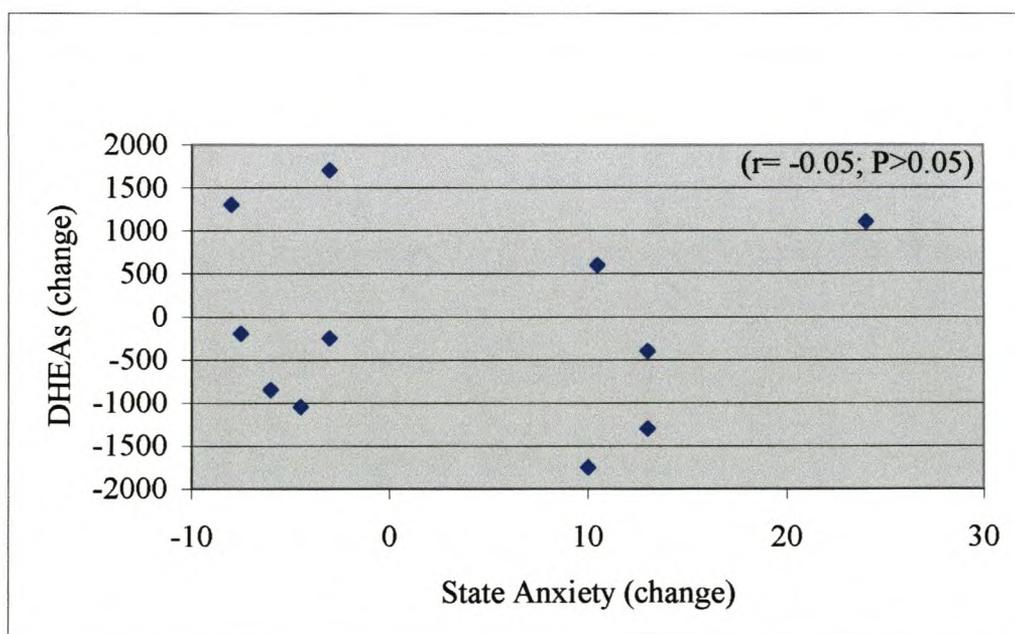
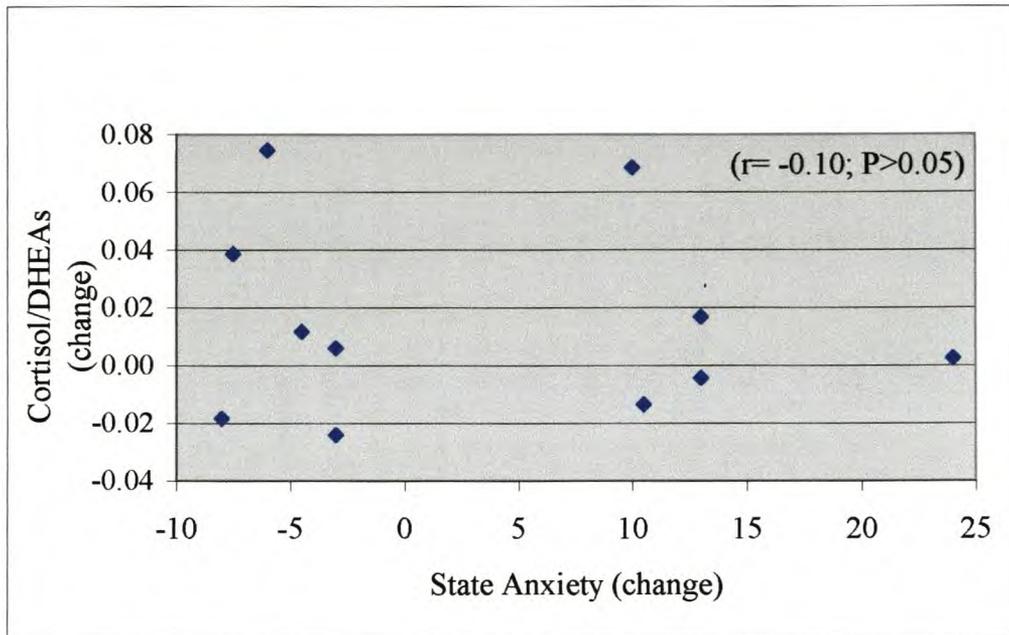


Figure 27: Change in State Anxiety across Baseline to Post massage, relative to changes in cortisol/DHEAs ratio



From the above 3 graphs, it is evident that 5 subjects' State Anxiety scores increased post-intervention relative to baseline. We grouped individuals according to this distribution i.e. those whose State Anxiety increased (n=5) versus those whose State Anxiety decreased following the massage intervention (n=6). With this grouping, I performed a t-test on their averaged baseline results and the personality scores. Subjects whose State Anxiety increased, were found to have lower Commitment scores. See Table 18 for physiological results and for psychological results see Table 19.

Table 18: Subject characteristics grouped according to State Anxiety response

Variable	State Anxiety decreased	State Anxiety increased	P value *
Age (yr)	32.66 ± 7.25	32.40 ± 4.72	NS
BMI (kg/m ²)	25.97 ± 2.21	25.66 ± 2.53	NS
Cholesterol (mmol/l)	5.43 ± 0.98	5.73 ± 0.55	NS
LDL (mmol/l)	3.51 ± 0.80	5.73 ± 0.61	NS
HDL (mmol/l)	1.35 ± 0.25	1.23 ± 0.17	NS
HDL/Tot.Cholesterol (%)	25.7 ± 7.0	21.6 ± 4.1	NS
Triglyceride (mmol/l)	1.27 ± 0.85	1.45 ± 0.72	NS
Cortisol (nmol/l)	541.3 ± 173.24	539.9 ± 165.6	NS
DHEAs (nmol/l)	5858 ± 2937	6230 ± 2379	NS
Cortisol/DHEAs	0.106 ± 0.046	0.089 ± 0.010	NS

* Statistical analysis: Mann Whitney U test
Abbreviations: NS: not significant, P ≥ 0.05

Table 19: Subject characteristics grouped according to State Anxiety response

Variable	Peripheral fat (WHR < 1)	Central fat (WHR ≥ 1)	P value *
Trait Anxiety	39.1 ± 10.1	37.2 ± 7.2	NS
Hardiness	7.5 ± 3.4	5.6 ± 3.0	NS
H - Control	1.5 ± 1.8	1.6 ± 1.1	NS
H - Commitment	3.5 ± 1.0	1.4 ± 1.5	P<0.05
H - Challenge	2.5 ± 1.5	2.6 ± 2.2	NS
Symptoms of Stress	33.1 ± 5.7	35.2 ± 8.4	NS
Job Satisfaction	86.3 ± 10.7	77.1 ± 11.3	NS
POMS	0.17 ± 12.8	4.8 ± 12.6	NS

* Statistical analysis: Mann Whitney U test

Abbreviations: NS: not significant, P≥0.05

H- subscales for Hardiness follow

4 DISCUSSION

4.1 *Baseline study*

All subjects declared themselves to be moderately to severely stressed on entry into the study. The study subsequently determined stress levels using a multidisciplinary approach. Although variability of most parameters was moderate to high, preventing confident conclusions on all aspects, some major conclusions could be reached. The main finding from this study was that resting cortisol as a physiological measure of stress is problematic. The second major finding was that personality factors play a large role in perceptions of stress and health outcomes.

