Stress, Anxiety, and Depression: Prevalence and Associations to Electroencephalography and Cognitive Performance in Healthcare Professionals

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I. Declaration

I declare that this thesis is submitted in fulfilment of the requirements for the award of Doctor of Philosophy (Science) in the School of Life Sciences at the University of Technology Sydney.

This thesis is wholly my own work unless otherwise referenced or acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis. This document has not been submitted for qualifications at any other academic institution.

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Signature of candidate: Production Note: Signature removed prior to publication. Date: 31.08.20

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III. Publications and Presentations

Publications

1. Maharaj, S., Lees, T., & Lal, S. (2018). Negative mental states and their association to the cognitive function of nurses. *Journal of Psychophysiology, 33*(3), 207–218. https://doi.org/10.1027/0269-8803/a000223

2. Maharaj, S., Lees, T., & Lal, S. (2019). Prevalence and Risk Factors of Depression, Anxiety, and Stress in a Cohort of Australian Nurses. *International Journal of Environmental Research and Public Health*, *16*(1), 61. https://doi.org/10.3390/ijerph16010061

3. Chalmers, T., Maharaj, S., Lees, T., Lin, C. T., Newton, P., Clifton-Bligh, R., McLachlan, C. S., Gustin, S. M., & Lal, S. (2020). Impact of acute stress on cortical electrical activity and cardiac autonomic coupling. *Journal of Integrative Neuroscience*, 19(2), 239–248. https://doi.org/10.31083/j.jin.2020.02.74

4. Ferreira, B., Maharaj, S., Simpson, A., Nassif, N., & Lal, S., (2020), The metabolic role of depression and burnout in nurses. *Translational Metabolic Syndrome Research,* 3, 9-11. https://doi.org/10.1016/j.tmsr.2020.03.002

5. Beehan-Quirk, C., Jarman, L., Maharaj, S., Simpson, A., Nassif, N., & Lal, S., (2020), Investigating the effects of fatigue on blood glucose levels – Implications for diabetes. *Translational Metabolic Syndrome Research,* 3, 17-20. https://doi.org/10.1016/j.tmsr.2020.03.001

6. Lees. T., Maharaj, S., Kalatzis, G., Nassif, N., Newton, P., & Lal, S. (2020) Electroencephalographic prediction of global and domain specific cognitive performance of clinically active Australian Nurses (*Accepted for publication, Journal: Physiological Measurement*)

Published abstracts

1. Lees, T, Maharaj, S and Lal, S. (2015). Electroencephalographic markers of subjective cognitive performance: implications towards electrophysiological prediction of early cognitive decline. Frontiers in Human Neuroscience Conference Abstract: ASP2015 - 25th Annual Conference of the Australasian Society for Psychophysiology

2. Maharaj, S, T, Lees, C, Zaslawski, K, Fatima-Shad, Lal, S. (2017), 'Assessing the link between negative mental states and cognitive performance in health professionals.' Conference Abstract: The 4th Annual Conference of the Australasian Cognitive Neuroscience Society

Conference proceedings

1. Maharaj, S, Lees, T, Lal, S. (2015), 'Cognitive function associations to mental states in nurses', The combined health science conference - New Horizons 2015 [poster], Sydney, 23-25 November

2. Lees, T, Maharaj, S, Lal, S. (2015), 'Electroencephalographic markers of subjective cognitive performance: implications towards electrophysiological prediction of early cognitive decline' ASP2015 - 25th Annual Conference of the Australasian Society for Psychophysiology, University of Newcastle, Sydney, December, 2-4

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Other (manuscripts currently submitted for publication)

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2. Lees T, Maharaj S, Kalatzis G, Nassif N, Newton P, Lal S., Anxiety and its relationship to the neurocognitive performance of Australian Nurses

3. Leong D, Akella A, Kumar Singh A, Lal S, Newton P, Clifton-Bligh R, McLachlan C, Gustin S, Maharaj S, Lees T, Cao J, Lin CT., Classifying the Level of Lab-induced Stress in a combined sample of nurses and non-health professionals using Auto-Encoder

4. Chalmers T, Maharaj S, Lal S., Assessing associations between workplace factors and Depression and Anxiety in Australian heavy vehicle truck drivers

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VII. Abbreviations

ABS = Australian Bureau of Statistics

ACTH = Adrenocorticotropic Hormone

AIHW = Australian Institute of Health and Welfare

AIN = Assistant in Nursing

ANOVA = Analysis of Variance

ANS = Autonomic Nervous System

β = Beta

B = Regression Coefficient

BMI = Body Mass Index

BP = Blood Pressure

Bpm **=** beats per minute

CANTAB **=** Cambridge Neuropsychological Test Automated Battery

CBT **=** Cognitive Behavioural Therapy

CRH = Corticotropin Releasing Hormone

°C = Degrees Celsius

DASS = Depression Anxiety Stress Scale

DC = Direct Current Value

EEG = Electroencephalography

ELISA = Enzyme-linked Immunosorbent Assay

EOG = Electro-oculogram

ESS = Epworth Sleepiness Scale

fMRI = Functional Magnetic Resonance Imaging

g('s) = Relative Centrifugal Force (RCF)

GHQ = General Health Questionnaire

GP = General Practitioner

HPA axis = Hypothalamic Pituitary Adrenal Axis

HR = Heart Rate

HREC = Human Research Ethics Committee

Hz = Hertz

IQ = Intelligence Quotient

LC-MS/MS = Liquid Chromatography Tandem Mass Spectrometry

MANCOVA = Multiple Analysis of Covariance

MCI = Mild Cognitive Impairment

MEG = Magnetoencephalography

mmHg = Millimetres Mercury

MMSE = Mini Mental State Examination

MRI = Magnetic Resonance Imaging

NC = No Change

NHC = Non-Healthcare comparative group

NS = Non-Significant

NSW = New South Wales

OMS = Ohms

PET = Positron Emission Tomography

qEEG = Quantitative Electroencephalography

R = Correlation Coefficient

r = Rho value

R^2 = Coefficient of determination

RN = Registered Nurse

SD = Standard Deviation

SE = Standard Error

µV = Microvolts

ug/dL = Micrograms per Decilitre

USA = United States of America

UTS = University of Technology Sydney

WAIS = Wechsler Adult Intelligence Scale

$\mu V/s^2$ = Microvolts per second squared

VIII. Abstract

Healthcare remains one of the most demanding careers available. Psychological distress is widespread among healthcare professionals. However, few studies have investigated the prevalence of stress and common mental health issues such as anxiety, and depression in Australian healthcare professionals, and their associations with electroencephalography (EEG) and cognitive performance. The present study assessed the prevalence of stress, anxiety and depression, and the relationships between these mental states and cognitive performance in healthcare professionals. It also investigated associations between cortisol and mental health/cognitive performance measures.

Data was obtained from 154 participants divided into four groups: nurses (n=81), allied health professionals (n=31), doctors (n=20), and non-healthcare professionals (n=22). The experimental protocol involved pre-study and post-study blood pressure measurements and the collection of salivary cortisol. A questionnaire battery obtained lifestyle, demographic, and work-related data. Mental health data was obtained using the Depression, Anxiety, Stress Scale, and the General Health Questionnaire. A 32-lead monopolar EEG was recorded over two five-minute phases (a resting baseline phase followed by an active phase involving the Stroop task). Finally, cognitive performance was assessed using the Mini-Mental State Examination and the Cognistat.

Prevalence rates in healthcare providers ranged between 26-60% for depression, 26-44% for anxiety, and 29-60% for stress. Stress was associated with decreases in repetition ($r=-0.46$, $p=0.039$), memory ($r=-0.49$, $p=0.029$), and attention ($r=-0.51$, $p=0.021$) in doctors, while anxiety was linked to decreased memory ($r=-0.23$, $p=0.047$) in nurses and global cognition ($r=-0.36$, $p=0.049$) in allied health professionals. Depression was also related to declines in memory ($r=-0.27$, $p=0.019$) in nurses. Conversely, stress was associated with better judgement ($r=0.61$, $p=0.004$) in doctors. Stress, anxiety, and depression were also associated with mixed findings in both high and low-frequency brain activities (decreased theta, increased delta, decreased alpha, increased beta, decreased gamma). No associations were found between cortisol and mental health/cognitive performance measures.

These findings provide insight into the prevalence of mental health symptomology in Australian health professionals and suggest that negative mental states are associated with both improvements and impairments in cognitive performance. Unique variations in electroencephalographic changes were also linked to stress, anxiety, and depression; giving insight into what brain rhythms may underlie stress, anxiety, and depression, and how they may relate to various cognitive processes. Further research exploring the effects of negative mental states on personal wellbeing and cognition could enable the development of industry-specific management, monitoring, and/or intervention strategies aimed at preserving the health and performance of health professionals.

Chapter 1 – Introduction

1.1 The Australian Healthcare Network

Advancements in healthcare, especially over the past few decades, have been immense; typified by the adopting of new technologies, wider and better-tailored treatment options, and more precise and accurate diagnostic tools - all enhancing the ability of the industry to improve the quality of human life. Healthcare expenditure in Australia currently costs approximately 185.4 billion dollars, which is around 1.2% higher than average over the past few years (Australian Institute of Health & Welfare (AIHW), 2019). With Australia's growing and ageing population, there has been a corresponding increase in the demand for healthcare services: according to published data, it is expected that healthcare expenditure will continue to rise at a rate of approximately 5% every year (Productivity Commission, 2005; Willis & Elmer, 2007; Deloitte, 2015; Private Healthcare Australia, 2019).

Due to ongoing development and constant expansion of the health and medical fields, there have been significant improvements in the overall health and quality-of-life of society (Theodoropoulos, 2010). However, as growth in the field continues, the demand for people skilled in medical and health services also increases. Given the services provided by healthcare professionals, efforts to maintain a highly skilled workforce and sustain their capacity to work optimally are often well supported by the general public. Thus, both the role and importance of the healthcare system and its employees stand well recognised within society.

Australia's healthcare system consists of a combination of public and private providers (AIHW, 2018) comprised of hospitals, clinics, and government/non-government agencies. These providers deliver a wide range of services, including primary and emergency health care, in-patient and out-patient hospital-based treatments, preventive health care strategies, rehabilitation, aged care, and palliative care (Willis & Elmer, 2007). Within this multi-faceted system, the staff network consists of approximately six-hundred-thousand employees (AIHW, 2016a; AIHW 2018) who comprise the multidisciplinary team of doctors, nurses, allied health staff, and support

staff that play a vital role in ensuring that patient care is delivered to a high standard. The distribution of healthcare professionals from various sectors can be viewed in Figure 1.1. Although the Australian health workforce has increased considerably over the past few years, staffing increases have not kept up with population demands. This has placed increased strain not only on the healthcare system but individual employees within this system (Willis & Elmer, 2007).

Figure 1.1: The distribution of registered health professionals in Australia in 2014-2015

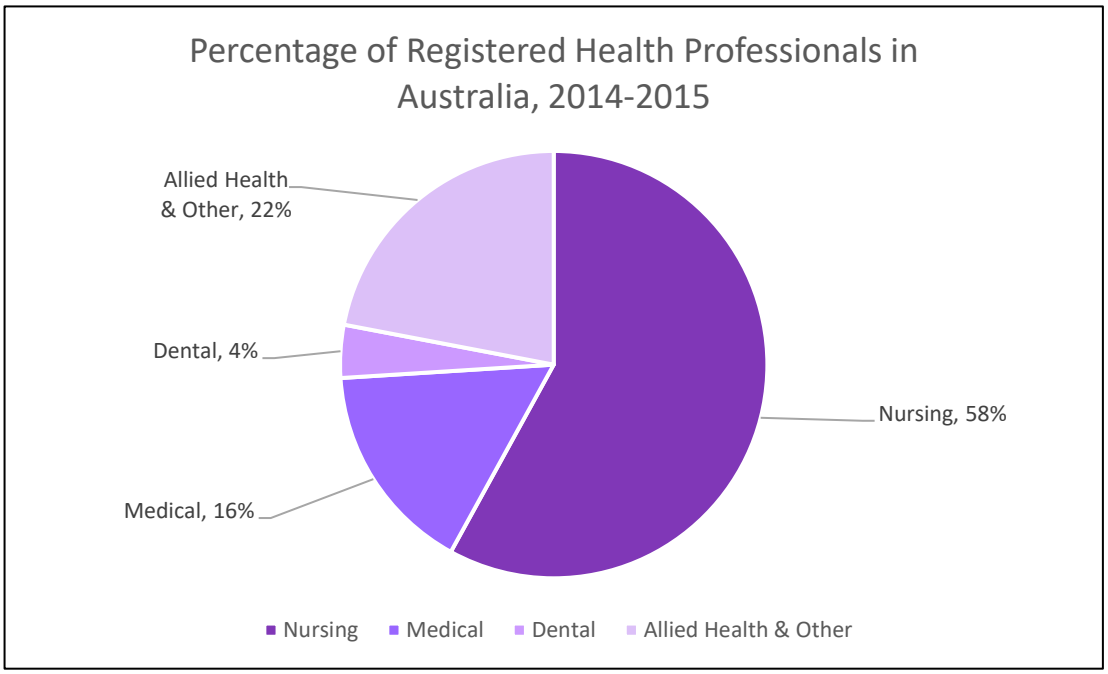


Figure 1.1 displays a pie chart with the percentage distribution of registered health professionals (by sector) in Australia for the period of 2014-2015. Nursing remains the largest sector, followed by allied health and medicine respectively (Australian Department of Health, 2019; AIHW, 2016a). *Image adapted from the Australian Institute of Health and Welfare (AIHW), 2016a.*

The effectiveness of a healthcare system, particularly in the provision of healthcare services, is strongly related to the various and unique roles associated with each professional who works within it (Theodopulous, 2010). Each professional group has a particular combination of training and experience that defines their roles and responsibilities (Australian Medical Association, 2011). Nurses have a broad workload as they provide support, care, and assistance to both patients and their families,

participate inpatient rehabilitation, and promote health education (Delucia et al., 2009). Such a broad and unique role allows nurses to work in many areas of the healthcare system and presents them with the most substantial amount of time spent with patients (Delucia et al., 2009). Therefore, they play an essential role in improving and promoting health services in the community.

Australia's medical system is also dominated by medical practitioners who train extensively to build upon expert knowledge (Willis & Elmer, 2007) and are thus primarily involved in clinical assessments, diagnosis, and prognosis of medical conditions. They also make critical judgments and decisions about the needs of their patients (Royal College of Physicians, 2005). They are also required to convey relevant medical information to other professionals while also empathically responding to the patient's and family's needs (Shaw, Brown, & Dunn, 2015). What makes their role so unique and complex is that medical practice is characterised by taking responsibility for overall clinical outcomes (Australian Medical Association, 2011), thus placing doctors in demanding leadership and management roles.

Finally, allied health professionals are support professionals who work in the healthcare team to assist in a person's medical care (Allied Health Professionals Australia, 2019). Together, allied health professionals represent the second largest sector of the health workforce and are estimated to deliver around 200 million health services annually (Allied Health Professionals Australia, 2019). The allied health workforce also continues to grow rapidly as demand grows across the aged care, mental health, disability, and health sectors overall (AIHW, 2016a; AIHW, 2018). Allied health professionals provide a broad range of diagnostic, technical, therapeutic, and direct health services; with each profession having a unique and demanding role that requires in-depth knowledge of their field (Allied Health Professionals Australia, 2019). Allied health professionals include but are not limited to physiotherapists, occupational therapists, pharmacists, imaging specialists (such as radiographers), optometrists, podiatrists, and psychologists (AIHW, 2016a; Allied Health Professionals Australia, 2019).

1.2 Mental Health in Healthcare Professionals

Despite their differing roles, previous studies have identified significant workplace stressors common to various health-related professions. For example, doctors have previously reported work-related stressors relating to heavy workloads, long working hours, the fear of making mistakes, and the high level of professional responsibility (Antoniou et al., 2016). Similarly, nurses have reported work-related stressors such as large workloads, long work hours, colleague's inexperience, meeting patients' needs, and a lack of support at work (Howard et al., 2014). Allied health professionals such as pharmacists, physiotherapists, and psychologists have also reported stressors associated with large workloads, time constraints, colleagues inexperience, a lack of support at work, lack of change (in their day to day role) and poor role autonomy (Cushway et al., 1994 & 1996; Lindsey et al., 2008; Santos, Barros, & Carolino, 2010; Wick, 2010). Heavy workloads and occupational demands placed upon healthcare providers have also been associated with poor mental health in both doctors and nurses (Chopra, 2009). While heavy workloads are widely acknowledged to adversely affect workplace performance and mental wellbeing, there is a lack of research exploring prevalence rates for stress and mental health disorders like anxiety and depression in Australian health professionals, especially in allied health professionals.

The stigma attached to mental health issues in medicine also compounds the issue. Doctors tend not to seek help and consequently have report higher rates of psychological distress compared to both the Australian general population and other Australian health professionals (BeyondBlue, 2013; Australian Medical Association, 2013). Prevalence rates for psychiatric distress seen in Australian medical professionals have ranged from around 20-42% and even 82% (BeyondBlue, 2013; Shehabi et al., 2008; Soares & Chan, 2016). Similarly, prevalence rates for psychiatric distress of approximately 25% have been seen in Australian medical students (Cheng et al., 2013). Globally, stress, depression, and anxiety rates in physicians range between 17-54% as seen in France (Kerrien et al., 2015), India (Saini et al., 2010), Pakistan (Khuwaja, Qureshi, & Azam, 2004; Atif et al., 2016), Tunisia (Marzouk et al., 2018), Iran (Assadi et al., 2007), China (Gong et al., 2014a), and the United Kingdom (Imo, 2017). Many studies (including the studies listed above) have also suggested that work-related

factors such as heavy workloads, long work hours, and low job satisfaction may contribute to a higher risk of developing negative mental states (Tyssen & Vaglum, 2002; Brooks, Gerada, & Chalder, 2011).

Prevalence rates for psychiatric distress in nurses are more heavily reported and remain similar to that of medical practitioners, with our own study of Australian nurses showing rates of 32%, 41%, and 41% for depression, anxiety, and stress, respectively (Maharaj, Lees, & Lal, 2019)[1]. By contrast, Australian Midwives have shown prevalence rates of 17% for depression (Creedy et al., 2017). Globally, rates for depression are wide-ranging from approximately 10-80% in countries such as the USA (Letvak, Ruhm, & McCoy, 2012; Welsh, 2009), Iran (Ardekani et al., 2008; Tabrizi & Kavari, 2011), China (Gong et al., 2014b; Cheung & Yip, 2015), and Brasil (Schmidt, Dantas, & Marziale, 2011), France and Canada (Ohler, Kerr, & Forbes, 2010; Nourry et al., 2014). A high incidence of anxiety in nursing professionals is also evident, with studies stating prevalence rates ranging from 20-66% in Australian Midwives (Creedy et al., 2017), Chinese nurses (Gao et al., 2012; Cheung & Yip, 2015), Iranian nurses (Nooryan et al., 2014), and Brasilian nurses (Veloso et al., 2016). Similarly, the few prevalence rates that have been presented for stress range from approximately 40–90% (Khan, Anwar, & Sayed, 2015; Al-Makhaita, Sabra, & Hafez, 2014; Gheshlagh et al., 2017; Kibria, 2018). Common predictive factors for having or acquiring a mental health disorder included poor job satisfaction, heavy workloads, shift work, sleep disturbance, and years employed (Ardekani et al., 2008; Welsh, 2009; Tabrizi & Kavari, 2011; Subih et al., 2011; Cheung & Yip, 2015; Khodadadi et al., 2016). Limitations in many of the studies listed above do exist as many (both locally and internationally) are confined to only registered/hospital nurses (excluding enrolled nurses and midwives) and also tend to focus on their occupational stress/coping and not their stress as a whole. Many also do not focus on depression and anxiety.

The various branches of allied health have shown similar rates of distress when assessing Australian professionals (Harris, Cumming, & Campbell, 2006). Rates have also been high in Pakistani physiotherapists at approximately 70%, 50% and 60% and

[1] See publication: Maharaj, S., Lees, T., & Lal, S. (2019). Prevalence and Risk Factors of Depression, Anxiety, and Stress in a Cohort of Australian Nurses. *International Journal of Environmental Research and Public Health,* 16(1), 61. https://doi.org/10.3390/ijerph16010061

Pakistani physiotherapy students at 48%, 68% and 53% for depression, anxiety, and stress respectively (Babur & Liaqat, 2018; Syed, Ali & Khan, 2018). Similarly, allied health students in Jordan have shown rates of approximately 60% for depression and anxiety, and 50% for stress (Almhdawi et al., 2018). Psychological wellbeing has not been commonly assessed in allied health professionals, presenting a major gap in current research. Therefore, despite assertions that rates of poor psychological wellbeing/psychiatric distress are elevated in all types of healthcare workers including allied health, the scope of the problem remains uncertain (Roy-Byrne, 1998).

Allied health professionals and nurses have however reported similar emotional strain. Many nurses have stated that they would leave the profession or choose not to practice due to a lack of professional support available at work (Hooper et al., 2010), which may exacerbate current staff shortages (Australian parliamentary inquiry, 2005; Delucia et al., 2009; Tuckett et al., 2015). Similar trends of absenteeism and poor retention of employees has also been seen in medical practitioners (Devi, 2011). Workplace stress plays such a substantial role in mental health issues such as depression and anxiety in healthcare professions, and the resultant cost to both the individual and industry is staggering (Centers for Disease Control and Prevention, 2008). The cost of workers' compensation claims associated with stress and stress-related mental disorders are noticeably greater in medicine and healthcare (costing approximately $200 million annually) compared to other occupations (Australia Safety & Compensation Council, 2006; Safework Australia, 2013). On average, individuals with mental health issues take approximately five days off work and have 11 days of reduced productivity annually (BeyondBlue, 2016). This equates to billions of dollars lost to absenteeism and lost productivity (Slade et al., 2009) which, if the same (or higher) levels of absenteeism and lost productivity are prevalent among health and medical professionals, are a substantial financial burden upon an industry that is already under financial strain. Absenteeism and lost productivity within the health workforce can also leave facilities understaffed and unable to meet patient demands, placing patients at risk.

Thus, with such demanding occupations, the ongoing strain faced by healthcare professionals may leave them at higher risk of developing stress, anxiety, or depression

(Stetz et al., 2007; Chopra, 2009; Chiang & Chang, 2012; BeyondBlue, 2013) as studies have shown that the ongoing stress faced by these professionals can have adverse effects on their psychological well-being (Chopra, 2009; BeyondBlue, 2013; Cheung & Yip, 2015; Jones et al., 2015). Poor mental health among healthcare providers may also hinder professional performance which can impact considerably on the quality of care they provide to patients (inevitably impacting negatively on patients' health) (Creedy et al., 2017; Maharaj, Lees, & Lal, 2019). Although it is broadly recognised that healthcare providers may be affected by poor mental health and that poor mental health may affect their ability to work optimally, little research has assessed just how prevalent negative mental states are. Also largely uninvestigated, are the impacts of stress, anxiety, and depression on the cognitive performance of clinically active healthcare professionals, even though previous literature has associated stress, anxiety, and depression with cognitive dysfunction (discussed further in Section 1.4). Given the around-the-clock nature of healthcare services, this should present a considerable concern, as any impact on the optimal cognitive performance of healthcare providers poses a risk to both professionals and their patients (Cecil & Glass, 2014).

1.3 Cognition

The human brain can be divided into four main lobes: the frontal, parietal, occipital and temporal lobes; each responsible for mediating different functions. While cognition can be sub-divided into individual constituent processes (discussed further below), mapping these directly onto the cerebral cortex becomes far more complex (Cambridge Cognition, 2019). Studies have localised specific brain regions that are heavily involved in distinct cognitive functions (as seen in Figure 1.2); however, mapping finite areas of the brain for all aspects of cognition remains challenging due to human variability and a lack of understanding with regards to underlying cortical neurobiology (Cambridge Cognition, 2019). Therefore, cognitive functioning is broadly defined as the sum of all cognitive processes resulting from communication from both within and between the different brain regions (Leto & Feola, 2014). Cognition fundamentally controls our thoughts and behaviours, which are precisely regulated by discrete brain circuits and neurotransmitter systems. Such systems include the dopaminergic, noradrenergic, serotonergic, and cholinergic systems (Bear et al., 2007; Cambridge Cognition, 2019).

The cognitive processes that underpin our daily lives include but are not limited to the way in which we perceive, manage, and utilise information. As such, cognition involves a variety of abilities categorised into domains, such as memory (which involves encoding, storing, and retrieving information), language (which involves speaking, comprehension and general communicative activities), visuospatial ability (involving the ability to identify visual and spatial relationships and being able to mentally represent and manipulate objects), and executive functioning (commonly used as a collective term for various higher-order functions - which are functions that require high loads of mental effort such as judgment, abstract reasoning, and problem solving) (Brandimonte et al., 2006; Ellis, 2019; Zlotnik & Vansintjan, 2019).

Cognitive skills play an essential role in day-to-day functioning and can influence mental alertness, workplace productivity, conscious decision-making, and personal well-being (Mograbi et al., 2014). Thus, declines in cognition may easily be associated with reductions in an individual's productivity, skill, and overall ability. Cognition can be assessed in various ways, including physiological measures and more commonly, psychometrics. Psychometric tools remain the most common form of assessing cognitive performance as they often provide a clear, direct, and often rapid measure of cognition (Fisher, Chacon, & Chaffee 2019).

