Who is Pre-disposed to Insomnia?

A Psychobiological Investigation

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Abstract

It has been hypothesised that a trait-like vulnerability to sleep disruption exists. This has been demonstrated in response to physiological stressors such as caffeine and phase advance. From this work the Ford Insomnia Responsivity to Stress (FIRST) questionnaire was designed, which aims to specify those who are vulnerable to stress related sleep disruption. Further to this, neuroticism and emotion focused coping have been shown to characterise the insomnia population, and suggested that these constitute risk factors for the development of an insomnia syndrome. However, there has been very little work which aims to define an at-risk population and none which aims to characterise this population from both a physiological and psychological perspective. The aim of this thesis is to define the vulnerable population with regards to psychology and psychobiology. . It was hypothesised that the vulnerable group would show greater stress reactivity, physiologically, higher levels of neuroticism relative to the resilient group, lower levels of conscientiousness and a greater inclination toward rumination and worry.

Over three studies measures of sleep, personality, stress perception and coping styles amongst others were taken as well as measuring, separately, 3 indices of physiological stress response:

Cortisol output: Salivary free cortisol was taken whilst a sample of good sleepers completed the Trier Social Stress Test (TSST) (n=32). Results indicate that the vulnerable group show significantly greater levels of cortisol at base line ($p<0.05$).This was mediated by conscientiousness ($\beta=0.39$). They were also higher in negative affect, rumination, stress and worry ($p<0.05$).The vulnerable group also showed an increase in insomnia symptoms in response to real life stress. This was also related to conscientiousness ($r= 0.55$, $p<0.05$)

Cardiovascular response: Heart Rate (HR) and Cardiac Vagal Tone (CVT) were measured while participants (n=31) completed a relaxation (baseline) and stressful task. There was found to be a main effect of group on HR response to the stress task relative to baseline, but this did not maintain when psychological variables of interest were entered (n=31) into the model. Conscientiousness was related to lower CVT change, interpreted as lower

CVT flexibility. Psychologically, the vulnerable group were again found to score higher on neuroticism, perceived stress and rumination relative to the resilient group ($p<0.05$).

Brain activation: fMRI data was collected whilst participants completed a stroop task, in which a siren indicated an increase in task difficulty (stress cue) (n=24). It was found that the vulnerable group showed significantly less activation bilaterally in the inferior parietal lobule (IPL) ($p<0.001$). In the left IPL activation was mediated by neuroticism ($\beta=0.607$).There was also significantly greater activation in the left postcentral gyrus (PG) ($p<0.001$), compared to the resilient group. This was mediated by FIRST score ($\beta=-0.61$). Again, the vulnerable group scored higher on measures of neuroticism and lower on conscientiousness ($p<0.05$).

Psychometric information gathered across the 3 studies was collapsed into one dataset (n=84). ANOVA revealed that the vulnerable group had significantly higher scores on measures of neuroticism, perceived stress, state stress, depressive feelings, depressive thinking, brooding, worry, emotion focused and problem focused coping and significantly lower scores on conscientiousness and extroversion ($p<0.05$).

Results indicate that the vulnerable group are higher on neuroticism across all 3 studies, and score higher on rumination and stress questionnaires in 2 of the studies. Physiological data suggests that the vulnerable group are more sensitive to stress anticipation, as opposed to showing greater reactivity to stress.

It is concluded that neuroticism is a risk factor for developing insomnia and that the vulnerable population show greater physiological responses whilst anticipating stress, a phenomena which represents the interaction between personality, rumination and the physiology of the stress system.

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Acknowledgement

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Lastly: to my friends and family, particularly my mum and dad. Thank you.

Author's Declaration

I declare that, except when explicit reference is made to the contribution of others, that this thesis is the result of my own work and has not been submitted for any other degree at the University of Glasgow or any other institution.

Signature:

Print Name:

Definitions/Abbreviations

The table below lists abbreviations with corresponding full term and a brief definition. Below are definitions of words used within the thesis which have a particular meaning within the context of the research presented.

Abbreviation	**Full Term and Definition (where appropriate)**
ACTH	Adrenocorticotropic Hormone: Produced by the pituitary gland, leads to the release of cortisol
AC-PC	Anterior-Commissure-Posterior Commissure: AC-PC refers to the AC-PC line. fMRI scans are collected through the AC-PC line i.e. the scanner collects data at an angle relative to the mid-point of these 2 structures
APS	Arousal Predisposition Scale
AUC	Area Under the Curve: Provides an index of change over time, and is generally used in measuring the half life of drugs or in investigating hormone levels. A mathematical technique based on integrals
AUCb	Area Under the Curve relative to baseline
AUCg	Area Under the Curve relative to absolute

	zero
AUCi	Area Under the Curve relative to increase
BDI	Beck Depression Inventory
BOLD	Blood Oxygenated Depended Level: the signal that fMRI records to provide brain activation levels
BSM	Behavioural Sleep Medicine
CAR	Cortisol Awakening Response: The typical pattern found upon awakening, where cortisol levels peak within 30 minutes from awakening
CRH	Corticotrophin-Releasing Hormone: Produced by the thalamus, triggers ACTH release from the pituitary gland and so an increase in cortisol
CVT	Cardiac Vagal Tone
DASS	Depression Anxiety and Stress Scale
DASSA	Anxiety sub-scale of the DASS
DASSD	Depression subscale of the DASS
DASSS	Stress subscale of the DASS
DSMIV	Diagnostic and Statistical Manual, fourth edition

EEG	Electroencephalogram: measures electrical impulses in the brain
EFC	Emotion Focused Coping: the likelihood that someone will focus on the emotional rather than the practical aspects of a problem
EKC/ECG	Electrocardiogram: measures heart-rate
ERP	Event Related Potential: any stereotyped electro-physical response to a stimulus
FIRST	Ford Insomnia Responsivity to Stress Test: Questionnaire designed to measure the likelihood that someone's sleep will be disrupted in response to stress
fMRI	Functional Magnetic Resonance Imaging: Technique for looking at brain activation patterns
GABA	γ-Aminobutyric acid: Chief inhibitory neurotransmitter in the mammalian central nervous system
HADS	Hospital Anxiety and Depression Scale: Questionnaire for measuring anxiety and depression levels
HPA	Hypothalamic-Pituitary-Adrenal axis: Part of the neuroendocrine system, largely responsible for controlling reactions to stress

HR	Heart Rate
ICD-10	International Classification of Diseases, 10th edition
ICSD-2	International Classification of Sleep Disorders, 2nd edition
ISI	Insomnia Severity Index: Questionnaire designed to measure insomnia severity over the past 2 weeks
LVS	Linear Vagal Scale: Method for extracting vagal tone
MMPI	Minnesota Multiphasic Personality Index: Questionnaire assessing personality. Arguably better suited to measuring psychopathology than theoretical constructs of personality
MRI	Magnetic Resonance Imaging
MSLT	Multiple Sleep Latency Test: A test for measuring daytime sleepiness
NEO-ffi	NEO-Five Factor inventory: NEO represents 3 of the 5 main personality domains (described below). Questionnaire for assessing personality based on the five factor model
NEOO	Openness subscale of the NEO-ffi

NEOC	Conscientiousness subscale of the NEO-ffi
NEOE	Extroversion subscale of the NEO-ffi
NEOA	Agreeableness subscale of the NEO-ffi
NEON	Neuroticism subscale of the NEO-ffi
nREM	Non-Rapid Eye Movement: a stage of sleep, also known as deep sleep
PFC	Problem Focused Coping: Measured by the brief-COPE questionnaire: the likelihood than an individual will focus on the practical aspects of a problem
PI	Psychophysiological Insomnia
POMS	Profile of Mood-states Questionnaire: Measures mood based on six factors: anxiety-tension;depression-dejection;anger-hostility;fatigue-inertia;vigour-activity;confusion-bewilderment
PSG	Polysomnography: considered the gold standard in object sleep measurement. Takes ECG, EEG, EMG, and respitory measures throughout the night to measure sleep, sleep stages and make diagnosis of any sleep disorders
PSQI	Pittsburgh Sleep Quality Index: Index which measures sleep quality over the last month

PSS	Perceived Stress Scale: Questionnaire designed to measure perception of stress: i.e. the extent to which one is likely to view a situation as stressful
PSW/WORRY	Penn State Worry Questionnaire: Designed to measure levels of worry
PTSD	Post Traumatic Stress Disorder: a Psychological disorder characterised by an intrusive 'reliving' of a negative event
QRS	Name for 3 of the graphical deflections seen on an electrocardiogram output (Q wave, R wave and S wave). Used to infer heart rate based on the distance between the 2 R-waves
REM	Rapid Eye Movement: A stage of Sleep characterised by rapid eye movements. Traditionally associated with dreaming, muscle atonia and an active EEG
ROI	Region of Interest: Specific brain area selected for further investigation, usually apriori
RSQ	Rumination Scale
RUMB	Brooding subscale of the RSQ
RUMB	Depressive thinking subscale of the RSQ
RUMR	Reflective thinking subscale of the RSQ

SE	Sleep Efficiency: Percent of time spent in bed spent sleeping
SFC	Salivary Free Cortisol: Cortisol levels in the saliva
SI	Situational Insomniacs: Good sleepers who find their sleep is disrupted in response to certain situations
SOL	Sleep Onset Latency: Time take to fall asleep
SPM	Statistical Parametric Mapping: Software used to analyse fMRI data
SQA	Scottish Qualifications Agency: Questions for chapter 5 are taken from exam administered by this organisation
STAI	State-Trait Anxiety Inventory: Questionnaire designed to measure state (dependent on situation) and trait (enduring characteristic) anxiety levels
SWS	Slow Wave Sleep
TIB	Time in Bed
TPQ	Tri-dimensional Personality Questionnaire: measures personality on 3 domains: novelty seeking harm avoidance and reward dependence. Each domain is posited to relate directly to activation of 3 neurobiological subsystem: dopaminergic,

	serotonergic and noradrenergic
TSST	Trier Social Stress Test: Robust lab based psycho-social stress test
TST	Total Sleep Time
UGSC	University of Glasgow Sleep Centre
VAS	Visual Analogue Scale: A line in which either end represent an extreme feeling or opinion. Individual is asked where they sit on that line in reference to the particular question
VLPO	Ventrolateral Preoptic Nucleus: Group of neurons in the hypothalamus, active during nREM sleep. Thought to control transition from sleep to wake
WASO	Wake After Sleep Onset: Time spent awake during the night before final awakening

Definitions

Hyperarousal: Taken from the hyperarousal model, describes the notion than an individual or a group of individuals demonstrate chronically increased nervous system activity, relative to a healthy group. This is present throughout the 24h cycle.

Arousability: Is used to mean the propensity an individual has to become aroused i.e. how they respond to their environment. A predisposition to arousability is used to describe an individual who is more prone to arousal of the central nervous system.

Outline

This section will provide a brief narrative account of the thesis, chapter by chapter.

Chapter1:

Chapter 1 provides a broad justification for the study of insomnia generally. Firstly the cost of insomnia is considered. This is explored from 2 points of view: the cost to the individual in terms of quality of life, reduced functioning and an increased likelihood of developing a secondary mental illness. Next, the cost to society regarding absence from work, increased accidents at work and decreased productivity are outlined. Adding to this is the cost of medication prescribed for insomnia. Cost-effectiveness of psychological interventions is considered.

Following this the theoretical models of insomnia which are pertinent to the theories advanced in this thesis are delineated: The 3-P model, the hyperarousal model, the cognitive model, the neurocognitive model, the attention-intention-effort pathway and the animal model. These models will be referred to throughout the thesis.

This chapter concludes that the cost of insomnia is high, and so research which aims to better understand the aetiology, prevention and improvement of treatment is essential. The models put forward so far make no attempt to explain which factors may predispose an individual to insomnia. This therefore represents a gap in the literature, and a lack of empirical research aimed at understanding predisposing factors.

Chapter 2:

Chapter 2 outlines the rationale behind believing that a vulnerable phenotype exists, and theorises on which constructs may define this phenotype. Firstly, familial aggregation of insomnia is investigated in order to demonstrate that there may be an inherited vulnerability. Next, genetic factors are considered and specifically the 5-HTT serotonin transporter polymorphism, suggesting that vulnerability to insomnia may be more related to a fault in the stress system rather than the sleep system.

Experimental work is then considered. Works which have shown a trait like vulnerability to sleep disturbance are evaluated. The role of psychological mechanisms is then considered, with a focus on neuroticism, conscientiousness and emotion focused coping. Theories on how genetics, psychobiology, personality and coping style interact are then put forward.

Chapter 3:

Chapter 3 outlines methods generic to all studies. Firstly, the screening process is explained. This process is exactly the same for chapters 4, 5 and 6, with additional screening steps added to chapter 6, pertaining to the use of fMRI.

The same psychometric scales are used throughout all 3 experimental chapters. These scales are outlined in chapter 3 with regards to their psychometric properties and a justification for why those scales in particular were chosen for the measure of the construct of interest.

Lastly pilot fMRI data is presented. This is here to outline the procurement of competencies relating to this brain imaging method. Its purpose in this chapter is not to outline experimental work or findings, but rather to represent skills acquired during the course of the Ph.D., and prior to running a larger fMRI based study

Experimental Chapters: 4-6:

Chapters 4-6 outline experimental work. These studies were initially designed to investigate stress reactivity in those defined as vulnerable compared to those defined as resilient to stress-related sleep disruption. Stress reactivity is measured using 3 different indices of the physiological stress response: salivary free cortisol (SFC), heart rate (HR) and Cardiac Vagal Tone (CVT) and then functional Magnetic Resonance Imaging (fMRI). In each study 2 groups are constructed retrospectively based on Ford Insomnia Responsivity to Stress Test (FIRST).

In each chapter, psychological variables are analysed first, then the physiological data is presented and where appropriate interactions between the 2 are investigated. Finally

results for each chapter are discussed, highlighting limitations, implications and future directions.

Chapter 7: Psychological Variables Across 3 Samples

To provide support to the experimental work conducted, data sets across all 3 samples were convolved giving a larger sample size in which to investigate psychological differences between the groups.

Chapter 8 Overall Discussion

This section focuses on the results of all 3 studies together. Given that each chapter has its own discussion section, the aim of this section is not to regurgitate this information, but to pull it all together into a theory of vulnerability to insomnia. Results of the experimental chapters are outlined briefly. Psychological variables are discussed separately from psychobiological variables and then there is discussion around the interaction between these two. These are then taken together to suggest a theory of what defines the vulnerable phenotype. Implications of this work as a whole, and future directions are then considered.

Chapter 1: Defining Features, Prevalence, Cost and Conceptualisation of Insomnia

1.1 Defining Features

The core symptomatology of insomnia as defined by the major disease and sleep disorder classification manuals- DSM IV [1], ICD-10 [2], ICSD-2 [3]- is a difficulty initiating or maintaining sleep, non-restorative or poor quality sleep and daytime impairments- either specific symptoms in terms of fatigue for example, or more global impairment such as social functioning (ICSD-2 and DSM-IV respectively) which are attributed by the patient to night-time sleep. For a diagnosis to be made these symptoms need to present for at least 3 nights a week [4] and not resultant from environmental disruptions- i.e. noise, bed partners, temperature- and be present for at least 1 month [1, 4].

DSM-IV	*ICSD-2*
Primary Insomnia	Adjustment Insomnia Psychophysiological Insomnia Paradoxical Insomnia Idiopathic Insomnia
Insomnia related to another Medical Disorder (Axis I or II) Insomnia Due to General Medical Condition Substance Induced Sleep Disorder	Insomnia Due to a Mental Disorder Insomnia Due to a Medical Condition Insomnia Due to a Drug Substance
	Inadequate Sleep Hygiene Behavioural Insomnia of Childhood Non-organic, Unspecified Physiologic (organic), Unspecified

Table 1 1 DSM-IV vs. ICSD-2 for Insomnia Subtypes

Currently, there are 2 dominant classification systems for insomnia: DSM-IV and ICSD-2, which differ somewhat in their conceptualisation of insomnia and insomnia subtypes. The ICSD-2 provides a long list of insomnia disorder sub-types, whilst the DSM-IV focuses on only a few (table 1 1: DSM-IV vs. ICSD-2 insomnia sub-typing).

Insomnia Sub-type	*Symptoms*
Psychophysiological Insomnia	Heightened arousal; Learned Sleep preventing associations; Decreased functioning during wakefulness
Paradoxical Insomnia	Complaint of severe insomnia in the absence of objective sleep disturbance; Daytime impairment not commensurate with degree of sleep disruption
Idiopathic Insomnia	Longstanding complaint with insidious onset during infancy or childhood; Causes distress or functional impairment; Is not better explained by any other disorder or condition

Table 1 2 ICSD-2 Insomnia Subtypes

Further, the ICSD-2 provides specific diagnostic features for each primary-insomnia phenotype (table 1 2 outlines the ICSD-2 diagnostic criteria for insomnia phenotypes), whereas the DSM-IV tends to view primary insomnia as only diagnosable if present in isolation. Understanding these insomnia sub-types, and having them thoroughly and correctly classified is important for research in this field, with work suggesting that different subtypes may present different aetiologies (work on familial aggregation, discussed later, suggests that those with a family member diagnosable as suffering from insomnia are more likely to report earlier onset, for example.) along with negative attitudes towards interventions[5]. It is important to note also that in the DSM-V the diagnostic features of insomnia will be altered, meaning a shift away from 'Primary Insomnia' which could not be diagnosed in the presence of another illness, to 'Insomnia Disorder'. This means that insomnia can be diagnosed alongside another disorder, rather than being relegated to the position of symptom. The DSM-V also highlights time courses for insomnia: acute, sub-acute and persistent, which the DSM-IV failed to do. This is linked more closely to the ICSD-2 and the notion of adjustment or acute insomnia. This highlights a general shift in the literature and the way in which insomnia is perceived: as a disorder in its own right with its own aetiology, treatment and consequences, independent of other factors.

1.2 Prevalence

Due to differing classification systems, amongst other things, the true prevalence of insomnia remains elusive. Ohayon[6] provides a comprehensive review of the epidemiological studies conducted up until that point: the prevalence of insomnia as defined by the DSM-IV is reported as 6% if the most stringent criteria are applied. That is

to say this number represents those who would receive a diagnosis of primary insomnia, as defined by the DSM-IV. Around one third of the population are reported as endorsing at least one insomnia symptom. Since 2002 a handful of other studies have been published in varying populations, reporting similar figures: in a French-Canadian cohort, insomnia syndrome is reported as being present in 9.5% of the population and 29.9% report insomnia symptoms[7]. This study used a combination of DSM-IV and ICD-10 criteria for insomnia diagnosis. In a Swedish cohort,[8] the prevalence of insomnia is reported as 6.5%, insomnia defined as a problem initiating or maintaining sleep or non-restorative sleep associated with daytime consequences at least 4 nights a week , however there was no minimum length of time applied to the presence of these symptoms to inform the diagnosis of insomnia. A study focusing mainly on children in Hong-Kong [9] found that insomnia was present in 4% of children, 12% of adult women and 9% of adult men, when diagnosis is based on a combination of DSM-IV and ICSD-2 criteria.

These 3 studies report similar figures in 3 differing populations, and all use very similar criteria in the diagnosis of insomnia- based mostly on DSM-IV guidelines. However, it has been pointed out that estimates range from as low as 5% to as high as 50% depending on criteria used [6], thus emphasising the point that a greater degree of standardisation needs to occur in this field of research if we are to truly understand the prevalence of insomnia.

1.3 Cost

The cost of insomnia is intrinsically linked to its prevalence: obviously the more common a condition is the greater its burden is going to be, relatively. Therefore until there is a consistency within the insomnia epidemiological research, the burden of insomnia will be constantly misunderstood. There are however, some methodologically strong studies which aim to delineate the cost of insomnia from various viewpoints, using similar criteria for the definition of insomnia as those in the studies mentioned above. In one of the more thorough assessments of the economic burden of insomnia, conducted in the province of Quebec, Canada, it was reported that the total annual cost of insomnia is $6.6 billion (Cdn $), in this one province alone. The authors report that this is likely a conservative estimate, but clearly demonstrate that there is a massive societal cost

attached to untreated insomnia, the largest contributor to the cost (76%) being that of lost productivity and work absence[10]. However it should be noted that it was the participants who relayed the attribution of this productivity loss to sleep: this has an inherent bias given that it is highly likely that insomnia suffers will underestimate their performance and are possibly more likely to attribute loss of productivity to sleep loss and not other factors, as per Harvey's cognitive model[11].

Kyle et.al.[12] highlight the burden of insomnia to the individual, in terms of health related quality of life, concluding that treating insomnia with either pharmacological treatments or psychological interventions leads to improvements in quality-of-life outcomes across several domains from physical through to emotional functioning. This improvement in quality of life to the individual is important when considering the cost-benefit of insomnia treatment. Botteman[13] highlights the cost- and clinical-effectiveness of pharmacological treatments for insomnia and points to the work of Morgan et.al.[14] who have demonstrated the cost-utility of CBT is well within the range considered to be acceptable by the NHS, meaning that the cost of implementing this treatment is far out-weighed by the gains to quality of life in the patient, as well as being a clinically effective treatment. Further to this, it has been shown those with remitted insomnia have lower healthcare and productivity costs vs. non-remitted patients[15]. The gain made in productivity under-writes the majority of treatment costs. Furthermore costs associated with psychological treatments could be minimised with the implementation of a stepped care model, which works on the premise that the majority of people will see improvements with the least intensive treatment type- i.e. online therapy or group sessions-and only the severe cases will see a specialist BSM practitioner[16].

It could be argued that again, cost-utility estimates are conservative given the emergence of data showing that insomnia is a risk factor for mental and physical ill-health. A recent meta-analysis concluded that the likelihood of developing major depression is two-fold in those who have insomnia vs. good sleepers[17], supported by work showing that the relationship between insomnia and depression is mediated by insomnia subtype[18]. Further, Taylor [19] concludes that treating insomnia may lead to better outcomes and improved quality of life in a range of comorbid disorders, from heart-disease through to cancer, and that rates of these disorders are higher in a poor-sleeping population. Brower

et.al. [20] demonstrate that treating sleep complaints in those receiving support for alcoholism halves relapse rates. Thus, there are clear benefits on an individual level, but also a wider societal level to treating insomnia in an otherwise healthy population, and also in those with comorbid conditions. Understanding the aetiology of insomnia and the differing subtypes is pivotal in providing individually-tailored, and therefore more robust, treatments but also in preventing chronic insomnia and therefore reducing the bill associated with sleep loss that arises from both direct and indirect costs.

1.4 The Insomnia Models: Concepts and Evidence

A thorough understanding of insomnia is fundamental in reducing the burden of this disorder. The mechanisms which lead to the manifestation and maintenance of sleep disruption remain elusive, in that there is no absolute answer as of yet. The major models of insomnia demonstrate how conceptualisation and understanding of chronic insomnia has evolved over-time, whilst also pointing a way for further research: what is still unclear and how might an understanding of this enrich the field of sleep research and therefore sleep-treatment and prevention programmes? Outlined below are the models which have proven most influential and which frame the rationale for this thesis.

1.4.1 The 3-P Model

Spielman's stress-diathesis, or 3-P model of insomnia[21] (Figure 1 1) purports that there are 3 components in the aetiology of insomnia: Predisposing factors- personality, coping-style, and genetics; Precipitating factors- life-stressors; and Perpetuating factors. In Spielman's initial outlay of this model these perpetuating factors are considered within a behavioural framework: sleep disruption is the result of classical conditioning. A sufficient stressor will lead onto disrupted sleep (in those who have some kind of vulnerability). The insomnia becomes early or sub-chronic insomnia due to maladaptive 'coping strategies' such as staying in bed longer to promote sleep opportunity. These coping strategies- which will later be referred to as safety behaviours- encourage the maintenance and continued development of early insomnia into chronic insomnia via classical conditioning: the sleeping environment becomes associated with wakefulness.

Spielman's broader stress-diathesis model is appealing in that it appears intuitively obvious, highlighting the close relationship between sleep disruption and stress.

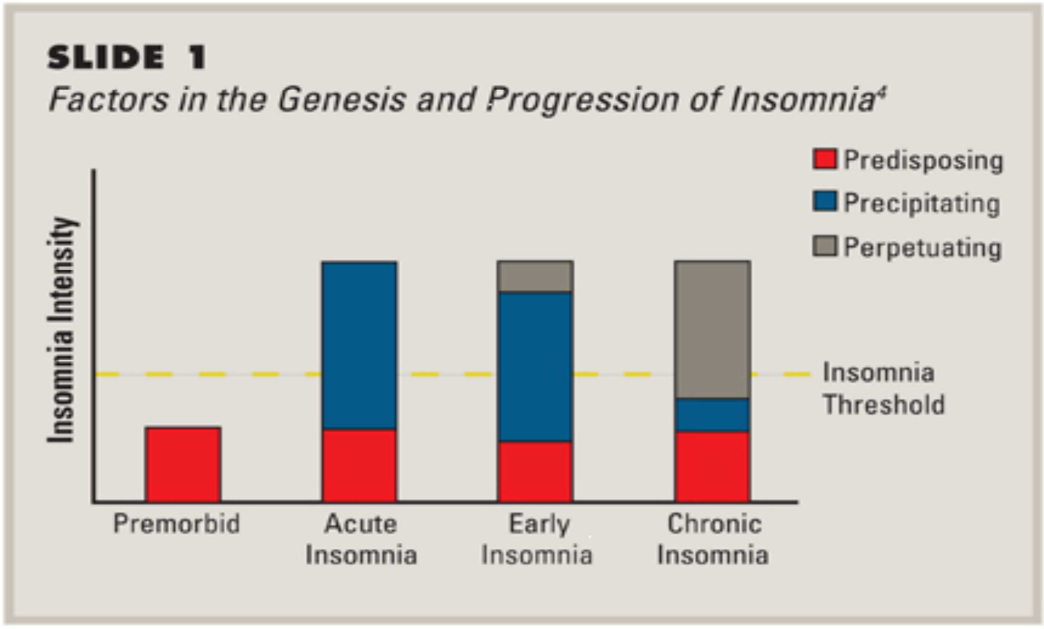


Figure 1 1 Spielman's 3-P Model

It has been widely endorsed throughout the sleep literature and, in terms of psychophysiological insomnia (PI), has proved a useful framework in conceptualising how this disorder develops and is maintained. However, the specific elements of each component remain equivocal. Physiological, behavioural and cognitive mechanisms have been studied in order to elucidate the aetiology of PI within this frame-work. These factors will be explored within the context of other models or theories of insomnia, as essentially these models are attempts to better understand the factors which underlie these 3 broad components, out-with a purely-behavioural- and wholly reductionist- view-point.

1.4.2 The Neuro-cognitive Model

The Neuro-cognitive model[22] (Figure 1 2) is essentially a behavioural explanation of the aetiology of insomnia, but with a particular focus on cortical arousal, as measured by high frequency EEG. While the behavioural model can explain some of the phenomenology associated with insomnia, such as the reverse first-night effect (whereby insomnia patients show improved sleep when in a novel environment, as opposed to disrupted

sleep as seen in good sleepers in this situation)[23] and the interventions derived from it have shown clinical efficacy [24] it cannot explain, what Perlis et.al. term 'the 4 paradoxes of insomnia'. Namely: that insomnia patients will report being awake during PSG verified sleep; PI patients will consistently overestimate how long it takes them to fall asleep and how long they are awake for during the night; when treated with hypnotics PI report disproportionate improvements in sleep relative to objectively measured improvement; and finally benzodiazepines do not normalise sleep, but still result in improvements in subjective reports.

The authors attempt to explain these paradoxes via the measurement of high-frequency EEG activity, an index of cortical arousal which is tightly associated-if not analogous to-cognitive arousal, whilst differentially associated with the various stages of normal sleep [25]. It has been known for some time that insomnia patients display increased high-frequency EEG activity- in the beta and gamma range[26]. It is proposed, therefore, that as one develops chronic insomnia, as guided by the principles of a behavioural model, there is an increase in high frequency EEG at sleep onset. This would indicate that there is maintenance of sensory processing and memory formation in a PI population[27]. Increase in high frequency EEG may then explain why an individual perceives sleep as wakefulness, due to the brain still processing environmental information, creating a more easily perturbed sleep. Misperceiving total sleep time and sleep latency may be due to a real perception of disengagement- how long it takes to inhibit high frequency EEG/ cognitive processes. As for the paradoxes surrounding drug use it is argued that benzodiazepines promote mesograde amnesia[28] and discourage memory formation, thus masking the effects of high frequency EEG whilst not producing improved PSG scores

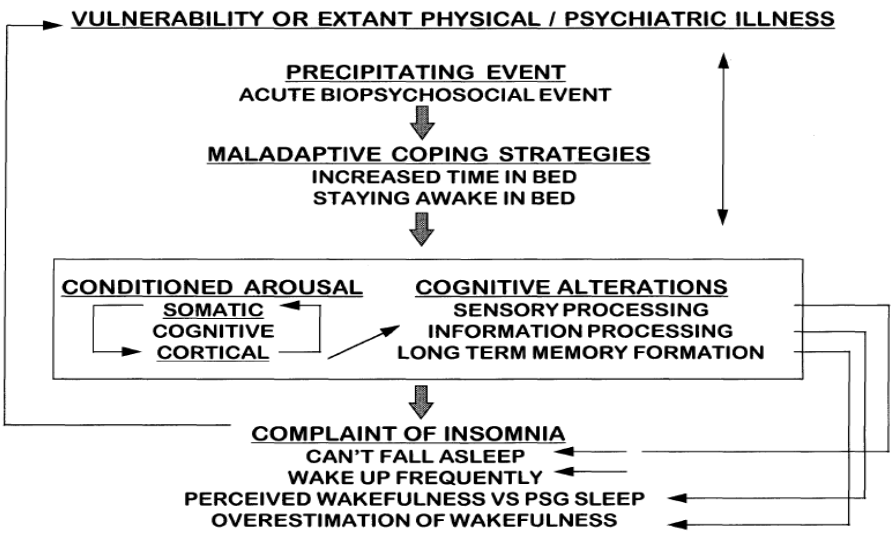


Figure 1 2 Perlis et.al. Neurocognitive model

The model has remained largely untested, with focus largely being on lower frequency EEG [29]. However, Perlis et.al.[30], in a small sample (n=9 per group) showed that PI versus good sleepers and poor sleepers with major depression demonstrate greater beta/gamma activity and that this occurs maximally in shallow sleep stages, as the model would predict and is a feature specifically of PI, and not insomnia and major depression. Bastien et.al.[31] have demonstrated, in line with the outlined model, that insomnia patients show reduced event related potentials (ERP's) relating to sleepiness in the evening, and increased ERP's relating to information processing, suggesting that an inability to inhibit waking processes and a propensity toward increased cortical arousal may both contribute to poor sleep. Nofzinger et.al.[32] have shown that beta EEG activity is conversely related to sleep quality, and also to differential brain activation patterns in a PI group.

This model represents an expansion on traditional behavioural conceptualizations, highlighting the interplay between psychology and biology and so in this sense is the first explicitly, fundamentally psychobiological model of insomnia, and has considerable overlap with the hyperarousal theory discussed later. Whilst paving a way for our understanding of the neurobiological mechanisms of insomnia, it does ignore certain aspects. Namely, the cognitive processes involved in insomnia, alluding to them vicariously through a presumed biological index. No hypotheses are made regarding how worry or rumination may feed increased gamma-activity at sleep onset, for example. It is unsatisfactory, also, in its lack of consideration for the daytime consequences of insomnia. A perceived impairment in daytime functioning is an essential feature of

insomnia in both the DSM-IV and ICSD-2. The model provides conjecture on what maintains disrupted sleep, but fails to explain insomnia in full.

1.4.3 The Cognitive Model

The cognitive model of insomnia[11] delineates the cyclical nature of the cognitive processes involved in the maintenance of insomnia, highlighting night-time and daytime cognitions and behaviours (Figure 1 3). It begins with negatively toned cognitive activity-rumination and worry. Anecdotally, the insomnia population is characterised by a 'racing mind'. This is also evidenced experimentally. Watts et.al.[33] have suggested that those suffering with insomnia feel less in control of their thinking, and further, split insomnia patients into 2 groups: worried insomnia sufferers and non- worried insomnia sufferers. The main difference between these groups is that worried insomnia-sufferers ruminations revolved around work whereas the thoughts of the non-worried insomniacs revolved around the sleep process itself. Nicassio et.al. [34] have shown that insomnia sufferers have more negative thoughts at bedtime than good sleepers, and more recent work has suggested that emotionally laden thoughts are the ones most likely to interfere with the sleep process[35].

This rumination, or racing mind, perpetuates insomnia as it leads to further cognitive but also somatic arousal (tension) and so eventually learned associations between the sleeping environment and feeling tense. It is important to note here that although the focus of this model is, obviously, the cognitive processes driving insomnia it is not dissociated from somatic or physiological arousal. Cognitive arousal leads to physiological arousal, as Lundh and Broman[36] point out in their paper discussing sleep interfering and sleep interpreting processes whereby cognitive or physiological arousal would be an interfering process as it impacts directly on sleep; dysfunctional beliefs about sleep or anxieties about sleep would be sleep interpreting processes as they lead to increased cognitive arousal.

It has been demonstrated that insomnia patients hold dysfunctional beliefs and attitudes with regards to sleep, and its impact the following day [37-39]. These are maintained via safety behaviours. Again, in parallel with the anxiety literature, safety behaviours are overt or covert strategies aimed at avoiding a feared outcome. However, they are likely to

interfere with the disconfirmation of the dysfunctional belief or attitude[40]. It has been suggested that insomnia patients employ certain safety behaviours in order to conserve energy, for example by only engaging in mundane activities or cancelling social engagements, or increasing sleep opportunity- by increasing time in bed[41, 42]. Such behaviours are posited to reinforce faulty beliefs about sleep and its daytime consequences and in the case of the latter example solidify the association between the bedroom environment and arousal. The cycle is complete, and becomes self-fulfilling.

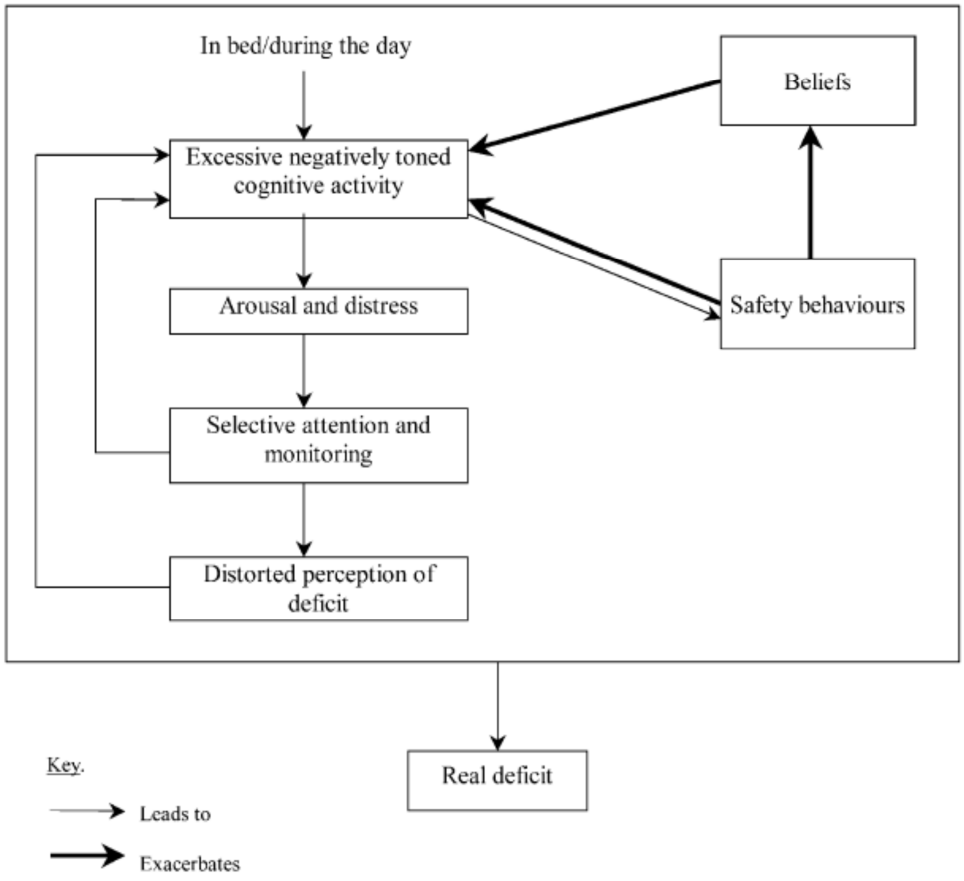


Figure 1 3 Harvey's Cognitive Model[11]

1.4.4 Attention-Intention-Effort Pathway

The Attention-Intention-Effort (AIE) pathway (figure 1 4)[43] explains insomnia with regards to the interaction between behavioural and cognitive processes, and how these interact with the physiology of arousal. This explanatory model has strong overlaps with aspects of the cognitive model, in that is provides theoretical explanations as to how faulty cognitions, and the ensuing arousal, may be maintained. In accordance with the cognitive model, rumination or worry about sleep and its negative impact the next day leads to a narrowing of attention to cues which indicate a lack of sleep or are indicative of

sleep loss/ wakefulness: selective monitoring or attentional biases to sleep cues. This line of thinking with regards to understanding the aetiology of insomnia is supported by work in anxiety which has demonstrated that those who are of an anxious disposition will display an attentional bias toward threat cues, and that this can be detected via various cognitive paradigms[44-46]. It has also been shown to exist in insomnia patients using various paradigms, of a similar nature to those employed in the anxiety literature [47-49]. Such an attentional bias heightens awareness to sleep loss, and therefore highlights the intention to fall asleep, thus leads to increased effort to fall asleep and therefore increased arousal [43]. This is what the AIE states: attention to lack of sleep leads to a direct effort to fall asleep. Effort by its very nature leads to arousal (either somatic or cognitive). This then further undermines the automaticity of the sleep process and further highlights cues which indicate a lack of sleep and so the cycle continues.

During the day this attentional-bias may manifest as selectively attending to cues which indicate reduced performance, and attributing this to sleep. Such an attentional bias has not been demonstrated experimentally. However, there is a well documented discrepancy between objective performance and subject performance in insomnia patients. Orff et.al.[50] show there is no differences on neuropsychological tests between an insomnia and good-sleeping group. The discrepancy between objective performance and subjective daytime complaints is explained in terms of attentional biases toward deficits: the patient becomes overly aware of mistakes made and so inflates their 'failure' at the task. Bastien et.al [51] extends a similar argument to Orff et.al., stating that differences in objective vs. subjective measures may be due to the insomnia population having to put in more effort to maintain good performance. This area has been thoroughly reviewed by Fulda and Schulz[52], concluding that there is little evidence of an objective deficit. Similarly insomnia patients are shown to consistently over estimate variables which equate to sleep loss [53]or to misperceive their sleep [54]. One possible explanation for this is the development of an attentional bias toward cues which reinforce the worry that one is not sleeping, and therefore an inflation of the problem. Both the day and night time misperceptions endow negatively toned cognitions, and potentially lead to further somatic arousal.

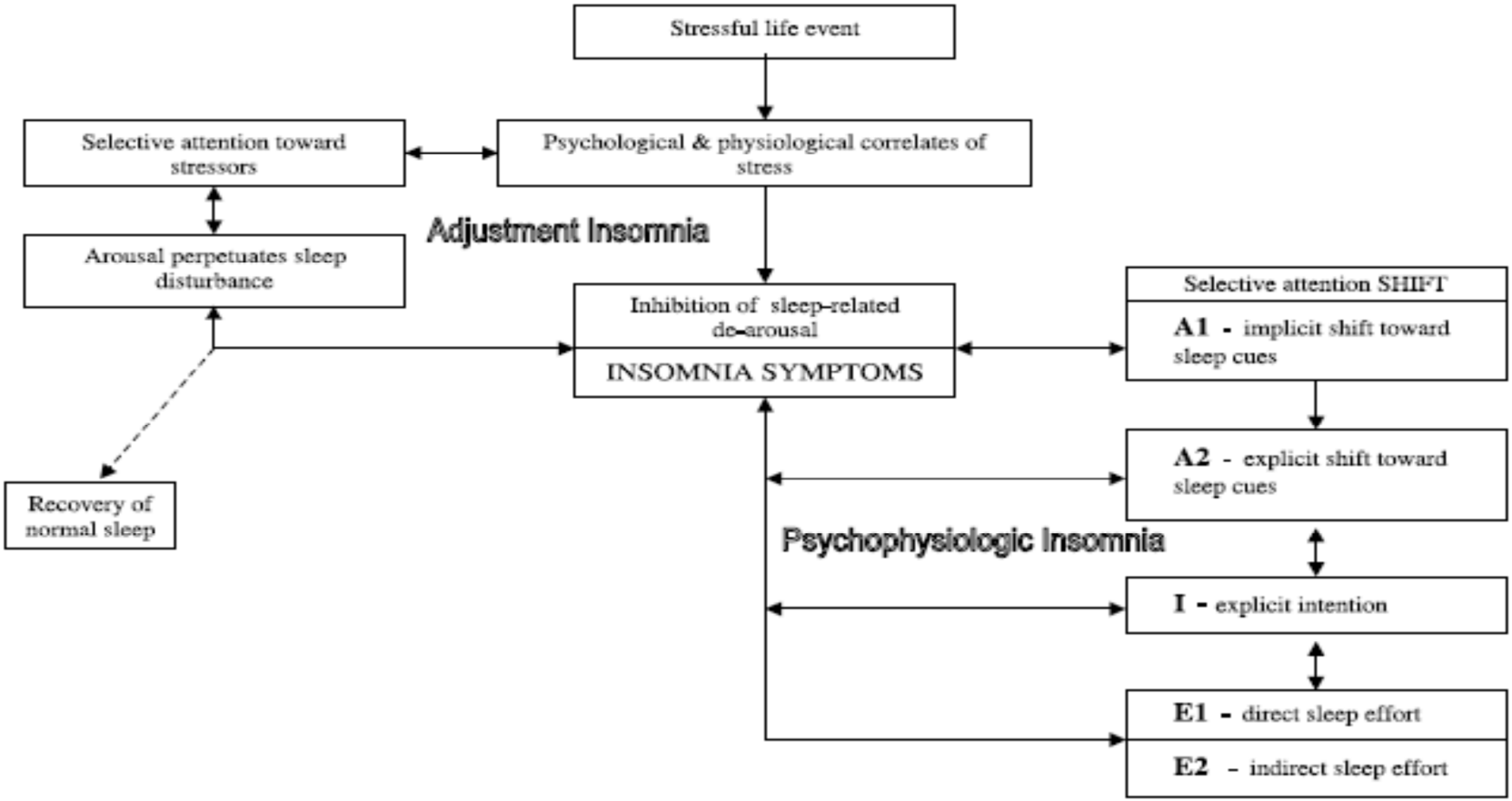


figure 1 4 Attention-Intention Effort Pathway for the maintenance of Insomnia. Taken from Espie et.al. 2002

1.4.5 The Hyperarousal Model

The hyperarousal model of insomnia states that insomnia is a disorder of the 24h cycle- unlike the neurocognitive model which is concerned only with problems at sleep onset, but similar to the cognitive model which takes into consideration the daytime consequences of insomnia- by which insomnia sufferers demonstrate consistently increased somatic and cognitive arousal. Unlike the aforementioned models, there is no explicit role of learned/ operant conditioning, the evidence for this model focusing on the physiology of sleep rather than the cognitive/ behavioural changes that are thought to occur in insomnia. Rather than competing with the 3-P, neurocognitive and cognitive model, it compliments them: acute insomnia caused by a stressor which then, in those who focus cognitively on their insomnia- i.e. sleep related ruminations- becomes an independent chronic condition. The hyperarousal model emphasises the interaction between both psychological and neurobiological systems in the aetiology and maintenance of insomnia and in this sense is integrative (figure 1 5). The theory has been reviewed comprehensively elsewhere [55, 56] so only the most relevant evidence is discussed here.

Bonnet and Arand [57] for example have demonstrated increased sympathetic nervous system activity, as measured by low frequency spectral power EKG, in the evening and throughout the sleep cycle, relative to sleep stage in chronic insomnia patients; Vgontzas et.al.[58] show that cortisol secretion- a marker of hypothalamic-pituitary-adrenal axis activity (HPA)- is significantly greater in the early part of the night in poor sleepers, but is also more pronounced across the 24h cycle, demonstrating the same circadian pattern as good sleepers, but with a greater number of cortisol and ACHT pulses throughout the circadian cycle and, particularly pronounced differences in the ‘valleys’ of the pulsatile curves, thus suggesting a disorder of the central nervous system rather than one of sleep loss or circadian misalignment. The same group have also demonstrated that 24-h urinary free cortisol levels are mildly, although significantly, correlated with total sleep time (r=0.33)

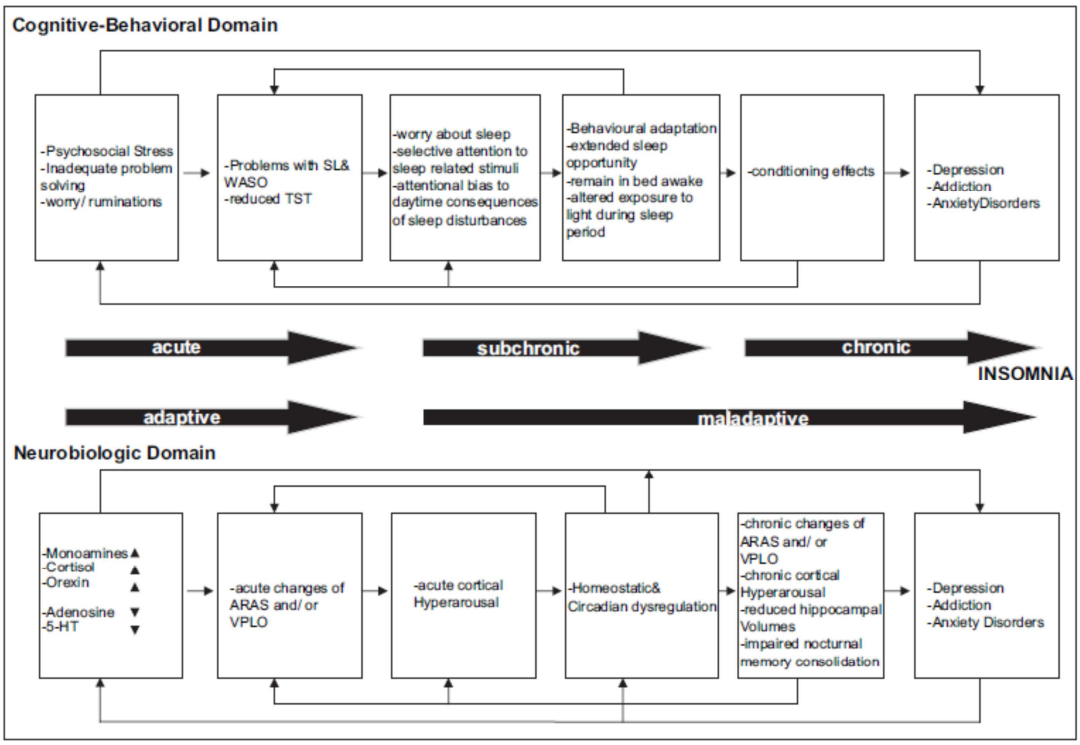


Figure 1 5 Neurocognitive model of insomnia
5-HT: Serotonin; ARAS: ascending reticular activating system; SL: sleep latency; TST: total sleep time; VLPO: ventrolateral preoptic area of the hypothalamus; WASO: wake after sleep onset. Acute insomnia: 1–90 days; sub chronic: 3–6 months; chronic>6 months. Note: the cognitive-behavioural and the neurobiological domain are depicted in a parallel way – it is assumed that both domains are strongly interconnected and not independent of each other. From Riemann et.al.[56]

. This may be compounded by the fact that sensitivity to stress hormones (corticotrophin releasing hormone (CRH)) seems to become greater as we age [59]. This should be a consideration when investigating hormonal activity and insomnia: absolute values may not capture the full extent of the hyperarousal, as sensitivity seems to change with age and probably on an intra-individual level. It may serve to have a secondary measure of sympathetic nervous system activity alongside cortisol levels in order to assess sensitivity differences across sleep groups and ages, such as spectral EKG, or core body temperature.

Nofzinger et.al.[60] have demonstrated that there is a smaller relative decrease from REM to nREM sleep in whole brain glucose metabolism, coupled with an increase in metabolism during wakefulness and consolidated nREM sleep. Winkelman et.al.[61] demonstrate reduced GABA in the PI patients brain, again suggesting that this population are constantly over-aroused, given GABA's function as a global inhibitor.

The hyperarousal theory has widespread support, through various different domains and does not occlude other theories of insomnia, expanding on the neurocognitive model,

whilst not discounting a cognitive approach to insomnia as indeed in this domain too insomnia patients seem to be 'hyperaroused'.

The common thread throughout all sleep models is the idea that stress (precipitant) leads to sleep difficulty, due to the resultant increased- or an over sensitivity to- arousal, and that this is then maintained via learned associations, increased worry, and a 24h arousal to combat lack of sleep (perpetuating). However, there is a paucity of research on what factors may predispose an individual to developing, and possibly maintaining, a sleep complaint after the resolution of a stressful life event- such as bereavement or sudden unemployment -and secondly how these factors interact with and mediate each other: that is to say there is a need to profile an 'at risk' population through a stronger understanding of the aetiology of primary sleep complaints and how this relates to the biological and psychological stress systems, a sentiment echoed in Drake et.al.'s[62] review of the development of insomnia in relation to comorbidity: Insomnia seems to be associated with a constantly increased sympathetic nervous system and this may account for the common psychiatric and physiological co morbidities- such as depression, anxiety, heart disease etc [19]- associated with chronic insomnia. Understanding which factors pre-date insomnia and which result from sleep loss will help in better understanding how to treat and prevent the disorder. Understanding causality is difficult because studies which support the models are, largely, conducted on those already diagnosable as suffering from insomnia meaning that there is very little information regarding what may act as a predisposing factor to insomnia. The causality of the demonstrable hyperarousal remains unknown, as does the nature of the relationship between psychological variables such as worry, rumination and neuroticism and arousability in this population. The animal model of insomnia may help to better understand the mechanisms through which stress affects the sleep system, on a very fine-grain scale.

1.4.6 The Animal Model

Saper, Chou and Scamell [63] propose the idea of a 'sleep switch'. Their paper outlines the neural mechanisms responsible in switching from awake to sleep and back. The switch is thought to dwell within the hypothalamus (figure 1 6). This model, and how it applies to the interaction of stress and sleep, has been further elucidated by Cano

et.al[64]. Their animal model for stress induced insomnia supports the hyperarousal theory, in that it suggests that there is a hierarchical organisation of neuronal groups responsible for the switch between wakefulness and sleep, and sleep disruption. The crux of this is the VentroLateral Pre-Optic nucleus (VLPO) switch. Located in the hypothalamus, this group of neurons is active mostly during nREM sleep. It secretes inhibitory neurotransmitters- GABA and galanin- which act on the locus ceruleus, a group of nuclei in the brain-stem involved heavily in the physiological stress/ panic response. It is proposed that the VLPO acts as a 'flip-flop' switch, by which it inhibits waking responses to allow sleeping responses to happen. However, upon dealing with stress this switch is unable to remain in the 'off' position due to increased activation of the limbic system, which in turn activates physiological responses, leading to sleep disruption. The methodology employed in the genesis of this model provides a more ecologically valid stress-induced insomnia state, in that the animals experience no sleep deprivation and although the stressor is more homogeneous than stressors experienced by people it provides an elegant method by which to investigate the effects of a species-specific psychological stressor on sleep-patterns and indeed did create a sleep pattern similar to that seen in human insomnia patients. That is to say: increased SOL, decrease in REM and more sleep disruption. Thereby, the model proposed highlights areas which may merit further research in a human population and more interestingly, corroborates the work done by Nofzinger et.al.[60], showing similar brain areas to be implicated in the disruption of the sleep cycle across species. In terms of predisposition to insomnia, it implies that stress-sensitivity is perhaps more implicated than a problem with the sleep-system, per se.

This model highlights again the role of the stress-arousal system in insomnia, demonstrating that although the sleep systems remain fully active- i.e. promoting sleep-, sleep disruption still occurs and is only attenuated upon deactivation of parts of the limbic-arousal system. The authors point out that this may have implications in understanding how best to treat insomnia: through the dampening of the stress response rather than the promotion of the sleep system- adding to the argument posed by Espie et.al.[43] and Bastien et.al.[31] in understanding the difference between hyperarousal and faulty inhibition.

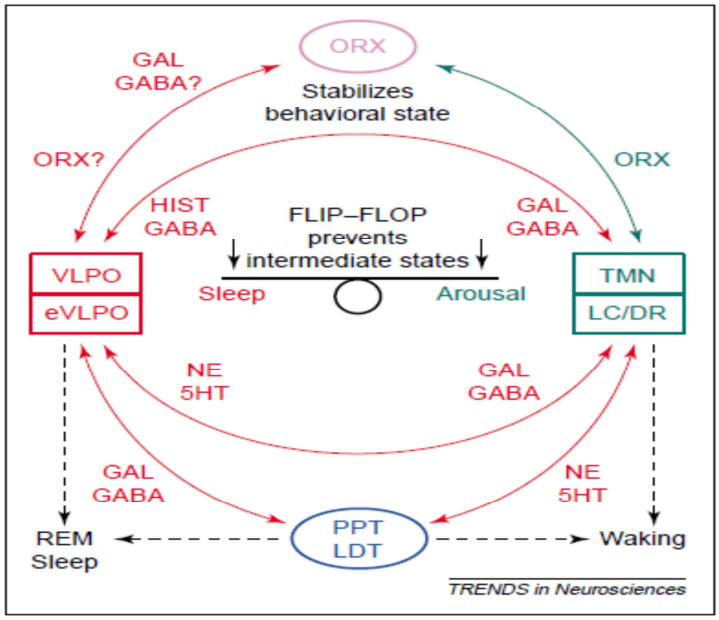


Figure 1 6 From Saper et.al. Animal Model[63]
Inhibitory pathways shown in red, and the excitatory pathways in green. The blue circle indicates neurons of the LDT and PPT; green boxes indicate aminergic nuclei; and the red box indicates the VLPO. Aminergic regions such as the TMN, LC and DR promote wakefulness by direct excitatory effects on the cortex and by inhibition of sleep-promoting neurons of the VLPO. During sleep, the VLPO inhibits amine-mediated arousal regions through GABAergic and galaninergic (GAL) projections. Most innervations of the TMN originates in the VLPO core, and input to the LC and DR predominantly comes from the extended VLPO. This inhibition of the amine-mediated arousal system disinhibits VLPO neurons, further stabilizing the production of sleep. The PPT and LDT also contain REM-promoting cholinergic neurons. The extended VLPO (eVLPO) might promote REM sleep by disinhibiting the PPT–LDT; its axons innervate interneurons within the PPT–LDT, as well asaminergic neurons that normally inhibit REM-promoting cells in the PPT–LDT. Orexin/hypocretin neurons (ORX) in the lateral hypothalamic area (LHA) might further stabilize behavioural state by increasing the activity of aminergic neurons, thus maintaining consistent inhibition of sleep-promoting neurons in the VLPO and REM-promoting neurons in the PPT–LDT. Unbroken lines represent neuronal pathways described in the text. Broken black lines indicate influences of specific regions on behavioural states. Abbreviations: DR, dorsal raphé nucleus; HIST, histamine; LC, locus coeruleus; LDT, laterodorsal tegmental nuclei; PPT, pedunculopontine tegmental nuclei; REM, rapid eye movement; TMN, tuberomammillary nucleus; VLPO, ventrolateral preoptic nucleus.

Who is Predisposed to Insomnia: a Review of Familial Aggregation, Stress-Reactivity, Personality and Coping Style

The aetiology of Insomnia from onset through to the development of an insomnia syndrome is poorly understood. Apart from a few epidemiological studies there is very little work investigating what may predispose certain individuals to insomnia. It has been estimated that 23-33% of the population are currently experiencing trouble with their sleep[7], while ~6-10% [65, 66] are suffering from chronic insomnia. This raises questions as to the factors that drive the minority into a chronic condition, and why some people experience sleep disruption in response to certain situations while others do not seem to develop a sleep-complaint. This chapter aims to review what is known about vulnerability to insomnia and suggest possible mechanisms that may lead to poor sleep in response to life-stressors. Two viewpoints are presented: first, the genetic and psychobiological factors that play a role; and secondly, psychological influences of personality and coping style will be examined. The interaction of these factors and the ways they may mediate one another in the onset and maintenance of insomnia will be examined within the framework of the 4 dominant models of insomnia: The 3-P (stress-diathesis) model[21], the hyperarousal theory of insomnia (for a review see Riemann et.al[55].); the neuro-cognitive model of insomnia[22] and the cognitive model[11](these models are outlined in chapter 1). The notion that a predisposed phenotype does exist will be discussed with reference to studies on the familial aggregation of insomnia and a discussion of which genes may be driving this, with a particular focus on genetics which may control response to stress. Lastly, psychological factors will be considered, concluding that a vulnerable phenotype does exist and that it is likely characterised by faulty stress-management, at both a physiological and psychological level. The merit of a more profound understanding of predisposing factors is in the ability to help prevent insomnia in those who are vulnerable, the development of education programmes, and in the provision of further insights into developing more robust, individually tailored, treatment programmes.

2.1 Familial Aggregation: At risk from birth

A strong genetic component has been demonstrated in healthy sleep, both in humans and in animals, leading to the mapping of several loci which may be involved in sleep regulation. Studies on normal sleep in twins have also demonstrated strong concordance in slow wave sleep, suggesting ~50% heritability, similarities in sleep onset latency and in sleep disruption that are not solely accounted for by environmental factors [67-70]. Further to this there seems to be a strong familial component in other sleep disorders such as narcolepsy, parasomnias, sleep apnoea, idiopathic insomnia, hypersomnia and delayed sleep phase syndrome. This would all suggest that there might be a genetic/ familial component to Psychophysiological Insomnia (PI), and this has an obvious bearing when considering predisposing factors and in understanding the psychobiology of PI.

Work on familial aggregation of PI is somewhat sparse (table 2 1 provides a summary of published studies which have a particular focus on familial aggregation and insomnia); however, there is a small body of work which does imply a role of heritability in the development of PI and that this may be related to anxiety, depression and stress-reactivity all of which are demonstrably intricately related. Dauvilliers et. al.[71] conducted analyses on 181 insomnia sufferers who were classified as either primary insomnia (n=77) or insomnia due to a psychiatric disorder (n= 104), in order to differentiate aetiologies. This work represents the most rigorous protocol in terms of screening procedures and history taking within the familial aggregation literature. The Spielberger State-Trait Anxiety Inventory (STAI) and Beck Depression Inventory (BDI) were used to help diagnose depression and anxiety, when scores correlated with observations from clinical interview allowing for classification of ‘insomnia due to psychiatric disorder’. Participant diagnosis for insomnia was achieved via clinical interview on the basis of DSM-IV and ICSD criteria whereby insomnia was diagnosed based on clinician agreement. Further to this, PSG was conducted to rule out other sleep disorders and a physical examination was also carried out by sleep-specialist physicians, thus allowing for assessment of the relative contribution of psychological, behavioural and medical factors to insomnia. This cohort represents the most thoroughly defined group within the published work in this field.

Results from the Primary Insomnia group suggest that the risk of developing insomnia is 6.65 times greater in those who have a first degree relative with PI, with the mother being the most commonly affected relative (42%). Interestingly, the risk value decreased to 1.63 for psychiatric insomnia, suggesting differing degrees of genetic contribution.This work is the first work to validate family history, and also to employ a control group of probands spouses (n=90) who were assessed with the Insomnia Severity Index (ISI) and via clinical interview. This goes someway to controlling for environmental factors i.e. if the current sleeping environment was contributing to poor sleep, this should be evident in those sharing the environment. However, the family members' sleep and health status was poorly defined: sleep status was confirmed only with the ISI, and there was no mental health or sleep history taken. This limits the inferences that can be made about common pathways between psychiatric disorders and sleep. Further the ISI only gives information on current sleep state, which may not provide an accurate picture of familial aggregation of insomnia: it could potentially be the case that a first degree relative may suffer periods of transient insomnia, which the ISI may fail to capture. This pattern could potentially be seen also in their relation. Furthermore, the study in no way allows inferences regarding familial environmental factors- i.e. factors in the childhood home which may have encouraged faulty attitudes towards sleep, and so doesn't allow one to conjecture on what may drive the heritability. Given the reportedly high accuracy with which patients can perceive and identify insomnia in family members (ROC analysis AUC=0.97;p<0.0001[71]) is it not possible that concern over sleep is learned implicitly in some cases? It would be interesting in a study such as this to investigate differences in polysomnographic (PSG) sleep, in order to establish a familial aggregation of paradoxical insomnia. Further to this, the age of the cohort ranged from 16-86. It is largely accepted that sleep becomes more problematic, subjectively, as one ages. Having an elderly representation in the sample may dilute the results somewhat as they may represent a population which are more vulnerable to insomnia for different reasons and so may report symptomology of insomnia, in the absence of familial aggregation.

Bastien and Morin[72] recruited a sample of 285 well-defined patients reporting to a sleep clinic and found that 35% of participants reported a first or second degree relative with a current or past sleep problem. The mother was the most commonly affected member, with 45% of mothers having a past problem and 39% a current problem with insomnia. Further, there was a trend towards a higher familial incidence in those

reporting earlier onset vs. those reporting a later onset- as suggested previously, representing the fact that insomnia in an older sample is likely due to differential aetiological factors. There was no attempt in this study to follow-up family members, or to verify the existence or severity of insomnia.

Beaulieu-Bonneau et. al [73] have supported this work, demonstrating, in a population based sample, a strong association between maternal insomnia (19.7% of cases report their mother as suffering with insomnia) and increased risk in offspring. There were significant group differences between those with a current sleep problem or reported past problems vs. good sleepers who endorsed never having any sleep problems. Furthermore, those who demonstrated a vulnerability to insomnia- i.e. currently diagnosable as an insomnia sufferer, or reporting past episodes of poor sleep- showed a trend toward reporting more anxiety related symptomatology and predisposition to arousal. This is important when we consider insomnia in light of the hyperarousal model (outlined in chapter 1), and may tentatively suggest that there is a predisposition to 'hyperarouse' in response to stress, which might eventually lead to chronic hyperarousal and insomnia. It also supports findings by LeBlanc et.al.[74] who demonstrate that arousal predisposition creates an odds ratio (OR) of 1.12 for the incidence of a new case of insomnia syndrome. The absolute differences in familial incidence between the good sleepers and the vulnerable group are relatively small (29% vs. 37%) and the groups are poorly defined, not assessing for psychiatric conditions that we know impact on sleep, or other comorbid conditions. The presence of an afflicted family member was identified based only on the participants' response to a 'yes'/ 'no' question and so may be biased- maybe not however, if PI are as accurate at assessing family members sleep as has previously been suggested.

Although there is no objective measure of sleep in the majority of these studies, they indicate that there is a familial component in self-reported insomnia. LeBlanc et.al. [74] point out that family history was the second strongest predictive factor in new case insomnia syndrome in their study. In terms of differing aetiologies, all of these studies report an association between early onset of sleep problems and reporting of 'positive' first-degree relatives. The implication here is that there is a familial predisposition in some: a vulnerable phenotype. It could be hypothesised that the mechanism here is through stress reactivity, making some more negatively responsive to stress and so more

likely to have an earlier onset- a stronger predisposition- of insomnia, or to report more periods of transient insomnia, whereas in those with no familial history it takes a longer period of consistent or a more severe life stressor before sleep disruption is evident, or perceived as a complaint. Drake et.al.[75] support this notion, showing that 37.2% of variation in responses to a validated and reliable questionnaire assessing vulnerability to sleep disruption (Ford Insomnia Responsivity to Stress Test (FIRST)) is accounted for by familial aggregation. This relationship remained after controlling for potential confounds including age, gender, shift schedule, and psychiatric history.

Authors	Objectives	Participants	Methods	Results	Interpretation	Critique
Dauvilliers et.al. 2005	Evaluate the prevalence of insomnia in first-degree relatives of chronic insomnia sufferers; differentiate chronic insomnia sufferers from those with psychiatric insomnia	181: 77 chronic insomnia patients; 104 patients with a co-morbid psychiatric complaint Insomnia mean age: 45.07 (S.D.= 13.53) Mean age of Onset: 32.17 (SD=13.39)	Clinical interview; BDI; STAI; PSG in cases where other disorders were suspected (n=92). ISI used to validate insomnia in 1st degree relatives in a sub-sample(n=74) Spouses also completed ISI	72.2% of insomnia patients reported familial insomnia; 43.3% in psychiatric group; 24.1% in non-insomnia control group. Mother most commonly affected Family history related to earlier onset in insomnia group	Familial aggregation present in insomnia, justifying need for further genetic studies particularly in those with early onset	ISI may not be sensitive to recurrent periods of transitional insomnia; no mental health/ sleep history of family member Wide age range may dilute results Only aggregation study to employ PSG, get some form of confirmation about family members insomnia (ISI) Attempts to control for effects of current sleeping environment (spouses ISI).
Bastien and Morin, 2000	Evaluate Familial incidence of insomnia among those with insomnia complaints	285 insomnia patients from a sleep clinic Mean age 41.7 (SD= 13.96) Mena age of onset: 31.8 (SD=16.4)	Semi-structured interview for diagnosis of insomnia Family history of 1st and 2nd degree relatives: is an affected member present and what is the nature of their sleep problem	35% of insomnia patients report family history. Mother is most commonly affected member Family history is related to earlier onset, and with sleep onset, as opposed to maintenance problems.	Family history is likely a potential risk factor for insomnia, however this study cannot elucidate familial from social factors i.e. is poor sleep learned?	1st and 2nd degree relatives considered. Probands relatives only assessed indirectly via propand
Beaulieu-Bonneau et. al 2007	Assess rates of family history of insomnia in good sleepers and insomnia patients. What characteristics do those with family history have in common?	545 insomnia patients (203 with family history of insomnia) 403 good sleepers (117 with family history of insomnia) Mean age: 43.9 (S.D.= 14.1)	Initial telephone screening then postal survey: ISI, PSQI, BDI, STAI, APS Questions about family history: "Do any of your immediate family members presently have or ever had sleep difficulties?"Follow-up questions to specify which relative(s) had a sleep problems and what type of problem. Is it current or past?	31.9% reported at least 1 first degree relative with insomnia Mother was most frequently affected Patients with a current or past history were more likely to report a family member with insomnia compared to good sleepers who had no past episodes (39.1% vs. 29%)	Provides further support for the role of family history in the development of insomnia	No direct assessment of family members. Entirely survey based. Large sample
Drake et.al. 2008	Assess the degree of familial aggregation in vulnerability to stress related sleep disruption in siblings	46 (23 sibling pairs) Mean age 51.1 (S.D.=12.1)	Non-twin sibling pairs recruited. ESS, FIRST DSM-IV criteria used to exclude insomnia TST, TIB for weekday and weekends taken at interview SE calculated from this	Correlational analyses showed 37.2% of variance in stress-related sleep disruption is accounted for by familial aggregation. This remained when controlling for age, psychiatric history and shift work	Suggests that vulnerability to sleep disruption may run in families, particularly in relation to stress	No validated measure of sleep Sample is older on average than other studies Poorly defined sample The implications of this work needs follow up. Only study to look at sibling pairs.

Table 2 1 Summary of Published study with a Focus on the Familial Aggregation of Insomnia/ Sleep Disruption

2.2 Genetics: Stress Rather Than Sleep

2.2.1 Twin Studies

Twin studies provide a valuable tool for understanding the heritability of a disorder, allowing one to investigate the co-occurrence of a specific outcome relative to the degree of genetic similarity in a twin-pair (mono- or di-zygotic). Twin studies can also help to control for shared environmental effects if both twins are raised in the same household. The higher degree of genetic similarity in twins is a strength compared to studies of familial aggregation. The twin study approach compares similarities within mono-zygotic twins to similarities within di-zygotic twins, allowing for the analysis of variance which is attributable to genetic and/or environmental influences. Twin-studies in the insomnia literature further support the presence of genetic factors that increase vulnerability to insomnia. It will be suggested that this is more likely related to the stress system rather than the sleep system.

Twin studies to date all suggest that insomnia-related traits are heritable. Partinen et.al. [76] found the heritability for sleep disruption and sleep length 44%. Barclay et.al[77] reported that genetic influences were present on 6 out of 7 components of sleep quality as measured by the PSQI, with a range of heritability-estimate from 0% to 46%, with the rest of the variance accounted for by non-shared environmental factors. This contradicts Partinen's finding somewhat, however, as Barclay et.al. point out the sample here is relatively young and so may be less susceptible to the genetic influences on sleep duration. The participants in this sample did not score in the extreme upper limit for any of the components of the PSQI, suggesting that they are not likely to suffer from an ongoing chronic insomnia; therefore what they are reporting on is a population with some insomnia symptoms. The reported variances may then speak more closely to a genetically controlled response to what is causing the mild disruption, rather than to a genetic common ground to the sleep system (I'm not arguing that there isn't one, but that this maybe isn't what Barclay et.al. have tapped into). This will be discussed more thoroughly when we look at specific genetic polymorphisms.

This point is maybe made clearer when we look at recent work by Drake et.al.[78]. In a comparable twin cohort it was found that there is a significant overlap between sleep

reactivity to stress- the likelihood that sleep will be disrupted in response to stress- and insomnia symptoms in terms of their genetic influences. Sleep-reactivity to stress was measured by the FIRST. The FIRST is a questionnaire which has been shown to differentiate those likely to show objective sleep disruption in response to stress, versus 'stable' sleepers (discussed in more detail later). It is argued that the findings from this study reflect the notion that sleep-reactivity may represent a genetic vulnerability to insomnia- interestingly the heritability was 43% for males and only 23% for females, suggesting different degrees of genetic influence between the genders. Insomnia in this sample was based on DSM-IV-TR criteria taking into consideration sleep and daytime impairment factors. Wust et.al.[79] have shown 48% heritability in cortisol awakening response, implying a genetic influence on HPA axis reactivity. Taking this all together, it could be the case that the heritability factor is one of an over-sensitive stress system, rather than an ineffective sleep system.

2.2.2 Genetic Polymorphism: 5-HTTLPR Serotonin Transporter Polymorphism

When we look next at the identification of genetic polymorphisms that may affect sleep, there is further support for the proposed notion that genes may exert their influence on insomnia through sleep-reactivity, or a differential stress response which may affect sleep. For example, Way and Taylor[80] using a laboratory based psychosocial stressor (the Trier Social Stress Test) found that genetic polymorphisms (5-HTTLP) are associated with increased cortisol response to the stress task. This same polymorphism has been found to be associated with vulnerability to sleep disruption. (See below) It would have proven interesting in the Way and Taylor study to have sleep history and current sleep assessed in this study in order to indicate causality i.e. does the polymorphism lead to increased cortisol response, or does it affect sleep and this increases cortisol response to stress? This work does imply however that the mechanism through which genetics contributes to insomnia may be via stress systems, and that there is a definite inclination toward disrupted sleep in some, echoing the findings of Drake et.al.[78].

Brummet et.al. [81] have demonstrated a significant interaction of life stress- caring for an Alzheimer's patient- and the 5-TTLPR genotype. Those who possess homozygosity for the s-allele demonstrated greater sleep disruption, as defined by the PSQI, in response to

care-giving stress compared to controls. This suggests a trait-like vulnerability to experience insomnia during periods of stress, the mechanism of which is the production and re-uptake of serotonin. The s/s allele of this gene seems to inhibit the re-uptake of serotonin. This appears counter intuitive. However there is an argument to suggest the expression of 5-HTT is critical in the development of the neonatal brain, but independent to its function in adults [82-85]. The presence of this homozygous genotype modulates responsiveness to stress indirectly via brain development early in life, particularly in emotion regions: this has implications when we will subsequently consider the role of personality and coping style in the onset and maintenance of PI and also when taking into account aspects of cognitive hyperarousal.

It is assumed in this study that each individual experiences the same stress in the same way i.e. there is no measure of subjective stress levels or of cognitive hyperarousal. Such information could provide useful insight into how stress biology affects cognition and vice versa. It can be concluded from this study that the presence of the s/s allele leads to a greater likelihood of a subjective complaint.

Deuschle et. al.[86] have also found an association between serotonin transporters length polymorphism and primary insomnia. Particularly interesting in this study is that they found no association between s-allele and PSG recordings, thus suggesting that the 5-HTTLPR s-allele genotype has a stronger relationship with self-reports of insomnia rather than objective measurement of sleep, supporting the previously mentioned study. Unlike the previously mentioned study, participants were screened for major depressive episodes, an important consideration given the relationships between depression and sleep and depression and serotonin transporters. The authors conclude that the 5-HTTLPR s-allele, combined with stress, contributes to the hyperarousal seen in PI, for example, in the increased activation seen the hypothalamic-pituitary-adrenal axis (HPA) during the early evening in PI sufferers, and that it may make them more vulnerable to negative conditioning of sleep related stimuli, due to the uncoupling in the brain in the areas of the pregenual cingulate and amygdala, areas which contribute to extinction of negative affect[87]. That is to say that carriers of the s/s allele of the 5-HTT find it more difficult to extinguish negative learning. This could suggest a possible genetic pathway by which insomnia is not only precipitated but also perpetuated. It also implies a trait-like hyperarousal as both a precipitant and perpetuator. This is in-line with other work which

has demonstrated that those who are in possession of at least one s-allele on the 5-HTT gene are more likely to develop depressive tendencies, depressive disorders and/or suicidal ideation, but only if such individuals also encounter severe, or many life stressors [88, 89]. A recent meta-analysis[90] has reviewed work highlighting the role of the s/s allele in modulating amygdala function in response to aversive stimuli. It seems that the s/s allele does confer a tendency to preferentially process aversive stimuli; however the authors conclude that the effects may not be as strong as initially though, due to the heterogeneity of studies and consistent under-powering. What the meta-analysis highlights however is a consistency in this finding, and an area of research which may prove to further elucidate the mechanisms by which the 5-HTTLPR polymorphism may lead to disrupted sleep and then insomnia (and speculatively, what drives the relationship between insomnia and depression).

Of course there is a lot of work still to be done in this area: looking at a broader range of stressful life events, further investigation into the common biological, genotypic, pathways between stress, insomnia and depression and work looking at possible protective factors. Secondly none of this work allows any inference about environmental factors to be made. For example, as in Drake et.al. [75], sibling pairs are the population of interest. While it is likely that siblings have had a similar environment growing up, there is no information on how environmental influences may have become divergent over-time. While all this work does support the idea that there is a trait-like vulnerability to sleep disruption-and therefore insomnia- it remains unclear what the environmental and genetic interactions are, what genotypes and loci are implicated and to what extent all of this implicates insomnia as a risk-factor for the development of further psychiatric problems, which seem to be under the control of similar systems. Work in this field would also benefit from better defined groups: absolutely screening for other sleep disorders and in the case of the majority of the work, taking a more complete psychiatric and health history from all participants and in the case of familial work, more stringent testing and screening of the ‘positive’ relatives. What has been done so far constitutes a starting point, and certainly highlights exciting and novel pathways for sleep research and although by no means equivocal, does serve to underscore the importance of stress, familial aggregation and genotyping in the aetiology of PI. At the core of this research is the notion that arousability, certainly from a biological perspective, may pre-exist PI. This

work all serves to imply that insomnia is a disorder of genetic and environmental interaction and is, essentially, a stress disorder.