Physiologically, stress was assessed by determining resting cortisol concentrations. There was a large variability in the range of cortisol concentrations, with 5 subjects falling in the lower half of the normal healthy range, 7 falling in the upper half of the normal healthy range and 5 above the normal healthy range. It is possible that the majority of our subjects were not that severely stressed. Had they all been more stressed it is likely that more subjects would have cortisol concentrations above the normal range. However, one study found that subjects with higher work loads actually had lower morning cortisol concentrations⁸⁵, possibly as a result of interrupted sleep-wake patterns or neuroendocrine exhaustion. There are theoretical arguments for higher or lower than expected values. The diurnal variation predicts early morning peak³⁴ but this could also be influenced by negative feedback³⁵. Another complication is that the other psychophysiological studies that assessed anxiety levels and cortisol^{78,85} measured salivary cortisol concentration, hence I was unable to make direct comparisons of our cortisol results relative to other published studies of groups with similar stress.

In this study, cardiovascular pathology (stress ECG) and depression were the main exclusion criteria. I did not screen for a specific cut-off level of stress assessed by a questionnaire. Rather, subjects volunteered themselves as fitting the criterion: “moderate to severely stressed”. The Trait Anxiety results revealed that 5 subjects fell within the lower half of the normal distribution and 6 in the upper half. Five subjects were above the normal upper limit and no subject below the normal limit. The State Anxiety results

revealed similar results: 6 subjects fell within the lower half of the normal range, and 7 in the upper half. There were 2 subjects whose State Anxiety score was above the normal upper limit and 1 whose score fell below the normal limit. One can conclude from these results that the stress levels of the subjects of the group were not severe, but rather moderate. The Symptoms of Stress scale used in this study has a possible score range of 21-84. The mean of the subject group was 33.13, indicating that the majority of the subjects fell within the first quartile of score for Symptoms of Stress. This reveals that the subjects' symptoms of stress were moderate, yet not one subject was symptom-free.

Our multidisciplinary assessment revealed that the subjects were moderately stressed, but as a group I was not able to classify them as severely stressed. In summary, the discussion that follows refers to a group of subjects who experience moderate stress.

4.1.1 The effects of moderate stress on health-related physiological parameters

As mentioned earlier in the discussion, an important finding of this study was that the group of subjects had a large range of baseline cortisol concentrations. This could be a characteristic of this particular group, namely that stress results in a wide variety of baseline cortisol concentrations. It has however, been suggested that there exist marked differences in the functioning of the HPA axis in healthy men ²¹⁶. Varying degrees of stress exposure and other factors, e.g. sleep pattern disturbances ⁸⁷ could possibly play a role in the broad range of cortisol concentrations observed in this study.

There were 7 subjects whose average baseline cholesterol concentrations were above the recommended value (Medical Research Council, Tygerberg South Africa), for which moderate work stress could be partially responsible. However, other factors not investigated could also have played a role e.g. unhealthy diet and lifestyle (which could also be partially influenced by stress and work commitments). Other factors, such as genetics, such also not be disregarded. The relationship between stress and CVD is quite clear, but whether this is mediated through the effects stress has on cholesterol is still uncertain. Under acute stress situation free fatty acids and cholesterol appear to become elevated ¹⁵⁷. The mechanisms of glucocorticoids have been described to produce insulin

insensitivity, which can lead to hyperglycaemia, hypertriglyceridaemia, hypercholesterolaemia and hyperinsulinaemia ¹³⁸

A possible confounding factor to the results is the age of the subjects. The influence of age on LDL and DHEAs is known. LDL has been shown to rise with increasing age ²¹⁷, and our results are consistent with this. DHEAs was shown to decrease with age in this particular subject group of relatively stressed working males between the ages of 24 and 42, which is what was expected, as DHEA has been shown to decrease with age in the normal population ⁹². The fact that cortisol correlated negatively with age, could also be a specific characteristic of this particular subject group, as cortisol is thought to remain constant with increasing age ⁶³. It has been suggested that the adrenal secretion of cortisol is maintained during aging at the expense of Δ 5-steroids, such as DHEA ⁶⁴, explaining the decrease in DHEA with age. Although “peripheral” glucocorticoid concentrations are maintained with age, adaptive changes at glucocorticoid receptor levels are suspected ²¹⁸. This can be assessed by using a stress-challenge in conjunction with dexamethasone suppression ¹⁷¹. Future studies should consider more detailed methods of assessment of the HPA axis e.g. functional stress testing such as the dexamethasone suppression test.

Despite co-varying for the effect of age, my results showed that those subjects with high WHR had a lipid profile of relative CVD risk. In contrast, the high BMI group only showed elevated HDL. Both BMI and WHR have been shown to be associated with risk factors of CVD ^{177,179}, but WHR has been proposed to be a better indicator of CVD risk ¹⁸⁰. My results also indicate that WHR is a better indicator of the presence of CVD risk than BMI. High WHR has been shown to independently be associated with CVD risk factors, but these effects are increased with weight gain (BMI) ²¹⁹.

However, subjects with relatively higher CVD risk did not exhibit higher stress as measured by either physiological or psychological indicators of stress or symptoms of stress. So, CVD health risk in this group of subjects did not seem to be influenced by

stress, unless the tools used in this present study for assessing stress did not adequately assess accumulation of stress i.e. chronic stress.

The discussion thus far has concluded that this particular subject population was moderately stressed and not severely stressed. The fact that the HRR test revealed only 2 subjects as having high HRR, supports the fact that the subjects were only moderately stressed. There are only two possible ways to interpret this: either, as previously stated, our subjects were not highly stressed, or the test is not sensitive to moderate stress. For this study I selected the cold pressor test, which has been shown to have the highest laboratory to real-life correlations relative to other laboratory stress testing techniques²²⁰. Cardiovascular reactivity has been shown to be much greater in relation to real-life stress than to that of any laboratory stress^{221,222}. My recommendation for future stress studies is that if one is wanting to assess cardiovascular reactivity, one needs to ensure that sufficient numbers are in either the high or low group. This could be achieved by either selecting a subject group that is more severely stressed or measuring reactivity in a more real-life stress test (such as a public speaking test). In the literature, some researchers have screened many subjects, and selected their 2 study groups from the extremes. I did not use this technique as I wanted assess the physiological reactivity of specific subject group i.e. working males experiencing stress.

There was very little difference between State Anxiety and POMS scores, as they were highly associated. State Anxiety and POMS assesses relatively similar states, hence one can conclude that the subjects were honest in their responses. In future research one could possibly select one of the scales. My recommendation would be to select the POMS using the 3 stress-related subscales. The POMS results showed a much broader range between subjects and the subscores assist in making interpretation more meaningful.

An example of the meaningfulness of breaking down the POMS score is illustrated in the relationship the POMS and its subscore results had with Symptoms of Stress. POMS itself, correlated highly with Symptoms of stress ($r = 0.71$; $P < 0.05$); in fact, far better

than with State Anxiety ($r = 0.50$; $P < 0.05$). Comparing the subscores, Tension-Anxiety had a far greater association with stress symptoms ($r = 0.72$; $P < 0.05$) than either Vigour or Fatigue ($r = -0.53$; $P < 0.05$ and $r = 0.62$; $P < 0.01$). Hence, it was tension-anxiety that had the most influential effect on symptoms of stress, greater than that of high fatigue or low vigour.

4.1.2 Trait-related relationships

Arnetz and Fjellner²²³ found that neuroendocrine and physiological reactions to stressors varied greatly from one individual to another. As mentioned earlier in this discussion, our subjects exhibited a large range in POMS scores. Arnetz and Fjellner also concluded that certain personality factors appear to play a large role in predicting stress-induced neurophysiological reactions. Stress-related personality types have been shown to be associated with increased baseline cortisol concentrations^{71,75,78,79}. The implication to understanding the individual differences in personality and state is that it may give insight into why some people develop illness during prolonged stress, while others do not.