Figure 1.2: The four lobes of the cerebrum and their associated functions

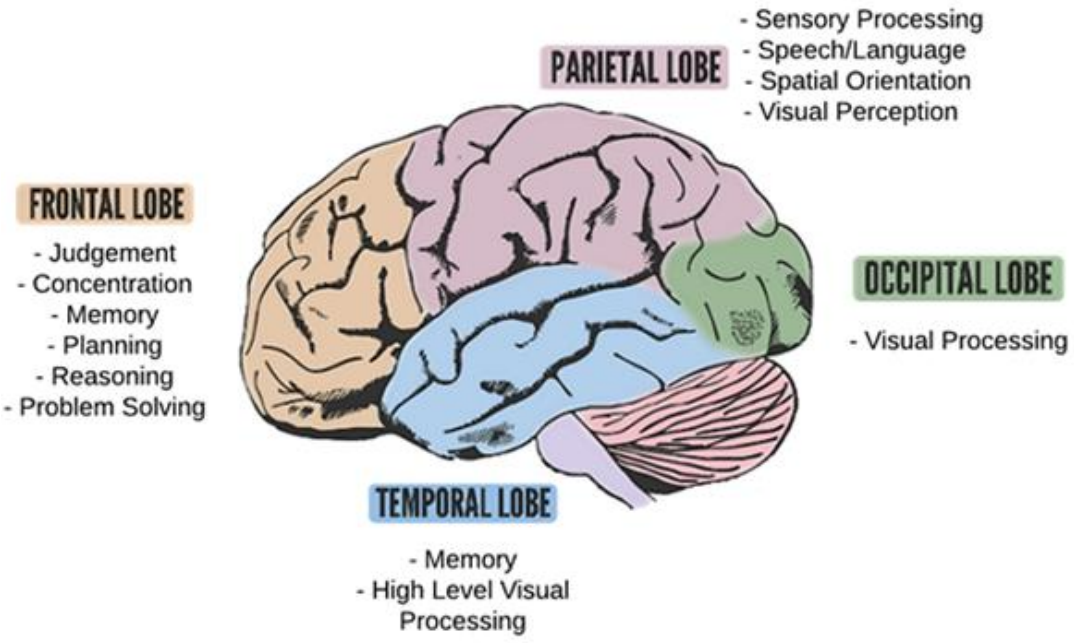


Figure 1.2 displays an image of the brain separated (by colour) into its four lobes. Accompanying each lobe is a list of functions associated with that particular brain region. Note: Each list contains **some** but **not all** of the functions associated with its corresponding lobe). *Image adapted from Mohsenin, 2012 [online].*

1.3.1 Psychometric Measures of Cognition

Psychometric tools are standardised scientific measures used to assess an individual's cognitive ability and are the most common form of measuring cognitive performance (Fisher, Chacon, & Chaffee 2019). Common psychometric test batteries used to assess cognitive performance include the Cambridge Neuropsychological Test Automated Battery (CANTAB) (Cambridge Cognition, 2019), the Wechsler Adult Intelligence Scale (WAIS) (Wechsler, 2008), the Mini Mental State Examination (MMSE) (Folstein et al., 1975), and the Cognistat (Mueller et al., 2007) (see Table 1.1 below for a comparison). Although the CANTAB and the WAIS are comprehensive and highly validated tools (Cronbach's alpha 0.65-0.87 and 0.87 respectively) that are commonly used in both clinical and research settings (Weschler, 2008; Holdnack et al., 2011; Smith et al., 2013; Kim et al., 2014; Syvaoja et al., 2015), both tools only measure a limited number of cognitive domains. They are also time-consuming to administer, expensive, and are not readily available without specialist qualifications (Climie & Rostad, 2011; Hartman, 2009; Pearson Clinical, 2019).

In contrast, the MMSE is a short and simple cognitive screening tool to administer, and it provides a measure of global cognitive performance. However, the MMSE may be affected by demographic factors such as age (Friedman, 2012) and its use of a single global score may also present the risk of false negatives. Thus, to increase sensitivity for identifying cognitive impairment, the MMSE is commonly used in combination with the Cognistat (Tombaugh & Mcintyre, 1992; Macaulay et al., 2003; Mueller et al., 2007). The Cognistat is a relatively short cognitive assessment tool that utilises a collection of abbreviated subscales that are modelled from more extensive and well-validated neuropsychological tests. Therefore, it allows for a more comprehensive assessment of cognitive status while being relatively short in duration (Logue et al., 1993; Allen, 2011). The Cognistat also presents its results as a graphic representation of strengths and weaknesses by domain (rather than a single global score), producing a differentiated profile of cognitive abilities. (Kiernan et al., 1987; Friedman, 2012). Both the MMSE and the Cognistat are reliable and validated measures (Chronbach's alpha 0.89 and 0.81 respectively) that are easily accessible, cost-effective, and time-efficient; allowing for a thorough cognitive assessment of both global and domain-specific performance whilst

assessing many cognitive domains (Hinkle, 2002; Mystakidou et al., 2007; Mueller et al., 2007). The MMSE and Cognistat are both used extensively in clinical and research settings to measure/screen for cognitive impairment and are also commonly used to estimate impairment severity and progression (by following cognitive changes in an individual over time) (Shim et al., 2017). Therefore, the MMSE and Cognistat were chosen to assess cognitive function in the present doctoral investigation.

Table 1.1: Comparison of four commonly utilised psychometric tools

Psychometric Tool	Qualification Restrictions/ Training required	Price Range ($)	Global or Domain Specific Assessment	Number of Cognitive Domains Assessed	Minimum Duration of Assessment
CANTAB	No/No	300 - 5000	Domain Specific	4	20 minutes
WAIS	Yes/Yes	800 - 2000	Both	4	60 minutes
MMSE	No/No	Free	Global	-	10 minutes
Cognistat	No/Yes	Free	Both	12	20 minutes

Table 1.1 displays a comparison of four commonly utilised psychometric tools that assess cognition & screen for cognitive impairment. The price range is for AUD.

Key: CANTAB = Cambridge Neuropsychological Test Automated Battery (Cambridge Cognition, 2019), WAIS = Wechsler Adult Intelligence Scale (Mueller et al., 2007), MMSE = Mini Mental State Examination (Folstein et al., 1975)

1.3.2 Psychometrics and Cognitive Performance

The Mini-Mental State Examination (MMSE) is a brief psychometric tool that screens for cognitive impairment in adults. It advantageously requires no specialised training or equipment for its administration (Lancu & Olmer 2006). As shown by Yuseph *et al.* (1997), when administered in combination with other neuropsychological measures, the MMSE can predict Mild Cognitive Impairment (MCI) and minor declines in cognitive performance with high accuracy (87%) in individuals with Alzheimer's (n=71, gender breakdown not stated, mean age=77±5.0 years). Reviews by Lancu & Olmer (2006) and Tsoi *et al.* (2015) also noted good construct validity and accuracy of the MMSE. Somewhat similar were the findings of a meta-analysis by Mitchell (2009) who indicated that the MMSE had high accuracy rates in individuals with dementia but

lower accuracy when needed to identify more subtle forms of MCI. Marsh *et al.* (2000) also concluded that the MMSE had poor predictive ability in participants with more subtle or non-verbal impairments in cognition (n=73, 36 females, mean age=75±13 years). Lannin & Scarcia (2004) found that the MMSE had good internal consistency but poor sensitivity when used alone, as it did not solely detect cognitive impairment in any of the subjects that they assessed (n=14, 5 females, mean age=56±15 years). Likewise, Larner (2018) also found the MMSE to show high specificity (0.80) but poor sensitivity (0.64) for identifying cognitive impairment. However, it is noteworthy that the MMSE's sensitivity for detecting impairments does increase with higher levels of impairment (Lancu & Olmer 2006). Therefore, the MMSE is a reliable and validated screening tool that is widely recommended for the screening of early cognitive impairment.

Previous literature has also established the clinical utility of the Cognistat in measuring cognitive status (Doninger et al., 2006; Lannin & Scarcia, 2004). Gupta and Kumar (2009) assessed the internal reliability of an Indian adaptation of the Cognistat in individuals with traumatic brain injury (n=30, 5 females, mean age=34±11 years) and healthy controls (n=55, 29 females, mean age=27±8.5 years). Gupta's study also noted a strong Cronbach's alpha value of 0.94, which was further supported by Hinkle (2002), who also showed good internal consistency with a Cronbach's alpha value of 0.81 when using the English version of the Cognistat (n=100, 49 females, mean age=65±15 years). Similarly, Nesset *et al.* (2014) also found that the Cognistat was able to significantly predict the progression of mild cognitive impairment to dementia (n=64, 49 females, mean age=74±7.9 years). Additionally, Johansson *et al.* (2014) found that the Cognistat was more sensitive than the MMSE with the same specificity (n=46, 22 females, mean age=79±5.2 years), thus making it more reliable than the MMSE alone. However, in Johansson's study, no discussion was given on domain-specific results, and thus, false positives may have occurred if only the screen measure of Cognistat was used (Pichitino & Green, 1999; Smith et al., 1999) rather than the screen and the metric measure together. The failure of the Cognistat screen questions is further supported by Smith *et al.* (1999) who administered the Cognistat to geriatric males (n=341, mean age=77 years) and found a combination of high screen failure rates and high metric pass rates, suggesting that the screen alone may not be an effective method of administration.

It should be noted that most studies that have utilised the Cognistat and the MMSE have assessed elderly populations which do not correlate with the age range being used in the present investigation (18-69 years). Further limitations may arise if studies only used the screen scoring system for the Cognistat, which as mentioned above, may yield false positives (Pichitino & Green, 1999).

1.3.3 Physiological Measures of Cognition

The brain remains one of the most complex organs in the human body. Due to its inherent complexity and its trillions of connections, it remains difficult to study (Woodruff, 2016). Direct measures of brain function allow scientists to identify minute changes in brain activity and are advantageous as they can provide information (such as the rate and the source of neural activity) that other physiological measures (e.g. heart rate variability and skin conductance) cannot (Woodruff, 2016). Several neurological techniques exist to assess brain function. These include Magnetic Resonance Imaging (MRI), Functional Magnetic Resonance Imaging (fMRI), Positron Emission Tomography (PET), and Magnetoencephalography (MEG). While these neuroimaging modalities afford researchers robust spatial resolution, they are often costly, invasive, time-consuming, lack portability, and/or are indirect (as they detect indirect metabolic signals rather than neuronal activity) (Crosson et al., 2010). Extensive formal training is also required for correct and proper usage of the aforementioned imaging modalities. One neurophysiological measure that does not present with such limitations is electroencephalography (EEG). Compared to the neuroimaging techniques outlined above, EEG is non-invasive, widely available, cost-effective, and requires minimal training. It also provides researchers with excellent temporal resolution and direct access to neuronal signalling (Crosson et al., 2010). Therefore, EEG was chosen as the objective physiological measure of cognition in the current study. A comparison between EEG, MRI, and fMRI can be seen in Figure 1.3. Furthermore, EEG can be measured easily under both resting and active conditions (Modi & Sahin, 2017). EEG also allows for the use of Event-Related Potentials (ERP) which are obtained from regular EEG recordings. However, ERP's are used to track specific responses to a specific stimulus (Woodman, 2010). The current investigation

did not aim to measure a specific response but rather a change in activity between two phases; hence, ERP was not utilised in the current investigation.

Electroencephalography provides a cost-effective tool for detecting subtle changes in brain activity and cognition, and its use is becoming increasingly popular (Al-Qazzaz et al., 2014). EEG specifically measures the electrical activity of cortical neurons distributed throughout the cerebral cortex (Al-Qazzaz et al., 2014). Neural oscillations arise from many brain regions and contribute to different functions in each of these regions (Modi & Sahin, 2017). This activity, which the literature broadly classifies as either low-frequency or high-frequency oscillations, falls into distinct bands/rhythms and indicate different behavioural states (Figure 1.4). Low-frequency oscillations (such as delta and theta activity) often underlie coordinated activity between distal regions and are therefore commonly associated with sleep and drowsiness, whereas high-frequency oscillations (such as alpha, beta, and gamma activity) often reflect local processing (Modi & Sahin, 2017) and more commonly underlie higher-order/active cognitive abilities. Declines in cognition are therefore most often associated with reduced activity in high-frequency brain rhythms (alpha, beta, and gamma) and increased activity in low-frequency brain rhythms (delta and theta) (Koenig et al., 2005; Aurtenetxe, 2013). As negative mental states may be associated with declines in cognitive performance, this decline may be measured using electroencephalography. Furthermore, the use of simple and non-invasive measures such as EEG may also present as a cost-effective and time-effective way to identify potential biomarkers for cognitive decline.

Figure 1.3: A comparison between Electroencephalography, Magnetic Resonance Imaging, and Functional Magnetic Resonance Imaging

	EEG	MRI	fMRI
Temporal resolution	High	Low	Low
Spatial resolution	Low	High	High
Measures brain activity?	Directly	Only structure	Indirectly (BOLD response)
Level of expertise needed	Some training	Extensive training	Extensive training
Cost	Accessible to many researchers	Requires extensive funding	Requires extensive funding
Portability	Both fully portable and semi-portable devices available	Not portable	Not portable

Figure 1.3 displays a comparison between electroencephalography (EEG), Magnetic Resonance Imaging (MRI), Functional Magnetic Resonance Imaging (fMRI), showing their advantages and disadvantages. *Image adapted from Farnsworth, 2019 [online].*

Figure 1.4: The five major brain rhythms measured by electroencephalography

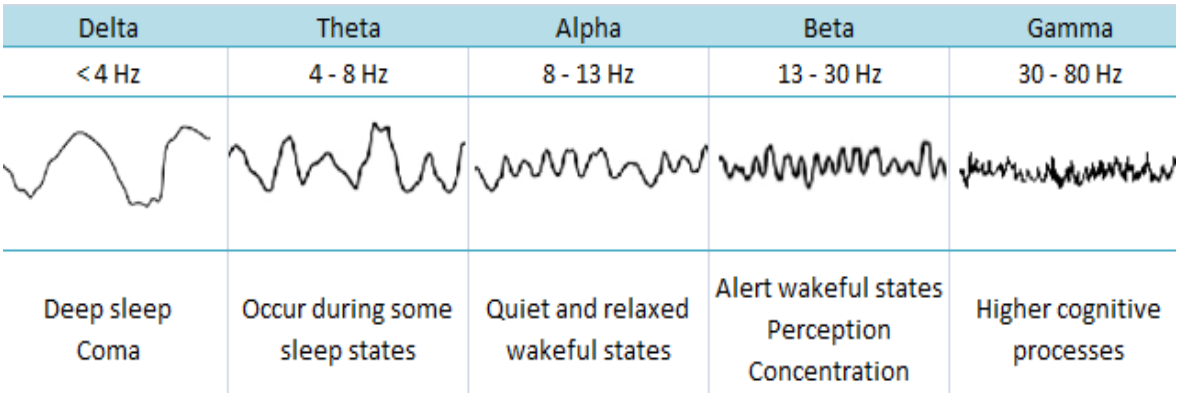


Figure 1.4 displays the five major brain rhythms; their frequency in hertz (Hz), their amplitude/what they look like, and the physiological states they pertain to. *Image adapted from Bear et al., 2007 – pg.598.*

1.3.4 EEG and Cognitive Performance

Fluctuations in gamma-band activity receive large amounts of interest due to their correlations with cognitive processes (Herrmann, Frund, & Lenz, 2010; Merker 2016; van Es & Schoffelen, 2019). Deficits in gamma rhythm maintenance and gamma rhythm generation are thought to reflect less efficient or degraded neural synchronisation and activity (Brenner et al., 2003) which are commonly considered important mediators of higher cognitive processes (Light et al., 2006; Cho et al., 2006). A study by Tao and Tian (2005) found that gamma-band coherence was lower during both rest and cognitive tasks in individuals with Alzheimer's (n=12, 7 females, mean age=96.4±9 years) and MCI (n=18, 10 females, mean age=70.3±13.3 years) when compared to controls (n=10, 5 females, mean age=67.9±9.6). Krishnan *et al.* (2009) additionally noted that a failure to maintain gamma-band oscillatory activity was also reflective of poorer cognitive performance in schizophrenics (n=21, 8 females, mean age=43±10 years). Similarly, Missonnier *et al.* (2010) and Lee *et al.* (2010) noted deficits in gamma activity for both MCI (n=29, gender breakdown not reported, age range=77–91 years) and Alzheimer's patients respectively (n=25, 20 females, mean age=74±7.2 years). This outcome was also supported by Basar *et al.* (2016), who found that cognitively impaired Alzheimer's patients showed heavily delayed gamma responses (n=15, 7 females, mean age=68±6.5

years). The trend of gamma deficiencies in cognitively impaired groups has also been supported by numerous other studies associating declines in cognitive activity with declines in gamma-band EEG activity (Yeragani et al., 2006; Brenner et al., 2003; Cho et al., 2006; Light et al., 2006; Pachou et al., 2008; Sharma et al., 2010). Though many studies show similar results, it should be noted that frequencies for specific brain activity may vary slightly between studies. For example, studies may present the upper and lower limits of gamma activity to be anywhere between 20-45Hz (also true for the other EEG brain rhythms such as delta, theta, alpha and beta) (Fisch & Spehlmann, 1999; Yeragani et al., 2005; Pachou et al., 2008). However, variations in upper and lower limits between studies are often minimal.

In contrast to the above findings, Van-Deursen *et al.* (2008) found an increase in gamma-band activity in individuals with Alzheimer's (n=15, 4 females, mean age=75±6.9 years) while no differences were seen in healthy controls (n=20, 8 females, mean age=70±6.1 years) or individuals with MCI (n=20, 8 females, mean age=71±7.2 years). Similarly, Wang *et al.,* (2017) also found enhanced gamma rhythm power (in addition to increased delta and alpha activity) in patients with Alzheimer's (n=8, 4 females mean age=76.9±0.7) compared to controls (n=12, 5 females, mean age=73.7±2.3); however, the small sample size remains a downfall as it limits the generalisability of Wang's study. While increases in gamma activity are often considered reflective of better cognitive functioning, it has been suggested that the increase in gamma activity seen in individuals who suffer from forms of cognitive impairment, may be reflective of increased effort and the use of more neural resources. This, in turn, may be viewed as a functional compensation mechanism; and would therefore not necessarily reflect better cognitive performance (Van-Deursen et al*.,* 2008; Wang et al., 2017). Furthermore, Moretti *et al.* (2009) found an increase in EEG theta/gamma ratio to be associated with memory impairment (n=49, 31 females, mean age=68.5±6.9 years) while Barr *et al.* (2010) found an increase in gamma-band activity in patients with schizophrenia (n=24, 10 females, mean age=37±11 years) and controls (n=24, 11 females, mean age=38±10 years) during a working memory task. It is possible that as task difficulty increased in Barr's study, gamma activity also increased as controls may use various cognitive strategies to cope with increasing task demands,

whilst schizophrenics utilised more cognitive resources for high-demand tasks (Başar-Eroğlu et al., 2007).

Increases in synchronous EEG activity may also reflect a major mechanism for integrating the activity of multiple brain regions, usually reflecting better cortical functioning (Tallon-Baudrey et al., 1988; Basar et al., 1999; Basar et al., 2013). As such, Stam *et al.* (2003) assessed cognitively impaired subjects and noted that declines in beta synchronisation were linked to declines in cognitive performance (n=54, 33 females, age range=51-89 years). However, declines in other EEG frequency bands were not observed, suggesting that beta activity may be of significant importance (Kim et al., 2009). The findings noted in Stam's study may reflect the specific pathology of Alzheimer's rather than the general ageing process (considering the upper age range for the study was quite high) as the two impaired groups showed similar impairments, despite the age difference between groups. Similarly, Pijenburg *et al.* (2004) assessed cognitive performance in patients with Alzheimer's during both a resting state and working memory task (n=14, 7 females, mean age=76±14 years) concluding that a decrease in beta synchronisation occurs, which is suggestive of a lack of functional interaction. This was further supported by both Missonnier *et al.* (2007), who noted declines in beta synchronisation in MCI patients (n=29, gender breakdown not stated, age range: 57–91), and Kim *et al.* (2009), who noted that decreased beta activity was associated with poorer cognitive performance (n=25, 21 females, mean age=74±7.7 years). Similar reductions in beta power and activity were also observed by Wang *et al.* (2013) who assessed cognitively impaired patients following cerebral infarcts (n=110, 30 females, mean age=71±11.9).

In contrast, Güntekin et al., (2013) found that healthy controls (n=17, 9 females, mean age=69±5.5 years) showed increases beta-band EEG activity during cognitive load, whilst subjects with MCI did not (n=17, 7 females, mean age=71 ± 5.6 years), suggesting that cognitive impairment is not associated with beta rhythm variations. Finally, a more recent study by Kaiser *et al.* (2017) also found increases in beta EEG activity to be associated with delayed memory recall in female geriatric patients (n=28, mean age=80.6 years). As previously discussed, the increase in high-frequency EEG activity seen in cognitively impaired individuals may reflect a compensatory mechanism where

individuals utilise more neural resources without improving performance (Jiang, 2005). Jiang (2005) supported this notion, finding that while psychometric cognitive scores between patients with MCI (n=35, 18 females, age range: 52-71 years) and healthy controls (n=34, 17 females, age range: 51-63 years) did not differ significantly, the MCI patients did show significant increases in both high and low-frequency EEG activity while controls did not.

A large cohort study by Koenig *et al.* (2005) examined EEG synchronisation in individuals with Alzheimer's and MCI (n=419, gender breakdown not stated, age range=58-63 years), noting decreased activity in all three high-frequency bands (alpha, beta, and gamma), increased delta activity, but no change in theta activity in cognitively impaired individuals. Reductions in alpha EEG power were also related to poorer cognitive performance in a study by Luckhaus *et al.* (2008) who assessed cognitively impaired individuals (n=132, 55 females, mean age=68±10 years) and Choi et al. (2019) who assessed healthy older individuals (n=496, 331 females, mean age=67.8 ± 9.8). Various other studies have also reported reductions in alpha EEG activity in cognitively impaired individuals with MCI and Alzheimer's (Jackson & Snyder, 2008; Babiloni et al., 2006a & 2016). However, both Trejo *et al.* (2005) and Rossini *et al.* (2006) had conflicting findings to the studies above, stating that alpha rhythms may actually increase in cognitive impairment when assessing healthy individuals (n=16, 4 females, mean age= 27±7.4 years) and subjects with MCI (n=69, 41 females, mean age=71.4 years) respectively. Moretti (2015) also found increases in alpha activity which were associated with cortical thinning in patients with MCI (n=74, 38 females, age range: 57-85). It is also possible that increases in high-frequency activity may be related to clinical affective disturbances such as anxiety (Huang et al., 2000; Isotani et al., 2001). This may result in cognitive impairment without a progressive course. Thus, increases in high-frequency alpha activity (potentially associated with negative affect) may still be associated with cognitive impairment. The overall conflicting nature of the above studies raises doubts about the certainty of not only alpha EEG activity but also beta and gamma EEG activity in cognitively impaired individuals. Therefore, this area of research warrants further investigation.

Although Koenig *et al.* (2005), found no change in theta activity in cognitively impaired patients (n=419, gender breakdown not stated, age range=58-63 years), Van der Hiele *et al.* (2007) showed increases in theta activity in addition to decreased alpha reactivity both related to decreases in cognitive performance in probable Alzheimer's patients (n=16, 7 females, mean age=78±8). Aurtenetxe *et al.* (2013) conversely found a significant increase in theta activity (in addition to finding decreases in delta activity) in patients with MCI suggesting the increase as a compensatory mechanism (n=25, gender breakdown not stated, mean age=75±4.8 years). Jelic *et al.* (2000) also found increases in theta power in individuals with MCI (n=27, 9 females, age range=47-69 years). Their work is supported by Huang *et al.* (2000), who also found an increase in low-frequency bands (delta and theta) and reduced alpha power in cognitively impaired patients (n=69, 37 females, mean age=63±7.1 years). In contrast, Missonnier *et al.* (2006) suggested that cognitive decline may be predicted by a decrease in theta power in MCI (n=24, 19 females, mean age=84±4.6 years), which was supported by Cummins *et al.* (2008) (n=12, 4 females, mean age=68±8.3 years) who also assessed individuals with MCI. Decreases in theta activity may be associated with cerebral atrophy (Devanand et al., 2007) and decreased white matter integrity (Müller et al., 2005) in medial temporal regions (associated with the generation of theta activity), possibly reflecting altered theta generation/transmission between the brain regions. While these neuropathological changes are commonly observed in patients with Alzheimer's and MCI, they may not be seen in all individuals with negative mental states.

Cognitively impaired individuals have also been shown to exhibit increases in delta activity (Brunovsky et al., 2003). However, this is not consistently reported in those with more minor/subtle cognitive impairments (Dimpfel, 2014; Fauzan & Amran, 2015). Conversely, Huang *et al.* (2000) found increases in delta activity in all of their cognitively impaired participants, including those who were only mildly impaired (n=69, 37 females, mean age=63±7.1 years). This was further supported by Brunovsky *et al.* (2003) who estimated the degree of cognitive impairment in Alzheimer's disease from EEG, noting that increases in delta power were associated with poorer cognitive performance (n=38, 21 females, mean age=71±7.4 years). In contrast, Babiloni *et al.* (2006b) showed findings that were only in partial agreement to those above as they found a significant increase in delta activity in Alzheimer's patients (n=28, 20 females,

mean age=77±1.3 years) but did not associate this activity with declines in cognitive ability. Further ambiguity was introduced in a review by Jackson & Snyder (2008) who in opposition suggested that the resting EEG of cognitively impaired individuals demonstrate a decrease in delta power. The discrepancies seen between these studies cast doubt on the role of delta activity in cognitive performance.