2.3 Defining the vulnerable

The work supporting the hyperarousal model of insomnia (see chapter 1) demonstrates that there is a clear psychobiological component to the maintenance of this disorder- an interplay between cognitive and physiological arousal. This too can be integrated into the 3-P model as factors which perpetuate PI. However, it has also been observed that an increased arousal may precede the onset of insomnia rather than being a symptom of or compensatory mechanism (as suggested by Drummond et.al[91]) to sleep deprivation. As already mentioned, Leblanc et.al.[92], report the greatest predictors of new onset insomnia syndrome in a population based sample as arousability, measured by the arousal predisposition scale (APS), with an odds ratios of 1.2; family history of insomnia (OR= 2.96) ; higher bodily pain and lower self-rated health. The first 2 mentioned variables do suggest a trait-like, possibly inherited, vulnerability. The work on familial aggregation and genetics also supports the idea of a vulnerable phenotype, which responds more sensitively to stress. Arousability as measured by the APS may reflect a vulnerability to the hyperarousal seen in insomnia as it asks questions behaviourally reflective of an up regulation and sustained activation of the sympathetic nervous system such as ‘I get flustered if I have several things to do at once’ or ‘Strong emotions carry over for one or two hours after I have left the situation which caused them’.

Experimentally, Bonnet and Arand [93] have shown sleep disruption to be consistent across different stressors:

1. ‘first night effect’: Spending the night in a new environment is considered a mild stressor, and leads to sleep disruption in good sleepers
2. Caffeine prior to sleep onset: Caffeine represents a mild physiological stressor. Being a stimulant, it is known to disrupt sleep. Participants were given 400mg half an hour prior to sleep onset.
3. 3h phase advance: Participants lights out (bed-time) is 3 hours earlier. This means that they are trying to sleep at a time when their circadian rhythm would not normally allow.
4. 6h phase advance: Participants lights out is 6 hours earlier.

It was found that those who demonstrated a clear sleep disruption on the first night in the sleep laboratory also demonstrated greater sleep disruption across the other 3 conditions, despite being good sleepers at screening and on baseline night (2nd night in the lab). The 'situational insomniacs' (SI) (i.e. those who demonstrated sleep disruption in response to the 3 stressor conditions, relative to baseline) compared to the 'super sleepers' (those whose sleep maintained across all conditions relative to baseline) also demonstrated increased heart-rate, increased low-frequency (indicative of sympathetic nervous system activity) and decreased high-frequency (a decrease in parasympathetic nervous system activity) EKG spectral power, and mimicked what would be expected of a PI group in Multiple Sleep Latency Tests (MSLT) scores. That is to say, greater MSLT scores suggesting a difficulty with de-arousal as longer MSLT times reflects an inability to fall asleep and is characteristic of the insomnia population. This suggests that the SI group- the vulnerable population- are more sensitive to stressors, both physiological- caffeine- and psychological- first night effect. Further, that the observed sleep disruption seen may be secondary to increased sympathetic nervous system activity: this is a marker for vulnerability to sleep disruption. Interestingly the SI group demonstrated no mood or personality differences- measured using the Minnesota Multiphasic Personality Inventory (MMPI)- at baseline, thus implying that the relationship seen between increased depression and anxiety scores and insomnia is resultant from sleep disruption and not vice-versa: insomnia is a precursor to mood disorders. Considering the polymorphisms which have been implicated, it could be hypothesised that this is most likely via the mechanisms that drive arousability and then hyperarousal

Drake et.al[94] , using the FIRST, found that those scoring high on the FIRST demonstrated greater MSLT scores, in accordance with the previously mentioned study. PSG scores during the first night in a sleep laboratory were also worse in those scoring higher on the FIRST. The PSG results remained significant even after exclusion of those with a past complaint of insomnia, and groups showed no differences on sleep diary measures obtained for 2 weeks prior to coming to the lab, thus indicating that the sleep disruption is likely due to 'the first night effect', rather than a faulty basal sleep system. Differences in MSLT scores became non-significant when those with a past complaint of insomnia were excluded. This is not surprising given the evidence suggesting that a past episode of insomnia is the greatest predictor of a new episode [74, 95]. Taken as a whole, the work suggests that a vulnerability to sleep disruption exists in good sleepers, prior to any

complaint and can be measured psychometrically, and further, that the severity of sleep disruption (i.e. on the MSLT) is plausibly worse in those who have experienced an episode of subjective sleep disruption in the past: past sleep disruption leads to a greater risk of future, and more severe, sleep disruption. What could be investigated further is the idea that a past episode leads to a weak learned association between bedtime environment and sleeplessness that becomes more easily aggravated in those that are already vulnerable- as has been suggested by Deuschle et al[86] stating that the 5HTTP-s allele may discourage distinction of negative learning due its expression in brain areas which are known to control this, and is more prevalent in those vulnerable to stress-related sleep disruption. This may mean then that behavioural conditioning is easier in the vulnerable group whereby a few nights of bad sleep due to the presence of a stressor may create negative associations around sleep during this period. This learning is not extinguished as effectively during preceding nights of good sleep and so in the face of a new stressor these negative associations are more easily activated. In this way it becomes easier to induce a new period of insomnia. This is of course speculative, but could provide an interesting avenue of research in terms of helping us better understand the mechanisms that drive chronic sleep disruption, and indeed which mechanisms bridge the gap between acute and chronic insomnia in the small percentage that does progress.

Interestingly, Pezawas et.al.[96] note that whilst performing an emotional task known to engage the amygdala, those with the s-allele of the 5HTTLPR polymorphism have increased amygdala reactivity to the task, and also are more anxiety prone in terms of their ‘temperament’, as measured by the Tridimensional Personality Questionnaire (TPQ). The TPQ is a psychometric test which aims to define personality in 3 components: reward dependency, harm avoidance and novelty seeking. It has been used widely in the field of personality genetics and different interactions of these 3 traits are thought to correspond to differences in dopaminergic, serotonergic and noradrenergic systems[97] . The authors interpret this as being reflective of the 5-HTT polymorphism’s role in depression genesis and maintenance; however it may be better interpreted as reflective of emotional arousability and may represent a pathway through which sleep disruption leads to depression. Furthering this hypothesis are 2 meta-analysis conducted in 2004[98, 99] which both conclude that the 5HTTP-LR polymorphism is tightly associated with anxiety-like traits, particularly neuroticism as measured by the NEO-ffi and a trend toward association with harm avoidance on the TPQ. This will have a particular bearing when we

go on to discuss personality as a risk factor in the development of insomnia. In the context of understanding the role of 5-HTTPLR polymorphism in the aetiology of insomnia, what these studies suggest is that the short allele contributes to a phenotype who is more reactive to stressful situations in terms of their physiological response, more reactive to emotional stimuli in terms of their brain activation patterns but also may be more prone to perceiving events as negative or stressful in terms of their personality- i.e. higher in neuroticism.

It is highly plausible therefore that a vulnerability to insomnia does exist and that this is driven by a tendency toward hyperarousal. If we accept that vulnerability does exist- that insomnia is not simply the result of learned associations, but the interaction between environment and a vulnerable phenotype- then we need to define and understand the mechanisms behind it, both biological and psychological. Physiologically, the evidence to date would support the contention that insomnia is a disorder of the stress-system. It makes sense then that psychologically we would want to investigate variables which regulate stress-perception, particularly given the evidence described above that such personality dimensions may be under the control of the same polymorphism implicated in the onset of sleep problems.

2.4 Personality and Coping style: Influence and mediation

What we know so far regarding the genetics of insomnia is suggestive, and it is obvious that the indicated polymorphism is not influence enough to account fully for stress-related sleep disruption: a large proportion of ‘carriers’ do not report disrupted sleep and vice versa- not to mention the fact that sleep regulation is likely an interaction between various genotypes, neurotransmitters and endocrine responses- sleep is a tightly regulated homeostatic drive. Besides other biological factors, a person’s psychology is likely to mediate their response to stress, and so their vulnerability to stress related sleep disruption and so insomnia.

Lundh and Broman[36] discuss the differences between sleep-interfering and sleep-interpreting processes, whereby hyperarousal would be seen as a sleep-interfering process, as arousability leads directly to sleep disruption. Sleep interpreting processes are

psychological constructs which lead to an over inflation of the sleep problem, or which lead to cognitive arousal, which in turn then triggers sleep-interfering processes (figure 2 1).

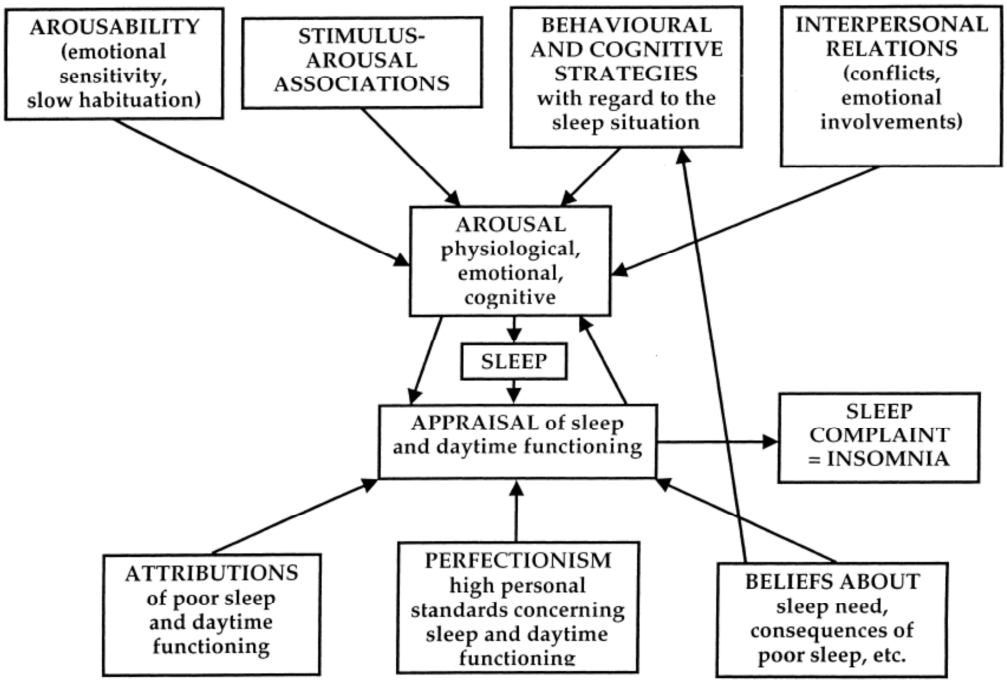


Figure 2 1 Lundh and Broman [36] Sleep Interpreting and Sleep Interfering Processes

The model highlights the interplay between subjective, cognitive and somatic arousal. Nicassio et.al.[34] and Lichstein et al [100] both demonstrate that cognitive arousal is perceived more strongly by insomnia patients than is somatic arousal. However, as Lundh and Broman point out, cognitive arousal- conceptualised as the racing mind, rumination, worry- is, in itself, physiological arousal in so much that negative thinking at sleep onset will lead to an emotionally induced physiological response. Taking this stance on insomnia highlights the importance not only of physiological markers to insomnia, but also psychological precursors and so the role of the interaction between the 2: cognitive arousal begets physiological arousal and vice versa; the degree to which a situation or stressors elicits an arousal- either in the terms of H-P-A activation, or a ruminative/ worry cycle- is bound to be driven by 1) an individual's basic physiology but also 2) psychological response, that is to say, their interpretation of how stressful the stressor actually is. This becomes a chicken and egg scenario. The point however is not which comes first, but that both lead to increased stress-reactivity and so an increased vulnerability to insomnia.

Considered below are psychological factors which may act as markers to stress-related sleep disruption.

Brosschot et.al.[101] define worry as a constructive problem solving process which is thwarted by cognitive predispositions, such as anxiety, and further conclude that preservative cognition- rumination and worry- work directly on somatic disease via cardiovascular, immune, neuroendocrine and neurovisceral systems i.e. similar to the hyperarousal demonstrated in insomnia, and the proposed pathway between insomnia and illness- and further highlighting the bi-directional relationship between cognitive and physiological arousal. In this way, worry becomes a deconstructive process. It may be that cognitive predispositions which lead to preservative cognition are also likely to lead to vulnerability, given that worry and rumination are characteristic of the insomnia population, as for example in Harvey's cognitive model. Daytime [102]and pre-sleep [35] worry have been shown to characterise the insomnia population, and to differentiate them from good sleepers Further to this worry has been shown to delay sleep onset in good sleepers[103].

Van de Laar et.al. [104] have reviewed the role of personality factors in insomnia so this won't be covered in fine detail here. Rather this information will be used to suggest a model by which personality, in interaction with coping style, creates an at-risk phenotype. They conclude that the insomnia population consistently show traits associated with 'neuroticism', 'internalization', anxious concerns and traits associated with perfectionism, and further, that future longitudinal studies should not view personality as a single predisposing factor, but assess it as a part of a larger group of interacting psychological and physiological factors involved in the predisposition to and perpetuation of chronic insomnia. Personality is not a discreet construct, but one which interacts with genes, environment and coping style.

This complex interaction has been demonstrated in other psychological disorders, particularly in depression. This will be used here in order to outline possible research avenues in insomnia, drawing parallels with the depression literature to provide clues as to how personality and coping may affect insomnia-vulnerability but also indicating how sleep may lead onto the genesis of mood disorders via these same mechanisms.

It is largely accepted that high levels of neuroticism predict experiencing a clinically significant depressive episode [105-107]. The mechanisms by which temperamental predispositions instigates depressive symptoms is not entirely clear. However, recent work has suggested that there is an interaction between neuroticism, conscientiousness, emotion focused coping and genetics. Leandro and Castillo [108] have shown in a sample of 274, strong positive correlations between neuroticism and emotion focused coping and avoidance coping, and that conscientiousness is associated with more positive coping styles. However, these results are correlational. They do, at best suggest that one of the factors through which neuroticism may lead to depression is through affecting coping style. Saklofske et.al.[109] have shown that perceived stress in a student population was significantly and positively correlated with neuroticism, emotion focused coping and negative affect. Conscientiousness and positive affect seemed to be protective against the perception of stress, or at least the reporting of stress. Again, the results are largely correlational but highlight the fact that negative affect is a combination of both personality and coping style, and specifically neuroticism and emotion focused coping.

When individuals who have never been depressed are compared to those who have, it has been shown that neuroticism as measured 6 years previously is related to current levels of depression in both groups and also associated with cognitive reactivity in both groups. Neuroticism seems to predict a ruminative response to low mood which could possibly mean that neuroticism leads to a process whereby in the face of low mood, one reflects on the mood and what caused it rather than engaging in a more active coping style. In terms of those who have suffered depression in the past, the higher they scored on neuroticism the more likely they were to respond to mild negative moods with thoughts of hopelessness or suicidality. The authors explain this in terms of ‘differential activation theory’: Associations are learned during a previous depressive episode linking depression, rumination and negative affect. An individual who has not had a previous episode does not experience this learning. In this explanation, neuroticism encourages depressive thinking, but in the previously depressed group, this seems to be more severe. This may be reflective of extreme emotion focused coping. An alternate explanation may be related to the previously mentioned genetics which seem to prevent the extinction of learned negative associations. Again, this is speculative but has some support in that neuroticism and anxiety/ depression do seem to have an overlapping genetic contribution[110] and the polymorphism most extensively studied/ implicated in sleep,

stress, anxiety and depression is the same: the 5-HTT serotonin transporter polymorphism.

It seems then that the role of personality and coping style in insomnia may be similar to that of depression. However, the extent to which personality factors mediate, and encourage the onset of insomnia is poorly assessed, as the majority of work to-date is defining those already suffering with a diagnosable complaint, and making judgements as to what is likely to be a predisposing factor is further complicated by the fact that insomnia seems to predict changes in personality, as suggested by Danielsson et.al[111], demonstrating that sleep-onset problems in adolescents predict neuroticism in middle-age, and not, as would be expected, the other way around. Possibly because sleep loss in adolescents may alter the development of neuroendocrine systems and gene expression, plus, lead to heightened anxiety, worry and rumination around bedtime. This may then result in the development of a neurotic trait, which in later life predicts and perpetuates insomnia. This study defined adolescent neuroticism based on the 16 factor Cattell [112-115] model of personality, and at follow-up on Eysenck's personality questionnaire[116]. Results would appear stronger and more reliable if the questionnaires used were consistent if for no other reason than to ensure a standardization of neuroticism at both time points. Secondly, it could be that personality is still developing during adolescence so scores obtained at younger ages may not be representative of true personality[117]. Other, possibly mediating factors were not measured, like other personality traits and coping styles- reflecting back on the depression literature it seems that an emotional coping style may be the mediator between neuroticism and depression, and that this may be learned over time and so possibly coping style may at baseline undermine relationships between neuroticism and sleep. Further, the study only considered sleep onset latency, assessed via one question, with no assessment of daytime functioning or distress, and is therefore unrepresentative of an insomnia syndrome.

Williams and Moroz [118] support the idea that neuroticism does predict sleep disruption during a period of transition but that this is mediated by conscientiousness- as with depression, conscientiousness seems to have a protective role- and daily hassles. Using subscales of the PSQI the authors assess how personality traits predict different aspects of sleep and sleep complaints in response to stress. The main findings were neuroticism (N) was negatively and conscientiousness (C) was positively related to sleep quality. Poor

sleep predicted greater depressive symptoms and poorer functional status for high-N/low-C participants, but not for other N and C profiles. That is to say that high N/ low C individuals are more likely to report impaired functioning due to sleep loss. This may be because high N individuals have a stronger propensity toward negative affect, coupled with low effortful-control- i.e. low C- may result in a propensity to interpret incoming information as a signal for daytime dysfunction which may then be attributed to poor sleep. High C may mediate this due to the possibility that sleep disruption, or more specifically less time in bed may be attributed to working harder, or in this population, staying up later to study- so high N high C may create a perfectionistic type personality who does not attribute daytime signs of tiredness to sleep loss, but rather to achievement. This, once again is speculative, however intuitive. Blagrove and Akehurst[119] have shown that N predicts mood disruption as measured on the POMS in sleep-deprived good sleepers and that change in reasoning performance was correlated with change in mood. Thus, providing further indication that N may make lead to increased vulnerability to sleep loss, and more sensitive to the negative effects of sleep loss. Possibly via similar mechanisms to which Williams and Moroz outline: certain N and C profiles may make an individual more aware of mistakes they are making, which may then cause anxiety over future errors, increasing the likelihood that they occur. This was not assessed in the study, but would provide a good understanding as to how these variables interact in the onset and perpetuation of insomnia.

In the face of ambiguous stimuli those with high scores on the neuroticism subscale of the NEO-ffi demonstrate a stronger inclination toward avoidance of and are reported to be more likely to interpret ambiguous stimulus as negative [120]. Such a profile-high N/Low C- may also lead to more worry and rumination around sleep onset as one becomes unable to control their 'racing mind'. There is an intuitive relationship between neuroticism and worry: neurotics are inclined toward anxiety-like responses, and conversely, worry may lead to neuroticism [121, 122]. Vincent et.al.[123] have also demonstrated that N is linked to short sleep (OR= 1.30). In terms of the phenomenology of insomnia it is easy to see how neuroticism may perpetuate the disorder as one interprets incoming signals from the environment as signs of not sleeping, or signs of functioning being reduced and this being attributed to sleep loss which then reinforces worry about sleep in an individual who is already prone to the effects of negative affect and probably inclined towards worry anyway. The role of neuroticism in predisposing an

individual to insomnia is again probably due to how it affects stress-perception and reaction to stress. High neuroticism is the experience of negative affect- i.e. being more likely to interpret incoming information as having a negative valence (and so possibly more likely to employ an emotion focused coping strategy). This means you are likely to experience more stress in your day to day life. The associations between N and worry create a situation where sleep can become easily compromised.

Personality variables, although equivocally, have a role to play not just in stress perception but in physiological reactions to stress. Nater et.al.[124] have found that neuroticism is associated with increased cortisol secretion throughout the day, and that the relationship between affect and stress-reactivity is mediated by conscientiousness, in so much that high C leads to a greater reduction in cortisol in response to positive affect- so it would seem that high C leads to a reduction in worry and also a greater detainment of positive affect. Mikolajczak et.al.[125] demonstrated in healthy men that flexibility of cortisol waking response (CAR) is predicted by, amongst others, neuroticism.

Although the work on biomarkers of personality is recent, sparse and conflicting there is an agreement between probable vulnerability traits, and the physiology of hyperarousal and stress reactivity, and the cognitive aspects regarding worry and avoidance in insomnia. What has been suggested so far in this review is a strong role for stress reactivity being a precursor to insomnia; however this is likely to be mediated by neuroticism and conscientiousness. With regards to how such personality variables may influence stress-reactivity, it is important to understand the other variant in stress-perception: coping style.

Coping style is defined as the response an individual makes to a stressor. In transactional models of coping, cognitive appraisal of the stressor is emphasised, highlighting the role of the individual in response to stress: a particular stressor will not have a blanket effect[126, 127]. Coping style then is key in understanding individual response to stress, and so is likely a strong mediator in understanding the psychobiology of individuals vulnerable to insomnia. Biobehavioural systems predict 2 models coping response: retreat or a ‘shut off’ response- i.e. retreating to sleep- or a ‘turn on’ response- i.e. hypervigilance [128] and these map directly onto specific coping styles, and the effect they have on sleep. Disengagement may lead to longer sleep, whereby sleep becomes an

escape, however emotion focused coping may lead to shorter or disrupted sleep and this may lead to increased worry and rumination coupled with an unwillingness' to disengage. Sadeh et.al.[129] demonstrate that in a group of good sleeping students, those who are high on emotion focused coping are more likely to show, in sleep diaries and actigraphy, a decrease in total sleep time during a stressful period- the week prior to an important interview. Morin et.al[130] have shown those who use emotion regulation strategies are likely to perceive their lives as more stressful, and that such techniques are more common in an insomnia population. Further, a recent meta-analysis [131] suggested link between 'problematic' coping strategies and neuroticism, one of these being emotion focused coping, implying a mediation of personality on chosen coping strategy. Interestingly, problem focused coping has been linked with a lower cortisol response throughout the day in healthy older adults[132], suggesting that this may be protective.

Contemporary models of coping imply that there is a choice in which strategy a person applies in a particular situation. Personality however is defined as ' the system of enduring inner characteristics of individuals that contribute to consistency in their thoughts, feelings and behaviours'[133] It seems probable then that personality will affect choice of coping strategy in a given situation: Individuals who experience greater negative affect- neuroticism- may be more inclined to engage in emotion focused strategies. This has a bearing on stress-perception and so the stress response, which in turn predicts sleep disruption which may then be maintained by ongoing negative cognitive activity, a hypervigilance for and attentional bias to cues which indicate lack of sleep, and so further worry, rumination and anxiety around sleep. Neuroticism and emotion focused coping and measures of arousal have been shown to characterise those rated as vulnerable to sleep problems (β=0.413 and β=0.222 respectively), based on the FIRST, and that vulnerable patients demonstrated comparable cognitive emotional arousal to insomnia patients[134], implying further that an observable predisposition does exists, one which is defined by not only physiological arousal but by cognitive-emotional arousal associated with neuroticism and emotion focused coping.

2.5 Discussion

It is accepted that stress interferes with sleep, and stressful-life events precipitate insomnia [135, 136]. However, there has been little work investigating predispositions to stress reactivity and how this affects subsequent sleep. There is clear evidence in the sleep literature that a trait-like vulnerability exists, that this may be inherited, and some work to suggest that this is mediated by different psychological variables- particularly neuroticism and emotion focused coping. It is suggested that vulnerability to insomnia is the result of both genetic, physiological systems and an individual's propensity toward stress-perception. Once again we are faced with a chicken/ egg scenario: does a genetic propensity toward increased stress-reactivity lead to neuroticism, EFC and so rumination and worry or does neuroticism etc result in an increased stress response- i.e. to what extent does cognitive arousal lead to physiological response and vice versa? In order to address this question longitudinal studies are required, assessing personality and coping style changes over time, and further, how this relates to stress-response not just in terms of cortisol and HPA axis activation but using other more global measures such as whole-body metabolism.

What this chapter highlights is a need to better understand the vulnerable phenotype, which in the long run may help us prevent, reduce the cost of, and improve our treatments of insomnia. It is suggested that stress-reactivity is the main predisposing factor. This, however, is a composite of various domains, and the interaction of these. Neuroticism predicts increased stress-reactivity and negative affect, and increases the perceived negative effects of sleep loss. This in itself may create worry over sleep. N may also lead to the deployment of negative coping styles in response to stress- EFC- as an increase in negative affect may seem to warrant a focus on emotion rather than practical problem solving. Both these factors are then likely to interact with the suggested polymorphism to create an individual that is vulnerable to stress related sleep disruption both psychologically and physiologically.

All 3 factors seem to pre-exist insomnia and are not subsequent to it, while also characterising the insomnia population. Understanding the links between all 3 in the face

of different kinds of stressors and how they influence different physiological systems is crucial to our understanding of the aetiology of insomnia from the point of good sleep.

Chapter 3: Methods and Competencies

To avoid unnecessary repetition, before experimental works are presented, an explanation of methodologies common to all experiments will be provided, as well as a delineation of skills practiced and gained throughout the course of the Ph.D. programme. Methods specific to a particular piece of work will be outlined in the relevant chapter. Initially, an outline of generic recruitment and screening processes is provided. Secondly, psychometric properties of scales employed through all 3 experimental studies are presented.

3.1 General Methods:

3.1.1 Recruitment and Screening

Participants for the most part (in all studies except a pilot study, reported later in this chapter) were recruited through the School of Psychology at the University of Glasgow. E-mails advertising for participants were sent round the 'subject pool'. This is an online database which students can sign up to if they wish to be contacted about taking part in research. It allows researchers to contact participants with consideration for inclusion and exclusion criteria- i.e. only those who have indicated a willingness to participate in brain imaging studies, or only those who are native English speakers for example. Further to this, posters advertising the study were placed in the waiting room of the School of Psychology. Willing participant left their name and/or contact number or e-mail address. Interested participants were contacted and screened by the researcher, using the University of Glasgow screening questionnaire (appendix I). This was conducted, without exception, over the phone. In brief, the interview asks questions regarding sleep onset time, wake after sleep onset time and how often during a week these aspects of sleep are seen to be problematic. It also asks questions regarding total sleep time and time in bed. In order to diagnose insomnia, there must also be the presence of daytime impairment, so participants are also asked how their sleep affects their function during the day and in which domain. Further to this the participant is required to give information on estimated weekly alcohol intake, the presence of any other sleep disorders, and any ongoing

physical and psychological disorders. If any are reported they are asked which treatments they are or have received for these.

In addition to the standard questions, for the purposes of the studies presented here participants were also asked about recreational drug use and caffeine intake. Primarily, participants were excluded if they reported the presence of any sleep disorder, or current psychological disorder even if medicated. Those who regularly used recreational drugs were also excluded (see appendix II for full exclusion criteria applied to all studies, except the pilot study discussed later in this chapter).

3.1.2 Questionnaire assessment

Psychometric assessment is a key tool within any area of psychological research and is employed extensively throughout the work presented here. As the same constructs are measured in all of the main studies, it is prudent that the tools used to measure them are presented here and referred to in proceeding chapters (appendix III provides the questionnaire booklet that participants were given). Primarily, 3 constructs were of interest: neuroticism, emotion focused coping and conscientiousness. Scales were based on their ability to reliability measure these constructs, and independently from psychopathology. A further consideration was participant burden, so the brief version of certain scales was employed (such as the brief-COPE). Groups are constructed using the Ford Insomnia Responsivity to Stress Test (FIRST) score. The other measures represent independent variables or co-varying factors. Sleep scales were employed as a second check that participants were sleeping well, and not suffering from insomnia.

Ford Insomnia Response to Stress Test (FIRST): The relation of insomnia to stress has been evaluated using the FIRST [94], where subjects are asked how likely they are to have difficulty sleeping following nine different types of stressful situations- such as knowing they have a presentation to give the next day. Responses are recorded on a 4-point categorical scale (not likely, somewhat likely, moderately likely and very likely). Patients with high FIRST scores are categorized as vulnerable to insomnia, while a low FIRST score indicates resilient sleepers. Reliability of this 9 item scale is high (Cronabach's alpha = 0.83). Drake et.al.[137] show that those classed as vulnerable show a more pronounced

reaction to a small dose of caffeine prior to bed, as measured by latency to persistent sleep, relative to the vulnerable group. Thus supporting the validity of this questionnaire, but also showing that relatively benign stimuli can be troublesome for those who are predisposed. The utility of this scale in selecting those who are vulnerable or resilient to stress related sleep disruption will be discussed in more depth in light of the experimental findings.

Pittsburgh Sleep Quality Index (PSQI): The PSQI has been shown to have high validity and reliability (cronbach alpha of 0.83), and has been used extensively on various populations. Although not a specific diagnostic tool for insomnia, the PSQI has a sensitivity of 89.6% and a specificity of 86.5% for detecting sleep difficulty[138] The score obtained- global PSQI score- comprises 7 components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction over the last month. The questions are marked on a 1-3 Lickert scale, with 3 representing the extreme negative. A global score of 5 or greater is considered to indicate a poor sleeper. The scale was originally used in primary care setting in older adults, although has been shown to have moderate to high validity and reliability in other populations and has been used in populations similar to the one in this study [47, 139, 140]. The high sensitivity of the scale ensures that those scoring below the cut off are good sleepers, but does not provide a diagnosis of insomnia to be made, but rather 'poor sleep'.

Insomnia Severity Index (ISI): The ISI[141] is a 7 item scale assessing perceived sleep difficulty and perceived consequences of insomnia and level of distress regarding insomnia, the contents of which correspond in part to the diagnostic criteria of insomnia as according to the Diagnostic and Statistical manuals 4 (DSM-IV). Recent validation of the scale as a screening measure for insomnia, and as an outcome measure of treatment has recently been assessed by Bastien et.al.[142]. They report that the internal consistency of the ISI was 0.74 (cronbach alpha) and that it had moderate correlations with sleep diary data. It has also been demonstrated in the same paper that the ISI is sensitive to detecting changes in perceived sleep quality in response to treatment, and demonstrate a good convergence between subjective ratings of severity and clinician ratings. It also provides cut-off points, allowing to measure, as the name suggests, an understanding of

the severity of an individual's sleep problem. In this way, it provides a good compliment to the PSQI within the context of the studies presented within this thesis.

Perceived stress Scale(PSS): The PSS[143] is a self report measure consisting of 14 items which ask the participant to rate on a 5-point Lickert scale (from 0- never to 4, very often) how often they felt or thought a certain way over the past month in response to stress. A high score indicates an individual who perceives stressful life events as out of their control, and unpredictable. Looking at stress perception is important in the context of understanding stress reactivity and its interactions with personality, given the rationale outlined in chapter 2: that personality may impact on stress response due to an increase perception of stress. The test retest reliability is adequate at 6 weeks follow up. The Cronbach's alpha is reported by Drake et.al. as 0.84, 0.85 and 0.86 across their 3 initial samples. This provides a measure of stress perception, rather than stress-levels.

Brief-COPE: The brief-COPE[144] is a shortened version of the COPE inventory[145]. It consists of 14 scales each with 2 items (28 items in total). It is answered on a 4 point Lickert scale, to represent the extent to which an individual believes they use a certain strategy to cope with stress (1= I haven't been doing this at all to 4- I've been doing this a lot). It has been well validated for use in various populations experiencing different psychological and physiological conditions. The 14 scales can be grouped, allowing for comparisons between emotion and problem focused coping.

Depression Anxiety Stress Scale (DASS-21): The DASS-21 is the abbreviated version of the DASS-42 [146]. It is composed of three scales: Depression, anxiety and stress. Cronabach's alpha for each of these, respectively being 0.88, 0.82, 0.90, and 0.93 overall, thus demonstrating adequate reliability. It asks participants to respond on a 4 point Lickert scale according to how applicable each statement is to them (0 being 'does not apply at all' to 3 being 'applied to me very much, or most of the time').

NEO-ffi: The Neo-ffi [147]is a brief- 60 item version- of the NEO-PI-R-180 items. It is a measure of the five factor model of personality, scoring on the following domains: Neuroticism, extroversion, openness, agreeableness and conscientiousness. Each item is scored on a 6-point scale, with several items reversed scored. Two week test-retest reliability has been found to be relatively high (0.86 to 0.90 for the five scales)[148]. The

internal consistency is reported as ranging from 0.68 to 0.86[147]. The NEO provides a more specific conceptualisation of personality compared to, for example, the Minnesota Multiphasic Personality Inventory. It has been used extensively in understanding the relationship between personality and stress responses, and so is used here because it is a psychometrically sound tool, and will allow a certain level of comparison between the experimental work here and other published data. Further to this it provides an overview of personality based on theoretical constructs, in a way that does not infer psychopathology, such as the MMPI might.

Ruminative response scale of Ruminative Style Questionnaire (RSQ): The Ruminative Responses Scale of the RSQ [149] includes 22 items asking people to rate to what degree they *generally* indulge in specific behaviours or thought process when feeling 'sad, blue or depressed', on a scale from 1 *(almost never)* to 4 *(almost always)*.Items relate to thought processes that are self focused, symptom focused or consequence/ cause focused. Nolen-Hoeksema reports the alpha coefficient to be to be 0.90 and the test-retest reliability at 1 year follow-up to be 0.67. It has also been suggested that this scale comprises 2 separate components of rumination: reflection and brooding and that high levels of either can have differential effects on treatment outcomes for depression[150])The Response styles questionnaire itself has adequate predictive validity [149]. Recent work in insomnia has suggested that rumination maybe more important in understanding and treating the insomnia population than worry, although this needs further investigation [151]

Penn State Worry Questionnaire (PSW): The PSW[152] is a 16 item scale asking participants to rate how typical each item is of them, rating from 1 (not typical of me at all) to 5 (very typical of me), with some items reversed scored such as 'I never worry about anything'. In the initial validation of the scale it was demonstrated that worry is a separate construct from depression or anxiety and that the scale itself did not overlap with other pre-therapy measures (STAI, BDI and the cognitive somatic anxiety questionnaire). It has a high internal consistency (coefficient alpha= 0.93 and 0.94). The test-retest reliability has been shown to be high at one month follow up (r (46) =0.93). Worry and rumination are suggested to be different constructs, with worry being defined as concern over the future, and rumination being concern over past failures and losses[153]. It is suggested that worry and rumination may differentially affect sleep. It is therefore important to capture both when assessing vulnerability factors [151].

3.2 Competencies: MRI, programming and sleep measurements

As alluded to previously in this chapter, a small pilot study was carried out prior to commencing a larger MRI based study (see chapter 6). The main purpose of this was firstly, to gain insight into the use of MRI and subsequent data analysis. Secondly, the paradigm employed in the larger MRI study is novel to the sleep field, and so it was used on a small number of patients to ascertain the extent to which it did lead to differential brain activation in insomnia patients versus good sleepers, before being employed in a population of good sleepers who have been classed as either vulnerable to stress related sleep disruption or resilient. Methods and findings will be outlined briefly here.

3.2.1 Aims:

To assess the extent to which those suffering with Psychophysiological Insomnia (PI) show increased activation in the insula in response to anticipation to a mild stressor.
It is hypothesised that the PI group will show grater activation of the insula in response to an anticipatory cue, and greater activation in areas responsible for successful task completion.

3.2.2 Methods:

3.2.2.1 Participants:

Participants were recruited through the University of Glasgow Sleep Centre, responding to posters placed in local G.P offices and community buildings such as local libraries. 10 participants were recruited, 5 good sleepers and 5 PI. 4 were excluded due to excessive movement in the scanner, rendering their data un-analysable. This left a sample of 3 insomnia patients and 3 good sleepers.

3.2.2.2 Questionnaires:

Participants completed a battery of psychological questionnaires, however given the small sample these were not analysed. Sufficed to say that no-one scored highly enough on the Hospital Anxiety and Depression scale (HADS) [154, 155] to suspect that they had a

comorbid condition. The PI group all scored above 15 on the ISI, and the good sleeping group scored as good sleepers.

3.2.2.3 The Paradigm:

A stroop task was employed. This was programmed using e-prime 2.0. The stroop task involves showing participants a word, printed in colour. The task is to identify the colour the word is printed in and ignore the words meaning. Words used are the same as in the bigger study and were either sleep related, anxiety related, neutral or positive in valence and had been previously validated (insert refs from chapter 6). Responses were made using the thumb and index finger of each hand, with each button corresponding to a particular colour. Participants were given an opportunity to practice responses, until they felt comfortable enough to continue with the scan.

Words would be presented on the screen for 1700ms with a 600ms fixation point between words. A siren would sound randomly and the task would speed up, requiring a faster response. Words were presented for 300ms with a 100ms fixation. It would then return to normal. This would repeat. The siren was intended as an anticipatory cue to the stressor.
Image acquisition was carried out on a Siemens 3T scanner, with a TR of 2 seconds.

3.2.3 Analysis:

Analysis was carried out using SPM8. Given the small sample size, uncorrected p-values are reported. Data were first pre-processed to account for roll pitch and yaw movement, and images were normalised to a standard brain image provided by SPM. This accounts for differences in brain shape, size and location of structures. A Gaussian filter of 4x4x4 was applied, smaller than the SPM default, reflecting the difficulty of measuring insula activity.

3.2.4 Results:

It was found, comparing speeded and normal conditions between groups, that the PI group show greater activation in the temporal, parietal and occipital lobes and around

limbic areas in the speeded (stressful) condition relative to good sleepers(global maxima t= 12.96, p< 0.001 [-30 50 30]) (figure 1)

Region of Interest (ROI) analysis, carried out using MARSBAR, revealed the PI group to show greater activation of the insula during anticipation relative to good sleepers.

3.2.5 Conclusions:

Obviously, the sample here limits any real conclusion that can be drawn from this study and it is worth highlighting again that the point of including this here is to demonstrate steps that were taken to pilot the experimental paradigm and gain a certain amount of competency with fMRI acquisition and analysis.

What the results do suggest however is that the paradigm is sufficiently stressful to induce differential brain activation in PI versus good sleepers, and that this activation relates to an increase in activity in areas needed for successful completion of the task, suggesting that the PI need to work harder to complete the task. The results from insula analysis suggest that the PI group show a stronger anticipation to stress as hypothesised, and the task seems to be able to elicit this.

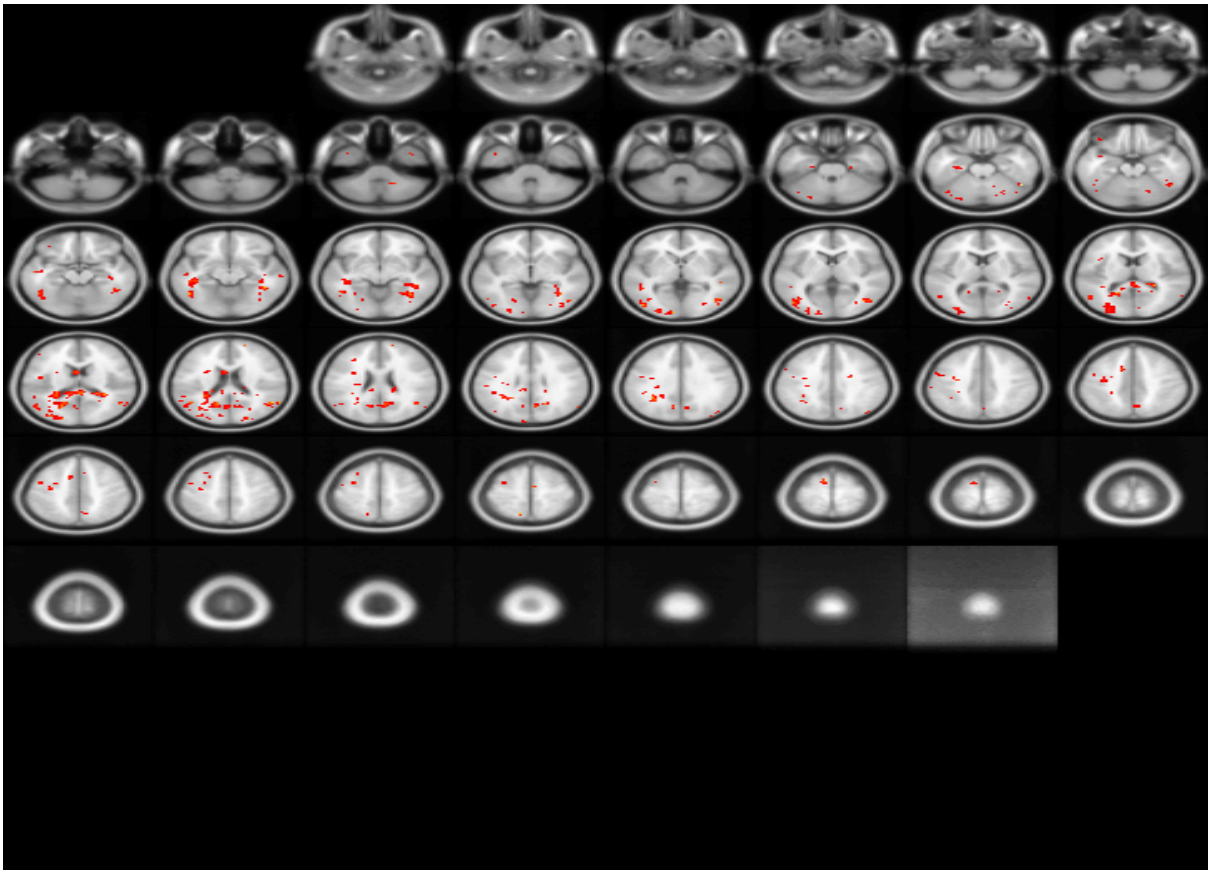


Figure 3 1 Brain activation in the insomnia group> good sleeping group.
Red represents areas of greater activation in the PI group relative to good sleepers during the speeded task

4.1 Introduction

As delineated in previous chapters, there is strong evidence to suggest that certain individuals are more vulnerable to stress-related sleep disruption than others (Bonnet and Arand [156] for example). Drake et.al.[94] have devised the Ford Insomnia Responsivity to Stress (FIRST) scale, which has been shown to accurately separate those who demonstrate disrupted sleep in response to stress from those who do not.

Such vulnerability is due, probably, to various factors including genetic polymorphisms which seem to induce a more sensitive stress response, or a predisposition to arousal[81], personality[104] and coping style [129]. Williams and Moroz [118] have shown that during a period of transition, high levels of neuroticism predict sleep disruption as a result of daily hassles, whilst conscientiousness seems to be protective, especially when coupled with low neuroticism. Sadeh et.al.[129] demonstrated that emotion focused coping predicts sleep disruption as measured by sleep-diary and actigraphy in the week prior to an important interview. However, there has been no work which aims to systematically define this vulnerable phenotype with consideration for all of these various domains: physiological stress and how this maybe mediated by personality and coping style to make an individual more likely to experience disturbed sleep.

In terms of stress-reactivity, the hyperarousal theory of insomnia (for a review see Riemann et.al[55]) posits that the insomnia population show increased arousal relative to good sleepers, not just at night time but throughout the 24 hour cycle. One line of evidence for this theory points to the hypo-pituitary-adrenal axis (HPA). Vgontzas et.al.[58, 59] have demonstrated differential cortisol profiles between insomnia sufferers and good sleepers, throughout the 24h cycle but especially in the first half of the evening, which implies that the HPA is more active in those sleeping badly, indicating a sensitive or over-active stress response. Based on the hyperarousal theory and the evidence that exists to support the notion of a vulnerable phenotype it is hypothesised that one of the defining characteristics may be a more sensitive physiological stress response, or a vulnerability to physiological hyperarousal, rather than a vulnerability of the sleep system per se. This would mean that vulnerability is conferred due to a more sensitive stress system, reacting non-commensurate to the stressor. Further to this, it is well established

that mood disorders are related to HPA dysregulation[157], and one of the most consistent findings in psychiatric disorders is hypercorticolism[158]. Given the close relationship between insomnia and mood disorders, particularly the idea that insomnia is the strongest predictor to new onset depression[159], it can readily be hypothesised that the common thread may be HPA dysregulation, which predisposes to insomnia, opening the doors to the associated sequelae.

Further to this certain personality factors seem to play a role in mediating biological stress responses (as measured by cortisol secretion). Oswald et.al.[160] demonstrated, using the Trier Social Stress Test (TSST) - a robust, laboratory based psychosocial stressor[161] -, that cortisol responses varied according to personality traits but also gender. Women who are high in neuroticism (i.e. high in negative affect) show a blunted cortisol response. Men with low extroversion also show a blunted cortisol response. Overall, openness- which generally represents good psychological well-being- was associated with a lower cortisol response. Such work serves to underline the value of assessing personality when considering stress response. In a sample of 104 working men, Nater et.al.[124] demonstrate that neuroticism is associated with increased cortisol output throughout the day, and conscientiousness with decreased cortisol output, but only if positive affect is also present.

Based on the evidence to date, reviewed briefly here and in more detail elsewhere in this thesis, it is hypothesised that those who appear to be vulnerable to stress related sleep disruption as predicted by the FIRST will show greater stress reactivity as measured by salivary free cortisol in response to the TSST. This will be mediated by personality and coping style, whereby neuroticism and emotion focused coping predict higher cortisol response. It is further hypothesised that conscientiousness will mediate the relationship between neuroticism and cortisol response. The aim here is to comprehensively describe the vulnerable phenotype from both a psychological and physiological stance. Other psychological variables known to characterise the insomnia population, such as worry and rumination will also be measured in order to conjecture on whether such constructs pre-exist a complaint of insomnia, or are encouraged by it.

In order to determine the extent to which these factors predict disrupted sleep in response to stress, participants will be followed up during a self-defined stressful and

normal week-2 weeks in total. It is hypothesised that the vulnerable group will show greater increases in sleep disruption during the stressful week compared to the resilient group and that this will be predicted by cortisol responses to the TSST (stress-reactivity), neuroticism and coping style. Again, it is hypothesised that conscientiousness will be protective.

4.2 Materials and Methods

4.2.1 Participants:

Participants were recruited from undergraduate psychology classes (n=50). They were all screened using the University of Glasgow Sleep Centre screening form (appendix I), and based on this, reported being good sleepers. As we were looking for good sleepers only, in order to assess vulnerability prior to any period of insomnia, anyone reporting insomnia symptoms or symptoms of another sleep disorder were excluded. Participants who reported a past episode of insomnia lasting more than 1 month were also excluded. Other psychological disorders or disorders of the central nervous system were excluded, as were individuals on any medications known to affect H-P-A regulation. Given that we were recruiting from an undergraduate sample, only people who were of a 'typical' student age were included (17-25 years) to prevent effects of age influencing the data. Those successful on screening were invited to the Psychology department to take part in an experiment investigating extraversion (in order to hide the true meaning of the experiment. See appendix IV for information sheet given to participant, and appendix V for consent form). Participants then completed the TSST, in which the outcome measure was salivary free cortisol (SFC). Ten were excluded for scoring too high on sleep measures and 6 were excluded due to insufficient saliva for analysis [n= 34; 18=female; average age= 21.1 (SD= 1.5) (table 4 1)]. Participants were paid for participation.

	Age (SD)	*Gender (no. female (% female))*
Resilient	21.12 (1.73)	7 (38.9)
Vulnerable	21.15 (1.46)	8 (50)

Table 4 1 Mean age (standard deviation in parenthesis) and gender (number and percent female) for resilient and vulnerable group

Participants completed a series of psychometrics upon completion of the TSST, to assess coping style, personality, rumination, worry, stress anxiety and depression. These questionnaires have been outlined in chapter 3 and can be viewed in appendix III.

4.2.2 The Trier Social Stress Test:

As already mentioned, the TSST is a robust laboratory based stressor, comprising of 2 components: a speaking task and a math task. In this way it taps into different kinds of psychosocial stress: social anxiety and performance anxiety. It has been used on various populations such as the depressed and anxious [162] and to validate stress management techniques such as compassion meditation[163], whereby the physiological response to the TSST has been shown to decrease in those trained in meditation. This has also been shown for mindfulness based stress management techniques [164]. Such works highlight the utility of the TSST as a lab based stressor, and more importantly the idea that physiological stress response can be mediated by psychological inputs.

4.2.2.1 TSST Procedure

On arrival the participant is welcomed by the experimenter and taken to experiment room 1 where they are asked to relax. After a 10 minute period a saliva sample is taken. In order to collect the salvia the participant is asked to put a swab under their tongue- the optimal positioning for gathering SFC- and told to keep it there for 2 minutes (the

experimenter times this). This time should allow optimal absorption of saliva.

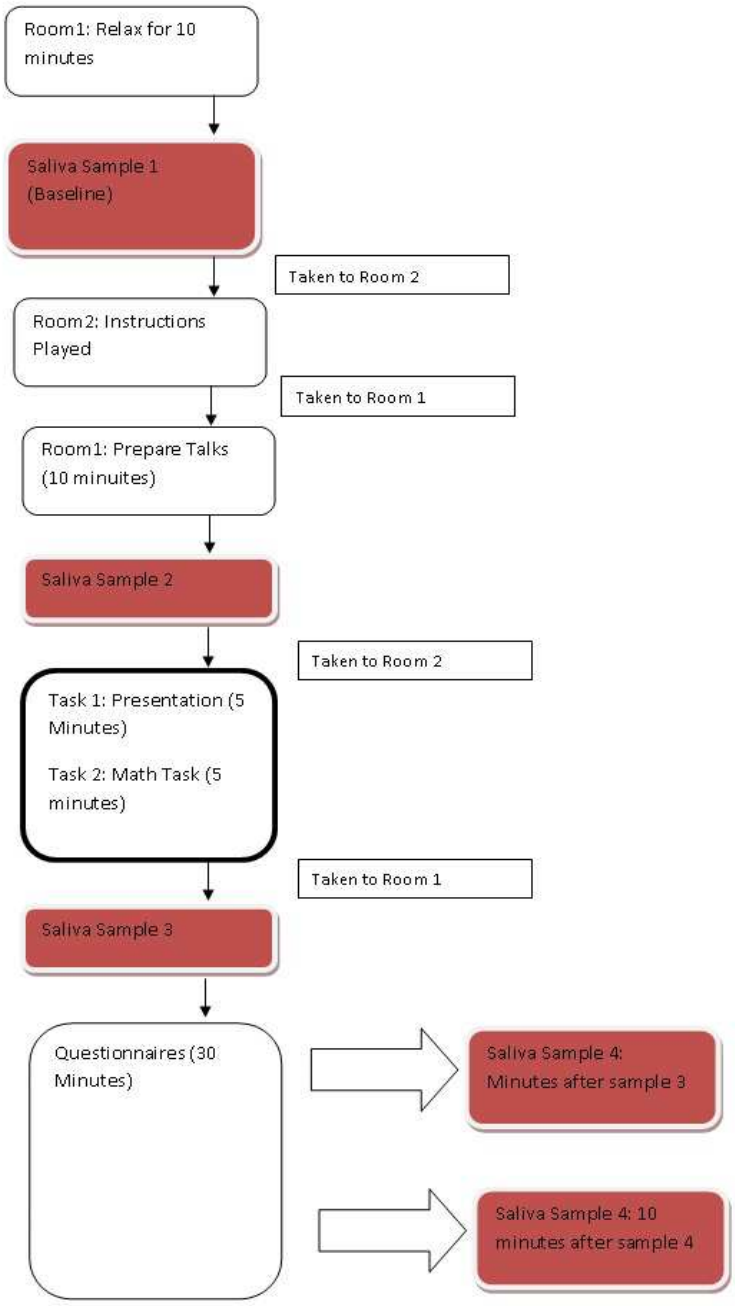


Figure 4 1 Flow Chart of TSST

The participant is then taken to experiment room 2, where they were faced with 2 interviewers. These were experimental confederates taking part in the study on a voluntary basis-, who are instructed to remain impassive throughout the study- i.e. not engage in any positive way with the participant. They are also instructed to maintain eye contact with the participant at all times, while taking notes. Appendix VI provides instructions that were given to the confederates. They also ran through some dummy trials in order to learn the flow of events. The participant also sees a laptop set up with a

camera, and a stop-watch. At this point the instructions are played to the participant over the laptop: they will have to deliver a speech in as though presenting at a job interview for which they are given 10 minutes to prepare, and informed that a second task will follow. They are asked to make a believable impression as the panel may ask follow up questions. They are also informed that they will be recorded throughout the talk for further analysis of body language and voice-pitch and continuity and that the panel are expertly trained in body and voice analysis- see appendix VII for transcript of recording played to participants. After instructions they are taken back to room 1 where they are given 10 minutes to make notes on their speech. They are informed in the recording that these notes are not to be taken into the interview room, but merely to allow the participant to organise their thoughts. After this 10 minute period a second saliva sample is taken. During the speech the panel are instructed not to engage with the participant as long as they are talking fluently. If there is a pause of 20s or more within the 5 minutes they are to ask questions such as 'What qualifies you for this position?' After the five minute period, one panel member informs the participant about the next task: to count backwards from 6033 in blocks of 13. If a mistake is made they must restart. This task lasts 5 minutes or until the participant reaches 0. The participant is then led to room 1 where another saliva sample is taken. At this point they are left to complete the questionnaires and saliva samples are collected every 10 minutes- 5 samples in total. Lastly the participant is debriefed and released. See figure 4 1 for flow chart of events.

Saliva swabs were stored at -20^{o}C, in an on-site refrigerator. Although cortisol is a relatively stable hormone, keeping its integrity for several hours at room temperature, it is advisable that samples are cooled straight away to ensure accurate analysis, especially if samples are to be stored until the end of a study. SFC was assessed by Salimetrics, LLC. using time-resolved fluorescence assay.

4.3 Analysis:

Data were first inspected for normality of distribution, using kurtosis descriptive statistic. All data appeared to be normal- see appendix VIII for values for each variable. Therefore parametric tests have been used. Correlation was then employed to assess potential overlap between psychometric constructs and to provide initial indication as to which variables may be related to vulnerability to sleep disruption, in the sample as a whole

initially and then within groups. Independent t-tests were carried out to assess differences in psychometric variables between the groups.

In order to understand the cortisol output in terms of change over time- as an indication of stress-reactivity- area under the curve was calculated for each participant using trapezoidal integration. This gives one outcome measure for the change in cortisol levels over the 5 time points. AUC with respect to ground, with respect to baseline and with respect to increase were calculated [165] (figure 4 2). AUC provides an index of change, allowing analysis of cortisol change over time without many multiple comparisons, and so conserves power.

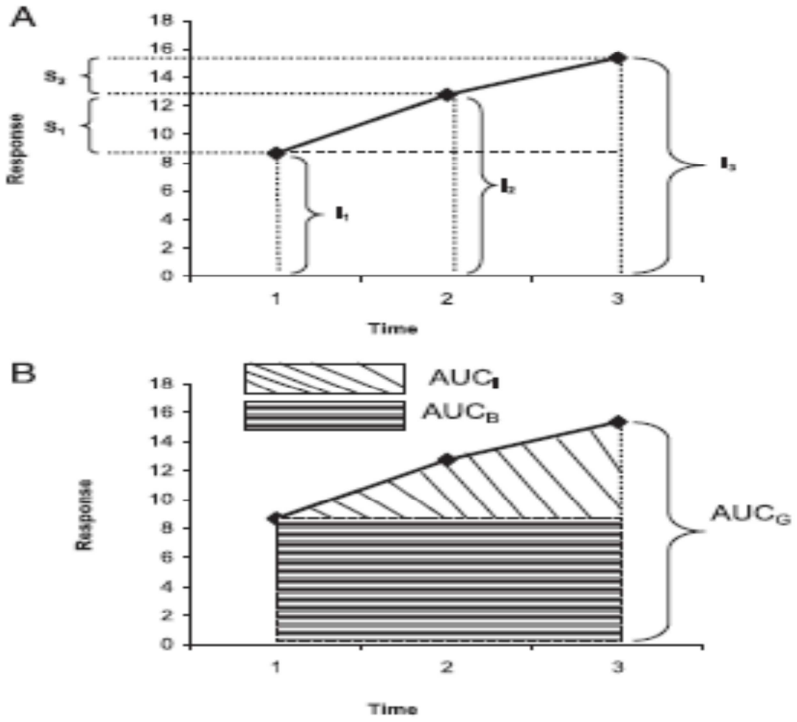


Figure 4 2 .Graphic depiction of AUC.
Taken from Fekedulegn et.al. (2007). Graph A represents repeated measures of different magnitude or intensity at each time point (I1, I 2, 13), and changes in the response over time, or sensitivity (S1, S 2). Graph B represents the 3 kinds of AUC.

Independent sample t-tests were carried out initially to investigate difference between groups in AUC and psychometrics. A mixed-design general linear model analysis was then computed to assess interactions between cortisol output and psychometrics. Based on the visual representation of the data individual time-points were also investigated. Exact p-values are reported with effect sizes reported as Cohen's *d*.

4.4 Results:

Two groups were created post-hoc based on FIRST scores: A vulnerable group (n= 18) and a resilient group (n=16). Groups were created based on the median score for the FIRST, which was 19.5 for this sample, in practice meaning that anyone scoring 19 or below was classed as resilient and anyone scoring 20 or above was classed as vulnerable. This is in line with published figures, reporting a median of 20 in a sample of 104[94]. Resilient and vulnerable groupings were calculated in that sample via use of the median also.

4.4.1 Psychological Variables

4.4.1.1 Correlation:

Bi-variate correlational analysis was carried out over the whole sample primarily to indicate which psychometric variables showed a relationship with FIRST scores. Further, to indicate if there was any strong overlap between psychological constructs measured by the psychometrics. It is important for further analysis that one can be sure of the independent nature of the proposed constructs when considering their relationship with the FIRST and their potentially mediating effects on physiological stress response. Scatter-Plots depicting significant correlations can be seen in appendix IX. The Full correlation matrix can be seen in appendix X.

It was found that FIRST score correlated significantly with PSQI ($r(31)=.36$, $p=.034$); DASSS ($r(31)=.47$, $p=.005$); NEON ($r(31)=.49$, $p=.003$); RUMD ($r(31)=.43$, $p=.01$); and WORRY ($r(31)=.473$, $p=.005$), and showed a trend toward RUMR ($r(31)=.37$, $p=.06$). It is worth noting here that the correlation with RUMR indicates that the critical r value is .36, meaning that correlations below this value which may be meaningful will not be considered so in this analysis.

All correlations are representative of weak to moderate associations. From the correlation matrix, it can be seen that where there is correlation between constructs, for example neuroticism and PSS, that these associations are weak to moderate (r values between .3 and .7). While this demonstrates a relationship between the variables of interest, it does suggest that they have substantial unshared variance.

4.4.1.2 Between-group analysis

Figure 4 3 shows the between group differences on the different psychometric scales. Independent sample t-tests were calculated to assess the difference. It was found that the vulnerable group scored significantly higher on the neuroticism subscale of the NEO-ffi (t (32)= -2.912, p=.006, *d=.99*); the depressive thinking subscale of the RSQ (t (32)=-2.389, p=.024, *d=.81*); the stress subscale of the DASS (t(32)= -3.015, p=.005, *d=1.03*); the PSW (t(32)= -3.321, p=.002, *d=1.13*) and on both the emotion (t(32)=-2.375, p=.024, *d=.82*) and problem focused coping (t(32)= -2.399, p=.022, *d=.83*) subscales of the brief-cope. Table 2 shows the averages and standard deviations. Cohen's *d* in all cases represents a large effect size, where *d*>.79.

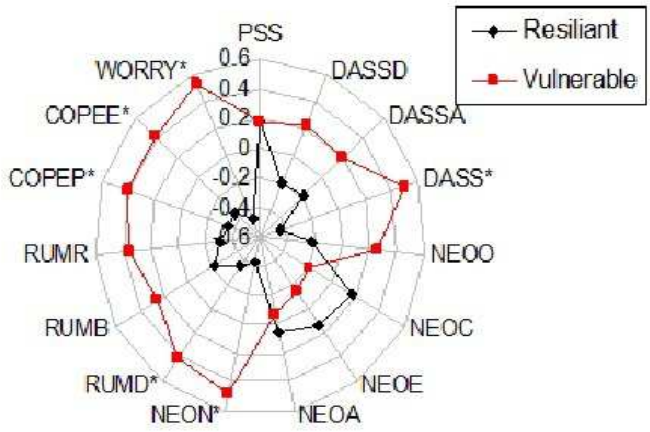


Figure 4 3 'Vulnerable' Vs 'Resilient' on psychometrics.
Abbreviations: PSS= Perceived Stress Sale; DASSD=Depression; DASSA=Anxiety; DASS=Stress; NEO=openness; NEOC=Conscientiousness; NEOE=Extraversion; NEOA=agreeableness; NEON=Neuroticism; RUMD=Depressive thinking; RUMB=Brooding; RUMR=reflective thinking; COPEP=Problem focused coping; COPE= Emotion focused coping

Scale	*Resilient (SD)*	*Vulnerable*
PSS	12.5 (7.1)	14.75 (6.0)
DASSD	4.00 (4.5)	6.00 (5.1)
DASSA	3.33(3.6)	4.63 (3.2)
DASSS	7.11 (4.8)	13.00 (6.5)
NEOO	50.11 (5.8)	53.00 (6.2)
NEOC	51.61 (8.6)	49.56 (5.0)
NEOA	53.5 (9.2)	52.50 (7.7)
NEON	29.29 (7.6)	38.75 (11.0)
RUMD	19.00 (5.5)	24.38 (7.6)
RUMB	8.39 (3.6)	10.19 (3.9)
RUMR	9.06 (3.1)	11.44 (3.9)
COPEP	10.00 (3.0)	12.44(2.9)
COPEE	11.00 (4.4)	14.31 (3.7)
WORRY	38.33 (7.7)	49.06 (11.0)

Table 4 2 Mean and standard deviation on the psychometric scales for each group. Highlighted in red are variables which differ significantly (p<0.05) between groups.

4.4.2 Cortisol

If more than 2 time-points were missing from the cortisol data then the participant was excluded. Where 2 or less were missing these values were replaced by the group mean for this time point. A total of 5 time-points were replaced in this way.

In order to assess differences on stress reactivity between group's independent t-tests were carried out on the 3 AUC values. There were no significant differences between groups in terms of AUC with respect to ground (t (32) =1.721; p=0.095, Cohen's d= 0.6) or AUC with respect to increase (t (32) =.25, p=.801) (table 3). GLM mixed design analysis showed a significant effect of time (F (4, 1) =7.912, p=.003) but no significant group by time interaction. Individual time points were then investigated (figure 4), using independent samples t-test. It was found that the vulnerable group had significantly higher SFC at time point 1 and 2 compared to the resilient group (t (32) = 2.641, p= .013 and t (32) = 2.662, p=.012 respectively), and this was shown to have a large effect (d= .92 and .93 respectively). There was no significant difference at any other time point. Appendix XI provides supplementary data, graphing the SFC response in the 10 poor sleepers which have been excluded from this analysis, but which may be of interest to the reader, and will be considered in the discussion.

	AUCg (SD)	*AUCi (SD)*
Resilient	264.36 (135.5)	42.79 (104.67)
Vulnerable	195.16 (102.93)	51.21 (86.49)

Table 4 3 AUC with respect to ground and increase for each group. Standard deviation in parenthesis

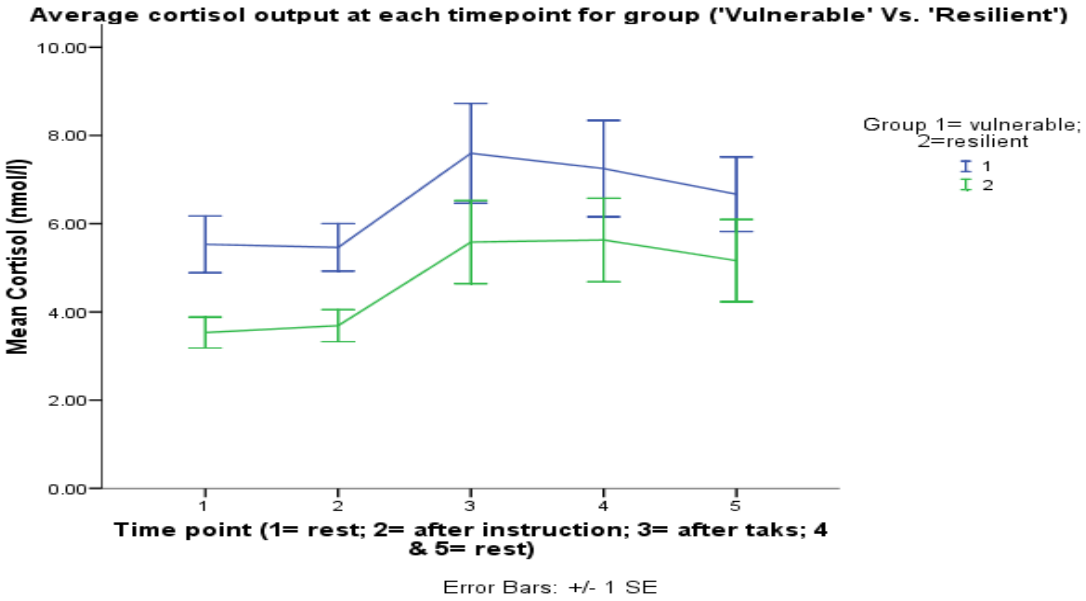


Figure 4 4 Average Cortisol out-put at each time point for each group Significant between group difference at time 1= before instruction and time 2= after hearing instructions for task and preparing. Time points 3-5= after task. Bars represent 1 standard error.

Step-wise Regression analysis was carried out in order to assess which factors contributed to the significant difference in baseline cortisol measure (table 4 4: regression output). Based on the between group differences in the psychometrics and our initial hypothesis- that greater neuroticism, low conscientiousness and greater EFC would lead to higher stress reactivity- NEON, NEOC, worry, DASS, RUMD, COPEP and COPEE were all entered into the model. The only covariate to survive the stepwise regression was NEOC. The regression co-efficient values suggest that as conscientiousness increases, so too does SFC at T1.

Within group correlations were then conducted, to get an insight into what factors conscientiousness is associated with, in each group. Frequency analysis was also conducted in order to get an idea of the distribution of high C high N, low C low N etc

between the groups. In the resilient group conscientiousness did not correlate significantly with any other variable. Within the vulnerable group conscientiousness significantly correlated with cortisol output at time point 1 and 2 (r (15) =.51, p=.046; r (15) =.69, p=.003, respectively) (Appendix XII shows scatter-plots depicting these relationships). Chi-square analysis reveals no significant difference in combination of conscientiousness and neuroticism distribution between groups (x^2 (1, *N* = 32) = .513, *p* = .637).

		B	*SE B*	Beta
Step 1				
	constant	7.52	1.16	
	Group	-2	0.76	-0.42
Step 2				
	Constant	1.24	2.08	
	Group	-1.71	0.73	-0.36
	NEOC	0.12	0.53	0.39

Table 4 4 Regression co-efficients.

4.5 Part 2: Follow-up

Upon completion of the TSST participants were invited to take part in a follow up study, to assess the degree to which sleep was disrupted in response to real life stressors, and if this varied by FIRST grouping. It was hypothesised that those who score higher on the first will show an increase in number of insomnia symptoms during the stressful week, compared to the normal week. It was further hypothesised that this would be mediated by neuroticism, conscientiousness, EFC and stress-response as measured by cortisol.

4.5.1 Methods:

Participants were given 2 weeks of sleep diaries, and instructed to fill these out during 'working week times'- i.e. Monday to Friday. These diaries are the standard University of Glasgow Sleep Centre diaries (appendix XIII). The participant is instructed to fill the diary

in as soon after wakening as possible. They are asked every morning about their sleep the night before. It assesses sleep parameters such as how long it took to fall asleep, how many awakenings they had, when they went to bed and got out of bed in the morning and how many hours sleep they achieved, and also asks participants to rate quality of sleep in terms of how tense they felt in bed and how satisfied they were with the previous night's sleep.

Participants were instructed to fill the diaries out during a 'normal' week. That is to say a week in which they do not anticipate any unusual stressors such as increased work-load, presentations, exams etc. and again during a week which they anticipated to be more stressful than usual. This could be a week leading up to exams or in which they had course deadlines. In order to assess that both weeks were perceived to vary in stress, 3 questions were added to the sleep diary:

'**In the last week how often have you felt nervous and/or 'stressed'?**

0 1 2 3 4

Not at all Fairly Often Very Often

1. **Have there been any events in the last week which have caused increased stress?**

   Yes/ no

2. **If so, what?**

4.5.2 Participants:

A total of 18 participants returned the sleep diaries. Given that all participants from part one agreed to take part, this represents a 36% drop out (6= female; average age 20.93 (SD= 1.33)). Reasons for drop out were not generally given, but when provided it was due to forgetting to complete the diary. Four were excluded for scoring too high on the PSQI and ISI (given the nature of the study, the second part commenced before responses to questionnaires in the first part had been scored) Final n= 14; 6 vulnerable.

4.6 Analysis:

Due to the small sample size and the non-normal distribution of the data (Kurtosis and skew in appendix XIV), Mann-Whitney analysis is carried out. Standard deviations are reported. This is not conventional for Mann-Whitney data, but may be more meaningful to the reader. Median and interquartile range values can be found in appendix XV.

4.7 Result:

In order to test that the stressful week was indeed considered more stressful than the normal week, a Mann-Whitney test were carried out on subjective stress ratings between the weeks. Results showed both groups subjectively rated week 2- the high stress week- as significantly more stressful than week 1 ($U= 21, p=<0.05$ and $U=36$, $P<0.05$ respectively). There were no significant differences between the groups on stress ratings for either week and no significant difference in change in stress scores between the groups. Without exception the reported stressor was increased workload.

As would be expected in a sample recruited as good sleepers, there were no significant differences in sleep parameters- SOL, WASO, number of awakenings, TST, TIB or SE in week 1.

Number of insomnia symptoms was also calculated for each participant for each week. A symptom was counted if:

SOL≥30min

WASO≥30 min

These parameters are based on Edinger et.al.'s Research Diagnostic Criteria [166]. A score of 1 was given for a particular night if either SOL, WASO or both met this criteria, meaning a maximum of 5 and a minimum of 0 were the possible extremes for each participant. Calculating number of symptoms will give an insight into the extent to which sleep is disrupted, in the absence of a diagnosable disorder.

During the high-stress week there is a trend toward number of awakenings to be greater in the vulnerable group ($U= 36.5$, $p=0.099$), and SE to be decreased ($U=11.0$, $p=0.093$).

The vulnerable group show significantly increased change score in number of symptoms from week1 to week2 compared to the resilient group (U=39.0, p<0.05) (figure4 5). No other change scores differed significantly. Descriptive statistics for the sleep variables are shown in table 4 5 and figure 4 6 (SOL and WASO). Change score in sleep variables are represented in figure 4 7. In terms of psychological variables (table 4 7) the vulnerable group were significantly higher in all subscales of the DASS (DASD: U= 42, p<0.05; DASA: U=4 40.5, P<0.05; DASS: U=39.5, p<0.05); the reflective thinking subscale of the rumination scale (U= 41, P<0.05) and in neuroticism (U= 76.5, P<0.01). No other variables differed significantly. The groups also did not differ significantly in their responses to the TSST, either on individual time points or AUC (table 4 6). Due to the small sample, and only having 2 groups data are not corrected for multiple comparisons.

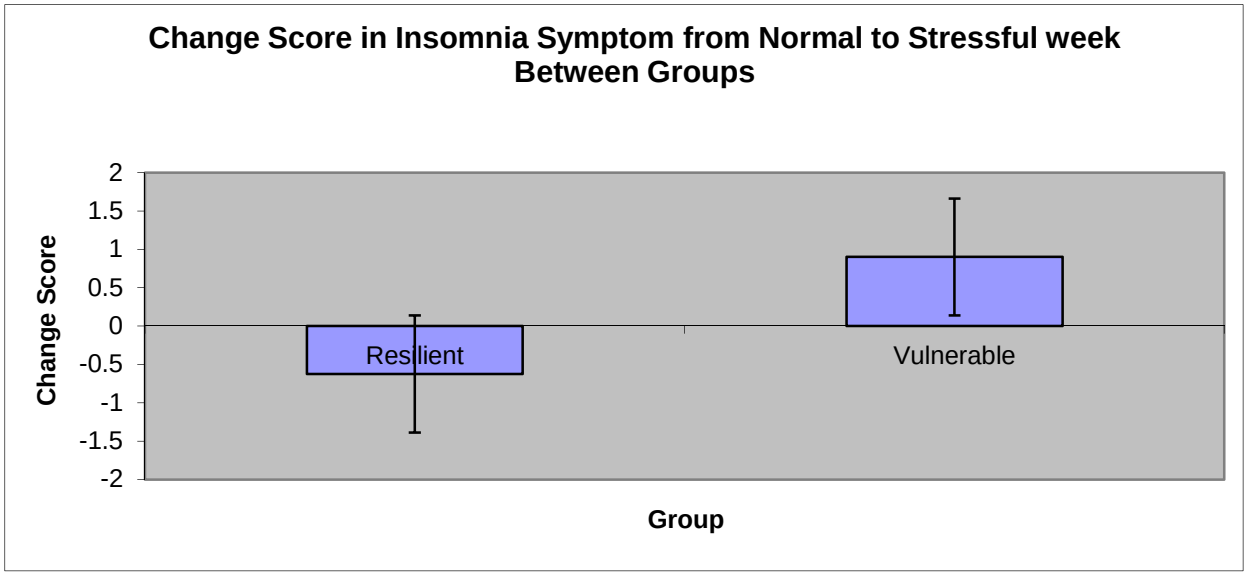


Figure 4 5 Average change score in insomnia symptoms between weeks, showing decrease in the resilient group and increase in the vulnerable (U=66.0, p<0.05)

	Sleep Paramaeters: Means (Standard Deviation)					
		SOL	*WAKENING*	*WASO*	*TST*	*TIB*	*SE*
Normal Week	*Resilient*	15.28 (8.89)	0.3 (0.34)	6.9 (10.53)	487.3 (49.28)	547.70 (73.30)	89.66 (9.00)
	Vulnerable	14.16 (9.91)	0.48 (0.32)	5.96 (5.33)	482.74 (51.51)	542.47 (57.86)	89.17 (5.55)
Stressful Week	Resilient	13.75 (7.54)	0.3 (0.45)	2.625 (3.87)	450.175 (29.55)	493.525 (45.79)	91.965 (6.60)
	Vulnerable	24.5 (23.79)	0.78 (0.60)	13.98 (17.50	424.14 (60.19)	490.14 (78.15)	86.909 (4.30)

Table 4 5 Average Values on Sleep Diary Variables for Normal and Stressful Week for Each Group (S.D.)