My results showed that committed individuals experience more vigour and less fatigue. One might initially expect the reverse i.e. highly committed individuals work hardest and should feel more fatigue. My results are best explained in a quote²²⁴ pg 32-34, illustrating the difference between the committed and the non-committed individual:

“I’ve never been able to sit idly by. It’s not that I can’t relax, because I can. But there are so many things to do in life that are interesting and rewarding. I’m almost never bored. Even when there’s something I have to do that doesn’t strike me as interesting at first (say at work), usually, once I get into it, I find it worthwhile in a way that teaches me something. Maybe it will involve a new way of using my calculating skills, or maybe it will just turn out to be more interesting or important than I thought. I’ve always liked to feel that I grow in life, rather than just stagnate.” In contrast to: *“Too often, my life seems like a rat race. I’m always trying to catch up, to meet deadlines imposed on me by other people. And most of the things I have to do, when you come down to it, aren’t even important. They’re just routine. So even though I’m nervous and tense about*

meeting deadlines, I'm also bored a lot of the time. Sometimes I think about taking early retirement – calling it a day. Maybe life on a houseboat would be better.”

The conclusion one can draw from this is that “commitment” goes hand-in-hand with a person being actively and energetically involved in what they are doing. It is feasible that the effort and attentiveness invested in activities actually positively enhances one’s perceived energy levels.

Commitment was also found to be positively associated with job satisfaction in this study. An involved and enthusiastic attitude towards one’s work is conducive to more satisfaction taken from it. Kobasa and Hilker²²⁵ found that the hardy executive expressed more job satisfaction with the three major aspects of the work environment – interpersonal, personal and systems – than did the non-hardy executives. This confirms the results of this study, however, only the Commitment score was a good predictor of job satisfaction and not the total Hardiness score. Total Hardiness score, as well as any of the three components of Hardiness, were found to be uncorrelated to symptoms of stress. This is contrary to what Kobasa *et al.* proposed: that hardiness should have a buffering effect on illness²⁷⁻²⁹. In contrast, a different personality trait, Trait Anxiety, was associated with increased stress symptomology (see section 3.1.5), but not any other physiological measurements. Van Eck *et al.*⁷¹, found that Trait Anxiety correlated positively with cortisol concentrations, but my study’s results did not reveal this same association.

From the results of this study, individuals with a low cortisol to DHEAs ratio had a high sense of control. This lower ratio is suggestive of a reduced physiological stress profile, due to the fact that DHEA shows antigluocorticoid effects in several systems¹⁰⁸. Conversely, a low sense of control is associated with an increased stress profile. Perceived stress scores have been found to correlate negatively to DHEAs concentrations¹⁰⁵. The antigluocorticoid properties of DHEA suggest that DHEA blocks the potentially deleterious effects of stress-induced cortisol release. Cortisol/DHEAs ratio is thought to be a better indicator of the stress related state as

cortisol production is assumed to occur at the expense of DHEA production, due to the fact that pregnenolone is the precursor for both DHEA and cortisol (see Figure 5 in literature review). The highly stressed state of long-term and acute illness^{106,107} has been shown to be associated increased cortisol/DHEAs ratio. This is the first study to measure cortisol and DHEAs and calculate the ratio, and correlate these endocrine profiles to psychological variables.

It is relevant that individuals who perceive a sense of control exhibit a physiological profile of reduced stress. People strong in Control believe and act as if they can influence the events taking place around them. Reduction in the sense of control occurs when a person feels unable to produce a set of actions that will restore a perceived discrepancy between reality and aims and ambitions. Power or mastery over the environment is likely to have an ameliorating effect on stress. In contrast, people who feel powerless believe and act as if they are victims of forces beyond their control. A sense of control appears to have a large impact on the physiological manifestation of stress.

Control has previously been thought to play an important role in job strain¹³⁹, with low control increasing the stress associated with work. Also, low job control has been shown to predict future cardiac events¹⁴⁶. Frankenhaesser and Johansson²²⁶ found that in the work environment, a lack of control was associated with feelings of distress, as well as a trend towards increased cortisol concentrations. Hence, personal control appeared to act as a buffer to the physiological manifestation of stress experienced at work as well. Bjorntorp introduced a model integrating the autonomic, neuroendocrine and endocrine consequences of reaction to stressful stimuli¹⁶⁴, which proposed a classification of individuals into different categories according to their responses. He proposed that a “sense of control” plays a very important role in determining the physiological stress response. I am unaware of any studies (from Bjorntorp himself, or other researchers) that confirm the association between sense of control and physiological stress, besides this one.

The determining factor explaining why some people have a stronger sense of control than others is controversial and is likely to differ from individual to individual. It has been postulated that current differences in control may reflect the overall proportion of mastery, as opposed to failure during previous experiences in early life²²⁴. As they grow older, children's developing physical and mental capabilities lead them to try to accomplish things. When children succeed, they have a sense of mastery – and when they fail, a sense of failure. Early successes, even if in easy tasks, set up positive feelings of control. The concept of control over events is possibly a behaviour learnt at an early age. Behavioural interventions that encourage an increased sense of control, e.g. teaching active coping strategies, could be successful interventions to reduce and manage stress, both psychologically and physiologically. Research on work related stress should include assessments of subjects' histories of accomplishment versus low control experiences.

4.1.3 State-related relationships

State-related psychological stress, assessed through questionnaires has been found to correlate with cortisol⁶⁶⁻⁶⁹. Negative mood has also been found to be associated with increased cortisol^{71,72}. The changes in cortisol, are likely to be mediated by psychophysiological mechanisms, although not all studies reveal a close relationship between state-related stress and cortisol^{70,71,80,82} or between other state-related psychological and physiological indicators of stress²²⁷.

In order to explain the non-correlation between state-related stress and cortisol observed in this study, it could be that I did not assess the psychological states effectively, with the questionnaires that I selected. Alternatively, the poor relationship obtained between state and physiology is as a result of one's conscious perception of stress being different to that of our unconscious experience of stress. This should not be underestimated. If our unconscious perception of stress differs significantly from the conscious judgment, then it is likely that our physiological indicator of stress will not reflect our perceived (conscious) perceptions (estimations). With this potential problem we included into the study design the HRR test, in the hope that it would assess unconscious stress reactivity,

although, this was not shown to be a useful tool in this particular subject group of moderately stressed working males, as previously discussed.

State-related results were associated with Job Satisfaction scores. Tension-Anxiety, State Anxiety, Vigour, Fatigue and POMS (in that order) were all equally good predictors of Job Satisfaction (ranging from $r = -0.51$; $P < 0.05$ to $r = -0.62$; $P < 0.05$). The finding that stress impacted negatively on job satisfaction highlights the necessity for stress management interventions in the workplace as an integral part of Human Resource Management. In order to enjoy one's work, one should try not to "stress" about it!

Our state-related results showed that, instead of a close relationship between state and physiology, this study showed psychological state to be highly related to job satisfaction and personality to be more related to physiological manifestations.

4.2 Intervention study

Variability

Biological variability refers to the amount of change inherent within the individual subject. One measures biological variation by taking repeated measures from an individual over a prescribed period of time and then calculating total variance or coefficient of variation. Normal biological variability (between-individual variability) is a natural physiological phenomena, but makes intervention studies difficult as subtle changes, as result of an intervention, are more difficult to detect. During this study, precautions were taken to ensure the method-error was kept to a minimum. Serum samples from baseline to post-intervention were analysed in the same assays by the same technician. As expected, between-individual variability was shown to be greater than within-individual variability. Within-individual variability cannot be avoided in dynamic biological systems, and in our study it was assessed as acceptable if CV was $< 15\%$, for all physiological systems except TG.