A summary of the various EEG findings discussed above in Section 1.3.4 can be seen in Table 1.2 (below).

Table 1.2: Summary of the EEG findings reviewed

Study	EEG Activity				
	Gamma	Beta	Alpha	Theta	Delta
Huang et al., 2000			↓	↑	↑
Jelic et al., 2000		↓		↑	
Brenner et al., 2003	↓				
Brunovsky et al., 2003			↓		↑
Stam et al., 2003		↓			
Pijenburg et al., 2004	↓	↓	↑		
Koenig et al., 2005	↓	↓	↓	NC	↑
Tao & Tian 2005	↓				
Trejo et al., 2005			↑		
Yeragani et al., 2006	↓	↓			
Babiloni et al., 2006					↑*
Jiang 2005		↑	↑	↑	↑
Missonnier et al., 2006				↓	
Rossini et al., 2006			↑	↑	↑
Missonnier et al., 2007		↓			
Van der Hiele *et al.* (2007)			↓	↑	
Cummins et al., 2008				↓	
Jackson & Snyder 2008			↓		↓
Luckhaus et al., 2008			↓		
Van-Deursen et al., 2008	↑				
Kim et al., 2009	↓	↓			↓
Krishnan et al., 2009	↓				
Moretti et al., 2009	↑			↑	
Barr et al., 2010	↑	↓*			
Lee et al., 2010	↓	↓			↑
Missonnier et al., 2010	↓				
Wang et al., 2013		↓			
Guntekin et al., 2013		NC			
Aurtenetxe et al., 2013	↓	↓	↓	↑	
Moretti 2015			↑		
Basar et al., 2016	↓				
Wang et al., 2017	↑		↑		↑
Kaiser *et al.,* 2017		↓			
Choi et al. (2019)			↓		

Table 1.2 displays a summary table of the studies looking at EEG activity and cognitive performance. * changes were observed but were not significantly correlated to cognitive performance.

Key: ↓ = Declines in activity ↑ = Increase in activity NC = No Change

1.4 Negative Mental States and Cognition

Australian government spending on mental health services has increased substantially over the past few years, now costing approximately $9 billion annually (AIHW, 2018b). Mental health issues affect approximately half of the Australian population at some point throughout their lifetime (AIHW, 2019). Given the prevalence of mental health disorders are increasing, so too are the economic, social, and individual impacts of these disorders (Doran, 2013).

Depressed and anxious workers tend to have trouble concentrating, are accident-prone, have limited ability to perform mental and interpersonal tasks, and struggle with time management. Productivity is also generally lower in those with depression or anxiety (Letvak, Ruhm, & McCoy, 2012; Marizitti et al., 2010). This decline in performance is detrimental to any workplace; however, in clinical settings, these declines are significant, as they may lead to declines in the quality of patient care provided and increases in the frequency and severity of adverse medical events and clinical errors (Berland et al., 2008; Lees & Lal, 2016). In Australia, the direct hospital costs associated with adverse medical events have been estimated at approximately $900 million a year which can add up to 18% to the total inpatient budget (Ehsani, Jackson, & Duckett, 2006). With approximately 200,000 adverse medical events possibly resulting from human error within the healthcare team (AIHW, 2013), and with stress already associated in over 50% of all adverse events (Wilson et al., 1999), it has become increasingly important to understand what factors may be influencing the number of these adverse events/errors.

1.4.1 Stress

Stress can commonly be defined as any shift or disturbance to an individual's internal/external environment, disrupting homeostasis (Stephens & Wand, 2012), and is usually caused by intrinsic or extrinsic adverse forces (stressors) (Tsigos, 2016). More conventionally, it can also be defined as feeling overloaded, worried, and tense; and can be either acute (short-lived) or chronic (ongoing) (Bear et al., 2007). Acute stress can further be defined as either beneficial (eustress) or detrimental (distress) to performance; while chronic stress can lead to an imbalance of stress hormone levels

due to the desynchronization of the Hypothalamic-Pituitary-Adrenal (HPA) axis (Lucassen & Cizza, 2012).

The human body aims to counteract stress using an intricate repertoire of physiologic and behavioural responses that ultimately aim to maintain and/or re-establish homeostasis (Tsigos, 2016). The physiological stress response primarily involves the autonomic nervous system (ANS) and the HPA axis (Habib et al., 2001). The autonomic response involves the sympathetic nervous system which engages the body's 'fight or flight' response and regulates bodily functions such as heart rate, pupil dilation, digestion, respiration, and temperature regulation (Anderson et al., 2019). A longer-term neuroendocrine response involving the HPA axis is also initiated. The HPA axis involves the stimulation of the hypothalamus by the amygdala which starts a chain of events resulting in cortisol release from the adrenal cortex (Figure 1.5 & 1.6) (Andreassi, 2000). This increase in cortisol levels is considered the main physiological correlate of stress (Anderson et al., 2019). The biological effects of glucocorticoids (steroid hormones such as cortisol) are usually adaptive; however, inadequate, or excessive HPA-axis activation may be disruptive long-term (Smith & Vale, 2006). Cortisol aims to help regulate the magnitude and duration of HPA activation by providing negative feedback to the hippocampus (Figure 1.6) to inhibit the stress response, preventing excessive exposure to stress hormones. However, as previously mentioned, chronic stress can lead to excessive amounts of cortisol, which can damage hippocampal cells responsible for regulating this feedback process (Bear et al., 2007).

Figure 1.5: The physiological stress response involving the Hypothalamic-Pituitary-Adrenal axis

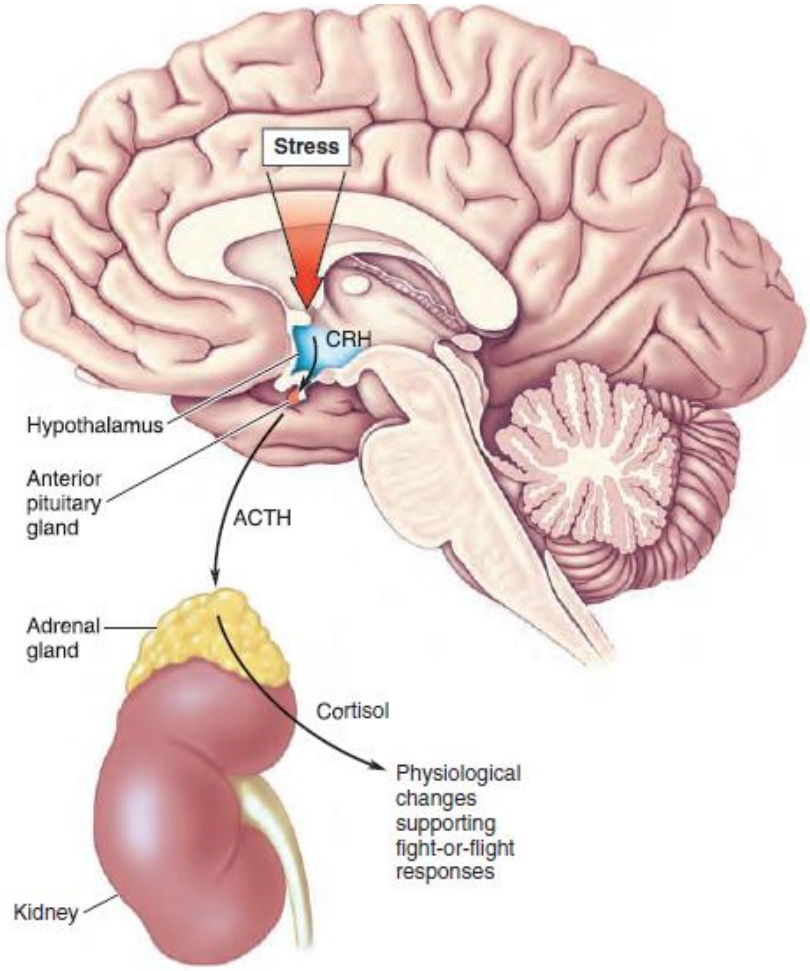


Figure 1.5 displays the physiological stress response via the Hypothalamic-Pituitary-Adrenal axis. Stressful stimuli activate the amygdala, which in turn activates the hypothalamus to release corticotropin-releasing hormone (CRH). CRH acts on the anterior pituitary gland to release adrenocorticotropic hormone (ACTH) which acts on the adrenal gland to synthesis and release cortisol. Cortisol release from the adrenal cortex also acts on the hippocampus to inhibit the HPA response via negative feedback (indicated by red lines). *Image adapted from Bear et al., 2007 – pg. 668.*

Figure 1.6: Regulation of the Hypothalamic-Pituitary-Adrenal axis

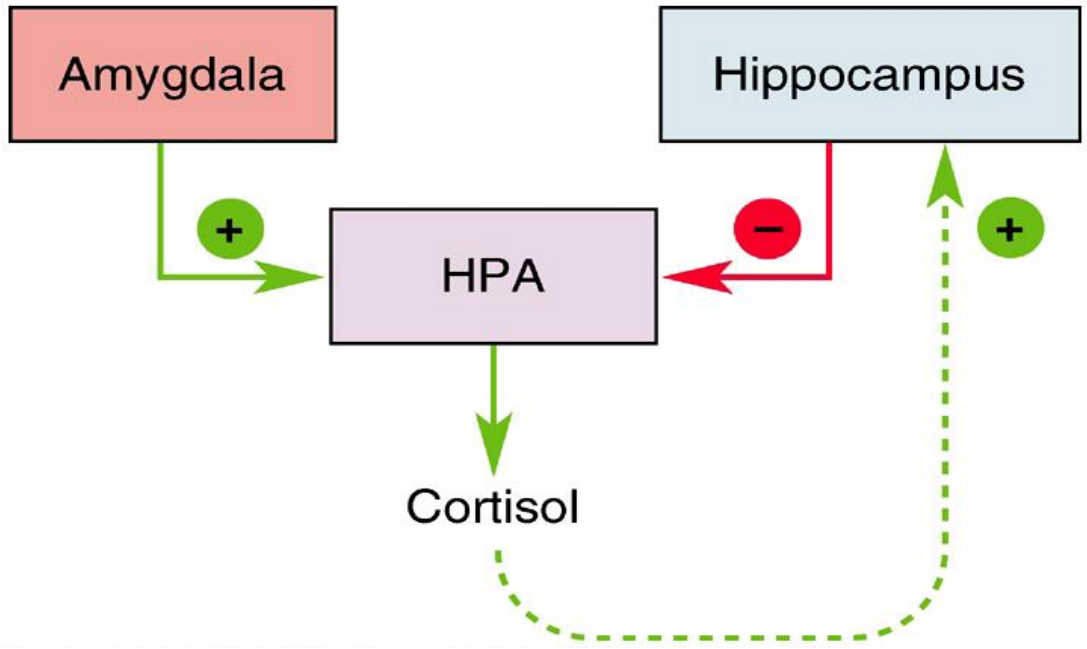


Figure 1.6 displays the regulation of the Hypothalamic-pituitary-adrenal (HPA) axis via both negative and positive feedback. Communication from the amygdala initiates the stress response involving the HPA axis. This response elicits the release of cortisol from the adrenal cortex which in turn acts on the hippocampus to inhibit the HPA response. *Image adapted from Bear et al., 2007 – pg.670.*

1.4.2 Stress and Cognitive Performance

Previous literature has investigated the link between stress and cognitive performance; however, the results between studies have often been contradictory. An early study by Keinan (1987a) found that individuals with higher levels of distress showed poorer task performance as they tended to rush and over-examine alternative answers. Thus, they made decisions earlier than necessary, resulting in a large number of errors (n=101, 59 females, age range=20-40 years). A second study by Keinan *et al.* (1987b) affirmed the proposition that high amounts of stress and anxiety impair attention and decision making as stressed subjects employed disorganised and incomplete scanning patterns, thereby lowering the quality of their decision outcomes (n=38, 14 females, age range=20-29 years). In contrast, a study by Duncko *et al.* (2007) examined the effects of acute stress exposure on visuospatial ability, learning, and memory performance (n=28,

males, mean age=26±4.8 years) and found that the stress group performed significantly better in each task when compared to controls. Schwabe *et al.* (2008) also found that stress could improve memory and recall (n=96, 48 females, age range=19-37 years), which was further supported by Human *et al.* (2013) who found improved memory performance after exposure to an acute stressor in healthy males (n=38, age range=18-23 years). Likewise, Beste *et al.* (2013) noted improved task processing efficiency/cognitive flexibility in males (n=36, mean age not stated) in addition to Bos *et al.* (2014) who noted better recall and fewer errors in a memory task following stress exposure (n=73, 41 females, age range=18-29 years). The improvements in performance seen following stress exposure may suggest a consistent pattern with the inverted U-shaped hypothesis (Yerkes & Dodson, 1908). Under this hypothesis, moderate levels of stress are able to support performance, whereas exceedingly high or low levels of stress may impair performance.

In agreement with the inverted U-hypothesis, which focuses on the amount of stress placed on an individual and the exposure time - other studies have also noted that the type of stress in addition to how it is perceived, can have a significant impact on cognitive abilities (Skinner & Brewer 2002; Payne et al., 2007; Kassam et al., 2009). It has been shown that receiving positive feedback after being placed in a stressful situation may allow for an individual to cognitively adjust more than those who experienced negative feedback when placed in the same situation (Kassam et al., 2009); suggesting that different stress profiles create differences in both mental and physical resources which lead to differences in adjustment (n=103, 71 females, mean age=22±3.4 years). As challenge states are generally characterised by a greater availability of resources compared to threat states (Mendes et al., 2007), participants who experience stress as a challenge rather than a threat may have more cognitive resources available to deal with their stress and more cognitive resources available to complete a task, and thus, are able to perform better.

Other research has also indicated that stress may impair cognitive functions such as attention, working memory, cognitive flexibility, and visuospatial ability (Stokes and Raby 1989; Kivimäki & Lusa, 1994). Studies by Domes *et al.* (2004) and Luethi *et al.* (2008) have also supported the impairing effect of stress on working memory

performance. However, Dome's study also noted that the impairing effects may be associated with the timing of the applied stressor. A study by Schwabe and Wolf (2010) also found that stress impaired calculation, memory, and recall performance in healthy individuals (n=48, 32 females, age range=19-39 years). In contrast, Mackenzie *et al.* (2007) assessed the cognitive performance of stressed informal caregivers (n=27, 19 females, mean age=59±13 years) and suggested that attention and not working memory may be impaired. The comprehensive neuropsychological test battery used by Mackenzie's team (2007) enabled the assessment of multiple cognitive domains, but, the mean age of the participants was quite high, which could have influenced the results; as it is suggested that with age, comes a general decline in cognition (Riddle, 2007). Furthermore, Murray and team (2010) introduced further dissimilarity, finding that acute stress caused no improvement or impairment in male pilots (n=40, age range=18-30 years), whilst Henderson *et al.* (2012) found that uncontrolled stress can be harmful to executive functioning (n= 109, 63 females, age range=18–24 years).

Finally, varying results have also been seen in studies assessing healthcare professionals. Leblanc *et al.* (2005 & 2012) examined paramedic performance in high and low-stress scenarios (2005: n=30, gender breakdown and mean age not stated; 2012: n=22, 5 females, mean age not stated) using mobile patient simulators. Both of Leblanc's studies found that the stress and anxiety caused by clinical encounters impaired performance, regardless of how experienced the participants were. However, a subsequent review by Leblanc (2009) did associate the clinical performance of physicians with the different levels of knowledge and skills that they had. In contrast, a recent study by Lees & Lal (2016) found no association between stress and cognitive performance in a cohort of nurses (n=36, 34 females, mean age=38±11 years), although, a later study by Maharaj *et al.* (2018)[2] noted that stress (in addition to anxiety and depression) were associated with impairments in memory performance in Australian nurses. Finally, another study by Leblanc *et al.* (2008) conversely found that acute stress improved junior surgeons' surgical skills (n=12, gender breakdown and mean age not stated). However, the surgical skills cohort in LeBlanc's 2008 study was relatively small, and most of their studies do not specify the gender or age of the

[2] See publication: Maharaj, S., Lees, T., & Lal, S. (2018). Negative Mental States and Their Association to the Cognitive Function of Nurses. *Journal of Psychophysiology*, 33(3), 207–218. https://doi.org/10.1027/0269-8803/a000223

participants; thus, the mixed results raise concerns about the varying effects of stress, especially in different healthcare populations.

1.4.3 Anxiety

Anxiety can be a natural, adaptive, and appropriate response in pressured situations, with the feeling of anxiousness usually ending when the stressful situation has ended, or the 'stressor' has been removed (Carney & Drevets, 2002; Martin et al., 2009; Grupe & Nitschke, 2013). However, when the response is prolonged or excessive, this disproportionate level of anxiety may become disruptive and interfere with an individual's ability to cope with situations (Steimer, 2002); and hence can be defined as an inappropriate and excessive expression of fear. Components of the anxiety disorders commonly involve a persistent state of heightened anxiety which may affect daily life, increased motor tension, autonomic hyperactivity, and increased vigilance (Teicher, 1988).

Anxiety disorders are characterised by a variety of neuroendocrine changes, neurotransmitter actions, and neuroanatomical disruptions (Martin et al., 2009). Anxiety can be rooted in stressful life events and is predominated by the stress response. Therefore, anxiety is also characterised by both sympathetic activation (such as sweating, hypertension, and tachycardia) and an increase in the neuroendocrine response - involving HPA axis activation (Andreassi, 2000; Bear et al., 2007). Symptoms of anxiety are also thought to partially result from disruptions in the limbic system of the brain which are crucial components for emotion regulation. In particular, the fear response is heavily associated with hyper-activation of the amygdala (seen as the emotional centre of the brain) and/or damaged/weakened hippocampal activity due to over activation of the HPA axis (Martin et al., 2009). In turn, limbic and HPA dysregulation are seen to be crucial biological components of anxiety disorders (Shin & Liberzon, 2010).

1.4.4 Anxiety and Cognitive Performance

Anxiety's relevance to clinical performance has also been shown in healthcare settings (Leblanc et al., 2007; Levita et al., 2016). Cumming and Harris (2001) examined the

effects of anxiety on the ability of senior radiography students (n=105, gender breakdown, mean age not stated) to make decisions, and found that the more anxious group was less accurate in the diagnostic decision-making task. Levita *et al.* (2016) also noted that psychologists with higher rates of anxiety were less efficient at delivering Cognitive Behavioural Therapy (CBT), and therefore may be considered as being unable to perform their tasks at optimal levels (n=38, 23 females, mean age=29±5.5 years). In contrast, Leblanc *et al.* (2007) found that doctors reported higher levels of anxiety in high-stress conditions compared to low-stress conditions, but that performance improved in the high-stress condition (n=48, gender breakdown and mean age not stated). It can be noted that all the residents in Leblanc's study (regardless of level) showed similar perceptions of anxiety, but though scores of junior doctors improved in the high-stress condition, scores for more experienced doctors did not change. Thus, experience may play a crucial factor in mediating performance as more experienced individuals may be less affected by stressors if they have developed coping mechanisms to protect performance (Driskell & Salas, 1996).

Contention regarding the association between anxiety and cognitive performance has also been expressed in non-healthcare samples. Asmundson and Stein (1994) used a broad neuropsychological test battery to assess memory, executive functioning abilities, cognitive flexibility, and concentration, in patients with anxiety (n=36, 13 females, mean age=37±9.4 years), finding that those with anxiety performed poorer in all cognitive tasks compared to healthy controls. A study by Wood, Mathews, and Dalgleish (2001) further found that anxious individuals would have a higher error rate as they made speedy decisions (n=34, 21 females, mean age=37.7 years). Wood's and colleagues study also noted that under normal conditions, both the anxious and control groups performed equally well, however, anxious participants performed worse than their non-anxious counterparts when placed under mental stress; showing the strong relationship between stress and anxiety. This was supported partially by Mantella *et al.* (2007), where anxious subjects again displayed cognitive impairments in short-term memory but not executive functioning (n=87, 58 females, age range=71±6.5 years).

Earlier studies by Avila and Parcet (1997) (n=245, 210 females, mean age=20±3.0 years) and Kellogg, Hopko, and Ashcraft (1999) (n=30, gender breakdown and mean age not

stated) both found that anxious and non-anxious participants performed equally. However, in some tasks, performance diminished in high-stress conditions; suggesting that stress alone, rather than anxiety, may increase task difficulty, leading to impaired performance. However, contention was introduced in a later study by Hu *et al.* (2012) who suggested that anxious individuals (n=19, 9 females, age range=18-29 years) may perform better than non-anxious individuals, as they cautiously approached tasks, swapping speed for accuracy. Anxiety vigilance was further supported by Robinson *et al.* (2013) who found that anxiety may reduce errors, thereby improving performance (n=22, 11 females, age range=20-34 years).

Once again, deteriorations in several domains of cognitive performance were further established by Ashcraft and Kirk (2001), Ashcraft (2002), and Ashcraft and Moore (2009) where anxiety was seen to impair problem-solving, calculation and working memory ability. Furthermore, Raffield *et al.* (2016) analysed diabetic patients with comorbid anxiety and depression symptoms, finding that they had poorer performance on all cognitive testing measures assessed (n=598, 300 females, age range=38-93 years). However, limitations arise as most of the studies above do not differentiate for subtypes of anxiety which causes contention among researchers as it is suggested that specific types of cognitive impairments may be associated with particular subtypes of anxiety (Purcell et al., 1998; Boldrini et al., 2005; Ghassemzadeh et al., 2012). An early study by Purcell *et al.* (1998) identified that individuals with anxiety (n=80, 56 females, mean age=39±11 years) show impairments in cognitive domains such as spatial working memory, spatial recognition, and executive functioning; compared to healthy controls (n=30, 18 females, mean age=41±13 years). However, different subtypes of anxiety were associated with various forms of cognitive impairment; supported by Airaksinen, Larson, and Forsell (2005) (n=112, 81 females, age range=20-64 years) who also found different impairments between subtypes and that some subtypes, such as generalised anxiety disorder, may show no impairment.

Contrasting most of the studies above, Castaneda *et al.* (2011) found no major cognitive impairments in young adults with anxiety (n=75, 56 females, age range=18-29 years). Likewise, Gladsjo *et al.* (1998) used a comprehensive neuropsychological test battery on individuals with panic disorder (n=69, 32 females, age range=19-61 years),

finding no differences in learning, memory, attention, visuospatial functioning, and psychomotor speed when compared to healthy controls (n=19, gender breakdown not stated, age range=19-59 years), even suggesting that anxiety severity did not affect neuropsychological test performance. However, Darke (1988) measured the working memory capacity in highly anxious and low anxiety subjects (n=64, gender breakdown and mean age not stated), finding that highly anxious subjects exhibited significantly smaller memory capacity compared to the low anxiety groups, suggesting that severity does affect performance. In contrast, Potvin *et al.* (2013) found that both mild and severe anxiety in older adults (n=756, 462 females, aged 75±6.0 years) is not necessarily damaging to cognitive performance, as it was beneficial to participant performance in their study.

1.4.5 Depression

Depression is an affective disorder manifesting itself as low moods, low self-esteem, guilt, sleep, cognitive disturbance, and suicidal tendencies (Andreassi et al., 2000). Depression affects around 1 in 6 people, causing distress and disruption to their daily life (BeyondBlue, 2016).

The physiological basis for depression is yet to be fully understood, but common theories do exist. The monoamine hypothesis states that depression is caused by a reduction in monoamine levels (Bear et al., 2007); in particular, a depletion of dopamine, norepinephrine, and serotonin levels (a hormone important for mood regulation). The second and more commonly accepted hypothesis is the Diathesis-Stress-Hypothesis (Figure 1.7) which implicates the HPA axis (Monroe & Simons, 1991). This hypothesis states that the greater an individual's vulnerability for developing depression, it will take less environmental stress for that individual to become depressed (Monroe & Simons, 1991); suggesting that both genetic factors and early childhood stressors alter the HPA axis which results in the diminished inhibition of cortisol release. Therefore, the model proposes that the two components (diathesis and stress) contribute synergistically to yield an effect greater than their combined separate effects to result in depressive symptomology (Colodro-Conde et al., 2018).