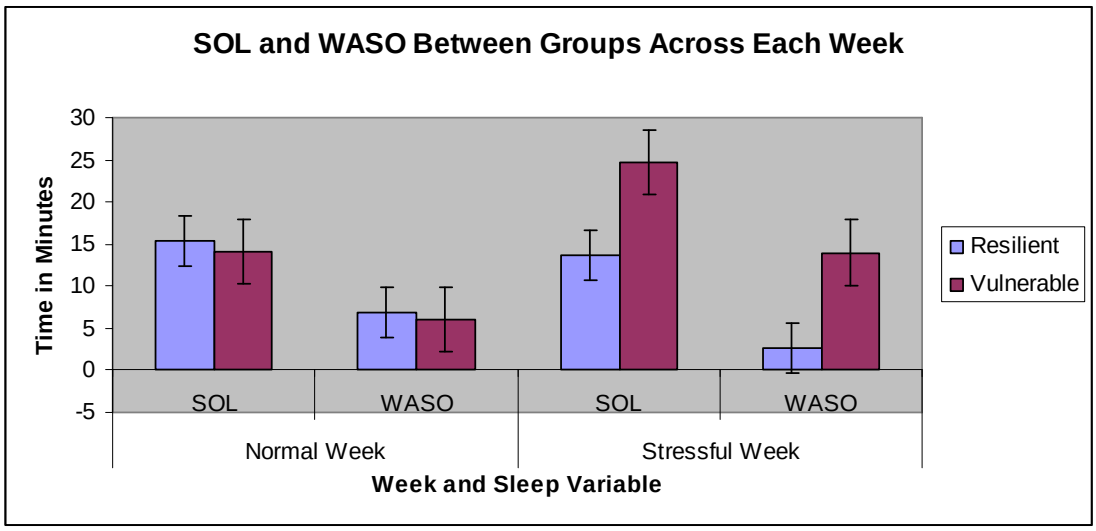


Figure 4 6 Average SOL and WASO between weeks between groups.
No Significant differences. Bar represents 1 SE

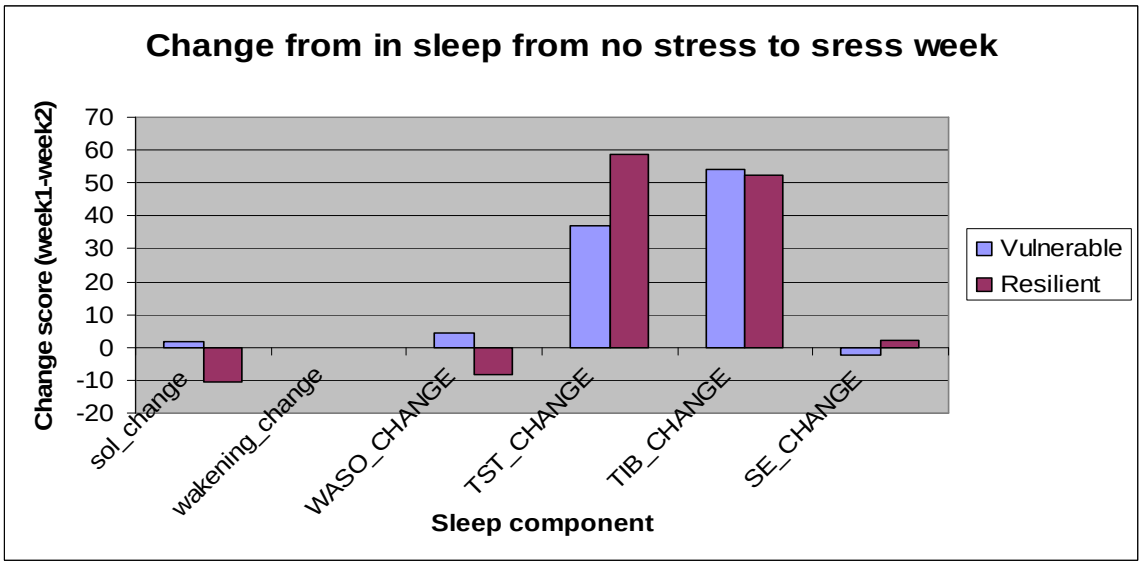


Figure 4 7 Change in sleep variables between normal and stressful week

The symptom change score correlates significantly with cortisol at time one (r= 0.55, p<0.05), and AUCg (r=-0.622, p<0.05). The amount of variance accounted for here is quite large, and so caution should be applied to the interpretation of such results, given the small sample. It is possible that these represent a type II error.

	T1	*T2*	*AUCg*	*AUCi*
Resilient	4.98 (2.55)	5.34 (2.24)	295.45(125.01)	79.28 (100.89)
Vulnerable	3.40 (1.43)	3.44 (1.56)	175.20 (100.45)	39.11 (63.92)

Table 4 6 Descriptive statistic for salivary free cortisol between the vulnerable and resilient group

Scale	*Resilient (SD)*	*Vulnerable*
PSS	9.50 (4.14)	15.13 (7.95)
DASSD	0.67 (1.03)	6.75 (6.14)
DASSA	1.33 (2.42)	5.50 (3.16)
DASSS	6.00 (3.10)	14.25 (8.58)
NEOO	45.33 (6.63)	55.25 (6.71)
NEOC	54.50 (9.87)	47.25 (9.82)
NEOE	59.00 (4.43)	49.75 (5.15)
NEOA	56.17 (6.49)	47.37 (7.25)
NEON	35.33 (7.66)	41.50 (13.15)
RUMD	17.5 (6.75)	24.13 (6.15)
RUMB	7.67 (3.08)	11.00 (4.38)
RUMR	7.17 (2.32)	12.13 (4.64)
COPEP	9.83 (3.19)	13.00 (2.98)
COPEE	11.17 (5.56)	15.13 (3.04)
WORRY	41.00 (5.69)	47.25 (12.98)

Table 4 7 Mean and Standard Deviation for Psychological variables for follow up sample

4.8 Discussion

Autonomic arousal is thought to characterise the insomnia population, not just at night but throughout the 24h cycle [55]. Vgontzas et.al. [58, 59] have supported this notion, demonstrating increased HPA activity, as assessed via cortisol output, to be higher in a group of insomnia patients compared to controls. Based on this idea coupled with the fact that a predisposition to insomnia has been posited to exist, it was hypothesised that those vulnerable to insomnia would demonstrate increased stress reactivity- increased change over time in SFC- to a laboratory based psychosocial stressor. This then is a precursor to hyperarousal. The FIRST questionnaire is designed to differentiate those who are vulnerable to stress-related sleep disturbance from those who are resilient. Results will be discussed first in terms of cortisol and then psychological variables before discussing the follow-up study.

It was found that the paradigm did show a robust effect, whereby the main effect of time is significant. We can be confident therefore that the paradigm is indeed affecting HPA activity. However, our results did not show any significant differences for cortisol change over time- i.e. stress-reactivity (AUC). There was however a trend for AUCg, and this showed a strong effect, suggesting the study may have been underpowered. However, it was demonstrated that the vulnerable group had higher cortisol levels on average at every time point, and significantly so at time points 1 and 2. This suggests firstly that the trend for AUCg is an artefact of baseline levels, given that AUCg considers differences from absolute zero rather than from respective baselines i.e. the trend denotes differences in baseline and not in reactivity, as area under the curve in this calculation would be higher in the vulnerable group, simply because it has a higher starting point that isn't accounted for in the AUCg calculation and not because reactivity is any different. Secondly, this may represent either an insomnia-like 'hyperarousal' in this group, whereby they are exhibiting a psycho-biological vulnerability to insomnia, and thus implying that the hyperarousal that has been demonstrated in insomnia is not due to lack of sleep but rather cause of and maintenance of. If this is the case it may explain why AUC was not significantly different, as you wouldn't necessarily expect stress-reactivity to be greater if the differences can be explained purely by elevated baseline levels. Given the piloting nature of the study, it is possible also that to detect such differences, if they do

exists, one would need more power. Alternatively, it may be the case that the vulnerable group show a heightened stress response to the anticipation of stress, which has increased their baselines levels of SFC. This will be discussed further within the context of the psychological differences. This also highlights the importance of a longer baseline period in order to support the conclusion we have drawn, but also if one believes anticipation to be responsible for the baseline differences shown here, then a true baseline has not really been recorded so a longer period of relaxation prior to beginning may be merited, or obtaining cortisol baseline levels at a different time from running the paradigm. Balodis et.al.[167] present an interesting discussion on the use of physiological variables in assessing stress reactivity and support the idea of a longer baseline period to truly assess baseline levels. Given the data we have however, the conclusions presented here are sensible.

The finding of greater baseline levels but not in stress-reactivity is inconsistent with our hypothesis, but provides an interesting avenue for future research. Further to this, on examination of appendix X which shows the pattern of response for the vulnerable group, resilient group and the 10 who were excluded for scoring as poor sleepers on the PSQI or classed as insomnia sufferers on the ISI. Bearing in mind that all these individuals endorse being good sleepers at baseline, this pattern of response may indicate a pathway into insomnia. What we see is a consistently increased response in the vulnerable group compared to the resilient group, which is significantly different at baseline. In the poor-sleeping group we see again a consistently increased response, but also a much sharper increase and decline in SFC i.e. a more labile stress-reactivity. This is of course speculative, but may suggest that what is demonstrated here are increasing levels of expression of vulnerability to insomnia whereby a vulnerable individual who is currently a good sleeper demonstrates increased baseline levels, and an individual who is vulnerable and currently experiencing mild sleep complaints begins to demonstrate an abnormal stress-response. Given that a past period of poor sleep is the strongest predictor of a new episode of poor sleep (LeBlanc et.al[74].), this seems a sensible conclusion to draw whereby repeated stress, coupled with a propensity toward negative affect, leads to continued HPA dysregulation and so an increase wear-and-tear on the system until a constant hyperarousal and insomnia develops. It needs to be emphasised though that this is mere speculation based on visual differences in the data. Given the small sample size,

this was not analysed and no hypotheses were constructed a-priori with regards to a poor sleeping population.

We have demonstrated that good sleepers who score high on the FIRST are significantly higher on measures which typically characterise the insomnia population, those being factors associated with negative affect, stress, rumination and worry. This implies that these qualities increase the likelihood of an individual developing a sleep complaint in response to stress, given that everyone in the sample endorsed good sleep during screening and on psychometrics.

In terms of increased baseline levels of SFC, this may be explained by anticipation of stress: If you have an individual who is prone to negative affect (neurotic) and rumination and worry it may be the case that coming in to do an experiment but not knowing exactly what the task is may be enough to elevate their stress-response as they already begin to ruminate and conjecture on what the task is and how well they will perform. An increased anticipation to stress is also reflected at time-point 2, after hearing what the task is and preparing. To tease these 2 theories out it would be beneficial to conduct this study with more baseline measures over a longer period at the start of the task, as suggested previously. Greater insight into the stress response would be gained by including more direct measures of stress such as oxygen metabolism, heart-rate or galvanic skin response. This would provide an insight into the stress-system as a whole and may allow for conjecture on parasympathetic versus sympathetic nervous system activity. A Investigation of other aspects of the stress system will provide a fuller explanation of the stress-reactivity in this population and may help to over-come the problem of large inter- and intra-individual variance in cortisol secretion, which has been widely documented in the stress and anxiety literature.

Regression analysis suggests that conscientiousness is the only factor which has a significant mediating effect on baseline levels of cortisol. As outlined in previous chapters, there is strong evidence to suggest that conscientiousness is protective against insomnia, particularly if it is coupled with low levels of neuroticism [118]. Whilst the vulnerable group did show, on average, lower scores on the conscientiousness subscale of the NEO-ffi, as would be expected, this did not reach significance. Further to this regression analysis would suggest that as conscientiousness increases so too does cortisol output at

time 1, given the positive value of Beta. This seems contradictory to the published data, and to our hypothesis. Given the nature of the task, it could be that conscientiousness would create an increased stress response, as this factor is likely to create a certain amount of performance anxiety, especially given that the vulnerable group in this study are characterised by increased neuroticism. This may undermine the protective aspects of conscientiousness by producing a phenotype which feels the need to do everything 'right', coupled with an increase in negative affect and rumination which may exacerbate worries about not being able to get it 'right'. In this sample, there were no significant between-group differences in terms of frequency for those scoring high on neuroticism, and low on conscientiousness or any other combination of these variables, so conclusions are, at the moment, speculative. In the vulnerable group conscientiousness correlated positively with baseline SFC, but not in the resilient group. Implying, therefore, that in the vulnerable group, who are characterised by neuroticism and other variables which may indicate sensitivity to negative affect, that conscientiousness does have a negative effect on SFC. Given the nature of the task an individual who is prone to organisation, thoroughness and effortful control may experience the TSST as more stressful given the time constraints in which to prepare for the task and the complete lack of control. This is then compounded by increased neuroticism, which encourages the interpretation of events towards being negative in valance. This is supported by previously mentioned work showing cortisol is reduced as a function of conscientiousness, via positive affect[124]. Conscientiousness exerts a protective effect by encouraging responses to positive events. If conscientiousness is then coupled with high neuroticism, which encourages negativity then conscientiousness may encourage an increased stress response by creating a perfectionist personality type, and there by loses its protective function. Again, this is supported by the work of William and Moroz[118] who suggest conscientiousness is protective, only when coupled with low neuroticism.

While these results are compelling, it needs to be highlighted that this work was carried out on a relatively small sample so results are suggestive. Secondly cortisol is known to have large intra-and inter-individual variability- as can be seen in the data presented here-, compounding the small sample size problem. This work would benefit from more participants and a secondary, more stable measure of the stress response. The results however do suggest that this is an area which merits a more intensive research effort.

4.8.1 Follow-up: Which factors predict Sleep Disruption in Response to Stress

To fully assess if the FIRST does actually identify those who are vulnerable to sleep disruption in response to stress a follow up study was conducted. In conjunction with phase1, this will allow conclusions to be drawn regarding the existence of a vulnerable phenotype but also what factors may define this group psychologically and physiologically, giving more gravitas to the arguments presented in the previous section.

As would be expected the groups did not differ on any sleep variables during the non-stress week, and none met criteria for insomnia confirming their good-sleeper status. Sleep diaries were given with the instruction to fill one out during a normal week, defined as one in which no unusual stressors were anticipated, and one during a stressful week. Subjectively, both groups rated their selected stress week as significantly more stressful so the manipulation appears valid.

Despite the high drop-out, the group who participated in the second part of the study seem to resemble the group in the first phase psychologically, in that the vulnerable group are higher in neuroticism, aspects of rumination and stress, suggesting that the FIRST is related to these constructs, and that this finding is reliable.

Results from the sleep diary further suggest that the FIRST does adequately specify those who are vulnerable to sleep disruption in response to real life stressors- namely, work load. The most interesting finding is the differences in symptom change score between the groups. The vulnerable group show a significantly higher change score compared to the resilient group, representing a significant increase in insomnia symptoms. While no participant in the final sample reached diagnostic criteria for insomnia during week 2, their sleep had become noticeably affected by stress, but only if they are vulnerable. It was demonstrated also that baseline levels of SFC in part 1 were significantly correlated with change scores. Between group correlations suggests that in the vulnerable group they are related positively, but for the whole sample related negatively. This may be due to the resilient group showing a reduction in symptoms during week 2 relative to week1. This again in itself is interesting. The resilient group show a decrease in number of symptoms. This could be explained by differences in personality perhaps. If the resilient

group are lower in neuroticism and slightly higher on average in conscientiousness then increased workload may create a better sleep if the individual feels a sense of achievement at the end of the day and is not prone to worry about the increase in workload. Folkman [168] discusses the case for positive emotion in stress reactivity, talking about the notion of positive stress: If an individual is excited by the prospect of a challenge and believe they can handle the challenge then this stress has a positive effect. This is one possible explanation for the finding of reduced symptoms in the resilient group, whilst highlighting the notion outlined in chapter 2, that conventionally mild stressors may be enough to induce stress-like changes in a vulnerable individual because they are more prone to negative affect and worry: more likely to view a situation as negative, rather than challenging. Therefore, it takes a small stressor perceived as a large stressor to induce changes in stress physiology and then affect sleep.

This work demonstrates that the vulnerable population have a distinct psychological profile, and elevated baseline measures of SFC, suggesting that both the psychology and physiology of the stress-system create the vulnerable phenotype. Conscientiousness seems to mediate the stress response; however more work with larger samples would help clarify this relationship. Based on previous work it is likely that this interacts with neuroticism in its effects on HPA activity. It also supports the FIRST in its ability to differentiate between a vulnerable and resilient population.

4.8.2 Implications

In a broader sense, the import of this work may prove to be in highlighting the need to educate about sleep before the onset of an insomnia episode. Preventative techniques such as mindfulness base stress management will likely prove to reduce levels of insomnia in the general population, and therefore reduce the associated negative sequelae of outcomes if they are introduced to the vulnerable population, especially considering the usefulness of these techniques in reducing SFC in response to TSST [164]. If the hypotheses presented here can be verified through replication and improvement, then it provides a strong advocacy for prevention, rather than cure.

4.8.3 Future Directions

Future work needs to focus on the role of psychological and physiological variables in the onset of insomnia symptoms. Whilst this work provides an important first step it has several limitations, such as small sample size, possibly too short a baseline to fully support the conclusions drawn and the use of only one marker of physiological stress. Secondly, the stressors in both parts of the study are based on performance (given that the reported stressor in the follow up period was unanimously workload). Investigating response to more emotional based stressors may also provide an interesting insight.

Chapter 5 Heart Rate, Cardiac-Vagal Tone and Personality and Coping in the Vulnerable

5.1 Introduction

In order to verify the results from the Trier study presented previously, we investigated stress-reactivity in an arguably more direct manner: assessing heart-rate (HR) and cardiac-vagal tone (CVT) in response to a performance based stressor.

Autonomic arousal as measured by HR has been shown in a small number of studies to characterise the insomnia population. Bonnet and Arand [57] demonstrated in a sample of 12 objectively (PSG) defined insomnia patients, compared to age- sex and weight-matched controls that the insomnia patients show an increase in heart-rate and significantly increased low-frequency and decreased high frequency power in the EKG throughout the sleep cycle. This translates to mean that the insomnia group demonstrate increased sympathetic nervous system activity, which the authors describe as 'sympathetic hyperactivity', during sleep. This provides some support for the notion of hyperarousal in this population. It would have proven interesting to investigate if these differences were present throughout the 24h cycle and not just during sleep, providing further support for the hyperarousal theory of insomnia. This study is not the first to demonstrate increased heart-rate in this population, but it is the first to control for sleep stages, taking into account natural variation between sleep stages. For example, nREM is characterised by an increase in parasympathetic activity (decreased heart-rate) and REM sleep is largely characterised by sympathetic nervous system activity (increased heart-rate) [169]. Periods of wakefulness in the insomnia group were also accounted for-considering that heart-rate will be increased during wakefulness, relative to during sleep. These are important considerations when investigating HR throughout the sleep cycle, as each stage of sleep has its own characteristic pattern of HR and transitioning between stages is a complex process in terms of the interaction between the different parts of the nervous system[170]. Studies to-date however do suggest that the insomnia population show increased sympathetic nervous system activity as measured via HR while asleep and in response to exercise and stress as demonstrated in classic studies[171-174]. This may

represent a pathway into cardiovascular disease, which has been associated with insomnia [175].

Such work implies that the CNS is chronically altered in the insomnia population, and not just in its response to stress. Further to this and of more relevance from the point of view of this thesis, is the effect of acute stress on HR and how this leads to disrupted nocturnal sleep. Hall et.al. [176] conclude from their study that acute stress alters HR variability during sleep. In a sample of 59 PSQI-defined good sleepers it was found that acute stress alters HR variability during sleep, and this was significantly associated with a decrease in sleep maintenance and a decrease in delta wave counts- i.e. reduced deep sleep. The stressor employed was one of anticipation, rather than completing a stressful task: those in the stress condition were told that the following morning they would have to prepare and give an oral presentation, which would be assessed on content and quality, whilst the control group would be asked to sit quietly and read a magazine whilst HR and blood pressure were monitored. What this study really demonstrates therefore is that anticipation to stress affects HR during the night. It would have been interesting in this study to assess which other factors may mediate this effect. Worry was controlled for as was ambient stress levels, however, personality, rumination and coping style were not. Such factors may have a bearing on how strong the physiological anticipation to a stressful situation is. Brosschot et.al.[101], upon review of the literature surrounding stress-related physiological activation highlight the need to better understand how factors such as worry and rumination may increase the physiological stress response in anticipation to the stressor, and further maintain the activation in the resolution of the stressor. Indeed Brosschot et.al.[177] report that trait worry and trait anxiety lead to heightened HR but reduced heart-rate variability throughout the course of one day, and that these effects further impinged on sleep the following night.

Both the work by Hall and Brosschot suggest that physiological response to stress during the day represents a risk factor for disrupted sleep at night. It is possible therefore that an increased sensitivity of the cardiovascular system may be endemic to the vulnerable population.

Cardiac Vagal Tone (CVT) is a marker for parasympathetic nervous system activity, and works in tandem with HR. Baglioni et.al.[178] have found that CVT is greater in insomnia

patients compared to good sleepers, in response to emotional stimuli. Higher CVT has been associated with greater reactivity to stimuli [179]and has been suggested as a predictor of stress vulnerability and stress-reactivity in both animals [180] and humans [181], whereby decreased vagal tone indicates an increased stress response. It has been shown that active coping tasks lead to an increase in HR (sympathetic nervous system activity) and a withdrawal of CVT (parasympathetic nervous system activity) [182] and dysregulation of CVT have been implicated in both anxiety and depression [183, 184].

The present study aims to assess HR and CVT in response to an active coping task, between a vulnerable and resilient group. As well as assessing worry and rumination, personality factors and coping styles will also be measured. This will allow a certain level of discursive comparison between results of this study and the TSST study. It has been delineated in previous chapters the pathway by which personality and coping style may contribute to a hypersensitivity to stress: neuroticism represents an increase in negative affect, and an increased likelihood of interpreting challenges as threatening [185-187]. This leads to an intensification of stress response and therefore a greater vulnerability to stress [188].

5.2 Aims

The primary aim of this study is to investigate stress reactivity in individuals vulnerable to sleep disruption, as assessed by the FIRST, in an attempt to support what has been found in previous work which has used cortisol in response to a psychosocial stressor (TSST). ECG recording provides the primary outcome measures, thus allowing inferences to be made about sympathetic (heart-rate) and para-sympathetic (cardiac-vagal tone) nervous system activity. Again, psychometrics measuring personality, coping style, worry, rumination, depression, anxiety and stress have been used to further assess which factors, psychologically, define the vulnerable population and how these may mediate physiological responses to stress.

5.2.1 Hypotheses

As with the previous study, this work is exploratory in nature. Hypotheses are based on the results of our previous study.

Heart-rate

It is hypothesised that the vulnerable group will show significantly increased arousal at baseline, relative to the resilient group, as measured by HR.

It is hypothesised that the vulnerable group will show greater heart-rate throughout and greater CVT throughout the paradigm compared to the resilient group, but the change between conditions will not be significantly different (i.e. stress-reactivity will be the same between groups)

Psychometrics

It is hypothesised that the vulnerable group will show a similar psychological profile to that seen in the insomnia population: higher in neuroticism, worry, rumination.

Conscientiousness will mediate the relationship between group and baseline heart-rate, as suggested by the previous study.

The vulnerable group will subjectively rate the task as more stressful.

5.3 Methods and Materials

5.3.1 Participants

Participants were recruited as per the previous study: through advertisements in the University Of Glasgow School Of Psychology. All participants were screened using the standard UGSC screening form (Appendix I). Full exclusion criteria can be seen in appendix II). In brief, participants who were deemed to suffer from insomnia or any other sleep disorder were considered ineligible to participate. Individuals currently diagnosed as having an ongoing mental illness or receiving any kind of psychological intervention (pharmacological or psychological) were also excluded. Participants who reported having heart problems, issues with blood pressure or were taking medication for such disorders were also excluded. Participants who had taken part in the previous study were also excluded.

On top of the standard questions asked in the screening form participants were also asked if they regularly took recreational drugs. If they reported taking drugs frequently they were excluded from the study. A question asking about caffeine intake was also added ('How many caffeinated drinks do you drink a day?'). If more than 5, they were excluded.

In total 31 participants completed the study: 13 vulnerable and 18 resilient (table 5.1 shows the demographics). Groups were constructed post-hoc based on median split of the FIRST. It was planned to exclude individuals who scored too high on the PSQI and ISI, however no-one did so in the analysis of the psychometrics the full sample was included. For the ECG data 4 participants were excluded due to increased artefact in their data, rendering it un-analysable. The total number of participants in this section of analysis is 28: 12 resilient and 16 vulnerable (demographics displayed in table 5.1). Age did not differ significantly between the groups, however gender representation did and so this will be entered into analysis as a covariate.

Psychometrics		**Age (mean(SD))**	**Gender (% female)**
	Resilient	22.23 (2.49)	72.2
	Vulnerable	21 (1.61)	92.3
ECG			
	Resilient	20 (2.48)	61.5
	Vulnerable	18 (1.61)	94.4

Table 5 1 Age and gender for sample.
Psychometrics reflects full sample. 'ECG' shows age and gender after excluding those with excess artefact in the data

5.3.2 Measures

The Psychometric measures are outlined in chapter 3, and can be seen in appendix III. To assess heart-rate, ECG was recorded continuously throughout the experiment and analysed in accordance with the Netscope method [189]. Therefore, heart-rate and cardiac-vagal tone (CVT)- based on the Linear Vagal Scale (LVS) [190]- were measured. This allows for a measure of both sympathetic and para-sympathetic nervous system activity, which can be thought of as opposing forces operating on the nervous system: Sympathetic nervous system activity leads to a quickening of heart-rate, whereas CVT slows it down. Understanding both gives a greater insight into how stress-reactivity may create an at risk phenotype: which force leads to the disruption.

In addition to the psychometrics and heart-rate measures, subjective stress was measured throughout the experiment. At the end of each period of relaxation, at the end of each period of stress and before beginning the experiment participants are asked to rate how they had felt during the previous minutes. They were presented with a visual analogue scale (VAS) which ranged from 0 (very calm) to 10 (very stressed). This would serve as a manipulation check, ensuring that the paradigm was stressful, subjectively.

5.3.3 Procedure: ECG set-up and Stress-paradigm

Participants who were successfully screened over the phone were invited to meet the experimenter at the University Of Glasgow School Of Psychology. They were instructed to avoid smoking or imbibing caffeinated beverages for at least 1 hour before coming in to the study. They were given an information sheet (appendix XVI) and given time to read this and ask any questions before signing the consent form (appendix XVII). Upon completion of this they were taken to a small room where the experiment would take place. The room was quiet, and had been tested for any electrical interference which might cause artefact in the ECG. Participants were run between 1300 and 1800 hours, all in the same room.

To record the ECG, four self-adhesive Ambu wet gel disposable ECG electrodes with popper lead connections were attached to the individual's torso. To ensure a strong connection, the skin was first prepared with an alcohol wipe and abrasive pad. Electrodes were placed one beneath left clavicle and one above the waist. Ground and reference leads were placed beneath the right clavicle roughly 1cm apart. ECG was recorded using a Lifelines Trackit Ambulatory device, with a poly-patient connector unit added on.

Once the electrodes were fitted and it was checked that the Trackit was recording properly participants were led to a semi reclined cushioned chair. This meant that they were in a semi-supine position, the intention being to reduce muscle movement and tension. The computer screen from which the participant would see the task was positioned roughly 50cm away, and the response pad was placed near their dominant hand on a small table, so that they could comfortably respond to the tasks. The participant was instructed that it was very important that they remain still throughout the experiment as body movements can have a large impact on the ECG recording, and so

were told to make themselves as comfortable as possible. Once the participant had instructed the experimenter that they were comfortable the lights were turned off and the experiment was started. The experimenter remained in the room with the participant, seated behind them. This was to allow the experimenter to record the verbal response to the VAS but also to note down the times at which the relaxation and stress phases began, as a safe-guard against any problems with the programme failing to record this information.

Before the paradigm began the participant went through a short training phase, in order to get them used to the button responses required for the rest of the experiment. The experiment would not continue until this was successfully completed. Response key can be seen in figure 51.

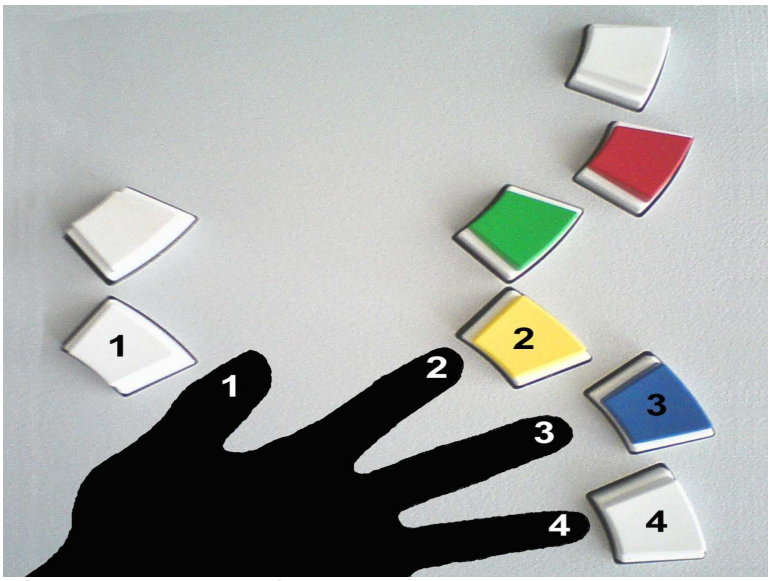
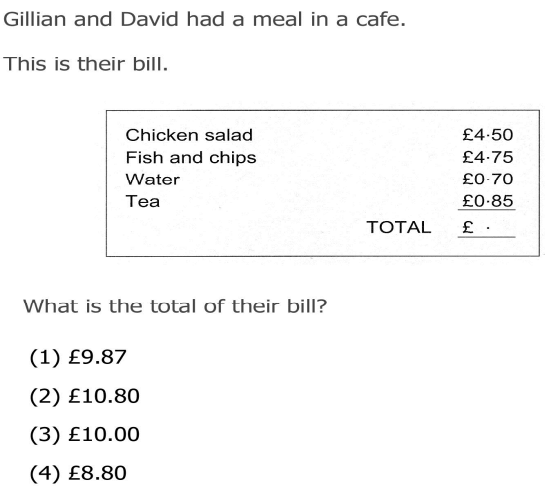


Figure 5 1 Response key

Once this was completed the VAS was administered. A line appeared on a screen with a 0 and one end and a 10 at the other. Participants were asked to respond verbally, choosing a number corresponding to how stressed they felt, 0 being not at all and 10 being very. The experimenter noted the response. The baseline condition was then run (the same procedure is applied to the relaxation condition mentioned later) in which the participant heard some relaxing music and saw on the screen a calm scene- a list of the music and accompanying images can be seen in appendix XVIII. This lasted for 5 minutes and was intended to induce relaxation.

After 5 minutes a message would be displayed telling the participant that the next phase was about to commence. During the stressor condition participants were presented with multiple choice questions, adapted from past foundation and general level standard grade examinations (SQA, 2010, figure 5 2 shows an example. Further examples can be seen in appendix XIX). Participants were told prior to commencing the experiment that they would be required to answer as quickly and as accurately as possible, and that their performance would be timed. To increase the pressure, a ticking clock played throughout the stressor phase, counting down the amount of time they had left in which to respond. Participants were given feedback on their performance in the form of a green tick when correct, a red cross when wrong and 'out of time, too slow' when they failed to answer the question within the time limit (these are also displayed in appendix XVIII). There were 24 questions for each stressor phase. The condition ended once each question had been seen. At the end of the stress phase the VAS was administered.

At the end of this stressor phase a relaxation phase took place and then a break, to allow the participant to move about. The participant dictated the length of the break. The 3 conditions were then repeated: baseline (relaxation); stressor; relaxation. This paradigm has previously been validated in our lab (unpublished data) and is similar to paradigms investigating mild stress on heart-rate, representing an active coping task. The paradigm was run using Superlab 4 (Cedrus Corporation, San Pedro, C.A.).


Gillian and David had a meal in a cafe.

This is their bill.

Chicken salad	£4·50
Fish and chips	£4·75
Water	£0·70
Tea	£0·85
TOTAL	£ ·

What is the total of their bill?

(1) £9.87

(2) £10.80

(3) £10.00

(4) £8.80

Figure 5 2 Example question given during the stress condition

5.3.4 Refining the ECG Data

Continuous ECG data was recorded throughout the duration of the study, while another channel recorded the timing pulse generated by Superlab in order to accurately time the onset of each phase (as stated this was also recorded manually). In order to obtain HR and CVT, data was processed using Neuroscope (Medifit Instruments Ltd., London). This process was carried out for each individual participant. First, a period of 50-100ms surrounding the QRS complex was selected (figure 5 3). Figure 5 4 shows an example of the selection process from the data. The software uses this selection as a template R wave, to then identify every R wave in the data thus allowing the R-R intervals to be calculated. R-R interval is the distance between 2 R waves. This was used to calculate HR and CVT values. These values were then processed using a second Neuroscope programme. Continuous HR and CVT data are displayed in the form of a tachogram, based on previously calculated RR intervals. Specific time periods are then selected using the cursors- the dotted lines shown in the figures. One minute epochs were selected, and mean HR and CVT calculated. Therefore, the data used in analysis is the average HR and CVT for each minute of the baseline, stress and recovery phases.

In some cases artefact was found. In the case of suspected artefact a Clinical Scientist was consulted as a second opinion and artefact removed manually (figure 5 5).

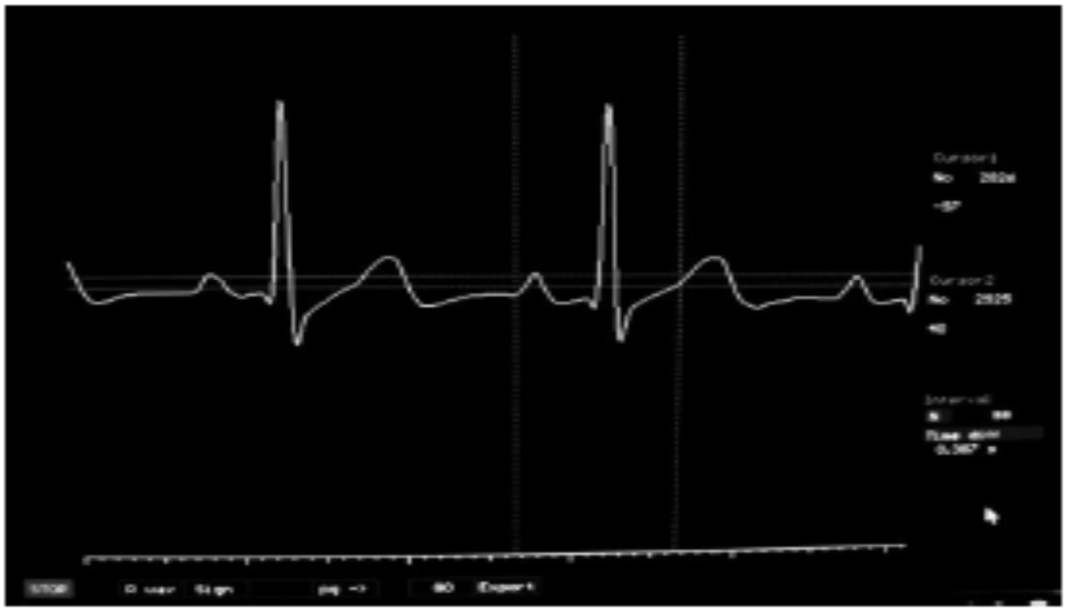


Figure 5 3 Defining QRS complex.
The Peak represents is the R wave. The distance between the peaks is the R-R interval. The dotted lines around the R wave are cursors used to select exemplar QRS complex.

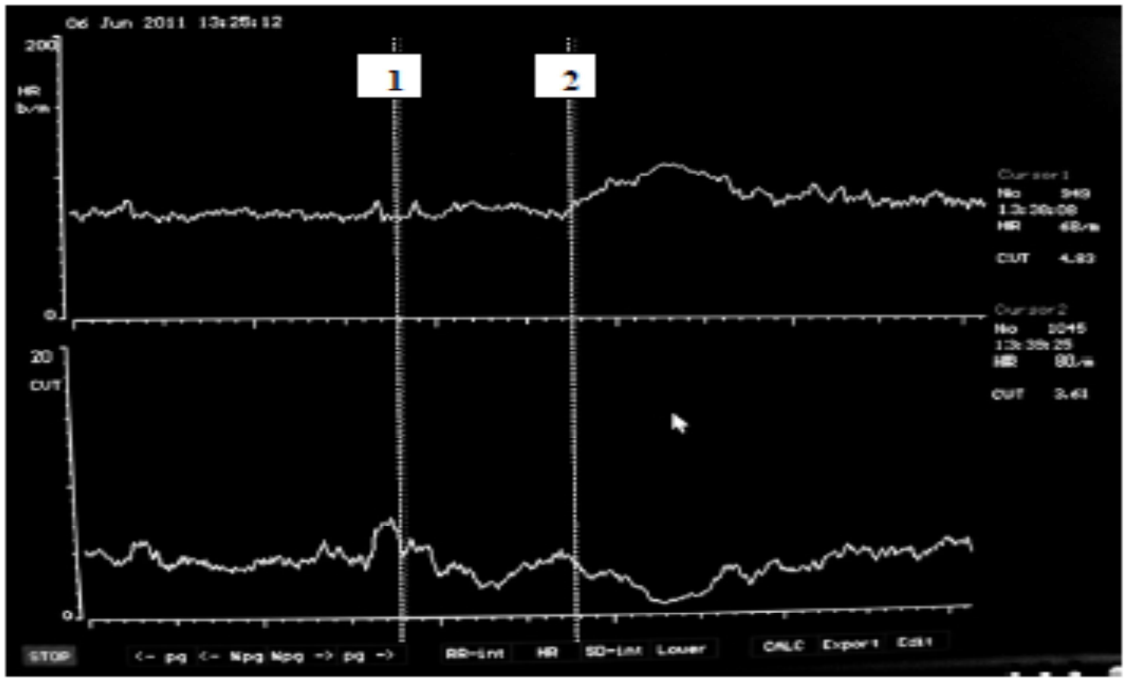


Figure 5 4. HR and CVT Data refining.
Taken from the end of baseline ECG data. Number 1 is the start of the selected epoch, and number 2 is the end of the selected epoch, at the beginning of the stress phase. The x axis is time and the Y axis is the value. The top graph represents HR and the bottom CVT. Data was selected in this fashion, using the 2 cursors to obtain HR and CVT values for every minute epoch of the paradigm.

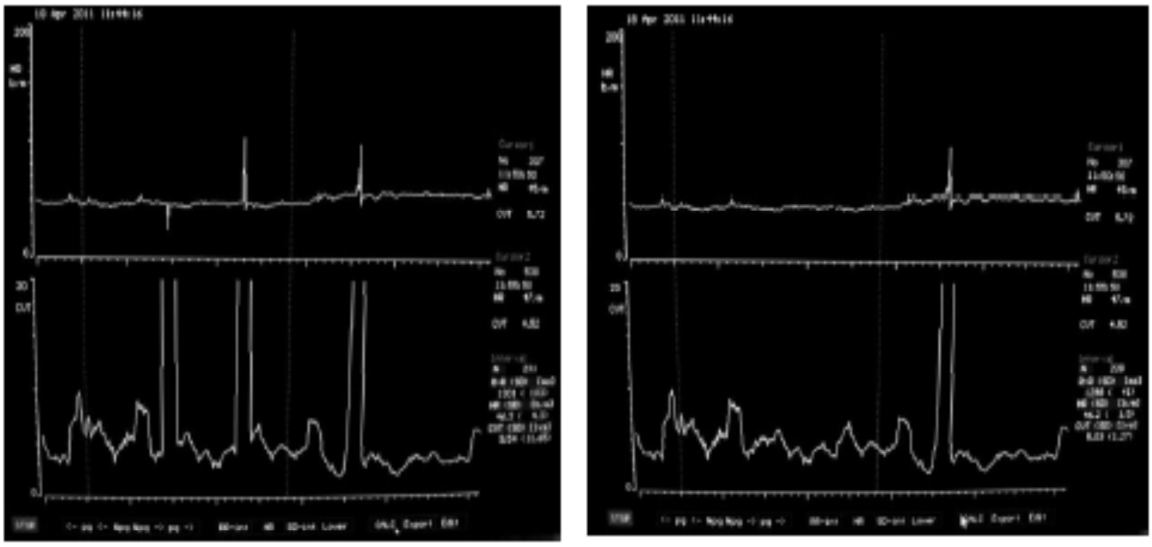


Figure 5 5 Example of ECG artefact
Left hand picture is before; Right hand picture is after artefact is removed. The first 2 peaks in the left hand graph are areas which are removed.

5.4 Results

5.4.1 Psychometrics

The median score of the FIRST was 18. This similar to published data. Drake et.al [94] report the median to be 20, and in the previous study the median is reported as 19.5.

Data were inspected for normality. Kurtosis and skeweness scores indicated that all the psychometrics were normally distributed (< +/- 3, as per Field, 2010) (appendix XX). The data was inspected initially via Pearson correlation. Full correlation table can be seen in appendix XXI. Scatter-plots displaying the relationship between FIRST and other psychological variables (where a significant correlation was found) are displayed in appendix XXII. It was found that first scores showed weak to moderate correlations with PSQI ($r(29)=0.43$, $p=0.15$), ISI ($r(29)=0.60$, $p<0.001$), PSS ($r(29)=0.61$, $p<0.001$), DASS_S ($r(29)=0.55$, $p=0.002$) and Neuroticism ($r(29)=0.39$, $p=0.31$). Neuroticism also correlates with DASS_S and PSS, but only moderately ($r(29)=0.5$, $p=0.005$); $r(29)=0.63$, $p<0.001$, respectively). This goes some way to supporting what can be seen in the previous study.

To asses between group differences, one-way ANOVA was carried out on the variables hypothesised to show differences- neuroticism, conscientiousness, rumination, worry, emotion focused and problem focused coping. T-tests were also carried out on anxiety and depression and on the sleep scales (DASSA and DASSD, PSQI, ISI) to ensure that groups did not differ significantly on these possibly confounding factors. Table 5.2 shows the mean and standard deviation for all the psychometric variables between groups. This is plotted visually in figure 4.1. Data is reported in the standard APA format, with F values and exact p-values, except where $p<0.001$. Effect sizes are reported as Cohen's *d*. It was found that groups differed significantly on Neuroticism ($F(1, 30) = 5.5$, $p = .026$, $d=0.86$), PSS ($F(1, 30) = 13.2$, $p = .001$, $d=1.31$) and RUMB ($F(1, 30) = 5.29$, $p = .029$, $d=0.86$). All showed large effects. They were also significantly different on in ISI scores ($F(1, 30) = 15.54$, $p < .001$), with the vulnerable group scoring higher on all the mentioned variables. No-one in the sample scored high enough on the ISI to be classed as having insomnia, so this between-group difference is not clinically significant, especially considering the non-significant difference in PSQI scores. However, analysis was re-run with gender and ISI entered into a general linear model as covariates. Neuroticism, PSS, and RUMB remained significant. This is supportive of what was found in the previous study, where the

vulnerable group are shown to be higher in variables denoting negative affect, rumination and stress.

	Vulnerable (mean (SD))	*Resilient (mean (SD))*
PSQI	4.56 (2.15)	3.23 (1.69)
ISI	5.33 (3.25)	1.46 (1.61)
FIRST	21.72 (3.48)	14.46 (2.02)
PSS	17.94 (5.46)	10.31 (6.18)
DAS_D	7.88 (6.61)	4.15 (5.06)
DAS_A	5.76 (5.91)	4.00 (4.07)
DAS_S	13.06 (7.52)	5.54 (4.70)
NEO_O	50.39 (5.93)	50.23 (8.41)
NEO_C	47.00 (10.35)	50.69 (9.16)
NEO_E	50.17 (8.66)	53.23 (9.44)
NEO_A	53.89 (6.62)	55.77 (7.15)
NEO_N	37.50 (9.13)	30.00 (8.29)
RUM_B	24.22 (6.21)	19.62 (4.31)
RUM_D	9.33 (3.36)	7.54 (2.26)
RUM_R	9.67 (4.00)	8.00 (2.63)
EFC	13.34 (3.33)	13.08 (4.65)
PFC	12.11 (2.35)	11.69 (3.38)
PSW	42.94 (14.24)	38.77 (8.41)

Table 5 2 Means and standard deviations for the psychometrics for each group.

NB: Highlighted red are variables which differed significantly

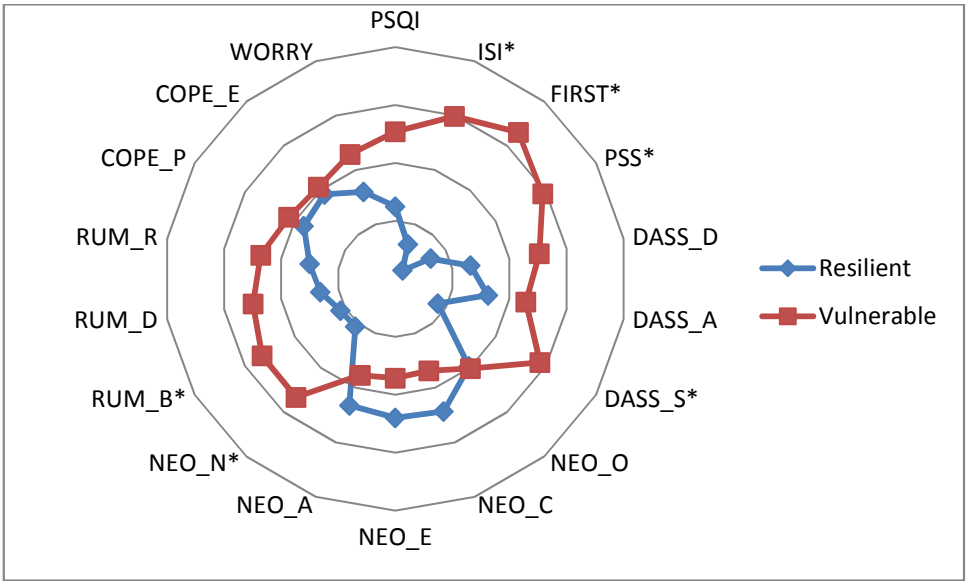


Figure 5 6 Spider chart showing between group differences on psychometrics. Red line represents the vulnerable group. * indicates significant between group difference (p<0.05). Created using z-score data. PSS= Perceived Stress Sale; DASS_D=Depression; DASS_A=Anxiety; DAS_S=Stress; NE_O=openness; NEO_C=Conscientiousness; NEO_E=Extraversion; NEO_A=agreeableness; NEO_N=Neuroticism; RUM_D=Depressive thinking; RUM_B=Brooding; RUM_R=reflective thinking; COPE_P=Problem focused coping; COP_E= Emotion focused coping

5.4.2 Heart-rate and Cardiac-Vagal Tone

Again, data is presented in the APA format, with effect sizes reported at Cohen's *d*, except in the case of ANOVA based analysis where partial eta squared is reported. Before HR/ CVT data was assessed, responses for the VAS scale were inspected to ensure that the task was deemed subjectively stress inducing. Baseline subjective stress was compared between groups. This did not differ significantly between groups (t (1, 30) = 0.573, p=.572). To assess that the paradigm was considered stressful, paired t-tests were performed to assess differences between baseline 1 and stressor 1 and between baseline 2 and stressor 2. The difference between baseline 1 and stressor 1 was significant (t (1, 27) =-7.215, p<.001). The difference between baseline 2 and stressor 2 was also significant (t (1, 27) =-8.32, p<0.001). Subjectively, over both phases participants rated the stress condition as significantly more stressful than the baseline.

Kurtosis and Skeweness values for the average CVT and HR data for each phase of the study indicate that some of the data is not normally distributed between groups. Further to this, there was found to be outliers in every condition of the paradigm. As the study is exploratory in nature, data was log transformed, rather than deleting the outlying cases, in order to preserve power and to allow the use of parametric testing with the natural log transformation. This normalised outliers and distribution. Average HR and CVT for each baseline, stress and recovery phase for each group can be seen in table 5 3. Figure 5.2 depicts the mean HR minute by minute over the 3 conditions, before and after the break. Figure 4.3 shows the same information except with CVT.

		Resilient		**Vulnerable**	
		HR(SD)	CVT(SD)	HR (SD)	CVT(SD)
Phase 1					
	Baseline	77.09 (12.76)	16.36 (10.28)	74.42 (11.10)	13.95 (10.88)
	Stressor	83.34 (11.38)	13.16 (9.71)	80.52 (11.29)	11.12 (8.27)
	Recovery	76.88 (11.09)	16.25 (9.77)	74.01 (9.88)	13.80 (11.45)
Phase 2					
	Baseline	76.29 (11.60)	16.71 (10.37)	72.66 (9.61)	14.77 (9.10)
	Stressor	78.90 (11.06)	16.48 (11.03)	77.25 (11.16)	12.97 (10.68)
	Recovery	78.25(10.21)	17.15 (12.93)	75.10 (7.55)	13.47 (10.07)

Table 5 3Average (Standard Deviation) HR and CVT

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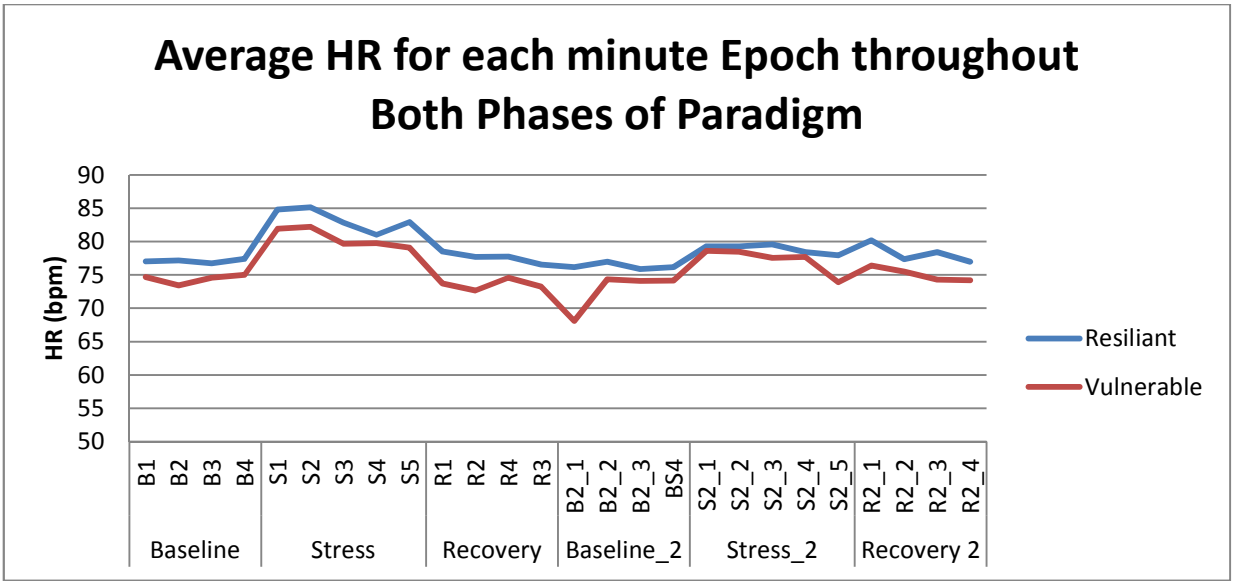


Figure 5 7Graph showing the average HR for each minute of the paradigm for both groups. It appears that the first phase has more of an effect on HR.

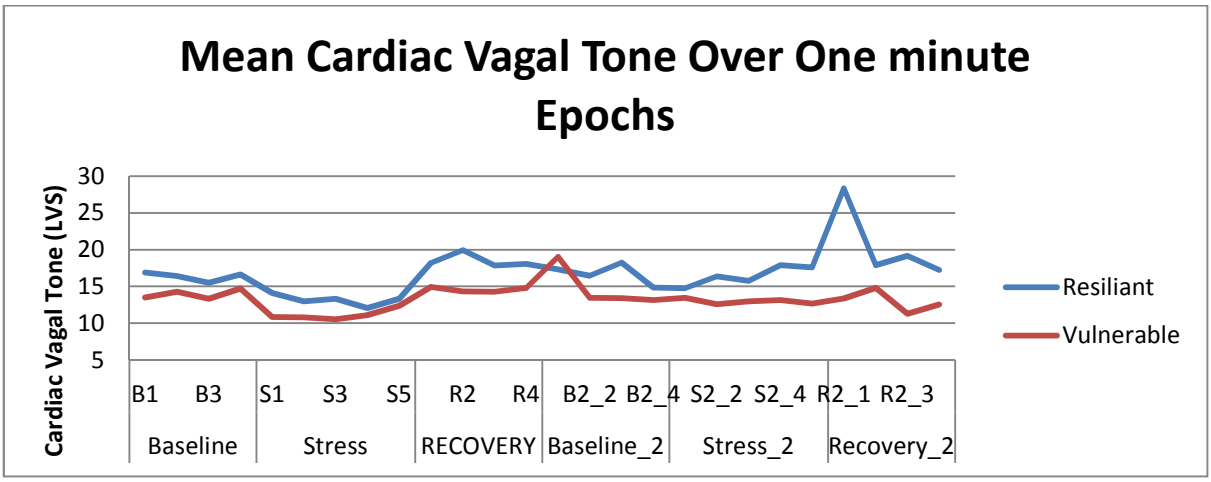


Figure 5 8 CVT for both groups averaged at each minute throughout the paradigm

Initial analysis was carried out on phase 1 only. This is because there was more missing data towards the end of the paradigm- possibly because participants were getting restless, and so moving more and creating artefact in the ECG recording.

Baseline levels were computed first. The log transformed average HR for baseline 1 was compared between groups in an independent t-test. Contrary to hypothesis, there was no significant difference at baseline (t (26) =.53, p= .60, *d*=.61). Repeated measure general linear model analysis revealed that there is a significant effect of condition on HR ($F(2,1)=15.006$, $P<0.001$, partial eta square= .347) and a significant effect of group ($F(2,1)=.4.90$, $p=.037$)but no condition by group interaction ($f(2,1)=.96$, $p=.76$). This

remained the case when age, gender and ISI were entered into the model as covariates. When psychometric variables of interest (neuroticism, PSS, EFC, RUMB and conscientiousness, based on hypotheses and significant between group differences) were entered into the model as covariates, the main effect of group becomes insignificant, although still pointing toward a trend (f(1,2)=3.748, p=.07, partial eta squared=.18). There is also a main effect of EFC= (F (1, 2) =5.404, p=.033, partial eta squared=.24). Parameter estimates suggest that as EFC increases, the difference in HR between conditions decreases.

Pairwise comparisons, corrected for multiple comparisons using bonferonni correction, revealed that there was a significant difference between Baseline and stress (p<0.001) and stress and recovery (p<0.001) but no significant difference between Baseline and recovery (p=.72). Demonstrably, the paradigm is inducing a physiological stress-response, whereby heart-rate increases in response to the stressor relative to baseline and recovery, and during the recovery phase heart-rate drops again to a level comparable to baseline. Given that the group by condition interaction is non-significant, this implies that the change in response between conditions is similar between groups, thus implying no significant difference in stress reactivity between the groups.

Cardiac vagal tone was analysed in the same way. There was no significant difference in cardiac vagal tone at base-line (t (26) =.66, p=.56, *d*= .23). Repeated measure general linear model analysis shows a trend for condition to have an effect on CVT (f (2, 1) =3.343, p=.065, partial eta squared = .2), controlling for age, gender, ISI, neuroticism, EFC, RUMB, PSS and conscientiousness. There is no group by condition interaction (f (1, 2) =.197, p=.168, partial eta squared=0.21) or main effect of group (f (2, 1) =.226, p=0.641, partial eta squared=.012). There was a significant interaction between conscientiousness and condition (f(1,2)=4.03, p=.042, partial eta squared=.182).To better understand this relationship within-group correlations were carried out, revealing that in the vulnerable group conscientiousness correlated negatively with change in CVT between the stress and relaxation conditions ((r(15)=-.67, p=0.006) (Pairwise comparison generated from the GLM reveals that the significant differences lie between baseline and stress and stress and recovery).

5.5 Discussion

Work Presented previously suggested that those vulnerable to insomnia demonstrate heightened levels of physiological arousal at baseline, as index by SFC. And that this was mediated by conscientiousness. Further it was found that the vulnerable group showed greater levels of negative affect, rumination, worry and perceived stress. To further test these findings, HR and CVT were measured in a new cohort of participants, whilst they engaged in an active coping task. Measures of personality, coping style, stress, depression, rumination and worry were taken. It was hypothesised that the vulnerable group would show elevated levels of HR at baseline compared to the resilient, and lower levels of CVT throughout the stress task, compared to the resilient group as lowered CVT has been shown to be a reliable index of stress vulnerability and further that active coping task lead to lower CVT in primary insomnia patients [178]. Further, it was expected that the vulnerable group would be higher in neuroticism, rumination, worry and perceived stress, as per previous work. Results will be discussed first looking at the psychological variables, then HR and then CVT.

Data from the psychometrics supports the idea that the vulnerable population seems to be characterised by neuroticism, brooding (the RUMB subscale of the RSQ) and perceived stress, as measured by the PSS. This supports what has been found in the previous chapter. Again, this suggests that the vulnerable group are prone toward negative affect and rumination and perceiving life as more stressful than the resilient group. Contrary to hypothesis, the groups did not differ at all on coping style, both groups showing nearly identical scores on the problem focused and emotion focused coping measures.

Heart-rate data and CVT demonstrates that the paradigm is inducing stress at a physiological level, showing a main effect of time. The vulnerable group also tended to lower HR, but this did not interact with condition. This may highlight a basic difference in the stress system between these groups which is not related to stress reactivity. This finding however did not hold up when psychological covariates were entered into the model, meaning that an individual's psychology may account for more of the variance in physiological stress response, than grouping by the FIRST. To check that the lower median reported in this sample was not responsible for these results i.e. if the vulnerable group were not vulnerable enough, analysis were carried out with groups defined based on a

score of 19.5 as per the Trier study. This did not alter the findings. CVT did not show a main effect of group or a group by time interaction. The negative correlation between change in CVT and conscientious shows that as conscientiousness increases change in CVT decreases. Based on this it could be speculated that those high in conscientiousness show a less flexible CVT response. Friedman [183] highlights the need to focus more on flexibility of the CVT response rather than absolute values, demonstrating that in anxiety there is generally a lower HR variability and a less flexible CVT response. Whilst such conclusions cannot be drawn from the data presented, it does provide an interesting speculation, especially when combined with results from the previous study: The vulnerable group report greater levels of neuroticism. Within this group conscientiousness is demonstrably related to changes in CVT between stressful and relaxing conditions. In line with conclusions drawn from the previous chapter and studies from the wider field[118], it could be hypothesised that conscientiousness coupled with high neuroticism may lead to a vulnerable phenotype which is characterised by reduced vagal tone flexibility. Again, it needs to be highlighted that this is speculative. The sample here is relatively small, and the data only hints at such conclusions. However, these theories seem sensible based on what has been reported within this thesis and elsewhere.

The lack of baseline elevation in HR in the vulnerable group, and indeed, a lower average HR is an interesting finding. In evaluating the Trier Kirschbaum et.al.[161] report no correlation between HR and cortisol output, although both react to the task. A stronger understanding of the interactions of the various parts of the autonomic nervous system will help clarify what this pattern of results means. In Post-Traumatic Stress Disorder (PTSD) patients it has been found that although there is an elevation relative to controls on all measures of autonomic activation, none of these measures correlate with each other[191]. It may be the case then that HR is a less robust marker of vulnerability to sleep disruption than cortisol is, the vulnerability being attached to the endocrine system. Conversely it may be that the vulnerable group do in fact show decreased sympathetic and parasympathetic activity. As stated, lower CVT is reported as a marker of depression, anxiety and stress-vulnerability so this may not be surprising. Perhaps in a small, healthy sample of good sleepers these differences are too subtle to really explore.

In terms of comparing between studies to gain insight into the interactions of the nervous system, there may be little merit in comparing the TSST with a computer based stressor.

5.5.1 Future Directions

This work needs to be replicated on a bigger sample, in order to allow the various highlighted factors to be properly investigated. The hypothesis and theories put forward in the previous section of the discussion may be better tested in the context of a more robust stressor, simultaneously collecting physiological data to understand the interactions between various parts of the nervous system in creating a vulnerable phenotype.

The main findings from this work are that, on average, the vulnerable group show differential HR and CVT levels, irrespective of condition, highlighting the idea that it is perhaps not stress-reactivity which defines a vulnerable phenotype but a basal difference in the autonomic nervous system.

The findings from the psychometric variables support the idea that as a group, those vulnerable have a specific psychological profile and that this can be detected by the FIRST.

Experimentally, there needs to be work with large samples using robust stressors, such as the TSST, and measuring various indices of physiological stress response in order to fully understand the driving mechanisms behind a vulnerability to sleep disruption, in a sample which is otherwise young and healthy.

Chapter 6: The Vulnerable Brain: The Role of the Insula in Defining the Vulnerable Phenotype

6.1 Introduction

Consistently, previous chapters have demonstrated that the FIRST can differentiate those who are vulnerable to sleep disruption, and that those who are vulnerable show a specific psychological profile which has been consistent across the 2 studies presented. The previous studies further suggest that the vulnerable population may show greater H-P-A activity. This is manifest as a general increase similar to the hyperarousal thought to exist in insomnia, meaning that they have consistently higher cortisol levels across all measured time points. Similar findings regarding cortisol have been demonstrated in the insomnia population [58, 59]. Given that this was only significantly different at baseline, this may imply a stronger response to anticipating stress. Secondly, it seems that the vulnerable population show cardiovascular activity patterns which mimics that of depression or anxiety- a lower CVT overall (however these results were not significant). This suggests, however tentatively, that the vulnerable population may show dysfunction in the para-sympathetic nervous system, before the onset of any sleep disorder, or other ensuing psychological disorder (such as depression, a condition for which insomnia is a risk factor).

The aim of the current study is to further understand the psychobiology of the vulnerable population by investigating brain activation patterns in response to a mild stressor, using fMRI. We will focus mainly on the brain networks involved in autonomic regulation, in particular the insula.

Brain imaging and its contribution to sleep will be reviewed briefly. The insula will be explained and the rationale behind the belief that this may be a promising region of interest (ROI) for sleep and stress researchers.

6.1.1 Neuroimaging Studies of Insomnia

Given the outline in Chapter 1 regarding the cost of insomnia, the benefits of effective treatments based on a thorough understanding of sleep dysfunction- from a subjective and objective stance- , and the aetiology of sleep disorders are important. The literature has previously had a strong focus on cognitive deficits and quality of life in insomnia [12, 52, 192]; however, there has recently been a growth of research employing neuroimaging techniques to investigate sleep disorders, thus allowing for a better understanding of the function of sleep and the underpinnings of its dysfunction, and allowing researchers to infer how this may relate to cognitive processes. Functional neuroimaging studies, using functional Magnetic Resonance Imaging (fMRI) and Positron Emission Tomography (PET), of normal sleep have demonstrated differential brain activity in slow-wave sleep (SWS) and REM sleep. During REM sleep there is a significant increase in activity in paralimbic and limbic areas, with least activation in areas of the brain responsible for executive function such as prefrontal cortex. SWS is characterised by a general de-arousal of the brain, specifically in thalamic structures, thus suggesting the function of NREM sleep is restorative or conservative [91, 193]. In the 'insomnia brain', it has been suggested by ERP studies, that the deregulation of the central nervous system does not occur as effectively as it does in good sleepers, a problem that may be compounded by the dysfunction of brain areas known to inhibit certain cognitive processes resulting in the inability to disengage from waking processes[194]. Such findings have lead to the hyperarousal theory of insomnia [60]which has been supported by functional neuroimaging studies. Nofzinger et.al.[195]were the first to investigate brain hyperarousal in insomnia using PET. They found a smaller decrease in relative metabolism from waking to NREM sleep in the ascending reticular activating system, hypothalamus, thalamus, insular cortex, amygdala, and the hippocampus in insomnia patients when compared to good sleepers. The anterior cingulate and medial prefrontal cortices also showed relatively smaller decreases in activation (table 6 1 provides information on some of the functions associated with the mentioned brain regions. This is not exhaustive, but is intended to provide an idea of what these areas do and why they might be important in understanding sleep-wake cycles and disorders of sleep.),. In terms of the reported experience of insomnia the involvement and hyperactivity of these areas seems plausible. An unrestorative sleep could be due to hyperarousal of sensory processing systems, combined with an inadequate disinhibition of areas responsible for consciousness control.

Attentional biases, increases in stress perception (or negative affect i.e. neuroticism) and problems with memory could be resultant of abnormal function of limbic and paralimbic areas. Further, cognitive deficits reported by insomnia patients could reflect the detrimental effect sleep loss has on hippocampal volume, as shown by a recent pilot study[196] (although this failed to be replicated in one study [197],but found to be depended on insomnia severity in another [198], so needs further replication before any solid hypotheses can be made). The causal pathway is however unclear here, and a smaller hippocampus may be the result of increased levels of cortisol caused by stress, rather than sleep loss. Possibly, smaller hippocampal volumes may predispose to insomnia. Thus, stress may cause sleep problems or may be caused or heightened by a lack of sleep. The direction of these relationships remains elusive. The implicated brain regions- and the reported subjective daytime effects- highlight and reinforce an already intuitive relationship between sleep and stress.

6.1.2 Stress and sleep

The relationship between sleep and stress is discussed elsewhere in this thesis and so is only summarised here. A widely recognised model of insomnia is Spielman's [21]stress diathesis (3-P) model: it is suggested that there are 3 components to the development and maintenance of insomnia: Predisposing factors such as rumination, which make a person more vulnerable to insomnia. Precipitating factors, or triggers for insomnia - i.e. stressful life events like the death of a loved one or losing your job - will cause an already vulnerable person to develop a sleep complaint. Finally perpetuating factors maintain the insomnia once the precipitating factor is no longer present. Recent studies suggest that poor sleepers show an attentional bias toward sleep cues, and this may perpetuate their insomnia. Their attention is drawn to stimuli which represent sleep, this in turn reinforces the insomnia, as it means their focuses is constantly taken back to sleep. Espie's attention-intention –effort model explains how attentional bias may maintain insomnia[43] One's attention is drawn to sleep cues, which highlight the intention to fall asleep. This then leads to an effort to sleep which causes further arousal and thus the cycle continues. All of these processes undermine the autonomy of good sleep. The 3-P model emphasises the importance of the relationship between sleep and stress: the inextricable links between these two states. Stress has a detrimental effect on sleep, and

a lack of sleep seems to effect perceived stress[199]. The relationship between stress and sleep is complex and cyclical.

Brain Area	Location	Examples of Attributed Functions
Ascending Reticular Activating System (ARAS)	Composed of several neuronal networks connected the brainstem to the cortex	Arousal; Sleep-wake transition; pain perception; attention; basic 'ancient' functions
Hypothalamus	Below the thalamus, above the brain stem	metabolic processes and regulation of the autonomic nervous system; circadian cycles, thirst, hunger, sleep,
Thalamus	Between the cerebral cortex and midbrain, near the centre of the brain	Relaying sensory information to the cerebral cortex, alertness, consciousness and sleep
Insular Cortex	Bilateral, in the sullcus between the temporal and frontal lobes	consciousness, homeostasis, perception, motor control, emotion perception: attaching salience to incoming cues
Amygdala	Part of the Limbic system. Bi-lateral in the medial-temporal lobes	Emotion processing, emotional memory
Hippocampus	Part of the Limbic System; Medial Temporal Lobe	memory, space
Anterior Cingulate	Frontal part of the cingulate cortex, surrounding the corpus callosum (which transmits information between hemispheres)	autonomic such as heart rate and blood pressure; cognitive functions such as reward anticipation decision making an d emotion
Medial Pre-frontal Cortex	Anterior part of the frontal lobes	Executive function; Emotion inhibition or inhibition of urges which are socially unacceptable; Personality expression.

Table 6 1 Brain areas Highlighted in the Insomnia Literature; their location and some proposed functions

The HPA is central to the stress response. Cortisol, produced by the adrenal glands, is responsible for restoring homeostasis after the effects of stress. Many studies have been carried out investigating cortisol levels in insomnia. Most of these studies would indicate that insomnia is indeed a disorder of 24 hour hyperarousal- not just during the night. Insomnia sufferers tend to show higher levels of cortisol throughout the day, and specifically in the evening and in the 1st half of the night, and a correlation has been shown between urinary free cortisol levels in insomniacs and total wake time[59]. Broadly speaking, sleep has a blunting effect on H-P-A activity[200]. The fact that insomnia sufferers show higher cortisol levels throughout the 24h cycle shows that it is an illness of hyperarousal and disinhibition rather than an illness of sleep loss. This also implies that it is affected by- if not is a disorder of- stress. For a comprehensive review of insomnia and the stress system see Basta et.al[201]. Whether specific parts of the brain are chronically hyperaroused (that is to say chronically hyper-active) is yet to be explored, but such findings do suggest, at least, an increased stress response, whilst implying that insomniac brains will demonstrate clearly the negative effects of prolonged cortisol exposure (for example, reduced hippocampal volume).

Brain imaging studies of psychological stress and anxiety implicate similar neural networks as those thought to be associated with insomnia. Wang et.al.[202]used perfusion functional MRI to look at patterns of cerebral blood flow under psychological stress and found that areas of the prefrontal cortex, the insula and the cingulate cortex were more active in those who showed a higher stress response to the task. The right prefrontal cortex showed sustained activation after the task, as did the insula, thus implying heightened vigilance to threat cues and negative emotion. Further, the limbic system has been shown to be hypersensitive i.e. shows a stronger Blood Oxygenated Level Dependent (BOLD) response- simply put, greater oxygen consumption in these brain areas-in response to stressful tasks in clinically anxious patients. Specifically in the amygdala, insula, anterior cingulate gyrus and medial prefrontal cortex, in various anxiety disorders, as well as being highlighted in the insomnia literature. This network of structures is important in generating effective responses to incoming stimulus and regulating the affective state of the individual. Paulus has written an extensive review on neuroimaging studies and anxiety[203].

Given the similar neural substrates underlying stress/ anxiety and insomnia, the increase in cortisol cause by all 3 states and the hyperarousal found in both anxiety and insomnia it is appropriate to suppose that insomnia could be viewed as an anxiety/ stress disorder, and furthermore, anxiety literature may provide a roadmap for sleep researchers, as anxiety research is far more developed. Further credence for this outlook is provided by the two most prominent models of insomnia. Firstly, Spielmen's model states a period of stress which results in insomnia. Secondly Harvey's cognitive model of insomnia highlights the daytime impairments that insomnia patients experience and how this leads to engagement in avoidance behaviours, a pattern that has been well documented in anxiety literature.

Recent research into anxiety has focused on the involvement of the insula, which forms part of the paralimbic system and is located deep in the lateral fissure. Due to its location in the brain it is difficult to measure- i.e. it is a relatively small structure, folded deep in the lateral sullcus between the temporal and frontal lobes-, which is why it may not have been investigated extensively to date. Paulus and Stein[204] have recently reviewed the involvement of the insula in anxiety disorders. One of the main functions of the insula is that of interoception, or embedded cognition: the sense of physiological conditions of the entire body. It is where signals representing the internal state of the body are integrated. It also has afferent and efferent connections with the amygdala, nucleus accumbens, medial cortex and anterior cingulate [204]. This means that the insula is perfectly positioned to attach salience to incoming environmental and somatic stimuli and integrate this into affective and physical state. The insula is seen to be more active in people suffering from anxiety, particularly when faced with the anticipation of a stressful event, rather than during the event itself [205] while also being correlated with intolerance of uncertainty[206] i.e. the insula is more active in anxiety prone individuals when they are faced with ambiguous stimuli. It is known that anxious individuals are more likely to interpret stimulus as dangerous. This might suggest that the insula has a key role to play in attaching salience to incoming stimulus: possibly a tendency to attach threat is a result of hyperactivation. Such a conjecture would fit with the predictive function of the insula- that is to say its role in anticipating how the body may feel given a certain stimulus, whether it is internal or environmental. The connections to the medial prefrontal cortex and anterior cingulate cortex means that the activation of the insula has an effect on self referent processing and the degree to which executive control is

deployed- it has been demonstrated that the degree of insula activation predicts safety behaviours- such as avoidance- during risky decision making tasks[207]. Further to this connections to the amygdala and nucleus accumbens mean that it may affect emotion processing and motivation. The interaction between the insula and the amygdala may be important in understanding both sleep and stress/anxiety responses: The insula interpreting incoming stimulus, and how this may affect homeostasis and the amygdala producing an emotional response to this. A hyperarousal of such a system may result in a hyperawareness of environmental and internal stimulus, and an increased emotional response. Through this system ambiguous stimuli may be more likely to be interpreted as negative or threatening when coupled with negative beliefs and faulty cognitions. The exact role of the insula in anxiety is only beginning to be understood, but it seems to be centrally involved in anxiety disorders and normal emotion and motivational processing.

6.1.3 Insula and Vulnerability to Insomnia

The insula has been implicated in the work supporting the hyperarousal theory of insomnia [60]. The anxiety literature provides a broad understanding of the role the insula may have to play in stress perception, and in the activation of a stress-response. Stein e.tal.[208] have shown that insula activation is greater in healthy controls prone to anxiety, versus those who are not prone (as measured by the STAI) in response categorisation of emotional faces. Further, this relates to neuroticism.

Based on what we know about the functions and connections of the insula as delineated above, it is hypothesised that:

I. Greater insula activation may characterise those who are vulnerable to stress-related sleep disruption, in response to stress-anticipation. It is expected that this will be mediated by conscientiousness, considering the data presented previously.

II. The vulnerable group will show a psychological profile consistent with our previous work: high in negative affect, worry and rumination.

6.2 Approach and Methods

6.2.1 Screening and Recruitment

Participants were recruited and screened as per chapter 3. Additional exclusion criteria for MRI safety can be found in appendix XX. In brief, anyone with metal implanted in their body were excluded. Those who passed initial screenings were invited to the School of Psychology to collect the information sheet (appendix XXIV), sign the consent form (appendix XXV) and collect a 2 week sleep diary to further ensure that only good sleepers were selected.

6.2.2 Procedures and Methods

Participants who were screened successfully with the sleep diary and actiwatch were invited to the scanning facility at the Centre for Cognitive Neuroimaging at the University of Glasgow. Prior to this they had completed a series of questionnaires assessing personality, coping, stress, anxiety, depression, rumination and worry (see appendix III).Once checklists had been completed (see appendix XXIII) to ensure the participant was MRI safe, the study task was explained. Once any queries were dealt with the participant was asked to change into MRI clothes and placed in the scanner. The participant completed a practice session; 2 attention bias sessions (not included in this thesis); a stress session; a resting state scan (again not included in this thesis) and a structural scan. Participants were given a small remuneration for their time.