The HPA axis has three main functional characteristics: i) basal activity leading to appropriate levels of cortisol production in a circadian pattern, ii) negative feedback

regulation that results in stimulation of the system when plasma cortisol concentrations fall and iii) responses to a variety of stresses which, if strong, will override the circadian and feedback controls (see section 1.5). Each one will be discussed below in terms of variability.

i) A large variability in serum cortisol concentrations both within- and between- individuals has been reported before^{58,228}. Even when control is exerted over time of day and samples are obtained within a specified morning interval i.e. between 8 a.m. and 9 a.m.^{65,229}, variation is still high, as seen in my results. Eight a.m. serum cortisol analysis has been shown to have better stability than other means of cortisol sampling e.g. saliva or urine. Correlation coefficients for 8 a.m. concentrations of plasma cortisol, nocturnal urinary and 24hr urinary cortisol/creatinine ratio have all been shown to have “moderate” reliability. However, salivary cortisol, nocturnal urinary cortisol/creatinine ratio and 24hr urinary cortisol were shown to have “even less” reliability⁶⁵ than 8 a.m. plasma samples. It could be argued that one serum sample for the assessment of cortisol is a weak basis for conclusions regarding effects of stress, or intervention on cortisol concentrations, because serum cortisol shows clear circadian variation. According to one study, the spontaneous variation in serum cortisol concentration from 7:30 a.m. to 9 a.m., when the blood samples of this current study were collected, is of a relatively small magnitude²³⁰, as the differences are much larger when very early morning samples are compared with evening samples. Furthermore, in this study, although samples were taken between 7:30 a.m. and 9 a.m., each subject returned at their own exact time for the different occasions. Thus, changes in mean serum cortisol could not be attributed to this circadian-related variation. Although I only measured two cortisol baseline serum samples (due to time and financial constraints), it has been suggested that three or more baseline measurements may be needed to obtain a satisfactory reliability of the mean⁶⁵. In the same paper 18 samples are recommended for salivary cortisol. These authors came to the conclusion by determining the ratio of biological variability to random error.

ii) Almost any kind of stress or threat to homeostasis will cause plasma glucocorticoid concentrations to rise. Research suggests that a large cortisol response to acute

stressors is beneficial in preventing stress-activated cortisol from overshooting and damaging the organism, since negative feedback kicks in appropriately^{37,231}. With reference to my results, a factor that may help explain the between- and possibly within--individual morning cortisol variation at baseline could be that I did not strictly control sampling time with reference to the time of awakening. Instead, I chose to control the chronological time of sampling. The basis for this possible flaw, is related to the hypothesis that the rise in cortisol in the early hours of the morning serves as the HPA axis's response to centrally driven input designed to provide the organism with sufficient energy to shift from resting to an active state⁵⁸ (although scientific evidence has yet to be provided). Sherman *et al.*⁸⁷ showed that older individuals' cortisol peak occurred earlier than that of younger individuals. They contributed this earlier peak to the fact that older individuals reported sleep disturbances and more specifically, reported earlier wakening. Although the current study found a correlation between age and cortisol, no inferences could be drawn since it was not known if the older individuals awakened earlier or not. Age has been found to be associated with disturbed sleeping and altered normal circadian rhythms²³². Recording the time of wakening is recommended for future studies where morning cortisol samples are taken, as it may help to explain some of this variation, for which one could then account.

iii) It is important for the HPA axis to be a dynamic, flexible system in order to respond varyingly to different situations, as both an absence of and an over abundance of glucocorticoids during stress have profound, pathophysiological consequences. "An inability to appropriately terminate glucocorticoid secretion at the end of a stressor can ultimately be as damaging as the inability to appropriately initiate secretion at the onset of a stressor"⁸⁴. Therefore variability has been regarded as a good characteristic of an endocrine system that serves adaptive functions in a quickly changing environment. As proper functioning of the HPA axis is crucial for survival and maintenance of health, it is not surprising that its regulation shows characteristics of plasticity, making it a very complex system.

A longitudinal analysis of weekly samples from 4 normal men, aged 36-59 years, revealed within-individual variability of DHEA (mean CV of 19%), and failed to demonstrate any monthly, seasonal, or annual rhythmicity⁹². My study showed less within-individual variability (CV of 7.3%). Orentreich *et al.*²³³ displayed large between- and within-individual variability of DHEAs among individuals within the healthy population (14.4% of the subjects had a CV between 10-19%, and 13.3% of the subjects had a CV of less than 10%, The other subjects all had a CV of > 19%). This variation could not be correlated with changes in life circumstances, health status, or any other discernible factors, hence this large variability still remains unexplained. Our results showed the within-individual DHEAs morning sample variability is much more stable than that of cortisol (mean CV was 7.3% vs 12.7%), although there appeared to be a large between individual variability, possibly as a result of the 18 year age range (24-42 yrs).

Cholesterol, LDL and HDL concentrations generally were more stable than the hormonal analyses, for both within- and between-individual variability. Large variabilities in HDL, LDL, total cholesterol and TG have been reported previously^{234,235}. Psychosocial variables have been shown to explain significantly the variability in TG, HDL and LDL²³⁶ beyond the relevant co variants such as age, gender, alcohol intake etc. The TG concentration had an exceptionally large between-subject variability in my study. The within-individual variability of 22.7% for the TG could possibly partially be explained by diet (i.e. fat intake varying the night prior or not adhering to the instructions to arrive fasted on the morning of the sampling). Other studies have shown that TG concentrations are much more variable in comparison to LDL and HDL (30% vs 11% and 15%)²³⁷.

Of the psychological variables, personality factors were only assessed once since they are known to be relatively stable over time. Of the state-related psychological scales the JSS was the most stable across time. There was a large between-individual variability in the POMS and the Tension-Anxiety subscale of the POMS. The POMS should be highly recommended for future research where one intends to use correlations as statistical

means of analysis as the large range of scores given by the POMS is more likely to elucidate certain associations through correlations. Hence the broad range of scores is quite useful for such purposes, but the large within-individual variability seen in the POMS would make the POMS a very difficult scale to use to assess the effect of an intervention, as it would mean that the change would have to be exceptionally large to overcome the normal variation that occurs at baseline. The State Anxiety scale would be the recommended scale for such purposes. The State Anxiety Index of the STAI and the Symptoms of Stress questionnaire has within- and between-individual variability that is similar to that of the hormonal measures indicated in this study.

4.2.1 Effects of the massage

One should also consider the fact that stress may be associated with attitudes and behaviours which do not relate to the maintenance of a healthy state. Health promoting behaviours include exercise and the practice of relaxation. Health threatening behaviours include smoking, excessive drinking lack of exercise and others, which could impact negatively on one's health and symptoms of stress. The subjects in this study were selected on the basis of specifically not doing regular exercise and on the basis that they did not practice any form of relaxation technique. All subjects had also not been for a professional massage in the past 6 months.

Eleven stressed working male individuals did not benefit significantly from 1 week of intensive massage, with respect to the selected psychological and physiological stress-related parameters measured. The variable nature of the parameters tested can be viewed as a major factor limiting our statistical power to assess the effect of massage. However, the inability to detect relatively subtle changes against such a high background of noise was not the only factor for non-significant results. Also, the subject numbers were relatively small, and subjects responded quite differently, so that the general average values remained almost the same.

The only visible trend was for baseline cortisol to increase after participation in the intervention, thus in a direction opposite to the expected, although not significantly. This

increase was accompanied by an increase in State Anxiety. There were 5 subjects whose State Anxiety increased quite substantially during the course of the study. During discussions at the time of feedback, these specific individuals reported an increase in stress as a result of outside circumstances (e.g. work-related deadlines). Hence, the difficulty of controlling this type of study is also a major factor influencing the results.

Two other factors to which consideration must be given with respect to the study design, were the intensive nature of the intervention (1 hr/day for 5 consecutive days), and also the fact that 2 days elapsed between the last massage and the post-testing time point. This study design was specifically selected to assess highly intensive intervention but one that still took place within a normal working week. These subjects were not specifically removed from this situation, as would have been the case if they had gone to a spa. The intervention was not to determine an acute effect of massage since the study did not take post-massage samples immediately, or even the very next morning. Hence, the study design was a design that could be introduced into the workplace.