Figure 1.7: The stress vulnerability model

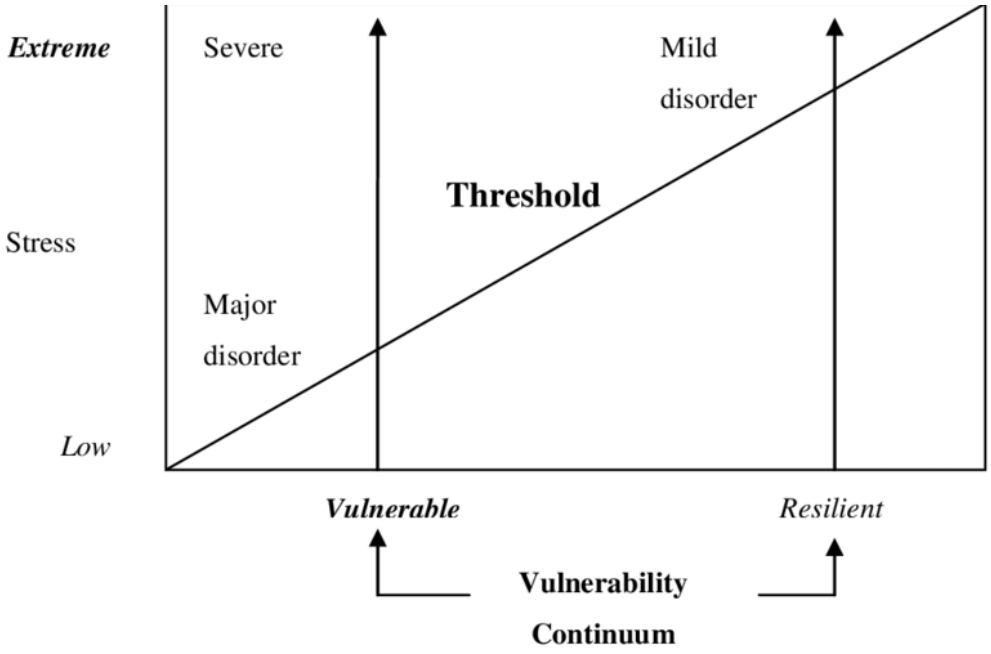


Figure 1.7 displays a stress vulnerability model which suggests that certain predispositions exist that make people more susceptible to developing diseases/disorders. As can be seen in the model, the more vulnerable an individual is, the less stress it will take for that individual to develop a disorder. In contrast, more resilient individuals are able to persevere through higher rates of stress before developing a disorder. *Image adapted from Ingram & Luxton, 2005.*

1.4.6 Depression and Cognitive Performance

Studies assessing the effects of depression on cognitive performance have generally had mixed findings (Austin et al., 1992; O'Brien et al., 2004; Hinkelmann et al., 2009). Austin *et al.* (1992) found that individuals with depression exhibited impairments in memory and recall but not executive functioning (n=40, 23 females, mean age=46±13 years); supported by the work of Sweeney, Kmiec, and Kupfer (2000) in non-bipolar patients with depression (n=93, 56 females, mean age=32±9.0 years). In contrast, Wang *et al.* (2006) found that young adults with depression (n=57, 48 females, mean age=31±10 years) exhibit no memory impairments compared to healthy controls (n=46, 35 females, mean age=27±9.5 years). Likewise, Fossati *et al.* (1999) did not find memory impairments in young patients with depression (n=34, 14 females, age range=18-45 years). However, they did report disturbances in executive functioning

ability, which was synonymous with both Smith, Muir, and Blackwood (2006) where major depressives (n=42, 29 females, mean age=21±1.9 years) did not differ significantly from controls (n=33, 19 females, mean age=22±2.3 years) in memory function but performed poorer in executive function tasks; and Mahurin *et al.* (2006) who found executive functioning and attention impairments in patients with major depression (n=30, 3 females, mean age=36±7.1 years). Executive functioning is a considerably important feature of adaptive human behaviour such as the ability to shift thoughts and respond to situations (Purcell et al., 1998; Fossati et al., 1999). Hence, impairments in this domain can be detrimental to the individual.

Further studies such as O'Brien *et al*. (2004) (n=60, 48 females, mean age=74±6.7 years) have also found impairments in attention, memory, learning, and executive function, supported by Rosenberg *et al.* (2010) who assessed episodic memory, psychomotor speed, and executive functioning in a large cohort of elderly (but non-demented) women (n=436, age range=70-80 years). Rosenberg's team also found that depressive symptoms were associated with cognitive decline in all of the aforementioned domains. This large longitudinal study (over 9 years) allowed Rosenberg's group to represent the older female population well, but the older age range is not reflective of the age range used in the current study (18-69). Conversely, some studies have suggested that depression does not cause any appreciable impairment in cognitive ability. Grant, Thase, and Sweeney (2001) found that un-medicated depressives (n=123, 75 females, mean age=39±10 years) showed a notable absence of cognitive impairment in attention, memory, and motor performance. Likewise, Castaneda *et al.* (2008) compared young depressives (n=68, 53 females, age range=21-35 years) to healthy controls (n=70, 35 females, age range=21-35 years) and found no significant impairments in short-term memory, verbal long-term memory, learning, attention, or executive functioning.

It is important to note that although the studies above may differ in their use of medicated and unmedicated individuals with depression, studies have noted no difference in cognitive performance between medicated versus unmedicated groups (Castaneda et al., 2008). While the reported impairments differ between studies, there remains a constant throughout; that depressed patients demonstrate a pattern of

cognitive deficits suggestive of frontal, prefrontal, and temporal dysfunction, as each of the impaired cognitive domains remains a central task of these particular brain regions (Elderkin-Thompson et al., 2011; Snyder, 2013).

Finally, links between depression and medication errors have been reported in hospital nurses as a review by Fry and Dacey (2007) noted that around 1 in 5 nurses had made either occasional or frequent medication administration errors. However, as it was a review, causal links could not be made. Conversely, the findings were supported by Saleh *et al.* (2014), who also found associations between depression and sleep disturbances, and medication administration errors in nurses (n=52, 51 females, average age=23±3.2 years). Cognitive symptoms tend to characterise one of the core features of depression, impacting on various functional outcomes (Barnes et al., 2006; Nakano et al., 2008), and so the public health implications of cognitive impairment associated with depression may be enormous, warranting further investigation (Papazacharias & Nardini, 2012).

1.5 Cortisol

Biochemical measures may be used as potential biomarkers for negative mental states and their associated cognitive decline. The stress hormone cortisol is secreted by the hypothalamic-pituitary-adrenal (HPA) axis and is not only implicated in the stress response but also in anxiety and depressive disorders (Varghese & Brown, 2001). Although cortisol production is highly regulated by the body's circadian rhythms (Figure 1.8), levels can rise independently to circadian rhythms in response to stress, anxiety, and depression, and each disorder has been associated with either hypo or hypercortisolemia (Burke et al., 2005; Bremmer et al., 2007). Increases in cortisol levels have also been commonly associated with impairments in memory (Lupien et al., 1999 & 2002).

Figure 1.8: Circadian variation in cortisol levels

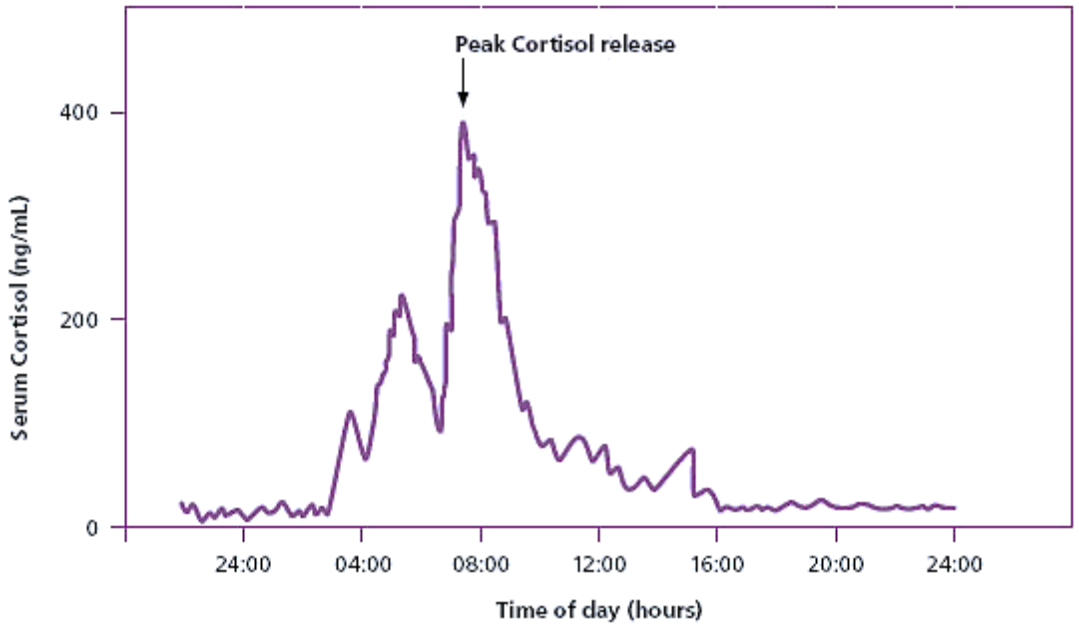


Figure 1.8 displays the natural circadian variation in cortisol levels over 24 hours. As can be seen, cortisol levels tend to peak in the morning and will decline steadily throughout the day. A small afternoon fluctuation (around 2-3pm) can also be seen. *Image adapted from Abudu, 2009 [online].*

1.5.1 Cortisol and Cognitive Performance

Lupien *et al.* (1999) found declines in working memory but not declarative memory when testing the effects of hydrocortisone in healthy elderly males (n=40, mean age=80±9.9 years). This early finding is important as impairments in working memory can have negative effects on the gaining and consolidation of information. This finding was synonymous with Lupien *et al.* (2002) who were able to modulate memory by manipulating cortisol levels in elderly participants, concluding that it is possible to improve or worsen verbal memory depending on glucocorticoid levels (n=17, 8 females, mean age=70±8.0 years). Furthermore, De'Quervain *et al.* (2003) used positron emission tomography (PET) to assess the effects of glucocorticoids on memory processes in males; finding that higher glucocorticoid levels were associated with reduced cerebral blood flow in the right posterior medial temporal lobe (De'Quervain et al., 2003) which was associated with impaired declarative memory (n=14, mean age=22±1.8 years). As memory is commonly impaired, it is possible that glucocorticoids

may also affect other medial temporal/hippocampal-dependent cognitive functions (Grossman et al., 2006; Lupien et al., 2007). However, limitations arise as most studies focus on assessing memory rather than other cognitive domains. Additionally, if impairments in temporal function (in turn, impairing memory function) are present in the nursing population, it raises concerns about their ability to accurately remember important patient details and medication dosages/times whilst working.

Similar to the studies above, Buchanan and Tranel (2008) had healthy individuals undertake a social stressor, followed by a delayed recall task (n=40, 20 females, mean age=20±2.0 years). They found that cortisol responders to the stress condition showed reduced memory retrieval, whereas non-responders had improved retrieval. The study noted an independent effect of both stress and cortisol on memory performance. However, Bohnen *et al.* (1990) introduced conflicting findings, reporting impaired attention but not memory in cortisol responders (n=24, all female, age range=41-69 years), an outcome supported by Vedhara *et al.* (2000) (n=60, 24 females, mean age=22±4.5 years). In contrast, Souza-Talarico *et al.* (2008) noted that an increase in cortisol levels was not associated with impaired working memory in individuals with Alzheimer's (n=40, 11 females, mean age=80±6.0 years). Conversely, Wingenfeld *et al.* (2012) suggested that higher cortisol levels, paradoxically, may improve memory in individuals with post-traumatic stress disorder (n=44, 38 females, age range=20-58 years).

Contrasting further, a study by Singh-Manoux *et al.* (2014) found no association between cortisol and cognition in healthy subjects (n=3229, 688 females, mean age=61±6.0 years). Initially, higher waking cortisol was associated with better reasoning performance. However, the five-year follow-up found that chronically elevated cortisol was not associated with cognitive performance, suggesting that variability in HPA function is not a strong contributor to cognition. The longitudinal nature of the study, considerable sample size and the fact that multiple salivary samples were collected for each individual allows the study to well represent the chronic effects of elevated cortisol in the general population, rather than the acute effects, as most other studies had assessed.

As mentioned, research tends to show that cortisol may impact memory. However, this may also be dependent on the individual's emotional state, as suggested by Abercrombie *et al.* (2006). Abercrombie noted that elevated cortisol levels may facilitate memory in individuals who report high stress-related negative affect. Furthermore, studies examining the additive effects of cortisol and negative mental states are of clinical importance. However, a limited number of studies examine this relationship (Egeland et al., 2005; Gomez et al., 2009; Abercrombie et al., 2011) and usually have conflicting results. Gomez *et al.* (2009) found that higher cortisol levels impaired memory performance in both depressives (n=37, 25 females, mean age=40±13 years) and healthy controls (n=37, 8 females, mean age=44±14 years). However, Abercrombie *et al.* (2011) conversely noted that cortisol affects recall performance in depressed individuals (n=19, 10 females, mean age=27±10 years) but not healthy controls (n=41, 23 females, mean age=28±8.0 years).

1.6 Relevance of the Current Study

The timely and accurate application of health services and technologies is vital, especially as these services and technologies are often administered in critical situations where errors can be fatal. However, the healthcare system and the professionals that work within it are under immense pressure to meet the demands for healthcare with a limited supply of resources and workforce (Willis & Elmer, 2007). The ongoing strain that these professionals undergo is unlike many other professions. While it has been recognised that health professionals are at risk of psychological distress, little is known about its prevalence or the effects that this distress has on their global and domain-specific cognitive performance (Hooper et al., 2010). Studies in the area of negative mental states and cognition have generally had conflicting results; therefore, this area of research requires further investigation. Many major neuropsychiatric disorders, such as depression and anxiety, may have important cognitive components. For example, they may arise from atypical learning behaviours, impaired attributional systems, and/or deficient cognitive control processes that are usually used to regulate emotional outputs and behavioural responses (Robbins, 2011). Furthermore, cortisol can be implicated in stress anxiety, and depression, but few studies have investigated the link between negative mental states, cortisol, and cognitive performance together.

Hence, such a thorough physiological, biochemical, and psychometric investigation into multiple cognitive domains would substantially increase the knowledge in this area.

As mentioned, literature assessing the effects of negative mental states on the cognitive performance of health professionals is scant. Few studies have assessed healthcare populations, let alone compared different healthcare samples. The current doctoral study also builds on this research as there is a need to more definitively determine the effects of negative mental states on cognitive performance in different types of healthcare workers as the link between these factors may be important in evaluating the impacts that they may have on clinical performance and outcomes (Russell et al., 2015). Since many countries are faced with the increasing cost of healthcare services and subsequently focus on cost-saving and efficiency, the issue of sub-optimal healthcare remains a concern (Theodoropoulos, 2010). Hence, the health and welfare of the professionals who deliver healthcare services should be a priority to not only ensure their health and well-being but to ensure their optimal performance and patient safety.

Additionally, even when knowing that health-related professions are high load professions that tend to take a toll on those employed in them, research into the prevalence rates for mental health disorders like stress, anxiety, and depression remain lacking in Australian health professions. Generally, research in this area focuses on the mental health of nurses and in some instances, medical doctors, but rarely do studies focus on allied health professions. As explored in Chapter 1, Section 1.2, there is literature building in the area of mental health in medical and nursing professionals, but many of these studies are also conducted in countries other than Australia. Literature exploring mental health in Australian health professionals is scarce. Medical and health professions are inherently stressful regardless of geographical region. However, organisational factors, demographics, and workloads etc. vary greatly between nations and thus additional research in Australian healthcare professionals is not without its merits. The determination of prevalence rates and risk factor analysis for stress, anxiety, and depression in Australian health professionals remains a contribution to the area as research like this may have wide-ranging impacts on policymakers, professionals, and patients alike.

Finally, research identifying potential biomarkers of early cognitive decline will allow for the identification of cognitive deterioration before substantial decline has occurred.

The present project intended to provide research-based groundwork that may enable further research to inform policymakers and authorities on the prevalence of negative mental state and the effects of stress anxiety, and depression on cognitive performance of nurses. It is possible that by examining the present results and mitigating any cognitive impairment, we could improve the performance of our health professionals, as well as understand and manage their mental wellbeing and hence enhance the quality of patient care and importantly, it may reduce the incidence and severity of adverse medical events and patient fatalities.

1.7 Aims & Hypotheses

Aims:

1. To assess the prevalence of negative mental states (i.e. stress, anxiety, and depression) in healthcare professionals.
2. To investigate links between negative mental states and cognitive performance (MMSE, Cognistat, EEG) in healthcare professionals.
3. To compare the effects of negative mental states on cognitive performance between different healthcare populations.
4. To assess the relationship between cortisol and negative mental states, and cortisol and cognitive performance.

Hypotheses:

1. Negative Mental States such as stress, anxiety, and depression will be prevalent in all healthcare professionals.
2. a) Negative mental states will lead to declines in cognitive performance (MMSE, Cognistat) in healthcare professionals.
   b) Negative mental states will lead to increases in low-frequency EEG activity and decreases in high-frequency EEG activity - reflective of potential cognitive dysfunction.

3. Each healthcare population will have a different cognitive impact profile associated with negative mental states.
4. That cortisol will be associated with both negative mental states and cognitive performance.

Chapter 2 – Methodology, Data Processing, & Statistical Analysis

2.1 Participant Recruitment

Participants consisted of various healthcare professionals (nurses, doctors, and allied health professionals) and non-healthcare professions (members of the general population) recruited from the local community. A total of 154 participants were recruited for this study via social media, electronic and physical posters (see Appendix), email promotions, online advertisements, and word-of-mouth communication. The study protocol involved a cross-sectional exploratory lab-based study that was conducted on campus at UTS in a lighting and temperature-controlled lab. Participants attended a single session which took approximately 2 hours to complete for each participant.

2.2 Ethics approval

This study received ethics approval from the UTS Human Research Ethics Committee (HREC) (HREC: 2014000110).

2.3 Inclusion/Exclusion Guidelines

To be included into the study, participants needed to be presently employed (for healthcare participants), aged between 18-69 years, be proficient in the English language, have no chronic disease or illness, no previous history of psychosis, and not be taking any medications that could limit compliance or that could affect results (e.g. the use of certain pain medications (e.g. codeine in Panadein Forte) may affect brain activity (Cao et al., 2016)). Individuals who drank in excess of 16 standard drinks a day, or smoked in excess of 10 cigarettes a day were also excluded. Furthermore, participants needed to have blood pressure (BP) below 160/100 mmHg (Figure 2.1) (as per UTS HREC requirements). Volunteers unable to meet the criteria outlined above were excluded from the study to reduce any interference that these factors may have on outcome measures, thus improving data reliability.

Before and after each testing session, three BP measurements were obtained using a reliable and non-invasive automated blood pressure monitor and then averaged to derive an overall BP value (resulting in pre-study and post-study averages). See Chapter 2, Section 2.4.2 (below) for further detail. Participants were required to have systolic and diastolic BP below 160/100 mmHg to be included in the study. If at any point they presented with BP above or equal to 160/100 mmHg (indicative of stage 2 hypertension (Rafey, 2013)) they were excluded from the study. Participants with BP above or equal to 140/90 mmHg but below or equal to 159/99 mmHg (indicative of stage 1 hypertension (Rafey, 2013; Unger et al., 2020)), were included in the study but were advised to seek medical attention.

Figure 2.1: Blood pressure inclusion/exclusion guidelines

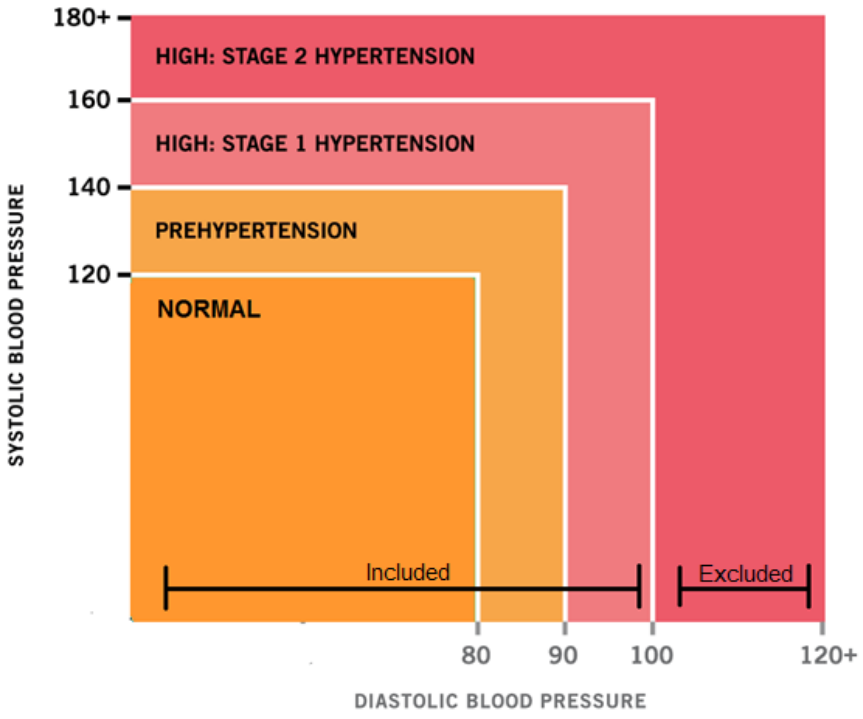


Figure 2.1 displays the normal range for blood pressure (120/80 mmHg) and the inclusion/exclusion guide used for the current study. Participants with blood pressure under or equal to 159/99 mmHg were included in the study. Individuals with blood pressure over or equal to 160/100 mmHg were excluded (Unger et al., 2020). *Image adapted from Wittwer, 2010 [online].*

2.4 Protocol

2.4.1 Consent

All participants provided informed consent prior to the commencement of the study. Before consent was obtained, participants received a detailed explanation about the study. Following the explanation, any remaining questions were answered. Written consent was then obtained via a consent form signed by both the researcher and the participant (who each retained a copy). A copy of the consent form can be found in the Appendix.

2.4.2 Blood Pressure

Following the study explanation and consent and procedures, participants were seated quietly for 5 minutes. Following this short rest period, three BP measurements were then obtained from the left arm using an automated blood pressure monitor (Omron IA1B, Japan). The automatic blood pressure monitor used for the present study and its correct cuff placement can be seen in Figure 2.2 and 2.3 respectively. Due to normal fluctuations in BP (Ogihara et al., 2009), three readings were taken and then averaged to increase accuracy. A 2 minute rest period was also given between each reading to avoid potential carry-over effects from the previous arm cuff compression (Yasuda et al., 2010) and to avoid discomfort to the participant. The three readings were then averaged to produce a single pre-study BP reading. Heart rate data (in beats per minute (bpm)) was also obtained for each recording. As per the BP inclusion guide in Section 2.3 above, if the participant's BP met the aforementioned inclusion guide of being below 160/100 mmHg, they then proceeded with the rest of the protocol.

Figure 2.2: Automated blood pressure monitor (Omron IA1B, Japan) used in the present study

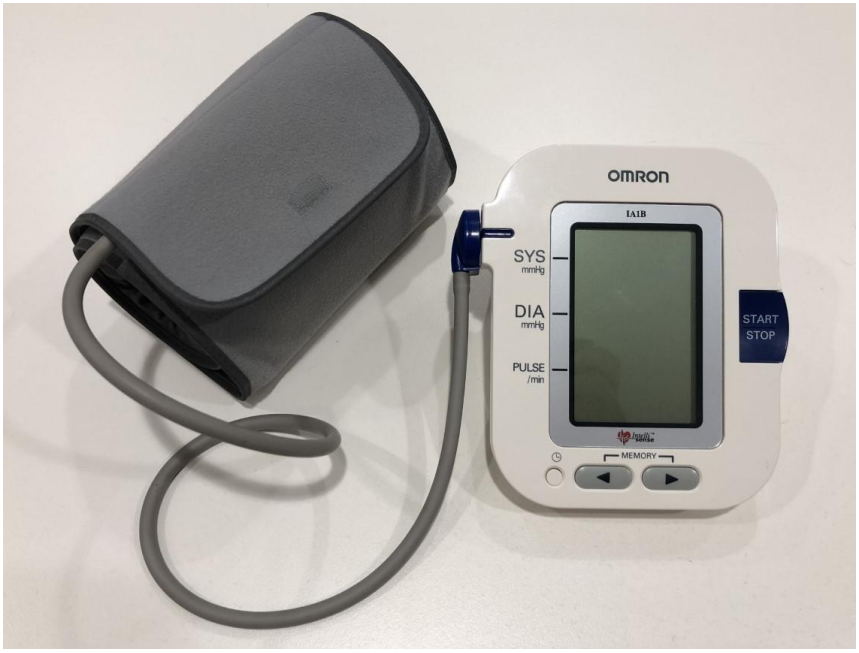


Figure 2.2 shows the Automated blood pressure monitor (Omron IA1B, Japan) used in the present study. The monitor displays systolic and diastolic blood pressure in addition to heart rate data.

Figure 2.3: Recording blood pressure with an automated blood pressure monitor

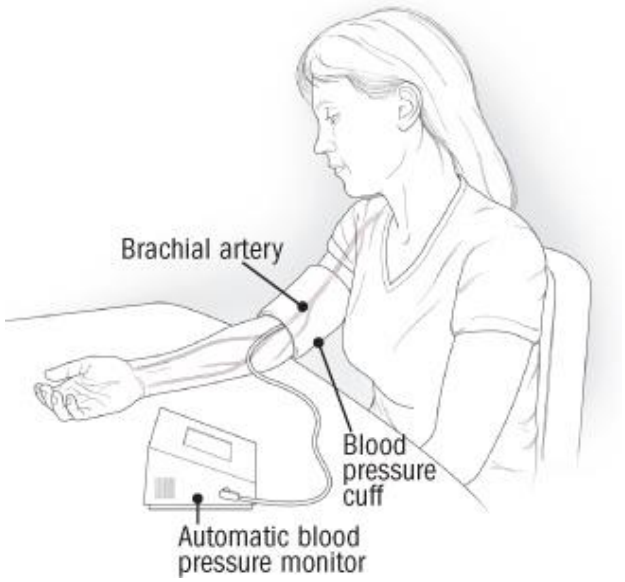


Figure 2.3 shows the correct sitting position and cuff placement (to ensure that the brachial artery is occluded) for recording blood pressure using an automated blood pressure monitor. *Image adapted from Harvard Medical School, 2009 [online].*

2.4.3 Cortisol

Following pre-testing and post-testing BP measurements, non-invasive salivary samples were obtained using a Salivette (Salimetrics Inc., USA). The Salivettes were later used to quantify cortisol levels. Before collection, participants were offered some water to increase salivation (Guest et al., 2007). Participants were then asked to place the cotton component of the Salivette into their mouth until saturated (usually around 2 minutes allows for the retrieval of an adequate saliva sample). Saliva collection is displayed in Figure 2.4. Following collection, salivary samples were stored at –20°C until analysed.