6.2.3 fMRI Paradigm

The paradigm employed is designed to assess hyperactivity of the insula in response to anticipated stress. A modified emotional stroop paradigm was used. The task involves identifying the ink colour that a word is presented in. Participants were asked to press the button corresponding to the colour of the ink. Accuracy and speed of response is affected by the nature of the word- i.e. anxious individual will have longer reaction times and lower accuracy to anxiety related words, and insomnia patients show the same responses to sleep related words, an effect known as attentional bias. The mechanisms of this however, are unclear with some authors suggesting it is a more a measure of delayed disengagement rather than attention bias (see Phaf et.al.[209] for a meta-analysis of the stroop). This aspect of the task is not important given the questions being answered here,

and served mainly to lull the participant into a false sense of security. The stress paradigm was run next after 2 attention bias scans. During this paradigm participants completed the same task as the emotional stroop condition; however words were not blocked as they were in the attention bias task (i.e. 16 neutral words then 16 sleep words) but rather collapsed into one list and randomised (a list of words used can be seen in appendix XXVI). The task would start as the previous attention bias tasks had but every so often a 500hz siren would sound indicating that the task was about to speed up. This would happen randomly, after at least 5 words of the slowed condition had been shown. At least 5 words were presented to allow brain activation patterns to 'normalise' back to baseline levels. There was a 6 second pause between the siren sounding and the speeded condition starting. This was built in to account for the delay between stimulus and BOLD response. During the speeded condition words were presented for 560 ms and the fixation cross for 100ms, as opposed to 1000ms and 300ms in the attention bias tasks. Participants were reminded prior to the task commencing of the importance of accuracy of response, in order to make the task more stressful. The siren served as an anticipatory cue. Participants heard the siren 30 times in total. Analysis of this task will focus on insula activation in response to the siren. After this scan, high resolution T1 weighted structural images were taken in 192 axial slices and isotropic voxels ($1mm^{3;}$ field of view: $256x256mm^2$, TR=1900MS, TE=2.92 ms, time to inversion= 900ms, FA=9^o). The anatomical scan is used in the pre-processing of fMRI data, in order to align functional images correctly

Functional images covering the whole brain (slices-32, field of view= 210x210mm, voxel size= 3x3x3mm) were gathered on a 3T Tim Trio Scanner (Siemens) with a 12 channel head coil. Echoplanner imaging sequence (interleaved, TR=2's, TE=30ms, Flip angle= 80^o) was used. There were 555 EPI volumes acquired throughout the stress paradigm (i.e. 555 images of the whole brain).

6.2.4 Participants:

Thirty- five participants agreed to take part in the study. Nine failed to show up for scan times, one was excluded after it was discovered that dental work rendered her ineligible for participation and another was excluded for showing poor sleep on the sleep diaries (SE of less than 80%) (n=24). 2 groups were created post-hoc based on the scores to the

FIRST questionnaire (see chapter 3 for an explanation of the questionnaire). The median value for scores on this questionnaire was 18, a similar number to our previous studies. Anyone scoring 18 or below was classed as resilient. The gender split is heavily biased toward females (15%= male). Table one shows age, gender and sleep-diary variables for each group. Some participants failed to return sleep diary information. In such cases the ISI and PSQI were relied upon to assess sleep status. Some participants failed to return sleep diaries so sleep diary data is available for 9 resilient participants and 12 vulnerable participants.

	Age (SD)	Gender (no male(% male))	SOL	WASO	TST	SE
Resilient	22.75 (3.62)	3 (25)	14.54 (7.41)	7.37 (5.75)	464.68 (30.60)	90.66 (5.00)
Vulnerable	23.5 (4.44)	1 (7.7)	17.00 (11.38)	7.17 (5.48)	454.10 (41.07)	88.00 (4.31)

Table 6 2 Age, Gender and Sleep

NB: SOL=Sleep Onset Latency (time to fall asleep); WASO=Wake After Sleep Onset (time awake during the night); TST=Total Sleep Time; SE=Sleep Efficiency (percent of time in bed spent

6.3 Analyses

6.3.1 Psychological and Sleep Variables

In order to compare the psychological profiles of the vulnerable and resilient group, psychometric scales will be analysed as per previous chapters. Normality was first inspected (see appendix XXVII for values). The depression sub-scale of the DASS (DASSD) was found to be non-normally distributed and so was log transformed. This normalised the distribution All sleep variables were normally distributed. One-way ANOVA was conducted on Sleep Onset Latency (SOL), Wake After Sleep Onset (WASO); Total Sleep Time (TST) and Sleep Efficiency (SE), to assess if subject sleep differs between the groups and therefore whether this should be a consideration in future analysis.

Whilst the vulnerable group show, on average, worse sleep than the resilient group (as can be seen in table 6 2), none of these differences are significant (SOL: F(1,19)=.317, p=.580; WASO: F(1,19)=.939,p=.939; TST:F(1,19)=.525;SE:F=(1,19)=1.724, p=.205), and the absolute differences are minimal. It can be assumed then that differences found in other variables are not due to current, subjective, sleep status and that the entire sample represents a good-sleeping student population.

Bi-variate correlation was carried out across the whole sample in order to investigate how the FIRST relates the other psychological variables across the whole sample (full correlation matrix can be found in Appendix XXVIII; scatterplots for significant correlations for the whole sample can be found in appendix XXIX). It was found that the FIRST correlates significantly with the PSS (r(23)=.565, p=.003); DASSS (r(23)=.527, P=.007); NEOC(r(23)=-.483, p=.024);NEOE (r(23)=-.518, p=.008); NEON (r(23)=.669, p<0.001); RUMB (r(23)=.590, p=.026); RUMD (r(23)=.590, p=.002). The direction of these relationships supports what has previously been stated in this thesis regarding the FIRST: that it is positively associated with measures of negative affect, stress and worry, but negatively associated with protective factors such as conscientiousness and extroversion

Differences in psychological variables of interest (see table 6 3 for averages and standard deviation; figure 6 1) were calculated using one-way ANOVA. Effect sizes for effects of interest are given as Cohen's *d*. PSQI did not differ significantly between groups (F (1, 23) =.070, p=.793), nor did ISI (F (1, 23) =.138, p=.714).Neither did age (F (91, 23) =.395, p=.536).These factors would have otherwise been considered as covariates. In this instance the only factor which will be entered as a covariate, outside of the psychological variables of interest, is gender.

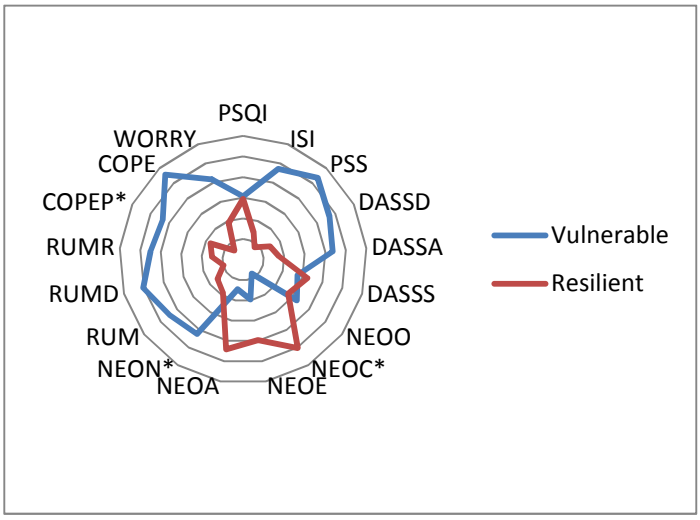


Figure 6 1 Plot of Psychological Variables.
Computed using z-scores.
***p=<0.05. PSS= Perceived Stress Sale; DASSD=Depression; DASSA=Anxiety; DASS=Stress; NEO=openness; NEOC=Conscientiousness; NEOE=Extraversion; NEOA=agreeableness; NEON=Neuroticism; RUMD=Depressive thinking; RUMB=Brooding; RUMR=reflective thinking; COPEP=Problem focused coping; COPE= Emotion focused coping**

	Vulnerable (mean (SD))	*Resilient (mean (SD))*
PSQI	4.25 (1.25)	4.08 (1.85)
ISI	3.42(2.68)	3.00 (2.92)
FIRST	22.00 (2.70)	15.08 (1.67)
PSS	17.67(6.96)	13.23 (7.22)
DAS_D	10.17(11.61)	3.23 (3.22)
DAS_A	4.67(4.70)	4.00 (4.90)
DAS_S	12.67(8.19)	7.08 (5.87)
NEO_O	50.58(6.17)	51.08 (6.51)
NEO_C*	48.5 (6.14)	55.85 (7.67)
NEO_E	44.5 (7.43)	51.77 (6.77)
NEO_A	54.5 (7.45)	58.69 (4.64)
NEO_N*	41.83(10.31)	31.62 (8.97)
RUM_B	24.72 (8.36)	20.15 (8.19)
RUM_D	10.82 (3.28)	8.38 (2.79)
RUM_R	10.91 (5.15	8.38 (3.78)
EFC	13.67(3.03)	12.92 (3.82)
PFC*	12.67(2.39)	10.15 (2.67)
WORRY	49.67 (13.08)	46.31 (13.17)

Table 6 3 Means and Standard deviations for Psychological Variables.

***p<0.05. See abbreviation list and chapter 3 for full explanation of abbreviation**

One-way ANOVA revealed that the vulnerable group were significantly higher on measures of neuroticism (F (1, 23) =7.02, p=.014; *d*=-1.06) and problem focused coping (F (1, 23) =6.108, p=.021; *d*=-.99), and significantly lower on conscientiousness (F (1, 23) =6.91, p=.015; *d*=1.06). There was also a trend for the vulnerable group to score higher on the DASSS (F (1, 23) =3.89, p=.061; *d*=-0.78) and on depressive thinking (F (1, 23) =3.87, p=.062; *d*=-.80). This goes someway to supporting previous work which has shown that the vulnerable group are prone to neuroticism, and this data would suggest also tend toward rumination and greater level of state-stress. Contrary to hypothesis, they show a greater level of problem focused coping, however this has also been shown in previous studies presented in this thesis.

6.3.2 Image Processing and Analyses

Data gathered from the scanner was analysed using SPM8 (Wellcome department of Imaging Neuroscience, London, UK). Region Of Interest (ROI) analysis was carried out using MARSBAR[210].

Before fMRI data can be analysed, the images need to be manipulated to account for individual differences in brain shape, size and position of landmarks, and also for movement. The pre-processing of images involved:

1. AC-PC plane correction. Structural images were spatially reoriented to position the AC-PC in the horizontal plane. Functional images were then re-orientated to this.

2. Images were then realigned to the first functional volume of the run.This step accounts for movements within subjects, or variances in head position. This stage generates a text file with movement parameters - roll, pitch and yaw. These parameters are entered into the final analysis as regressors of non interest to account for movement in the statistical models.

3. Images are next co-registered to the mean volume to account for changes in head position between scans

4. Structural images are then segmented. Output from this step is used to normalise images, so that they all sit on the same coordinate system. This step creates a probability map from the template: for each voxel, the probability of it being white matter, grey matter or cerebral spinal fluid (CSF) is calculated. Functional images are then segmented into the 3 different kinds of matter mentioned above.

5. Normalisation is the next step. The point of this step is to ensure that every participant's brain sits on roughly the same co-ordinate system. The parameter files from the segmentation step are used to ensure that brain areas map onto a standard space. They were mapped onto Montreal Neurological Institute (MNI) space.

6. Images are then smoothed. This reduces the effect of inter-individual variability in brain anatomy and improves statistical power in the GLM analysis. Images were smoothed with a Gaussian function (4x4x4: it has been suggested that a smaller smoothing parameter is used when

investigating smaller areas of the brain which is why a filter of 4x4x4 is employed).

6.3.3 Whole Brain Analysis

The results presented here are uncorrected for multiple comparisons (statistical tests performed on 10000 voxels). This needs to be borne in mind when considering the results presented. The whole brain analysis data did not hold-up when correction for multiple comparisons were applied. However, given the piloting nature of this work it is reasonable to consider the uncorrected data as a viable first step, which may provide insight and direction for future research.

Analysis was initially carried out on the entire group, in order to understand the effects of the paradigm in general. The analysis therefore considers data taken at the point of the siren, and for the 2 seconds afterwards (the minimum duration of the speeded task is 2 seconds), compared to during the normal, non-speeded task. MNI co-ordinates are reported.

Clusters of more than 20 voxels and $p<0.001$ are reported (see table 6 4 and figure 6 2; the full report of cluster activations are brain areas contained within each cluster can be seen in appendix XXX)). Amongst the regions that showed more activity during the stress (siren) trials as compared to the non-stress trials are areas related to emotion perception and arousal like the bilateral putamen and the thalamus. Lowering the extent threshold to 10 voxels also revealed activation in the hippocampus.

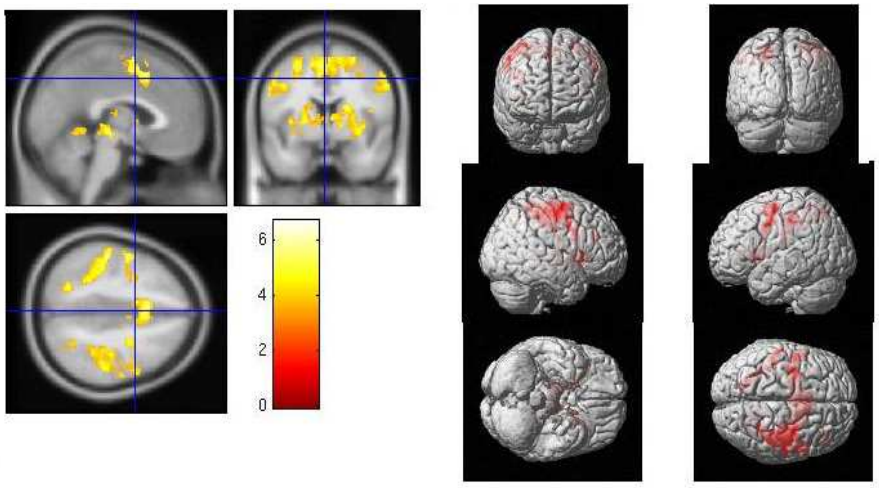


Figure 6 2 Whole brain activation. Difference between point of siren and baseline task for the whole sample. Clusters significant at uncorrected $p<0.001$; $k\geq 20$

Region	K	Maximum activation structure	X	Y	Z
Inferior Frontal Gyrus	Siren> baseline 4237	Right Insula	40	24	2
Left Frontal Lobe and Basal Ganglia	Siren> baseline 41	Thalamus	-20	30	-2
Left Frontal Lobe	Siren> baseline 41	Left Insula	-36	0	4
Left Frontal Lobe	Siren> baseline 5942	Postcentral Gyrus	-46	12	48
Left Cerebellum	Siren> baseline 58	Culmen	0	-48	4
Right Frontal Lobe	Siren> baseline 5924	Postcentral	46	-12	48
Parietal Lobe	Siren> baseline 95	Superior parietal Lobule (Broadmann area 7)	95	-60	48

Table 6 4 Clusters of Activation with peak area of activation reported.
All significant at uncorrected p<0.001.K= number of voxels in cluster; x, y, and z are MNI co-ordinates for area of maximum activation within the cluster

6.3.3.1 ROI analysis: The Insula.

ROI analysis was carried out for our a-priori region of interest: the insula. Analysis was carried out using MARSBAR. This is a toolbox which operates via MATLAB. It is designed specifically for ROI analysis. First, regions of interest were defined using MNI co-ordinates to select specific regions (see appendix XXXI for a visual representation of what the ROI's looked like, and co-ordinates used.). Two regions of interested were created- one for the left and right insula. A between sample t-test was then run in MARSBAR comparing only these selected regions of the brain. The 2 sample t-test compares activation in voxels within the selected region between groups.

It was found that both the right and left insula were significantly more activated in response to the siren relative to baseline (see figure 6 3): Left insula: t (24) =3.54, p=0.0018: Right Insula: t (24) =2.08, p=0.048 (both Bonferonni corrected for multiple comparisons). This supports the use of the paradigm, suggesting that in general population is sufficient to induce increases in insula activity, and conforms the findings of the whole-brain analysis.

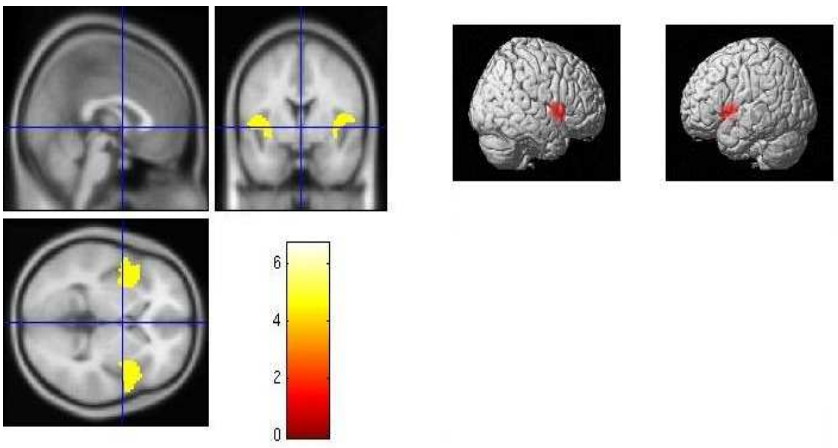


Figure 6 3 Bilateral insula activation in response to the siren. Two ROI's, one on each hemisphere. Centre co-ordinate for each region: 45, 5,-4; -47, 5,-1. For left insula corrected p= 0.0018; for right insula corrected p=0.048, siren>baseline

6.4 Between Group Analysis

In order to test if the differences between conditions differed between groups a between group analysis was carried out. A t-contrast was carried out looking at the change in

activation between conditions between groups. Table 6 5 outlines clusters of significant activation, and figure 6 4 shows whole brain activation, with uncorrected p>0.001. 5 clusters were identified with a voxel size greater than 20. The full list can be found in appendix XXXII. The maximum difference in activation is in the left pre- central gyrus (PG), and this remained after bonferonni corrections (t (12) =2.63, p=0.007; [-28, -36, 52]). Further, the vulnerable group also showed less activation bilaterally in the inferior Parietal Lobule (IPL), which remained after bonferonni corrections: right (t (24) =3, p =0.007; [52, -46, 58; -44.62) and left IPL (t (24) =2.63, p =0.01. [52, -46, 58]) compared to the resilient group.

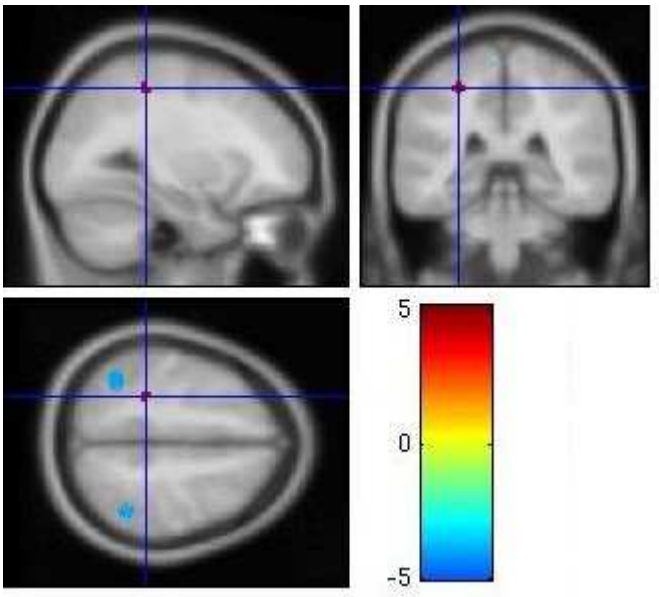


Figure 6 4. Bilateral hypoactivation in the inferior parietal lobule and increased activation in the left Postcentral gyrus
Vulnerable group >resilient group in response to the siren. Global Maxima -28, -36, 52, uncorrected p<0.001. IPL=blue; PG=red

Region	K	Maximum activation structure	X	Y	Z
Parietal Lobe	Siren> baseline, between groups 22	Right inferior parietal lobule	52	-46	48
Parietal Lobe	Siren> baseline, between groups 24	Post-central Gyrus	-28	-36	52

Table 6 5 Clusters of Activation for siren>baseline for the vulnerable group compared to the resilient group.
All significant at uncorrected p<0.001.K= number of voxels in cluster; x, y, and z are MNI co-ordinates for area of maximum activation within the cluster.

6.4.1 ROI Analysis Between Groups

In order to test our hypothesis that the insula would be more active in anticipation to stress, ROI analysis was carried out investigating insula activation in response to the siren, between groups. Bilaterally, the insula was seen to be more active in the vulnerable group, but this was not significant (figure 6 5) for the Left (t (24) =0.21, p (corrected) =0.8) or the right insula (t (24) =-0.12, p (corrected) =0.70) between groups.

To follow up the whole brain between group analyses results, beta values were also extracted for the bilateral IPL and the PG in order to assess relationships between activation in this area and psychological variables. The Beta values extracted were the average beta values for each participant at during the 2 conditions and can be seen in table 6 6.

6.5 Relationship Between Brain Activation and Psychological Variables

Given the results presented in the previous section, beta values for the left and right inferior parietal lobule were extracted (table 6 6). It can be seen that the vulnerable group had lower values on average in the right and left inferior parietal lobule, and as stated above this is significant. Paired t-tests show that in the resilient group the left IPL is significantly more activated than the right IPL(t(11)=2.90, p=0.015). The left and right IPL were not differentially activated in the vulnerable group (t (11) = 1.11, p=0.29). For the overall sample activation of the left IPL was negatively associated with factors related to negative affect: FIRST (r (22) =0.61, p=0.002); PSS (r (22) =-0.43, p=0.04) and NEON (r (22) = -0.43, p=0.04) (see appendix XXXIV for full matrix and appendix; scatterplots can be found in appendix XXXVI). Within the vulnerable group activation in the left IPL correlated significantly and negatively with openness (considered a marker of generally good psychological health) (r(22)=0.61, p=0.035 (see appendix XXXV for full matrix and appendix XXXVII).Within the resilient group activation of the left IPL correlated negatively with FIRST (r(10)=-0.644, p=0.024); PSS (r(10)=-0.68, P=0.015); DASSS (r(10)=-0.061, P=0.034); NEON (r(10)=0.62, P=0.032); WASO (r(10)=-0.72, p=0.043) and positively with PFC (r=0.079,p=0.002) (appendix XXXVIII displays scatter-plots for these relationships).

For the overall sample activation of the left IPL was negatively associated with factors related to negative affect: FIRST (r (22) =0.61, p=0.002); PSS (r (22) =-0.43, p=0.04) and NEON (r (22) = -0.43, p=0.04).

	Vulnerable	Resilient
	Mean (SD)	Mean (SD)
Left Parietal Lobule	-0.38 (1.20)	0.61 (0.65)
Right Parietal Lobule	-0.71 (0.63)	0.03 (0.55)
Left Postcentral Gyrus	0.75 (0.63)	0.23 (0.32)

Table 6 6 Average Beta values and standard deviations for left and right inferior parietal lobule and left postcentral gyrus

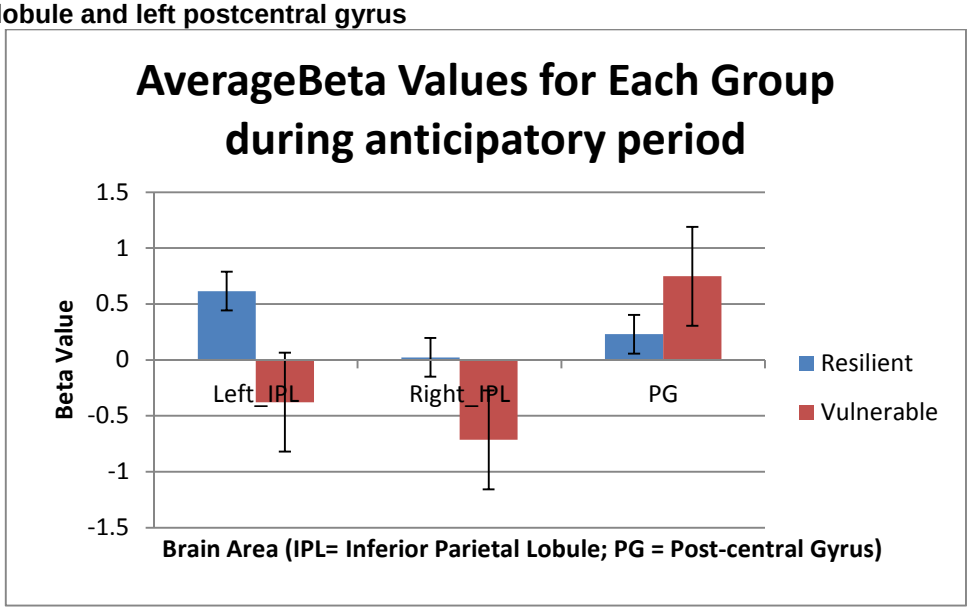


Figure 6 5 Graph Showing Beta values between groups of Left IPL, Right IPL and Post-central Gyrus. Bar represent 1 standard error

Multiple regression analysis was carried out for the left IPL (given that the right IPL showed no correlations with any of the psychological data). This was to test the extent to which activation in the highlighted areas is mediated by psychological variables. Based on our initial hypothesis and findings from previous work NEON, NEOC, PSS, RUMB, RUMD, COPEE and FIRST score were entered into the model in a stepwise fashion. A significant model was found (adjusted R squared = 0.35, f (1, 21) =12.77, p=0.002) with FIRST score being the only significant predictor (β=-0.62, p=0.002).

6.6 Discussion

The aim of this study was to investigate whether those defined as vulnerable to insomnia demonstrate increased activation in the insula in response to stress anticipation. We also replicated results from our previous studies: it was found that the vulnerable population showed higher levels of neuroticism, perceived stress and rumination.

In terms of the brain imaging data, the paradigm used was found to induce significant insula activation across the entire sample. On average, the vulnerable group showed higher insula activation in response to the siren compared to the vulnerable group. This was not significant, however. This suggests that the paradigm is robust and that the vulnerable population do not show differences in insula activation in anticipation to stress. Given the small sample size, the study may have been under-powered to show differences in insula activation between groups. Post-hoc power calculations show the power to be 0.053 (β-1). Therefore, the study is underpowered to show these effects at a statistically significant level, as (β-1) = 0.8 is considered the cut off for detecting differences at $p<0.05$. Power calculations were carried out using G-power, based on the effect size of the difference in insula activation between groups.

Increasing the sample, or the number of trials or employing more stringent cut offs in defining the groups may help to reduce problems with power in future studies. Compounding the problem of power is the nature of the sample. The work implicating the insula is conducted, largely, on clinical samples. The sample here is healthy. Perhaps the insula is a good marker in clinical disorder, but not as a predisposing factor. If insula activation does have a role to play in making an individual vulnerable then larger samples are clearly needed to detect this.

Interestingly, the inferior parietal lobule did seem to be differentially activated between groups. The inferior parietal lobule has been shown previously to be hypoactive in depressed, drug naïve adolescents[211], to have less density in individuals with social anxiety disorder[212] and to be hypoactive in PTSD patients in response to provocative, trauma related stimulus [213, 214]. The authors suggest that alterations of the IPL affect attention to conditioned fear response when under stress. Further to this, the inferior parietal lobule has been shown to play a role conditioned fear responses [215]. Perhaps the vulnerable population may demonstrate a faulty encoding process, whereby the siren becomes more readily associated with negative events- if we think about PTSD, the same processes may be happening but on a much more severe scale.

IPL activation may be protective against stress vulnerability. Mindfulness-based stress therapy has been shown to increase activation on the inferior parietal lobule, and increase connectivity between this area and fronto-limbic structures. This implies that increased activation of the IPL is protective against stress vulnerability [216]. It has also been shown that successful treatment of depression results in increased IPL activation at follow-up[217]

The parietal lobe is generally associated with integrating sensory information from different modalities, visiospatial processing and the direction of attention and object manipulation. Wagner et.al.[218] have put forward a theory of the parietal lobes role in memory retrieval, by which stimulus- sensory input- become attached to a history. This is known as the mnemonic accumulator hypothesis. In order to be acted upon, or for a decision to be made regarding sensory input, the input has to be interpreted. This is achieved via the integration of the accumulated history of that input. Essentially, the parietal lobe not only integrates sensory information but also the history of that sensory information i.e. its learned associations. Such a theory would explain the findings well suggesting that hypoactivation in this area represents a faulty retrieval of stimulus history i.e. interpreting it more negatively.

Given that the vulnerable group are demonstrably and consistently higher in neuroticism, this may make sense: a neurotic individual is more prone to negative affect and more likely to view ambiguous events as negative. This could be because their attentional system is more prone towards focusing on negativity. Or it could be that a more easily

learned negative association means that neutral events become more readily attached to negative feelings, leading to a neurotic type individual. Probably both explanations work in tandem. This makes someone vulnerable to insomnia by increasing the amount of negative emotions that they perceive, coupled with a likelihood for rumination (which, in this study has been associated with activation of the IPL) leading to disrupted sleep. Bringing this back to thinking about insomnia syndrome, someone who has been a good sleeper, and in facing life stress becomes a poor sleeper, may be more vulnerable to the threat of not sleeping well and this threat becomes more easily conditioned. Theoretically this relates well to the A-I-E and cognitive model [43, 219] delineated in chapter 2.This is of course speculative based on the finding that the resilient group show a negative correlation between neuroticism and IPL activation. To really test these theories this would need to be replicated in a larger sample, to understand how neuroticism interacts with IPL activation in the vulnerable population.

In terms of hyperactivation, the vulnerable group showed significantly increased activation in the Postcentral gyrus (PG). The PG is traditionally associated with the homunculus: the representation in the brain of the body. Increased activation in the motor cortex may represent compensation: having to work harder to fulfil the task. The idea of compensatory recruitment has been suggested to operate in sleep deprivation.[220]. Alternatively to this, activation of the PG has been studied in various disorders and is posited to affect working memory negatively in depression [221],schizophrenia[222] and obsessive compulsive disorder[223]. Further, positive outcome in treatment for depression has been associated with increased PG activity[224]. Increased activation in the PG may then represent an increased effort to fulfil the task during the speeded condition, not just in terms of coordinating hand movement, but also in mobilising working memory, as participants need to remember which buttons correspond to which colour. Speculatively, these results support a theory in which these 2 distinct areas interact to produce incongruent emotional responses to stimuli.

Considering that PG activation was predicted by neuroticism score, this implies that activation in this area is the result of negative affect and this is somewhat supported by the literature on depression and recovery from depression. Activation in this area seems more related to neuroticism than vulnerability to sleep disruption, reinforcing the idea that neuroticism- as measured by the NEO-ffi and considered to be an enduring

propensity toward negative affect- may be a unique risk factor to vulnerability. Given that the vulnerable population tend to be high in neuroticism, such findings could be easily masked.

The predictive value of FIRST score in IPL activation shows that as FIRST score increases, IPL activation is likely to decrease. This suggests that IPL hypoactivation is a marker for vulnerability to insomnia, whereas hyperactivation of the PG is a marker of neuroticism

Overall these results support the idea that the vulnerable population are characterised by neuroticism, worry and an increase in perceived stress. In the brain, this seem to corresponds to a differential recruitment of areas involved in attentional deployment and the learning of negative associations similar to what has been reported in post-traumatic stress disorder, for example. The pathway into insomnia may therefore not be stress-reactivity per se but rather a proclivity for negative associations. This then leads to an overall increase in perceived stress, not because areas of the brain which are primary to stress perception (i.e. the insula) are dysfunctional but because ambiguous events become more readily attached to negativity (possibly due to differential IPL activity), and then encoded more strongly in working memory (due to over activation of the PG). If this is in fact the case then the lack of support for the insula hypothesis is not surprising. Further to this, increased activation in the left IPL was negatively associated with psychological variables relating to negative affect and stress, suggesting that hypoactivation may be a risk factor, whilst increase activation represents a protective mechanism, or resiliency.

Whilst these results were unexpected, they are none the less interesting, and may provide a novel area of further investigation for the field. It needs to be highlighted though that the sample here is small. However, given that differences can be found in people who report and are assessed as being healthy, good-sleepers provides valid support for the theory of a predisposed phenotype, and tentatively suggests the neural mechanisms which may underpin this i.e. those involved in attention and emotional learning. This work also provides further support for neuroticism as a key risk factor to the development of insomnia.

Chapter 7: Psychological Variables Across the 3 Samples

7.1 Introduction

Given that the same psychometric data was gathered across all 3 studies, this allows for comparisons to be made between the 3 samples. This will create a larger dataset and provide support and clarification for the results already obtained regarding psychological characteristics of the vulnerable group.

7.1.1 Hypothesis

The vulnerable group will score higher on levels of neuroticism, perceived stress, rumination, worry and emotion focused coping and lower on openness

7.2 Methods and Participants

Data sets were collapsed into one file. Those who were excluded from the analysis of psychological variables in the individual studies were removed from the respective data sets before the files were collapsed. This exclusion was based on ISI and PSQI score and sleep diary, where available (n= 84). Table 7 1 provides information on age, gender and the mean and standard deviation for psychometric scale scores.

7.2.1 Analysis and Results

Bi-variate correlation was conducted. This demonstrated that across the whole sample FIRST score correlated positively with PSS ($r(82)=0.41$, $P<0.001$), DASSD ($r(82) = 0.32$, $p=0.002$), DASSA ($r(82) = 0.28$, $p=0.010$), DASSS ($r(82) = 0.47$, $p<0.001$), NEON ($r(82) = 0.57$, $p<0.001$), RUMB ($r(82) = 0.29$, $p=0.007$), RUMD ($r(82) = 0.28$, $p=0.011$), RUMR ($r(82) = 0.36$, $p<0.001$), COPEP ($r(82) = 0.36$, $p<0.001$), COPEE ($r(82) = 0.21$, $p=0.013$) and WORRY ($r(82) = 0.42$, $p<0.001$). It correlated negatively with NEOC ($r(82) =-0.26$, $p=0.017$) and NEOE ($r(82) =- 0.41$, $p=0.007$) (these relationships are displayed as scatter-plots in appendix XXIX).

ANOVA was carried out to assess between group differences. It was found that the vulnerable group had significantly higher scores on PSS (F (1, 82) = 5.76, p= 0.019; *d*= -0.53), DASSD (F (1, 82) = 10.24, p= 0.002; *d*= -0.69), DASSS (F (1, 82) = 16.78, p< 0.001; *d*= -0.89), NEON (F (1, 82) = 23.32, p< 0.001; *d*= -1.05), RUMD (F (1, 82) = 5.01, p=0.03; *d*= 0.50), RUMR (F (1, 82) = 7.86, p< 0.006; *d*= -0.61), COPEP (F (1, 82) = 18.36, p< 0.001; *d*= -0.94), COPEE (F (1, 82) = 4.90, p< 0.003; *d*= -0.48)and WORRY (F (1, 82) = 6.11, p=0.015; *d*= -0.54) and significantly lower on NEOC (F (1, 82) = 12.37, p= 0.001; *d*= 0.77) and NEOE (F (1, 82) = 10.91, p= 0.001; *d*= 0.72) (depicted in figure 7 1)

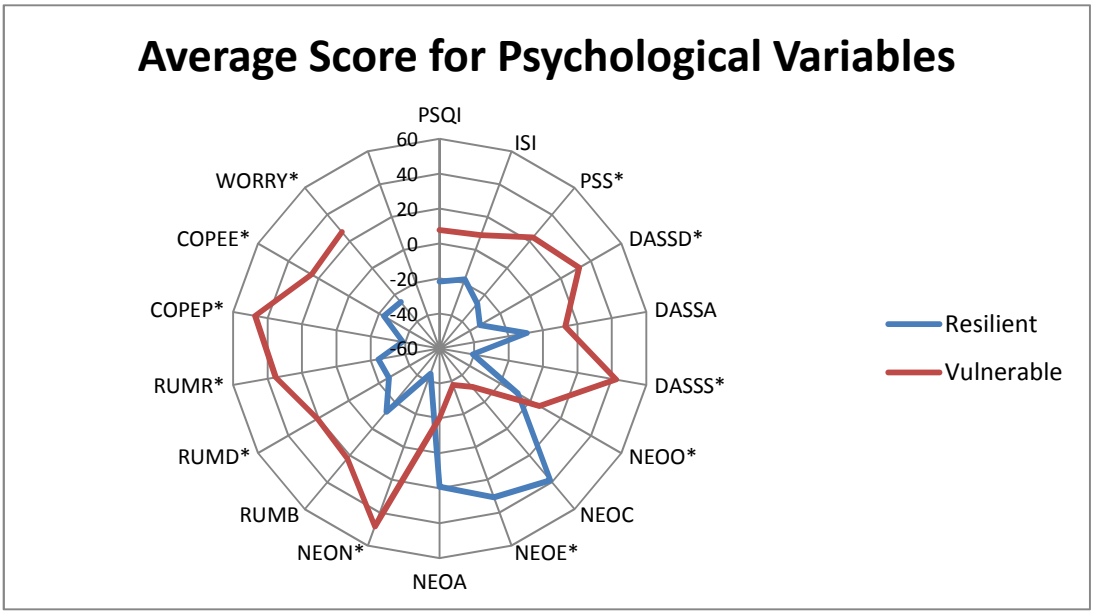


Figure 7 1 Mean score on the Psychological variables across 3 samples between groups. *p<0.05. PSQI=Pittsburgh Sleep Quality Index, ISI=Insomnia Severity Index; PSS=Perceived stress Scale; DASSD=Depression; DASSA=anxiety; DASSS=stress; NEOO=openness, NEOC=conscientiousness; NEOE=extroversion; NEOA=agreeableness; NEON= Neuroticism; RUMB=brooding; RUMD= depressive thinking; RUMR=reflection; COPEP=problem focused coping; COPEE=Emotion focused coping. Computed using z-score*100

7.3 Discussion

This short chapter provides valuable support for the results found in the previous experimental chapters. Collapsing data-sets together to create a larger sample and so more robust results, further confirms that the vulnerable group are higher on neuroticism, perceived stress, state stress, rumination and worry compared to the resilient group. They also score significantly higher on both the problem and emotion focused subscale of the brief-COPE.

	Resilient	(SD)	Vulnerable	(SD)
Gender (% female)	61		75	
Age	22.07	(3.01)	22.83	(3.80)
PSQI	3.86	(1.70)	4.38	(1.33)
ISI	3.02	(2.74)	3.80	(2.71)
PSS	12.93	(7.01)	16.50	(6.57)
DASSD	3.55	(3.71)	8.50	(9.51)
DASSA	3.73	(4.33)	4.65	(4.04)
DASSS	7.09	(5.33)	12.80	(7.34)
NEOO	50.68	(6.10)	51.55	(6.15)
NEOC	54.11	(7.02)	48.75	(6.94)
NEOE	51.68	(7.41)	46.53	(6.85)
NEOA	56.57	(7.23)	53.70	(7.42)
NEON	30.70	(8.30)	40.60	(10.44)
RUMB	15.34	(8.77)	18.61	(9.84)
RUMD	12.73	(6.66)	16.53	(8.69)
RUMR	8.66	(3.43)	11.13	(4.54)
COPEP	10.09	(2.74)	12.58	(2.56)
COPEE	12.14	(4.07)	13.92	(3.25)
WORRY	43.05	(11.67)	49.43	(11.96)
FIRST	15.00	(2.13)	22.18	(2.43)

Table 7 1 Means and Standard deviations for psychological and descriptive variables across all 3 samples, between groups

This may reflect an inability of this scale to differentiate between these 2 coping strategies or it may reflect a general heightened awareness of coping within the vulnerable population: possibly they are characterised by an inconsistent coping style, or a larger arsenal of coping mechanisms.

The resilient group are shown to be significantly higher on conscientiousness. As discussed previously, conscientiousness is generally considered a protective factor. However, coupled with high neuroticism is can become a risk factors for sleep disruption [118]. It is not surprising therefore that the vulnerable group are lower on conscientiousness. The interaction between these 2 variables is interesting. The vulnerable population is seen also to be lower on extraversion. Extraversion can be considered as a trait which infers an out-going nature: getting pleasure from the company of others. It has been suggested that those high on extraversion show less cortical arousal to stimuli than those low on extraversion, and that their reactivity to sensory information is lower[225]. Although no hypotheses were made regarding extraversion, the finding that the vulnerable population are lower on this trait is not surprising and may merit further investigation, in terms of understanding the psychobiological profile of the vulnerable phenotype.

Overall these results support the conclusions drawn so far: that the vulnerable group are higher on negative affect, rumination and stress, relative to the resilient groups. Further to this, extroversion becomes significant, showing that vulnerable group are lower on this trait. The same is true of conscientiousness. The effect size values, reported as Cohen's *d.*, indicate that the effects are strong for most of the variables (ranging from 0.5 to 1.05). These effect sizes are larger than what has been reported in previous chapters. The comparison across studies represents an important strength of the work contained within this thesis.

Chapter 8: Overall Discussion: Who is Predisposed?

In this section the results from the 3 experimental chapters will be pulled together to outline a cohesive theory of vulnerability to insomnia (summarised in table 8 1). Results from the psychological variables will be reviewed first, and then the psychobiological data and then they will be pulled together. It is important to bear in mind however, that whilst constructs like neuroticism and conscientiousness will initially be discussed within psychology, that these are psychobiological constructs, theorised to have characteristic effects on the stress system.

8.1 Psychology

Psychologically, the defining feature of this population seems to be a neurotic disposition, evidenced across all 3 studies. This is defined as tendency toward negative affect. That is to say an enduring tendency to experience negative, emotional stress. That being said, controlling for neuroticism does not eradicate the statistical significance found in the physiological measures, demonstrating that neuroticism alone is not enough to account for vulnerability.

In both the Trier and the HR/CVT study the vulnerable group were significantly higher in aspects of rumination, as well as neuroticism and this showed strong effects. In the fMRI study rumination was strongly correlated with right inferior parietal lobule activation in anticipation to stress. It makes sense therefore that this would infer vulnerability to insomnia. If neuroticism is defined as an enduring propensity toward experiencing negative emotion, this increases the likelihood of experiencing stress as the individual is more likely to interpret situations as being negatively toned. Coupled with rumination; this may compound the effects of neuroticism, as negative emotions are reflected on excessively.

In both the Trier and HR/CVT study, conscientiousness was shown to be associated with the respective physiological index of stress. It has been shown in the literature that conscientiousness, coupled with neuroticism leads to an increased likelihood of sleep disruption[118]. This may represent a perfectionistic personality type. Future studies

should measure perfectionism directly, using, for example, the Almost-Perfect Scale-Revised (PAS-R)[226]. This scale differentiates those who are high on perfectionism from those who are low but has the added benefit of allowing one to parse out maladaptive perfectionists (i.e. those who believe personal standards are not being met). In the fMRI study the vulnerable group were significantly higher in both conscientiousness and neuroticism. This is maybe one of the better defined groups as sleep diary data was gathered as part of the screening process. That being said, only one participant was excluded based on this, suggesting the other screening methodologies applied are probably sufficient (i.e. phone interview and assessment with the PSQI and ISI). Further, the fMRI study had the smallest sample. Based on the theories put forward previously in this chapter, the sample in this study should represent the highest level of vulnerability, given that they are higher on neuroticism and conscientiousness. Taken together, these results highlight the need to measure both these variables, as in the first 2 conscientiousness was the only significant mediating factor and in the third study, this particular construct seems to characterise the vulnerable group. Reflecting upon the vulnerable phenotype and the tasks employed in these studies this seems an intuitive conclusion to make. Whilst conscientiousness has been deemed as a protective factor when not coupled with neuroticism, the addition of a neurotic trait can make this maladaptive. If an individual is conscientious i.e. diligent, careful and neurotic i.e. susceptible to negative emotion, particularly in relation to stress, it becomes easy to see how this may act as a precursor to psychological dysfunction. In the face of stressful situations conscientiousness creates a drive to get things right.

Trait neuroticism contributes towards anxiety that things might go wrong, and a perceptual bias toward cues (or a negative interpretation of ambiguous cues) which may indicate that it has indeed gone wrong. This creates a greater anticipation to stress, and a prolonged elevation of the stress response (i.e. a consistent pattern in the stress response). Rumination on the stressful event may then lead to a reliving of the stressful experience. In terms of the phenomenology of insomnia, this could easily become the ‘racing mind’ and interfere with sleep. The tasks employed in this study all emphasise the importance of performance, either in terms of responding correctly or quickly to stimuli, or the judgement of a presentation. The stressor reported in the short follow-up is unanimously increased work load which again could be considered a performance based stressor. Under such conditions, an increase in the desire to do well coupled with a

greater likelihood of processing situations negatively could lead to belief that one is not performing correctly and an increase in anxiety results from this.

Psychologically then the results of the 3 studies presented makes theoretical sense. The consistency in greater levels neuroticism across the 3 studies in 3 independent samples, and the consistent finding that conscientiousness and rumination are related to physiological measures demonstrates that the vulnerable population does have its own psychological profile, which differentiates it from the resilient population and further, that this can be detected using the FIRST. This is further supported by the analysis on the combined data-set, showing the vulnerable group are increase in negative affect, perceived stress, rumination and worry.

Chapter 7 provides further support for the results found in the 3 experimental chapters. Across all 3 samples is can be seen that the vulnerable group are characterised by neuroticism, conscientiousness, perceived stress, depressive thinking, reflective thinking, state-levels of stress and worry. They also score significantly higher on problem focused and emotion focused coping. This may represent an unstable coping style. They were also found to be lower on extraversion.

8.2 Psychobiology

The biological indices of stress across the 3 studies prove to be quite interesting. It was hypothesised initially that the vulnerable group would demonstrate an increase in stress reactivity. However, this has consistently failed to garner support. Combined, the 3 studies all suggest that the autonomic nervous system is differently active in the vulnerable group, however, the nature of this difference does not appear to be in terms of reactivity. Further to this, the inconsistencies across the 3 different methods may imply that different parts of the nervous system are affected differentially, and so may demonstrate varying degrees of utility in specifying the vulnerable population. Firstly, cortisol output was elevated during the anticipation phases of the TSST- time points 1 and 2- in the vulnerable group. HR and CVT were consistently lower in the vulnerable population, and it has been argued that they demonstrate a decrease in CVT flexibility. There were no differences at baseline (in anticipation to the stressor). The fMRI study demonstrated that the vulnerable population showed greater activation in the left

postcentral gyrus (PG) and a bi-lateral hypoactivation in the inferior parietal lobule (IPL), in anticipation to stress. This has been argued as representing a deeper encoding of the negative association between the siren and the stressful task.

Study Chapter	Main Finding
Chapter 4	1. The vulnerable population are higher on negative affect, stress and worry 2. They show increased levels of cortisol at baseline (or in anticipation) 3. This is mediated by conscientiousness 4. They show an increase in insomnia symptoms in response to real life stress
`Chapter5	1. The insomnia population are higher on negative affect 2. They show reduced HR and reduced CVT consistently across stress and baseline measures. 3. CVT change is mediated by conscientiousness. 4. May indicate reduced CVT flexibility.
Chapter 6	1. The vulnerable group show greater levels of neuroticism. 2. The vulnerable population show an increase in activation in the left Postcentral Gyrus (PG) 3. This is mediated by neuroticism 4. The vulnerable group show hypoactivation bi-laterally in the Inferior Parietal Lobule (IPL) 5. This is mediated by FIRST score 6. This may reflect a stronger learned association between the siren and an increase in task difficulty.

Table 8 1 Summary of main findings

Further to this, there was some interesting data on the cortisol profile of those who were excluded from the Trier study analysis for scoring as poor sleepers (see appendix X). This demonstrated that on average, this small group of poor sleepers had larger SFC levels at every time point, and further their reactivity pattern (i.e. the shape of the graph) was much sharper, showing a steeper incline in response to the stressor but also a steeper decline towards baseline during the final resting phases. It would be interesting to follow these results up with an insomnia group in order to do a more stringent comparison. What these results suggest however is that the vulnerable group show an SFC response which lies somewhere between that of a good sleeper and that of a poor sleeper: the pattern of results may indicate a pre-clinical sample, that is to say a true representation of the vulnerable population. In a broader sense, this may mean that vulnerability to insomnia is characterised by a strong reaction of the HPA to the possibility of stress over time and in the face of more or increasingly severe stressors this becomes a marked change in stress-reactivity, as sleep begins to deteriorate. The worsening of sleep may then lead to further dysregulation of the HPA axis, and so chronically increased levels of cortisol that has been evidenced in the insomnia population[58]

Supporting this hypothesis is the brain activation of the IPL. If indeed it does represent the faulty encoding of emotional associations as suggested, then perhaps from a top-down perspective this leads to more situations in which the individual anticipates stress over time: if negative associations are more readily encoded within this population then it becomes easier for random events to become associated. For example, a student has to give a presentation. It goes badly. For a resilient individual this is written off as a bad presentation. For a vulnerable individual the bad experience becomes associated with the negative outcome and so anytime a presentation is needed it is associated with negative emotions and so the association strengthens. Hyperactivation in the PG has been previously implicated in working memory. This may then provide credence to the theories delineated above.

Thinking about the psychological implications of trait neuroticism, these associations may be compounded. Neuroticism leads to negative interpretations, which means that an even larger array of situations become negative, due to a focus- and subsequent rumination-on the negative aspects. To elaborate on the example given: A student gives an overall well received presentation. However, they forgot to mention one of their key

findings. This in itself is not a big deal, and probably there will be an opportunity to ask questions and mention this after and overall the presentation went down well and was considered interesting by the audience. However, the neurotic, vulnerable individual focuses on the aspect which they forgot, or the aspect which they failed. This again leads to an association between presenting and notions of 'I am no good at this'; 'this will go badly'; 'I am anxious'. Coming back to sleep, this pathway may represent one way in which poor sleep is maintained. If an individual who is usually a good sleeper has a bad night's sleep due to events that day or events coming up the next day which they are anxious about, and they embody the vulnerable phenotype then they may be more sensitive to the negative associations of sleep loss, or more likely to interpret lack of sleep as threatening. This mirrors somewhat the ideas put forward in the A-I-E pathway for explaining chronic insomnia[43]

As outlined above, day-to-day stress levels increase as more and more situations become stress inducing. There are then more situations in which the HPA axis becomes over active, as the anticipation of stress becomes more frequent. The suggested lack of flexibility of CVT may represent an inability to dampen the processes of the autonomic nervous system. Over time, as sleep begins to falter and further impact on the central nervous system, this becomes the hyperarousal seen in insomnia and possibly a more reactive stress system.

8.3 Strengths and Limitations

Limitations for each chapter are presented in the discussion for each chapter, so only broad limitations will be discussed here.

Whilst these results are interesting and complement each other nicely, several caveats must be considered. Firstly, the conclusions put forward in this overall discussion are largely speculative, based on sound theory but nonetheless still need to be tested. Whilst they are sensible, to really draw out these hypotheses a much bigger sample is needed, following changes in CNS indices over time, in relation to changes in sleep and number of perceived stressful life events. It would also be necessary, to truly answer the questions posed, to have the same sample undergo all 3 stress paradigms, so that relationships

between different components of the CNS can be directly compared, rather than speculatively across 3 different samples.

The selection of the vulnerable group is based solely on the FIRST. This may then represent a very specific kind of vulnerability to insomnia. The validation of the FIRST scale was conducted using primarily physiological stressor- caffeine and phase advance ((Cronbach's alpha = 0.83, test retest reliability co-efficient = 0.92)[137]. The studies presented here, then, represent the primary example of the FIRST in relation to psychological stress. This then may provide some validation for the scale, given the consistency in findings. This however is a secondary outcome and not the aim of this thesis. Interestingly, the studies highlight the importance of stress anticipation. The FIRST scale however poses 3 questions regarding stress anticipation-how much your sleep is likely to be disturbed *before* a stressful event (items 1, 8 and 9).- and 6 questions about how you feel *after* a stressful event. Given the results presented, this might indicate a weakness of the scale if increased stress reactivity, or prolonged maintenance of increased stress levels is not what characterises this population i.e. the FIRST may select those who show strong anticipation to stress rather than those who are vulnerable to sleep disruption. . Further to this, the FIRST scale has not been validated against other scales which may measure similar constructs such as the Arousal Predisposition Scale[227]. The benefit of the FIRST over the APS however, is that the FIRST asks directly about how sleep will be affected given a certain situation, whereas the APS is a more general questionnaire assessing arousability. Given that the aim of this thesis is to differentiate those vulnerable to sleep disruption, the APS would at best have provided an interesting comparison between those who are high in arousability but not vulnerable. This may be an important comparison to make in future studies in order to allow inferences about protective factors, but not essential when considering vulnerability factors. Supporting the use of the FIRST scale is the finding that the vulnerable group do show an increase in subjectively reported insomnia symptoms in response to real-life stress – although the stress reported is consistently work load i.e. performance based stressor. None the less, this does suggest that the FIRST is a valid scale.

The small sample size and bias toward females in the 2 latter samples has to be considered also. Given that insomnia is more frequently observed in females[6], this may not be an issue, and may in fact add to the validity of the results. Gender was covaried

for in analysis where appropriate and did not have a significant influence, but this may be an artefact of large under-representation of males in the latter 2 studies.

The effects sizes reported throughout this thesis are mostly in the moderate to large range. This therefore implies that the effects found are genuine. If conducted in larger samples, this may help to illuminate on some of the inconsistencies between studies, particularly on some of the psychological variables and may further show significant results where only trends have been found here.

8.4 Future Directions and Implications

Considering the limitations outlined above, future studies should aim to recruit larger samples with an even representation of males and females. As already suggested, longitudinal work needs to be done, assessing changes over time to indicate which factors most strongly predict these changes. In an ideal situation, the study which will best answer the questions posed will follow a large genotyped cohort from childhood through to adulthood, periodically assessing them on various physiological and psychological domains. Realistically, the next step is replication. Further, replication on larger samples and follow-up times extending beyond 2 weeks. Once this has been achieved, , investigation of protective factors will prove merited for example looking at arousability, using the APS for example, compared to the FIRST, and assessing those who are predisposed to arousal, but not vulnerable, again considering both psychological and physiological domains.

The implications of this work are primarily within the domain of prevention. Given the cost outlined in chapter 1, both to the individual and at a societal level, there is an obvious merit in preventative measures. The existence of a vulnerable phenotype, in practical terms, may not result in targeting individuals but will aid in our understanding of which factors needs to be targeted, generally. This will inform educational programmes and preventative interventions. Given the results of this thesis, prevention should focus on stress management and the rationalisation of intrusive or unrealistic thoughts: teaching objectivity, in order to reduce the negatively laden emotional burden of trait neuroticism. By proxy, this work may also provide some insight into the insomnia mind. It is posited that stress reactivity changes over time; however the constructs of personality

are considered enduring. This could possibly then provide direction for more robust, individually tailored treatment programmes for those suffering chronic insomnia.

The results of this thesis also highlight the issue of transdiagnosis within mental health. The constructs hypothesised to characterise those vulnerable to insomnia are also known to be strongly associated with depression and anxiety disorders- such as worry, rumination and negative affect. In terms of the physiological stress response, comparisons are drawn between the vulnerable population, the insomnia population, the depressed population and in the brain imaging chapter, with the PTSD population. These factors may then not be specific to the development of insomnia, but rather to psychological disorder generally. Groups in this thesis were constructed based on a scale aimed at assessing vulnerability to sleep disruption, therefore only vulnerability to sleep disruption can be confidently concluded upon. It could be the case however, that targeting risk factors to insomnia may result in not only a reduction of insomnia syndrome prevalence but also a reduction in depression and anxiety disorders.

8.5 Concluding Remarks

The work presented in this thesis is piloting. No work has been published to date which aims to systematically define the vulnerable population. As such, this works represents novel and interesting avenues of research for the field. It has been demonstrated that differences between the vulnerable and resilient groups are considerably consistent, suggesting that this is indeed a distinct population, that can be reliably selected by the FIRST scale. Ultimately, this work represents a tentative first step in understanding the interaction between psychology and stress biology in defining the vulnerable population

Appendices

I. University of Glasgow Standard Screening Form

PLEASE MAKE SURE THAT ALL OF THE FORM IS FILLED IN CLEARLY INCLUDING WHO TOOK THE CALL AND THE DATE AND TIME. NOTES SHOULD BE KEPT ON SEPARATE PIECE OF PAPER.

Source

How did you find out about the University of Glasgow Sleep Centre?	
Why have you contacted us?	
Method of initial contact (mobile, email, office phone)?	

Personal

Full Name:	*Date of Birth:*	*Age:*
Telephone:	*Address:*	
Alternative Telephone:		
When is a good time to call?		
What GP practice do you attend, and who is the GP you normally see?		

Sleep

Do you have difficulty sleeping at the moment? (Y/N)	
Have you always been a poor sleeper? (Y/N)	
How long have you had a sleep problem?(yr)	

Do you have difficulty falling asleep? (Y/N)	
How many nights per week do you have difficulty falling asleep? (out of 7)	
How long does it normally take you to fall asleep?(min)	
Do you have a difficulty with waking up during the night?(Y/N)	
How many nights per week do you have a difficulty with waking up during the night?(out of 7)	
How long are you normally awake during the night, in total? (min)	
What time do you normally go to bed? (time)	
What time do you normally get up?(time)	
How long do you normally sleep?(hr/min)	
Do you any other difficulties with your sleep (e.g. restless legs, breathing problems, sleep walking)?	
Do you work shifts, night shifts?	
Roughly, how many units of alcohol do you drink per week? *(Remember: One standard (175ml) glass of wine = 2 unit* *One pint of standard lager = 2.3 units* *Spirit & Mixer = 1 unit)*	
Does your sleep disturbance affect how you feel and function during the day (e.g. fatigue, sleepiness, concentration, memory, mood, motivation, irritable, work/social functioning etc.)? If yes, specify most salient.	

Health

Do you keep in good health physically? (Y/N)	
What physical health problems do you have (if applicable)?	

What medicines do you take for your physical health? (if applicable)	
Do you keep in good health mentally? (Y/N)	
What physical health problems do you have (if applicable)?	
What medicines do you take for your mental health? (if applicable)	
Do you give your consent for us to contact your GP if necessary regarding your health?	
If you are not suitable for any of the studies ongoing at the moment are you happy for your details to be kept on a database so that you may be contacted in the future should a suitable study start?	

Notes

For Office Use
Enquiry taken by: At (time): On (date): Information sent:

[study name]	**[study name]**	**[study name]**	**[study name]**
[study name]	**[study name]**	**[study name]**	**[study name]**
[study name]	**[study name]**	**[study name]**	**[study name]**

On (date):

II. Exclusion criteria (Chapters 4,5,6)

- Presence Sleep disorder
- If any of the following sleep symptoms are presented, even if participant does not reach diagnostic criteria:
- complaint about sleep
- Dissatisfied with amount of sleep
- Feeling that sleep is non-restorative
- Current psychological Disorders (Depression, Anxiety etc)
- Currently receiving treatment for psychological disorders.
- Disorders of the central nervous system (Cushington's disease, epilepsy for example)
- Heart/ blood pressure problems
- Currently taking medications, except contraceptive pill, or inhalers
- Regularly taking recreational drugs (more than once a week)
- Excessive caffeine intake (more than 5 caffeinated beverages per day)
- Excessive alcohol consumption (more than 20 units per week, on average)
- Travelled across time-zones in the last month
- Participated in other studies which are part of this thesis

III. Questionnaire Booklet

Name:
Age:
Date of Birth:
Gender:

Please remember with while answering the questionnaires that your first response is usually the most representative. Don't be tempted to over think the questions

PSQI

INSTRUCTIONS: The following questions relate to your usual sleep habits **during the past month *only***. Your answers should indicate the most accurate reply for the *majority* of days and nights in the past month. Please answer all the questions.

1. **During the past month, when have you usually gone to bed at night?**

   Usual Bed Time: ……

2. **During the past month, how long (in minutes) has it usually taken you to fall asleep each night?**

   Number of Minutes: ……

3. **During the past month, when have you usually got up in the morning?**

   Usual Getting Up Time: ……

4. **During the past month, how many hours of *actual sleep* did you get at night? (This may be different than the number of hours you spend in bed)**

   Hours of Sleep per Night: ……

For each of the remaining questions, ***circle the response that fits best****. Please answer all the questions.*

5. **During the past month,** how often have you had trouble sleeping because you…

(a). Cannot get to sleep within 30 minutes.	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
(b). Wake up in the middle of the night or early morning.	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
(c). Have to get up to use the bathroom.	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week

(d). Cannot breathe comfortably.	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
(e). Cough or snore loudly.	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
(f). Feel too cold.	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
(g). Feel too hot.	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
(h). Had bad dreams	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
(i). Have pain.	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week

(j). Other reason(s), please describe _____

_____

_____

How often during the past month have you had trouble sleeping because of this?

Not during the past month	Less than once a week	Once or twice a week	Three or more times a week

6. During the past month, how would you rate your sleep quality overall?

Very Bad	Fairly Bad	Fairly Good	Very Good

7. During the past month, how often have you taken medicine (prescribed or 'over the counter') to help you sleep?

Not during the past month	Less than once a week	Once or twice a week	Three or more times a week

8. During the past month how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?

Not during the past month	Less than once a week	Once or twice a week	Three or mor times a weel

9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

No problem at all	Only a very slight problem	Somewhat of a problem	A very big problem

10. Do you have a bed partner or roommate? Please circle:

No bed partner or roommate

Partner / roommate in other room

Partner in same room, but not same bed

Partner in same bed

If you have a roommate or bed partner, ask him / her how often in the past month you have had……

a. Loud snoring

Not during past month	Less than once a week	Once or twice a week	Three or more times a week

b. Long pauses between breaths while asleep

Not during past month	Less than once a week	Once or twice a week	Three or more times a week

c. Legs twitching or jerking while you sleep

Not during past month	Less than once a week	Once or twice a week	Three or more times a week

d. Episodes of disorientation or confusion during sleep

Not during past month	Less than once a week	Once or twice a week	Three or more times a week

e. Other restlessness while you sleep: please

describe_____

_____

_____

Not during the past month	Less than once a week	Once or twice a week	Three or more times a week

ISI

1. Please rate the current (i.e., last two weeks) severity of your insomnia problems(s) by *circling* a response.

	None	Mild	Moderate	Severe	Very
a. Difficulty falling asleep:	0	1	2	3	4
b. Difficulty staying asleep:	0	1	2	3	4
c. Problem waking up too early:	0	1	2	3	4

2. How satisfied/dissatisfied are you with your current sleep pattern?

Very Satisfied	Satisfied	Neutral	Dissatisfied	Very Dissatisfied
0	1	2	3	4

3. To what extent do you consider your sleep problem to interfere with your daily functioning (e.g. daytime fatigue, ability to function at work/daily chores, concentration, memory, mood, etc.)

Not at all Interfering	A little	Somewhat	Much	Very much Interfering
0	1	2	3	4

4. How noticeable to others do you think your sleeping problem is in terms of impairing the quality of your life?

Not at all Noticeable	A little	Somewhat	Much	Very much Noticeable
0	1	2	3	4

5. How worried/distressed are you about your current sleep problem?

Not at all Worried	A little	Somewhat	Much	Very much Worried
0	1	2	3	4

FIRST

When you experience the following situations, how likely is it for you to have difficulty sleeping? *Circle* an answer even if you have not experienced these situations recently.

Before an important meeting the next day

Not likely Somewhat likely Moderately likely Very likely

After a stressful experience during the day

Not likely Somewhat likely Moderately likely Very likely

After a stressful experience in the evening

Not likely Somewhat likely Moderately likely Very likely

After getting bad news during the day

Not likely Somewhat likely Moderately likely Very likely

After watching a frightening movie or TV show

Not likely Somewhat likely Moderately likely Very likely

After having a bad day at work

Not likely Somewhat likely Moderately likely Very likely

After an argument

Not likely Somewhat likely Moderately likely Very likely

Before having to speak in public

Not likely Somewhat likely Moderately likely Very likely

Before going on vacation the next day

Not likely Somewhat likely Moderately likely Very likely

PSS

The questions in this scale ask you about your feelings and thoughts **during the last month**. In each case, you will be asked to indicate by writing a number, *how often* you felt or thought a certain way:

0 = Never 1 = Almost Never 2 = Sometimes 3 = Fairly Often 4 = Very Often

1. In the last month, how often have you been upset because of something that happened unexpectedly?.....

2. In the last month, how often have you felt that you were unable? to control the important things in your life?.....

3. In the last month, how often have you felt nervous and “stressed”? .....

4. In the last month, how often have you felt confident about your ability to handle your personal problems?.....

5. In the last month, how often have you felt that things were going your way?.....

6. In the last month, how often have you found that you could not cope with all the things that you had to do? .....

7. In the last month, how often have you been able to control irritations in your life?.....

8. In the last month, how often have you felt that you were on top of things?....

9. In the last month, how often have you been angered because of things that were outside of your control? .....

10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?.....

DASS21

Please read each statement and insert a number 0, 1, 2 or 3 which indicates how much the statement applied to you *over the past week*. There are no right or wrong answers. Do not spend too much time on any statement.

The rating scale is as follows:

0 Did not apply to me at all
1 Applied to me to some degree, or some of the time
2 Applied to me to a considerable degree, or a good part of time
3 Applied to me very much, or most of the time

1 I found it hard to wind down

2 I was aware of dryness of my mouth

3 I couldn't seem to experience any positive feeling at all

4 I experienced breathing difficulty (eg, excessively rapid breathing, breathlessness in the absence of physical exertion)

5 I found it difficult to work up the initiative to do things

6 I tended to over-react to situations

7 I experienced trembling (eg, in the hands)

8 I felt that I was using a lot of nervous energy

9 I was worried about situations in which I might panic and make a fool of myself

10 I felt that I had nothing to look forward to

11 I found myself getting agitated

12 I found it difficult to relax

13 I felt down-hearted and blue

14 I was intolerant of anything that kept me from getting on with what I was doing

15 I felt I was close to panic

16 I was unable to become enthusiastic about anything

17 I felt I wasn't worth much as a person

18 I felt that I was rather touchy

19 I was aware of the action of my heart in the absence of physical exertion (eg, sense of heart rate increase, heart missing a beat)

20 I felt scared without any good reason

21 I felt that life was meaningless

NEO-ffi

Below are a number of characteristics which may or may not apply to you. Please indicate your degree of agreement based on the following scale.

Disagree strongly	**Disagree**	**Disagree more than agree**	**Agree more than disagree**	**Agree**	**Agree strongly**
1	**2**	**3**	**4**	**5**	**6**

1	I am not a worrier.	
2	I like to have a lot of people around me.	
3	I don't like to waste my time daydreaming.	
4	I try to be courteous to everyone I meet.	
5	I keep my belongings clean and tidy.	
6	I often feel inferior to others.	
7	I laugh easily.	
8	Once I find the right way to do something, I stick to it.	
9	I often get into arguments with my family and co-workers.	
10	I'm pretty good at pacing myself so as to get things done on time	
11	When I'm under a great deal of stress, sometimes I feel like I'm going to pieces	
12	I don't consider myself to be especially "light-hearted".	
13	I am intrigued by the patterns I find in nature and art.	
14	Some people think I'm selfish and egotistical.	
15	I am not a very methodical person.	
16	I rarely feel lonely or blue.	
17	I really enjoy talking to people .	
18	I believe letting students hear controversial speakers can only confuse and mislead them.	
19	I would rather cooperate with others than compete with them.	
20	I try to perform all the tasks assigned to me conscientiously.	
21	I often feel tense and jittery.	
22	I like to be where the action is.	
23	Poetry has little or no effect on me.	

24	I tend to be cynical and sceptical of others' intentions.	
25	I have a clear set of goals and work towards them in an orderly fashion.	
26	Sometimes I feel completely worthless.	
27	I usually prefer to do things alone.	
28	I often try new and foreign foods.	
29	I believe that most people will take advantage of you if you let them.	
30	I waste a lot of time before settling down to work.	
31	I rarely feel fearful or anxious.	
32	I often feel as if I'm bursting with energy.	
33	I seldom notice the moods or feelings that different environments produce.	
34	Most people I know like me	
35	I work hard to accomplish my goals.	
36	I often get angry at the way people treat me.	
37	I am a cheerful, high-spirited person...	
38	I believe we should look to our religious authorities for decisions on moral issues	
39	Some people think of me as cold and calculating.	
40	When I make a commitment, I can always be counted on to follow through	
41	Too often, when things go wrong, I get discouraged and feel like giving up.	
42	I am not a cheerful optimist.	
43	Sometimes when I am reading poetry or looking at a work of art, I feel a chill or wave of excitement.	
44	I'm hard-headed and tough-minded in my attitudes.	
45	Sometimes I'm not as dependable or reliable as I should be.	
46	I am seldom sad or depressed.	
47	My life is fast-paced.	
48	I have little interest in speculating on the nature of the universe or the human condition.	
49	I generally try to be thoughtful and considerate.	
50	I am a productive person who always gets the job done.	
51	I often feel helpless and want someone else to solve my problems	
52	I am a very active person.	

53	I have a lot of intellectual curiosity.	
54	If I don’t like people, I let them know.	
55	I never seem to be able to get organised.	
56	At times I have been so ashamed I just wanted to hide.	
57	I would rather go my own way than be a leader of others.	
58	I often enjoy playing with theories or abstract ideas.	
59	If necessary, I am willing to manipulate people to get what I want.	
60	I strive for excellence in everything I do.	

Rumination Scale

People think and do many different things when they feel depressed. Please read each of the items below and indicate whether you almost never, sometimes, often, or almost always think or do each one when you feel down, sad, or depressed. Please indicate what you *generally* do, not what you think you should do.

1*= almost never* ***2****= sometimes* ***3****= often* ***4****= almost always*

1. Think about how alone you feel……
2. Think “I won’t be able to do my job if I don’t snap out of this”……
3. Think about your feelings of fatigue and achiness……
4. Think about how hard it is to concentrate……..
5. Think “What am I doing to deserve this?”……..
6. Think about how passive and unmotivated you feel……
7. Analyze recent events to try to understand why you are depressed……
8. Think about how you don’t seem to feel anything anymore……
9. Think “Why can’t I get going?”…….
10. Think “Why do I always react this way?”…….
11. Go away by yourself and think about why you feel this way……
12. Write down what you are thinking about and analyze it……
13. Think about a recent situation, wishing it had gone better……
14. Think “I won’t be able to concentrate if I keep feeling this way.”…….
15. Think “Why do I have problems other people don’t have?”……..
16. Think “Why can’t I handle things better?”……
17. Think about how sad you feel……
18. Think about all your shortcomings, failings, faults, mistakes……
19. Think about how you don’t feel up to doing anything……
20. Analyze your personality to try to understand why you are depressed…….
21. Go someplace alone to think about your feelings……..
22. Think about how angry you are with yourself……..

Brief-COPE

These items deal with ways you've been coping with the stress in your life. I want to know to what extent you've been doing what each item says. How much or how frequently. Don't answer on the basis of whether it seems to be working or not—just whether or not you're doing it. Use these response choices. Try to rate each item separately in your mind from the others. Make your answers as true FOR YOU as you can. Please write the appropriate number at the end of each question.

***1** = I haven't been doing this at all; **2** = I've been doing this a little bit*

***3** = I've been doing this a medium amount; **4** = I've been doing this a lot*

1. I've been turning to work or other activities to take my mind off thing…..
2. I've been concentrating my efforts on doing something about the situation I'm in…..
3. I've been saying to myself "this isn't real."…
4. I've been using alcohol or other drugs to make myself feel better….
5. I've been getting emotional support from others…
6. I've been giving up trying to deal with it….
7. I've been taking action to try to make the situation better….
8. I've been refusing to believe that it has happened…
9. I've been saying things to let my unpleasant feelings escape…
10. I've been getting help and advice from other people…
11. I've been using alcohol or other drugs to help me get through it…
12. I've been trying to see it in a different light, to make it seem more positive…
13. I've been criticizing myself…
14. I've been trying to come up with a strategy about what to do…
15. I've been getting comfort and understanding from someone...
16. I've been giving up the attempt to cope…
17. I've been looking for something good in what is happening…
18. I've been making jokes about it…
19. I've been doing something to think about it less, such as going to movies,
    watching TV, reading, daydreaming, sleeping, or shopping…
20. I've been accepting the reality of the fact that it has happened…
21. I've been expressing my negative feelings...
22. I've been trying to find comfort in my religion or spiritual beliefs…

23. I’ve been trying to get advice or help from other people about what to do...
24. I've been learning to live with it...
25. I've been thinking hard about what steps to take…
26. I’ve been blaming myself for things that happened…
27. I've been praying or meditating…
28. I've been making fun of the situation…

PSWQ

Please use the scale below to express to what extent each statement is typical to you (write the number that represents you the best at the end of each statement).

1= *not at all typical;* ***2****= a little typical****; 3=*** *moderately typical;* ***4=****very typical;* ***5=*** *extremely typical*

1. If I do not have enough time to do everything, I do not worry about it…..
2. *My* worries overwhelm me…..
3. I do not tend to worry about things…..
4. Many situations make me worry…..
5. I know I should not worry about things, but I just cannot help it…..
6. When I am under pressure I worry a lot…..
7. I am always worrying about something…..
8. I find it easy to dismiss worrisome thoughts…..
9. As soon as I finish one task, I start to worry about everything else I have to do…..
10. I never worry about anything…..
11. When there is nothing more I can do about a concern, I do not worry about it any more…..
12. I have been a worrier all my life…..
13. I notice that I have been worrying about things…..
14. Once I start worrying, I cannot stop…..
15. I worry all the time…..
16. I worry about projects until they are all done…..

IV. Information Sheet for TSST Study (Chapter 4)

Participant Information Sheet

Title: Stress reactivity and insomnia

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

The Study
This study will be conducted through the University of Glasgow Sleep Centre. You have been invited to take part in this study based on your responses to previous part of the study or because you have passed the screening process. This second part of the study (phase 2) in which you are being asked to take part is designed to help us profile the relationships between sleep problems, perceived stress, personality and coping styles and stress reactivity. Hopefully this type of research will help us improve our understanding of insomnia, and give an insight into how insomnia can be prevented.

Do I have to take part?
Taking part in the research is entirely voluntary. This means that it is up to you to decide whether or not you would like to take part. If you do not wish to take part it will not affect the case or your rights in any way. If you decide to take part in the study, you can keep this information sheet and contact the researcher for further information. If you do decide to take part, you can change your mind and withdraw from the study at any time, even after the study has finished.

What does taking part involve?
If you decide to take part all you have to do is come to Psychology Department at the University of Glasgow where you will be asked to run through 2 different tasks and periodically provide saliva samples. The saliva samples allow us to collect information on the activity of certain hormones during the tasks. You will be in the department for roughly an hour and this will be paid (£10).

Would my results be kept confidential? What will happen to the results of the study?
All the information that is collected during the course of the study will remain strictly confidential. This means that all information will be kept secured in locked filling cabinets and only the researcher will be able to access these. You will be given a unique code that will ensure confidentiality and anonymity of all your data. Saliva samples will be sent securely for analysis, and no genetic data will be collected. The results of this study will be

published in a relevant journal so that the general public is also aware of these findings. However any information regarding your identity will not be revealed in these.

What are the potential benefits or disadvantages of taking part?
Taking part will provide us with information of how to improve treatments and aid in prevention of insomnia. There are no risks or disadvantages associated with taking part. You will also be given advice on how to promote better sleep during times of stress.

Who is organising and paying for the research?
The research study is organised by Christopher-James Harvey, doctorial research student and is funded by The Sackler Institute of Psychobiological Research.
Educational supervision of this research is provided by Prof Colin Espie and Dr. Jonathan Cavanagh

If I decide to take part what happens next?
If you decide to take part you will be invited to come to the Psychology Department and given the opportunity to ask any questions about the research before commencing the study.