I conclude that ideally a study such as this should be conducted within a framework of a minimum possible demand on the subjects' time as this can enhance rather than reduce stress. In my study massage was not done on-site. This is a major limitation to the study design. Attempts were made to conduct the study in several organisations, on-site, but no businesses could be found that were willing to do it that way. Using subjects in real-life situations is nonetheless still very relevant for this form of research and future studies. Work stress experienced by the subject cannot always be predicted and cannot be controlled for by the investigator. Since varying work stress can act as a confounding factor, future studies should have a matched control group subjected to the same work stress. Also, a study design utilising a control group is suggested, possibly in the form of just relaxation in a massage chair or on a massage table.

Massage, commonly used in the nursing setting, has been shown to be beneficial in reducing anxiety in patients¹⁹² and in relaxing patients¹⁹³. Studies report that patients and other subjects, such as healthy individuals and people with stress-related disorders

e.g. PTSD and depression, benefit from massage through its relaxation effect (see literature review section 1.13). Although there is an understanding pertaining to the effects of massage on soft and connective tissue, as studied in Physiotherapy and Chiropractic, not much is known about how massage, as a relaxation intervention, influences physiology of the endocrine system. If massage has claims to be such a “relaxation” modality, the question I asked was “what are the effects it has on the physiological indicators of stress?”

Subjectively, the subjects reported feeling relaxed during and after the massage, but no standardised measures were taken of the acute effect of massage. It is acknowledged that therapeutic massage has a strong acute relaxation effect ¹⁹⁸ measured physiologically (assessed via EEG). Studies of the acute effects of massage (measuring anxiety and mood before and after) show significant changes towards decreased anxiety and mood improvement ^{194,201}. Statements by some subjects to the effect that they were “fortunate” to be part of the study, indicated subjectively the importance of this non-invasive relaxation intervention.

However, the objective of my study was to assess the effects of massage on the psychological state over the time-span of days rather than as an acute intervention. Hence, the study was designed to allow two days after the last massage before the post-massage assessments. The effect of massage on psychological state in this time-frame was not sufficiently answered by this study. What can be concluded is that a one-week intensive intervention with massage is unlikely to be effective if the subjects remain in the stress-inducing environment. Nevertheless, massage in the workplace is a very effective means of addressing the musculoskeletal symptoms of stress experienced at work ²⁰⁵. Also, on-site massage has been shown to increase alertness and mathematical ability, and decrease anxiety and job stress ^{200,202,204}. This appears to be true for when assessments are made directly before and after the massage. The longer-term effects are still unclear. If massage is to become recognized as a health enhancing therapeutic tool, research on its health enhancing effects needs to be documented. For future research I would recommend a less intensive (once or twice a week), longer duration (1 - 2 months +)

intervention, as opposed to a high intensity, short duration intervention. How long the acute effects of massage last is still questionable. Whether or not massage intervention is able to sufficiently influence hormonal indicators of cardiovascular markers of stress is unclear. Although massage has acute effects, it does not require lifestyle change. An alternative possibility is to recommend a relaxation intervention that is directed at altering the lifestyle of the individual.

An interesting finding was that those subjects, whose anxiety scores increased towards the end of the study, had significantly lower Commitment scores. This personality trait refers to individuals who are involved and committed to the task at hand. The non-committed individuals appeared to get more anxious as the study progressed. I hypothesised that individuals with high Commitment, don't allow extraneous factors e.g. extra demands placed on time as a result of being part of the study to increase their stress levels, whereas, individuals with low Commitment allow outside factors to increase their stress levels. Possibly, those individuals who exhibit low Commitment may be more likely to be distracted from the job at hand, allowing them to feel more stressed.

4.2.2 Conclusion

The literature review provided a foundation for the view that stress interferes with normal physiological function via neuro-endocrine responses and that these may be detrimental to one's health. The value of integrating psychological and physiological aspects in research is that one begins to view the body via its integrated psychophysiological processes. The benefit of using more parameters and fewer subjects (as done in this study) can help to elucidate a few key parameters for use in later studies. The results show that personality differences played a stronger role in the experience of stress and physiological manifestations of stress than state differences between subjects. On the other hand, state impacted negatively on job satisfaction and reported symptoms of stress. Low job satisfaction also played a detrimental role in CVD risk. Hence, human resource managers in organizations should pay particular attention to, or should monitor, symptoms of stress and employees' levels of job satisfaction.

4.3 Implications for future research

Methodological:

This study was successful in recruiting mainly moderately stressed subjects. One possible explanation for this was the fact that the study was a “relaxation” intervention programme and it possibly only attracted those individuals interested in “relaxing”. Those with higher stress levels might not have volunteered themselves, possibly as a result of them “not having enough time to relax”. It may be suggested in future relaxation intervention studies that the investigator should screen individuals according to a stress questionnaire and only accept those above a certain cut-off. I would recommend the total POMS which was used in this study (see methods 2.4). This scale gave the best (largest) range of results (see results 3.2.1).

Psycho-neuro-endocrine studies should, considering the variable nature of the measures, increase the number of baseline measures to three to obtain a more satisfactory reliability of the mean (or median if that seems more appropriate).

The stress questionnaires used in this study were very general perceptions of stress. Although the job satisfaction questionnaire was intended to isolate various areas of work-related satisfaction and dissatisfaction, it may have been more appropriate to attempt to isolate specific work-related areas of stress, such as stress that might arise from employment. Examples of specific employment related stressors are: low job security, inadequate pay, interpersonal conflicts with co-workers or customers, irregular schedule, difficulties juggling family demands and work demands.

Health-related:

Although job-strain has been shown to increase CVD risk ^{140,141}, my study is the first to show an association between job satisfaction and a low risk of CVD. Future studies should i) investigate whether or not these two variables are associated and ii) investigate the impact of improving job satisfaction on CVD risk profiles.

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Appendix 1

The 45 minute **massage protocol** was developed to encourage relaxation and reduction of stress, it was created by Adrienne Judes a massage therapist working in the therapeutic massage industry of over 15 years. The massage procedure was designed to combine the deep tissue work together with the more relaxing elements of the most popular bodywork modalities. The procedure included Swedish, Shiatsu massage, Acupressure and lymph drainage in a well-integrated standardised-set protocol. The deep tissue massage was included to eliminate the heavy muscle tension and maximise the relaxation after effects of more deep tissue work. Several lighter techniques such as superficial effleurage and pertissage (kneading) were included to all muscle groups, interspersed with deep effleurage when moving from one muscle group to another. Some brisk techniques were included to stimulate and invigorate peripheral blood circulation. A number of slower strokes were used for a more comforting and relaxing effect (techniques used described below). Weiss asserted that moderate intensity appeared to be the least and heavy or light intensity the most therapeutic ²³⁸. Wood stresses that the regulation of the pressure is an important determinant of the effect of massage, concluding that heavy pressure produces stimulation, while light pressure produces relaxation ¹⁸⁹. Varying the intensity as well as the different techniques is a vital component of a beneficial, therapeutic and relaxing massage as described by the research. This principle of continual variety was applied in a standardised manner throughout the massage procedure.

Weiss describes the component involved in the act of touching and the modifications one can make to tactile arousal ²³⁸. The components of the act of touching include: duration, location, action, sensation, intensity and frequency. These components described by Weiss are synonymous with those components of massage identified by Beard and Wood ¹⁸⁹, namely duration, area to be touched (location), rate of movement (action), type of movement (sensation), pressure (intensity) and direction. These components were always kept in mind during the massage as the intention was to achieve an optimum state on a continuum of tactile arousal. These components play a large role in determining whether or not the subject achieves a state of relaxation during the massage.