Before attending the study, participants were instructed to refrain from eating, drinking (except water), or brushing their teeth an hour before their allocated session to avoid contamination of the samples from food, blood, and other materials that may remain in the mouth (Nicolson, 2008). As cortisol release is dependent on the diurnal rhythm of the HPA axis in addition to circadian variations (Abudu, 2009), salivary samples were only taken between the hours of 9am-11am in order to prevent inaccuracies. The collection of salivary cortisol remains an accepted non-invasive alternate for serum-free cortisol (Bartanusz et al., 2014) as it reliably estimates serum levels and has the added advantage of being easier to obtain (Vining et al., 1983; Dorn et al., 2007). Blood and saliva remain the most common samples used to measure cortisol, and thus it is important to recognise that changes in cortisol levels have a time delay following a stressful event. Cortisol levels usually increase approximately 20-30 minutes following exposure to a stressor (Kirschbaum & Hellhammer, 1989; Vogel & Schwabe, 2016; Gerber et al., 2020) as is reflected in both blood and salivary levels. Thus, any changes in cortisol that occur due to participation in the study may be observed by comparing the pre-testing and post-testing measures. Salivary cortisol remains unaffected by freeze/thaw cycles (Kirschbaum & Hellhammer, 1989) and thus, all salivary samples were stored frozen at -20°C until assayed.

Figure 2.4: Directions for collecting salivary samples with a Salivette

Figure 2.4 displays saliva collection via a salivette. The participant first removes cap then removes the cotton swab from the Salivette (image 1-2), places the cotton swab into their mouth for a couple of minutes until saturated (image 3), then returns the swab back into the Salivette and places the cap back on (images 4-5). *Image adapted from The Sarstedt Salivette instruction manual: Sarstedt, 2019 – pg.1.*

2.4.4 Questionnaire Battery

Following the collection of salivary samples, participants completed a questionnaire battery which collected demographic, lifestyle, work, and psychological data. A brief set of instructions and explanations about each of the questionnaires was given to participants prior to filling out the battery.

Lifestyle Questionnaire

A 21-item in-house designed lifestyle questionnaire (adapted from the Lifestyle Appraisal Questionnaire (Craig, Hancock, & Craig, 1996) was used to collect relevant demographic and lifestyle data regarding age, ethnicity, education, medical history, alcohol intake, nicotine consumption, exercise habits, etc. This questionnaire was also used to determine the inclusion/exclusion criteria for the study as outlines in Chapter 2, Section 2.3.

Work Appraisal Questionnaires

The Work Appraisal Questionnaires were also in-house designed questionnaires developed to collect relevant work-related data including length of employment, level of qualification, job satisfaction, coping strategies for fatigue, and shift work data. A specific questionnaire was developed for each group (Nurses, Doctors, Allied health professionals, and Non-healthcare workers) to ensure that questions were specific to

the professional group being assessed. Each questionnaire contained a total of 16 open-ended and YES/NO style questions. Copies of the work questionnaires used for the nurse, allied health, and doctor cohorts can be found in the Appendix.

Epworth Sleepiness Scale

Sleep data was collected using the Epworth Sleepiness Scale (ESS) (Johns, 1991). The ESS is an 8-item self-report questionnaire assessing general levels of daytime sleepiness by assessing how likely an individual is to fall asleep in a particular situation (Johns, 1992). Each of the 8 items is scored from 0 to 3, which are then tallied to produce a total score ranging from 0 to 24. Higher scores are indicative of greater daytime sleepiness (Knutson et al., 2006). The ESS is a reliable and well-validated measure with a Cronbach's alpha value of 0.88 (Johns, 1992; Al-Abri et al., 2013). The ESS was collected to be used in the risk factor analysis (refer to Chapter 4) as sleepiness/sleep issues may exacerbate symptoms of stress, anxiety, and depression or vice versa where symptoms of stress, anxiety, and depression may affect sleep (Leggett, Burgard, & Zivin, 2016; Milojevich & Lukowski, 2016; Freeman et al., 2017).

General Health Questionnaire

The General Health Questionnaire (GHQ) is a well-validated (Cronbach's alpha 0.82-0.86) 60-item questionnaire (Goldberg, 1978). Each of the 60 items are accompanied by four possible responses; being 'not at all', 'no more than usual', 'rather more than usual' and 'much more than usual' (Goldberg, 1978; Jackson, 2007). The GHQ-60 produces a single overall score which is compared to a prescribed threshold value where scores above the threshold are indicative of less sound psychological wellbeing/psychiatric 'caseness'. The term psychiatric caseness is used probabilistically to refer to respondents who, if presented in general practice, would most likely receive further attention (Jackson, 2007). The GHQ scoring method was chosen over the Likert scoring method as the bimodal GHQ method avoids 'end-user scoring' and is therefore considered superior at reducing bias whilst also providing a prescribed cut-off value for interpretation and comparisons (Goldberg, 1978). Using the GHQ scoring method, 'not at all', 'no more than usual', are scored as '1' and rather more than usual' and 'much more than usual' are scored as '2'. When responses are tallied, athe GHQ groups

individuals into two categories based on the probability of an individual showing psychiatric caseness. As previously mentioned, scores above 12 are indicative of less sound psychological wellbeing/psychiatric 'caseness'.

Depression Anxiety Stress Scale

The Depression Anxiety Stress Scale (DASS) (Lovibond & Lovibond, 1995) is a 42-item Likert-style questionnaire that comprehensively assesses symptom severity of depression, anxiety, and stress; while allowing for the maximum discrimination between the three states (Lovibond & Lovibond, 1995; Brown et al., 1997). The DASS consists of three scales (one for each mental state) containing 14 items each. Together, the three scales identify psychological/emotional disturbances by assessing a wide range of psychological distress symptoms (listed below) (Lovibond & Lovibond, 1995). The score for each scale (depression, anxiety, and stress) is tallied and then compared to normative ranges to evaluate how severe an individual's symptoms are. The thresholds for depression, anxiety, and stress symptomology to be considered within the normal range are scores of <10, <8, and <15, respectively.

Depression Symptoms: Dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest/involvement, anhedonia, inertia
Anxiety Symptoms: Autonomic arousal, skeletal muscle effects, situational anxiety, subjective experience of anxious affect
Stress Symptoms: Difficulty relaxing, nervous arousal, being easily upset/agitated, irritable/over-reactive impatience

2.4.5 Electroencephalography

Following the completion of the questionnaire battery, brain activity was non-invasively measured using 32-channel electroencephalography (EEG) via the NeuroScan EEG system (SynAmps 2, Compumedics Limited, Australia). A 32 channel EEG was selected as it enabled a thorough full head investigation. The 32 electrode sites use in the present doctoral study can be viewed in Figure 2.5.

To set up, an EEG cap was placed directly onto the participants head. The EEG cap has electrodes integrated into the cap which automatically provide suitable electrode

placement with the appropriate interelectrode distances according to the standard international 10-20 system of electrode placement (Jasper, 1958; Windhorst & Johansson, 2012). The 10-20 system was designed to reliably place electrodes over the same brain regions regardless of any difference in head size and shape (Atkinson, 2006). Once the cap was secured on the participants head, a blunt tip (drawing up) needle was used to fill the ground, reference, and 30 active electrode sites with conductive gel (Signa Gel, Parker Laboratories, USA) (Figure 2.6) until an appropriate direct current (DC) value was obtained (less than 5kΩ). Two electrooculogram (EOG) electrodes were also filled with gel and secured above and below the participant's left eye, using surgical tape. The use of the EOG allowed for the tracking of eye movements and blinking, permitting the removal of any artefacts during the pre-processing stage. Once set up, participants were seated comfortably in front of a blank computer screen and were informed to sit quietly for 5 minutes while observing the blank screen so that a baseline phase recording could be obtained. The use of the blank screen for baseline measures allows participants to remain in a passive resting state where they are not actively processing significant amounts of information. Following the baseline recording, an active phase recording was obtained for 5 minutes during cortical stimulation with the Stroop task (Stroop, 1935). A raw EEG tracing from the 32-channel EEG can be viewed in Figure 2.7 while the completed EEG experimental set up can be seen in Figure 2.8.

The Stroop task (Figure 2.8 and Figure 2.9) is a standard and reliable task commonly used in neuropsychological assessments (Scarpina & Tagini, 2017). During the task, the participant undertakes a colour-word interference task requiring them to suppress a habitual response while processing incongruent stimuli; in turn stimulating cortical activation (Moering et al., 2004). The task generates an interference effect known as the "Stroop interference effect" which is also considered as a measure of cognitive flexibility and executive functioning (Uttl & Graf, 1997; Moering et al., 2004). The Stroop task (Stroop, 1935) was completed via computer using an in house designed software (as seen in Figure 2.8). The two sessions (baseline and active) allowed for the change in brain activity from a resting/baseline state to an active state - during cognitive engagement - to be examined.

Figure 2.5: The 32 electrode sites used in the current protocol

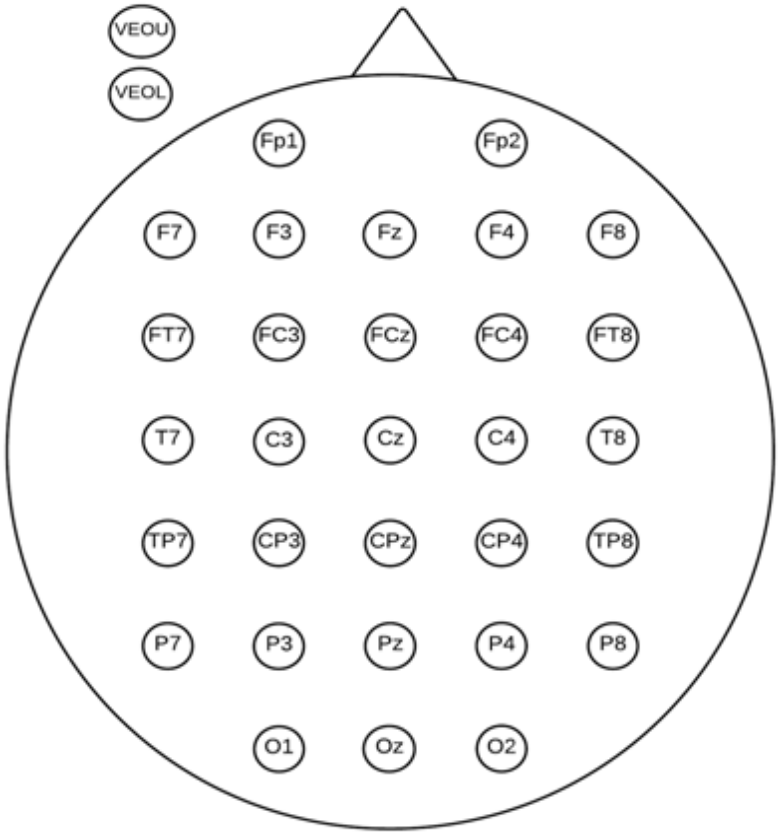


Figure 2.5 displays the EEG electrodes used in the current protocol (in accordance to the international 10-20 system (Jasper, 1958)). Electrodes are named with letters combined with a number. Letters correspond to the general brain region to which the electrodes overlie. Numbers indicate the location relative to the midline (even numbers represent electrodes that overlie the right hemisphere, odd numbers represent electrodes overlying the left hemisphere of the brain) (Boutros et al., 2011).

Key: FP = Frontal-polar F = Frontal FT = Fronto-temporal
FC = Fronto-central T = Temporal C = Central
P = Parietal O = Occipital TP = Temporal-posterior
CP = Centro-parietal Z = electrodes that overlie the centre/midline
VEOU = Vertical electrooculogram upper VEOL = Vertical electrooculogram lower

Figure 2.6: Conductive Signa gel and blunt-tip needle

Figure 2.6 displays the conductive gel (Signa Gel, Parker Laboratories, USA) and blunt-tip needle that are used to fill individual EEG electrodes.

Figure 2.7: Raw EEG tracing

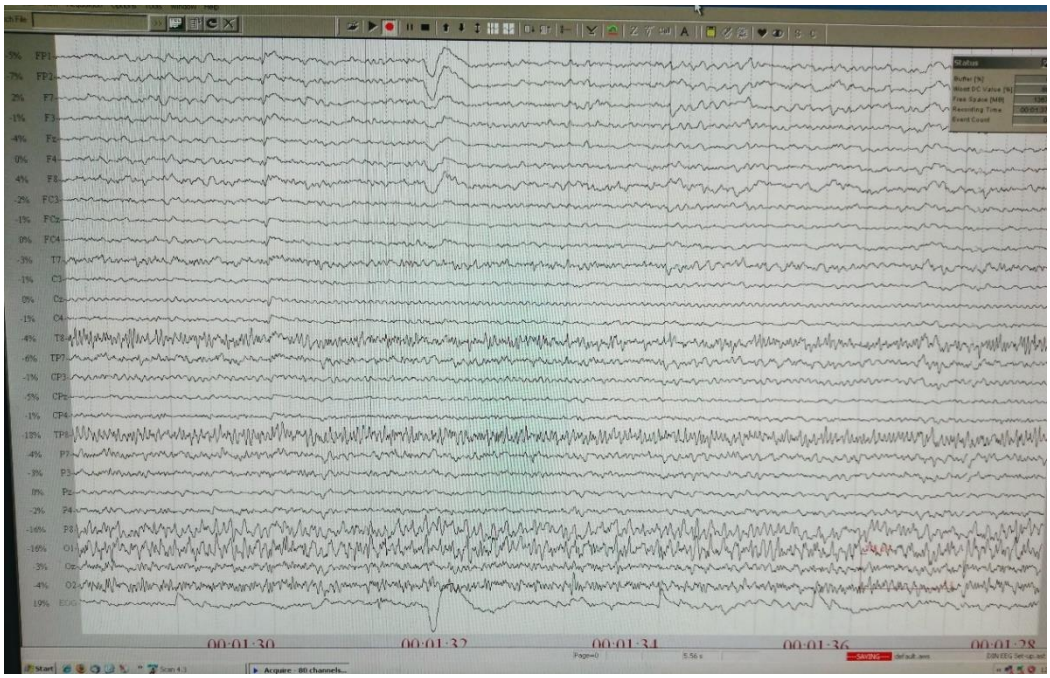


Figure 2.7 displays a raw 32-channel EEG trace from the present study. Each of the channels is labelled with an electrode location (e.g. FT8, P3, C4) and time in seconds can be seen on the X-axis.

Figure 2.8: The experimental set up used in the present study

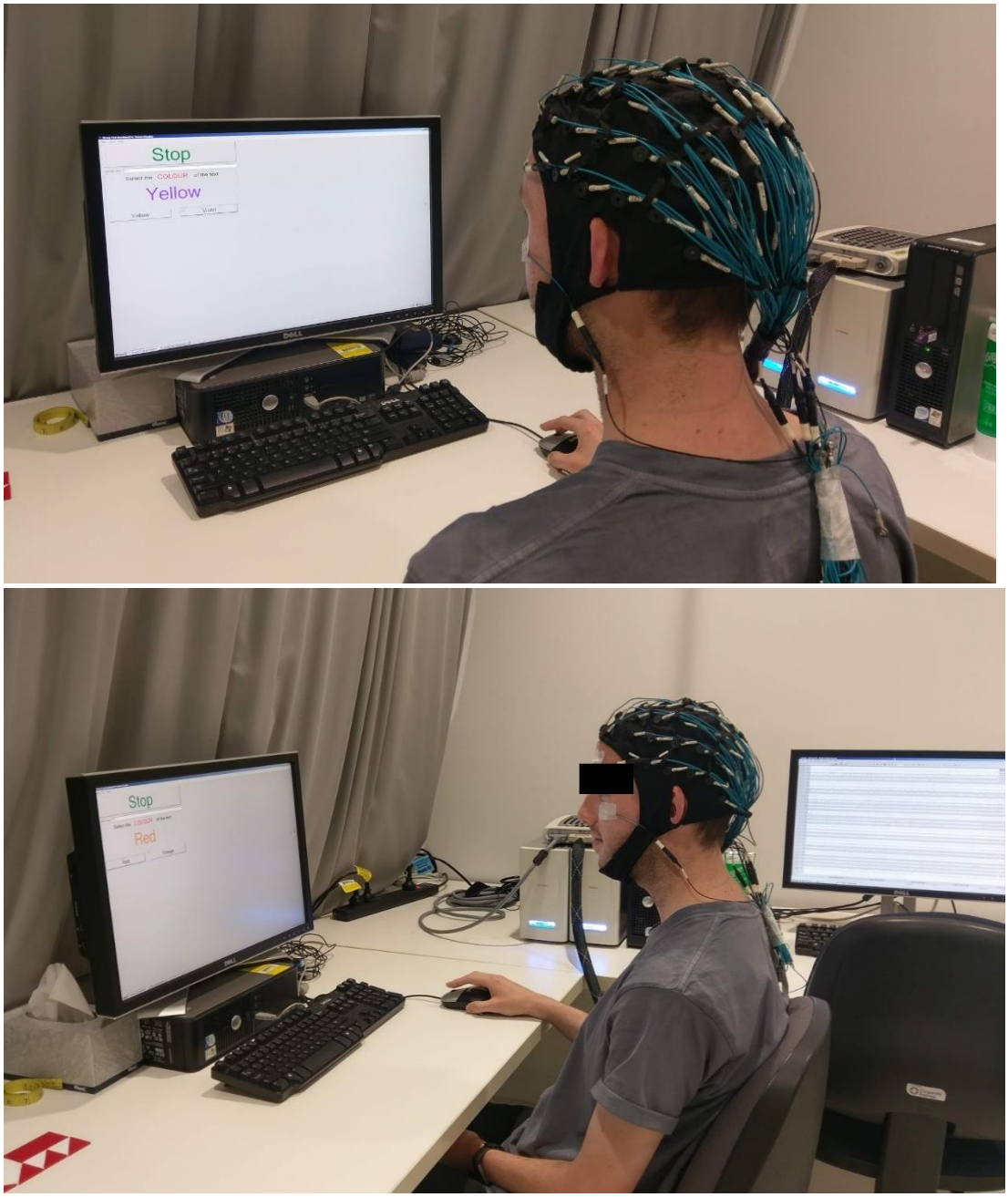


Figure 2.8 displays an image of a participant connected to an EEG in the laboratory setting. The computer screen displays the Stroop task (Stroop, 1935) being undertaken during the active phase EEG recording. *Permission was obtained from the participant to reproduce the image.*

Figure 2.9: The Stroop task

Figure 2.9 displays the Stroop task (Stroop, 1935). During the active electroencephalography session, participants are required to select the colour of the word, not what the word says. For example, for the word, **BLUE**, the correct answer would be “red".

2.4.6 Psychometrics

Following the completion of the two EEG recordings, the Mini-Mental State Exam (MMSE) (Folstein et al., 1975) and the Cognistat (Mueller et al., 2007) were used to measure cognitive function. The two cognitive tests were administered in a randomised order to avoid any potential order effects.

The Mini-Mental State Examination (MMSE)

The MMSE (Folstein et al., 1975) is a rapid 30-point examination used to assess global cognitive functioning. Administration takes approximately 5 minutes and consists of 11 questions, divided into two parts. Part 1 of the MMSE examines orientation, memory, and attention, while part 2 examines reading, writing, recall, comprehension and visual construction (Folstein et al., 1975). The total score for both parts are then tallied to provide a single overall score, with scores less than 23 out of the 30 possible points being suggestive of potential cognitive impairment (Schwamm et al., 1987). However, as noted in Chapter 1, Section 1.3.1, the MMSE may have limitations when identifying more subtle cognitive impairments (Yuseph et al., 1997). Thus, it is commonly

administered in conjunction with the Cognistat - allowing for a more sensitive and comprehensive assessment of both global and domain-specific cognitive performance (Macauley et al., 2003).

The Cognistat

Similar to the MMSE, the Cognistat (Mueller et al., 2007) is a relatively short assessment taking approximately 20 minutes. However, the Cognistat offers a more comprehensive breakdown of domain-specific performance by providing individual scores for each domain assessed. The cognitive domains assessed by the Cognistat include orientation, attention, language, construction, memory, calculation, and reasoning (Mueller et al., 2007). The language domain is further divided into comprehension, repetition, and naming. Likewise, reasoning is further divided into similarities and judgement (Mueller et al., 2007). Each of the domains assessed has its own impairment threshold score, where scores close to the threshold are indicative of poorer cognitive performance, and scores less than or equal to the threshold are indicative of cognitive impairment for that domain. During administration, a "screen" question of average difficulty is asked first, to which a correct answer indicates normal cognitive functioning for that domain (Deutinger, 2007; Mueller et al., 2007). If the individual fails the screen question, a series of "metric" questions from the same domain, but of increasing difficulty are asked, providing a more exhaustive assessment of the level of impairment (Deutinger, 2007; Mueller et al., 2007). Both the screen and metric questions were administered for the present study to improve data reliability. An example of a task completed during the Cognistat is shown in Figure 2.10.

Performance for each domain was then scored and tallied. Participant scores were then compared to threshold values to display the level of impairment (normal, mild, moderate, or severe) for each domain, allowing for the identification of more precise brain processes and/or areas that may be implicated in cognitive impairment.

Figure 2.10: An example of a participant completing a Cognistat task

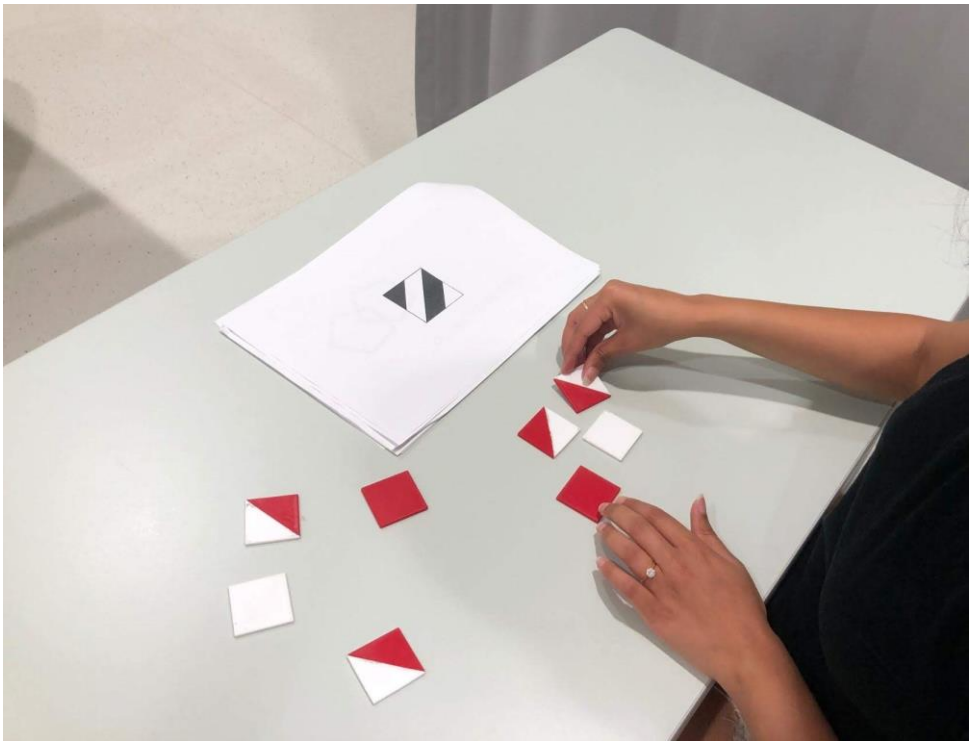


Figure 2.10 displays a participant completing the construction task of the Cognistat (Mueller et al., 2007). This task requires the participant to build a design (as shown on the white paper) using the coloured squares. *Permission was obtained from the participant to reproduce the image.*

2.4.7 Conclusion of Protocol

Following the psychometric assessment, post-testing BP and saliva samples were taken, after which, the study was concluded and study summary sheet was completed (as per UTS HREC requirements). A copy of the study summary sheet can be found in the Appendix. An overview of the entire study protocol is displayed in Figure 2.11 (below).