Thank you for reading this information. If there is anything that is not clear or if you have any questions regarding this study you can e-mail the researcher at

c.harvey.1@research.gla.ac.uk or call:

or call Chris on 0141 232 7566

If you would like some independent advice from someone who is not involved in the study, please contact Dr Maria Gardani +44 (0)141 232 7700 or M.Gardani@clinmed.gla.ac.uk

V. Consent Form for TSST Study (Chapter 4)

University of Glasgow | Sleep Centre

Participant Identification Number for this study:

CONSENT FORM

Title of Project: Stress reactivity and Insomnia (Phase 1)

Mr. Christopher-J. Harvey, Prof. Colin Espie, Dr. Jonathan Cavanagh

Please initial box

1. I confirm that I have read and understand the information sheet and received my own copy dated 20th April 2010 (version 1) for the above study. ☐

2. I have had the opportunity to consider the information provided, ask questions and have had these answered satisfactorily. ☐

3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐

4. I understand that data collected during this study may be looked at by responsible individuals from the research team or from regulatory authorities where it is relevant to them taking part in research.
I give permission for these individuals to have access to my records. ☐

5. I consent to the results (in anonymised form) of this study being published in relevant journals. ☐

6. I agree to be contacted in the future from the Glasgow Sleep Research Centre. ☐

7. I agree to take part in the above study. ☐

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Researcher	Date	Signature

VI. Instruction Sheet Given to Confederates During Training

Materials:

- 2 rooms
- Audio and visual recording device
- 2 notepads
- Scripted material: for introduction to tasks, task debriefing procedures
- Timers with alarms
- Salivettes for saliva collection
- Questionnaires (MEQ)
- Bland reading material

People:

- Experimenter: Responsible for guiding the subject to and from rooms, administering questionnaires, collecting saliva and debriefing participant
- Confederates-
    - At least 2
    - No prior contact with participant prior to TSST
    - Only one has verbal communication with the participant throughout the experiment

Environment:

- Preparatory/Resting room
    - Somewhat comfortable and secluded
    - Bland reading material
    - Paper and pen with writing desk for participant
    - Used before and after TSST for resting periods and note making

- Testing Room
    - Plain room with a desk and 2 chairs
    - Screen showing recording of participant- as microphone will not be visible it is important participants are made aware that the laptop has in build microphone
    - Speech and math task conducted in this room.

Procedures:

All participants will be tested between 1300 and 1800 hours as this a period of relative quiescence of the HPA axis- responsible for cortisol production- thus ensuring that natural circadian peaks in cortisol levels do not interfere or present a confound to our results

Participants will be instructed not to eat, smoke or ingest caffeine within at least an hour of testing. Participants will be instructed that this will ruin results and can be detected in the saliva.

Arrival:

I. Participant will be greeted by the experimenter in the waiting room and escorted to the preparatory room
II. They will be asked to rest for 10 minutes, feeling free to use the reading material provided.
III. Saliva sample is taken at the end of 10 minutes.

Speaking task:

I. Researcher gives participant instruction on speaking task- see appendix a.
II. If Ps asks any questions the researcher should give neutral responses such as 'Do what you think is best' or 'I do not have any further details'.

Preparation:

I. In prep room a timer is set for 10 minutes and Ps is told to make notes on their speech and that these, however, will not be allowed into the testing room
II. After the alarm goes off researcher returns to room and a second saliva sample is taken.

Speaking Task:

I. Researcher leads Ps back to testing room, knock on door and waits for reply from confederate1. Ps is led inside and researcher remains outside.
II. Confederates are to remain expressionless throughout this and the math task, and only confederate1 is to talk.
III. Timer is set to 5 minutes and confederate tells Ps to begin.
IV. Confederate 2 should take notes every minute or so as if noting the Ps performance, however these should be kept brief as it is essential that eye contact is maintained as continuously as possible.
V. If Ps stops speaking for more than 20s confederate1 should interject 'You still have more time. Please continue'.
VI. If Ps asks any questions again replies should be kept as neutral as possible:
    a. 'Do what you think is best'
    b. 'Say what comes into your head'
    c. 'Be as creative as you like' (for example)
VII. At the sound of the buzzer confederate 1 should say 'your time is up. Please stop.'

Math Task:

I. Confederate 1 then tells participant 'Now we would like you to subtract 13 from 6233 and keep subtracting from the remainder until we tell you to stop. You should be as fast and as accurate as possible'
II. Whenever an error is made the Ps must restart. Confederate 1 should say 'That is incorrect. Please begin again at 6233'
III. At the end of the 5 minutes the Ps is instructed 'Your time is up. You may return to your room'
IV. If Ps asks questions about responses confederate 1 must report 'I cannot give you this information. Someone else will tell you later'

Rest Period:

I. Participant is led back to resting room where they will rest for 30mins.
II. Saliva samples will be taken immediately on arrival and then every 10 minutes until 30 minutes is up. This will provide in total 5 saliva samples per participant for the whole paradigm.

Debriefing:

I. Participant is told nature of study – see appendix B.
II. Participant meets confederates who explain that they were cold as this was necessary for the experiment. If they are unavailable for debriefing the researchers explains this to them.
III. Payment is made.

In-case of Adverse Reaction

If the participant becomes unduly stresses- crying or overly agitated- confederate 1 should ask 'Are you OK to continue?' and then 'Do you wish to stop?'

If the participant indicates that they do wish to stop then the researcher in charge should be notified immediately, the experiment ended and the participant debriefed and calmed down.

VII. Transcript of Recording Played to Participants

Please listen carefully. I am about to explain the task that you are being asked to complete. [Pause]

The 2 trained interviewers sitting before you are waiting to assess how outgoing, gregarious and comfortable you are in a situation where you need to project an air of expertise. This is a type of personality test for a trait known as extroversion. [Pause]

You will be given a hypothetical situation in which you are applying for your ideal job, a job which you have dreamed of working in for as many years as you can remember.[Pause]

After seeing an advertisement for this job and applying, you have received an invitation to attend an interview. [Pause]

The job has a high salary and a lot of other candidates with whom you are competing. [Pause]

The final decision will be based on *your* ability to convince the interviewers that your experience, abilities and education make you better suited than all the other candidates. You are trying to convince the panel that *you* are the best candidate for this position. [Pause]

You will be given 10 minutes to prepare a detailed speech. You will then return to the interview room, which you are in now, to deliver your speech to the interviewers'. The purpose of the speech is to explain why you should get the job. The notes you make during preparation may not be taken into the interview room, but are merely to help you organise your thoughts. [Pause]

Following this you will be given a mental arithmetic task. [Pause]

It is important to remember that these interviewers are specifically trained to monitor and assess the rate of your speech for believability and convincingness and to also assess non verbal cues. Further it is important to remember that you will be compared against those who have already completed this task. [Pause]

Your speech will be recorded to allow us to go back through it to rate the contents and non verbal behaviour. [Pause]

You will now be given time to prepare.

You may leave the interview room.

[End]

VIII. Normality Values (Kurtosis and Skewness) for the Resilient and Vulnerable group (TSST; Chapter 4)

Mean, Skewness and Kurtosis values for the Resilient group (SPSS output)

Descriptive Statistics[a]

	N	Mean	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
PSQI	18	3.5556	.487	.536	-.705	1.038
ISI	18	3.0556	.898	.536	.170	1.038
PSS	18	12.5000	1.115	.536	2.210	1.038
DASSD	18	4.0000	1.265	.536	1.084	1.038
DASSA	18	3.3333	.760	.536	-.801	1.038
DASSS	18	7.1111	1.020	.536	1.833	1.038
NEOO	18	50.1111	-.469	.536	-.060	1.038
NEOC	18	51.6111	.616	.536	.604	1.038
NEOE	18	51.5556	.041	.536	-1.101	1.038
NEOA	18	53.5000	-.839	.536	.070	1.038
NEON	18	29.3889	-.446	.536	-.934	1.038
RUMD	18	19.0000	.558	.536	-.452	1.038
RUMB	18	8.3889	1.521	.536	2.907	1.038
RUMR	18	9.0556	.774	.536	1.368	1.038
COPEP	18	10.0000	.136	.536	-.725	1.038
COPEE	18	11.0000	.539	.536	-1.020	1.038
WORRY	18	38.3333	.340	.536	-.394	1.038
FIRST	18	14.8889	.224	.536	-1.271	1.038
Cortisol_T1	18	5.5322	1.093	.536	.624	1.038
Cortisol_T2	18	5.4627	.891	.536	.520	1.038
Cortisol_T3	18	7.5962	1.388	.536	1.572	1.038
Cortisol_T4	18	7.2493	1.556	.536	2.642	1.038
Cortisol_T5	18	6.6679	.874	.536	-.179	1.038
AUCg	18	264.0816	1.561	.536	2.838	1.038
AUCb	18	221.2876	1.093	.536	.624	1.038
AUCi	18	42.7940	-.277	.536	-.246	1.038
Valid N (listwise)	18					

a. 1= resilient; 2= vulnerable = 1.00

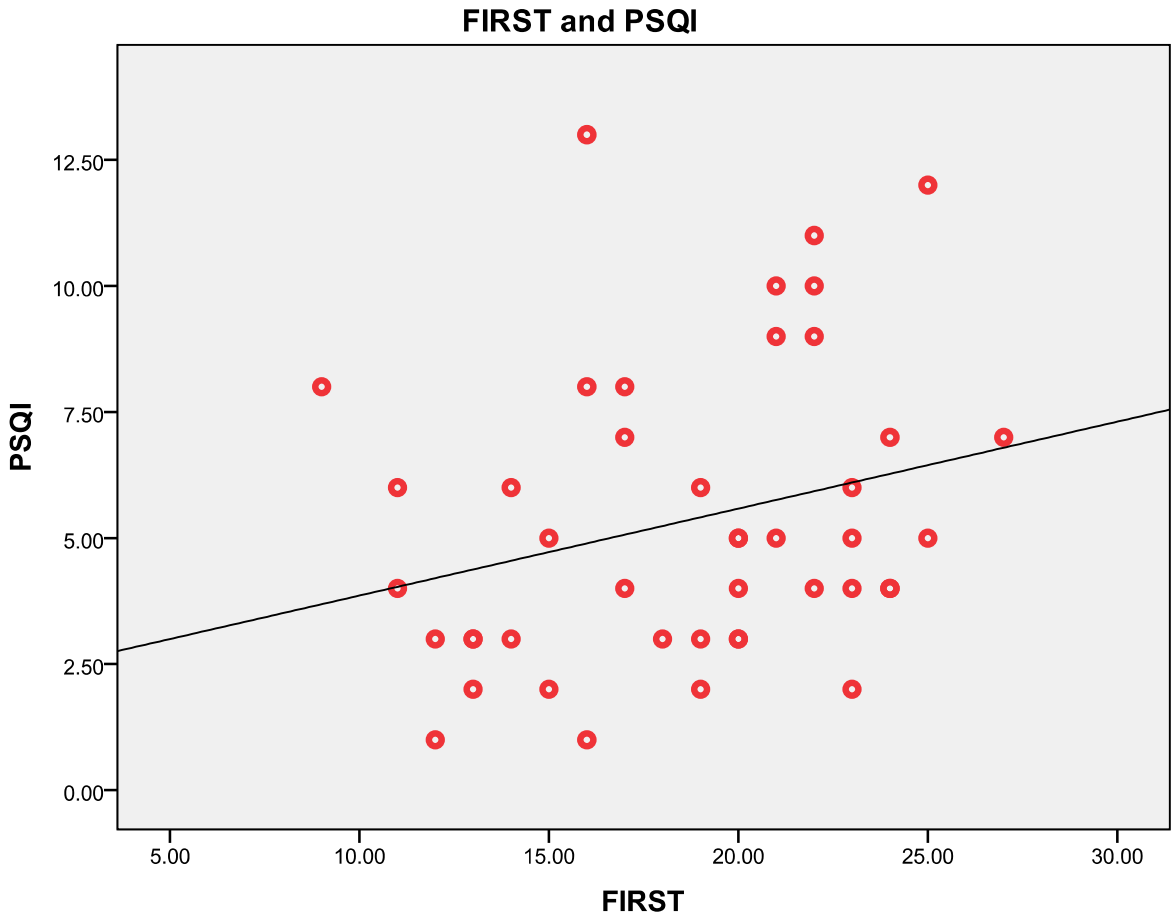
Mean, Skewness, Kurtosis values for the Vulnerable Group (SPSS output)

Descriptive Statistics[a]

	N	Mean	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
PSQI	16	4.5625	.210	.564	.042	1.091
ISI	16	4.3750	.657	.564	.670	1.091
PSS	16	14.7500	-.201	.564	-.463	1.091
DASSD	16	6.0000	1.122	.564	.525	1.091
DASSA	16	4.6250	-.127	.564	-1.003	1.091
DASSS	16	13.0000	.315	.564	.417	1.091
NEOO	16	53.0000	.854	.564	.635	1.091
NEOC	16	49.1250	-.079	.564	-.418	1.091
NEOE	16	49.5625	-.295	.564	-.891	1.091
NEOA	16	52.5000	-.789	.564	-.243	1.091
NEON	16	38.7500	-.160	.564	-.998	1.091
RUMD	16	24.3750	-.427	.564	-1.033	1.091
RUMB	16	10.1875	1.231	.564	.673	1.091
RUMR	16	11.4375	.157	.564	.277	1.091
COPEP	16	12.4375	.027	.564	1.330	1.091
COPEE	16	14.3125	.024	.564	-1.060	1.091
WORRY	16	49.0625	-.719	.564	.818	1.091
FIRST	16	22.4375	.383	.564	-.428	1.091
Cortisol_T1	16	3.5323	1.480	.564	2.222	1.091
Cortisol_T2	16	3.6894	.212	.564	-.640	1.091
Cortisol_T3	16	5.5826	.692	.564	-.723	1.091
Cortisol_T4	16	5.6311	.892	.564	.111	1.091
Cortisol_T5	16	5.1627	.836	.564	-.740	1.091
AUCg	16	192.5067	.408	.564	-1.239	1.091
AUCb	16	141.2921	1.480	.564	2.222	1.091
AUCi	16	51.2146	1.072	.564	.599	1.091
Valid N (listwise)	16					

a. 1= resilient; 2= vulnerable = 2.00

IX. Scatterplots for Whole-Sample Correlations between FIRST and Psychological Variables


FIRST and PSQI
PSQI
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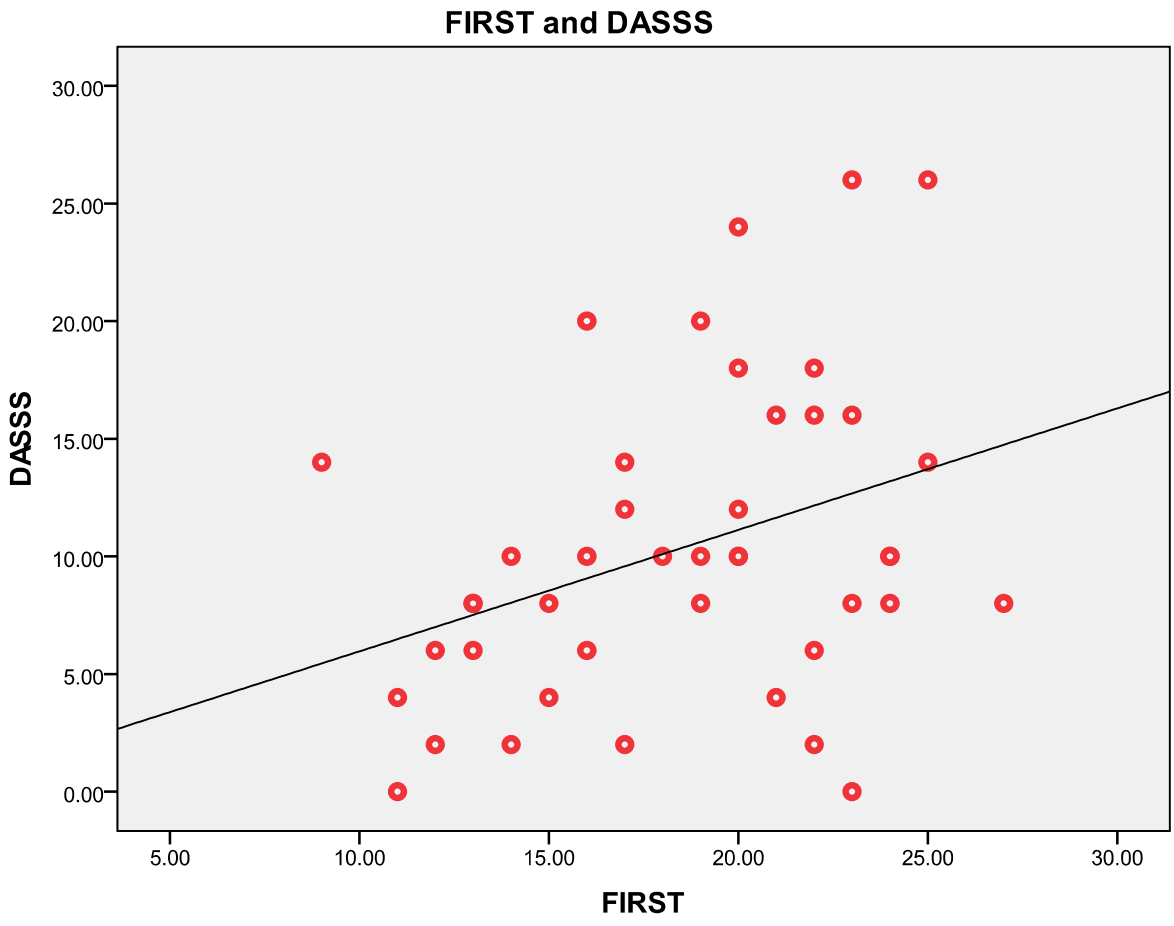
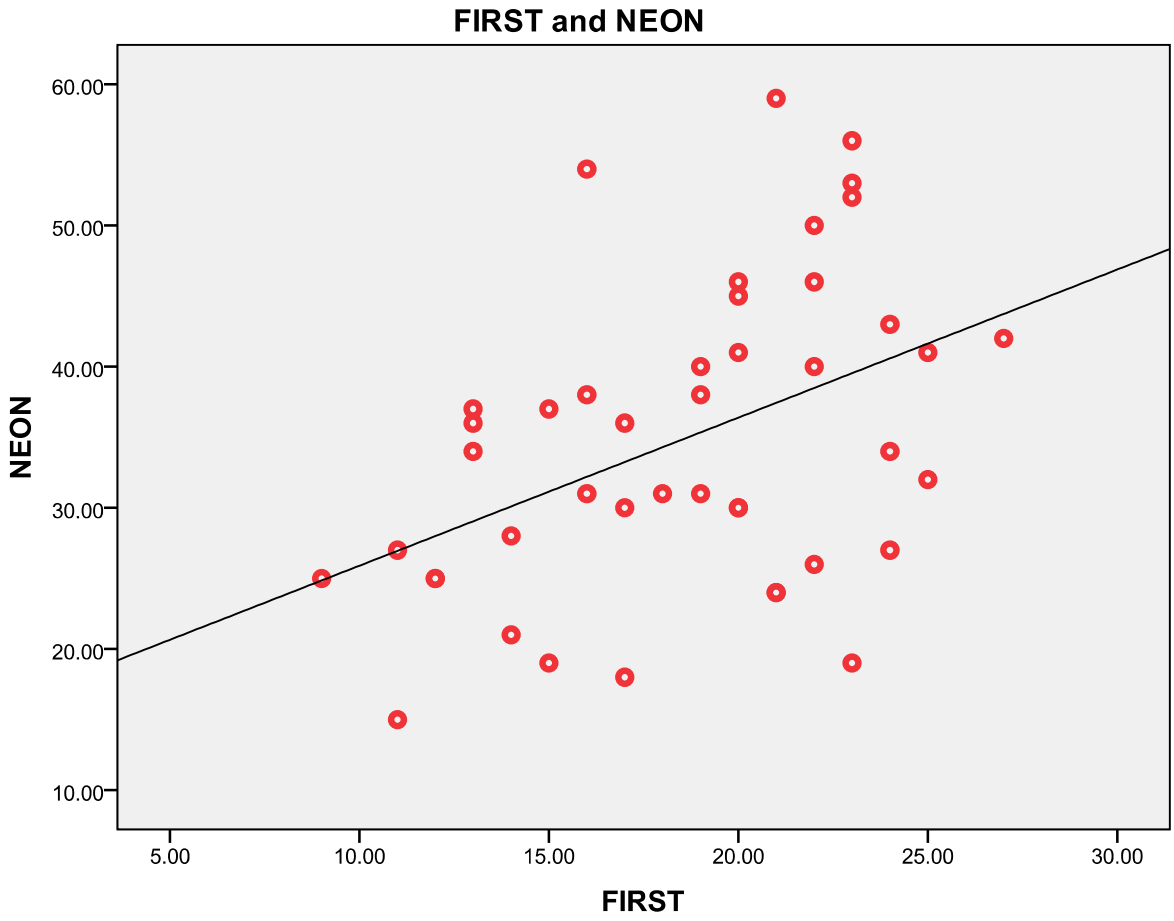
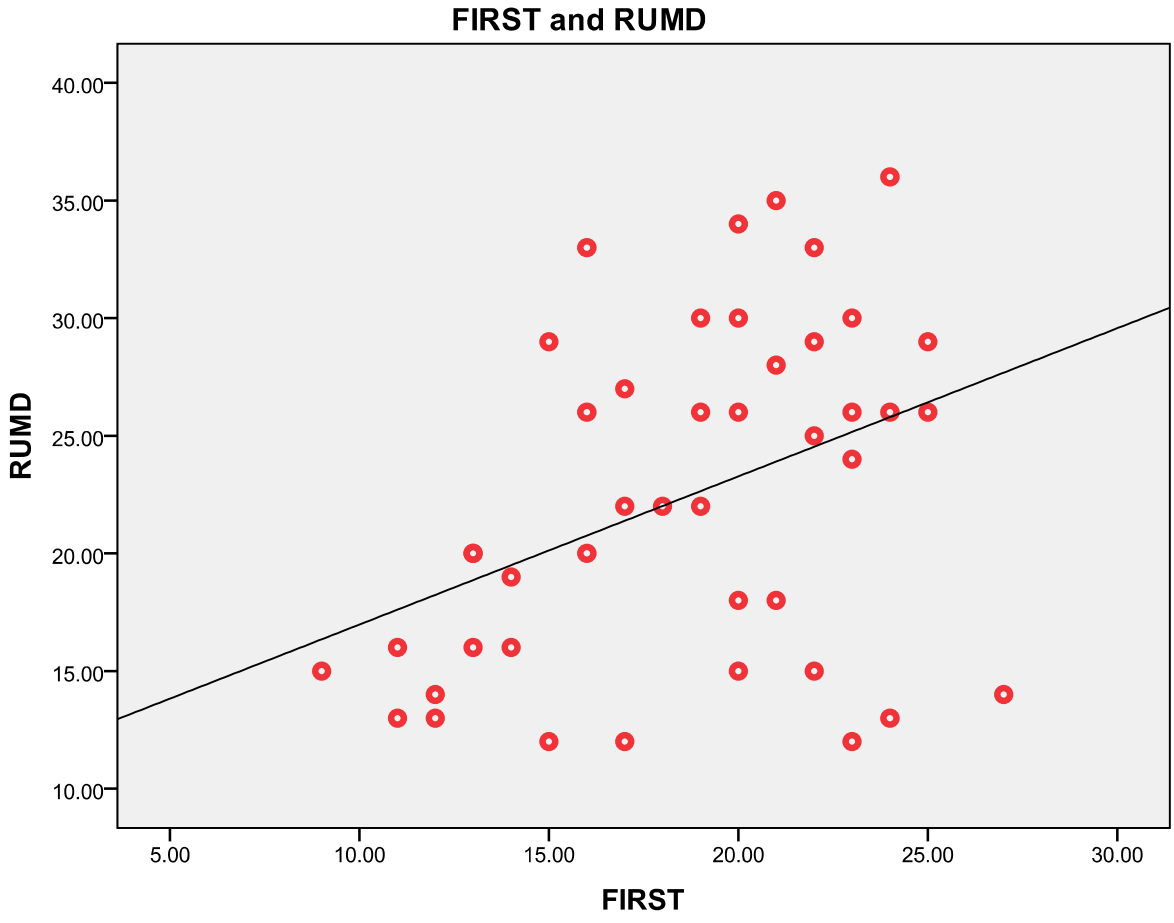
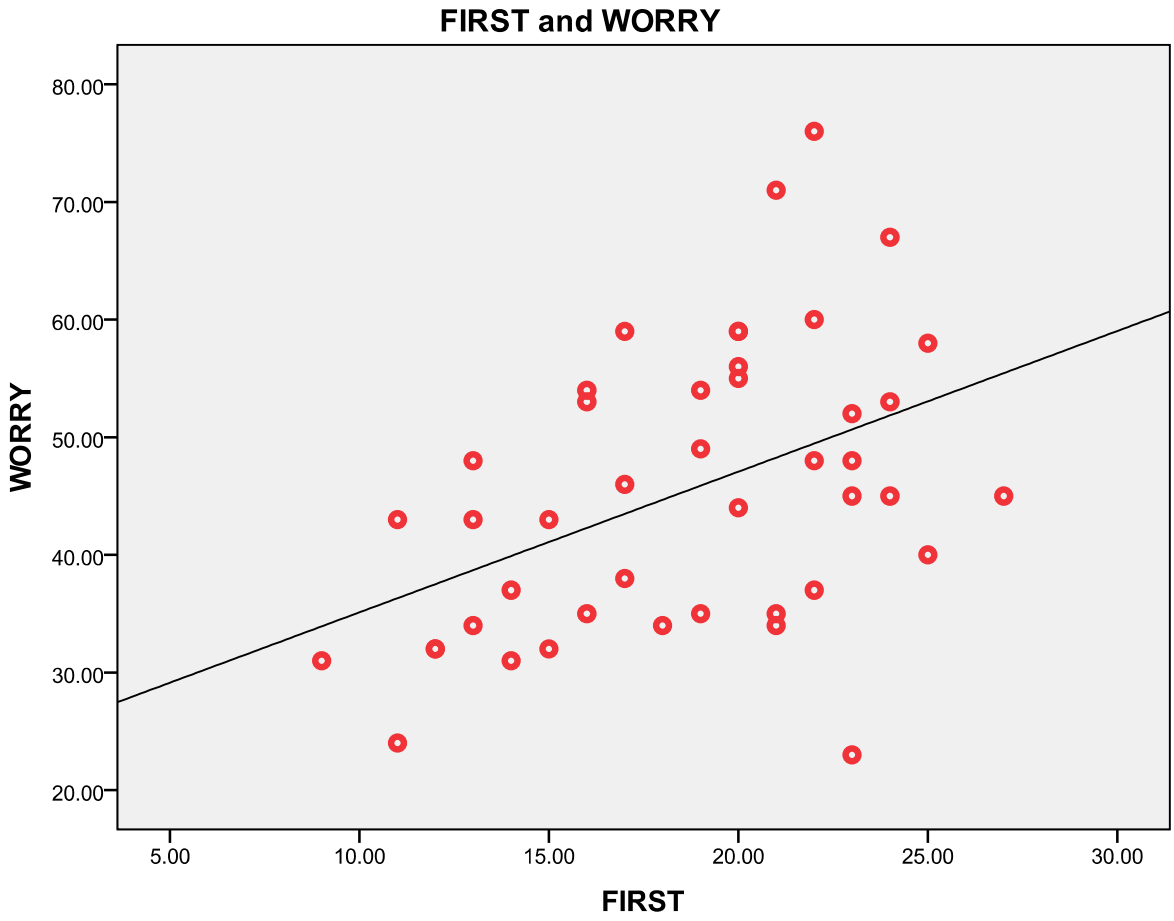
10.00
7.50
5.00
2.50
0.00
5.00
10.00
15.00
20.00
25.00
30.00
FIRST


FIRST and DASSS
DASSS
30.00
25.00
20.00
15.00
10.00
5.00
0.00
5.00
10.00
15.00
20.00
25.00
30.00
FIRST


FIRST and NEON
NEON
60.00
50.00
40.00
30.00
20.00
10.00
5.00
10.00
15.00
20.00
25.00
30.00
FIRST


FIRST and RUMD
RUMD
40.00
35.00
30.00
25.00
20.00
15.00
10.00
5.00
10.00
15.00
20.00
25.00
30.00
FIRST


FIRST and WORRY
WORRY
80.00
70.00
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40.00
30.00
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5.00
10.00
15.00
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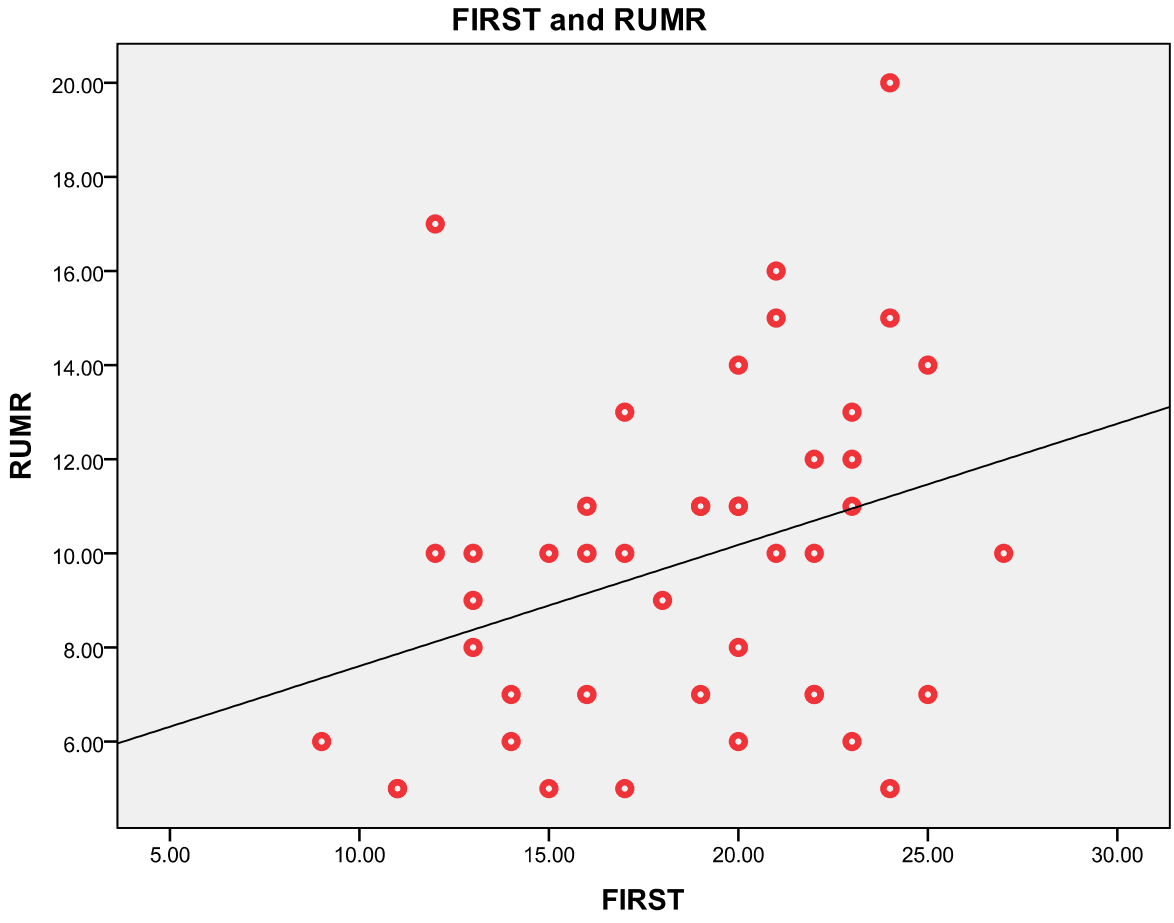
25.00
30.00
FIRST


FIRST and RUMR
RUMR
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14.00
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8.00
6.00
5.00
10.00
15.00
20.00
25.00
30.00
FIRST

X. Correlation Matrix for Psychological Variables(TSST; Chapter 4)

Correlations

		PSQI	ISI	PSS	DASSD	DASSA	DASSS	NEOO	NEOC	NEOE
PSQI	Pearson Correlation	1	.393*	-.009	.060	.090	.208	-.011	-.110	-.024
	Sig. (2-tailed)		.020	.958	.730	.607	.229	.949	.530	.891
	N	35	35	35	35	35	35	35	35	35
ISI	Pearson Correlation	.393*	1	.327	.280	.283	.434**	-.140	.196	.051
	Sig. (2-tailed)	.020		.055	.103	.100	.009	.423	.260	.772
	N	35	35	35	35	35	35	35	35	35
PSS	Pearson Correlation	-.009	.327	1	.651**	.468**	.501**	-.254	-.077	-.447**
	Sig. (2-tailed)	.958	.055		.000	.005	.002	.142	.660	.007
	N	35	35	35	35	35	35	35	35	35
DASSD	Pearson Correlation	.060	.280	.651**	1	.553**	.531**	-.034	-.259	-.452**
	Sig. (2-tailed)	.730	.103	.000		.001	.001	.846	.132	.006
	N	35	35	35	35	35	35	35	35	35
DASSA	Pearson Correlation	.090	.283	.468**	.553**	1	.612**	.118	-.073	-.309
	Sig. (2-tailed)	.607	.100	.005	.001		.000	.499	.677	.071
	N	35	35	35	35	35	35	35	35	35
DASSS	Pearson Correlation	.208	.434**	.501**	.531**	.612**	1	-.077	-.058	-.316
		PSQI	ISI	PSS	DASSD	DASSA	DASSS	NEOO	NEOC	NEOE
	Sig. (2-tailed)	.229	.009	.002	.001	.000		.661	.739	.064
	N	35	35	35	35	35	35	35	35	35
NEOO	Pearson Correlation	-.011	-.140	-.254	-.034	.118	-.077	1	-.231	-.191
	Sig. (2-tailed)	.949	.423	.142	.846	.499	.661		.182	.272
	N	35	35	35	35	35	35	35	35	35
NEOC	Pearson Correlation	-.110	.196	-.077	-.259	-.073	-.058	-.231	1	.291
	Sig. (2-tailed)	.530	.260	.660	.132	.677	.739	.182		.090
	N	35	35	35	35	35	35	35	35	35

NEOE	Pearson Correlation	-.024	.051	-.447**	-.452**	-.309	-.316	-.191	.291	1
	Sig. (2-tailed)	.891	.772	.007	.006	.071	.064	.272	.090	
	N	35	35	35	35	35	35	35	35	35
NEOA	Pearson Correlation	-.180	-.392*	-.404*	-.507**	-.382*	-.436**	.119	.145	.218
	Sig. (2-tailed)	.301	.020	.016	.002	.023	.009	.496	.407	.208
	N	35	35	35	35	35	35	35	35	35
NEON	Pearson Correlation	.193	.234	.645**	.637**	.443**	.649**	-.145	-.244	-.497**
	Sig. (2-tailed)	.266	.176	.000	.000	.008	.000	.406	.158	.002
	N	35	35	35	35	35	35	35	35	35
RUMD	Pearson Correlation	.243	.247	.348*	.331	.512**	.561**	.103	-.205	-.232
		PSQI	ISI	PSS	DASSD	DASSA	DASSS	NEOO	NEOC	NEOE
	Sig. (2-tailed)	.160	.152	.040	.052	.002	.000	.558	.238	.180
	N	35	35	35	35	35	35	35	35	35
RUMB	Pearson Correlation	.131	.284	.495**	.591**	.616**	.629**	-.036	-.047	-.276
	Sig. (2-tailed)	.454	.098	.003	.000	.000	.000	.837	.789	.108
	N	35	35	35	35	35	35	35	35	35
RUMR	Pearson Correlation	.166	.162	.155	.155	.324	.367*	.174	-.127	-.272
	Sig. (2-tailed)	.342	.352	.375	.375	.058	.030	.316	.466	.114
	N	35	35	35	35	35	35	35	35	35
COPEP	Pearson Correlation	-.001	.193	.231	.186	.300	.284	.133	-.045	-.027
	Sig. (2-tailed)	.996	.266	.181	.285	.080	.098	.445	.797	.876
	N	35	35	35	35	35	35	35	35	35
COPEE	Pearson Correlation	.077	.113	.151	.140	.396*	.204	.122	-.139	.073
	Sig. (2-tailed)	.660	.516	.386	.422	.019	.240	.485	.426	.679
	N	35	35	35	35	35	35	35	35	35
WORRY	Pearson Correlation	.263	.407*	.374*	.196	.248	.562**	-.145	.052	-.242
	Sig. (2-tailed)	.127	.015	.027	.260	.151	.000	.405	.768	.162
	N	35	35	35	35	35	35	35	35	35
FIRST	Pearson Correlation	.377*	.132	.211	.241	.223	.450**	.071	-.146	-.226
	Sig. (2-tailed)	.026	.450	.224	.162	.199	.007	.685	.403	.191
	N	35	35	35	35	35	35	35	35	35

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

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

Correlations

		NEOA	NEON	RUMD	RUMB	RUMR	COPEP	COPEE	WORRY	FIRST
PSQI	Pearson Correlation	-.180	.193	.243	.131	.166	-.001	.077	.263	.377*
	Sig. (2-tailed)	.301	.266	.160	.454	.342	.996	.660	.127	.026
	N	35	35	35	35	35	35	35	35	35
ISI	Pearson Correlation	-.392*	.234	.247	.284	.162	.193	.113	.407*	.132
	Sig. (2-tailed)	.020	.176	.152	.098	.352	.266	.516	.015	.450
	N	35	35	35	35	35	35	35	35	35
PSS	Pearson Correlation	-.404*	.645**	.348*	.495**	.155	.231	.151	.374*	.211
	Sig. (2-tailed)	.016	.000	.040	.003	.375	.181	.386	.027	.224
	N	35	35	35	35	35	35	35	35	35
DASSD	Pearson Correlation	-.507**	.637**	.331	.591**	.155	.186	.140	.196	.241
	Sig. (2-tailed)	.002	.000	.052	.000	.375	.285	.422	.260	.162
	N	35	35	35	35	35	35	35	35	35
DASSA	Pearson Correlation	-.382*	.443**	.512**	.616**	.324	.300	.396*	.248	.223
	Sig. (2-tailed)	.023	.008	.002	.000	.058	.080	.019	.151	.199
	N	35	35	35	35	35	35	35	35	35
		NEOA	NEON	RUMD	RUMB	RUMR	COPEP	COPEE	WORRY	FIRST
DASSS	Pearson Correlation	-.436**	.649**	.561**	.629**	.367*	.284	.204	.562**	.450**
	Sig. (2-tailed)	.009	.000	.000	.000	.030	.098	.240	.000	.007
	N	35	35	35	35	35	35	35	35	35
NEOO	Pearson Correlation	.119	-.145	.103	-.036	.174	.133	.122	-.145	.071
	Sig. (2-tailed)	.496	.406	.558	.837	.316	.445	.485	.405	.685
	N	35	35	35	35	35	35	35	35	35
NEOC	Pearson Correlation	.145	-.244	-.205	-.047	-.127	-.045	-.139	.052	-.146
	Sig. (2-tailed)	.407	.158	.238	.789	.466	.797	.426	.768	.403
	N	35	35	35	35	35	35	35	35	35
NEOE	Pearson Correlation	.218	-.497**	-.232	-.276	-.272	-.027	.073	-.242	-.226
	Sig. (2-tailed)	.208	.002	.180	.108	.114	.876	.679	.162	.191
	N	35	35	35	35	35	35	35	35	35

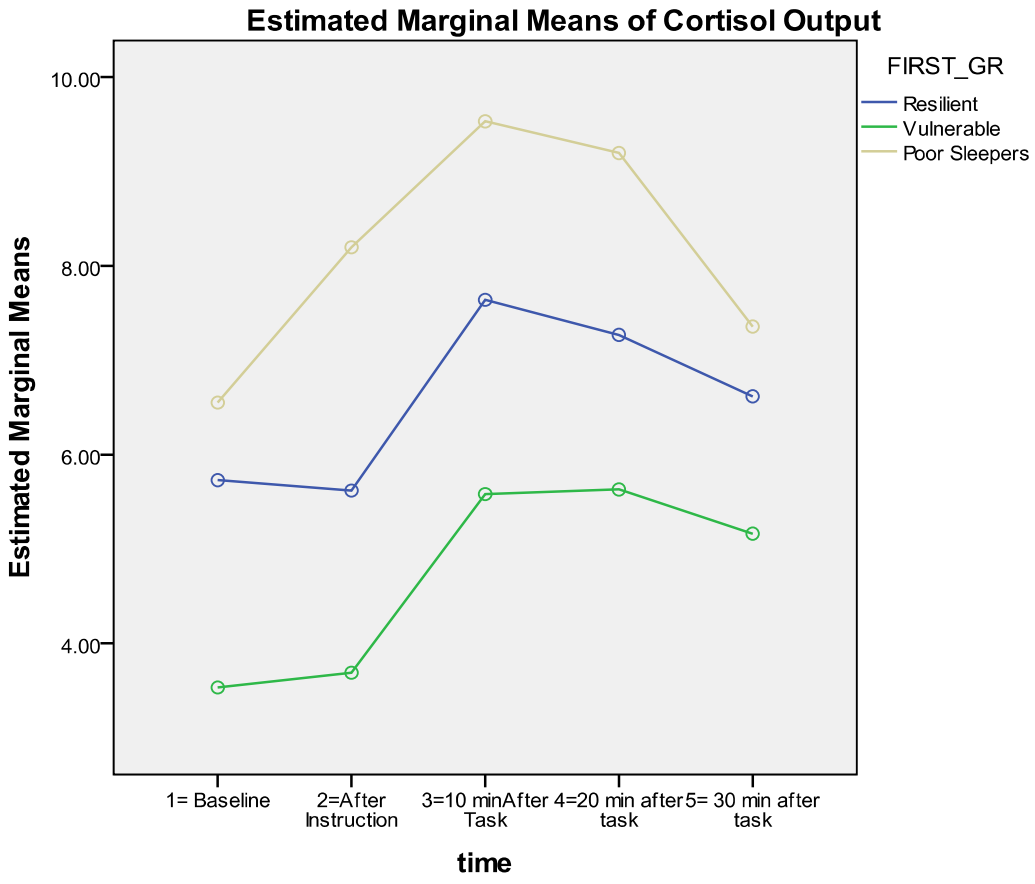
NEOA	Pearson Correlation	1	-.337*	-.124	-.527**	-.208	-.138	-.089	-.107	-.072
	Sig. (2-tailed)		.048	.477	.001	.230	.429	.612	.542	.683
	N	35	35	35	35	35	35	35	35	35
NEON	Pearson Correlation	-.337*	1	.507**	.572**	.357*	.409*	.222	.658**	.463**
	Sig. (2-tailed)	.048		.002	.000	.035	.015	.200	.000	.005
	N	35	35	35	35	35	35	35	35	35
RUMD	Pearson Correlation	-.124	.507**	1	.629**	.583**	.493**	.380*	.399*	.439**
	Sig. (2-tailed)	.477	.002		.000	.000	.003	.024	.018	.008
	N	35	35	35	35	35	35	35	35	35
RUMB	Pearson Correlation	-.527**	.572**	.629**	1	.428*	.394*	.203	.409*	.327
	Sig. (2-tailed)	.001	.000	.000		.010	.019	.243	.015	.055
	N	35	35	35	35	35	35	35	35	35
RUMR	Pearson Correlation	-.208	.357*	.583**	.428*	1	.694**	.650**	.196	.363*
	Sig. (2-tailed)	.230	.035	.000	.010		.000	.000	.260	.032
	N	35	35	35	35	35	35	35	35	35
COPEP	Pearson Correlation	-.138	.409*	.493**	.394*	.694**	1	.783**	.196	.309
	Sig. (2-tailed)	.429	.015	.003	.019	.000		.000	.260	.071
	N	35	35	35	35	35	35	35	35	35
COPEE	Pearson Correlation	-.089	.222	.380*	.203	.650**	.783**	1	.078	.322
	Sig. (2-tailed)	.612	.200	.024	.243	.000	.000		.654	.059
	N	35	35	35	35	35	35	35	35	35
WORRY	Pearson Correlation	-.107	.658**	.399*	.409*	.196	.196	.078	1	.453**
	Sig. (2-tailed)	.542	.000	.018	.015	.260	.260	.654		.006
	N	35	35	35	35	35	35	35	35	35

		NEOA	NEON	RUMD	RUMB	RUMR	COPEP	COPEE	WORRY	FIRST
FIRST	Pearson Correlation	-.072	.463**	.439**	.327	.363*	.309	.322	.453**	1
	Sig. (2-tailed)	.683	.005	.008	.055	.032	.071	.059	.006	
	N	35	35	35	35	35	35	35	35	35

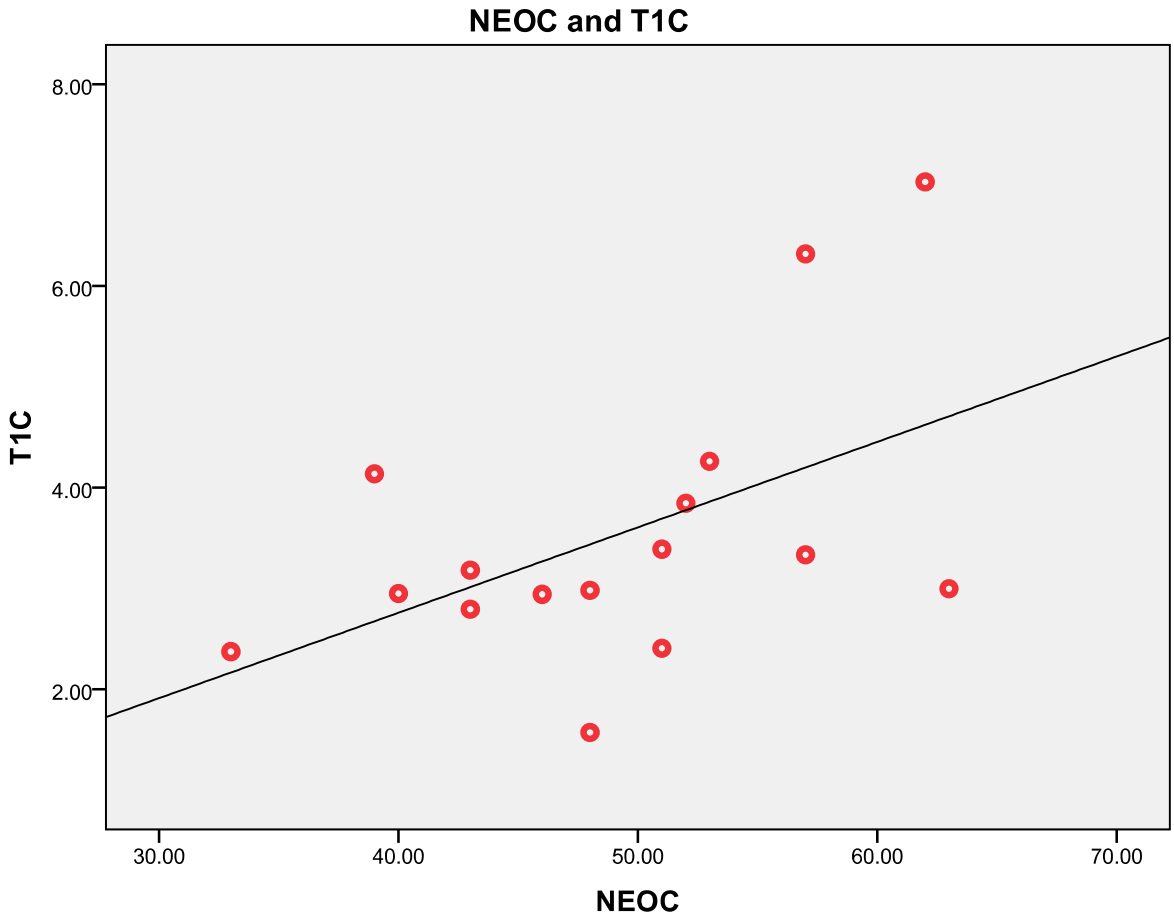
*. Correlation is significant at the 0.05 level (2-tailed).

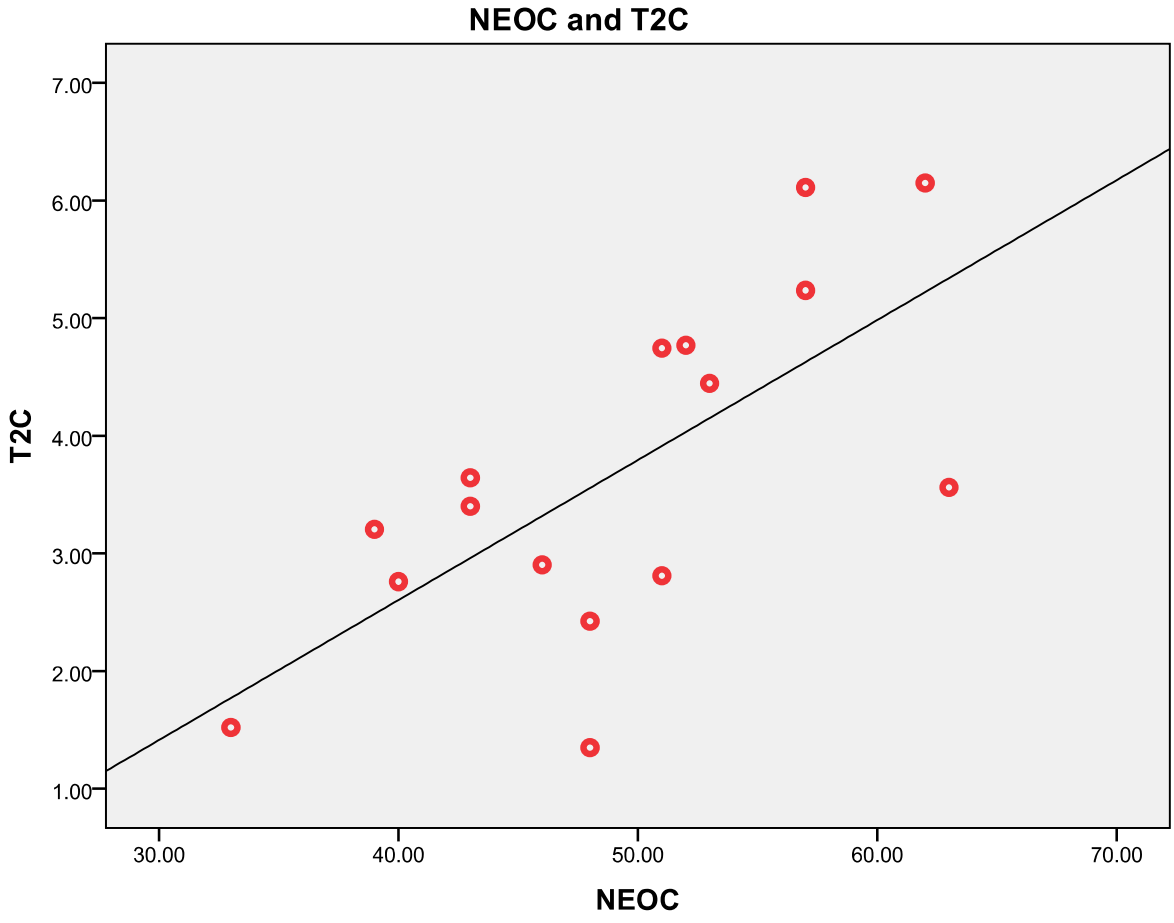
**. Correlation is significant at the 0.01 level (2-tailed).

XI. Estimated Marginal Means of Cortisol Output: Vulnerable, Resilient and poor sleeping Group (Chapter 4)



XII. Scatter-plot for correlation between Cortisol output at time 1 and NEOC (Chapter 4)


NEOC and T1C
8.00
6.00
4.00
2.00
T1C
30.00
40.00
50.00
60.00
70.00
NEOC


NEOC and T2C
7.00
6.00
5.00
4.00
3.00
2.00
1.00
T2C
30.00
40.00
50.00
60.00
70.00
NEOC

XIII. **Sleep Diary Used in Follow- up (Chapter 4)**

Name_____

Week Beginning_____

MEASURING THE PATTERN OF YOUR SLEEP

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
1. What time did you wake this morning?							
2. At what time did you rise from bed?							
3. At what time did you go to bed last night?							
4. Lights Out:- At what time did you put the light out to go to sleep?							
5. How long did it take you to fall asleep (minutes)? (After Lights Out)							
6. How many times did you wake up during the night?							
7. How long were you awake during the night (in total)?							
8. About how long did you sleep altogether (hours/mins)?							
9. Did you take sleeping pills to help you sleep? (please describe)							
10.Did you take alcohol before going to bed? (please describe)							
11. Did you take painkillers last evening or night? (please describe)							
12. Did you take pills for depression or anxiety? (please describe)							

MEASURING THE QUALITY OF YOUR SLEEP

1. How well do you feel this morning? 0 1 2 3 4 not at all moderately very							
2. How enjoyable was your sleep last night? 0 1 2 3 4 not at all moderately very							
3. How mentally alert were you in bed last night? 0 1 2 3 4 not at all moderately very							
4. How physically tense were you in bed last							

night? 0 1 2 3 4 not at all moderately very							

In the last week how often have you felt nervous and/or 'stressed'?

0 1 2 3 4

not at all Fairly Often Very Often

Have there been any events in the last week which have caused increased stress?

Yes/ no

If so, what?

XIV. Mean, Skewness and Kurtosis for follow up data (Chapter 4; SPSS output)

	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
SOL_1	6	15.8667	.914	.845	.332	1.741
WAKENING	6	.2000	.000	.845	-3.333	1.741
WASO_1	6	6.8333	2.165	.845	4.872	1.741
TST_1	6	480.2333	.166	.845	-2.381	1.741
TIB_1	6	526.4333	.994	.845	2.872	1.741
SE_1	6	91.9033	-1.597	.845	2.018	1.741
ALCH_1	6	1.1000	2.289	.845	5.303	1.741
PILL_1	6	.0000	.	.	.	.
FEEL_1	6	3.1333	-.095	.845	-1.825	1.741
ENJOYABLE_1	6	3.1333	-.115	.845	-2.658	1.741
ALERT_1	6	1.4333	-.040	.845	-.799	1.741
TENSE_1	6	.6667	.643	.845	.306	1.741
STRESSED_1	6	.6667	-.968	.845	-1.875	1.741
RECODE_Symtpom_1	6	1.3333	.919	.845	-1.205	1.741
no_nights	6	1.1667	1.095	.845	-1.115	1.741
FIRST	0					
SOL_2	6	15.4333	.876	.845	-.262	1.741
WAKENING_2	6	.1667	.456	.845	-2.390	1.741
WASO_2	6	1.6667	2.023	.845	4.202	1.741
TST_2	6	437.2333	-.188	.845	-1.637	1.741
TIB_2	6	477.0333	1.869	.845	4.017	1.741
SE_2	6	92.5408	-.917	.845	1.341	1.741
ALCH_2	6	2.1333	1.323	.845	.214	1.741
PILL_2	6	.0000	.	.	.	.
FEEL_2	6	2.6000	-.574	.845	-1.633	1.741
ENJOYABLE_2	6	2.5667	-.302	.845	-1.419	1.741
ALERT_2	6	1.7000	-.894	.845	1.020	1.741
TENSE_2	6	1.2000	.076	.845	.115	1.741
STRESSED_2	6	2.6667	.857	.845	-.300	1.741
RECODE_Symptom_2	6	.8333	1.207	.845	-.459	1.741
no_nights_2	6	1.3333	1.270	.845	1.531	1.741
SOL_CHANGE	6	.4333	.417	.845	-2.097	1.741
WAKENING_CHANGE	6	.0333	-.440	.845	1.335	1.741
WASO_CHANGE	6	5.1667	2.307	.845	5.414	1.741
TST_CHANGE	6	43.0000	.112	.845	-1.437	1.741
TIB_CHANGE	6	49.4000	-.701	.845	-.217	1.741
SE_CHANGE	6	-.6375	1.105	.845	-.369	1.741
PSQI	6	3.8333	.418	.845	-.859	1.741
ISI	6	3.5000	.876	.845	-.048	1.741

PSS	6	9.5000	.509	.845	-1.725	1.741
DASSD	6	.6667	.968	.845	-1.875	1.741
DASSA	6	1.3333	1.952	.845	3.657	1.741
DASSS	6	6.0000	.000	.845	-1.875	1.741
NEOO	6	45.3333	.128	.845	-.665	1.741
NEOC	6	54.5000	.313	.845	-1.969	1.741
NEOE	6	59.0000	-.415	.845	.576	1.741
NEOA	6	56.1667	-.285	.845	.577	1.741
NEON	6	25.3333	.651	.845	-1.191	1.741
RUMD	6	17.5000	1.205	.845	.474	1.741
RUMB	6	7.6667	.778	.845	-1.680	1.741
RUMR	6	7.1667	.568	.845	-2.001	1.741
COPEP	6	9.8333	.226	.845	-1.626	1.741
COPEE	6	11.1667	.306	.845	-2.545	1.741
COPEAD	3	8.3333	.331	1.225	.	.
COPEM	3	18.6667	-.230	1.225	.	.
WORRY	6	41.0000	-.371	.845	.932	1.741
T1C	6	4.9804	1.004	.845	.273	1.741
T2C	6	5.3388	.278	.845	-1.995	1.741
T3C	6	10.0160	-.454	.845	-1.436	1.741
T4C	6	9.6214	-.437	.845	-1.574	1.741
T5C	6	7.9111	-.125	.845	-2.778	1.741
AUCg	6	295.4485	-.147	.845	-1.418	1.741
AUCi	6	79.2783	.186	.845	-1.494	1.741
stress_change	6	2.0000	.000	.845	-3.333	1.741
Valid N (listwise)	0					

Table represents kurtosis and skeweness values for data used in the follow up analysis for the resilient group. Data with '_1' represent values from the non stress week. '_2' represents non stress value. Abbreviations can be found in the abbreviations section. 'Feel', 'Enjoyable', 'Alert' and 'Tense' relate to questions from 'measuring the quality of your sleep' from the sleep diary.

Descriptive Statistics[a]

	N	Mean	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
SOL_1	8	15.4250	.582	.752	-1.274	1.481
WAKENING_1	8	.4500	-.292	.752	-1.914	1.481
WASO_1	8	5.1250	.971	.752	-.046	1.481
TST_1	8	487.7255	-.410	.752	-.931	1.481
TIB_1	8	537.0813	-1.019	.752	2.019	1.481
SE_1	8	90.9238	-.300	.752	-1.101	1.481
ALCH_1	8	.9000	.212	.752	-2.464	1.481
PILL_1	8	.0000	.	.	.	.
FEEL_1	8	2.5000	-.723	.752	-.695	1.481
ENJOYABLE_1	8	2.7500	-.280	.752	.283	1.481
ALERT_1	8	1.7000	-.415	.752	1.505	1.481
TENSE_1	8	.9500	.225	.752	-1.216	1.481
STRESSED	8	1.0000	.935	.752	.350	1.481
RECODE_Symtpom_1	8	.3750	1.951	.752	3.205	1.481
no_nights	8	1.1250	.876	.752	-.706	1.481
SOL_2	8	28.0000	2.367	.752	5.874	1.481
WAKENING_2	8	.6000	.000	.752	-1.811	1.481
WASO_2	8	13.9750	1.767	.752	2.997	1.481
TST_2	8	420.0500	.114	.752	-1.227	1.481
TIB_2	8	488.4250	.367	.752	-1.568	1.481
SE_2	8	86.2470	.089	.752	-1.145	1.481
ALCH_2	8	.4000	1.440	.752	.000	1.481
PILL_2	8	.0250	2.828	.752	8.000	1.481
FEEL_2	8	2.2250	-.868	.752	-.359	1.481
ENJOYABLE_2	8	2.5500	.759	.752	.443	1.481
ALERT_2	8	1.7625	.240	.752	-.119	1.481
TENSE_2	8	1.4750	-1.792	.752	3.701	1.481
STRESSED_2	8	3.0000	.000	.752	-.700	1.481
sYMPTOM_2	8	3.8750	1.773	.752	3.404	1.481
RECODE_Symptom_2	8	1.5000	1.663	.752	3.422	1.481
no_nights_2	8	2.3750	.644	.752	-2.240	1.481
SOL_CHANGE	8	-12.5750	-1.622	.752	2.664	1.481
WAKENING_CHANGE	8	-.1500	-.611	.752	-.021	1.481
WASO_CHANGE	8	-8.8500	-1.439	.752	1.776	1.481
TST_CHANGE	8	67.6756	.375	.752	-.725	1.481
TIB_CHANGE	8	48.6563	.330	.752	-.553	1.481
SE_CHANGE	8	4.6767	-.075	.752	-.311	1.481
PSQI	8	4.6250	-.302	.752	-.165	1.481
ISI	8	4.1250	.874	.752	-.043	1.481
PSS	8	15.1250	-.426	.752	-1.436	1.481
DASSD	8	6.7500	.874	.752	-.051	1.481
DASSA	8	5.5000	-.325	.752	-.037	1.481

DASSS	8	14.2500	-.186	.752	-.385	1.481
NEOO	8	55.2500	.917	.752	.433	1.481
NEOC	8	47.2500	.269	.752	-.544	1.481
NEOE	8	49.7500	-.051	.752	-1.082	1.481
NEOA	8	47.3750	-.194	.752	-1.293	1.481
NEON	8	41.5000	-1.002	.752	-.164	1.481
RUMD	8	24.1250	-1.328	.752	1.093	1.481
RUMB	8	11.0000	1.037	.752	.255	1.481
RUMR	8	12.1250	.111	.752	.077	1.481
COPEP	8	13.0000	1.257	.752	1.402	1.481
COPEE	8	15.1250	-.036	.752	-1.828	1.481
WORRY	8	47.2500	-1.049	.752	.282	1.481
T1C	8	3.4024	1.167	.752	2.163	1.481
T2C	8	3.4448	.247	.752	.094	1.481
T3C	8	4.9066	.346	.752	-1.796	1.481
T4C	8	5.0529	.403	.752	-2.073	1.481
T5C	8	4.8300	1.005	.752	-.035	1.481
AUCg	8	175.2048	.436	.752	-1.428	1.481
meancort	8	4.3273	.537	.752	-1.107	1.481
AUCi	8	39.1092	.561	.752	-1.259	1.481
stress_change	8	2.0000	.935	.752	.350	1.481
Valid N (listwise)	0					

Table represents kurtosis and skeweness values for data used in the follow up analysis for the Vulnerable group. Data with '_1' represent values from the non stress week. '_2' represents non stress value. Abbreviations can be found in the abbreviations section. 'Feel', 'Enjoyable', 'Alert' and 'Tense' relate to questions from 'measuring the quality of your sleep' from the sleep diary.

XV. Median and Interquartile Ranges for Follow-up Data (Chapter 4)

	N			Percentiles		
	Valid	Missing	Median	25	50	75
SOL_1	6	0	14.0000	6.4500	14.0000	24.7500
WAKENING_1	6	0	.2000	.0000	.2000	.4000
WASO_1	6	0	2.5000	.0000	2.5000	12.0000
TST_1	6	0	477.5000	452.0000	477.5000	511.1000
TIB_1	6	0	520.5000	497.9000	520.5000	551.5000
SE_1	6	0	96.1450	84.1500	96.1450	98.5425
ALCH_1	6	0	.0000	.0000	.0000	2.1500
PILL_1	6	0	.0000	.0000	.0000	.0000
FEEL_1	6	0	3.1000	2.7000	3.1000	3.6500
ENJOYABLE	6	0	3.2000	2.5500	3.2000	3.6500
ALERT_1	6	0	1.4000	.6500	1.4000	2.3000
TENSE_1	6	0	.7000	.2000	.7000	.9500
STRESSED_1	6	0	1.0000	.0000	1.0000	1.0000
RECODE_Symtpom_1	6	0	.5000	.0000	.5000	3.2500
SOL_2	6	0	13.0000	8.9500	13.0000	23.0000
WAKENING_2	6	0	.1000	.0000	.1000	.4000
WASO_2	6	0	.5000	.0000	.5000	3.2500
TST_2	6	0	436.5000	422.7500	436.5000	455.5500
TIB_2	6	0	468.0000	455.6500	468.0000	494.0000
SE_2	6	0	93.0764	87.0001	93.0764	99.4929
ALCH_2	6	0	.0000	.0000	.0000	5.6000
PILL_2	6	0	.0000	.0000	.0000	.0000
FEEL_2	6	0	2.8000	1.7500	2.8000	3.2500
ENJOYABLE_2	6	0	2.6000	2.1500	2.6000	3.0000
ALERT_2	6	0	1.8000	1.1500	1.8000	2.3000
TENSE_2	6	0	1.1000	.6000	1.1000	1.9500
STRESSED_2	6	0	2.5000	2.0000	2.5000	3.2500
RECODE_Symptom_2	6	0	.0000	.0000	.0000	2.2500
SOL_CHANGE	6	0	-.3000	-2.8500	-.3000	4.2500
WAKENING_CHANGE	6	0	.0000	-.1000	.0000	.2500
WASO_CHANGE	6	0	.0000	-1.2500	.0000	10.5000
TST_CHANGE	6	0	41.0000	33.7500	41.0000	55.2500
TIB_CHANGE	6	0	53.9000	28.9000	53.9000	68.7500
SE_CHANGE	6	0	-2.2851	-3.5646	-2.2851	3.2921
PSQI	6	0	3.5000	2.7500	3.5000	5.2500
ISI	6	0	3.0000	1.0000	3.0000	5.7500
PSS	6	0	8.5000	5.7500	8.5000	14.2500
DASSD	6	0	.0000	.0000	.0000	2.0000
DASSA	6	0	.0000	.0000	.0000	3.0000

DASSS	6	0	6.0000	3.5000	6.0000	8.5000
NEOO	6	0	46.0000	38.5000	46.0000	50.5000
NEOC	6	0	52.5000	46.0000	52.5000	65.5000
NEOE	6	0	59.5000	55.7500	59.5000	62.0000
NEOA	6	0	55.5000	52.0000	55.5000	62.0000
NEON	6	0	23.5000	18.7500	23.5000	32.5000
RUMD	6	0	15.0000	12.0000	15.0000	23.7500
RUMB	6	0	6.5000	5.0000	6.5000	11.2500
RUMR	6	0	6.5000	5.0000	6.5000	10.0000
COPEP	6	0	9.5000	6.7500	9.5000	13.2500
COPEE	6	0	10.0000	6.0000	10.0000	17.2500
WORRY	6	0	42.0000	36.5000	42.0000	44.5000
T1C	6	0	4.4312	2.9201	4.4312	6.7758
T2C	6	0	5.2219	3.2989	5.2219	7.2195
T3C	6	0	10.9337	5.2889	10.9337	14.2871
T4C	6	0	10.0892	5.6835	10.0892	13.8731
T5C	6	0	8.2414	3.9344	8.2414	11.7259
AUCg	6	0	293.3734	179.7381	293.3734	431.7675
Mean Cort	6	0	8.4682	4.2872	8.4682	10.3294
AUCi	6	0	62.4507	-6.6585	62.4507	196.4361

Median and Interquartile ranges for the resilient group in the follow-up section '_1' denotes data from the normal weeks diary. '_2' indicates data from the stressful weeks diary. For abbreviation list see abbreviation section

Statistics[a]

	N			Percentiles		
	Valid	Missing	Median	25	50	75
SOL_1	8	0	11.5000	7.6500	11.5000	27.6000
WAKENING_1	8	0	.5000	.0500	.5000	.8000
WASO_1	8	0	3.0000	.5000	3.0000	9.5000
TST_1	8	0	496.5020	437.5500	496.5020	541.0000
TIB_1	8	0	548.0000	506.0000	548.0000	571.2000
SE_1	8	0	90.4800	87.1725	90.4800	95.7300
ALCH_1	8	0	.6000	.0000	.6000	2.0000
PILL_1	8	0	.0000	.0000	.0000	.0000
FEEL_1	8	0	2.7000	2.0000	2.7000	3.0000
ENJOYABLE	8	0	2.9000	2.2500	2.9000	3.1500
ALERT_1	8	0	1.8000	1.1500	1.8000	2.1500
TENSE_1	8	0	.9000	.1000	.9000	1.6000
STRESSED_1	8	0	1.0000	.0000	1.0000	1.7500
RECODE_Symtpom_1	8	0	.0000	.0000	.0000	.7500
SOL_2	8	0	18.0000	12.0000	18.0000	32.7500
WAKENING_2	8	0	.6000	.0500	.6000	1.1500
WASO_2	8	0	2.8000	.3000	2.8000	24.5000
TST_2	8	0	415.9998	346.0000	415.9998	496.1000
TIB_2	8	0	466.0000	411.6000	466.0000	579.5000
SE_2	8	0	86.4346	82.1235	86.4346	90.2968
ALCH_2	8	0	.0000	.0000	.0000	1.2000
PILL_2	8	0	.0000	.0000	.0000	.0000
FEEL_2	8	0	2.4000	1.7000	2.4000	2.7500
ENJOYABLE_2	8	0	2.4000	1.9000	2.4000	3.0000
ALERT_2	8	0	1.7000	.7500	1.7000	2.5750
TENSE_2	8	0	1.6000	1.2500	1.6000	2.0000
STRESSED_2	8	0	3.0000	2.2500	3.0000	3.7500
RECODE_Symptom_2	8	0	1.0000	.2500	1.0000	2.0000
SOL_CHANGE	8	0	-3.0000	-27.6000	-3.0000	5.0000
WAKENING_CHANGE	8	0	-.1000	-.3500	-.1000	.0000
WASO_CHANGE	8	0	-.3000	-20.2500	-.3000	.0000
TST_CHANGE	8	0	59.2022	-7.2500	59.2022	151.7500
TIB_CHANGE	8	0	62.0250	-39.7500	62.0250	106.4000
SE_CHANGE	8	0	5.5859	-2.0702	5.5859	8.3395
PSQI	8	0	5.0000	3.2500	5.0000	5.7500
ISI	8	0	3.5000	1.0000	3.5000	7.2500
PSS	8	0	16.0000	7.2500	16.0000	23.0000
DASSD	8	0	5.0000	2.0000	5.0000	11.5000
DASSA	8	0	5.0000	4.0000	5.0000	8.0000
DASSS	8	0	14.0000	8.5000	14.0000	22.5000
NEOO	8	0	54.5000	49.0000	54.5000	59.5000
NEOC	8	0	45.5000	40.0000	45.5000	55.7500

NEOE	8	0	49.5000	45.5000	49.5000	54.5000
NEOA	8	0	48.5000	40.0000	48.5000	54.0000
NEON	8	0	45.5000	28.7500	45.5000	51.2500
RUMD	8	0	26.0000	19.5000	26.0000	28.7500
RUMB	8	0	10.0000	8.0000	10.0000	14.7500
RUMR	8	0	12.5000	7.2500	12.5000	14.7500
COPEP	8	0	12.0000	11.0000	12.0000	14.7500
COPEE	8	0	15.0000	12.2500	15.0000	18.0000
WORRY	8	0	50.5000	36.7500	50.5000	58.2500
T1C	8	0	3.0898	2.4785	3.0898	4.0641
T2C	8	0	3.4804	1.9417	3.4804	4.4878
T3C	8	0	4.1124	1.9879	4.1124	7.9826
T4C	8	0	4.0296	1.8734	4.0296	8.8672
T5C	8	0	3.6473	1.7919	3.6473	8.1455
AUCg	8	0	151.3170	76.9419	151.3170	280.3642
Mean cort	8	0	3.7478	1.9243	3.7478	6.7897
AUCi	8	0	21.7350	-19.2061	21.7350	103.0895

Median and Interquartile ranges for the Vulnerable group in the follow-up section '_1' denotes data from the normal weeks diary. '_2' indicates data from the stressful weeks diary. For abbreviation list see abbreviation section

XVI. Information sheet for Heart-Rate Study (Chapter 5)

Participant Information Sheet

Title: Stress reactivity and Sleep

You are being invited to take part in a research study. You are being invited to take part because you responded to one of our advertisements and successfully completed the screening interview. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

The Study

This study will be conducted through the University of Glasgow Sleep Centre and the School of Psychology. You have been invited to take part in this study based on your responses to the screening process. The study in which you are being asked to take part is designed to help us profile the relationships between sleep problems, perceived stress, personality and coping styles and stress reactivity. Hopefully this type of research will help us improve our understanding of insomnia, and give an insight into how insomnia can be prevented.

Do I have to take part?

Taking part in the research is entirely voluntary. This means that it is up to you to decide whether or not you would like to take part. If you do not wish to take part it will not affect the case or your rights in any way. If you decide to take part in the study, you can keep this information sheet and contact the researcher for further information. If you do decide to take part, you can change your mind and withdraw from the study at any time, even after the study has finished.

What does taking part involve?

If you decide to take part all you have to do is come to School of Psychology at the University of Glasgow where you will be asked to run through a math task while we monitor your heart-rate. Heart rate information will allow us to collect information on the activity of your nervous system during the task. You will be in the department for roughly an hour and a half

. To measure heart-rate 4 electrodes will be placed on your torso: one below your right clavicle (near your shoulder), 2 below your left clavicle and one near the bottom of your left rib-cage. These will be connected to an ambulatory track-it device which is a standard device tested and used for collecting this kind of information.

During the math task you will alternately be presented with relaxing scenes, accompanied by soothing music and then with multiple choice math tasks which you need to answer within a set time. This takes roughly 45 minutes.

Upon completion of the task you will be asked to fill out some questionnaires relating to stress, personality, coping style, sleep, worry, rumination anxiety and depression.

You are free to withdraw from the study at any time and omit any questions which you do not feel comfortable with.

Would my results be kept confidential? What will happen to the results of the study?
All the information that is collected during the course of the study will remain strictly confidential. This means that all information will be kept secured in locked filling cabinets and only the researcher will be able to access these. You will be given a unique code that will ensure confidentiality and anonymity of all your data. The results of this study will be published in a relevant journal so that the general public is also aware of these findings. However any information regarding your identity will not be revealed in these.

What are the potential benefits or disadvantages of taking part?
Taking part will provide us with information on how to improve treatments and aid in prevention of insomnia. There are no risks or disadvantages associated with taking part. You will also be given advice on how to promote better sleep during times of stress. If you are a first year undergraduate psychology student you will receive 2 course credits or £10. Otherwise you will receive £10.

Who is organising and paying for the research?
The research study is organised by Christopher-James Harvey, doctorial research student and is funded by The Sackler Institute of Psychobiological Research.
Educational supervision of this research is provided by Prof Colin Espie and Dr. Jonathan Cavanagh

If I decide to take part what happens next?
If you decide to take part you will be invited to come to the Psychology Department and given the opportunity to ask any questions about the research before commencing the study.