The massage was applied with the subject in supine position. The massage began at the legs and progressed to the upper and lower back. The subject then rolled over onto their back and the shoulder and neck massage was applied. The massage took approximately 50 minutes in total, approximately 15 minutes for both legs, 25 minutes for the back and 10 minutes for the shoulder, neck and head. The massage procedure included the following techniques:

Effleurage involves slow rhythmic stroking hand movements, moulded to the shape of the skin. During this technique firm pressure was applied in the direction of venous or lymph flow. The palm of the hand was used for this technique. The masseuse attempted to mould the hands in order to conform to the contour of the body being treated. This technique was used interspersed in the procedure and as the introductory and closing technique. The variations of the effleurage techniques utilised in the massage procedure are described in ²³⁹.

Petrissage is a deeper technique than effleurage and is directed towards the muscles. The fingers and closed thumbs worked like tongs grasping the tissue gently. The tissue was squeezed gently and rolled in circular motion by alternately tightening and loosening the grasp. As the movement was repeated the grasping hands moved slightly forwards or backward as the movement was repeated. As hands worked together, the direction of movement was from distal to proximal centripetally. A distinction has been made between petrissage and kneading in that more tissue is lifted, squeezed and moved in kneading ²⁴⁰ while petrissage acts more deeply. Variants of the original technique were also included in the massage namely “picking up”. Petrissage is a particularly useful technique for stretching contracted or adherent fibrous tissue and will relieve muscle spasm. The variations of the petrissage techniques utilized in the massage procedure are described in ²³⁹.

Friction: (or rubbing) was done in slow small, circular movements, using the ball of the thumb or the fingertips or heel of the hand, according to the area being covered. Friction

always began lightly and progressed slowly to deeper pressure (depending on the underlying condition of the tissue). Contact with the skin was maintained. The aim of the technique is not to move the fingers on the skin, but to move the tissue under the skin.

Cross friction refers to a deep friction stroke that applies the pressure across the muscle fibre rather than along the longitudinal axis of the muscle fibres. This technique was applied with the ball of the thumb or fingertips or the knuckles in a linear back and forth motion across the muscle fibres. Deep friction is very effective at reducing pain, possibly via the pain gate theory. Pain relieving effects of massage are described in full ²⁴¹.

Lymph drainage was included in the massage procedure. Lymph spaces and lymph vessels of various sizes permeate the deep fascial and investing sheaths of muscles and other tissues. Passive exercise in the form of massage greatly enhances the movement of tissue fluids and lymph in the spaces and vessels of the deep fascia and muscles. The presence of the valves in the lymph vessels ensures a unidirectional movement of fluid forward, draining towards the heart when compressed. This technique was always applied after the massage work had been completed to that particular area. This technique would encourage the venous and lymphatic return, allowing for any toxin or metabolic end products that had been mobilised during the massage work to be most effectively transported out of the tissue. This encourages the detoxification process of the massage as the toxins are encouraged to be later eliminated via the kidneys or liver.

Acupressure refers to the use of finger pressure to key points (acupressure points) on the surface of the skin. These points have been said to correspond to physiological and anatomical features such as peripheral nerve junctions. Acupuncture and acupressure use the same points, but acupuncture employs needles, while acupressure uses the gentle but firm pressure of the hands. An important concept used by acupuncturists is that of the "trigger point". This is an area of increased sensitivity within a muscle that causes a characteristic pattern of referred pain in a related segment of the body. Trigger points generally correspond to the acupuncture/acupressure points. Firm pressure was applied to selected acupressure points (or trigger points) with a thumb or fingertip or a knuckle

if more pressure was required. Pressure was applied gradually and steadily and held without any movement until the tension was felt to be released. The pain experienced by the subject was monitored during all acupressure applications. Their pain tolerance was never exceeded, but when pain was experienced deep breathing techniques were employed. All the acupressure techniques utilized during our massage procedures are described in Gach acupressure manual²⁴².

The massage techniques that were not included during this procedure included: tapotement (or hacking), (gentle blows given with the border of each hand), vibration or shaking of the limbs. These techniques were eliminated from the massage as they are very invigorating techniques and were eliminated due to the fact that they are very disruptive to achieving relaxation.

The following basic principles of massage were followed throughout the experiment:

1. The hands were adjusted to the contours of the part; the pressure on the return movement was lighter; contact of the hands with the person being massaged was not interrupted.
2. An even rate of movement and rhythm was maintained at all times during the massage.
3. The subject was suitably draped at all times, if the lower limbs were exposed, the back was draped and vice versa.
4. A non-aromathmatic base oil (grape seed oil) was selected with a non-invasive mild scent. Oil was chosen instead of powder as it softens the skin, makes the skin smooth and slippery and easy to massage. Oil also prevents the friction that may be caused by the pulling of body hair. The oil I needed was to be non-aromathmatic to prevent aromatherapy from been a confounding variable in the effects of the massage.
5. Consideration for the subjects was given at all times: hands were warmed by rubbing them together before placing them on the subject, and the temperature of the room was adjusted to afford relaxation (24°C). Additional blankets were

available on request and the subject's temperature was monitored through the massage (this is quite common when lying still for long periods of time).

6. The choice of massage movements and the sequence of techniques were well planned and thought through well in advance. The masseuse was well practiced in the techniques and the routines of the specific procedure prior to the commencement of the study. An even tempo was applied and physical contact was maintained throughout the duration of the massage.
7. The procedure was planned to minimize the number of times the masseur had to move around the table and hence help avoid unnecessary disruptions. The procedure also gave consideration to minimizing the amount of time the subject had to move, keeping it to its minimal.
8. A pillow was placed under the hips and ankles when the subject was lying face down and removed when he rolled onto the back for the head, neck and shoulder-part of the massage. The rationale behind this was to alleviate unnecessary tension on the lower back area.
9. The size and height of the treatment table was the correct height for the therapist. This is vital as the therapist, herself, needs to be comfortable in order to give an effective massage. The recommended posture was adopted by the therapist of a broad foot stance and a straight back, wherever possible.

APPENDIX 2

Stress and Massage study

Please find here attached an **information sheet** with more information about the study, the **schedule sheet** with dates and appointment information, **directions sheet** and the **personal information sheet**, with information required for subject profiles.

After reading the **information sheet**, please complete and return the **schedule sheet**, filling in the times you would like to book, and the **personal information sheet**. You can e-mail them back to me at: loop@freemail.absa.co.za , or mail them to me at "Lucy Saunders, P.O. Box 500, Somerset West 7129".

INFORMATION SHEET

The University of Stellenbosch Department of Human and Animal Physiology

Project Title: Psycho-immunoendocrinology of work-related stress and effects of relaxation intervention.

Co-ordinator: Lucy Saunders
E-mail: loop@freemail.absa.co.za

Telephone: 021 – 808 4564
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Project Investigators: Lucy Saunders, Carine Smith

Project supervisors: Prof. Kathy Myburgh
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Telephone: 021 – 808 3148

Medical Practitioner: Dr J van der Merwe
(In case of emergency: 083 598 6183– available on a 24 hour basis – subject to driving from Paarl)

Explanation of study:

For this study we are interested in looking at how your body reacts to stressful conditions. The stress associated with work, is escalating in our society and is becoming a major health concern. If you agree to take part in this study, we would measure certain baseline physiological parameters, attempt to relax (de-stress) you for a week, and then reassess the impact of the relaxation on various systems of the body. Massage will be the relaxation technique used in this study. All participants will receive a massage once a day for 45 minutes, for a working week (i.e. 5 consecutive days).

Cortisol is a stress hormone released from the adrenal gland during stressful situations. Hyperglucocorticoidemia (a situation in one's body where stress hormones are found in large concentrations) is considered to be an important contributing factor in a number of age related diseases (such as heart disease, some types of diabetes, osteoporosis, and some nerve abnormalities). It is thought that stress may speed up the ageing process and we will attempt to clarify this issue by measuring levels of some hormones, cholesterol and other related substances in your blood and comparing these objective values with your subjectively assessed stress level.