Figure 2.11: Overview of the experimental protocol for the current study

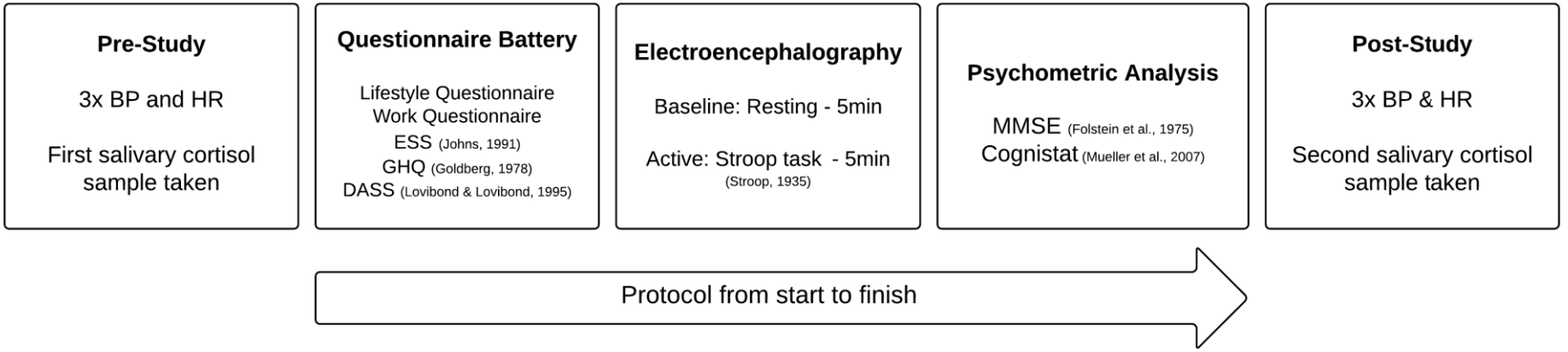


Figure 2.11 displays a flow chart summarising the experimental protocol used in the current study.

Key: BP = Blood Pressure
HR = Heart rate
ESS = Epworth Sleepiness Scale (Johns, 1991)
GHQ = General Health Questionnaire (Goldberg, 1978)
DASS = Depression Anxiety Stress Scale (Lovibond & Lovibond, 1995)
MMSE = Mini Mental State Examination (Folstein et al., 1975)

2.5 Cortisol Analysis

Cortisol analysis was conducted independently via Stratech Scientific (APAC PTY Ltd)

Samples were stored frozen at -20°C until assay, and all samples underwent one freeze-thaw cycle. For the assays, the samples were thawed and analysed using a commercially available ELISA assay kits (Salimetrics, USA) according to the manufacturer's instructions. Thawed samples were centrifuged at 1500 x *g* for 15 min to collect clear saliva, and this saliva was used without further processing for all assays. The samples were all brought to room temperature before adding to the assay wells, and all samples were analysed in duplicate.

The Salimetrics cortisol assay kits are specifically designed to measure salivary cortisol via competitive immunoassay. The kit utilises a specific monoclonal antibody which competitively binds to endogenous salivary cortisol and a pre-specified concentration of added horseradish peroxidase labelled cortisol. The degree of competition between the added and the endogenous cortisol can then be calculated, from which the amount of salivary cortisol can be measured (Stratech Scientific (APAC PTY Ltd)).

Assay performance is noted below:

Salivary cortisol correlates well with matched serum cortisol concentrations; r = 0.91.
Assay sensitivity = 0.003 µg/dL.
Intra assay variability (within assay) 4.2%
Inter-assay variability (between assays) 4.8%

2.6 Data Processing - Electroencephalography

Preceding statistical analysis, the raw EEG data sets obtained for both the baseline and active phases were processed according to the steps stipulated below. The raw EEG data was recorded at a sampling frequency of 1000 Hz.

1. The raw EEG data was filtered prior to analysis using an IIR Butter-worth band pass filter set at 13 and 50 Hz followed by a Hanning window.

2. The Aligned-artifact average procedure (Croft & Barry, 1998) was then utilised to minimise any ocular artefacts which may have been present in the recordings.
3. After pre-processing, each set of recordings (baseline and active) was sectioned into one-second epochs and the EEG activity in the selected frequency bands: delta (<4 Hz), theta (4-8), alpha (8-13 Hz), beta (13-30 Hz), and gamma (30-80 Hz), was calculated via Periodogram power spectral density estimate.
4. The epoch values of each recording were scanned for outliers, which were removed using a modified Z-score statistic that was calculated using the following equation (below).

$$z = \frac{X - \tilde{x}}{MAD}$$

Where:

X = Epoch value $\tilde{x}$ = Median value MAD = Median Absolute Deviation

Median Absolute deviation can be calculated using the following equation:

$$MAD = \tilde{x}_i \left(|X_i - \tilde{x}_j(X_j)| \right)$$

Where:

$\tilde{x}$ = Median X = Epoch value

Epoch values were rejected and removed if their *z* statistic was greater than or equal to 10.

5. The activity values for each of the epochs were then averaged to derive a single value for each frequency band at each electrode site. The activity values in each frequency band were also averaged, providing an overall average EEG activity value.
6. A reactivity value was generated by subtracting the baseline EEG activity from the active phase for each of the respective frequency bands. This value was

generated to allow the change in EEG activity between the baseline and active phases to be examined.

7. Finally, after all the EEG data had been collated, outlying values were removed using the modified Z-score statistic that was previously applied to the epoch values.

All EEG values were recorded in microvolt's (μV).

2.7 Statistical Analysis

All statistical analysis was performed using SPSS Version 23.0 for the Windows platform (SPSS Inc.; Chicago, IL, USA). The level of statistical significance for all analyses was defined as $p < 0.05$.

The data analysed for the current study included:

- Demographic data, lifestyle data, and work data.
- Blood Pressure and Heart Rate data (both pre-study and post-study measurements).
- Depression, Anxiety, and Stress severity as assessed by the DASS (Lovibond & Lovibond, 1995).
- General psychological wellbeing/psychiatric caseness as measured by the GHQ (Goldberg, 1978).
- Global cognitive function as assessed by the MMSE (Folstein et al., 1975) and domain-specific cognitive functioning as measured by the Cognistat (Mueller et al., 2007).
- Cognitive functioning as measured by electroencephalography (EEG). All 5 brain rhythms (delta, theta, alpha, beta, and gamma) were assessed in the current analysis. Note: EEG data is presented as reactivity values (the difference between the active and baseline phases) to display the change in activity between the two EEG phases.

Sample size estimation

Statistical significance is directly related to sample size, where larger sample sizes will increase the reliability of results and increase the possibility that a correlation is reflective of a true relationship (Biau et al., 2008; Peacock & Peacock, 2011). The sample power of a study also increases with increasing sample size (Biau et al., 2008). The larger the sample power, the less risk for Type II errors and the higher the chances of detecting a difference or relationship when it exists. Therefore, it is important that studies are planned with an adequate sample size in mind so that meaningful conclusions can be determined and without testing too many subjects, which may be considered unethical (Biau et al., 2008).

The sample size estimations for the current thesis were based on a study by Cohen (1992) who demonstrated that the minimum sample size required for the analysis conducted below (e.g. analysis of variance (ANOVA) and Pearson's correlations), with a sample power of approximately 0.80 and moderate to large effect size (0.5-0.8), is approximately 30. The current study aimed to recruit representative samples of at least 30 people for each test group. Where necessary, for groups of less than n=30, non-parametric alternatives (such as Spearman's rank correlation) were utilised.

Previous research published from our research unit (Lees & Lal, 2016; Rothberg et al., 2016; Maharaj, Lees, & Lal, 2018; Chalmers et al., 2020) have utilised similar sample sizes to the ones presented in the current thesis. Additionally, other studies assessing areas such as cognition (Austin et al., 1992; Mahurin et al., 2006; Hu et al., 2012; Human et al., 2013; Levita et al., 2016), and cortisol (Lupien et al., 2002; Buchanan & Tranel, 2008; Almela et al., 2010; Berger et al., 2017; Gerber et al., 2020) have also utilised smaller sample sizes ranging from approximately n=16 to n=50 for some of the test groups in the studies listed.

Demographics and Blood Pressure Data

Data was initially subject to descriptive statistical analysis. Dependent sample t-tests were then used to assess within-group differences in pre-testing and post-testing blood pressure measurements. One-way Analysis of Variance (ANOVA) followed by Tukey's

post hoc analysis (Brown, 2005) was also used to determine between-group differences in blood pressure readings.

Prevalence & Risk Factor Analysis

Prevalence of stress, anxiety, depression and psychiatric caseness (for the GHQ) was calculated as the percentage of participants with a cut-off score above the normal threshold of 12 for the GHQ, 10 for depression, 8 for anxiety, and 15 for stress. For the risk factor analysis, variables were first dichotomised to enable a good comparison of outcomes; again, participants with a cut-off score of >12 for the GHQ and >10 in depression, >8 in anxiety, and >15 in stress were considered as having these disorders as referenced by the GHQ & the DASS (Goldberg, 1978; Lovibond & Lovibond, 1995). A forward-stepwise (conditional) binominal logistic regression (Maharaj, Lees, & Lal, 2019) was then applied to measure the strength of associations between variables in order to identify significant predictors for the outcomes of interest to the study.

Additionally, one-way ANOVA followed by Tukey's post-hoc analysis (Brown, 2005) was also used to compare group means for each mental state and determine any between-group differences.

Overview of Cognitive Performance Assessments

Data was subjected to further analysis to allow for comparisons of group performance against threshold values for each cognitive performance measure. As performance on subjective cognitive measures may be influenced by age and total years of education (Friedman, 2012), a multivariate analysis of covariance (MANCOVA) controlling for age and years of education was then used to determine between-group differences in cognitive performance.

Relationships Between Negative Mental States and Cognitive Performance

Associations between each of the mental health measures (as measured via the DASS (Lovibond & Lovibond, 1995) and GHQ (Goldberg, 1978)) and cognitive performance (as measured by electroencephalography, the MMSE (Folstein et al., 1975) and the Cognistat (Mueller et al., 2007)) were assessed via Partial Pearson’s correlation (controlling for age and years of education) and non-parametric Spearman’s correlation

for groups with a sample size less than n=30 (Cohen, 1992). Correlation analysis produces a correlation co-efficient known as the r (rho) value between -1 and 1. The direction of the relationship can be either positive ($r>0$) or negative ($r<0$). Negative linear relationships are when one variable increases as the other variable decreases equally and are indicated by negative r values. Positive linear relationships are when one variable increases as the other variable increases equally, and are indicated by positive r values (Bewick et al., 2003). The closer the r value is to 1 or -1 indicates the strength of the linear relationship (Bewick et al., 2003).

In the case of multiple testing, where there were a considerably large number of variables being assessed/correlated (specifically with the EEG data), a Holm-Bonferroni correction was applied following correlation analysis in order to avoid type I errors (Gaetano, 2013). The family-wise α (a) level was set at 0.05.

From the correlation analyses, if a dependent variable had three or more significant correlations following post-hoc corrections ($p<0.05$), a regression analysis was conducted to determine the most significant predictor of that dependent variable (Bewick et al., 2003).

Relationships Between Cortisol and Negative Mental States / Cortisol and Cognitive Performance

Data was subject to descriptive analysis to allow for general comparisons in cortisol levels. Dependant (paired) sample t-tests were then used to determine any differences in pre-testing and post-testing cortisol levels. Cortisol measures were then broken down into pre-testing measure, post-testing measure, the change between pre-testing and post-testing cortisol measures, and average cortisol levels. Partial Pearson's correlation (controlling for age) was then used to determine associations between cortisol measures and negative mental states (DASS (Lovibond & Lovibond, 1995) and GHQ (Goldberg, 1978). A Partial Pearson's correlation (controlling for age and years of education) was also used to determine associations between cortisol measures and cognitive performance as measured by the MMSE (Folstein et al., 1975) and the Cognistat (Mueller et al., 2007).

Chapter 3 – Demographics, work characteristics, and blood pressure data

3.1 Results

Demographics and work characteristics

A total of 154 participants were recruited for the present study. Demographic and work-related data are displayed in Table 3.1.

The cohort breakdowns show a percentage distribution of 52.6% nurses (n=81), 20.1% allied health professionals (n=31), 13.0% doctors (n=20), 14.3% non-healthcare workers (n=22); with nurses being the largest cohort recruited for the current study. As seen in Table 3.1, mean ages for the groups ranged between the late 20's to late 30's for the healthcare groups (nurses=31.9±12.4 years, allied health=28.2±7.7 years, doctors=39.8±11.8 years) and early 20's for the NHC's (23.1 ± 3.4 years). Body mass index (BMI) was similar between the groups (nurses=25.6±5.0, allied health=22.9±3.8, doctors=23.6±2.2, NHC=22.6±3.4) however, gender distributions varied. Majority of the participants in the nursing cohort were females (81%) working as AIN's. The Allied health group was also dominated by females (74%) and mostly comprised of pharmacists and physiotherapists. The doctor cohort was predominantly male (80%) whilst the NHC gender distribution was almost evenly distributed (54% female).

Majority of the nursing group also worked in hospital (37%) and aged care settings reflecting the large number of AIN's (48.1%) and registered nurses (35.8%) in the cohort. The allied health group mostly worked in private practice (80.6%), whilst the doctor cohort were almost evenly split between hospital (55%) and private practice (45%) settings. Most nurses assessed in the current study engaged in shift work (72%), unlike the allied health (25.8%) and doctors' groups (40%) who less than half of each group were shift workers. Average time in role was highest for the doctors (14.5±11.1 years). However, hours per shift were similar within the healthcare groups compared to the NHC's. All groups reported a higher rate of positive job satisfaction; however, rates

of job satisfaction were lowest in the nursing (48.1%) and non-healthcare groups (50%) and highest in the allied health (64.5%) and doctor (70%) cohorts.

Sleepiness, as measured by the ESS, was also similar between the nursing, allied health, and NHC groups whilst the doctors reported the lowest rate of daytime sleepiness as measured by the Epworth Sleepiness Scale (ESS).

Table 3.1: Comparison of demographic and work data between groups (n=154)

	Nurses (n=81)	**Allied Health (n=31)**	**Doctors (n=20)**	**NHC (n=22)**
	Mean ± SD, ratio, or %			
Age (years)	31.9 ± 12.4	28.2 ± 7.7	39.8 ± 11.8	23.1 ± 3.4
Sex ratio M:F	15:66	8:23	16:4	10:12
Body Mass Index	25.6 ± 5.0	22.9 ± 3.8	23.6 ± 2.2	22.6 ± 3.4
Years of Education	15.3 ± 2.3	17.0 ± 1.4	23.4 ± 6.1	15.7 ± 2.0
Professional Type:	RN/Midwife 35.8% AIN 48.1% Other 16.0%	Pharmacist 29% Physiotherapist 29% Other 41.9%	Specialist 50% GP 30% Other 20%	n/a n/a n/a
Time in Role (years)	6.5 ± 8.3	5.2 ± 7.2	14.5 ± 11.1	3.0 ± 1.4
Shift worker	72%	25.8%	40%	40.9%
Shift Type: Mixed	50.6%	0%	30%	18.2%
Hours per Shift	8.2 ± 2.0	7.4 ± 1.4	8.4 ± 1.2	6.3 ± 2.2
Facility: Hospital	37%	19.4%	55%	n/a
Facility: Other	50.6%	80.6%	45%	n/a
Job satisfaction: Yes	48.1%	64.5%	70%	50%
Job satisfaction: No	33.3%	35.5%	30%	50%
Sleepiness (ESS)	6.7 ± 4.7	6.5 ± 5.1	5.2 ± 3.4	6.4 ± 4.5

Note: mixed shift type refers to individuals who worked a mix of both day and night shifts

Key: AIN = Assistant in Nursing, ESS = Epworth sleepiness scale, GP = general practitioner, NHC = Non-Healthcare Professional, SD = Standard Deviation, RN = Registered Nurse

Blood pressure data

Table 3.2 displays the mean pre-testing and post-testing blood pressure (BP) and heart rate (HR) measures for each cohort.

Dependent sample t-tests noted that within-group differences in pre-testing and post-testing blood pressure (BP) parameters were found to be non-significant for each group. One-way analysis of variance (ANOVA) also found no significant between-group

differences for pre-testing BP measures. However, ANOVA's did note significant between-group differences in post-testing systolic BP (p=0.026) and post-testing heart rate (p=0.035). Tukey's post hoc analysis further indicated that the doctors post-systolic BP differed significantly to the nursing (p=0.027) and allied health groups (p=0.03). Additionally, Tukey's post hoc analysis noted that the Nurses post-testing HR bordered on being significantly different from the Allied Health group (p=0.05).

Table 3.2: Comparison of blood pressure data between groups (n=154)

BP Parameter	Nurses (n=81)	Allied Health (n=31)	Doctors (n=20)	NHC (n=22)	P value
	Mean ± SD				
Pre Systolic BP	113.4 ± 12.2	110 ± 10.4	118.6 ± 8.8	112.3 ± 10.5	.108
Pre Diastolic BP	75.4 ± 8.0	74.1 ± 6.9	77.8 ± 6.9	74.2 ± 4.7	.275
Pre Heart Rate	76.6 ± 10.0	74.3 ± 9.0	70.8 ± 9.2	75.1 ± 12.3	.138
Post Systolic BP	111.0 ± 11.8	109.9 ± 10.5	118.8 ± 7.5	110.7 ± 11.6	.026*
Post Diastolic BP	74.6 ± 7.6	74.5 ± 5.0	77.5 ± 6.1	74.8 ± 5.7	.367
Post Heart Rate	72.9 ± 8.9	67.1 ± 7.3	68.8 ± 7.5	72.3 ± 9.6	.035*

Note: P-values marked in red with an asterisk indicate statistically significant between-group differences in blood pressure as determine by the Analysis of Variance (ANOVA).

Key: BP = Blood pressure in beats per min (bpm), NHC = Non-Healthcare Professional, SD = Standard Deviation

3.2 Discussion

Overall, the demographic breakdown for each of the medical cohorts well reflects the Australian health workforce (AIHW, 2016a; AIHW 2018). The total cohort breakdown showed that nurses dominated the recruited participants making up just over half of all the participants that were recruited for the present study; followed by the allied health, non-healthcare, and doctor groups respectively. The total cohort breakdown and the individual group gender breakdowns well represent the current healthcare industry in Australia, which is also heavily dominated by female nurses (AIHW, 2015; AIHW, 2018). The Australian allied health profession is also predominantly female and many allied health professionals work in private practice settings (AIHW, 2016a; AIHW 2018; Allied Health Professionals Australia, 2019) which was also seen in the present study cohort. The medical profession in Australia is also primarily male (Australian Medical Association, 2011; AIHW, 2016a; AIHW 2018) which was evident in our current

demographic breakdown as well. However, the mean ages for all our groups were slightly younger than population norms (AIHW 2018). Total years of education for each group in the present study also reflected population norms as nurses commonly hold undergraduate degrees while allied health and medical professionals commonly hold post-graduate degrees resulting in higher total years of education (Australian Medical Association, 2011; Australian Department of Health, 2013 & 2019; Allied Health Professionals Australia, 2019). The NHC group also consisted mostly of individuals with undergraduate qualifications.

Work characteristics revealed that nurses showed the highest rate of shift work, consistent with current employment trends in Australian nursing professionals (Willis & Elmer, 2007; NSW Nurses and Midwives Association 2019). Shift work in the current allied health group remained minimal which were also consistent with Australian work trends as allied health professionals are frequently employed in private practice and out-patient settings that usually run between the consistent hours of around 9am-5pm (Allied Health Professionals Australia, 2019). It can also be noted that job satisfaction was higher in the Allied Health and Doctor cohorts which may be associated with greater role autonomy, greater job flexibility, and lower workloads [for allied health professionals] (Willis & Elmer, 2007; Australian Department of Health, 2013 & 2019). While the healthcare groups represented their professions well, the low time in role and poor job satisfaction seen in the NHC group may have been influenced by many of the NHC participants consisting of students working part-time in roles such as retail and hospitality.

Though between-group differences in blood pressure were seen for post-systolic measures and post-HR measures, all blood pressure data was still within the normal expected range, not falling into the hypo or hyper-tensive ranges (Izzo & Taylor 1999; Wittwer, 2010). Changes in blood pressure before and after testing were also not significant suggesting that participants did not find the testing interventions used in the present study stressful (which would have resulting in an increase in BP) (Kulkarni et al., 1998; Spruill, 2010).

Chapter 4 – Prevalence of mental health symptoms and risk factor analysis

4.1 Results

Prevalence of Stress, Anxiety, and Depression

Prevalence was determined as any individual who scored above the normal range in each psychological measure. The prevalence rate and mean scores for the GHQ/DASS are displayed in Table 4.1.

Mean scores of the GHQ were within the normal range (below 12) for the allied health (9.7±10.5) and NHC groups (7.0±9.4) whilst the nursing and doctor groups fell into the mild range (scoring 15.5±14.7 and 14.7±14.5 respectively) indicating higher rates of psychological distress. Likewise, mean scores for stress were in the mild category for both the nurse (15.0±10.3) and doctor (15.0±8.4) populations but were within the normal range (below 15) for the allied health (10.8±9.0) and NHC (8.2±8.2) populations. Anxiety also fell into the mild category for the nursing (9.3±8.6) cohort but were within the normal range (below 8) for the allied health (6.0±8.5), doctor (7.3±6.2), and NHC (5.5±8.1) groups. Finally, mean scores for depression were within the normal range (below 10) for the nursing (9.4±9.5), allied health (7.8±9.1), and NHC (4.0±5.8) groups but were mild for the doctor cohort (11.1±7.3). Overall, both the nursing and doctor cohorts reported higher levels of distress in all mental health measures compared to the allied health and NHC groups.

Prevalence rates for each mental state were higher in the nursing and doctor cohorts for each of the mental health measures. The prevalence of poorer psychological wellbeing (measured via the GHQ) were considerably high in nurses and doctors with approximately half of each group scoring above the normal range (nurses 56%, doctors 50%). Though some individuals did not have scores over the normal threshold, 86.3% of all the nurses tested and 95% percent of all the doctors tested did report some degree of psychological distress. Additionally, prevalence rates for stress were much higher in

doctors (60%) and nurses (46%) compared to allied health (29%) and NHC's (23%). When including scores below the clinical threshold cut-offs, 100% doctors and 94% of nurses reporting some degree of stress. Within the doctor group, 50% of those respondents fell into the mild/moderate stress while 10% showed sufficient scores for severe stress. In the nurses, 24% showed mild/moderate stress while 22% showed sufficient scores for severe stress. The nursing (44%) and doctor (40%) cohort also showed higher prevalence rates for anxiety compared to the allied health (26%) and NHC (23%) groups. Though some scores were below clinical cut-offs, 90% of doctors 93% of nurses reporting some level of anxiety compared to 74% for allied health and 80% of NHC's. Finally, prevalence rates for depression were slightly lower for the nurse (37%), allied health (26%), and NHC (14%) groups but considerably high for the doctor cohort (60%). Of those doctors who scored above the normal threshold for depression, 25% fell into the mild/moderate categories while 35% showed sufficient scores for severe depression.

One-way ANOVA also demonstrated significant between-group differences in mean depression scores ($p=0.046$) and mean stress scores ($p=0.025$). Tukey's post-hoc analysis further revealed that the doctor's mean depression scores differed significantly to the NHC's mean depression scores ($p=0.047$), whilst the nurses mean stress scores differed significantly to the NHC's mean stress scores ($p=0.040$).

Table 4.1: Prevalence and mean scores for Stress, Anxiety, Depression and General Psychological Wellbeing (n=154)

Measure	Cohort	Mean ± SD	Interpretation	Prevalence
GHQ Threshold: < 12	Nurses	15.5 ± 14.7	**Mild**	56%
	Allied Health	9.7 ± 10.5	Normal	35%
	Doctors	14.7 ± 14.5	**Mild**	50%
	NHC	7.0 ± 9.4	Normal	23%
Stress Threshold: < 15	Nurses	15.0 ± 10.3	**Mild**	46%
	Allied Health	10.8 ± 9.0	Normal	29%
	Doctors	15.0 ± 8.4	**Mild**	60%
	NHC	8.2 ± 8.2	Normal	23%
Anxiety Threshold: < 8	Nurses	9.3 ± 8.6	**Mild**	44%
	Allied Health	6.0 ± 8.5	Normal	26%
	Doctors	7.3 ± 6.2	Normal	40%
	NHC	5.5 ± 8.1	Normal	23%
Depression Threshold: < 10	Nurses	9.4 ± 9.5	Normal	37%
	Allied Health	7.8 ± 9.1	Normal	26%
	Doctors	11.1 ± 7.3	**Mild**	60%
	NHC	4.0 ± 5.8	Normal	14%

Key: GHQ = General health questionnaire, NHC = Non-healthcare professional, SD = Standard Deviation

Binominal Logistic Regressions - (Risk Factor Analysis)

The logistic regression models for stress, anxiety, depression, and general psychological wellbeing (measured via the GHQ) were all non-significant in the nursing and doctor cohorts. The association between the study variables showed no significance between mental health measures and the following: age, gender, time in role, working at more than one facility, shift work, shift-type, sleepiness, casual employment, shift length, job satisfaction, physical complaints, and cognitive performance.

Within the allied health group: the logistic regression model for depression was significant ($p = 0.01$), explaining 28% (Nagelkerke R2) of the variance in depression, and correctly classified 74.2% of cases. Physical issues/complaints significantly predicted depression (S.E. = 0.657, Exp(B) = 5.71, df = 1, $p = 0.036$) with individuals who reported physical issues such as headaches, backaches, migraines or sleep disturbance being more likely to present with symptoms of distress. The regression model for anxiety was also significant ($p = 0.01$) and correctly classified 74.2% of cases. However, the

regression models for stress and general psychological wellbeing (via the GHQ) were non-significant.