Thank you for reading this information. If there is anything that is not clear or if you have any questions regarding this study you can e-mail the researcher at

c.harvey.1@research.gla.ac.uk or call:

or call Chris on 0141 232 7566

If you would like some independent advice from someone who is not involved in the study, please contact Dr Maria Gardani +44 (0)141 232 7700 or M.Gardani@clinmed.gla.ac.uk

XVII. Consent Form for HR study (Chapter 5)

University of Glasgow | Sleep Centre

Participant Identification Number for this study:

CONSENT FORM

Title of Project: Stress reactivity and Sleep

Please initial box

2. I confirm that I have read and understand the information sheet and received my own copy dated 21st September 2011 (version 1) for the above study. ☐

2. I have had the opportunity to consider the information provided, ask questions and have had these answered satisfactorily. ☐

3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐

4. I understand that data collected during this study may be looked at by responsible Individuals from the research team or from regulatory authorities where it is relevant to them taking part in research.
I give permission for these individuals to have access to my records. ☐

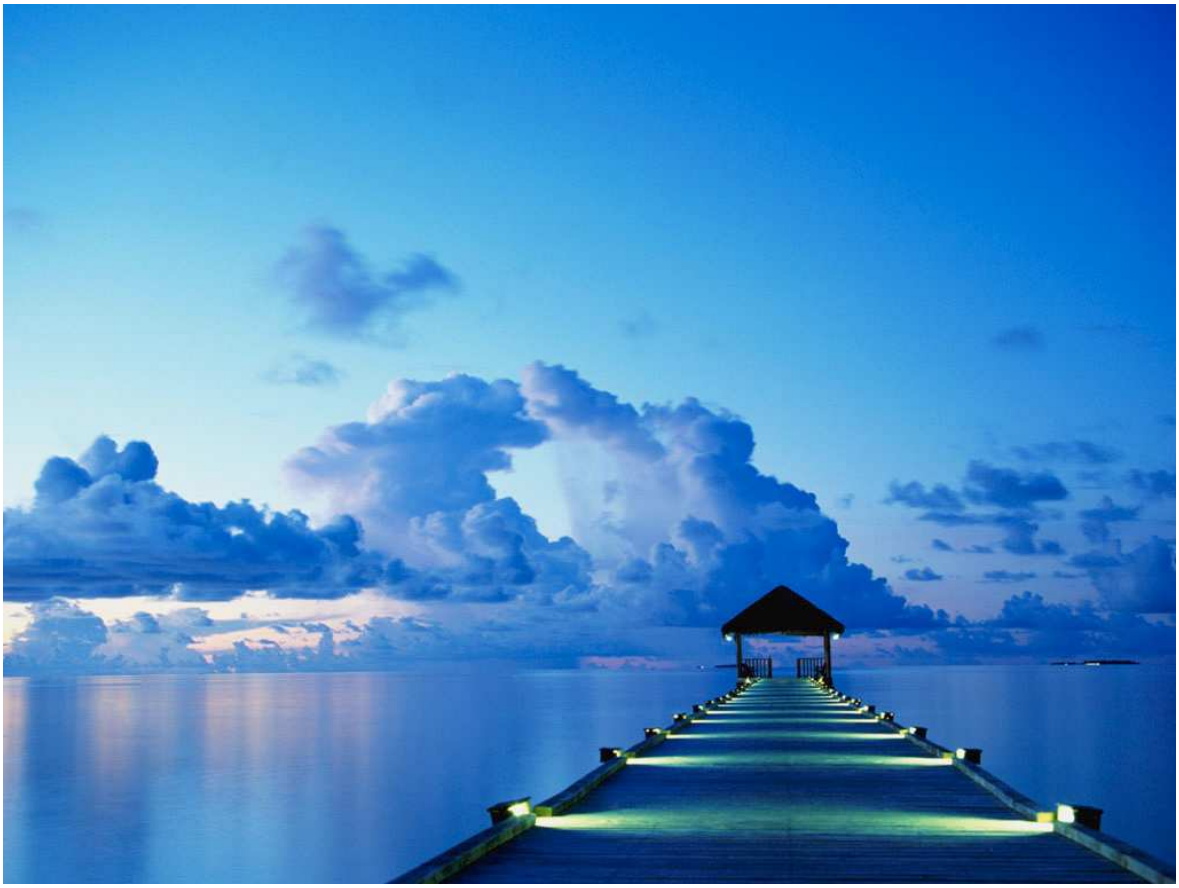
5. I consent to the results (in anonymised form) of this study being published in relevant journals. ☐

6. I agree to be contacted in the future from the Glasgow Sleep Research Centre. ☐

8. I agree to take part in the above study. ☐

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Researcher	Date	Signature

XVIII. Stimuli for Baseline/ Relaxation Conditions of Heart-Rate Study (Chapter 5)



Pier and Clouds, Accompanied by Beethoven's Sonata 14 (moonlight) in c sharp minor

Tree in Field, accompanied by Shostakovich - concerto para piano no 2 - andante

Water and Rock. Accompanied by `Grieg Solveig's Song- Peter Gynt Op. 23.`

XIX. Stimulus for Stressor Condition (Chapter 5)

The timetables below show the times of the ferries between Ardrossan and Brodick.

Ardrossan	Brodick
Depart	*Arrive*
07 00	07 55
09 45	10 40
12 30	13 25
15 15	16 10
18 00	18 55

Brodick	Ardrossan
Depart	*Arrive*
08 20	09 15
11 05	12 00
13 50	14 45
16 40	17 35
19 20	20 15

One day Sophia took the first ferry from Ardrossan to Brodick and the last ferry back. How long did Sophia spend in Brodick?

(1) 9 hours 55 minutes

(2) 10 hours 25 minutes

(3) 11 hours 25 minutes

(4) 11 hours 55 minutes

Example question for stress condition

A double-glazing firm pays its employees a bonus each month based on their sales.

The table below shows how the bonus is calculated.

Sales	Bonus
Less than £10 000	£0
From £10 000 to £20 000	6% of sales
More than £20 000	12% of sales

Martha sells £16 000 worth of double glazing.

What is her bonus?

(1) £0

(2) £160

(3) £560

(4) £960

Example Question for stress condition

A bottle of wine contains 750 millilitres.

Six glasses can be filled from one bottle of wine.

How much wine does each glass contain?

(1) 125 ml

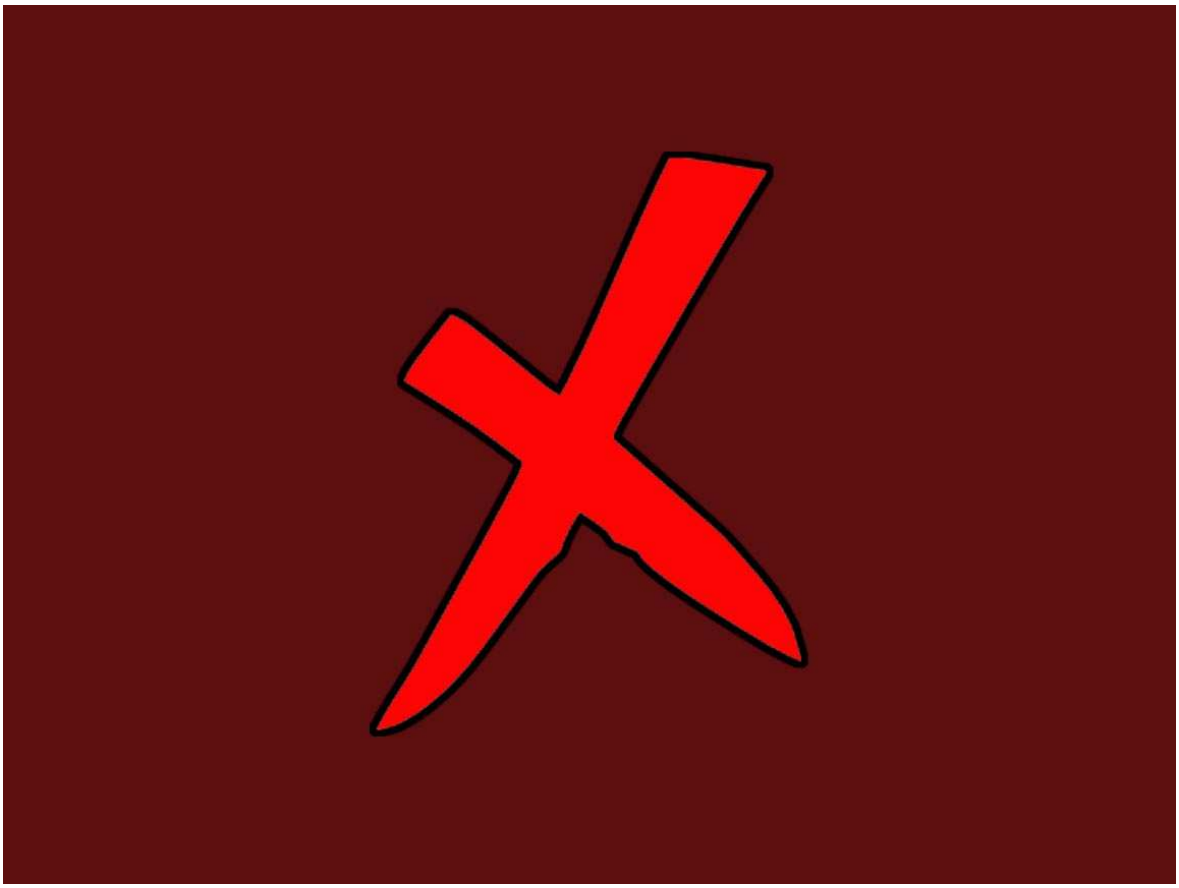
(2) 150 ml

(3) 175 ml

(4) 135 ml

Example Question for stress condition

Feedback screen for correct answer



Feedback screen for incorrect answer

XX. Mean, Kurtosis and Skewness of Psychological Variables' (Chapter 5)

Descriptive Statistics[a]

	N	Mean	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
PSQI	13	3.2308	.430	.616	1.615	1.191
ISI	13	1.4615	.504	.616	-1.447	1.191
FIRST	13	14.4615	-1.107	.616	1.225	1.191
PSS	13	10.3077	-.325	.616	-1.352	1.191
DASS_D	13	4.1538	1.937	.616	4.287	1.191
DASS_A	13	4.0000	.740	.616	-1.081	1.191
DASS_S	13	5.5385	.827	.616	-.286	1.191
NEO_O	13	50.2308	-.008	.616	-1.027	1.191
NEO_C	13	50.6923	.394	.616	-.759	1.191
NEO_E	13	53.2308	-1.133	.616	.643	1.191
NEO_A	13	55.7692	-.496	.616	-1.159	1.191
NEO_N	13	30.0000	1.406	.616	1.832	1.191
RUM_B	13	19.6154	.495	.616	.597	1.191
RUM_D	13	7.5385	1.094	.616	1.694	1.191
RUM_R	13	8.0000	1.509	.616	1.982	1.191
COPE_P	13	11.6923	.329	.616	-.728	1.191
COPE_E	13	13.0769	.844	.616	-.424	1.191
Valid N (listwise)	13					

Mean, Kurtosis and Skew for the resilient group. Abbreviations can be found in the 'Abbreviations' section. Table taken directly from SPSS

Descriptive Statistics[a]

	N	Mean	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
PSQI	18	4.5556	.816	.536	.126	1.038
ISI	18	5.3333	1.197	.536	1.653	1.038
FIRST	18	21.7222	.281	.536	-1.551	1.038
PSS	18	17.9444	.373	.536	-1.039	1.038
DASS_D	17	7.8824	.905	.550	.450	1.063
DASS_A	17	5.7647	1.694	.550	2.701	1.063
DASS_S	17	13.0588	.649	.550	.046	1.063
NEO_O	18	50.3889	.384	.536	-.124	1.038
NEO_C	18	47.0000	-.271	.536	-.118	1.038
NEO_E	18	50.1667	-.260	.536	-.061	1.038
NEO_A	18	53.8889	-.857	.536	1.009	1.038
NEO_N	18	37.5000	.246	.536	-.110	1.038
RUM_B	18	24.2222	.514	.536	-.232	1.038
RUM_D	18	9.3333	1.223	.536	1.005	1.038
RUM_R	18	9.6667	.778	.536	-.601	1.038
COPE_P	18	12.1111	-.487	.536	-.182	1.038
COPE_E	18	13.3889	-.427	.536	-.542	1.038
Valid N (listwise)	17					

Mean, Kurtosis and Skew for the vulnerable group. Abbreviations can be found in 'Abbreviations' section. Table take directly from SPSS.

XXI. **Correlation Table for Psychometric Data (Chapter 5)**

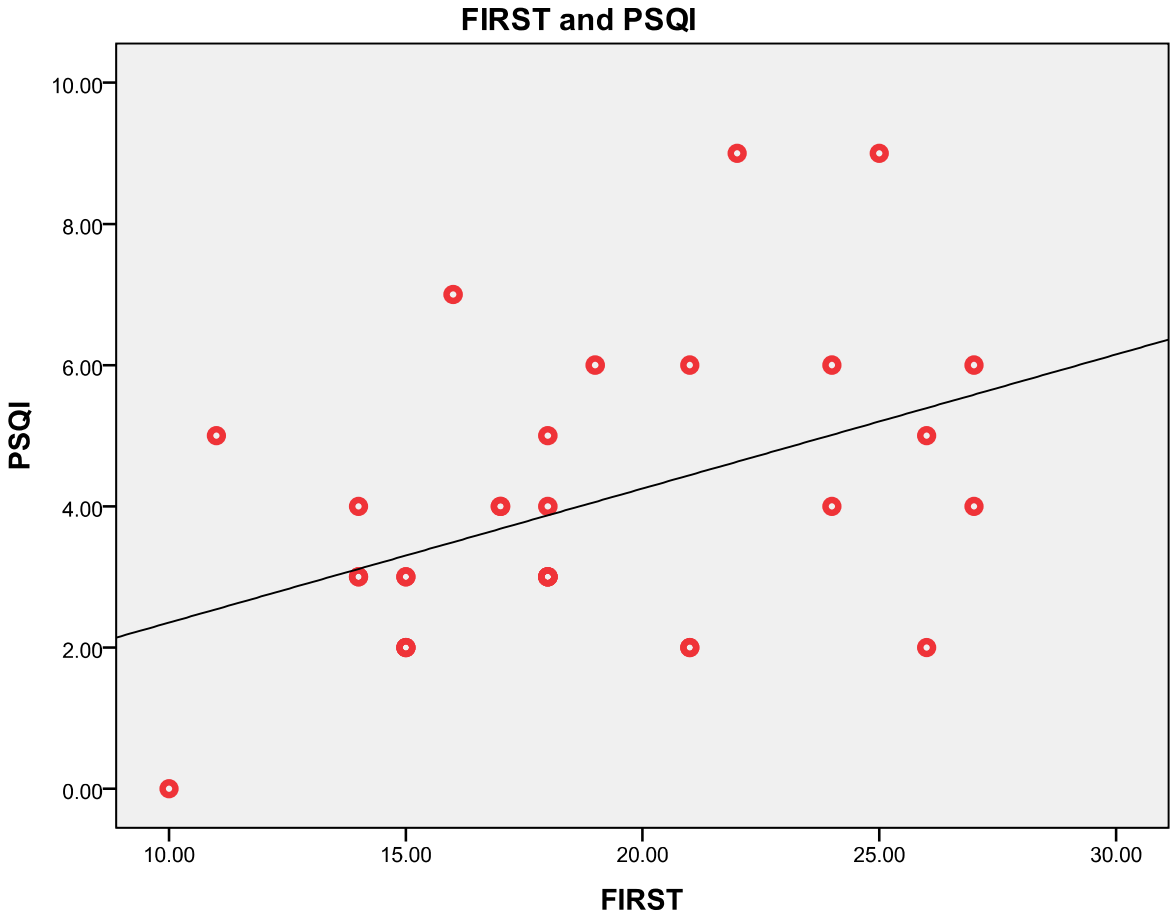
Correlations

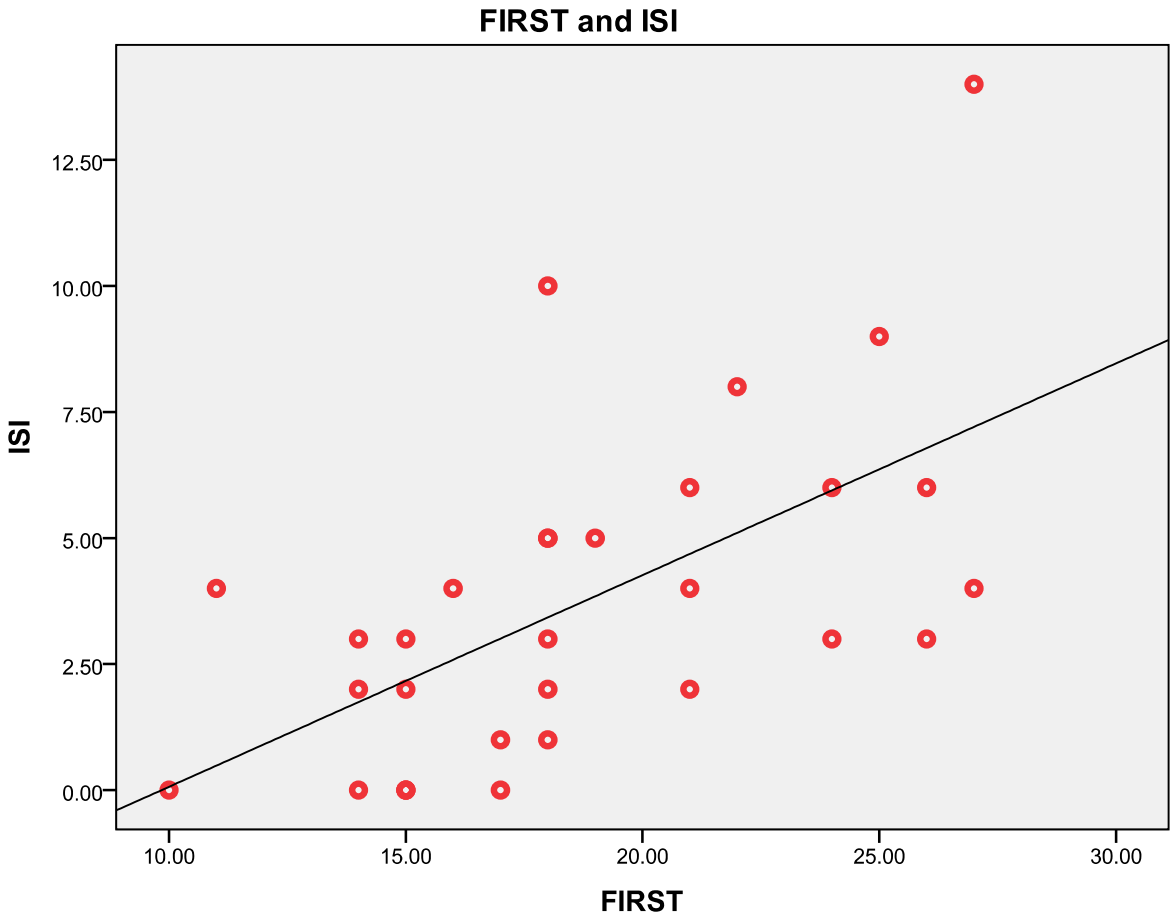
		AGE	PSQI	ISI	FIRST	PSS	DASS_D	DASS_A	DASS_S	NEO_O
AGE	Pearson Correlation	1	-.125	-.245	-.175	.014	-.133	-.025	.051	.071
	Sig. (2-tailed)		.502	.183	.347	.939	.485	.898	.788	.704
	N	31	31	31	31	31	30	30	30	31
PSQI	Pearson Correlation	-.125	1	.692**	.432*	.570**	.511**	.477**	.521**	.098
	Sig. (2-tailed)	.502		.000	.015	.001	.004	.008	.003	.599
	N	31	31	31	31	31	30	30	30	31
ISI	Pearson Correlation	-.245	.692**	1	.596**	.661**	.623**	.353	.641**	.112
	Sig. (2-tailed)	.183	.000		.000	.000	.000	.055	.000	.548
	N	31	31	31	31	31	30	30	30	31
FIRST	Pearson Correlation	-.175	.432*	.596**	1	.608**	.318	.181	.549**	.019
	Sig. (2-tailed)	.347	.015	.000		.000	.087	.338	.002	.920
	N	31	31	31	31	31	30	30	30	31
PSS	Pearson Correlation	.014	.570**	.661**	.608**	1	.588**	.381*	.652**	.061
	Sig. (2-tailed)	.939	.001	.000	.000		.001	.038	.000	.743
	N	31	31	31	31	31	30	30	30	31
DASS_D	Pearson Correlation	-.133	.511**	.623**	.318	.588**	1	.402*	.426*	-.027
	Sig. (2-tailed)	.485	.004	.000	.087	.001		.028	.019	.887
	N	30	30	30	30	30	30	30	30	30
DASS_A	Pearson Correlation	-.025	.477**	.353	.181	.381*	.402*	1	.478**	-.153
	Sig. (2-tailed)	.898	.008	.055	.338	.038	.028		.008	.420
	N	30	30	30	30	30	30	30	30	30
DASS_S	Pearson Correlation	.051	.521**	.641**	.549**	.652**	.426*	.478**	1	.103
	Sig. (2-tailed)	.788	.003	.000	.002	.000	.019	.008		.587
	N	30	30	30	30	30	30	30	30	30
NEO_O	Pearson Correlation	.071	.098	.112	.019	.061	-.027	-.153	.103	1
	Sig. (2-tailed)	.704	.599	.548	.920	.743	.887	.420	.587	
	N	31	31	31	31	31	30	30	30	31
NEO_C	Pearson Correlation	.039	-.362*	-.160	-.201	-.510**	-.423*	-.354	-.029	.022

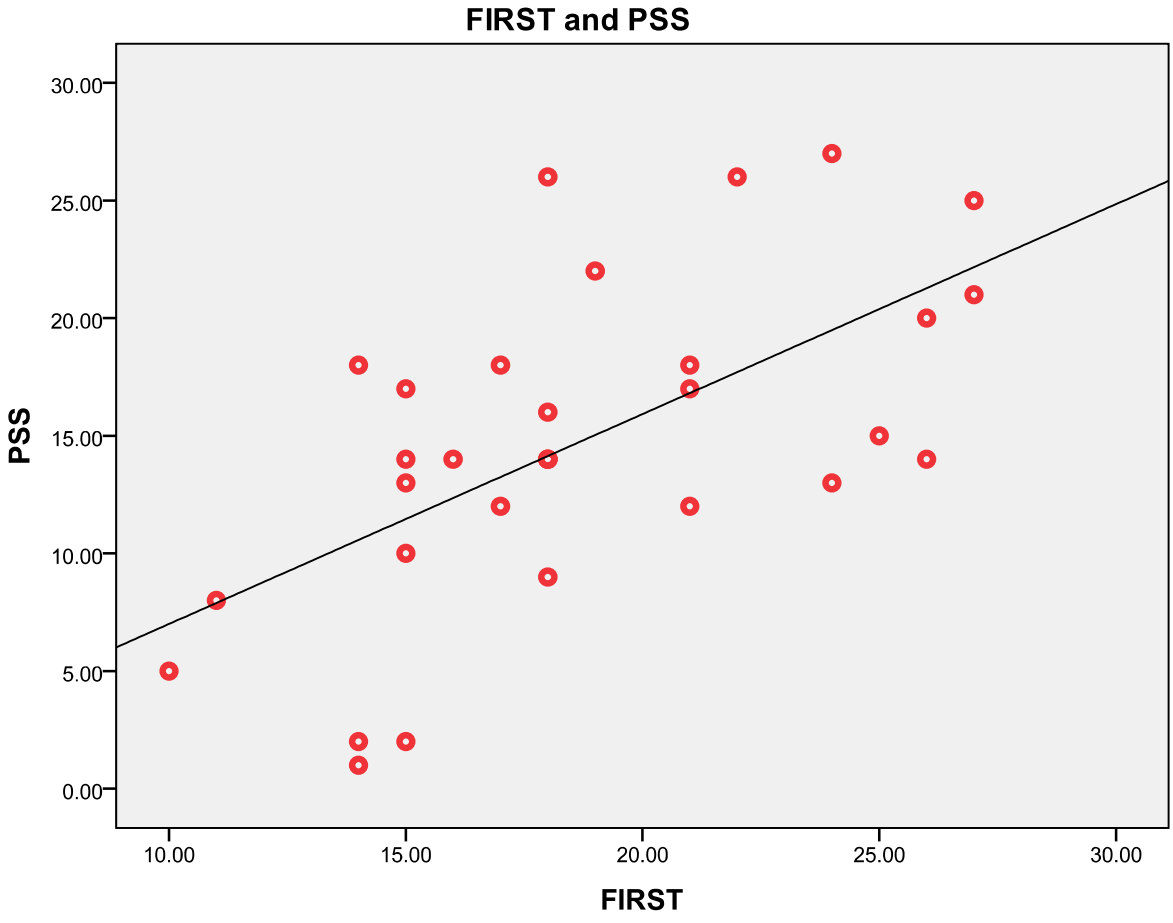
	Sig. (2-tailed)	.834	.045	.390	.277	.003	.020	.055	.880	.908
	N	31	31	31	31	31	30	30	30	31
NEO_E	Pearson Correlation	-.124	.087	-.142	.032	-.266	-.174	-.113	.045	-.062
	Sig. (2-tailed)	.507	.642	.445	.863	.148	.359	.552	.811	.739
	N	31	31	31	31	31	30	30	30	31
NEO_A	Pearson Correlation	-.115	-.390*	-.395*	.103	-.358*	-.461*	-.325	-.249	.103
	Sig. (2-tailed)	.537	.030	.028	.582	.048	.010	.080	.185	.581
	N	31	31	31	31	31	30	30	30	31
NEO_N	Pearson Correlation	.014	.335	.310	.388*	.628**	.522**	.598**	.499**	-.064
	Sig. (2-tailed)	.940	.066	.090	.031	.000	.003	.000	.005	.733
	N	31	31	31	31	31	30	30	30	31
RUM_B	Pearson Correlation	-.242	.395*	.627**	.340	.471**	.548**	.377*	.419*	.224
	Sig. (2-tailed)	.191	.028	.000	.061	.007	.002	.040	.021	.227
	N	31	31	31	31	31	30	30	30	31
RUM_D	Pearson Correlation	-.191	.150	.227	.133	.169	.165	.372*	.245	-.079
	Sig. (2-tailed)	.303	.421	.219	.474	.363	.385	.043	.192	.674
	N	31	31	31	31	31	30	30	30	31
RUM_R	Pearson Correlation	-.225	.138	.347	.221	.041	.246	.056	-.007	.325
	Sig. (2-tailed)	.223	.458	.056	.233	.826	.190	.769	.970	.075
	N	31	31	31	31	31	30	30	30	31
COPE_P	Pearson Correlation	-.150	-.152	-.112	.075	-.113	-.077	-.056	-.121	.384*
	Sig. (2-tailed)	.421	.414	.550	.687	.545	.684	.771	.524	.033
	N	31	31	31	31	31	30	30	30	31
COPE_E	Pearson Correlation	-.096	.059	.024	-.014	-.152	-.130	.069	.051	.475**
	Sig. (2-tailed)	.608	.753	.896	.942	.413	.492	.715	.787	.007
	N	31	31	31	31	31	30	30	30	31
WORRY	Pearson Correlation	.079	.195	.249	.211	.397*	.206	.351	.511**	.029
	Sig. (2-tailed)	.673	.292	.176	.254	.027	.274	.057	.004	.876
	N	31	31	31	31	31	30	30	30	31

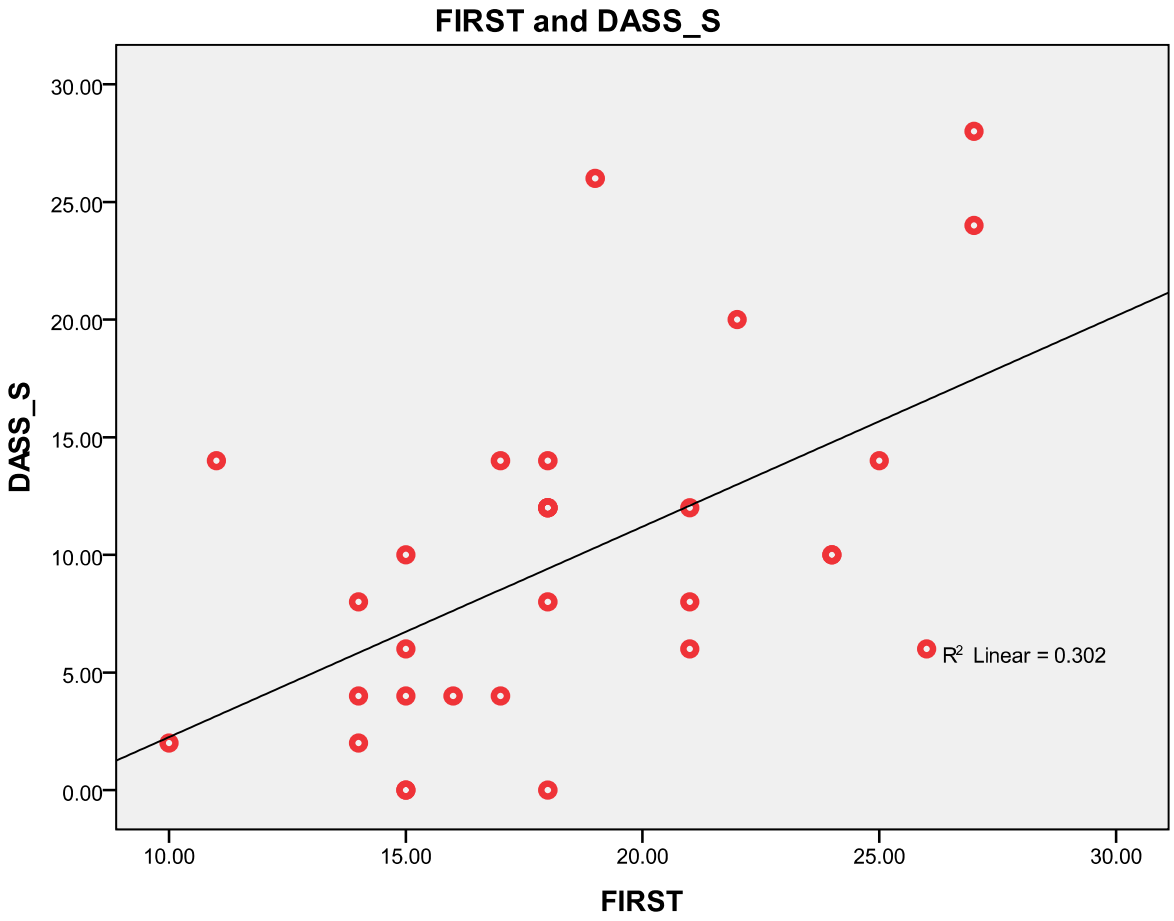
Correlation matrix generated in SPSS, showing correlation for all psychometric variables

XXII. Scatter-plots for Whole-Sample showing relationship between FIRST scale and other Psychological Variables (Chapter 5)




FIRST and ISI
ISI
12.50
10.00
7.50
5.00
2.50
0.00
10.00
15.00
20.00
25.00
30.00
FIRST


FIRST and PSS
PSS
30.00
25.00
20.00
15.00
10.00
5.00
0.00
10.00
15.00
20.00
25.00
30.00
FIRST


FIRST and DASS_S
DASS_S
30.00
25.00
20.00
15.00
10.00
5.00
0.00
10.00
15.00
20.00
25.00
30.00
FIRST
R² Linear = 0.302

XXIII. **MRI Checklist**

CENTRE FOR COGNITIVE NEUROIMAGING

University of Glasgow

3.0T MRI SCREENING FORM

Date _____ Principal investigator / Lab _____ Subject ID _____

Name _____ Height _____ Weight _____
Last name First name M.I.

Birthdate _____ Email Address _____

Address _____ City _____

State _____ Zip Code _____ Phone (H) (___) _____ (W) (___) _____

GP's name & address _____

1. Have you ever had surgery or other invasive procedures? ☐Yes ☐No If yes, please list below.
Type: _____ Date: _____
Type: _____ Date: _____

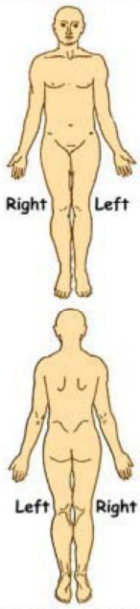
2. Have you had any previous MRI studies? ☐Yes ☐No If yes, please list below..

_____ _____ _____
Area of Body Date Facility Name & Location

3. Have you ever worked as a machinist, metal worker, or in any profession or hobby grinding metal? ☐Yes ☐No
or had an injury to the eye involving a metallic object (e.g., metallic slivers, shavings, foreign body)? ☐Yes ☐No
4. Are you pregnant, experiencing a late menstrual period, or having fertility treatments? ☐Yes ☐No
5. Are you currently taking or have recently taken any medication? ☐Yes ☐No Please list: _____
6. Do you have drug allergies or have you had an allergic reaction? ☐Yes ☐No Please list: _____

⚠ **Some of the following items may be hazardous to your safety or may interfere with the MRI exam. Please check the correct answer for each of the following. If you checked yes, please give more information. E.g. Type of material? How long ago? Use the diagram to indicate where on our body?**

☐Yes ☐No Cardiac pacemaker
☐Yes ☐No IUD or diaphragm
☐Yes ☐No Aneurysm clip or brain clip
☐Yes ☐No Carotid artery vascular clamp
☐Yes ☐No Neurostimulator
☐Yes ☐No Insulin or infusion pump
☐Yes ☐No Implanted drug infusion device
☐Yes ☐No Spinal fusion stimulator
☐Yes ☐No Harrington rods (spinal rod)
☐Yes ☐No Aortic clips
☐Yes ☐No Internal pacing wires
☐Yes ☐No Venous umbrella
☐Yes ☐No Artificial heart valve/prosthesis
☐Yes ☐No Artificial limb or joint
☐Yes ☐No Coloured contact lenses
☐Yes ☐No Wig, toupee, or hair implants
☐Yes ☐No Body piercing(s)
☐Yes ☐No Metal or wire mesh implants
☐Yes ☐No Pessary or bladder ring
☐Yes ☐No Swan-Ganz catheter
☐Yes ☐No Claustrophobia



☐Yes ☐No Shrapnel, buckshot, or bullets
☐Yes ☐No Implant held in place by a magnet
☐Yes ☐No Shunt (spinal or intraventricular)
☐Yes ☐No Tattooed eyeliner or eyebrows
☐Yes ☐No Transdermal delivery patch (nicoderm)
☐Yes ☐No Metal fragments (eye, head, ear, skin)
☐Yes ☐No Facelift or other cosmetic surgery
☐Yes ☐No Implanted cardiac defibrillator
☐Yes ☐No Cochlear, otologic, or ear implant
☐Yes ☐No Stents, filters, coils for blocked arteries
☐Yes ☐No Electrodes (on body, head or brain)
☐Yes ☐No Wire sutures or surgical staples
☐Yes ☐No Prosthesis (eye/orbital, penile, etc.)
☐Yes ☐No Metal rods in bones; joint replacements
☐Yes ☐No Bone/joint pin, screw, nail, wire, plate
☐Yes ☐No Asthma or breathing disorders
☐Yes ☐No Seizures or motion disorders
☐Yes ☐No Vascular access port or catheters
☐Yes ☐No Other implants in body or head
☐Yes ☐No Hearing aid ***(Remove before scan)***
☐Yes ☐No Dentures ***(Remove before scan)***

Please remove **all metallic objects** before the MR examination including: keys, hair pins, barrettes, jewelry, watch, safety pins, paperclips, money clip, credit cards, coins, pens, belt, metal buttons, pocket knife, & clothing with metal in the material. **Earplugs are required during the MRI examination.**

_____ _____ _____ _____
Your Signature Date MR Staff Name MR Staff Signature

XXIV. Participant Information sheet (Chapter 6)

Study Information Sheet - MRI

Title of Project: From Acute to Chronic Insomnia: The Role of the Insula
(Standard Functional Magnetic Resonance Imaging (fMRI) Study)

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. If anything is unclear or you would like more information, please ask us. Take time to decide whether or not you wish to take part.
Thank you for reading this.

What is the purpose of this study?
This study will use functional magnetic resonance imaging (fMRI) to take pictures of the activity of your brain while responding to neutral and emotive words in order to investigate possible differences between poor and good sleepers. Prior to the scan you will be asked to fill out some questionnaires, keep a sleep diary for 2 weeks to assess your sleep and wear a small wrist-device which will also monitor your sleep.

Why have I been chosen?
You have been chosen because you have already volunteered to participate in the Centre for Cognitive Neuroimaging Research Panel, coordinated at Psychology Department, or you volunteered to participate in research studies using functional magnetic resonance imaging, or because you have contacted the University of Glasgow Sleep Centre with an interest in taking part in our research.

Who is organizing this study?
This study is organized by Christopher-James Harvey

What will happen to me if I take part?
Before you take part a member of staff will ask you some questions to ensure that you have no metal within you before you enter the strong magnetic field of the MRI scanner. You may be asked to remove coloured contact lenses and to change (we provide training suits in case there is metal on your clothes). You will then be asked to lie in the scanner and the scanning will start. The scanning can be noisy so we shall give you headphones or earplugs to reduce this noise. If you are very claustrophobic, that is if you feel very uncomfortable in small closed environment, then it may not be appropriate for you to be scanned.

During the scan you will be view different stimuli through a pair of goggles and fitted with earphones. You will also be given 2 button boxes in order to make the responses required

during the experiment. We will also monitor and record your physiological responses: This will involve placing small sensors (electrodes) on your arms, hands and/or chest. Whatever the nature of the task, it will always be explained to you before you sign the consent form, and will never involve any painful stimulation. We will repeat the instructions before each task. At all times you will remain in contact with us through the intercom and you will have a buzzer in your hand, in case you want us to stop the scan and come in the scanner room. We will ask you in all cases to try to keep your head as still as possible. To help you do so, we will place foam pads under your neck and on the side of your head.
The scanning session will take about one and a half hours, although you will not actually be scanned for more than 60 minutes of this time.

What is the device involved?
We can learn a great deal about how the brain works by looking at the blood flow to different parts of the brain whilst the brain performs different tasks. We measure brain function using images taken with a magnetic resonance imaging scanner. This scanner uses a strong magnetic field to create detailed images of brain structure and function. By taking a series of images whilst you perform a task we can build up a picture of the brain areas activated by this type of task. The scan does not involve any injections or X-rays.

What are the possible risks/side effects of taking part?
The scanner can be loud when it takes images, and you will be given earplugs and/or headphones to block out some of the sound. Also, the scanner space is quite reduced, and people who are uncomfortable in small or confined spaces may not be able to participate. If this applies to you, remember that you may withdraw from the study at any time without explaining why. MRI is generally thought to be a safe, non-invasive imaging technique. There are no known risks or side effects, except that in less than 5% of people the scanning might induce a peripheral nerve stimulation (felt as small twitches); this is not dangerous but might induce discomfort. In some very rare cases, being in the magnetic field may also trigger vertigo (dizziness). In the unlikely case you experience one of these feelings, please alert us and withdraw from the study, should you wish to do so. Although there is no evidence of danger, as a natural precaution we do not wish to include any women who may either be pregnant or have any reason to believe they may be pregnant.

What are the possible benefits of taking part?
We will reimburse you for your time and travel, and you will have the pleasure of knowing that you have made a contribution to our understanding of the relationship between brain and behaviour. If you suffer from insomnia you will be offered group therapy aimed at treating this.

What happens at the end of the study?
The results of this study may be published in a journal or used for teaching purposes. The results may also be presented at scientific meetings, or in talks at academic institutions. Results will always be presented in such a way that data from individual volunteers cannot be identified.

Confidentiality - who will have access to the data?
The data will be stored on a secure network and only members of the Centre for Cognitive Neuroimaging (CCNI) of the Psychology Department at University of Glasgow will have access to the data. It is possible that the data may be used by researchers working with CCNi for other similar ethically approved research protocols, where the same standards of

confidentiality will apply. In all cases your name will not be used and your data will be identified only by a 5 digit code.

Will my General Practitioner (GP) be informed?

This is not a diagnostic scan. Your GP will not be routinely informed if your participation in this study has been as a normal volunteer. Brain images will NOT be routinely examined for abnormalities by a trained neuro-radiologist. Like faces, brains come in all shapes and sizes, however, so that there are many normal variations of what the scan shows. There is a chance of less than 1:100 that your scan may, by chance, show a significant abnormality of which you are unaware.

There is no guarantee that abnormalities will be picked up. It is possible, however, that an abnormality is detected, by chance, in the scan of a normal volunteer by the radiographer or one of the investigators. This is referred to as incidental finding. If this happens, your brain scan will be examined by a trained neuro-radiologist who will provide an expert opinion on the importance of the incidental finding for your health, and on the potential health benefit of disclosing this information to you. There are three possible cases:

- Unlikely net benefit: If the incidental finding is a condition not likely to be of serious importance for your health, or whose likely health importance cannot be ascertained, that finding will not be disclosed to you or your GP.
- Possible net benefit: If the incidental finding consists of a nonfatal condition that could possibly be grave or serious but that cannot be avoided or improved, then when you are likely to deem that information important, that finding will be disclosed to you with appropriate guidance. You may also choose not to be informed should such an unlikely finding apply to you. In that case, please tick the appropriate box on the consent form.
- Strong net benefit: In the very unlikely case of a life threatening condition or a condition likely to be grave and that can be treated or improved, this information will be disclosed to you and you will be appropriately advised. Further action will be decided which could involve further imaging and/or a discussion between you and your GP or an appropriate clinician.

What if new information becomes available?

If the new information pertains specifically to the health of the volunteer, the volunteer may be informed (see previous paragraph). Otherwise, new information will be published through traditional scientific channels (journal articles, conference presentations).

What will happen to the study results?

In accordance with good research practice, they will be kept securely for a minimum of 10 years and possibly indefinitely in the CCNi data archive.

Will I receive a financial compensation?

Yes; you will receive £6 per hour for your participation in this study.

Can I ask questions about the research project?

Yes; we will answer all questions you may have that are related to the research project to which you agree to participate (see contact details below)

Can I withdraw from the study?

Yes. Your participation to this research project is voluntary, and you may withdraw from the research at any time and for any reason, without explaining why, and this will not affect your medical care or legal rights.

Can the investigators interrupt the study?
The research may be interrupted by the researchers at any time, and for several possible reasons such as new requirements for the selection of participants, for example.

Are there compensation arrangements if something goes wrong?
In the unlikely event of anything untoward happening, the University of Glasgow provides insurance for claims.

This research study has been approved by the Ethics Committee of the Faculty of Information and Mathematical Sciences at University of Glasgow.

Contact details
Name
Address
Telephone Email

Thank you for considering taking part in this study. Our research depends entirely on the goodwill of potential volunteers such as you. If you require any further information, we will be pleased to help you in any way we can.

XXV. Study Consent (Chapter 6)

STUDY INFORMED CONSENT - MRI
(This form must be completed prior to any scanning)

Study title: From Acute to Chronic Insomnia: The Role of the Insula

☐ I confirm that I have read and understood the Study Information Sheet provided to me for the above study and have had the opportunity to ask questions.

☐ I understand the risks and contraindications including pregnancy.

☐ I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason, without my medical care or legal rights being affected.

☐ I understand that this is not a diagnostic scan but that should, by chance, something abnormal be noticed, an expert neuro-radiologist will examine my scans. There is no guarantee, however, that if there is an abnormality, it will be detected.

☐ I do not wish to be informed if a nonfatal condition likely to be grave or serious but that cannot be avoided or ameliorated is discovered in my brain (non mandatory for participating).

☐ I understand that the research data may be accessed by researchers working at or in collaboration with the CCNi in similar ethically approved studies but that at all times my personal data will be kept confidential in accordance with data protection guidelines.

I have initialled the above boxes myself and I agree to take part in the study.

_____
SIGNATURE OF VOLUNTEER

Name: _____ Date: _____

_____
SIGNATURE OF WITNESS

Name: _____ Date: _____

XXVI. **Words Used for Chapter 6 Paradigm**

Neutral	*Sleep*	*Anxiety*	*Positive*
stimulus praise nation set intellect drawing playful sandwich television shuffle address turn cream bottle after pear balcony point study Saturday texture	night alert exhausted tossing fatigue tired overactive restless snoring dream bed sleepy arousal lethargy wakeful silence pillow sheets dark naps	failure stupid inferior lonely inept embarrassment hated criticised foolish pathetic indecisive inadequate	confident relaxed optimistic assured holiday welcome melody windfall bold entertainment capable aloof

XXVII. Normality values for Psychological Variables (Chapter 6)

Descriptive Statistics[a]

	N	Mean	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
PSQI	11	4.4545	.092	.661	1.873	1.279
ISI	11	3.4545	.630	.661	-.906	1.279
PSS	11	12.9091	.327	.661	-1.428	1.279
DASSD	11	2.7273	.951	.661	.373	1.279
DASSA	11	3.2727	.546	.661	-1.686	1.279
DASSS	11	6.0000	.085	.661	-1.111	1.279
NEOO	11	50.5455	-.036	.661	.184	1.279
NEOC	11	56.6364	-.401	.661	-1.077	1.279
NEOE	11	51.2727	-.734	.661	-.939	1.279
NEOA	11	58.3636	-.997	.661	.766	1.279
NEON	11	31.0000	-.204	.661	-.823	1.279
RUMB	11	20.1818	1.164	.661	1.043	1.279
RUMD	11	8.0000	1.278	.661	3.379	1.279
RUMR	11	8.3636	1.764	.661	3.614	1.279
COPEP	11	10.1818	.508	.661	-1.468	1.279
COPEE	11	12.9091	-.772	.661	-.565	1.279
WORRY	11	46.4545	.062	.661	-.729	1.279
Valid N (listwise)	11					

Descriptive Statistics[a]

	N	Mean	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
PSQI	11	4.4545	.092	.661	1.873	1.279
ISI	11	3.4545	.630	.661	-.906	1.279
PSS	11	12.9091	.327	.661	-1.428	1.279
DASSD	11	2.7273	.951	.661	.373	1.279
DASSA	11	3.2727	.546	.661	-1.686	1.279
DASSS	11	6.0000	.085	.661	-1.111	1.279
NEOO	11	50.5455	-.036	.661	.184	1.279
NEOC	11	56.6364	-.401	.661	-1.077	1.279
NEOE	11	51.2727	-.734	.661	-.939	1.279
NEOA	11	58.3636	-.997	.661	.766	1.279
NEON	11	31.0000	-.204	.661	-.823	1.279
RUMB	11	20.1818	1.164	.661	1.043	1.279
RUMD	11	8.0000	1.278	.661	3.379	1.279
RUMR	11	8.3636	1.764	.661	3.614	1.279
COPEP	11	10.1818	.508	.661	-1.468	1.279
COPEE	11	12.9091	-.772	.661	-.565	1.279
WORRY	11	46.4545	.062	.661	-.729	1.279
Valid N (listwise)	11					

Means, standard deviation and normality values for the psychological variables, for the resilient group. It can be seen that DASSD is not normal and so was log transformed.

Descriptive Statistics[a]

	N	Mean	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
PSQI	12	4.6667	.846	.637	.996	1.232
ISI	12	4.1667	.357	.637	-.839	1.232
PSS	12	17.0000	.602	.637	.108	1.232
DASSD	12	10.5000	1.164	.637	.458	1.232
DASSA	12	4.6667	1.288	.637	1.922	1.232
DASSS	12	12.6667	.921	.637	1.882	1.232
NEOO	12	51.4167	.494	.637	-1.073	1.232
NEOC	12	46.3333	-.784	.637	2.432	1.232
NEOE	12	43.6667	.338	.637	.020	1.232
NEOA	12	54.1667	-.907	.637	2.691	1.232
NEON	12	41.6667	.515	.637	-.603	1.232
RUMB	11	25.2727	.089	.661	-1.264	1.279
RUMD	11	10.4545	.446	.661	-.064	1.279
RUMR	11	11.0000	.424	.661	-1.469	1.279
COPEP	12	12.5833	-.356	.637	-.509	1.232
COPEE	12	14.0000	-.277	.637	.799	1.232
WORRY	12	48.6667	.845	.637	-.557	1.232

Means, standard deviations and normality values for the vulnerable group

XXVIII. **Correlation Matrix for Psychological Variables (Chapter 6)**

Correlations

		PSQI	ISI	FIRST	PSS	DASSD	DASSA	DASSS	NEOO	NEOC
PSQI	Pearson Correlation	1	.664**	.166	.220	-.123	.115	.066	-.018	-.362
	Sig. (2-tailed)		.000	.428	.292	.557	.586	.754	.931	.075
	N	25	25	25	25	25	25	25	25	25
ISI	Pearson Correlation	.664**	1	.245	.305	.280	.367	.277	-.059	-.378
	Sig. (2-tailed)	.000		.238	.139	.175	.071	.180	.780	.063
	N	25	25	25	25	25	25	25	25	25
FIRST	Pearson Correlation	.166	.245	1	.565**	.420*	.326	.527**	.103	-.483*
	Sig. (2-tailed)	.428	.238		.003	.037	.112	.007	.625	.014
	N	25	25	25	25	25	25	25	25	25
PSS	Pearson Correlation	.220	.305	.565**	1	.620**	.483*	.659**	.244	-.370
	Sig. (2-tailed)	.292	.139	.003		.001	.015	.000	.240	.069
	N	25	25	25	25	25	25	25	25	25
DASSD	Pearson Correlation	-.123	.280	.420*	.620**	1	.297	.721**	.286	-.156
	Sig. (2-tailed)	.557	.175	.037	.001		.150	.000	.166	.456
	N	25	25	25	25	25	25	25	25	25
DASSA	Pearson Correlation	.115	.367	.326	.483*	.297	1	.606**	.303	-.359
	Sig. (2-tailed)	.586	.071	.112	.015	.150		.001	.141	.078
	N	25	25	25	25	25	25	25	25	25
DASSS	Pearson Correlation	.066	.277	.527**	.659**	.721**	.606**	1	.316	-.210

	Sig. (2-tailed)	.754	.180	.007	.000	.000	.001		.124	.314
	N	25	25	25	25	25	25	25	25	25
NEOO	Pearson Correlation	-.018	-.059	.103	.244	.286	.303	.316	1	.054
	Sig. (2-tailed)	.931	.780	.625	.240	.166	.141	.124		.799
	N	25	25	25	25	25	25	25	25	25
NEOC	Pearson Correlation	-.362	-.378	-.483*	-.370	-.156	-.359	-.210	.054	1
	Sig. (2-tailed)	.075	.063	.014	.069	.456	.078	.314	.799	
	N	25	25	25	25	25	25	25	25	25
NEOE	Pearson Correlation	-.159	-.351	-.518**	-.231	-.410*	-.272	-.403*	-.145	.456*
	Sig. (2-tailed)	.447	.086	.008	.267	.042	.188	.046	.488	.022
	N	25	25	25	25	25	25	25	25	25
NEOA	Pearson Correlation	-.235	-.117	-.215	-.090	-.014	-.127	-.216	.144	.475*
	Sig. (2-tailed)	.257	.578	.301	.668	.946	.547	.300	.491	.016
	N	25	25	25	25	25	25	25	25	25
NEON	Pearson Correlation	.176	.227	.669**	.675**	.481*	.599**	.690**	.218	-.519**
	Sig. (2-tailed)	.399	.276	.000	.000	.015	.002	.000	.295	.008
	N	25	25	25	25	25	25	25	25	25
RUMB	Pearson Correlation	-.243	.069	.452*	.539**	.613**	.408*	.573**	.223	-.020
	Sig. (2-tailed)	.253	.749	.026	.007	.001	.048	.003	.294	.927
	N	24	24	24	24	24	24	24	24	24
RUMD	Pearson Correlation	-.137	-.010	.590**	.702**	.427*	.490*	.490*	.308	-.225
	Sig. (2-tailed)	.523	.962	.002	.000	.037	.015	.015	.144	.291
	N	24	24	24	24	24	24	24	24	24
RUMR	Pearson Correlation	-.254	-.051	.335	.383	.566**	.178	.329	.254	-.002
	Sig. (2-tailed)	.231	.812	.109	.065	.004	.404	.117	.231	.991

	N	24	24	24	24	24	24	24	24	24
COPEP	Pearson Correlation	.080	.163	.375	.252	.262	.275	.251	-.040	-.195
	Sig. (2-tailed)	.705	.435	.064	.224	.205	.183	.226	.851	.351
	N	25	25	25	25	25	25	25	25	25
COPEE	Pearson Correlation	.152	.260	.242	.522**	.313	.487*	.398*	.157	-.214
	Sig. (2-tailed)	.468	.209	.243	.007	.128	.014	.049	.453	.305
	N	25	25	25	25	25	25	25	25	25
WORRY	Pearson Correlation	-.106	-.010	.392	.557**	.184	.364	.304	-.204	-.206
	Sig. (2-tailed)	.615	.962	.052	.004	.378	.073	.139	.329	.322
	N	25	25	25	25	25	25	25	25	25
Zscore(DASSD)	Pearson Correlation	-.121	.154	.149	.665**	.794**	.478*	.660**	.459*	-.120
	Sig. (2-tailed)	.563	.462	.477	.000	.000	.016	.000	.021	.569
	N	25	25	25	25	25	25	25	25	25

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

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

Correlations

		NEOE	NEOA	NEON	RUMB	RUMD	RUMR	COPEP	COPEE
PSQI	Pearson Correlation	-.159	-.235	.176	-.243	-.137	-.254	.080	.152
	Sig. (2-tailed)	.447	.257	.399	.253	.523	.231	.705	.468
	N	25	25	25	24	24	24	25	25
ISI	Pearson Correlation	-.351	-.117	.227	.069	-.010	-.051	.163	.260
	Sig. (2-tailed)	.086	.578	.276	.749	.962	.812	.435	.209

	N	25	25	25	24	24	24	25	25
FIRST	Pearson Correlation	-.518**	-.215	.669**	.452*	.590**	.335	.375	.242
	Sig. (2-tailed)	.008	.301	.000	.026	.002	.109	.064	.243
	N	25	25	25	24	24	24	25	25
PSS	Pearson Correlation	-.231	-.090	.675**	.539**	.702**	.383	.252	.522**
	Sig. (2-tailed)	.267	.668	.000	.007	.000	.065	.224	.007
	N	25	25	25	24	24	24	25	25
DASSD	Pearson Correlation	-.410*	-.014	.481*	.613**	.427*	.566**	.262	.313
	Sig. (2-tailed)	.042	.946	.015	.001	.037	.004	.205	.128
	N	25	25	25	24	24	24	25	25
DASSA	Pearson Correlation	-.272	-.127	.599**	.408*	.490*	.178	.275	.487*
	Sig. (2-tailed)	.188	.547	.002	.048	.015	.404	.183	.014
	N	25	25	25	24	24	24	25	25
DASSS	Pearson Correlation	-.403*	-.216	.690**	.573**	.490*	.329	.251	.398*
	Sig. (2-tailed)	.046	.300	.000	.003	.015	.117	.226	.049
	N	25	25	25	24	24	24	25	25
NEOO	Pearson Correlation	-.145	.144	.218	.223	.308	.254	-.040	.157
	Sig. (2-tailed)	.488	.491	.295	.294	.144	.231	.851	.453
	N	25	25	25	24	24	24	25	25

NEOC	Pearson Correlation	.456*	.475*	-.519**	-.020	-.225	-.002	-.195	-.214
	Sig. (2-tailed)	.022	.016	.008	.927	.291	.991	.351	.305
	N	25	25	25	24	24	24	25	25
NEOE	Pearson Correlation	1	.290	-.572**	-.478*	-.241	-.443*	-.291	-.225
	Sig. (2-tailed)		.159	.003	.018	.256	.030	.159	.279
	N	25	25	25	24	24	24	25	25
NEOA	Pearson Correlation	.290	1	-.249	.021	-.028	-.096	-.350	-.334
	Sig. (2-tailed)	.159		.229	.924	.895	.657	.086	.102
	N	25	25	25	24	24	24	25	25
NEON	Pearson Correlation	-.572**	-.249	1	.584**	.639**	.339	.323	.355
	Sig. (2-tailed)	.003	.229		.003	.001	.105	.116	.081
	N	25	25	25	24	24	24	25	25
RUMB	Pearson Correlation	-.478*	.021	.584**	1	.702**	.762**	.168	.179
	Sig. (2-tailed)	.018	.924	.003		.000	.000	.432	.403
	N	24	24	24	24	24	24	24	24
RUMD	Pearson Correlation	-.241	-.028	.639**	.702**	1	.680**	.371	.382
	Sig. (2-tailed)	.256	.895	.001	.000		.000	.074	.065
	N	24	24	24	24	24	24	24	24
RUMR	Pearson Correlation	-.443*	-.096	.339	.762**	.680**	1	.271	.184

	Sig. (2-tailed)	.030	.657	.105	.000	.000		.200	.390
	N	24	24	24	24	24	24	24	24
COPEP	Pearson Correlation	-.291	-.350	.323	.168	.371	.271	1	.723**
	Sig. (2-tailed)	.159	.086	.116	.432	.074	.200		.000
	N	25	25	25	24	24	24	25	25
COPEE	Pearson Correlation	-.225	-.334	.355	.179	.382	.184	.723**	1
	Sig. (2-tailed)	.279	.102	.081	.403	.065	.390	.000	
	N	25	25	25	24	24	24	25	25
WORRY	Pearson Correlation	-.282	.083	.638**	.599**	.584**	.302	.108	.209
	Sig. (2-tailed)	.172	.693	.001	.002	.003	.152	.608	.317
	N	25	25	25	24	24	24	25	25
Zscore(DASSD)	Pearson Correlation	-.214	.016	.463*	.596**	.518**	.524**	.198	.461*
	Sig. (2-tailed)	.304	.938	.020	.002	.009	.009	.342	.020
	N	25	25	25	24	24	24	25	25

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

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

Correlations

		WORRY	Zscore(DASSD)
PSQI	Pearson Correlation	-.106	-.121
	Sig. (2-tailed)	.615	.563
	N	25	25

ISI	Pearson Correlation	-.010	.154
	Sig. (2-tailed)	.962	.462
	N	25	25
FIRST	Pearson Correlation	.392	.149
	Sig. (2-tailed)	.052	.477
	N	25	25
PSS	Pearson Correlation	.557**	.665**
	Sig. (2-tailed)	.004	.000
	N	25	25
DASSD	Pearson Correlation	.184	.794**
	Sig. (2-tailed)	.378	.000
	N	25	25
DASSA	Pearson Correlation	.364	.478*
	Sig. (2-tailed)	.073	.016
	N	25	25
DASSS	Pearson Correlation	.304	.660**
	Sig. (2-tailed)	.139	.000
	N	25	25
NEOO	Pearson Correlation	-.204	.459*
	Sig. (2-tailed)	.329	.021
	N	25	25
NEOC	Pearson Correlation	-.206	-.120
	Sig. (2-tailed)	.322	.569
	N	25	25
NEOE	Pearson Correlation	-.282	-.214

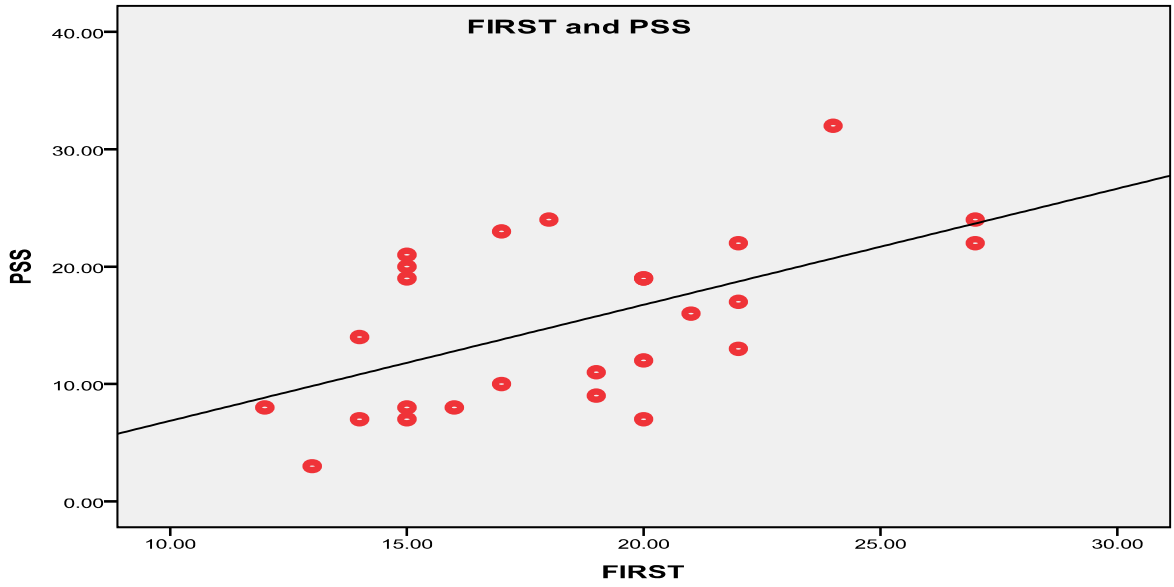
	Sig. (2-tailed)	.172	.304
	N	25	25
NEOA	Pearson Correlation	.083	.016
	Sig. (2-tailed)	.693	.938
	N	25	25
NEON	Pearson Correlation	.638**	.463*
	Sig. (2-tailed)	.001	.020
	N	25	25
RUMB	Pearson Correlation	.599**	.596**
	Sig. (2-tailed)	.002	.002
	N	24	24
RUMD	Pearson Correlation	.584**	.518**
	Sig. (2-tailed)	.003	.009
	N	24	24
RUMR	Pearson Correlation	.302	.524**
	Sig. (2-tailed)	.152	.009
	N	24	24
COPEP	Pearson Correlation	.108	.198
	Sig. (2-tailed)	.608	.342
	N	25	25
COPEE	Pearson Correlation	.209	.461*
	Sig. (2-tailed)	.317	.020
	N	25	25
WORRY	Pearson Correlation	1	.257
	Sig. (2-tailed)		.214

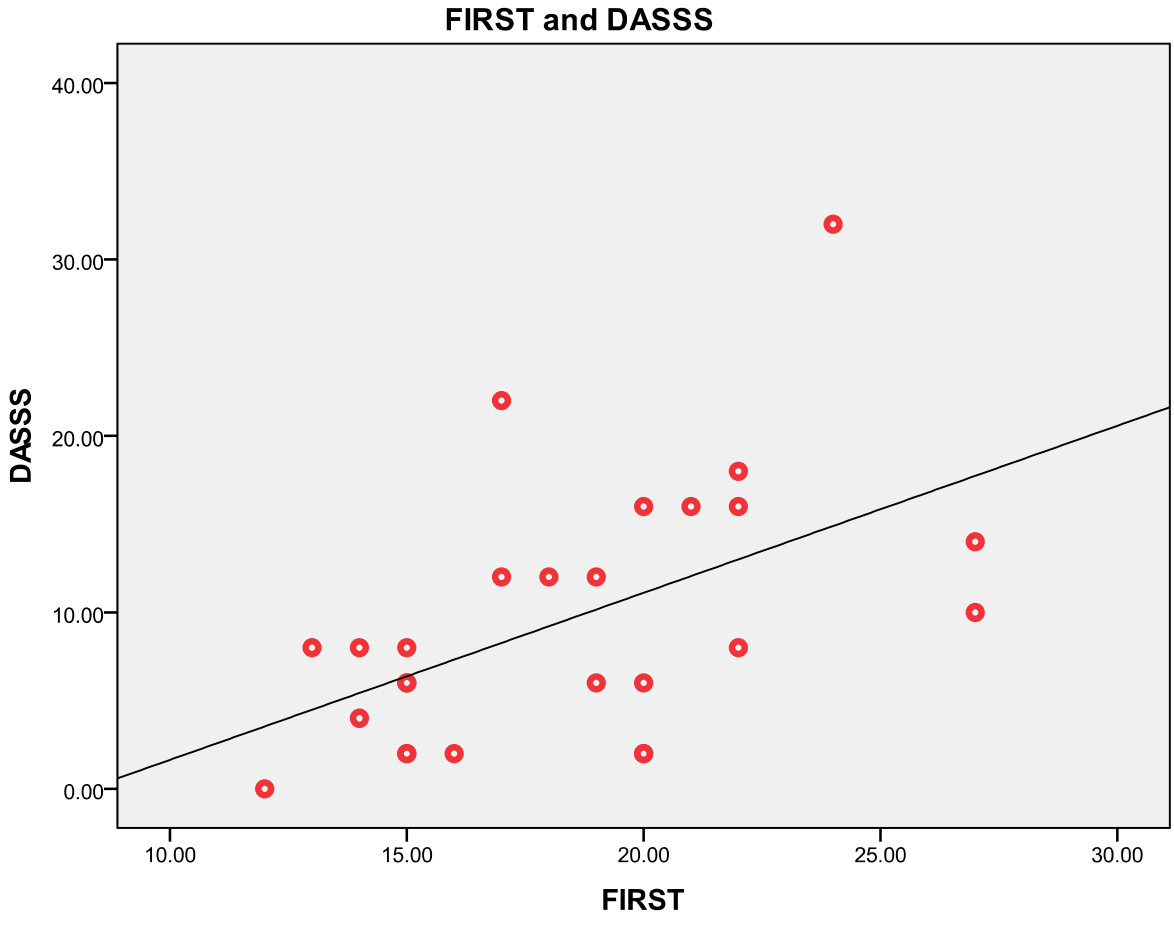
	N	25	25
Zscore(DASSD)	Pearson Correlation	.257	1
	Sig. (2-tailed)	.214	
	N	25	25

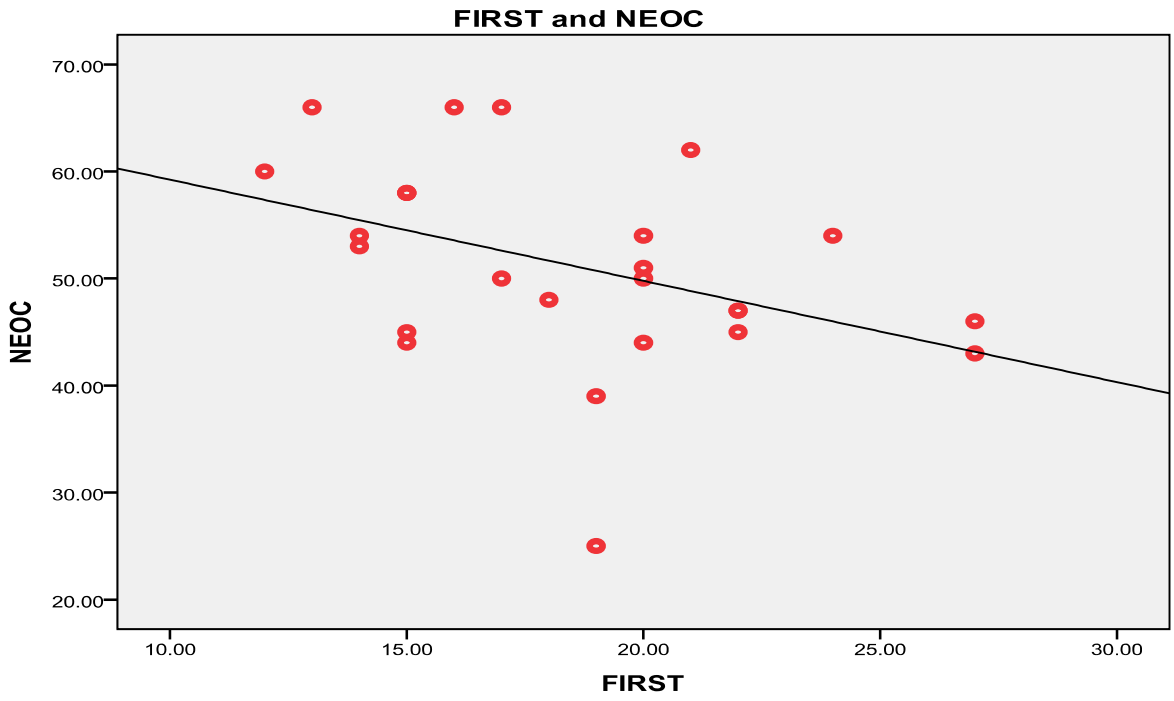
**. Correlation is significant at the 0.01 level (2-tailed).

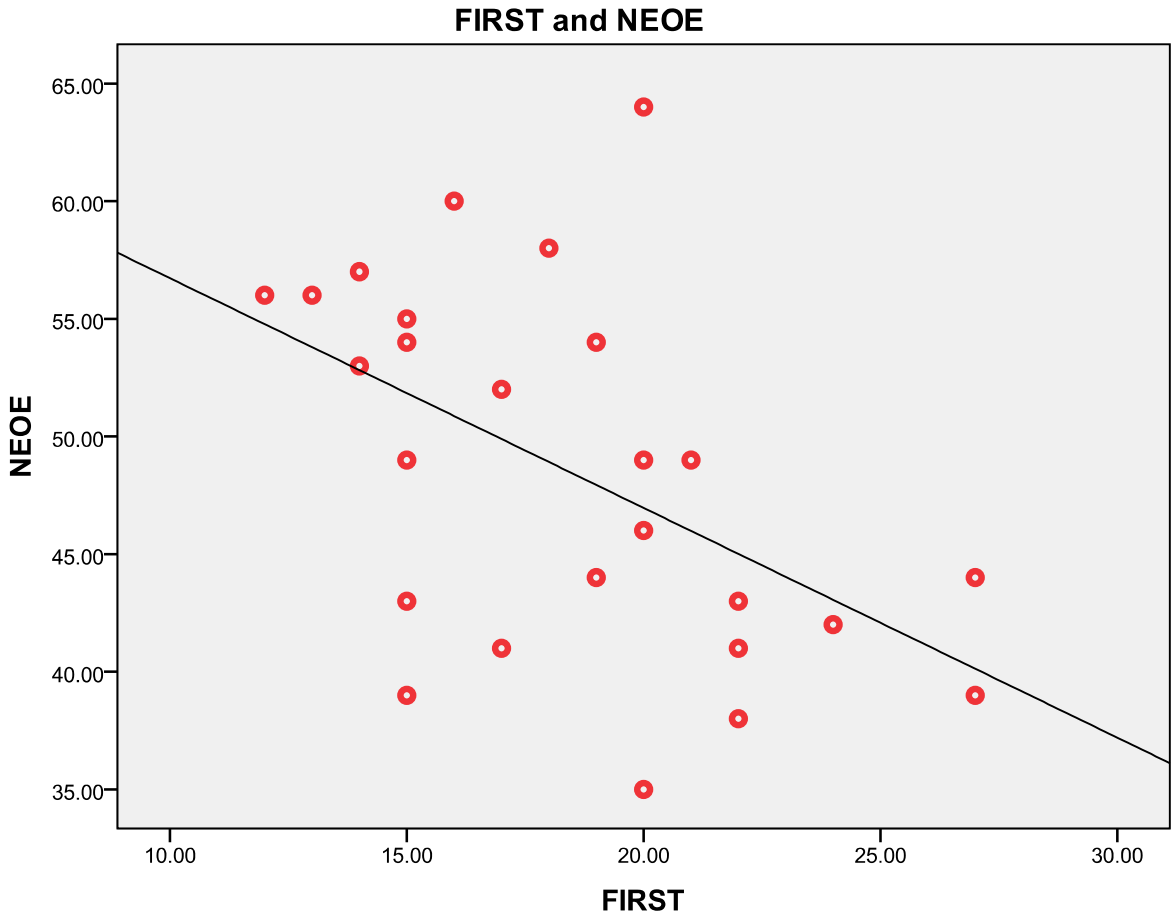
*. Correlation is significant at the 0.05 level (2-tailed).