For the study, you will need to visit the exercise laboratory at Stellenbosch University for a one hour appointment, where we will perform a clinical medical assessment, a 12 lead ECG and test your stress levels via a cardiovascular reactivity test. All participants will be asked to fill out some questionnaires. On different days, see below, blood will be taken on three different occasions.

On our team we have a Medical doctor, who will perform the health checks and be on standby (during hours and after hours) if you feel any discomfort at any time. Ethics approval has been given by the Ethics Committee (Subcommittee C) of the University of Stellenbosch.

You will need to complete the following:

Saturday the 27th October (or a scheduled appointment) is the day we have booked to do the stress levels checked.

This will entail:

- Consent & Indemnity forms
- Filling in trait-related questionnaires (personality assessments)
- Doing an ECG
- Having a clinical health assessment
- Doing a fitness test (at the same time as the ECG test)
- Doing a heart rate reactivity test

You may eat fairly lightly before this visit. Please mark your name at a suitable time on the schedule.

For 24 hours before this appointment: please do not consume any alcohol.

Monday the 29th October and 5th and 12th November: are days for the blood analysis and 3 state questionnaires to be completed. This shouldn't take more than 10 minutes, but it is very important that you get the blood samples taken at the same time each Monday. This is due to hormonal variation that occurs through the day, and we hope to avoid this from interfering in the results.

The day before (Sunday): "the day of rest", it is quite important that you **don't** do anything too vigorous in terms of **serious exercise**, as this may interfere with your immune status.

The night before (Sunday night): We are analyzing cholesterol in your blood, it is important not to eat fatty meat the night before. Please try to make your Sunday evening meal a carbohydrate-based meal as opposed to a fatty/protein based meal. This will avoid droplet of fat appearing in the blood. It would be very helpful to us if you try to standardize your Sunday evening meal (as much as possible).

The Monday morning: it is vital that you arrive the morning *fasted*. This means not eating or drinking anything after your evening meal on Sunday, i.e. **no breakfast or coffee or tea!** You may drink water. It's a good idea to make yourself a sandwich, which you can eat after the blood samples.

The week of the 5th to the 9th November is the massage week, where you will receive a daily massage. The massage is a leg, back, neck and shoulders massage including a variety of different massage techniques as well as some acupressure points. Each massage will last 45 minutes to an hour. Please check your diaries for that week and try to give me some indication of a time that will suit you. I am available all day and can schedule you in after hours if that suits you better.

Any further questions that you may have relating to the study will be answered in full, either by the co-ordinator or project investigators (see previous page for numbers). Please use this phone number in case of any problems regarding this study (Lucy Saunders: 082 411 1198).

4. EXERCISE PROFILE:

HOW MANY TIMES A WEEK DO YOU EXERCISE ON AVERAGE? (estimate according to your exercise programme over the last 6 months)?

FOR HOW LONG ON AVERAGE DO YOU EXERCISE IN ONE EXERCISE SESSION?

5. HEALTH PROFILE:

HAVE YOU HAD A MEDICAL CHECK IN THE LAST 3 YEARS? Yes No

If yes did it include an ECG test? Yes No

HAVE YOU EVER BEEN DIAGNOSED WITH:

Cancer? Yes No

Depression? Yes No

Diabetes Mellitus? Yes No

Coronary Heart disease (e.g. heart attacks)? Yes No

High blood pressure? Yes No

High blood cholesterol? Yes No

Thyroid disease? Yes No

Any endocrine-related disorders? Yes No

HAVE YOU EVER EXPERIENCED:

Immune system dysfunction? Yes No

If yes, was this due to any of the following: (check only if your answer is **yes**)

Medications after organ transplantation?
Medicines causing immune dysfunction (e.g. cortisone)?
Auto-immune diseases (e.g. rheumatoid arthritis)?
Other?

ARE YOU CURRENTLY USING ANY OTHER MEDICATIONS? Yes No

If **yes** please describe:

6. STRESS PROFILE:

HOW WOULD YOU DESCRIBE YOUR STRESS LEVELS OVER THE PAST 2 **YEARS**

Very relaxed Not at all stressed Moderately stressed Severely stressed

HOW WOULD YOU DESCRIBE YOUR STRESS LEVELS OVER THE PAST 2 **MONTHS**

Very relaxed Not at all stressed Moderately stressed Severely stressed

TO WHAT FACTORS DO YOU PERSONALLY ASCRIBE THE ABOVE STRESS?

HAVE YOU HAD A PROFESSIONAL THERAPEUTIC MASSAGE WITHIN THE LAST 2 **MONTHS**?

Yes No

DO YOU PRACTISE ANY FORM OF FORMAL RELAXATION TECHNIQUE ON A REGULAR BASIS? (e.g. meditation/yoga/tai chi)

Yes No

If yes which?

Appendix 4

CONSENT AND INDEMNITY FORM

Exercise Science Laboratory

Department of Animal and Human Physiology
University of Stellenbosch

Project title: PSYCHO-ENDOCRINOLOGY OF WORKSITE STRESS AND RELAXATION.

Statement of understanding:

I have read and understand the explanations of procedures below. I have had the opportunity to ask the investigator any question and understand that I am free to withdraw from the tests at any time should I so choose.

I confirm that:

1. I have been invited to participate in the research project at the Physiology Department at the University of Stellenbosch.
2. It has been explained that:
 - 2.1) The aims of the study will be: To measure the response of the immune and endocrine systems to occupational stress to occupational stress and relaxation procedures. Also to determine which individuals are more susceptible to stress, and which are more influenced by relaxation.
 - 2.2) Informed consent is required following procedures as part of the methods used in the study:
 - 2.2a) Blood drawing – Blood samples will be withdrawn for chemical analysis. Each time approximately 5ml of blood will be withdrawn with a syringe. A needle will be inserted into the elbow vein. (No more than 4 samples per visit, 21 ml). Performed three times, once a week over a three week period.
3. I have been informed of any possible side effects, discomfort or detrimental effects by participating in this study.
4. All the possible advantages of the study have been explained.
5. Information gathered in this study will be confidential. My name will not be coupled to my individual results when the results are made available for publication, since every subject will be represented by a number. The results will be used for a scientific assignment, publication or thesis, or all of these.
6. Results will be made available regarding the complete project, and I will receive a report on my individual results, once the project is completed.

7. I am free to withdraw from the study or any procedure at any time and that the researcher has the authority to remove me from the project, without impeding any participation at the relevant department in any other activity.
8. The information was presented in a language that I can understand and that I had the opportunity to ask any questions and that my questions were answered.
9. My participation was of my own choice without any pressure from the researcher or my employer and I am allowed to withdraw at any given time.
10. My participation will not involve any personal monetary costs.
11. If I experience any discomfort, I must contact Dr J. Brink tel.: 021 – 887 2820 or 083 598 6183 at any time.
12. I agree that I will not hold the University of Stellenbosch or any of its participating staff members or student liable for any injuries sustained by me during participation in this study.

I, _____ am _____ years of age and hereby give consent to undergo all the above procedures according to the explained protocol.