In the non-healthcare group: the logistic regression model for depression was significant (p = 0.002), explaining 44% (Nagelkerke R2) of the variance in depression, and correctly classified 90.5% of cases. Physical complaints again significantly predicted depression (S.E. = 0.23, Exp(B) = 5.679, df = 1, p = 0.035) with individuals who reported physical issues such as headaches, backaches, migraines or sleep disturbance being more likely to present with symptoms of distress. The regression model for anxiety was also significant (p=0.009), explaining 46% (Nagelkerke R2) of the variance in anxiety, and correctly classified 81% of cases. Physical issues/complaints and job satisfaction significantly predicted anxiety (S.E. = 0.636, Exp(B) = 8.93, df = 1, p = 0.049; S.E. = 0.93, Exp(B) = 2.0, df = 1, p=0.020). Finally, the logistic regression model for stress was non-significant but was significant for general psychological wellbeing (p=0.023), explaining 38.8% (Nagelkerke R2) of the variance in GHQ scores, and correctly classified 76.2% of cases. Physical issues/complaints significantly predicted depression (S.E.=1.289, Exp(B) = 17.3, df = 1, p = 0.027).

4.2 Discussion

The present study assessed the prevalence of stress, anxiety, and depression symptomology in representative samples of Australian nurses, allied health professionals, doctors, and non-healthcare professionals (consisting of members of the general population). Considerably little research has been conducted to directly assess the prevalence of stress, anxiety, and depression symptomology in Australian healthcare professionals, especially nurses and allied health professionals. The results of the current chapter indicated a worryingly high rate of negative mental state symptoms among nursing professionals and doctors, which could have a largely negative impact on overall healthcare provision. The current analysis indicated that factors at personal and organisational levels contributed little to each mental state in healthcare professionals, however, efforts made to counter personal and organisational problems in order to reduce mental strain should still be considered.

The present study demonstrated that levels of distress were high with over 20% of the NHC and allied health group, 40% of the nursing sample, and 60% of the doctor sample complying with the DASS cut-off criteria for stress (scores of 15 and above). The nursing and doctor cohorts also scored above the normal threshold, showing mild levels of stress (when observing the mean scores for each mental state) suggesting that they may experience higher rates and/or worse symptoms of stress compared to allied health professionals and especially compared to non-healthcare professionals (as the mean scores for nurses were also significantly different to NHC's). This is also emphasised as multiple individuals from the doctor and nursing groups also presented with severe levels of distress. Our prevalence rates for nurses, allied health professionals, and doctors were also comparable to those of other countries (Caplan, 1994; Opie et al., 2011; Al-Makhaita et al., 2014; Khan Anwar, & Sayed, 2015; Gheshlagh et al., 2017; Kibria, 2018; Almhdawi et al., 2018). Additionally, general psychological wellbeing was also assessed to account for individuals who may not have shown specific signs of stress, anxiety, or depression. The prevalence of poor psychological wellbeing and psychiatric caseness was also common among each sample group at over 20% in NHC's, 30% in allied health professionals, and over 50% for nurses and doctors – reflecting the prevalence rates seen with the DASS. Additionally, the mean scores for the nurses and doctors were above threshold norms entering into the mild range for the GHQ – suggestive of poorer psychological wellbeing and higher rates of psychiatric caseness overall compared to the NHC and allied health groups.

Likewise, the prevalence of anxiety symptoms was common among each sample group at over 20% in NHC's and allied health professionals and over 40% for nurses and doctors compared to approximately 14% of the general Australian population (ABS, 2019). Again, more than a quarter of each cohort complied with the DASS cut off criteria for anxiety (8 and above). The prevalence of anxiety among healthcare professionals in our study also fell within the ranges previously reported in healthcare professionals (ranging between 20–60%) (Caplan, 1994; Erdur et al., 2006; Schmidt, Dantas, & Marziale, 2011; Gao et al., 2012; Sun et al., 2012; Veloso et al., 2016; Creedy et al., 2017; Ghods et al., 2017). Whilst the higher rate of anxiety in the NHC group may be accounted for by considering how population norms are calculated [as mentioned previously], the higher prevalence of anxiety (and psychological symptoms in general)

in the healthcare groups may reflect work-related factors as poor mental health in healthcare professions are commonly described in available literature (Lindwall et al., 2014). The nursing group not only showed the highest prevalence for anxiety but also had mild levels of anxiety overall (when looking at mean scores for each mental state). This suggests that's nurses may experience higher rates and/or worse symptoms of anxiety compared to other healthcare professions and to non-healthcare professionals.

Depressive symptoms were also common in each healthcare professional group with prevalence rates of over 20% for allied health professionals, 30% for nurses, and 60% for medical professionals, compared to population norms of only 4% in the general Australian population (Australian Bureau of Statistics (ABS), 2019). However, it can also be noted that the NHC group for the current study also showed a higher prevalence of depression than general population norms (ABS, 2019), suggesting that depression may be more pervasive than expected. The higher rate of depression in the NHC group compared to general population norms could also be associated with population norms only considering individuals who have been formally diagnosed with depression (ABS, 2019), not accounting for those with subthreshold and milder forms mental illness who may not meet diagnostic criteria or who may not seek help (Olfson, Blanco, & Marcus, 2016). Additionally, not only were the prevalence rates for depression considerably high in the doctor group (60%), but their mean depression score was above the normal range – entering the mild category and their scores differed significantly to NHC scores. This suggests that they may have higher rates of depression compared to NHC's and other health professionals. The results of the present study also indicated that more than a quarter of each healthcare group complied with DASS cut-off criteria for depression (scores of 10 and above). Notably, multiple individuals in the nurse and doctor cohorts had presented with severe depressive symptoms. Depression prevalence among the healthcare professional groups in the present study reflected rates seen in previous literature from around the world with depression rates ranging from approximately 16–53% in doctors (Demir et al., 2007; Sadeghi et al., 2007; BeyondBlue, 2016) and nurses (Ardekani et al., 2008; Welsh, 2009; Schmidt, Dantas, & Marziale, 2011; Cheung & Yip, 2015; Creedy et al., 2017). Currently, little research is available in allied health professions to be able to compare current findings. However, prevalence rates of depression in the allied health group also fit within the

aforementioned ranges seen in nurses and doctors but were slightly lower than those reported in Pakistani allied health workers (Babur & Liaqat, 2018; Syed, Ali & Khan, 2018).

As previously mentioned, rates of stress, anxiety, and depression in our healthcare groups and even in our NHC group were much higher than population norms. Overlooking the signs of anguish and depression presented by healthcare professionals may not only increase the amount of physical and emotional strain placed on the individual but may also lead to low output – possibly resulting in low-quality patient care and higher burdens on establishments (Marazziti et al., 2010). Literature also suggests that poor mental health may lead to a decrease in cognitive performance (explored further in Chapter 6) which could further result in inadequate performance (de Vargas & Dias 2011; Maharaj, Lees, & Lal, 2018). Such consequences in the workplace could endanger human lives and increase the risk of adverse medical events (Berland et al., 2008; Johnson et al., 2018) whilst increasing rates of turnover, absenteeism, and lost productivity within the health workforce leave facilities understaffed and unable to meet patient demands (Tuckett et al., 2015; Johnson et al., 2018).

The current findings suggested that there were limited demographic and occupational variables associated with an increased incidence of developing symptoms of stress, anxiety, and depression - as only one lifestyle factor and one work-related factor were associated with poor mental health outcomes. Physical issues (such as backaches, migraines, and sleep disturbances) were associated with an increased risk of distress, anxiety, depression, and poor general psychological wellbeing in the allied health and NHC groups whilst job dissatisfaction significantly increased the likelihood of developing anxiety in the NHC group. However, previous literature has implicated additional demographic and work-related predictors for the relatively high prevalence of negative mental states among different healthcare providers. In contrast to the present study, previous studies have found common predictors such as age, years of employment, sex, job dissatisfaction, sleep disturbance, shift-work, colleague relationships, and marital status to increase the likelihood of developing stress, anxiety, and depression in nurses and doctors (Brewin & Firth-Cozens, 1997; Firth-Cozens, 1998;

Ruggiero, 2005; Ardekani et al., 2008; Welsh, 2009; Tabrizi & Kavari, 2011; Lindwall et al., 2014; Maharaj, Lees, & Lal, 2019). It, therefore, remains important to continue assessing associations between highly stressful work and its impact on mental wellbeing as we may still need to consider interventions aimed at improving working conditions to reduce personal and occupational strain in employees, thereby preventing or at the least, alleviating symptoms of stress, anxiety, and depression (Johnson et al., 2018).

The results seen in the present nursing group (prevalence: stress 46%, anxiety 44%, and depression 37%) remain similar to our previously published research (Maharaj, Lees, & Lal, 2019)[3]. Our 2019 paper outlining the prevalence of negative mental states in Australian nurses utilised the same statistical analysis and similarly showed prevalence rates of 41.2% for stress, 41.2% for anxiety, and 32.4% for depression. The risk factor analysis undertaken in the paper also identified job dissatisfaction as a predictor for both depression and stress (Maharaj, Lees, & Lal, 2019), unlike the present analysis which did not identify any predictors for poor mental health outcomes in nurses. The discrepancy in risk factor findings may be attributed to the larger sample size in the paper (n=102) compared to the current analysis (nurses n=81).

Limitations (discussed further in chapter 9) such as small representative samples and a cross-sectional study design do impact the current study and limit its applicability to the larger doctor, nursing, and allied health professions in Australia. Hence a larger sample size in addition to longitudinal study designs to fully determine predictors of stress, anxiety, and depression would be beneficial. Additionally, a more comprehensive assessment of demographic, personal, and work-related factors may also be beneficial.

Patient care is heavily reliant upon the entire healthcare team and their ability to work together, work optimally, and deliver the best care possible (Lindwall et al., 2014; Gatchel, 2018). It is becoming increasingly recognised that not only nurses but also doctors and allied health professionals are heavily affected by symptoms of stress, anxiety, and depression (Caplan, 1994; Schmidt, Dantas, & Marziale, 2011; Creedy et

[3] See publication: Maharaj, S., Lees, T., & Lal, S. (2019). Prevalence and Risk Factors of Depression, Anxiety, and Stress in a Cohort of Australian Nurses. *International Journal of Environmental Research and Public Health,* 16(1), 61. https://doi.org/10.3390/ijerph16010061

al., 2017; Gheshlagh et al., 2017; Babur & Liaqat, 2018; Syed, Ali & Khan, 2018). The prevalence of healthcare providers affected by negative mental states in the current study was high and must be addressed. Poor mental health can be detrimental to the individual, the industry, and to patients (Chiang & Chang, 2012; Brandford & Reed 2016) and no single sub-profession is immune to the pervasiveness of mental illness. There should also be a priority in developing both short-term and long-term support strategies and interventions targeted at improving the mental health needs of health professionals to combat the physical and psychological exhaustion associated with these mental states. The stress, depression, and anxiety experienced by healthcare providers may not be entirely preventable but realising its prevalence in the workplace remains considerably important as a healthy workforce is paramount in ensuring that both personal wellbeing and quality patient outcomes are achieved (Brandford & Reed, 2016).

Chapter 5 – Cognitive performance comparisons between groups

5.1 Results

Comparison and overview of cognitive performance between the healthcare and non-healthcare groups

Table 5.1 displays the scores for the cognitive assessment measures (both global and domain-specific) for each cohort. Global cognitive performance (measured by the MMSE (Folstein et al., 1975)) was found to be within normal range for all four cohorts, staying above the 25-point threshold value (Folstein et al., 1975). However, the nurse cohort fell below the impairment threshold of 11 in repetition performance (10.8±1.7) and below the impairment threshold of 4 for the judgement domain (3.4±1.5). Likewise, the NHC group scored below the impairment threshold of 4 for the judgment domain (scoring 3.6±1.8). Finally, the doctor cohort also showed domain-specific cognitive impairment in the memory domain, scoring 8.9 ± 3.1, which was below the 10-point normative threshold. The information from Table 5.1 is also presented graphically in Figures 5.1 and 5.2 to allow for a clearer visual depiction of cognitive performance scores between groups.

Multivariate analysis of covariance (MANCOVA) controlling for age and years of education was also used to determine between-group differences in cognitive performance measures (also seen in Table 5.1). The MANCOVA showed that there was a statistically significant difference between groups after controlling for age and years of education, $F (11, 404) = 1.88$, $p = .003$, Wilks' $\Lambda = .657$, partial $\eta 2 = .131$. Significant between-group differences were seen in global cognitive performance (as measured by the MMSE) and domain-specific measures for attention, repetition, naming, construction, memory, similarities, and judgment (as measured by the Cognistat).

Between group comparisons (via independent sample t-tests) indicated that for global cognitive performance, the nurse scores differed significantly to the allied health group ($p=<0.001$), doctor group ($p=0.017$), and NHC group ($p=<0.001$). For attention, the between group comparisons revealed no further significant differences. For repetition,

the nurses and doctors scores were significantly different from the NHC group (p=0.010, p=0.046). In the naming domain, the nursing and NHC scores showed further significant differences (p=0.007). The nurse group additionally showed differences to the allied health and NHC group for construction performance (p=0.004, p=0.028). Comparisons also revealed that the memory scores differed significantly between nurses and doctors (p=0.001), allied health professionals and doctors (p=0.003), doctors and NHC's (p=0.005). For construction, the nurses differed to the NHC's (p=0.014). For the similarities domain, significant differences were found between the nurse and allied health, doctor, and NHC scores (p=0.013, p=0.03, p=0.002 respectively). Finally, for judgment, between-group comparisons revealed no further significant differences.

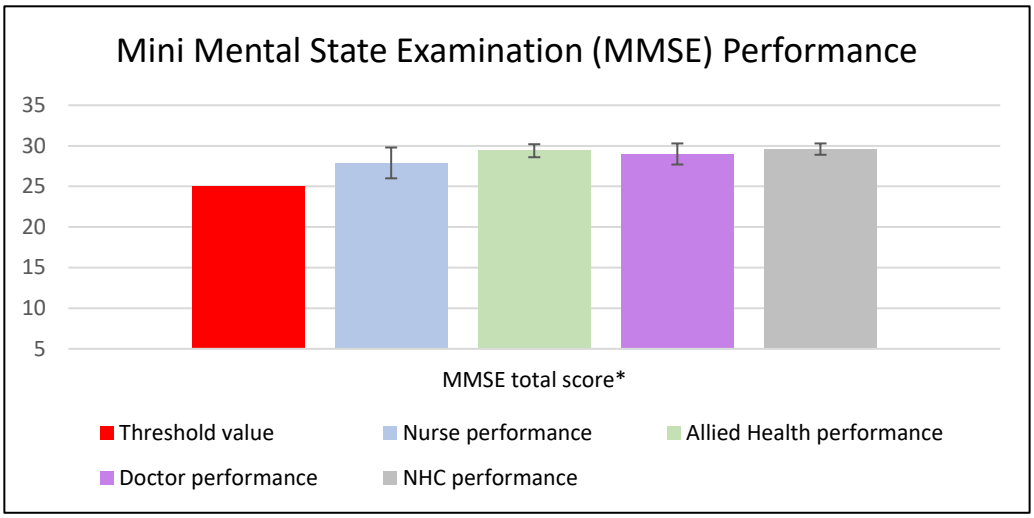
Table 5.1: Comparison of cognitive performance in each of the neurocognitive assessment measures

Cognitive Domain	Impairment Threshold	Nurses (n=81)	Allied Health (n=31)	Doctors (n=20)	NHC (n=22)	
		Mean ± SD				p-value
MMSE Total	< 25	27.9 ± 1.9	29.4 ± 0.8	29.0 ± 1.3	29.6 ± 0.7	<.001*
Orientation	< 10	12.0 ± 0.2	12.0 ± 0	12.0 ± 0	12.0 ± 0	.212
Attention	< 6	7.0 ± 1.0	7.4 ± 0.9	7.5 ± 0.8	7.6 ± 0.6	.012*
Comprehension	< 5	5.4 ± 0.7	5.7 ± 0.5	5.7 ± 0.6	5.6 ± 0.6	.054
Repetition	< 11	10.8 ± 1.7*	11.3 ± 1.3	11.3 ± 0.8	12.0 ± 0	.001*
Naming	< 7	7.2 ± 1.0	7.5 ± 0.9	7.6 ± 0.6	7.9 ± 0.3	<.001*
Construction	< 4	5.3 ± 1.1	6.0 ± 0.5	5.8 ± 0.6	5.9 ± 0.4	<.001*
Memory	< 10	10.6 ± 1.9	10.8 ± 2.3	8.9 ± 3.1*	11.0 ± 1.5	.001*
Calculation	< 3	3.6 ± 0.7	4.0 ± 0.2	4.0 ± 0	3.9 ± 0.5	.201
Similarities	< 5	6.0 ± 1.5	6.9 ± 1.4	7.0 ± 1.2	7.3 ± 1.1	.001*
Judgement	< 4	3.4 ± 1.5*	4.0 ± 1.8	4.0 ± 2.2	3.6 ± 1.8*	.002*

Note: performance values marked in red with an asterisk indicate scores that fell below the impairment threshold indicating mild cognitive impairment for that assessment. P-values marked in red with an asterisk indicate statistically significant differences in cognitive performance scores as determine by the Multivariate analysis of covariance (MANCOVA).

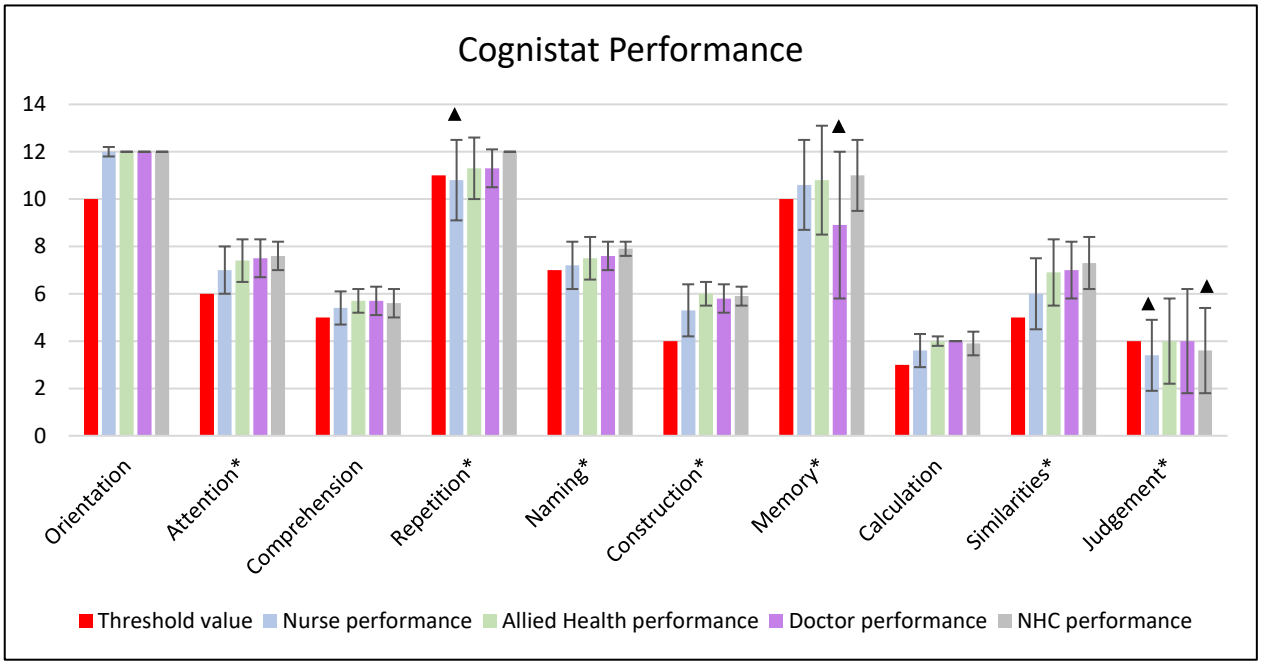
Key: MMSE = Mini Mental State Examination, SD = Standard Deviation

Figure 5.1: Graphical comparison of the MMSE scores between groups



Note: Cognitive domains (on the x-axis) marked with an asterisk indicate statistically significant differences in cognitive performance scores as determined by the Multivariate analysis of covariance (MANCOVA).

Figure 5.2: Graphical comparison of the Cognistat scores between groups



Note: performance domains marked with a triangle (▲) indicate scores that fell below the impairment threshold value, indicating mild cognitive impairment for that assessment. Cognitive domains (on the x-axis) marked with an asterisk indicate statistically significant differences in cognitive performance scores as determined by the Multivariate analysis of covariance (MANCOVA).

5.2 Discussion

The current chapter compared cognitive performance measures (MMSE and Cognistat) between the different healthcare and non-healthcare groups. Cognitive performance tended to differ significantly between the groups, specifically for global cognition and the domains of attention, repetition, naming, construction, memory, similarities, and judgement. Overall, nurses also tended to perform lower in all the cognitive tasks compared to the other healthcare and non-healthcare groups. Comparisons of cognitive performance in healthcare professionals have not been reported in previous literature and thus, the current findings are novel.

Ample evidence suggests that there is some degree of cognitive decline as part of the normal ageing process and that age can account for differences in cognitive ability (particularly in cognitive flexibility, short term memory, and problem solving) (Christensen, 2001; Trollor & Valenzuela, 2001; Adler & Constantinou, 2008). However, cognitive decline associated with old age is most commonly compounded by declines in hearing or visual ability (Peisah, & Wilhelm, 2002). There is also an increasing body of evidence to suggest that level of education may influence cognitive ability even as we age (Wilson et al., 2009; Parisi et al., 2012; Zahodne, Stern, & Manly, 2015; Guerra-Carrillo, Katovich, & Bunge, 2017). Highly educated individuals may be at lower risk of age-related cognitive decline due to increased cognitive reserve and thus, years of education may become an additional factor when considering a comparison of cognitive ability between groups of people. Though changes in cognition are often linked to age and can also be affected by years of education, the effects of both these confounding variables were accounted for in the current analysis and thus should not have impacted findings.

Group differences seen in the current findings may, however, be attributable to coping mechanisms that are commonly employed by individuals. Coping mechanisms are ways of reducing internal stress and discomfort acquired from various sources (Nooryan et al., 2014). When used effectively, coping mechanisms help an individual adjust their emotions, reducing any negative effects they may cause (Chinaveh, 2013; Cameron & Wally, 2015). Doctors commonly utilise problem-solving based coping strategies rather

than emotion-based strategies, which are associated with less mood disturbance (Lemaire & Wallace, 2010) and may help them perform better cognitively compared to the other healthcare groups (Lemaire & Wallace, 2010; Zhu et al., 2019). The differences in performance may also be associated with differing levels of cognitive reserve and neuroplasticity (Kivipelto et al., 2018) which is defined as the brain's ability to cope with damage/change and still function adequately. In addition to positive lifestyle factors and positive coping mechanisms, increased cognitive reserve and plasticity can also result from cognitive remediation (high cognitive activity) and high levels of education (Vance, McNees, & Meneses, 2009; Vance & Wright, 2009; Kivipelto et al., 2018). Cognitive remediation is a way of maintaining, improving, or mitigating the loss of cognitive capacity by continually challenging existing cognitive abilities, which in turn promotes the formation of new connections in the brain that increase cognitive functioning (see Figure 5.3) (Vance, McNees, & Meneses, 2009).

Figure 5.3: The relationship between cognitive remediation and cognitive reserve

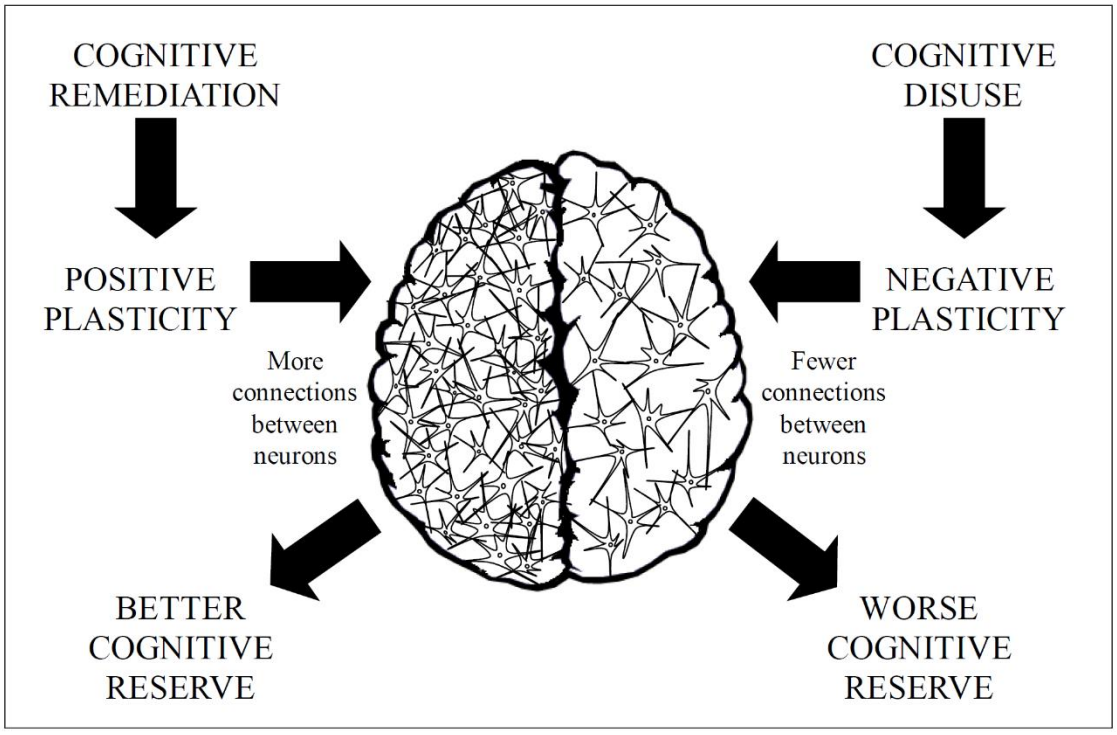


Figure 5.3 displays the relationship between cognitive remediation and cognitive reserve. Cognitive remediation results in positive neuroplasticity which in turn results in better cognitive reserve. In contrast, cognitive disuse leads to negative neuroplastic changes which in turn reduces cognitive reserve. *Image adapted from Vance, McNees, & Meneses, 2009.*

In addition to between-group differences, the nursing group scored below the impairment threshold displaying mild impairments in repetition and judgment performance whilst the doctor cohort showed mild impairments in memory, and the NHC group demonstrated impairments in judgement performance. Repetition, memory, and judgement are crucial abilities to maintain within a hospital setting. The varying pressures present at any given time are unique to each healthcare discipline; however, all health professionals rely heavily on their ability to notice minor changes in patient conditions and use past knowledge to work optimally whilst remembering important patient details. They additionally need to relay information to patients and their families, and other staff members; making memory, repetition (language), and judgement abilities crucial skills to maintain. It is also important to note that many individuals with mild cognitive impairments may also progress further into more severe impairment and later to dementia (Knopman & Petersen, 2015), making it important to identify and combat declines in cognition as early as possible.