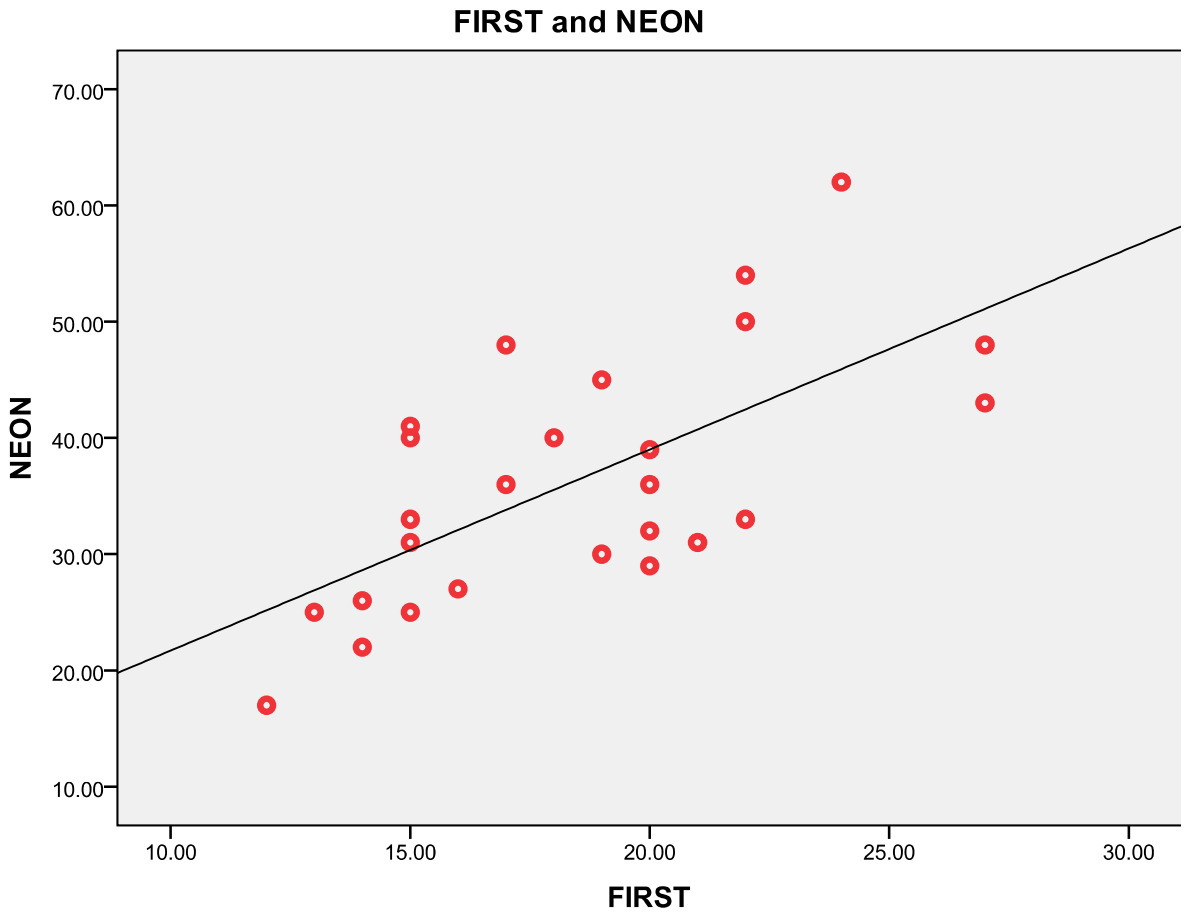
XXIX. Scatterplot Showing Relationship Between FIRST and other Psychological Variables in the Whole Sample

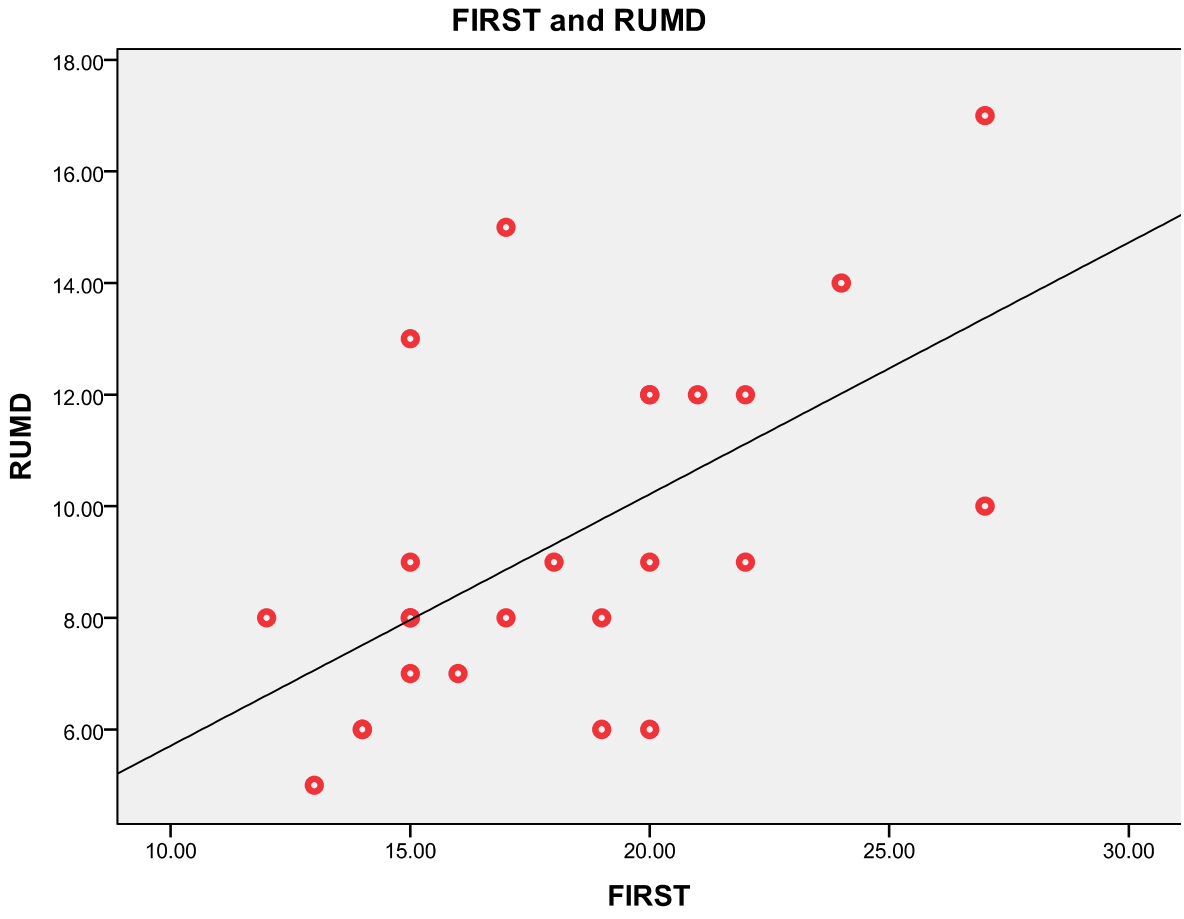


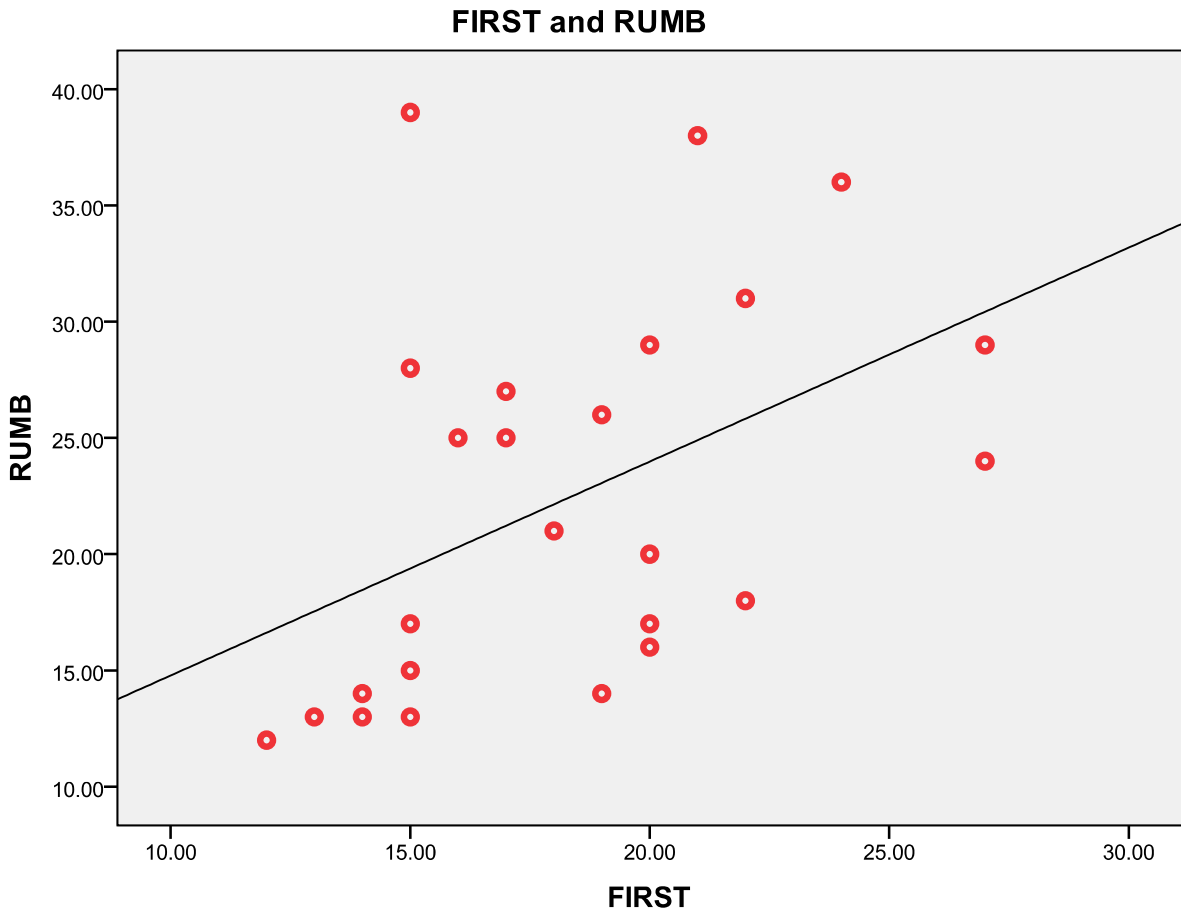



FIRST and NEOC
NEOC
70.00
60.00
50.00
40.00
30.00
20.00
10.00
15.00
20.00
25.00
30.00
FIRST


FIRST and NEOE
NEOE
65.00
60.00
55.00
50.00
45.00
40.00
35.00
10.00
15.00
20.00
25.00
30.00
FIRST


FIRST and NEON
NEON
70.00
60.00
50.00
40.00
30.00
20.00
10.00
10.00
15.00
20.00
25.00
30.00
FIRST


FIRST and RUMD
RUMD
18.00
16.00
14.00
12.00
10.00
8.00
6.00
10.00
15.00
20.00
25.00
30.00
FIRST


FIRST and RUMB
RUMB
40.00
35.00
30.00
25.00
20.00
15.00
10.00
10.00
15.00
20.00
25.00
30.00
FIRST

XXX. Whole Brain Report (Chapter 6)

```
analyse/Project0071/group/spmT_0002.img,1
Type: T
df: 22
Threshold
-- p value = 0.001
-- intensity = 3.505
-- cluster size = 20
Number of clusters found: 16
----------------------
Cluster 1
Number of voxels: 4237
Peak MNI coordinate: 40  24   2
Peak MNI coordinate region:  // Right Cerebrum // Frontal
Lobe // Inferior Frontal Gyrus // Gray Matter // brodmann
area 47 // Insula_R (aal)
Peak intensity: 6.2282
# voxels        structure
 4237    --TOTAL # VOXELS--
 3495    Sub-lobar
 2442    Gray Matter
 2194    Right Cerebrum
 1565    Left Cerebrum
 1338    White Matter
 1004    Lentiform Nucleus
  986   Extra-Nuclear
  981   Thalamus
  850   Putamen
  659   Thalamus_R (aal)
  556   Putamen_R (aal)
  477   Midbrain
  463   Putamen_L (aal)
  440   Thalamus_L (aal)
  340   Insula
  278   Insula_R (aal)
  265   Right Brainstem
  238   Frontal Lobe
  210   Left Brainstem
  195   Inferior Frontal Gyrus
  190   Insula_L (aal)
  186   Caudate_R (aal)
  179   Ventral Lateral Nucleus
  166   Medial Dorsal Nucleus
  117   brodmann area 13
  115   Pulvinar
  111   Caudate_L (aal)
  107   Caudate
   92   Lateral Globus Pallidus
   88   Pallidum_R (aal)
   76   Caudate Body
```

```
   63   Pallidum_L (aal)
   61   Medial Globus Pallidus
   61   Ventral Anterior Nucleus
   52   Claustrum
   49   Red Nucleus
   48   brodmann area 47
   43   Ventral Posterior Lateral Nucleus
   39   Sub-Gyral
   39   Frontal_Inf_Tri_L (aal)
   35   Lateral Posterior Nucleus
   32   Subthalamic Nucleus
   31   Caudate Head
   25   Mammillary Body
   24   Frontal_Inf_Oper_L (aal)
   23   Frontal_Inf_Tri_R (aal)
   20   Lateral Dorsal Nucleus
   20   Ventral Posterior Medial Nucleus
   19   Cerebro-Spinal Fluid
   17   brodmann area 45
   14   Lateral Ventricle
   13   Rolandic_Oper_L (aal)
   11   Frontal-Temporal Space
   10   Hippocampus_R (aal)
   10   Superior Temporal Gyrus
   10   Temporal Lobe
   10   Frontal_Inf_Oper_R (aal)
   10   Substania Nigra
    9   Midline Nucleus
    7   Subcallosal Gyrus
    6   brodmann area 22
    5   Lateral Geniculum Body
    5   Third Ventricle
    4   Frontal_Inf_Orb_L (aal)
    4   Limbic Lobe
    3   brodmann area 44
    3   Precentral Gyrus
    3   Inter-Hemispheric
    3   Olfactory_R (aal)
    2   Parahippocampa Gyrus
    2   brodmann area 27
    2   Temporal_Pole_Sup_L (aal)
    1   Frontal_Inf_Orb_R (aal)
    1   Middle Frontal Gyrus
----------------------
Cluster 2
Number of voxels: 58
Peak MNI coordinate: 0 -48  -4
Peak MNI coordinate region:  // Left Cerebellum // Cerebellum
Anterior Lobe // Culmen // undefined // undefined //
Vermis_4_5 (aal)
Peak intensity: 4.378
# voxels        structure
   58   --TOTAL # VOXELS--
   58   Culmen
```

```
   58   Cerebellum Anterior Lobe
   53   Left Cerebellum
   44   Vermis_4_5 (aal)
   14   Cerebelum_4_5_L (aal)
    5   Right Cerebellum
----------------------
Cluster 3
Number of voxels: 21
Peak MNI coordinate: 14 -70  -4
Peak MNI coordinate region:  // Right Cerebrum // Occipital
Lobe // Lingual Gyrus // Gray Matter // brodmann area 18 //
Lingual_R (aal)
Peak intensity: -4.08
# voxels        structure
   21   --TOTAL # VOXELS--
   21   Lingual Gyrus
   21   Lingual_R (aal)
   21   Occipital Lobe
   21   Right Cerebrum
   13   Gray Matter
   10   brodmann area 18
    8   White Matter
----------------------
Cluster 4
Number of voxels: 41
Peak MNI coordinate: -20 -30  -2
Peak MNI coordinate region:  // Left Cerebrum // Sub-lobar //
Thalamus // Gray Matter // undefined // undefined
Peak intensity: 4.7261
# voxels        structure
   41   --TOTAL # VOXELS--
   34   Left Cerebrum
   31   Sub-lobar
   24   Gray Matter
   19   Thalamus
   11   White Matter
    9   Extra-Nuclear
    9   Thalamus_L (aal)
    8   Hippocampus_L (aal)
    5   Midbrain
    5   Left Brainstem
    3   Parahippocampa Gyrus
    3   Limbic Lobe
    3   Lateral Geniculum Body
    2   brodmann area 27
    1   Pulvinar
----------------------
Cluster 5
Number of voxels: 24
Peak MNI coordinate: -30 -54  -2
Peak MNI coordinate region:  // Left Cerebrum // Temporal
Lobe // Sub-Gyral // White Matter // undefined // undefined
Peak intensity: -4.5078
# voxels        structure
```

```
   24   --TOTAL # VOXELS--
   24   Sub-Gyral
   24   White Matter
   24   Left Cerebrum
   19   Lingual_L (aal)
   15   Occipital Lobe
    9   Temporal Lobe
    1   Fusiform_L (aal)
----------------------
Cluster 6
Number of voxels: 451
Peak MNI coordinate: 58 -10   4
Peak MNI coordinate region:  // Right Cerebrum // Temporal
Lobe // Superior Temporal Gyrus // White Matter // undefined
// Temporal_Sup_R (aal)
Peak intensity: -7.3446
# voxels        structure
  451   --TOTAL # VOXELS--
  451   Right Cerebrum
  326   Temporal Lobe
  289   Superior Temporal Gyrus
  251   Temporal_Sup_R (aal)
  241   White Matter
  174   Gray Matter
  126   Heschl_R (aal)
  116   Sub-lobar
  113   Insula
   87   brodmann area 22
   65   Insula_R (aal)
   62   brodmann area 13
   39   Transverse Temporal Gyrus
   20   brodmann area 41
   10   Precentral Gyrus
    9   Frontal Lobe
    5   Rolandic_Oper_R (aal)
    2   brodmann area 6
----------------------
Cluster 7
Number of voxels: 471
Peak MNI coordinate: -52 -16   8
Peak MNI coordinate region:  // Left Cerebrum // Temporal
Lobe // Superior Temporal Gyrus // White Matter // undefined
// Heschl_L (aal)
Peak intensity: -7.2773
# voxels        structure
  471   --TOTAL # VOXELS--
  471   Left Cerebrum
  260   Temporal Lobe
  231   White Matter
  222   Gray Matter
  200   Sub-lobar
  182   Insula
  180   Superior Temporal Gyrus
  176   Temporal_Sup_L (aal)
```

```
  150   Heschl_L (aal)
  117   brodmann area 13
   75   Transverse Temporal Gyrus
   66   Insula_L (aal)
   50   brodmann area 41
   45   Rolandic_Oper_L (aal)
   44   brodmann area 22
   22   Extra-Nuclear
   11   Precentral Gyrus
   11   Frontal Lobe
    5   brodmann area 43
    1   Sub-Gyral
    1   brodmann area 42
----------------------
Cluster 8
Number of voxels: 71
Peak MNI coordinate: -36   0   4
Peak MNI coordinate region:  // Left Cerebrum // Sub-lobar //
Claustrum // Gray Matter // undefined // undefined
Peak intensity: 4.8635
# voxels        structure
   71   --TOTAL # VOXELS--
   71   Left Cerebrum
   71   Sub-lobar
   48   White Matter
   48   Insula
   32   Insula_L (aal)
   23   Gray Matter
   20   Rolandic_Oper_L (aal)
   17   brodmann area 13
   17   Extra-Nuclear
    6   Claustrum
    3   Putamen_L (aal)
----------------------
Cluster 9
Number of voxels: 33
Peak MNI coordinate: 54  12   6
Peak MNI coordinate region:  // Right Cerebrum // Frontal-
Temporal Space // undefined // undefined // undefined //
Frontal_Inf_Oper_R (aal)
Peak intensity: 4.6859
# voxels        structure
   33   --TOTAL # VOXELS--
   33   Right Cerebrum
   33   Frontal_Inf_Oper_R (aal)
   26   Frontal Lobe
   17   Precentral Gyrus
   15   brodmann area 44
   15   Gray Matter
   10   White Matter
    8   Inferior Frontal Gyrus
    7   Frontal-Temporal Space
----------------------
Cluster 10
```

```
Number of voxels: 20
Peak MNI coordinate: -4  48  14
Peak MNI coordinate region:  // Left Cerebrum // Frontal Lobe
// Medial Frontal Gyrus // Gray Matter // brodmann area 10 //
Cingulum_Ant_L (aal)
Peak intensity: -4.7151
# voxels        structure
   20   --TOTAL # VOXELS--
   20   Left Cerebrum
   17   Frontal Lobe
   17   Medial Frontal Gyrus
   13   Cingulum_Ant_L (aal)
   11   Gray Matter
    9   White Matter
    8   brodmann area 10
    7   Frontal_Sup_Medial_L (aal)
    3   Anterior Cingulate
    3   brodmann area 32
    3   Limbic Lobe
----------------------
Cluster 11
Number of voxels: 5942
Peak MNI coordinate: 46 -12  48
Peak MNI coordinate region:  // Right Cerebrum // Frontal
Lobe // Precentral Gyrus // White Matter // undefined //
Precentral_R (aal)
Peak intensity: 6.7446
# voxels        structure
 5942    --TOTAL # VOXELS--
 4163    Right Cerebrum
 4117    Frontal Lobe
 2867    White Matter
 2561    Gray Matter
 1749    Left Cerebrum
 1363    Precentral Gyrus
 1291    Parietal Lobe
 1224    brodmann area 6
 1165    Precentral_R (aal)
  925   Middle Frontal Gyrus
  920   Postcentral_R (aal)
  807   Postcentral Gyrus
  725   Precentral_L (aal)
  670   Medial Frontal Gyrus
  653   Sub-Gyral
  592   Cingulate Gyrus
  517   Supp_Motor_Area_L (aal)
  504   Limbic Lobe
  497   Supp_Motor_Area_R (aal)
  348   Inferior Frontal Gyrus
  331   Frontal_Sup_R (aal)
  258   brodmann area 32
  255   Cingulum_Mid_R (aal)
  254   Inferior Parietal Lobule
  249   brodmann area 4
```

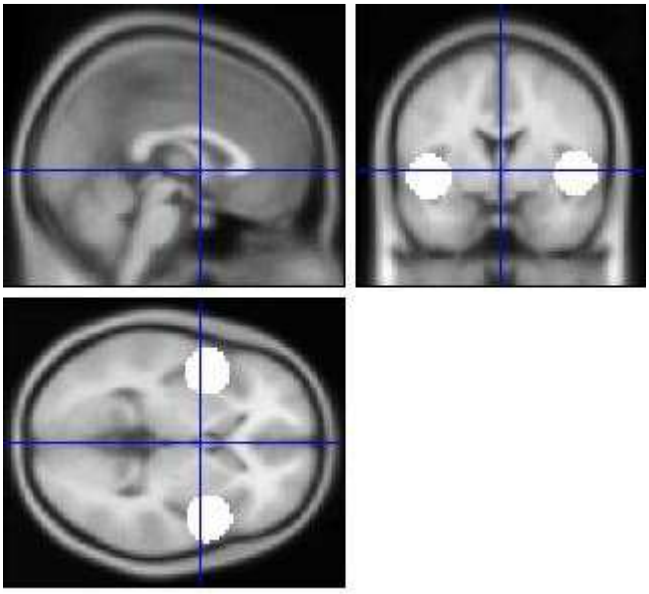
```
  218   Superior Frontal Gyrus
  193   Parietal_Inf_R (aal)
  193   brodmann area 40
  192   brodmann area 3
  154   Frontal_Mid_R (aal)
  146   Parietal_Sup_R (aal)
  138   SupraMarginal_R (aal)
  133   Frontal_Sup_L (aal)
  121   brodmann area 9
  116   Frontal_Mid_L (aal)
  109   brodmann area 24
   99   brodmann area 2
   96   Cingulum_Mid_L (aal)
   92   Frontal_Inf_Oper_R (aal)
   56   Postcentral_L (aal)
   52   brodmann area 7
   49   Superior Parietal Lobule
   28   Inter-Hemispheric
   27   Precuneus
   23   Frontal_Inf_Oper_L (aal)
   23   brodmann area 5
   20   brodmann area 8
   12   Frontal_Sup_Medial_L (aal)
    8   brodmann area 1
    7   brodmann area 45
    6   Anterior Cingulate
    6   brodmann area 44
    6   Cingulum_Ant_R (aal)
    1   Frontal_Inf_Tri_R (aal)
    1   Rolandic_Oper_L (aal)
    1   Paracentral_Lobule_L (aal)
    1   Precuneus_R (aal)
----------------------
Cluster 12
Number of voxels: 1349
Peak MNI coordinate: -50 -26  44
Peak MNI coordinate region:  // Left Cerebrum // Parietal
Lobe // Postcentral Gyrus // White Matter // undefined //
Parietal_Inf_L (aal)
Peak intensity: 6.1829
# voxels        structure
 1349    --TOTAL # VOXELS--
 1348    Left Cerebrum
 1334    Parietal Lobe
  830   White Matter
  513   Parietal_Inf_L (aal)
  467   Gray Matter
  426   Postcentral Gyrus
  355   Parietal_Sup_L (aal)
  281   Postcentral_L (aal)
  257   Inferior Parietal Lobule
  240   Sub-Gyral
  227   Precuneus
  204   brodmann area 7
```

```
  185   Superior Parietal Lobule
  119   brodmann area 2
  112   brodmann area 40
   62   SupraMarginal_L (aal)
   33   Precuneus_L (aal)
   27   Occipital_Mid_L (aal)
   20   brodmann area 3
   14   Frontal Lobe
   10   brodmann area 4
    7   Precentral Gyrus
    6   Supramarginal Gyrus
    2   Rolandic_Oper_L (aal)
    2   Occipital_Sup_L (aal)
    1   brodmann area 1
    1   brodmann area 5
----------------------
Cluster 13
Number of voxels: 56
Peak MNI coordinate: -2 -88  26
Peak MNI coordinate region:  // Left Cerebrum // Occipital
Lobe // Cuneus // Gray Matter // brodmann area 19 // Cuneus_L
(aal)
Peak intensity: -4.4678
# voxels        structure
   56   --TOTAL # VOXELS--
   55   Cuneus
   55   Occipital Lobe
   45   Cuneus_L (aal)
   40   Left Cerebrum
   32   Gray Matter
   18   brodmann area 19
   18   White Matter
   15   Right Cerebrum
   13   brodmann area 18
   11   Cuneus_R (aal)
    1   brodmann area 7
    1   Inter-Hemispheric
----------------------
Cluster 14
Number of voxels: 140
Peak MNI coordinate: 38  34  22
Peak MNI coordinate region:  // Right Cerebrum // Frontal
Lobe // Middle Frontal Gyrus // White Matter // undefined //
Frontal_Mid_R (aal)
Peak intensity: 5.7978
# voxels        structure
  140   --TOTAL # VOXELS--
  140   Frontal Lobe
  140   Right Cerebrum
  137   White Matter
  100   Middle Frontal Gyrus
   89   Frontal_Mid_R (aal)
   51   Frontal_Inf_Tri_R (aal)
   40   Sub-Gyral
```

```
    3   brodmann area 46
    3   Gray Matter
----------------------
Cluster 15
Number of voxels: 269
Peak MNI coordinate: -8 -42  34
Peak MNI coordinate region:  // Left Cerebrum // Limbic Lobe
// Cingulate Gyrus // White Matter // undefined //
Cingulum_Mid_L (aal)
Peak intensity: -5.499
# voxels        structure
  269   --TOTAL # VOXELS--
  213   Limbic Lobe
  209   Cingulate Gyrus
  145   Left Cerebrum
  144   Cingulum_Mid_L (aal)
  125   Gray Matter
  117   brodmann area 31
  110   Right Cerebrum
   98   White Matter
   66   Cingulum_Mid_R (aal)
   44   Precuneus_R (aal)
   30   Precuneus
   27   Parietal Lobe
   15   Frontal Lobe
   14   Inter-Hemispheric
   13   Cingulum_Post_L (aal)
   11   Paracentral Lobule
    8   brodmann area 7
    5   Sub-Gyral
    2   Precuneus_L (aal)
----------------------
Cluster 16
Number of voxels: 95
Peak MNI coordinate: 28 -60  48
Peak MNI coordinate region:  // Right Cerebrum // Parietal
Lobe // Superior Parietal Lobule // Gray Matter // brodmann
area 7 // Angular_R (aal)
Peak intensity: 4.3743
# voxels        structure
   95   --TOTAL # VOXELS--
   95   Parietal Lobe
   95   Right Cerebrum
   63   White Matter
   47   Angular_R (aal)
   38   Superior Parietal Lobule
   34   Sub-Gyral
   32   Gray Matter
   30   brodmann area 7
   20   Precuneus
   15   Parietal_Sup_R (aal)
    7   Occipital_Sup_R (aal)
    7   Occipital_Mid_R (aal)
```

```
3   Inferior Parietal Lobule
2   brodmann area 39
```

XXXI. **Insula ROI Definition(chapter 6)**



Centre co-ordinate of left insula: -45, 5, -4; Diameter of 10mm

“ “ “ “ Right Insula: 47, 5, -1; Diameter of 10mm

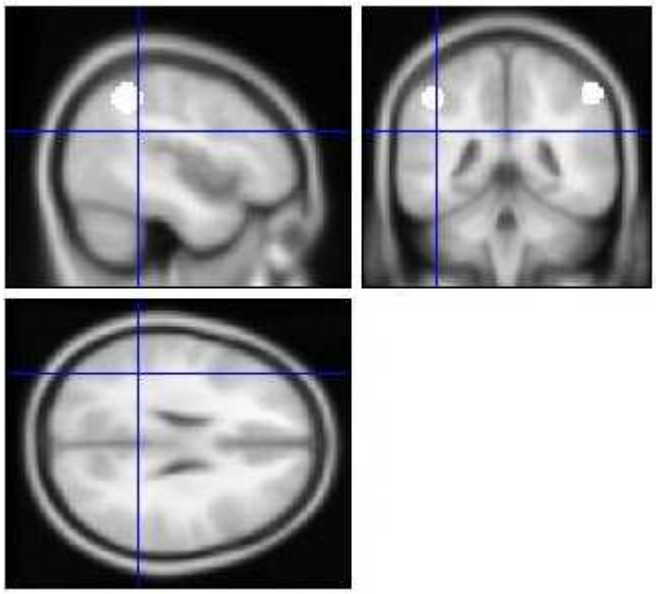
XXXII. Between Group Whole Brain Report (Chapter 6)

```
Threshold
-- p value = 0.001
-- intensity = 3.505
-- cluster size = 5
Number of clusters found: 5
----------------------
Cluster 1
Number of voxels: 7
Peak MNI coordinate: -50 -48  44
Peak MNI coordinate region:  // Left Cerebrum // Parietal Lobe //
Inferior Parietal Lobule // Gray Matter // brodmann area 40 //
Parietal_Inf_L (aal)
Peak intensity: -3.7651
# voxels        structure
    7   --TOTAL # VOXELS--
    7   Inferior Parietal Lobule
    7   Left Cerebrum
    7   Parietal Lobe
    7   Parietal_Inf_L (aal)
    4   White Matter
    3   brodmann area 40
    3   Gray Matter
----------------------
Cluster 2
Number of voxels: 22
Peak MNI coordinate: 52 -46  48
Peak MNI coordinate region:  // Right Cerebrum // Parietal Lobe //
Inferior Parietal Lobule // White Matter // undefined // Parietal_Inf_R
(aal)
Peak intensity: -4.9938
# voxels        structure
   22   --TOTAL # VOXELS--
   22   Inferior Parietal Lobule
   22   Parietal Lobe
   22   Parietal_Inf_R (aal)
   22   Right Cerebrum
   14   Gray Matter
   14   brodmann area 40
    8   White Matter
----------------------
Cluster 3
```

```
Number of voxels: 6
Peak MNI coordinate: -42 -58  50
Peak MNI coordinate region:  // Left Cerebrum // Parietal Lobe //
Inferior Parietal Lobule // Gray Matter // brodmann area 40 //
Parietal_Inf_L (aal)
Peak intensity: -3.6952
# voxels        structure
    6   --TOTAL # VOXELS--
    6   Inferior Parietal Lobule
    6   Left Cerebrum
    6   Parietal Lobe
    6   Parietal_Inf_L (aal)
    4   Gray Matter
    4   brodmann area 40
    1   White Matter
----------------------
Cluster 4
Number of voxels: 24
Peak MNI coordinate: -28 -36  52
Peak MNI coordinate region:  // Left Cerebrum // Parietal Lobe //
Postcentral Gyrus // Gray Matter // brodmann area 3 // Postcentral_L
(aal)
Peak intensity: 5.1318
# voxels        structure
   24   --TOTAL # VOXELS--
   24   Left Cerebrum
   24   Parietal Lobe
   24   Postcentral Gyrus
   24   Postcentral_L (aal)
   12   Gray Matter
   12   White Matter
   11   brodmann area 3
    1   brodmann area 40
----------------------
Cluster 5
Number of voxels: 5
Peak MNI coordinate: -6 -34  68
Peak MNI coordinate region:  // Left Cerebrum // Frontal Lobe //
Paracentral Lobule // Gray Matter // brodmann area 6 //
Paracentral_Lobule_L (aal)
Peak intensity: -3.8157
# voxels        structure
    5   --TOTAL # VOXELS--
```

```
5   Frontal Lobe
5   Left Cerebrum
5   Paracentral Lobule
5   Paracentral_Lobule_L (aal)
3   White Matter
2   brodmann area 6
2   Gray Matter
```

XXXIII. **Parietal ROI (Chapter 6)**



Centre co-ordinate of Left inferior parietal lobule: -46, -49, 47; Diameter: 10mm

Centre co-ordinate of Right inferior parietal lobule: 53, -49, 50; Diameter: 10mm

XXXIV. Whole group correlation matrix including Beta values (Chapter 6)

		PSQI	ISI	FIRST	PSS	DASSD	DASSA	DASSS	NEOO	NEOC	NEOE
PSQI	Pearson Correlation	1	.739**	.157	.125	-.089	.003	.004	.069	-.551**	-.060
	Sig. (2-tailed)		.000	.444	.543	.666	.989	.983	.736	.004	.770
	N	26	26	26	26	26	26	26	26	26	26
ISI	Pearson Correlation	.739**	1	.232	.219	.265	.244	.203	.021	-.532**	-.247
	Sig. (2-tailed)	.000		.254	.283	.190	.230	.320	.921	.005	.223
	N	26	26	26	26	26	26	26	26	26	26
FIRST	Pearson Correlation	.157	.232	1	.557**	.421*	.315	.521**	.106	-.412*	-.509**
	Sig. (2-tailed)	.444	.254		.003	.032	.117	.006	.606	.037	.008
	N	26	26	26	26	26	26	26	26	26	26
PSS	Pearson Correlation	.125	.219	.557**	1	.611**	.493*	.663**	.220	-.233	-.244
	Sig. (2-tailed)	.543	.283	.003		.001	.011	.000	.281	.253	.230
	N	26	26	26	26	26	26	26	26	26	26
DASSD	Pearson Correlation	-.089	.265	.421*	.611**	1	.286	.714**	.287	-.146	-.400*
	Sig. (2-tailed)	.666	.190	.032	.001		.157	.000	.155	.476	.043
	N	26	26	26	26	26	26	26	26	26	26
DASSA	Pearson Correlation	.003	.244	.315	.493*	.286	1	.611**	.264	-.185	-.291
	Sig. (2-tailed)	.989	.230	.117	.011	.157		.001	.192	.364	.150
	N	26	26	26	26	26	26	26	26	26	26

DASSS	Pearson Correlation	.004	.203	.521**	.663**	.714**	.611**	1	.293	-.114	-.411*
	Sig. (2-tailed)	.983	.320	.006	.000	.000	.001		.146	.581	.037
	N	26	26	26	26	26	26	26	26	26	26
NEOO	Pearson Correlation	.069	.021	.106	.220	.287	.264	.293	1	-.051	-.118
	Sig. (2-tailed)	.736	.921	.606	.281	.155	.192	.146		.805	.565
	N	26	26	26	26	26	26	26	26	26	26
NEOC	Pearson Correlation	-.551**	-.532**	-.412*	-.233	-.146	-.185	-.114	-.051	1	.287
	Sig. (2-tailed)	.004	.005	.037	.253	.476	.364	.581	.805		.155
	N	26	26	26	26	26	26	26	26	26	26
NEOE	Pearson Correlation	-.060	-.247	-.509**	-.244	-.400*	-.291	-.411*	-.118	.287	1
	Sig. (2-tailed)	.770	.223	.008	.230	.043	.150	.037	.565	.155	
	N	26	26	26	26	26	26	26	26	26	26
NEOA	Pearson Correlation	-.163	-.072	-.213	-.098	-.012	-.137	-.221	.154	.346	.297
	Sig. (2-tailed)	.425	.725	.297	.634	.954	.504	.277	.453	.083	.141
	N	26	26	26	26	26	26	26	26	26	26
NEON	Pearson Correlation	.087	.148	.660**	.679**	.473*	.606**	.694**	.194	-.352	-.579**
	Sig. (2-tailed)	.671	.469	.000	.000	.015	.001	.000	.342	.077	.002
	N	26	26	26	26	26	26	26	26	26	26
RUMB	Pearson Correlation	-.156	.104	.454*	.522**	.613**	.383	.559**	.234	-.069	-.459*
	Sig. (2-tailed)	.457	.622	.023	.007	.001	.059	.004	.260	.744	.021
	N	25	25	25	25	25	25	25	25	25	25

RUMD	Pearson Correlation	-.166	-.055	.584**	.705**	.422*	.497*	.495*	.287	-.127	-.251
	Sig. (2-tailed)	.427	.795	.002	.000	.036	.011	.012	.164	.546	.226
	N	25	25	25	25	25	25	25	25	25	25
RUMR	Pearson Correlation	-.296	-.120	.325	.394	.554**	.202	.338	.223	.089	-.455*
	Sig. (2-tailed)	.150	.569	.113	.051	.004	.334	.099	.284	.671	.022
	N	25	25	25	25	25	25	25	25	25	25
COPEP	Pearson Correlation	-.055	.039	.358	.271	.247	.305	.266	-.076	-.021	-.313
	Sig. (2-tailed)	.790	.851	.073	.180	.223	.129	.189	.711	.920	.119
	N	26	26	26	26	26	26	26	26	26	26
COPEE	Pearson Correlation	.121	.226	.242	.521**	.312	.482*	.397*	.152	-.165	-.225
	Sig. (2-tailed)	.555	.267	.234	.006	.121	.013	.045	.457	.419	.269
	N	26	26	26	26	26	26	26	26	26	26
WORRY	Pearson Correlation	-.160	-.069	.384	.564**	.178	.380	.314	-.221	-.089	-.296
	Sig. (2-tailed)	.434	.736	.052	.003	.384	.056	.119	.277	.666	.142
	N	26	26	26	26	26	26	26	26	26	26
par_left	Pearson Correlation	-.185	-.051	-.601**	-.426*	-.291	-.217	-.359	-.471*	.235	.340
	Sig. (2-tailed)	.386	.812	.002	.038	.168	.309	.085	.020	.269	.104
	N	24	24	24	24	24	24	24	24	24	24
par_right	Pearson Correlation	.130	.158	-.393	-.231	-.226	.102	-.139	-.078	.408*	.184
	Sig. (2-tailed)	.544	.462	.058	.277	.289	.636	.518	.718	.048	.389
	N	24	24	24	24	24	24	24	24	24	24

left_PG_beta	Pearson Correlation	.148	.319	.535**	.317	.438*	.415*	.405*	-.033	-.341	-.418*
	Sig. (2-tailed)	.491	.129	.007	.131	.032	.044	.050	.877	.103	.042
	N	24	24	24	24	24	24	24	24	24	24

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

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

Correlations

		NEOA	NEON	RUMB	RUMD	RUMR	COPEP	COPEE	WORRY	par_left
PSQI	Pearson Correlation	-.163	.087	-.156	-.166	-.296	-.055	.121	-.160	-.185
	Sig. (2-tailed)	.425	.671	.457	.427	.150	.790	.555	.434	.386
	N	26	26	25	25	25	26	26	26	24
ISI	Pearson Correlation	-.072	.148	.104	-.055	-.120	.039	.226	-.069	-.051
	Sig. (2-tailed)	.725	.469	.622	.795	.569	.851	.267	.736	.812
	N	26	26	25	25	25	26	26	26	24
FIRST	Pearson Correlation	-.213	.660**	.454*	.584**	.325	.358	.242	.384	-.601**
	Sig. (2-tailed)	.297	.000	.023	.002	.113	.073	.234	.052	.002
	N	26	26	25	25	25	26	26	26	24
PSS	Pearson Correlation	-.098	.679**	.522**	.705**	.394	.271	.521**	.564**	-.426*
	Sig. (2-tailed)	.634	.000	.007	.000	.051	.180	.006	.003	.038
	N	26	26	25	25	25	26	26	26	24
DASSD	Pearson Correlation	-.012	.473*	.613**	.422*	.554**	.247	.312	.178	-.291
	Sig. (2-tailed)	.954	.015	.001	.036	.004	.223	.121	.384	.168
	N	26	26	25	25	25	26	26	26	24
DASSA	Pearson Correlation	-.137	.606**	.383	.497*	.202	.305	.482*	.380	-.217
	Sig. (2-tailed)	.504	.001	.059	.011	.334	.129	.013	.056	.309
	N	26	26	25	25	25	26	26	26	24
DASSS	Pearson Correlation	-.221	.694**	.559**	.495*	.338	.266	.397*	.314	-.359
	Sig. (2-tailed)	.277	.000	.004	.012	.099	.189	.045	.119	.085
	N	26	26	25	25	25	26	26	26	24
NEOO	Pearson Correlation	.154	.194	.234	.287	.223	-.076	.152	-.221	-.471*
	Sig. (2-tailed)	.453	.342	.260	.164	.284	.711	.457	.277	.020
	N	26	26	25	25	25	26	26	26	24

NEOC	Pearson Correlation	.346	-.352	-.069	-.127	.089	-.021	-.165	-.089	.235
	Sig. (2-tailed)	.083	.077	.744	.546	.671	.920	.419	.666	.269
	N	26	26	25	25	25	26	26	26	24
NEOE	Pearson Correlation	.297	-.579**	-.459*	-.251	-.455*	-.313	-.225	-.296	.340
	Sig. (2-tailed)	.141	.002	.021	.226	.022	.119	.269	.142	.104
	N	26	26	25	25	25	26	26	26	24
NEOA	Pearson Correlation	1	-.256	.027	-.035	-.105	-.356	-.335	.072	-.091
	Sig. (2-tailed)		.208	.900	.870	.618	.074	.095	.726	.674
	N	26	26	25	25	25	26	26	26	24
NEON	Pearson Correlation	-.256	1	.566**	.643**	.351	.339	.355	.644**	-.432*
	Sig. (2-tailed)	.208		.003	.001	.085	.090	.075	.000	.035
	N	26	26	25	25	25	26	26	26	24
RUMB	Pearson Correlation	.027	.566**	1	.687**	.735**	.142	.177	.578**	-.168
	Sig. (2-tailed)	.900	.003		.000	.000	.498	.398	.002	.443
	N	25	25	25	25	25	25	25	25	23
RUMD	Pearson Correlation	-.035	.643**	.687**	1	.684**	.381	.382	.589**	-.223
	Sig. (2-tailed)	.870	.001	.000		.000	.060	.060	.002	.307
	N	25	25	25	25	25	25	25	25	23
RUMR	Pearson Correlation	-.105	.351	.735**	.684**	1	.297	.184	.316	.011
	Sig. (2-tailed)	.618	.085	.000	.000		.150	.379	.123	.961
	N	25	25	25	25	25	25	25	25	23
COPEP	Pearson Correlation	-.356	.339	.142	.381	.297	1	.707**	.136	-.269
	Sig. (2-tailed)	.074	.090	.498	.060	.150		.000	.509	.205
	N	26	26	25	25	25	26	26	26	24
COPEE	Pearson Correlation	-.335	.355	.177	.382	.184	.707**	1	.209	-.355
	Sig. (2-tailed)	.095	.075	.398	.060	.379	.000		.305	.089
	N	26	26	25	25	25	26	26	26	24
WORRY	Pearson Correlation	.072	.644**	.578**	.589**	.316	.136	.209	1	-.179
	Sig. (2-tailed)	.726	.000	.002	.002	.123	.509	.305		.402
	N	26	26	25	25	25	26	26	26	24
par_left	Pearson Correlation	-.091	-.432*	-.168	-.223	.011	-.269	-.355	-.179	1
	Sig. (2-tailed)	.674	.035	.443	.307	.961	.205	.089	.402	
	N	24	24	23	23	23	24	24	24	24

par_right	Pearson Correlation	-.092	-.390	-.034	-.151	.097	-.027	.065	-.229	.566**
	Sig. (2-tailed)	.671	.060	.877	.491	.661	.900	.763	.282	.004
	N	24	24	23	23	23	24	24	24	24
left_PG_beta	Pearson Correlation	-.244	.610**	.385	.418*	.340	.166	.120	.239	-.010
	Sig. (2-tailed)	.251	.002	.070	.047	.112	.438	.575	.260	.962
	N	24	24	23	23	23	24	24	24	24

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

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

Correlations

		par_right	left_PG_beta
PSQI	Pearson Correlation	.130	.148
	Sig. (2-tailed)	.544	.491
	N	24	24
ISI	Pearson Correlation	.158	.319
	Sig. (2-tailed)	.462	.129
	N	24	24
FIRST	Pearson Correlation	-.393	.535**
	Sig. (2-tailed)	.058	.007
	N	24	24
PSS	Pearson Correlation	-.231	.317
	Sig. (2-tailed)	.277	.131
	N	24	24
DASSD	Pearson Correlation	-.226	.438*
	Sig. (2-tailed)	.289	.032
	N	24	24
DASSA	Pearson Correlation	.102	.415*
	Sig. (2-tailed)	.636	.044
	N	24	24
DASSS	Pearson Correlation	-.139	.405*
	Sig. (2-tailed)	.518	.050
	N	24	24
NEOO	Pearson Correlation	-.078	-.033
	Sig. (2-tailed)	.718	.877
	N	24	24
NEOC	Pearson Correlation	.408*	-.341
	Sig. (2-tailed)	.048	.103
	N	24	24
NEOE	Pearson Correlation	.184	-.418*
	Sig. (2-tailed)	.389	.042
	N	24	24

NEOA	Pearson Correlation	-.092	-.244
	Sig. (2-tailed)	.671	.251
	N	24	24
NEON	Pearson Correlation	-.390	.610**
	Sig. (2-tailed)	.060	.002
	N	24	24
RUMB	Pearson Correlation	-.034	.385
	Sig. (2-tailed)	.877	.070
	N	23	23
RUMD	Pearson Correlation	-.151	.418*
	Sig. (2-tailed)	.491	.047
	N	23	23
RUMR	Pearson Correlation	.097	.340
	Sig. (2-tailed)	.661	.112
	N	23	23
COPEP	Pearson Correlation	-.027	.166
	Sig. (2-tailed)	.900	.438
	N	24	24
COPEE	Pearson Correlation	.065	.120
	Sig. (2-tailed)	.763	.575
	N	24	24
WORRY	Pearson Correlation	-.229	.239
	Sig. (2-tailed)	.282	.260
	N	24	24
par_left	Pearson Correlation	.566**	-.010
	Sig. (2-tailed)	.004	.962
	N	24	24
par_right	Pearson Correlation	1	-.099
	Sig. (2-tailed)		.647
	N	24	24
left_PG_beta	Pearson Correlation	-.099	1
	Sig. (2-tailed)	.647	
	N	24	24

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

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

NB: par_left= left inferior parietal lobule; par_right= right inferior parietal lobule; PG= left postcentral gyrus

XXXV. **Between group correlations (chapter 6)**

Resilient group correlations

		PSQI	ISI	FIRST	PSS	DASSD	DASSA	DASSS	NEOO	NEOC	NEOE
PSQI	Pearson Correlation	1	.789**	.107	.286	-.017	.166	-.008	.173	-.358	-.025
	Sig. (2-tailed)		.001	.728	.344	.955	.588	.979	.573	.230	.935
	N	13	13	13	13	13	13	13	13	13	13
ISI	Pearson Correlation	.789**	1	.224	.047	-.107	.268	-.117	.057	-.432	-.051
	Sig. (2-tailed)	.001		.461	.878	.729	.375	.704	.853	.140	.869
	N	13	13	13	13	13	13	13	13	13	13
FIRST	Pearson Correlation	.107	.224	1	.569*	.575*	.431	.608*	.440	-.215	-.162
	Sig. (2-tailed)	.728	.461		.042	.040	.141	.027	.133	.480	.598
	N	13	13	13	13	13	13	13	13	13	13
PSS	Pearson Correlation	.286	.047	.569*	1	.754**	.363	.442	.382	-.518	-.047
	Sig. (2-tailed)	.344	.878	.042		.003	.223	.130	.197	.070	.880
	N	13	13	13	13	13	13	13	13	13	13
DASSD	Pearson Correlation	-.017	-.107	.575*	.754**	1	.698**	.736**	.576*	-.404	-.124
	Sig. (2-tailed)	.955	.729	.040	.003		.008	.004	.040	.171	.688
	N	13	13	13	13	13	13	13	13	13	13
DASSA	Pearson Correlation	.166	.268	.431	.363	.698**	1	.719**	.569*	-.497	-.196

	Sig. (2-tailed)	.588	.375	.141	.223	.008		.006	.042	.084	.521
	N	13	13	13	13	13	13	13	13	13	13
DASSS	Pearson Correlation	-.008	-.117	.608*	.442	.736**	.719**	1	.779**	-.155	-.081
	Sig. (2-tailed)	.979	.704	.027	.130	.004	.006		.002	.612	.792
	N	13	13	13	13	13	13	13	13	13	13
NEOO	Pearson Correlation	.173	.057	.440	.382	.576*	.569*	.779**	1	-.305	-.383
	Sig. (2-tailed)	.573	.853	.133	.197	.040	.042	.002		.311	.196
	N	13	13	13	13	13	13	13	13	13	13
NEOC	Pearson Correlation	-.358	-.432	-.215	-.518	-.404	-.497	-.155	-.305	1	.211
	Sig. (2-tailed)	.230	.140	.480	.070	.171	.084	.612	.311		.489
	N	13	13	13	13	13	13	13	13	13	13
NEOE	Pearson Correlation	-.025	-.051	-.162	-.047	-.124	-.196	-.081	-.383	.211	1
	Sig. (2-tailed)	.935	.869	.598	.880	.688	.521	.792	.196	.489	
	N	13	13	13	13	13	13	13	13	13	13
NEOA	Pearson Correlation	-.386	-.339	.112	-.378	-.285	-.066	.050	-.258	.312	-.090
	Sig. (2-tailed)	.193	.258	.716	.203	.346	.831	.871	.394	.299	.770
	N	13	13	13	13	13	13	13	13	13	13
NEON	Pearson Correlation	.098	.051	.754**	.650*	.768**	.603*	.620*	.563*	-.448	-.535
	Sig. (2-tailed)	.751	.869	.003	.016	.002	.029	.024	.045	.125	.059
	N	13	13	13	13	13	13	13	13	13	13
RUMB	Pearson Correlation	-.172	-.160	.509	.301	.536	.266	.256	.220	-.075	-.611*
	Sig. (2-tailed)	.575	.601	.076	.318	.059	.380	.398	.470	.807	.027

	N	13	13	13	13	13	13	13	13	13	13
RUMD	Pearson Correlation	-.103	-.174	.463	.645*	.910**	.562*	.534	.449	-.321	-.375
	Sig. (2-tailed)	.737	.569	.111	.017	.000	.046	.060	.124	.285	.207
	N	13	13	13	13	13	13	13	13	13	13
RUMR	Pearson Correlation	-.112	-.257	.035	.299	.520	.225	.055	.131	-.055	-.449
	Sig. (2-tailed)	.715	.396	.910	.321	.068	.459	.858	.670	.857	.124
	N	13	13	13	13	13	13	13	13	13	13
COPEP	Pearson Correlation	.268	.193	.035	.292	.383	.280	.127	-.001	.099	.030
	Sig. (2-tailed)	.377	.529	.910	.334	.196	.354	.680	.998	.748	.923
	N	13	13	13	13	13	13	13	13	13	13
COPEE	Pearson Correlation	.214	.082	.238	.602*	.605*	.356	.369	.268	-.043	.041
	Sig. (2-tailed)	.483	.789	.433	.030	.028	.232	.215	.375	.889	.894
	N	13	13	13	13	13	13	13	13	13	13
WORRY	Pearson Correlation	-.354	-.380	.388	.408	.411	.080	.047	-.070	-.098	-.428
	Sig. (2-tailed)	.236	.201	.190	.166	.163	.795	.879	.820	.749	.145
	N	13	13	13	13	13	13	13	13	13	13
par_left	Pearson Correlation	-.186	.098	-.644*	-.682*	-.509	-.327	-.614*	-.570	.141	.288
	Sig. (2-tailed)	.564	.761	.024	.015	.091	.300	.034	.053	.662	.363
	N	12	12	12	12	12	12	12	12	12	12
par_right	Pearson Correlation	.357	.376	-.024	-.168	.034	.257	.129	.062	.363	.129
	Sig. (2-tailed)	.255	.229	.941	.602	.917	.420	.688	.847	.246	.690
	N	12	12	12	12	12	12	12	12	12	12

left_PG_beta	Pearson Correlation	.279	.497	.143	-.165	.270	.502	.188	.146	-.001	-.232
	Sig. (2-tailed)	.379	.100	.657	.609	.396	.096	.558	.651	.997	.469
	N	12	12	12	12	12	12	12	12	12	12

Resilient

		NEOA	NEON	RUMB	RUMD	RUMR	COPEP	COPEE	WORRY	par_left
PSQI	Pearson Correlation	-.386	.098	-.172	-.103	-.112	.268	.214	-.354	-.186
	Sig. (2-tailed)	.193	.751	.575	.737	.715	.377	.483	.236	.564
	N	13	13	13	13	13	13	13	13	12
ISI	Pearson Correlation	-.339	.051	-.160	-.174	-.257	.193	.082	-.380	.098
	Sig. (2-tailed)	.258	.869	.601	.569	.396	.529	.789	.201	.761
	N	13	13	13	13	13	13	13	13	12
FIRST	Pearson Correlation	.112	.754**	.509	.463	.035	.035	.238	.388	-.644*
	Sig. (2-tailed)	.716	.003	.076	.111	.910	.910	.433	.190	.024
	N	13	13	13	13	13	13	13	13	12
PSS	Pearson Correlation	-.378	.650*	.301	.645*	.299	.292	.602*	.408	-.682*
	Sig. (2-tailed)	.203	.016	.318	.017	.321	.334	.030	.166	.015
	N	13	13	13	13	13	13	13	13	12
DASSD	Pearson Correlation	-.285	.768**	.536	.910**	.520	.383	.605*	.411	-.509
	Sig. (2-tailed)	.346	.002	.059	.000	.068	.196	.028	.163	.091
	N	13	13	13	13	13	13	13	13	12
DASSA	Pearson Correlation	-.066	.603*	.266	.562*	.225	.280	.356	.080	-.327
	Sig. (2-tailed)	.831	.029	.380	.046	.459	.354	.232	.795	.300
	N	13	13	13	13	13	13	13	13	12
DASSS	Pearson Correlation	.050	.620*	.256	.534	.055	.127	.369	.047	-.614*
	Sig. (2-tailed)	.871	.024	.398	.060	.858	.680	.215	.879	.034
	N	13	13	13	13	13	13	13	13	12
NEOO	Pearson Correlation	-.258	.563*	.220	.449	.131	-.001	.268	-.070	-.570
	Sig. (2-tailed)	.394	.045	.470	.124	.670	.998	.375	.820	.053

	N	13	13	13	13	13	13	13	13	12
NEOC	Pearson Correlation	.312	-.448	-.075	-.321	-.055	.099	-.043	-.098	.141
	Sig. (2-tailed)	.299	.125	.807	.285	.857	.748	.889	.749	.662
	N	13	13	13	13	13	13	13	13	12
NEOE	Pearson Correlation	-.090	-.535	-.611*	-.375	-.449	.030	.041	-.428	.288
	Sig. (2-tailed)	.770	.059	.027	.207	.124	.923	.894	.145	.363
	N	13	13	13	13	13	13	13	13	12
NEOA	Pearson Correlation	1	.033	.244	-.241	-.097	-.520	-.584*	.308	-.094
	Sig. (2-tailed)		.915	.421	.427	.752	.069	.036	.306	.771
	N	13	13	13	13	13	13	13	13	12
NEON	Pearson Correlation	.033	1	.741**	.787**	.458	.131	.216	.637*	-.619*
	Sig. (2-tailed)	.915		.004	.001	.116	.669	.479	.019	.032
	N	13	13	13	13	13	13	13	13	12
RUMB	Pearson Correlation	.244	.741**	1	.728**	.766**	.075	.112	.785**	-.368
	Sig. (2-tailed)	.421	.004		.005	.002	.808	.715	.001	.239
	N	13	13	13	13	13	13	13	13	12
RUMD	Pearson Correlation	-.241	.787**	.728**	1	.761**	.484	.567*	.557*	-.339
	Sig. (2-tailed)	.427	.001	.005		.002	.094	.043	.048	.281
	N	13	13	13	13	13	13	13	13	12
RUMR	Pearson Correlation	-.097	.458	.766**	.761**	1	.382	.338	.592*	-.078
	Sig. (2-tailed)	.752	.116	.002	.002		.198	.259	.033	.810
	N	13	13	13	13	13	13	13	13	12
COPEP	Pearson Correlation	-.520	.131	.075	.484	.382	1	.794**	-.089	.152
	Sig. (2-tailed)	.069	.669	.808	.094	.198		.001	.772	.636
	N	13	13	13	13	13	13	13	13	12
COPEE	Pearson Correlation	-.584*	.216	.112	.567*	.338	.794**	1	-.019	-.303
	Sig. (2-tailed)	.036	.479	.715	.043	.259	.001		.950	.339
	N	13	13	13	13	13	13	13	13	12
WORRY	Pearson Correlation	.308	.637*	.785**	.557*	.592*	-.089	-.019	1	-.416
	Sig. (2-tailed)	.306	.019	.001	.048	.033	.772	.950		.179
	N	13	13	13	13	13	13	13	13	12
par_left	Pearson Correlation	-.094	-.619*	-.368	-.339	-.078	.152	-.303	-.416	1
	Sig. (2-tailed)	.771	.032	.239	.281	.810	.636	.339	.179	

	N	12	12	12	12	12	12	12	12	12
par_right	Pearson Correlation	-.269	-.105	-.135	.093	.110	.794**	.496	-.469	.301
	Sig. (2-tailed)	.399	.746	.676	.774	.734	.002	.101	.124	.342
	N	12	12	12	12	12	12	12	12	12
left_PG_beta	Pearson Correlation	-.230	.224	.304	.294	.234	.469	.322	-.069	.025
	Sig. (2-tailed)	.473	.483	.337	.353	.463	.124	.307	.831	.939
	N	12	12	12	12	12	12	12	12	12

		par_right	left_PG_beta
PSQI	Pearson Correlation	.357	.279
	Sig. (2-tailed)	.255	.379
	N	12	12
ISI	Pearson Correlation	.376	.497
	Sig. (2-tailed)	.229	.100
	N	12	12
FIRST	Pearson Correlation	-.024	.143
	Sig. (2-tailed)	.941	.657
	N	12	12
PSS	Pearson Correlation	-.168	-.165
	Sig. (2-tailed)	.602	.609
	N	12	12
DASSD	Pearson Correlation	.034	.270
	Sig. (2-tailed)	.917	.396
	N	12	12
DASSA	Pearson Correlation	.257	.502
	Sig. (2-tailed)	.420	.096
	N	12	12
DASSS	Pearson Correlation	.129	.188
	Sig. (2-tailed)	.688	.558
	N	12	12
NEOO	Pearson Correlation	.062	.146
	Sig. (2-tailed)	.847	.651
	N	12	12
NEOC	Pearson Correlation	.363	-.001
	Sig. (2-tailed)	.246	.997
	N	12	12
NEOE	Pearson Correlation	.129	-.232

	Sig. (2-tailed)	.690	.469
	N	12	12
NEOA	Pearson Correlation	-.269	-.230
	Sig. (2-tailed)	.399	.473
	N	12	12
NEON	Pearson Correlation	-.105	.224
	Sig. (2-tailed)	.746	.483
	N	12	12
RUMB	Pearson Correlation	-.135	.304
	Sig. (2-tailed)	.676	.337
	N	12	12
RUMD	Pearson Correlation	.093	.294
	Sig. (2-tailed)	.774	.353
	N	12	12
RUMR	Pearson Correlation	.110	.234
	Sig. (2-tailed)	.734	.463
	N	12	12
COPEP	Pearson Correlation	.794**	.469
	Sig. (2-tailed)	.002	.124
	N	12	12
COPEE	Pearson Correlation	.496	.322
	Sig. (2-tailed)	.101	.307
	N	12	12
WORRY	Pearson Correlation	-.469	-.069
	Sig. (2-tailed)	.124	.831
	N	12	12
par_left	Pearson Correlation	.301	.025
	Sig. (2-tailed)	.342	.939
	N	12	12
par_right	Pearson Correlation	1	.488
	Sig. (2-tailed)		.107
	N	12	12
left_PG_beta	Pearson Correlation	.488	1
	Sig. (2-tailed)	.107	
	N	12	12

Vulnerable Group Correlations

		PSQI	ISI	FIRST	PSS	DASSD	DASSA	DASSS	NEOO	NEOC	NEOE
PSQI	Pearson Correlation	1	.681*	.031	-.119	-.235	-.178	-.085	-.037	-.731**	.031
	Sig. (2-tailed)		.010	.921	.699	.440	.561	.782	.905	.005	.921
	N	13	13	13	13	13	13	13	13	13	13
ISI	Pearson Correlation	.681*	1	.173	.318	.347	.217	.349	-.013	-.610*	-.327
	Sig. (2-tailed)	.010		.571	.289	.245	.477	.243	.966	.027	.275
	N	13	13	13	13	13	13	13	13	13	13
FIRST	Pearson Correlation	.031	.173	1	.691**	.116	.623*	.375	.066	.144	-.390
	Sig. (2-tailed)	.921	.571		.009	.706	.023	.206	.832	.639	.188
	N	13	13	13	13	13	13	13	13	13	13
PSS	Pearson Correlation	-.119	.318	.691**	1	.628*	.658*	.789**	.061	.256	-.236
	Sig. (2-tailed)	.699	.289	.009		.022	.015	.001	.842	.398	.438
	N	13	13	13	13	13	13	13	13	13	13
DASSD	Pearson Correlation	-.235	.347	.116	.628*	1	.237	.706**	.302	.191	-.357
	Sig. (2-tailed)	.440	.245	.706	.022		.436	.007	.316	.532	.231
	N	13	13	13	13	13	13	13	13	13	13
DASSA	Pearson Correlation	-.178	.217	.623*	.658*	.237	1	.600*	-.076	.080	-.411
	Sig. (2-tailed)	.561	.477	.023	.015	.436		.030	.805	.796	.163
	N	13	13	13	13	13	13	13	13	13	13
DASSS	Pearson Correlation	-.085	.349	.375	.789**	.706**	.600*	1	-.034	.224	-.459

	Sig. (2-tailed)	.782	.243	.206	.001	.007	.030		.912	.461	.115
	N	13	13	13	13	13	13	13	13	13	13
NEOO	Pearson Correlation	-.037	-.013	.066	.061	.302	-.076	-.034	1	.163	.103
	Sig. (2-tailed)	.905	.966	.832	.842	.316	.805	.912		.594	.738
	N	13	13	13	13	13	13	13	13	13	13
NEOC	Pearson Correlation	-.731**	-.610*	.144	.256	.191	.080	.224	.163	1	.001
	Sig. (2-tailed)	.005	.027	.639	.398	.532	.796	.461	.594		.997
	N	13	13	13	13	13	13	13	13	13	13
NEOE	Pearson Correlation	.031	-.327	-.390	-.236	-.357	-.411	-.459	.103	.001	1
	Sig. (2-tailed)	.921	.275	.188	.438	.231	.163	.115	.738	.997	
	N	13	13	13	13	13	13	13	13	13	13
NEOA	Pearson Correlation	.039	.160	.091	.232	.211	-.185	-.208	.455	.189	.354
	Sig. (2-tailed)	.900	.601	.767	.446	.489	.544	.495	.118	.536	.235
	N	13	13	13	13	13	13	13	13	13	13
NEON	Pearson Correlation	-.041	.119	.513	.649*	.305	.719**	.658*	-.093	.045	-.437
	Sig. (2-tailed)	.895	.698	.073	.016	.311	.006	.014	.762	.883	.135
	N	13	13	13	13	13	13	13	13	13	13
RUMB	Pearson Correlation	-.230	.336	.360	.684*	.696*	.529	.733**	.242	.243	-.176
	Sig. (2-tailed)	.472	.286	.250	.014	.012	.077	.007	.448	.447	.584
	N	12	12	12	12	12	12	12	12	12	12
RUMD	Pearson Correlation	-.336	-.029	.623*	.708**	.212	.482	.362	.127	.360	.078
	Sig. (2-tailed)	.285	.930	.030	.010	.508	.113	.248	.695	.250	.809

	N	12	12	12	12	12	12	12	12	12	12
RUMR	Pearson Correlation	-.520	-.068	.330	.402	.560	.182	.412	.304	.450	-.375
	Sig. (2-tailed)	.083	.835	.295	.196	.058	.571	.183	.336	.142	.229
	N	12	12	12	12	12	12	12	12	12	12
COPEP	Pearson Correlation	-.522	-.229	.081	.071	.051	.358	.171	-.167	.326	-.364
	Sig. (2-tailed)	.067	.452	.793	.819	.868	.230	.577	.587	.277	.222
	N	13	13	13	13	13	13	13	13	13	13
COPEE	Pearson Correlation	-.030	.380	.358	.402	.278	.660*	.437	-.005	-.237	-.492
	Sig. (2-tailed)	.923	.201	.229	.173	.357	.014	.135	.988	.435	.088
	N	13	13	13	13	13	13	13	13	13	13
WORRY	Pearson Correlation	.001	.191	.689**	.725**	.104	.698**	.493	-.388	.003	-.149
	Sig. (2-tailed)	.998	.532	.009	.005	.737	.008	.087	.191	.992	.627
	N	13	13	13	13	13	13	13	13	13	13
par_left	Pearson Correlation	-.219	-.127	-.357	-.205	-.085	-.189	-.065	-.610*	-.040	.106
	Sig. (2-tailed)	.495	.694	.255	.524	.792	.557	.841	.035	.902	.744
	N	12	12	12	12	12	12	12	12	12	12
par_right	Pearson Correlation	-.003	.055	.253	-.059	-.041	.044	.062	-.302	.073	-.252
	Sig. (2-tailed)	.993	.865	.427	.856	.899	.892	.848	.340	.822	.429
	N	12	12	12	12	12	12	12	12	12	12
left_PG_beta	Pearson Correlation	.068	.296	.320	.441	.331	.467	.314	-.104	-.284	-.287
	Sig. (2-tailed)	.833	.350	.311	.151	.293	.126	.320	.748	.372	.366
	N	12	12	12	12	12	12	12	12	12	12

Correlations[a]

		NEOA	NEON	RUMB	RUMD	RUMR	COPEP	COPEE	WORRY	par_left
PSQI	Pearson Correlation	.039	-.041	-.230	-.336	-.520	-.522	-.030	.001	-.219
	Sig. (2-tailed)	.900	.895	.472	.285	.083	.067	.923	.998	.495
	N	13	13	12	12	12	13	13	13	12
ISI	Pearson Correlation	.160	.119	.336	-.029	-.068	-.229	.380	.191	-.127
	Sig. (2-tailed)	.601	.698	.286	.930	.835	.452	.201	.532	.694
	N	13	13	12	12	12	13	13	13	12
FIRST	Pearson Correlation	.091	.513	.360	.623*	.330	.081	.358	.689**	-.357
	Sig. (2-tailed)	.767	.073	.250	.030	.295	.793	.229	.009	.255
	N	13	13	12	12	12	13	13	13	12
PSS	Pearson Correlation	.232	.649*	.684*	.708**	.402	.071	.402	.725**	-.205
	Sig. (2-tailed)	.446	.016	.014	.010	.196	.819	.173	.005	.524
	N	13	13	12	12	12	13	13	13	12
DASSD	Pearson Correlation	.211	.305	.696*	.212	.560	.051	.278	.104	-.085
	Sig. (2-tailed)	.489	.311	.012	.508	.058	.868	.357	.737	.792
	N	13	13	12	12	12	13	13	13	12
DASSA	Pearson Correlation	-.185	.719**	.529	.482	.182	.358	.660*	.698**	-.189
	Sig. (2-tailed)	.544	.006	.077	.113	.571	.230	.014	.008	.557
	N	13	13	12	12	12	13	13	13	12
DASSS	Pearson Correlation	-.208	.658*	.733**	.362	.412	.171	.437	.493	-.065
	Sig. (2-tailed)	.495	.014	.007	.248	.183	.577	.135	.087	.841
	N	13	13	12	12	12	13	13	13	12
NEOO	Pearson Correlation	.455	-.093	.242	.127	.304	-.167	-.005	-.388	-.610*
	Sig. (2-tailed)	.118	.762	.448	.695	.336	.587	.988	.191	.035
	N	13	13	12	12	12	13	13	13	12
NEOC	Pearson Correlation	.189	.045	.243	.360	.450	.326	-.237	.003	-.040
	Sig. (2-tailed)	.536	.883	.447	.250	.142	.277	.435	.992	.902
	N	13	13	12	12	12	13	13	13	12
NEOE	Pearson Correlation	.354	-.437	-.176	.078	-.375	-.364	-.492	-.149	.106

	Sig. (2-tailed)	.235	.135	.584	.809	.229	.222	.088	.627	.744
	N	13	13	12	12	12	13	13	13	12
NEOA	Pearson Correlation	1	-.232	.041	.264	-.008	-.116	-.134	-.015	-.345
	Sig. (2-tailed)		.445	.899	.408	.980	.707	.663	.960	.272
	N	13	13	12	12	12	13	13	13	12
NEON	Pearson Correlation	-.232	1	.294	.409	.157	.263	.510	.709**	-.121
	Sig. (2-tailed)	.445		.353	.186	.625	.385	.075	.007	.709
	N	13	13	12	12	12	13	13	13	12
RUMB	Pearson Correlation	.041	.294	1	.586*	.694*	-.002	.219	.347	.113
	Sig. (2-tailed)	.899	.353		.045	.012	.995	.494	.270	.741
	N	12	12	12	12	12	12	12	12	11
RUMD	Pearson Correlation	.264	.409	.586*	1	.592*	.105	.157	.631*	.067
	Sig. (2-tailed)	.408	.186	.045		.043	.744	.626	.028	.845
	N	12	12	12	12	12	12	12	12	11
RUMR	Pearson Correlation	-.008	.157	.694*	.592*	1	.114	.003	.079	.263
	Sig. (2-tailed)	.980	.625	.012	.043		.724	.993	.808	.435
	N	12	12	12	12	12	12	12	12	11
COPEP	Pearson Correlation	-.116	.263	-.002	.105	.114	1	.651*	.307	-.232
	Sig. (2-tailed)	.707	.385	.995	.744	.724		.016	.307	.468
	N	13	13	12	12	12	13	13	13	12
COPEE	Pearson Correlation	-.134	.510	.219	.157	.003	.651*	1	.500	-.477
	Sig. (2-tailed)	.663	.075	.494	.626	.993	.016		.082	.117
	N	13	13	12	12	12	13	13	13	12
WORRY	Pearson Correlation	-.015	.709**	.347	.631*	.079	.307	.500	1	-.014
	Sig. (2-tailed)	.960	.007	.270	.028	.808	.307	.082		.967
	N	13	13	12	12	12	13	13	13	12
par_left	Pearson Correlation	-.345	-.121	.113	.067	.263	-.232	-.477	-.014	1
	Sig. (2-tailed)	.272	.709	.741	.845	.435	.468	.117	.967	
	N	12	12	11	11	11	12	12	12	12
par_right	Pearson Correlation	-.362	-.248	.374	.038	.433	-.227	-.290	.022	.484
	Sig. (2-tailed)	.248	.437	.258	.911	.184	.477	.360	.945	.110
	N	12	12	11	11	11	12	12	12	12
left_PG_beta	Pearson Correlation	-.080	.649*	.339	.301	.263	-.362	.005	.390	.351

	Sig. (2-tailed)	.805	.022	.308	.369	.434	.248	.987	.210	.263
	N	12	12	11	11	11	12	12	12	12

Correlations[a]

		par_right	left_PG_beta
PSQI	Pearson Correlation	-.003	.068
	Sig. (2-tailed)	.993	.833
	N	12	12
ISI	Pearson Correlation	.055	.296
	Sig. (2-tailed)	.865	.350
	N	12	12
FIRST	Pearson Correlation	.253	.320
	Sig. (2-tailed)	.427	.311
	N	12	12
PSS	Pearson Correlation	-.059	.441
	Sig. (2-tailed)	.856	.151
	N	12	12
DASSD	Pearson Correlation	-.041	.331
	Sig. (2-tailed)	.899	.293
	N	12	12
DASSA	Pearson Correlation	.044	.467
	Sig. (2-tailed)	.892	.126
	N	12	12
DASSS	Pearson Correlation	.062	.314
	Sig. (2-tailed)	.848	.320
	N	12	12
NEOO	Pearson Correlation	-.302	-.104
	Sig. (2-tailed)	.340	.748
	N	12	12
NEOC	Pearson Correlation	.073	-.284
	Sig. (2-tailed)	.822	.372
	N	12	12
NEOE	Pearson Correlation	-.252	-.287
	Sig. (2-tailed)	.429	.366
	N	12	12
NEOA	Pearson Correlation	-.362	-.080
	Sig. (2-tailed)	.248	.805
	N	12	12
NEON	Pearson Correlation	-.248	.649*
	Sig. (2-tailed)	.437	.022

	N	12	12
RUMB	Pearson Correlation	.374	.339
	Sig. (2-tailed)	.258	.308
	N	11	11
RUMD	Pearson Correlation	.038	.301
	Sig. (2-tailed)	.911	.369
	N	11	11
RUMR	Pearson Correlation	.433	.263
	Sig. (2-tailed)	.184	.434
	N	11	11
COPEP	Pearson Correlation	-.227	-.362
	Sig. (2-tailed)	.477	.248
	N	12	12
COPEE	Pearson Correlation	-.290	.005
	Sig. (2-tailed)	.360	.987
	N	12	12
WORRY	Pearson Correlation	.022	.390
	Sig. (2-tailed)	.945	.210
	N	12	12
par_left	Pearson Correlation	.484	.351
	Sig. (2-tailed)	.110	.263
	N	12	12
par_right	Pearson Correlation	1	.111
	Sig. (2-tailed)		.732
	N	12	12
left_PG_beta	Pearson Correlation	.111	1
	Sig. (2-tailed)	.732	
	N	12	12

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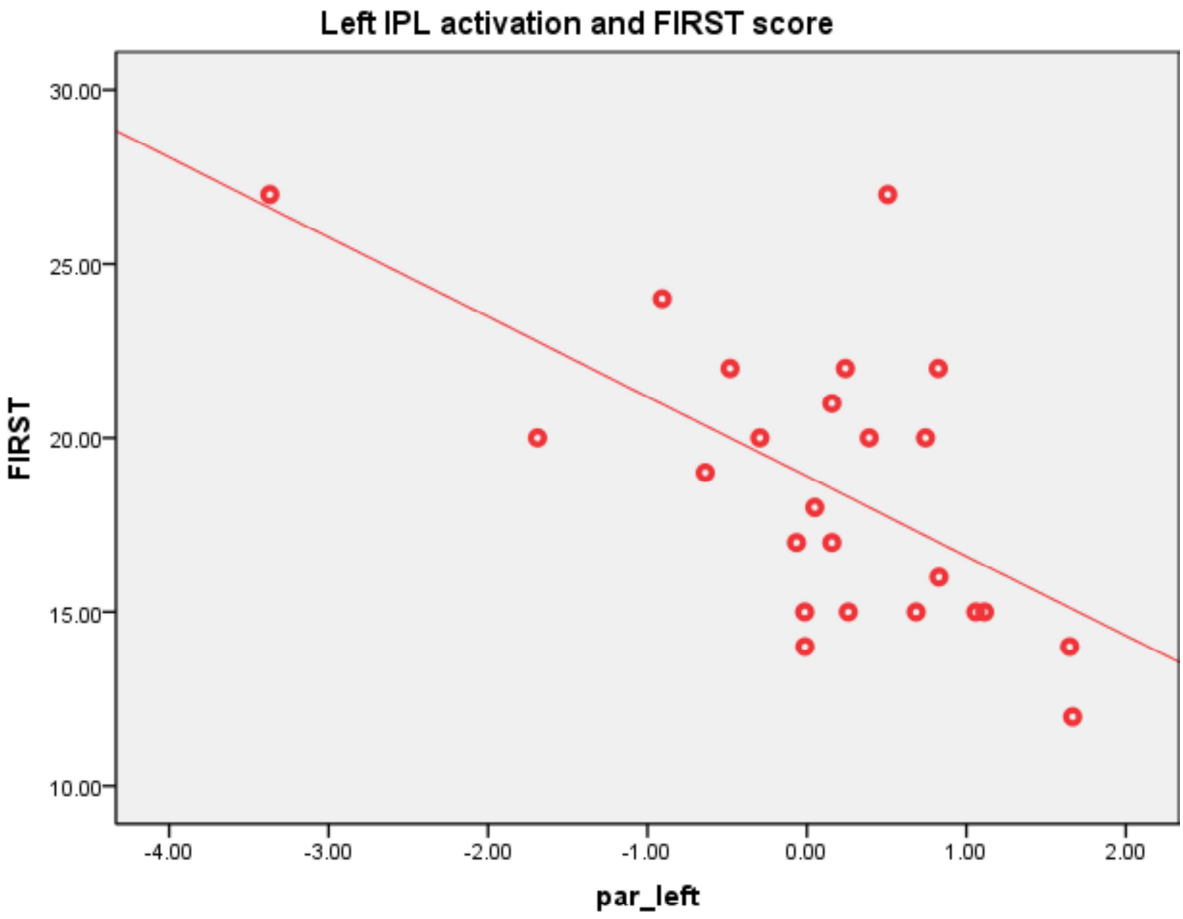
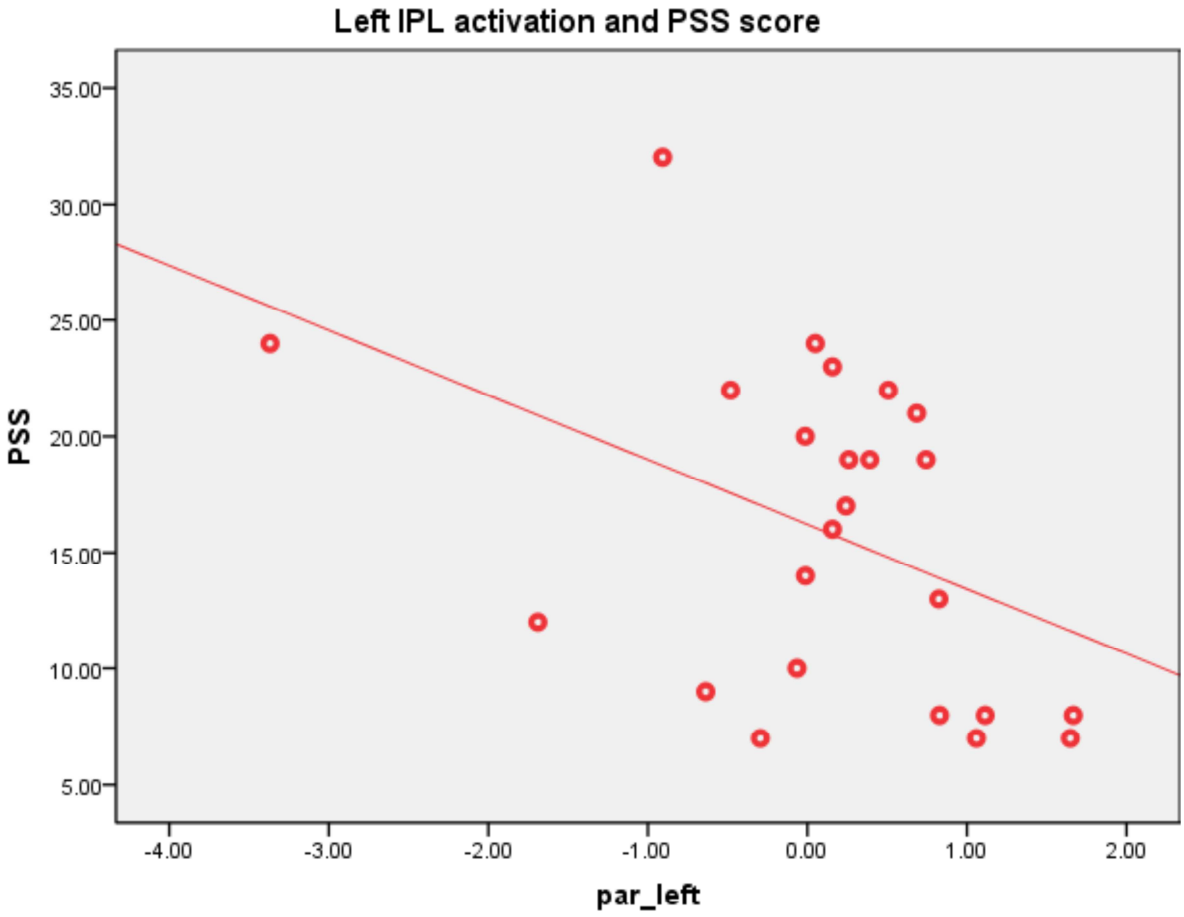
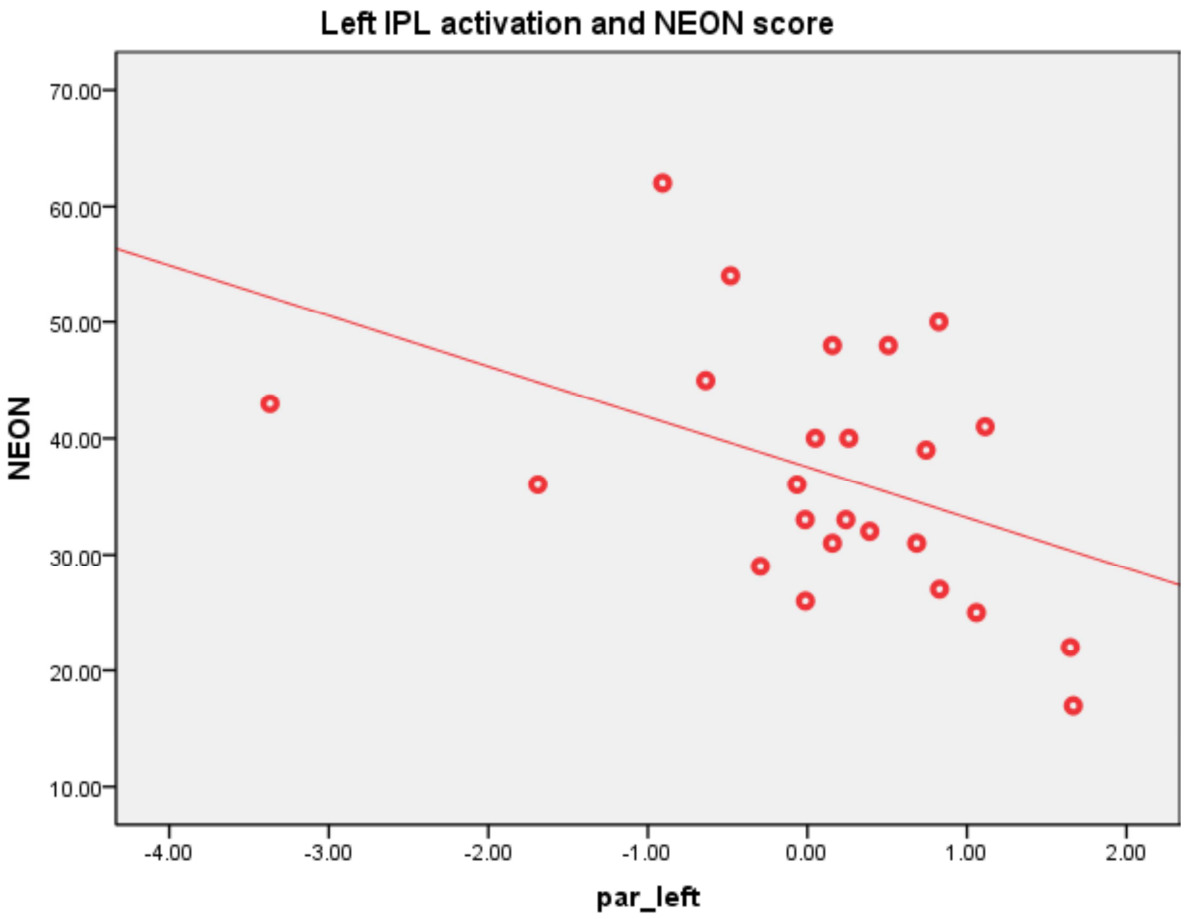
NB: Par_left = left inferior parietal lobule; Par_right= right inferior parital lobule; left_PG_beta= left postcentral gyrus