Signatures:

Subject: _____ ID _____

Date: _____

Address: _____

Witness: _____ ID _____

Date: _____

Appendix 5

THE HARDINESS SCALE					
Developed by Kobasa, S. L.					
Write down how much you agree or disagree with the following statements, using this scale:		Strongly disagree	Mildly disagree	Mildly agree	Strongly agree
1	Trying my best at work makes a difference.	0	1	2	3
2	Trusting to fate is sometimes all I can do in a relationship.	0	1	2	3
3	I often wake up eager to start on the day's projects.	0	1	2	3
4	Thinking of myself as a free person leads to great frustration and difficulty.	0	1	2	3
5	I would be willing to sacrifice financial security in my work if something really challenging came along.	0	1	2	3
6	It bothers me when I have to deviate from the routine or schedule I've set for myself.	0	1	2	3
7	An average citizen can have an impact on politics.	0	1	2	3
8	Without the right breaks, it is hard to be successful in my field.	0	1	2	3
9	I know why I am doing what I'm doing at work.	0	1	2	3
10	Getting close to people puts me at risk of being obligated to them.	0	1	2	3
11	Encountering new situations is an important priority in my life.	0	1	2	3
12	I really don't mind when I have nothing to do.	0	1	2	3

Appendix 6

TRAIT ANXIETY INDEX					
Developed by Charles D. Spielberger in collaboration with R. L.Gorsuch, R. Lushene, P. R. Vagg, & G. A. Jacobs					
A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number to the right of the statement to indicate how you <i>generally</i> feel. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe how you generally feel.		Almost never	Sometimes	Often	Almost always
		1	2	3	4
1	I feel pleasant	1	2	3	4
2	I feel nervous and restless	1	2	3	4
3	I feel satisfied with myself	1	2	3	4
4	I wish I could be as happy as others seem to be	1	2	3	4
5	I feel like a failure	1	2	3	4
6	I feel rested	1	2	3	4
7	I am "calm, cool, and collected"	1	2	3	4
8	I feel that difficulties are piling up so that I cannot overcome them	1	2	3	4
9	I worry too much over something that really doesn't matter	1	2	3	4
10	I am happy	1	2	3	4
11	I have disturbing thoughts	1	2	3	4
12	I lack self-confidence	1	2	3	4
13	I feel secure	1	2	3	4
14	I make decisions easily	1	2	3	4
15	I feel inadequate	1	2	3	4
16	I am content	1	2	3	4
17	Some unimportant thought runs through my mind and bothers me	1	2	3	4
18	I take disappointments so keenly that I can't put them out of my mind	1	2	3	4
19	I am a steady person	1	2	3	4
20	I get in a state of tension or turmoil as I think over my recent concerns and interests	1	2	3	4

Appendix 7

STATE ANXIETY INDEX					
Developed by Charles D. Spielberger in collaboration with R. L.Gorsuch, R. Lushene, P. R. Vagg, & G. A. Jacobs					
Read each statement and then circle the appropriate number to the right of the statement to indicate how you feel <i>right now</i> , that is, <i>at this moment</i> . There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.		Not at all	Somewhat	Moderately so	Very much so
1	2	3	4	5	6
1	I feel calm	1	2	3	4
2	I feel secure	1	2	3	4
3	I am tense	1	2	3	4
4	I feel strained	1	2	3	4
5	I feel at ease	1	2	3	4
6	I feel upset	1	2	3	4
7	I am presently worrying over possible misfortunes	1	2	3	4
8	I feel satisfied	1	2	3	4
9	I feel frightened	1	2	3	4
10	I feel comfortable	1	2	3	4
11	I feel self-confident	1	2	3	4
12	I feel nervous	1	2	3	4
13	I am jittery	1	2	3	4
14	I feel indecisive	1	2	3	4
15	I am relaxed	1	2	3	4
16	I feel content	1	2	3	4
17	I am worried	1	2	3	4
18	I feel confused	1	2	3	4
19	I feel steady	1	2	3	4
20	I feel pleasant	1	2	3	4

Appendix 8

PROFILE OF MOOD STATE (POMS)						
Below assesses 3 of the 6 subscores of the total POMS as developed by Douglas M. McNair, Maurice Lorr & Leo F. Droppleman						
Please circle the one number for each word which best describes HOW YOU HAVE BEEN FEELING DURING THE PAST WEEK INCLUDING TODAY.		Not at all	A little	Moderately	Quite a bit	Extremely
1	Tense	0	1	2	3	4
2	Worn out	0	1	2	3	4
3	Lively	0	1	2	3	4
4	Shaky	0	1	2	3	4
5	Listless	0	1	2	3	4
6	Active	0	1	2	3	4
7	On Edge	0	1	2	3	4
8	Energetic	0	1	2	3	4
9	Panicky	0	1	2	3	4
10	Relaxed	0	1	2	3	4
11	Uneasy	0	1	2	3	4
12	Restless	0	1	2	3	4
13	Fatigued	0	1	2	3	4
14	Nervous	0	1	2	3	4
15	Cheerful	0	1	2	3	4
16	Exhausted	0	1	2	3	4
17	Anxious	0	1	2	3	4
18	Sluggish	0	1	2	3	4
19	Weary	0	1	2	3	4
20	Alert	0	1	2	3	4
21	Full of pep	0	1	2	3	4
22	Carefree	0	1	2	3	4
23	Vigorous	0	1	2	3	4
24	Bushed	0	1	2	3	4

Appendix 9

JOB SATISFACTION SURVEY						
Developed by Paul. E. Spector						
Please circle the one number for each question that comes closest to reflecting your opinion about it.	Disagree very much	Disagree moderately	Disagree slightly	Agree slightly	Agree moderately	Agree very much
1 When I do a good job, I receive the recognition for it that I should receive.	1	2	3	4	5	6
2 Many of our rules and procedures make doing a good job difficult.	1	2	3	4	5	6
3 I like the people I work with.	1	2	3	4	5	6
4 I sometimes feel my job is meaningless.	1	2	3	4	5	6
5 Communication seems good within this organization.	1	2	3	4	5	6
6 I do feel that the work I do is appreciated.	1	2	3	4	5	6
7 My efforts to do a good job are seldom blocked by red tape.	1	2	3	4	5	6
8 I find I have to work harder at my job because of the incompetence of people I work with.	1	2	3	4	5	6
9 I like doing the things I do at work.	1	2	3	4	5	6
10 The goals of this organization are not clear to me.	1	2	3	4	5	6
11 There are few rewards for those who work here.	1	2	3	4	5	6
12 I have too much to do at work.	1	2	3	4	5	6
13 I enjoy my coworkers.	1	2	3	4	5	6
14 I often feel that I do not know what is going on with the organization.	1	2	3	4	5	6
15 I feel a sense of pride in doing my job.	1	2	3	4	5	6
16 I have too much paperwork.	1	2	3	4	5	6
17 I don't feel my efforts are rewarded the way they should be.	1	2	3	4	5	6
18 There is too much bickering and fighting at work.	1	2	3	4	5	6
19 My job is enjoyable.	1	2	3	4	5	6
20 Work assignments are not fully explained.	1	2	3	4	5	6

Appendix 10

THE SYMPTOMS OF STRESS QUESTIONNAIRE					
Selected from various treatises on mental stress and are generally assumed to be common in people undergoing stressful life periods.					
Please circle the appropriate number to the right of the statement to indicate how you have felt DURING THE PAST WEEK by circling the appropriate answer.		Never	Seldom	Sometimes	Often or continuously
1	Heartburn or acid troubles	1	2	3	4
2	Poor appetite	1	2	3	4
3	Nausea or vomiting	1	2	3	4
4	Abdominal pains	1	2	3	4
5	Diarrhea or irregular bowel function	1	2	3	4
6	Difficulties falling asleep or waking during the night	1	2	3	4
7	Nightmares	1	2	3	4
8	Headache	1	2	3	4
9	Dizziness	1	2	3	4
10	Tachycardia or irregular heart beats	1	2	3	4
11	Tremor of hands	1	2	3	4
12	Excessive perspiration without physical effort	1	2	3	4
13	Breathing difficulties or irregularities	1	2	3	4
14	Lack of energy	1	2	3	4
15	Fatigue or feebleness	1	2	3	4
16	Anxiety or nervousness	1	2	3	4
17	Irritability or fits of anger	1	2	3	4
18	Muscle pains	1	2	3	4
19	Heavy arms or legs	1	2	3	4
20	Tight feeling in head or neck	1	2	3	4
21	Heart racing or pounding	1	2	3	4