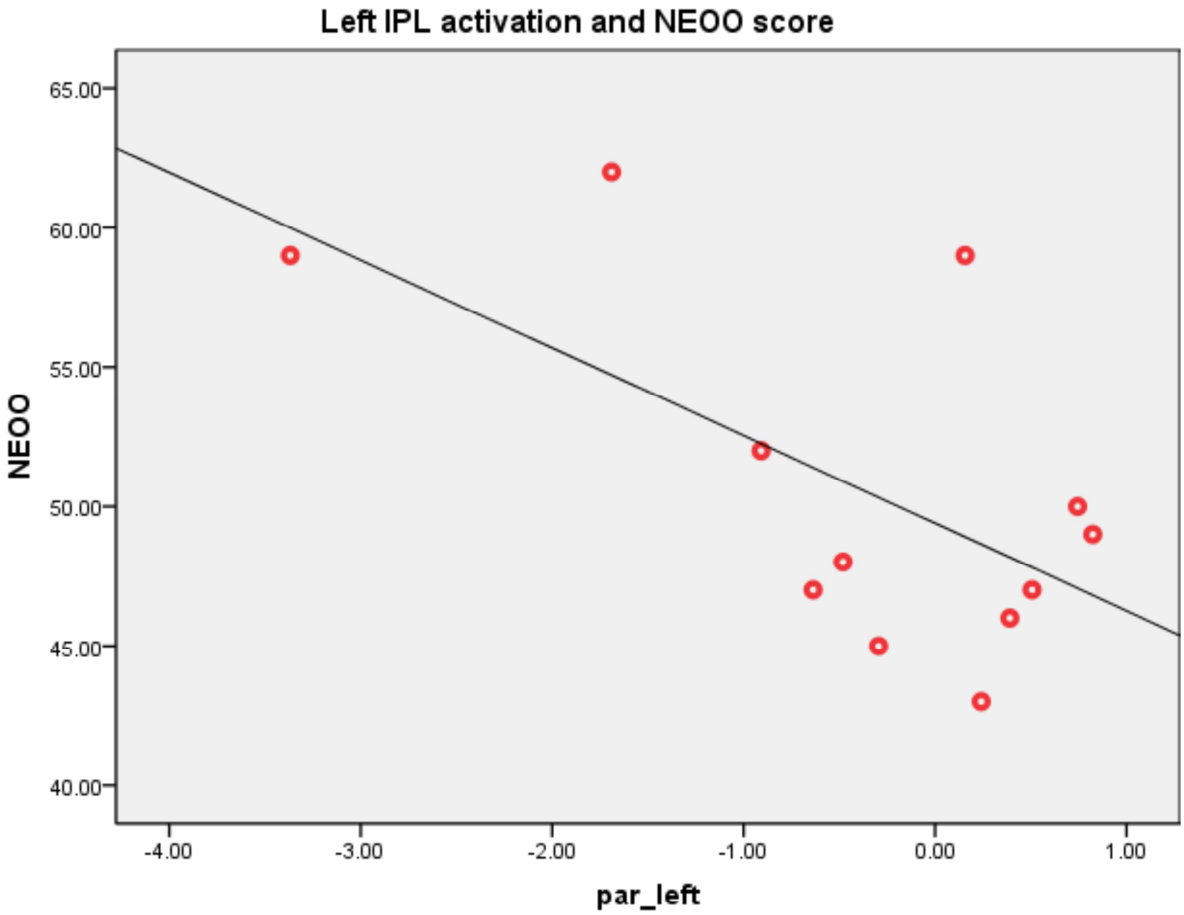
XXXVI. Scatter-plots for Left IPL beta values and Psychological Variables


Left IPL activation and FIRST score
FIRST
30.00
25.00
20.00
15.00
10.00
-4.00
-3.00
-2.00
-1.00
0.00
1.00
2.00
par_left

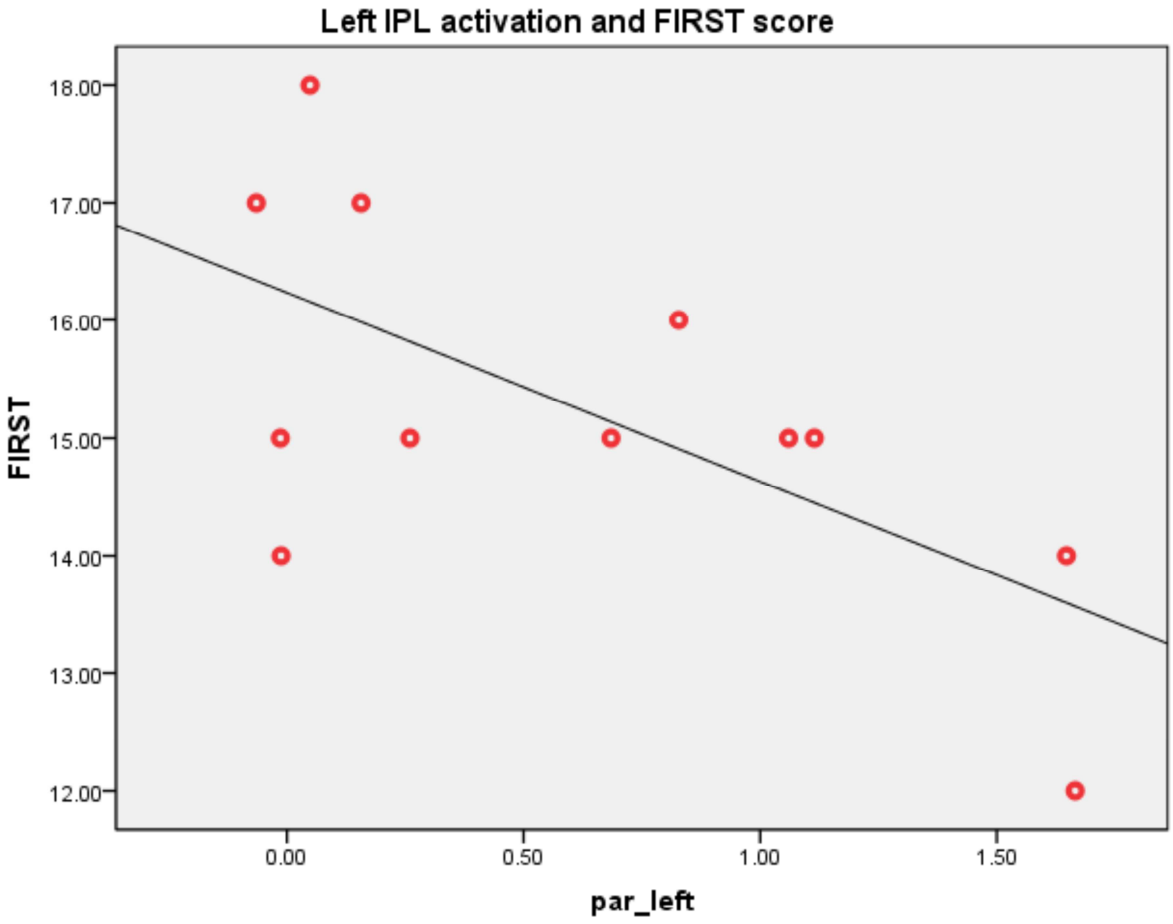

Left IPL activation and PSS score
PSS
35.00
30.00
25.00
20.00
15.00
10.00
5.00
-4.00
-3.00
-2.00
-1.00
0.00
1.00
2.00
par_left

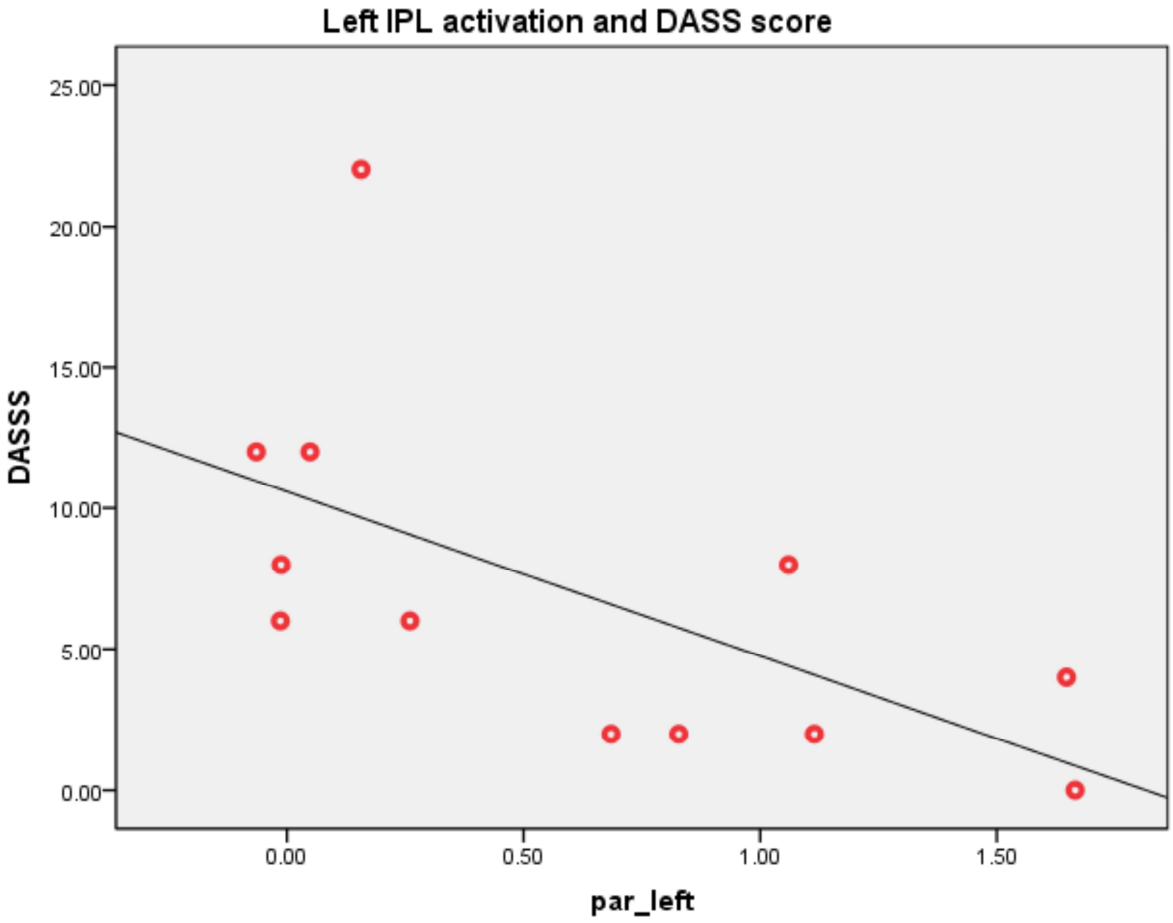

Left IPL activation and NEON score
NEON
70.00
60.00
50.00
40.00
30.00
20.00
10.00
-4.00
-3.00
-2.00
-1.00
0.00
1.00
2.00
par_left

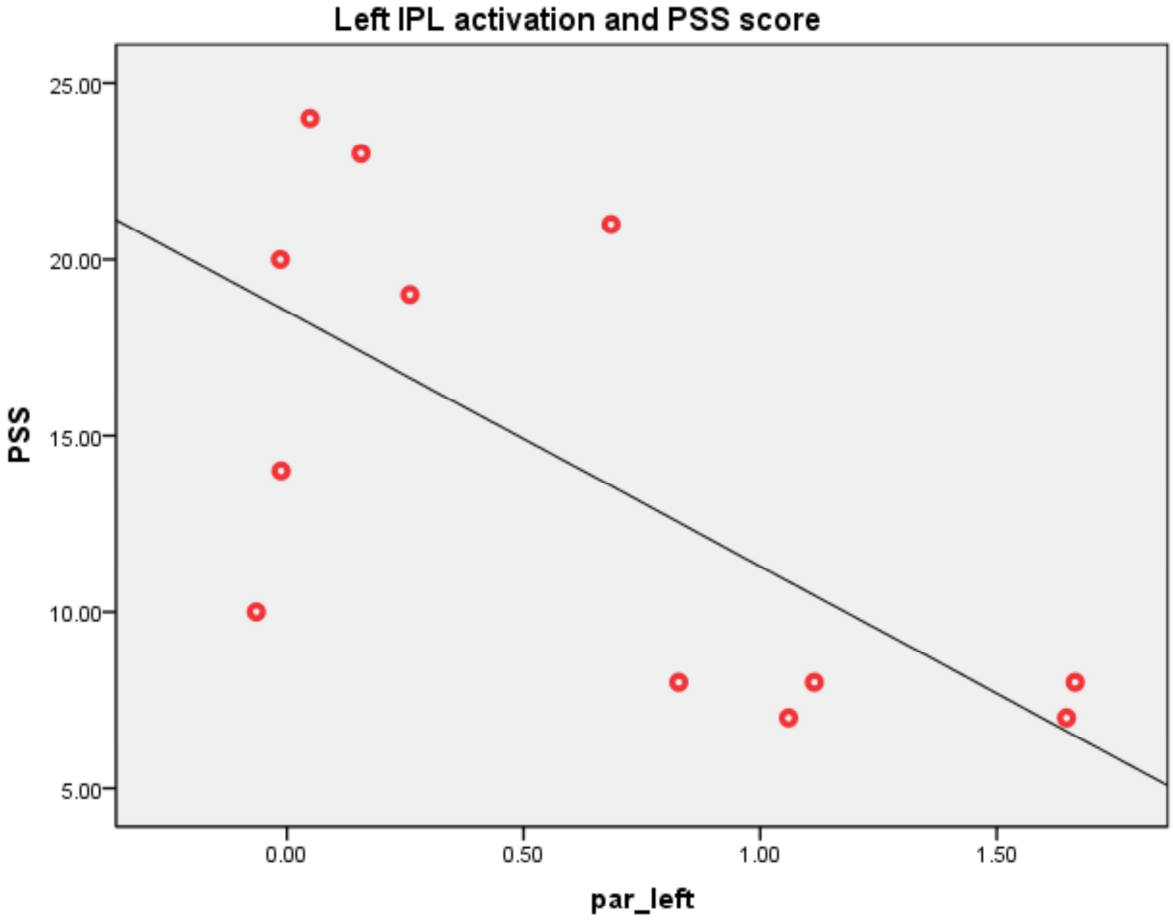
XXXVII. Scatter-Plots showing Relationship between left IPL and openness in the Vulnerable group

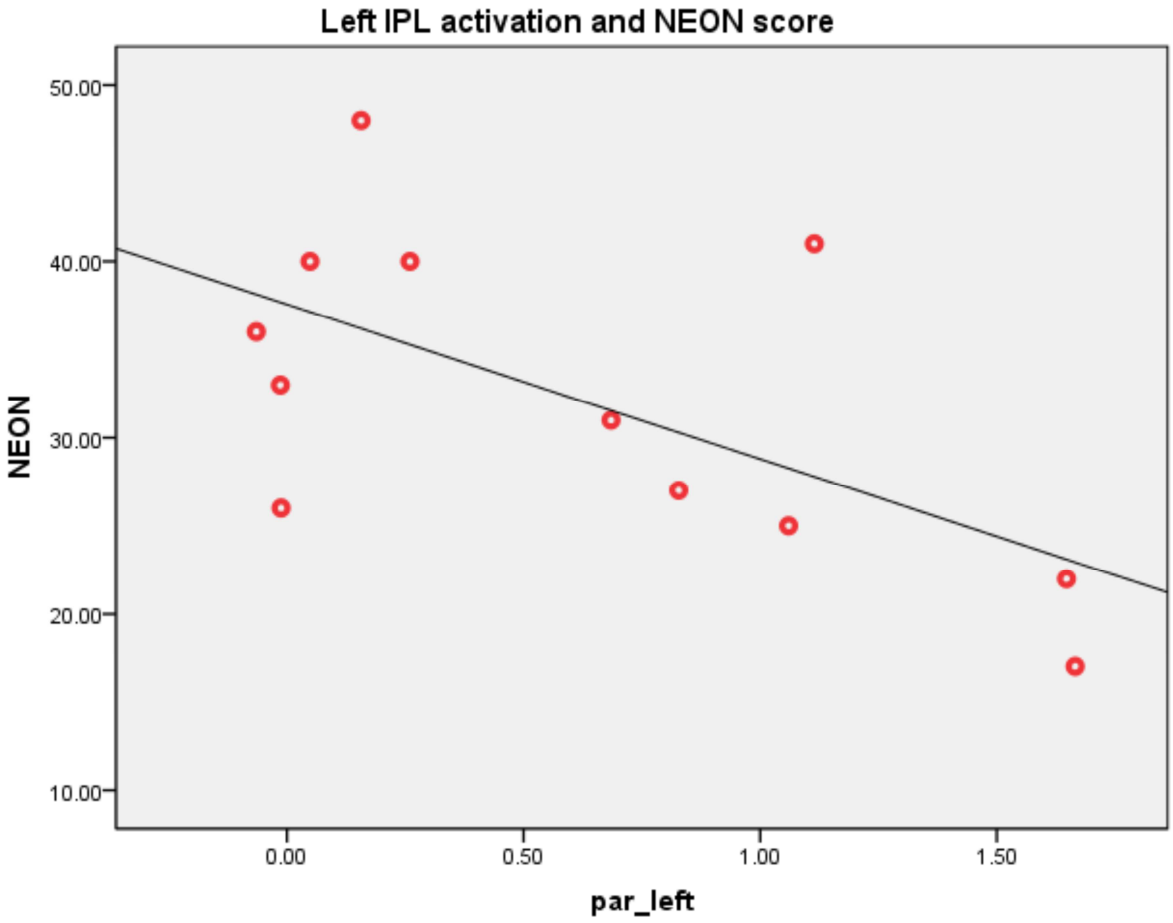


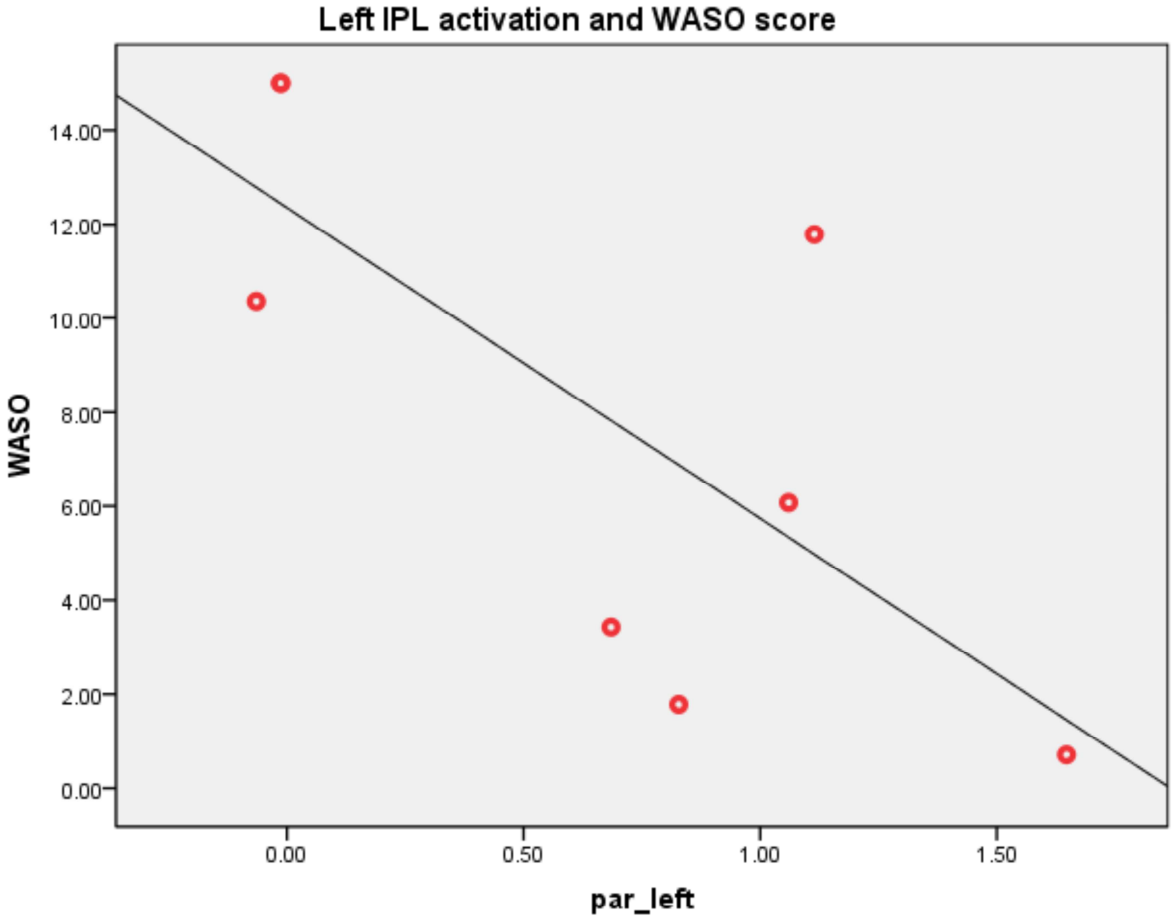
XXXVIII. Scatter-plots showing relationship between left IPL beta values and Other Psychiological Variables in the Resilient Group

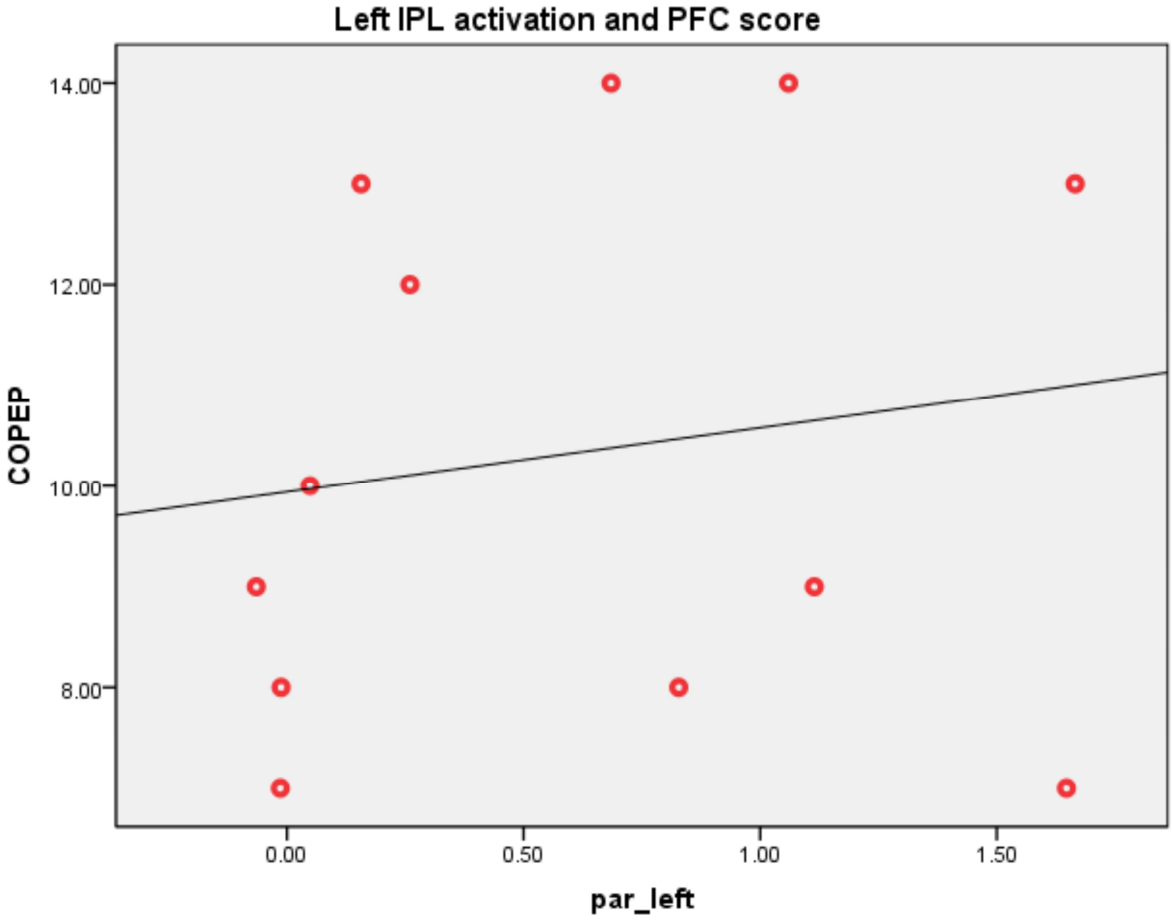



Left IPL activation and DASS score
DASSS
25.00
20.00
15.00
10.00
5.00
0.00
0.00
0.50
1.00
1.50
par_left

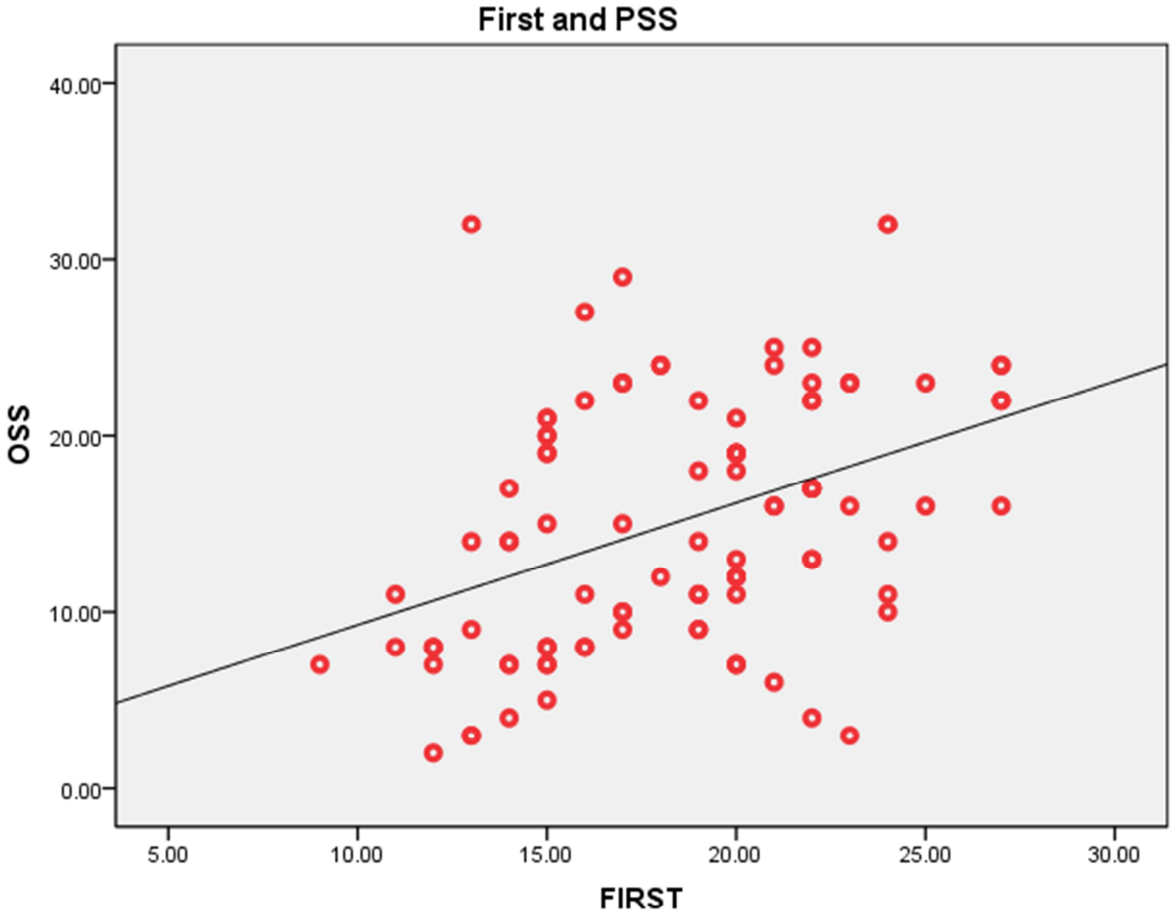

Left IPL activation and PSS score
PSS
25.00
20.00
15.00
10.00
5.00
0.00
0.50
1.00
1.50
par_left

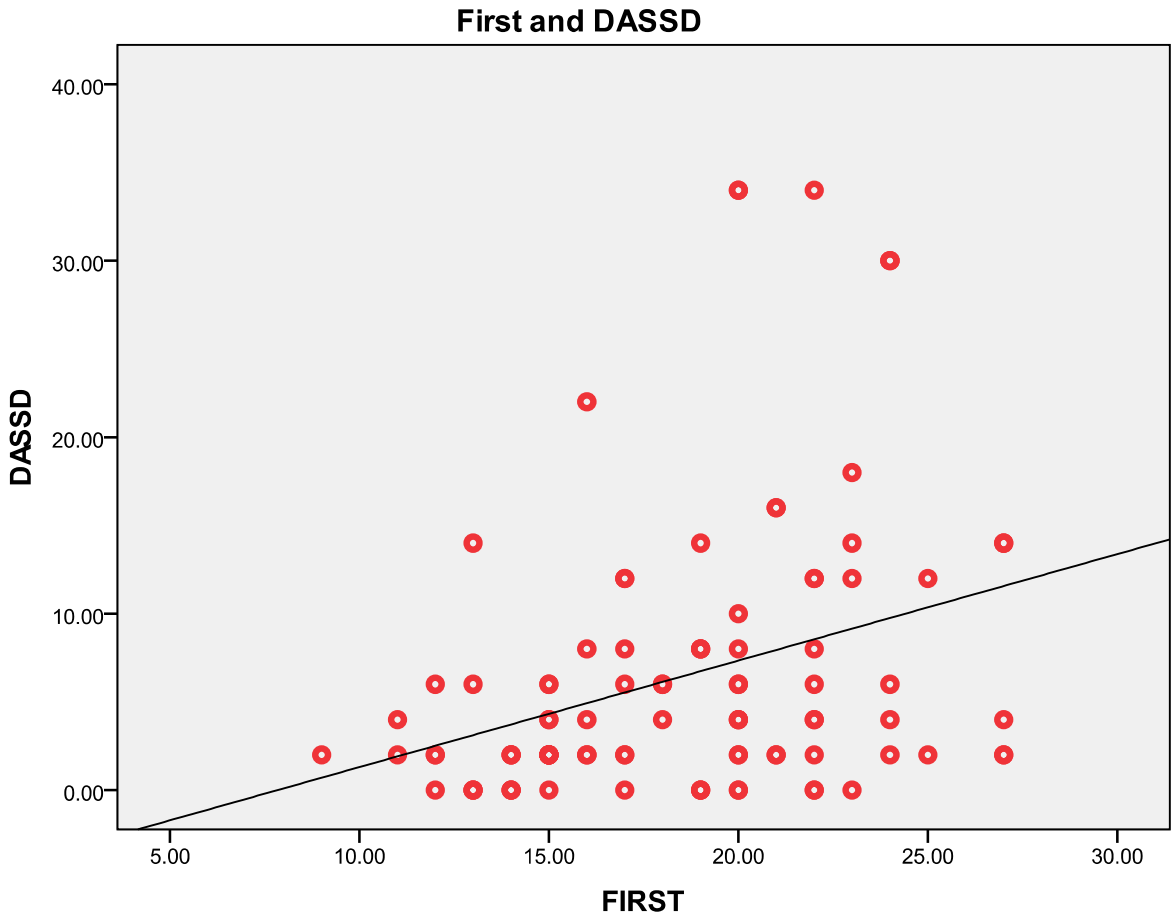

Left IPL activation and NEON score
NEON
50.00
40.00
30.00
20.00
10.00
0.00
0.50
1.00
1.50
par_left

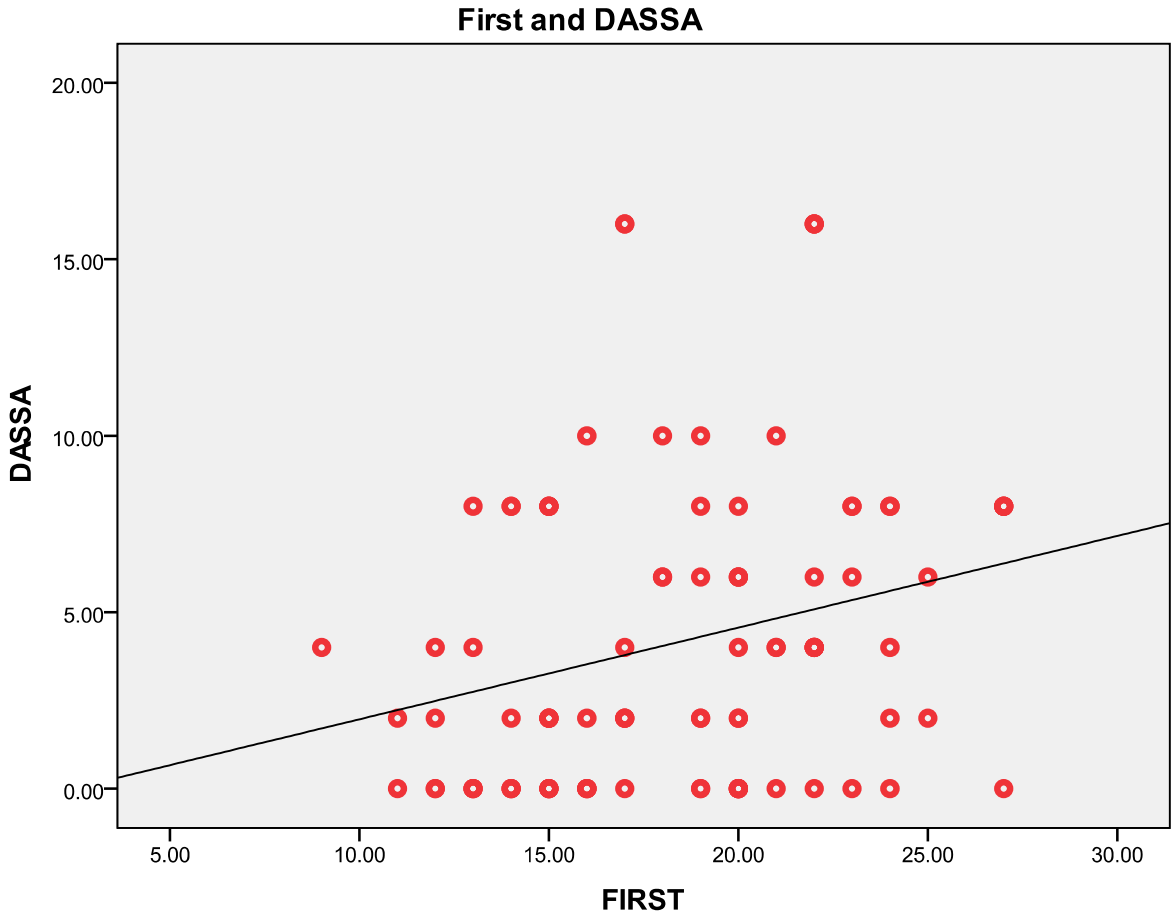

Left IPL activation and WASO score
WASO
14.00
12.00
10.00
8.00
6.00
4.00
2.00
0.00
0.00
0.50
1.00
1.50
par_left

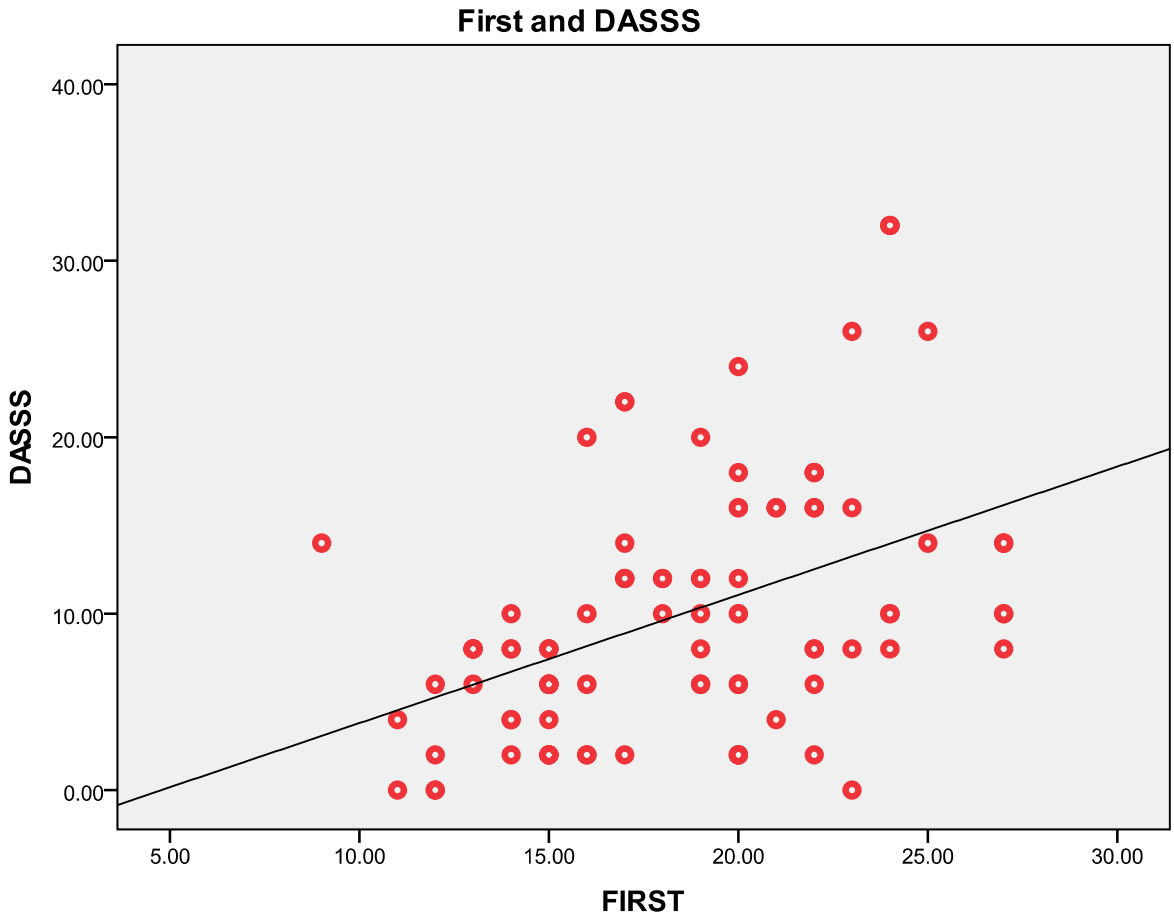

Left IPL activation and PFC score
14.00
12.00
10.00
8.00
COPEP
0.00
0.50
1.00
1.50
par_left

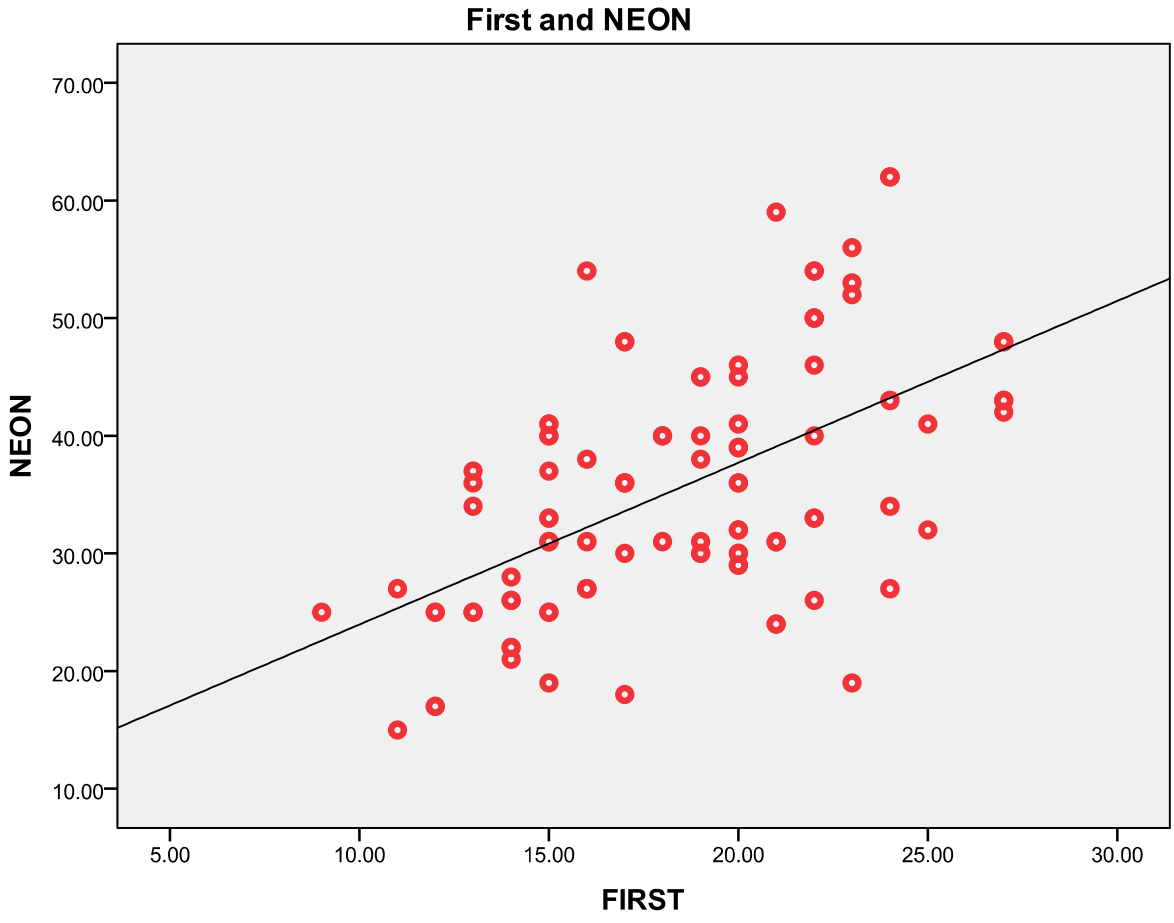
XXXIX. Scatter-Plots Showing Relationships between FIRST and other Psycchological Variables across the whole Sample, Across all 3 studies (Chapter 7)

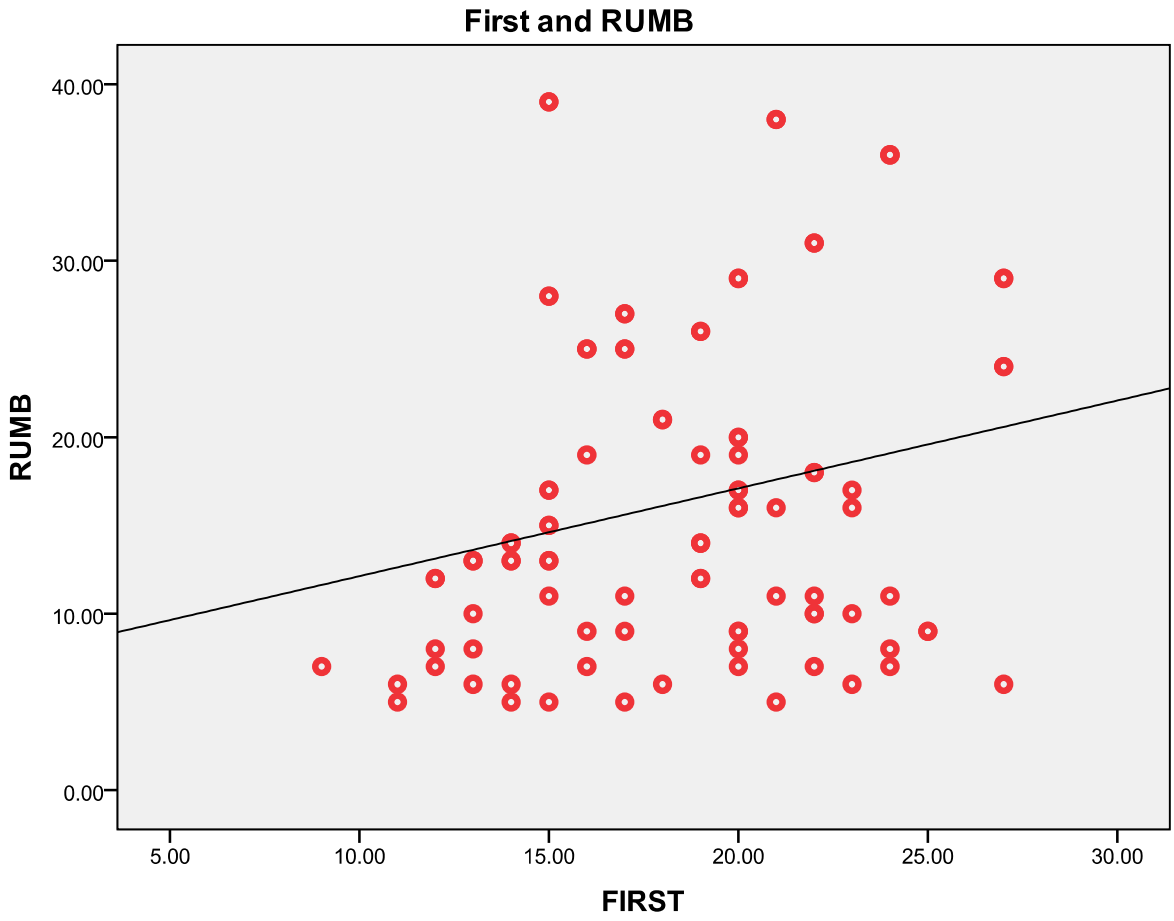

First and PSS
40.00
30.00
20.00
10.00
0.00
OSS
5.00
10.00
15.00
20.00
25.00
30.00
FIRST

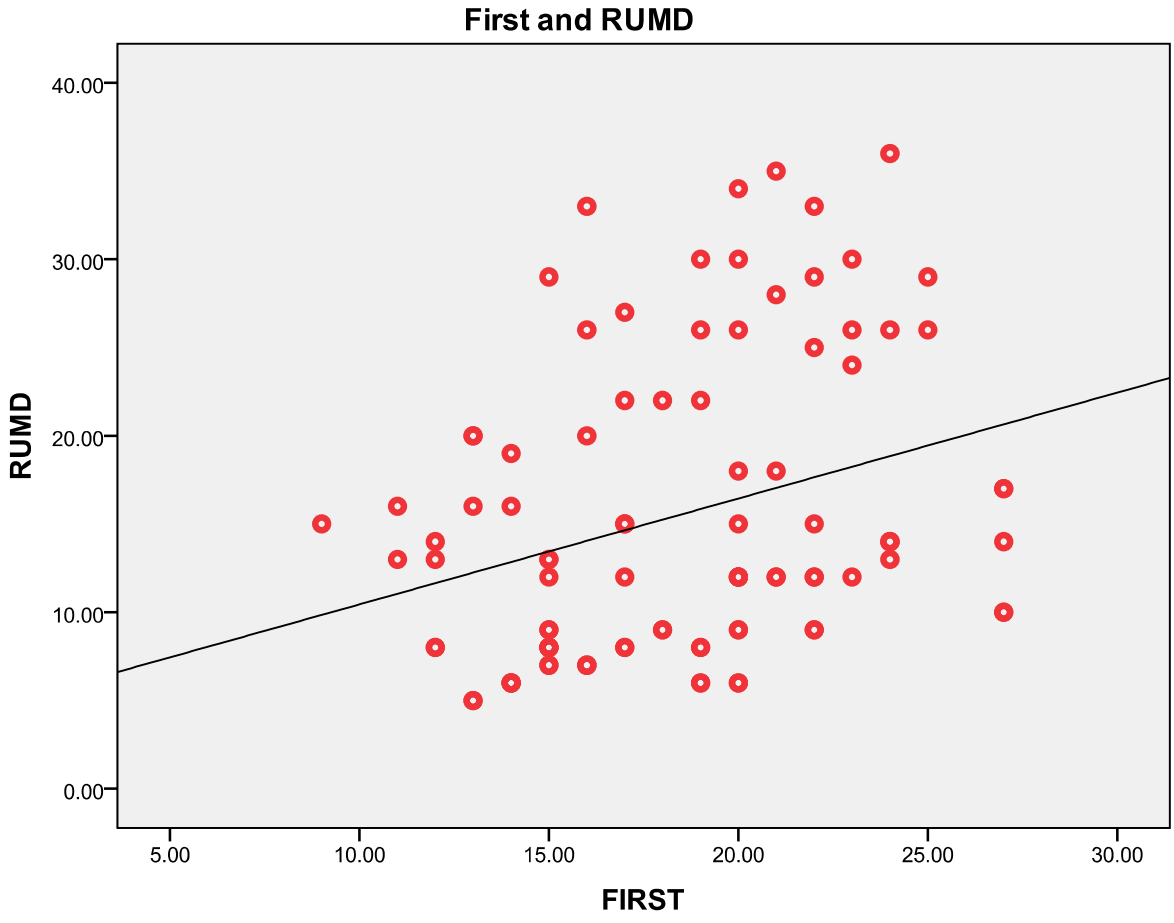

First and DASSD
DASSD
40.00
30.00
20.00
10.00
0.00
5.00
10.00
15.00
20.00
25.00
30.00
FIRST

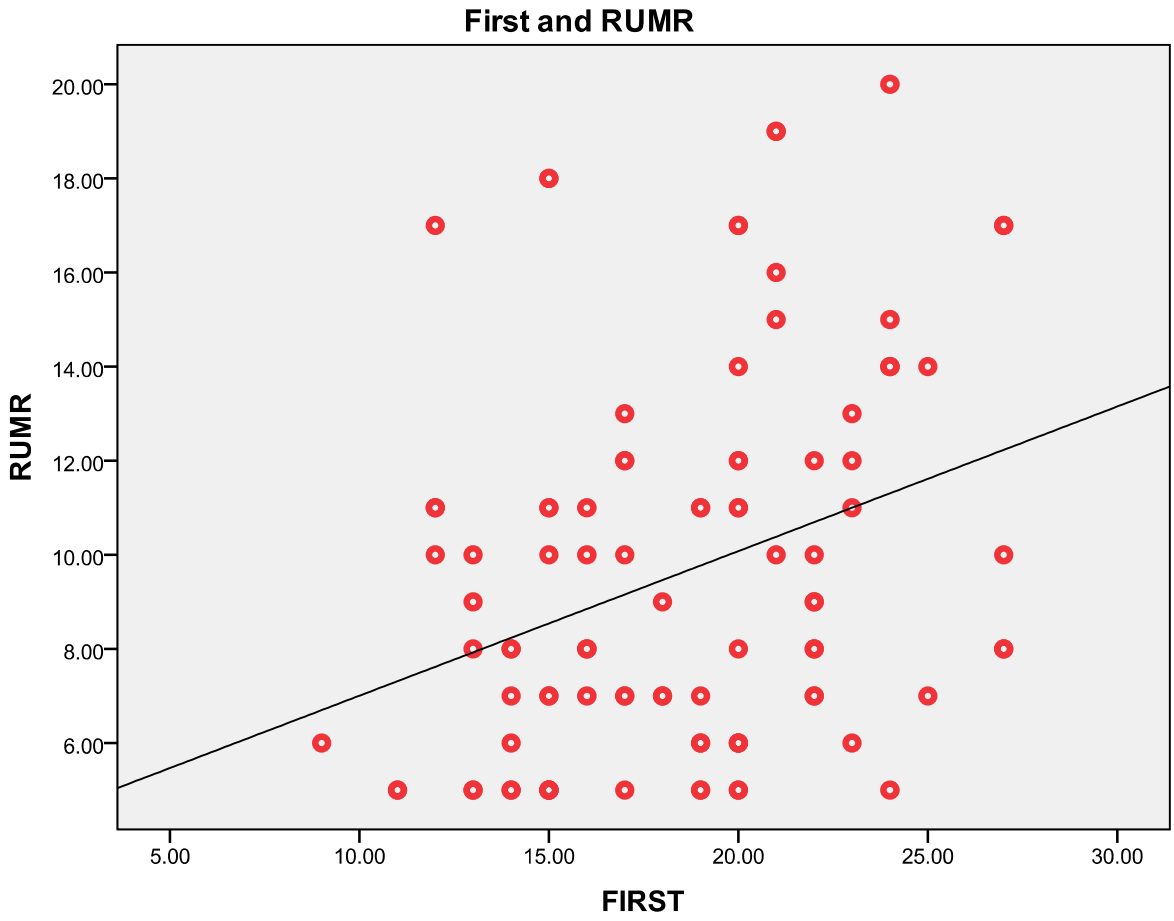

First and DASSA
DASSA
20.00
15.00
10.00
5.00
0.00
5.00
10.00
15.00
20.00
25.00
30.00
FIRST

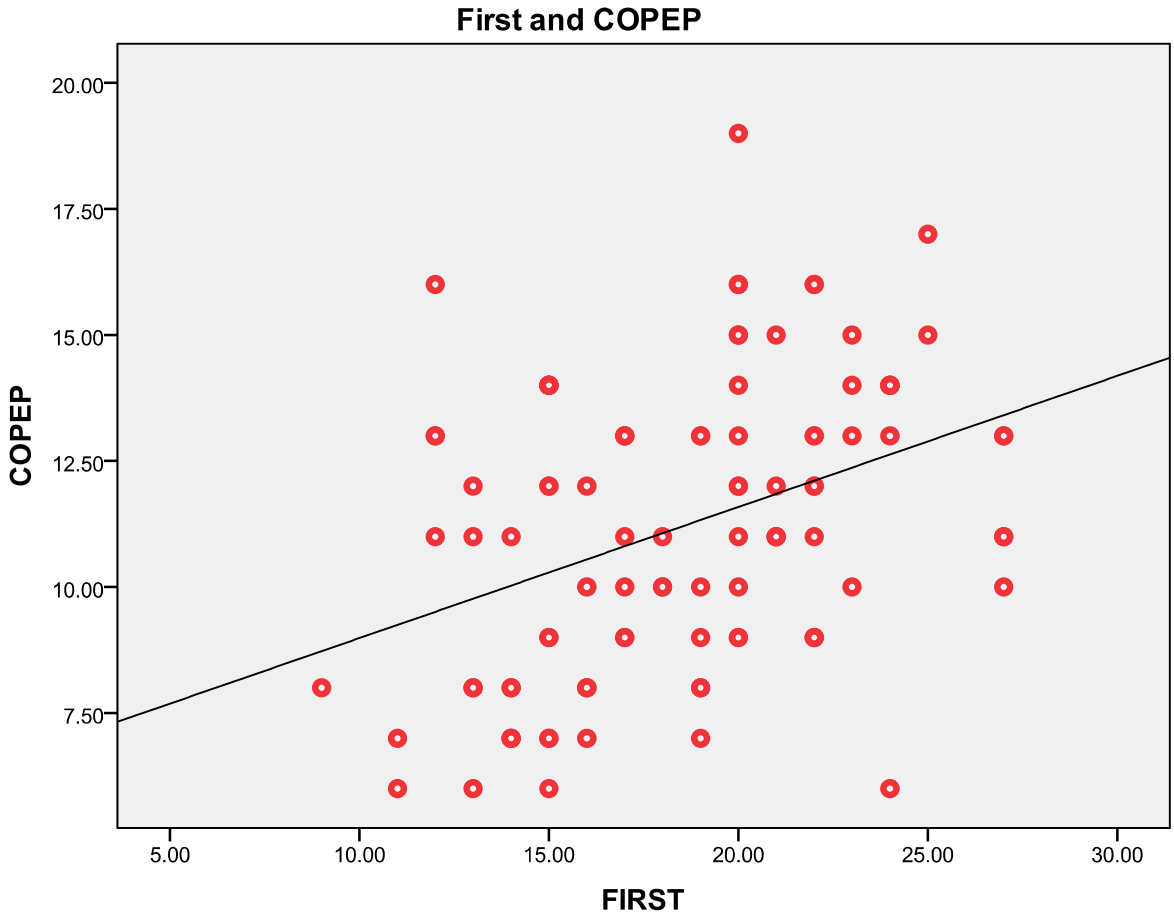

First and DASSS
DASSS
40.00
30.00
20.00
10.00
0.00
5.00
10.00
15.00
20.00
25.00
30.00
FIRST

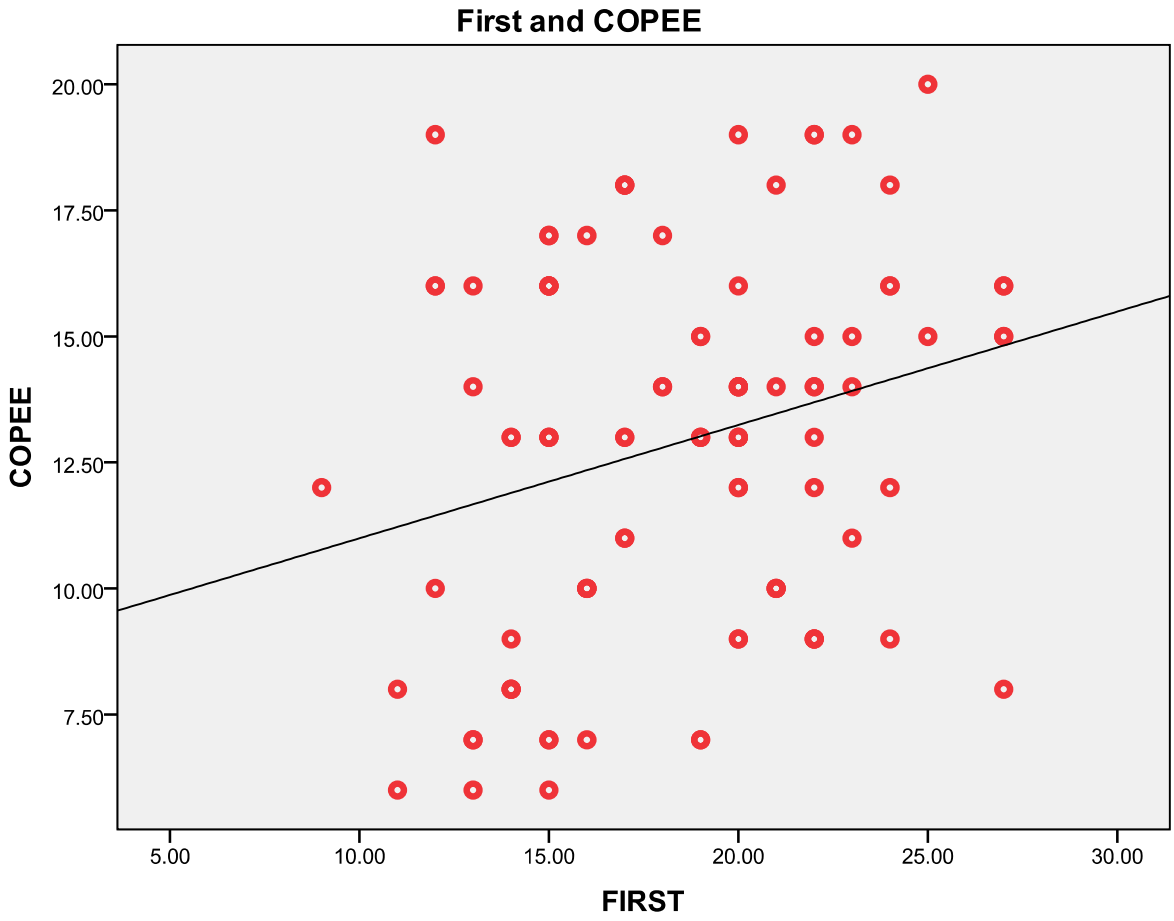

First and NEON
NEON
70.00
60.00
50.00
40.00
30.00
20.00
10.00
5.00
10.00
15.00
20.00
25.00
30.00
FIRST

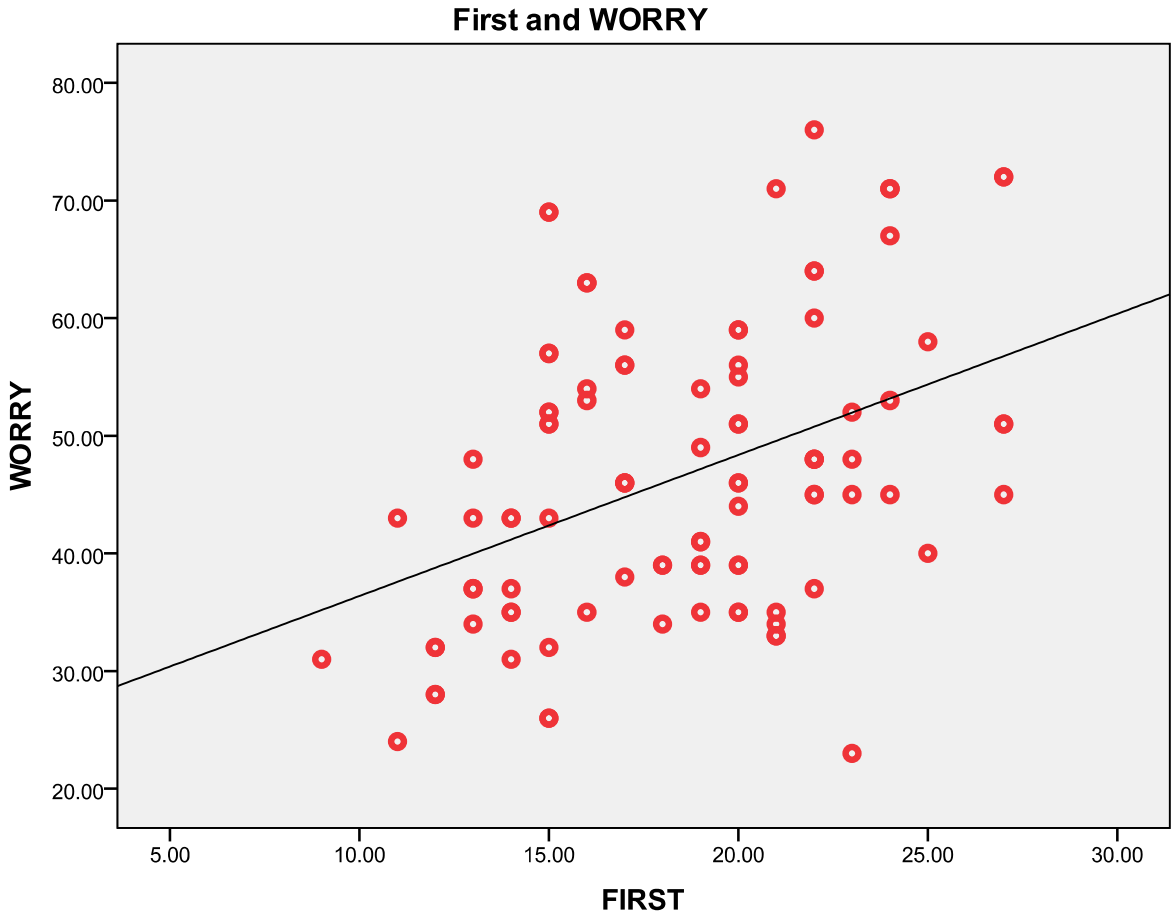

First and RUMB
RUMB
40.00
30.00
20.00
10.00
0.00
5.00
10.00
15.00
20.00
25.00
30.00
FIRST

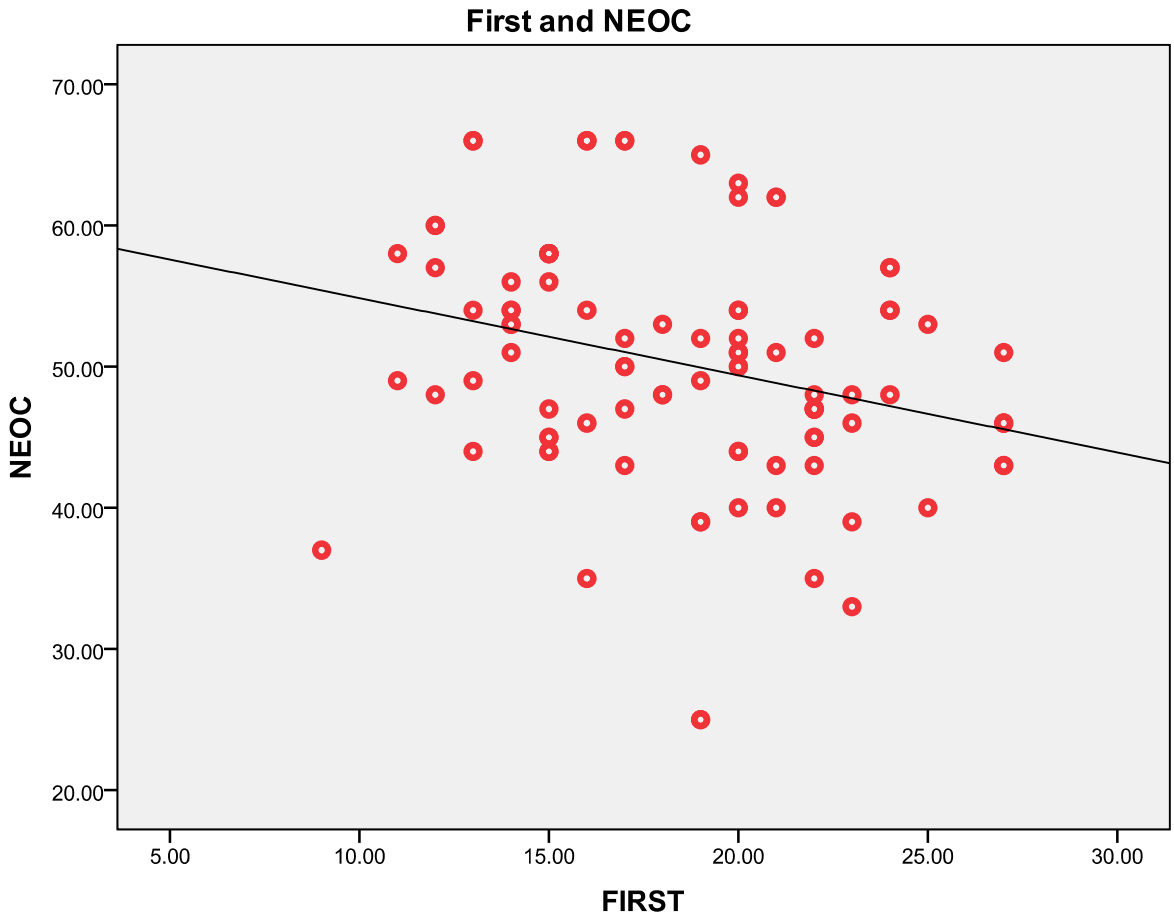

First and RUMD
RUMD
40.00
30.00
20.00
10.00
0.00
5.00
10.00
15.00
20.00
25.00
30.00
FIRST

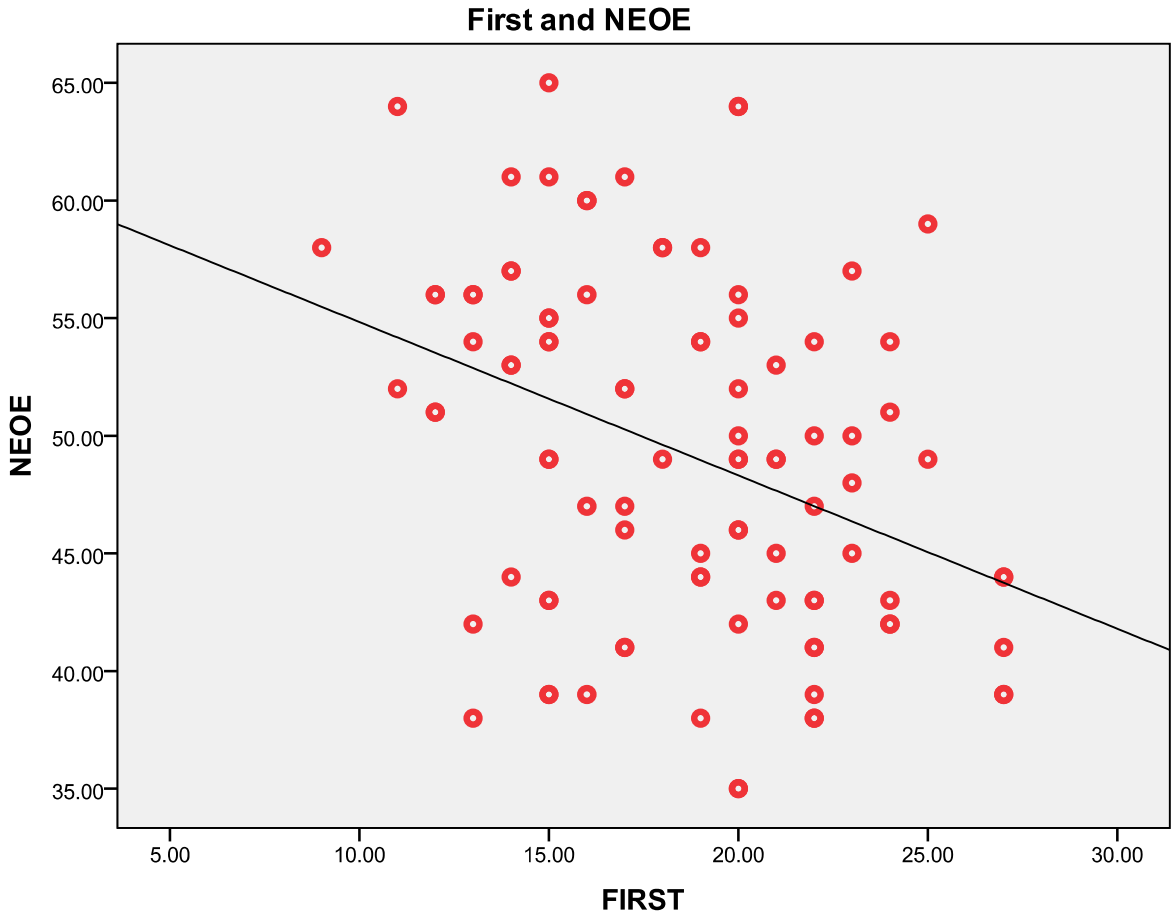

First and RUMR
RUMR
20.00
18.00
16.00
14.00
12.00
10.00
8.00
6.00
5.00
10.00
15.00
20.00
25.00
30.00
FIRST


First and COPEP
COPEP
20.00
17.50
15.00
12.50
10.00
7.50
5.00
10.00
15.00
20.00
25.00
30.00
FIRST


First and COPEE
COPEE
20.00
17.50
15.00
12.50
10.00
7.50
5.00
10.00
15.00
20.00
25.00
30.00
FIRST


First and WORRY
WORRY
80.00
70.00
60.00
50.00
40.00
30.00
20.00
5.00
10.00
15.00
20.00
25.00
30.00
FIRST


First and NEOC
NEOC
70.00
60.00
50.00
40.00
30.00
20.00
5.00
10.00
15.00
20.00
25.00
30.00
FIRST


First and NEOE
NEOE
65.00
60.00
55.00
50.00
45.00
40.00
35.00
5.00
10.00
15.00
20.00
25.00
30.00
FIRST

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