In addition to differences seen in the cognitive abilities for each of the groups assessed in the present study, the impairments seen should highlight potential declines in the ability of working health professionals. Professionalism in the medical and health industry relies on both the encouragement and celebration of good practice in addition to the protection of patients from sub-optimal practice (Irvine, 2006). Poor cognitive performance in healthcare professionals cannot be ignored as it can directly affect output and in turn, places both professionals and patients at risk, and thus there is a strong need for more research in the area to identify long term changes in cognition.

Chapter 6 – Associations between Negative Mental States and Cognitive Performance (MMSE & Cognistat)

6.1 Results

Associations between Negative Mental States and Cognitive Performance

The present chapter reports on correlations between negative mental states as measured by the DASS (Lovibond & Lovibond, 1995) and cognitive performance as measured by the MMSE (Folstein et al., 1975), the Cognistat (Mueller et al., 2007). Significant associations between negative mental states and global and domain-specific cognitive performance are displayed in Table 6.1. Overall, as stress, anxiety, and/or depression severity increased, global or domain-specific performance decreased.

Psychological wellbeing (via the GHQ (Goldberg, 1978)) was negatively correlated to global cognitive performance in the nursing cohort (r=-0.51, p=0.013) (Figure 6.1) and repetition performance in the doctor cohort (r=-0.46, p=0.039). Thus, poorer psychological wellbeing (indicated by higher GHQ scores) was associated with poorer global and domain-specific cognitive performance.

Negative relationships were found between stress and domain-specific cognitive performance for the following domains: repetition (r=-0.46, p=0.039), memory (r=-0.49, p=0.029), and attention (r=-0.51, p=0.021) in the doctor cohort. In contrast, a positive correlation was found between stress and judgement performance in the doctor cohort (r=0.61, p=0.004). Thus, as stress levels increased, domain-specific cognitive performance in repetition, memory and attention decreased, whilst judgement increased.

Anxiety was negatively correlated to both memory (r=-0.23, p=0.047) (Figure 6.1) and global cognitive (r=-0.36, p=0.049) performance in the nursing and allied health cohorts respectively. Thus, as anxiety levels increased, global cognition and memory performance were seen to decrease.

Finally, negative correlations were also found between depression and memory performance in the nursing cohort (r=-0.27, p=0.019) (Figure 6.1); demonstrating that as depression levels increased, memory performance decreased.

Multiple regression analysis

As there were multiple cognitive variables (three or more) that were significantly correlated to stress in the doctor population, a multiple regression analysis (Table 6.2) was performed to determine the strongest predictor for stress.

The regression analysis for stress was found to be significant at p=0.02. Collectively, repetition, memory, judgment, and attention significantly predicted a substantial 52% of the variability in depression (F=4.06, df=4,15, p=0.02, R=0.721, R2=0.52, Adjusted R2=0.391). Individually, the strongest of the three predictors was judgement (p=0.014).

Table 6.1: Correlations between mental health (DASS & GHQ) measures and cognitive performance

Cohort	Mental State	Cognitive Measure	r	p
Nurses (n=81)	GHQ	MMSE	-0.51	.013*
	Depression	Memory	-0.27	.019*
	Anxiety	Memory	-0.23	.047*
	Stress	NS		NS
Allied Health (n=31)	GHQ	NS		NS
	Depression	NS		NS
	Anxiety	MMSE	-0.36	.049*
	Stress	NS		NS
Doctors (n=20)	GHQ	Repetition	-0.46	.039*
	Depression	NS		NS
	Anxiety	NS		NS
	Stress	Repetition	-0.46	.039*
		Memory	-0.49	.029*
		Judgement	0.61	.004*
		Attention	-0.51	.021*

Note: Significant correlations are marked in red with an asterisk. No rows were included for the NHC group as no significant correlations were found for that cohort.

Key: GHQ = general health questionnaire, MMSE = Mini Mental State Examination, NS = non-significant, SD = Standard Deviation

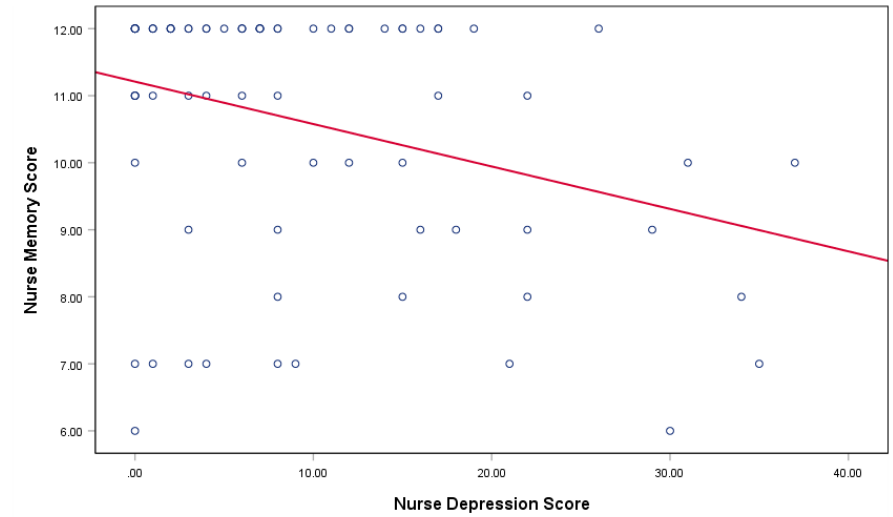
Table 6.2: Regression analysis for stress in doctors

Regression Summary for Dependent Variable: Stress R=0.721, R_2=0.52, Adjusted R_2=0.391, F (4,15) = 4.06 p=0.02, SE of estimate = 6.53					
	β	**SE of β**	**B**	**t**	**p-value**
Intercept	41.07	23.98		1.71	.107
Repetition	-2.67	2.10	-.26	-1.27	.222
Memory	-.753	.588	-.280	-1.28	.220
Judgment	2.05	.735	.547	2.79	.014*
Attention	.354	2.47	.035	.143	.888

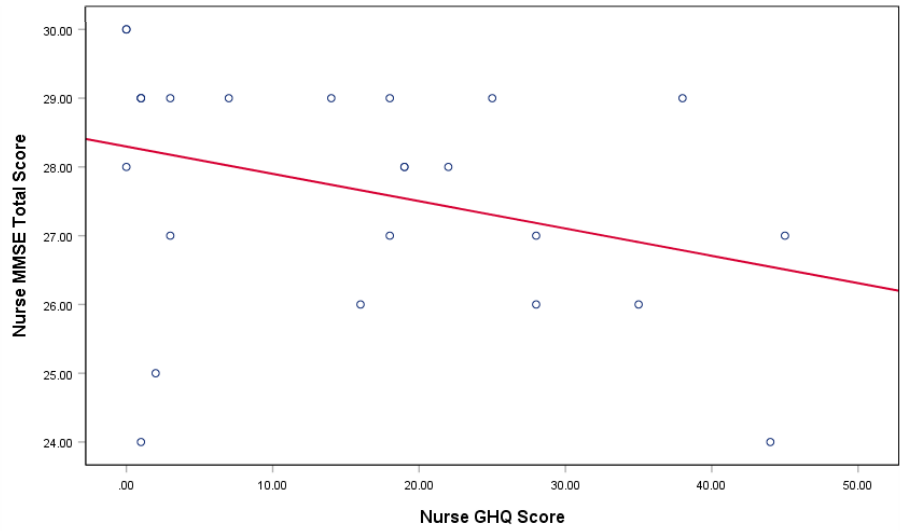
Note: Significant correlations are marked in red with an asterisk.

Key: β = beta, B = Regression coefficient, R = Correlation coefficient, R2 = Coefficient of determination, SE = Standard error

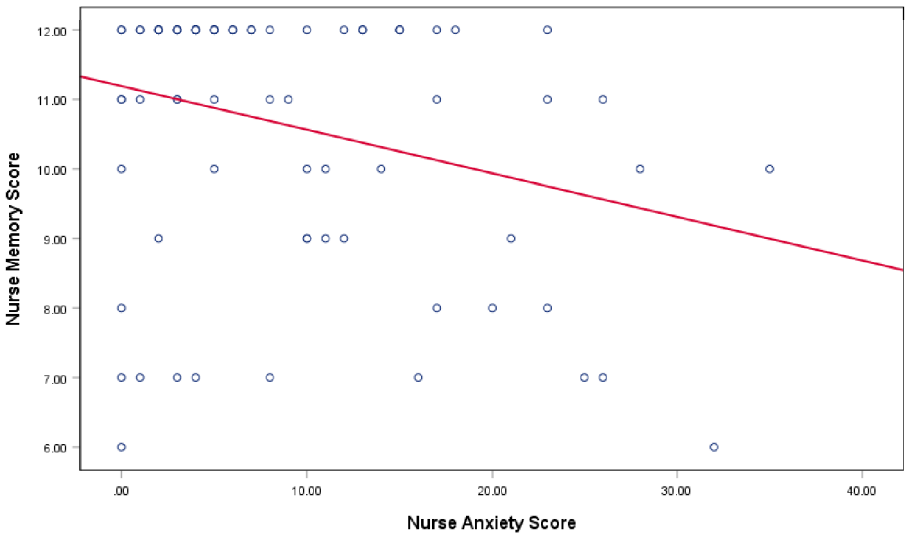
Figure 6.1: Correlation graphs for mental health and cognitive performance variables



Graph A



Graph B



Graph C

Figure 6.1 displays correlation graphs showing the relationship between:
a) Depression and memory performance in nurses (r=-0.27, p=0.019)
b) GHQ scores and global cognitive performance in nurses (r=-0.51, p=0.013)
c) Anxiety and memory performance in nurses (r=-0.23, p=0.047)

6.2 Discussion

Associations between negative mental states (stress, anxiety, and depression) and cognitive performance were found for the three healthcare groups but not for the non-healthcare group. The findings are discussed below.

Stress

The present study noted significant negative correlations between stress and performance in repetition, memory, and attention cognitive domains. Conversely, a positive relationship was found between stress and judgement performance. All associations between stress and cognitive performance were observed in the doctor cohort.

Literature assessing the effects of stress on memory performance has yielded inconsistent findings, with studies generally following the inverted U hypothesis (Yerkes & Dodson, 1908). In accordance with this theory, it has been suggested that small amounts of stress/acute stress can improve memory and recall performance while higher amounts of stress/chronic stress may impair memory performance. However, overall, the literature has consistently supported a strong association between stress and impaired memory performance (Schoofs, Wolf, & Smeets, 2009; Luethi et al., 2008). The impairing effects of stress may be ascribed to physiological and endocrine changes (cortisol) on memory processes (Oei et al., 2006; Schwabe and Wolf, 2010; Ness & Calabrese, 2016). Although the present study found no link between cortisol and cognition (discussed further in Chapter 8), previous studies commonly indicate elevated cortisol levels as the primary determinant of both stress and anxiety-induced memory impairments (Kuhlmann, Kirschbaum, & Wolf, 2005; Kuhlmann & Wolf, 2006; Buchanan & Tranel, 2008; Schwabe & Wolf, 2010) due to its interactions with brain regions such as the hippocampus, prefrontal cortex, and temporal regions. These areas play important roles in supporting various learning and memory phases such as storage, encoding, consolidation, or retrieval (De'Quervain et al., 2003; Bermúdez-Rattoni, 2007; Smeets, 2011). Elevated cortisol levels have also been associated with structural deterioration and a loss of synaptic connections between neurons in these brain regions, potentially explaining how stress may impair memory performance. The

detrimental effects of stress have also been supported by Wiegert *et al.* (2006) who associated stress with reduced neural excitability in the hippocampus post cortisol administration.

In addition to *where* cortisol may be exhibiting its effects, another factor is *when* (Gagnon & Wagner, 2016). Payne *et al.* (2007) suggested that the timing of stress induction may determine which stage of memory will be adversely affected by cortisol elevations. Stress experienced just prior to memory retrieval, (when cortisol levels are not yet elevated) may have very different effects compared to stress experienced one hour before retrieval (when cortisol levels have peaked and are exerting their effects) (Schwabe & Wolf, 2014). Similarly, stress around the time of learning may enhance memory; however, stress long before learning has been shown to blunt new learning (De'Quervain et al., 2000) and can even disrupt the successful encoding of new information (Zoladz et al., 2011).

Stress has also been shown to cause atypical hippocampal activity and connectivity when processing mental schema, which was linked to poorer memory ability (Kluen et al. 2017; Vogel et al., 2018). This infers that stress may also interfere with the efficient use of prior knowledge. Prior knowledge, aka 'mental schema', allows us to learn from previous events and form expectations, hence making the world around us more predictable and easier to navigate. Schemas further help us to organise, interpret, and remember information. Consequently, optimum schema-related processing is essential (Kluen et al. 2017; Vogel et al., 2018). Therefore, stress may not only impair memory by interrupting processes such as encoding and retrieval but may also interfere with memory updating, which can occur by decreasing cognitive flexibility while adopting a rigid cognitive stance (Vogel & Schwabe, 2016). Taken together, these stress-induced changes associated with cortisol and processing ability may explain memory-related difficulties under stress (Vogel & Schwabe, 2016).

In addition to memory impairments, stress was also seen to impair attention performance in the present study, which is commonly supported by previous literature. Eysenck *et al.* (2007) have suggested that stress may impair attention by interfering with attentional control which refers to an individual's ability to focus their attention. According to the attentional control theory – when stressed or anxious, attentional

resources are allocated widely as individuals may preferentially assign resources to irrelevant tasks and stimuli (e.g. their intrusive thoughts or worries) rather than directing resources to focus on a task at hand (Eysenck et al., 2007; Derakshan & Eysenck, 2009; Sadeh & Bredemeier, 2011; Sänger et al., 2014). As attentional resources are allocated widely, rather than directing them to relevant stimuli, attentional control is diminished and in turn, performance is impaired (Sadeh & Bredemeier, 2011; Sänger et al., 2014). Doctors are often exposed to emergency or clinical situations that require them to pay close attention to detail, focus, and shift focus when necessary. In a clinical situation, a lack of and/or lapses in attention can easily result in failure to recognise and respond to patient deterioration (Fry & MacGregor, 2014; Massey, Chaboyer, & Anderson, 2017), negatively impacting patient outcomes. The current study suggests that stress is related to domain-specific cognitive impairments in attention, which may be attributed to a lack of attentional control.

Stress was also linked to poorer repetition performance in the doctor cohort. Verbal repetition falls within the cognitive domain of language, as it involves both sustained language processing and general cognitive control abilities (Ghazi-Saidi & Ansaldo, 2017). Current literature supports the notion that stress may impair language performance in both bilingual and monolingual individuals (Blumenthal et al., 2006; Hashemi, 2011; Zheng & Cheng, 2018). However, relatively little is known about the nature and extent of how stress may impair language. Explanations of the cognitive and linguistic mechanisms driving language performance are also limited and unclear. Linguistic mechanisms may be hindered by tasks that are inherently more demanding and require sustained effort (Mohamadi, 2013). Tasks with greater difficulty may utilise additional amounts of finite cognitive resources that would otherwise be allocated to other processes that underlie language performance. These other processes in turn suffer, which can result in language performance errors such as omissions, additions, and word-substitutions (Green, 1986; Blumenthal et al., 2006). Language errors in medical professionals may result in poor patient notes and handovers, in addition to poor communication with patients and other professionals.

The potential impacts of stress on human judgment is also of paramount importance to healthcare personnel. Medical doctors continually make critical decisions that require sound judgment to diagnose and treat patients whilst preventing injury or, at worse,

the loss of human life. Most critical judgments are also frequently made under conditions of temporary or prolonged stress. Therefore, the relationship between stress and judgment is critical. Contrary to available literature, the present study found that stress was associated with improved judgment performance, rather than impaired performance. Similar to the attentional control theory discussed above, information processing bias (Hayes & Hirsch, 2007; Weber, 2008) suggests that under stress, individuals tend to adopt a simpler mode of information processing where they narrow their focus and do not fully explore alternative options (Kowalski-Trakofler & Vaught, 2003). Thus, they focus on key elements of information while ignoring the rest and tend to offer solutions or make decisions earlier than necessary - without utilising all available information and/or before considering all possible outcomes (Keinan et al., 1987a and 1987b). As focus shrinks, the individual concentrates on only critical issues and elements of information that is being presented to them. This focused/bias attention was assumed to be bad as the individual may fail to gather the right information, but it may, in fact, improve judgement and decision making as it eliminates nonessential information whilst highlighting only the most important points that may be needed (Kowalski-Trakofler & Vaught, 2003). Doctors are commonly required to process vast amounts of information and, in some instances, are under severe time constraints when doing so. Thus, this narrowed focus may be beneficial to their judgment and decision making in these situations.

In addition to information processing bias, it is also crucial to include the concept of perception when discussing the relationship between stress and judgment/decision-making. Stress is induced when there is an imbalance between an individual's external demands and their internal ability to cope with those "perceived demands" (Lazarus & Folkman, 1984). This ability to cope with stress is dependent upon an individual's perception or interpretation of an event or challenge and thus it is based on the perceived experience of distress (Lazarus & Smith, 1988; Delahaye et al., 2015). Stress' effects on attention, therefore, depend on an individual's subjective experience (Palacios-García et al., 2017). If perceived distress is minimal, or if stress is perceived as positive (i.e. a challenge rather than a threat), it may lead to improved judgment rather than impaired judgment, which may have been the case for the doctor cohort in the current study (Palacios-García et al., 2017).

Anxiety

Significant negative correlations between anxiety and memory in the nursing cohort, and anxiety and global cognition in the allied health cohort, were also found.

Similar to stress, the constructs and mechanisms behind anxiety-induced cognitive impairments tend to be similar if not identical. Low levels of anxiety have also been seen to increase arousal and thus improve overall performance due to its motivating properties (Eysenck et al., 2007; Jamieson et al., 2010) and by introducing caution as an influencing factor in performance. Anxious individuals have been shown to adopt a cautious approach to tasks, trading slower speed for better performance accuracy (Hu et al., 2012). However, higher levels of anxiety are generally seen to impair performance, especially in memory-related domains. This impairing effect extends to memory performance in nurses and in turn the quality of care they provide to their patients (Berland et al., 2008). In accordance with the current study findings seen in the nursing cohort; Lucas *et al.* (1991), similarly noted that anxiety was related to impairments in verbal memory. This was later supported by research from Asmundson and Stein (1994) and Okereke & Grodstein (2013), who both observed impairments in verbal memory in patients with anxiety.

In addition to the possible effects of cortisol, anxiety is proposed to impair memory by degrading attentional control and limiting processing efficiency (Eysenck & Calvo, 1992; Wilson, 2008), reducing both the storage and processing capacity of working memory (Darke, 1988). Similar to stress, individuals with anxiety are prone to dedicating cognitive resources to their unpleasant and intrusive thoughts and worries rather than the necessary stimuli or task (Ashcraft et al., 2002; Wilson, 2008). Thus, breakdowns in performance while under pressure or while anxious are more likely to occur when anxiety is either higher or during complex, attentionally demanding tasks that rely on large amounts of cognitive resources to be dedicated to working memory for the short-term storage and manipulation of information (Wilson, 2008). The cognitive assessment used in the present investigation (the Cognistat) assesses working memory/short-term recall (Mueller et al., 2007) which relies heavily on efficient attentional control. It is thus possible that the decrements in the allocation of attentional resources associated with anxiety may account for the current findings.

Unlike the nursing cohort, the allied health cohort demonstrated impairments in global cognition as anxiety levels increased. Anxiety has previously been associated with impairments in various cognitive abilities, such as problem-solving and (Kellogg, Hopko, & Ashcraft, 1999), decision making (Cumming & Harris, 2001), mathematics (Ashcraft, 2002), memory (Berland et al., 2008), and attention (Derakshan & Eysenck, 2009). The overall decline in global cognition observed in the allied health group may reflect the wide-ranging effects anxiety has on cognitive performance. Though non-specific when compared to domain-specific cognitive impairments, declines in global cognitive ability may have more subtle decrements in general everyday abilities. This may subsequently impact the quality of care provided by allied health staff to patients.

Depression

Present study analysis revealed a single significant negative correlation between depression and memory in the nursing cohort. Prior literature in the area supports the present finding linking depression to impaired memory performance (Strömgren, 1977; Glass et al., 1981; Brand et al., 1992; Burt et al., 1995; Gomez et al., 2006; Hinkelmann et al., 2009).

Colby & Gotlib (1988), Brand *et al.* (1992), and Kizilbash *et al.* (2002) all found that depression adversely affected memory and recall performance. This was also seen to worsen with comorbid anxiety (Kizilbash et al., 2002). The damaging effects of depression on memory were also supported by Hinkelmann *et al.* (2009), who found that individuals with depression had impairments in verbal memory and working memory whilst also implicating cortisol which exhibits its effects primarily on the hippocampus and thus, in particular, hippocampal-dependent cognitive domains, such as memory, may be impaired. Neuroimaging studies have also correlated abnormal cerebral blood flow to the prefrontal cortex and medial temporal lobe with increased cortisol (De'Quervain et al., 2003) and reductions in hippocampal volume in subjects with depression (Drevets, 2001; Hickie et al., 2005) which may additionally attribute to possible memory dysfunction as these areas of the brain are important to various memory processes. However, it has been suggested recently that memory impairments in depressive disorders may be supplemented by changes in dopaminergic activity, as activation of the mesolimbic dopaminergic reward circuit enhances encoding and

information retention while depression is characterised by reward circuit dysfunction (Dillon, 2015). Those with depression and/or higher rates of depressive symptomology may also lack cognitive effort, which can impact the memory retrieval processes that rely on the allocation of cognitive effort to recover and utilise information (Brand et al., 1992). Nurses rely heavily on their ability to remember patient information throughout a shift whilst utilising past knowledge to care for their patients to the best of their ability. Impairments in memory can be detrimental to their ability to provide high-quality, safe patient care. Thus, the present study findings raise the possibility that memory impairments related to depression may be caused by both physiological and psychological factors, all of which remain detrimental to an individual's cognitive output.

General Psychological Wellbeing (as measured by the GHQ)

The GHQ was found to be linked to declines in global cognitive ability in the nursing cohort, and repetition performance in the doctor cohort.

Higher GHQ scores have previously been associated with higher error rates/cognitive failures and variability in cognitive performance measures (Bunce et al., 2008; Mackenzie et al., 2009; Day, Brasher, and Bridger, 2012). The association between poor psychological wellbeing and impaired global cognition/memory may be compounded by the mechanisms that moderate the relationship between cognitive impairments and stress, anxiety, and depression as discussed above (e.g. poor attentional control and processing efficiency).

Though the present results did not find an association between stress and memory or anxiety and attention in the nursing group, the present results do partly support our previously published research (Maharaj, Lees, & Lal, 2018)[4], where depression and anxiety were also associated with memory impairments. This slight discrepancy seen between the studies may be attributed to the differing sample size or the more

[4] See publication: Maharaj, S., Lees, T., & Lal, S. (2018). Negative Mental States and Their Association to the Cognitive Function of Nurses. *Journal of Psychophysiology*, 33(3), 207–218. https://doi.org/10.1027/0269-8803/a000223

stringent analysis used in the current analysis, as confounding variables were accounted for during correlation analysis during the present analysis.

A cross-sectional study design was utilised for the present study, only allowing for short-term variations in cognition to be assessed. Short term assessments provide an initial insight into the potential cognitive disposition facing working professionals but do not provide information on long-term changes which would require a longitudinal study design. Additionally, the cognitive assessment tools used in the current analysis provide a thorough investigation of cognitive performance but do not provide a total measure of cognition. Thus, additional cognitive assessment tools may provide a more robust assessment of cognitive performance.

The present chapter found that negative mental states were associated with cognitive performance (in most cases declines in performance) within healthcare professionals. It was also noted that associations differed slightly between the various healthcare and non-healthcare groups and it is suggested that the varying levels of distress, anxiety, or depression (as noted in Chapter 4, Section 4.1) may account for the different associations seen between negative mental states and cognitive performance. Overall, the current findings support hypothesis 2 and 3: that negative mental states will lead to declines in cognitive performance in the healthcare professional group and that different healthcare populations will show different cognitive effect profiles related to negative mental states.

Chapter 7 – Associations between Negative Mental States and electroencephalography (EEG)

7.1 Results

The present chapter explored correlations between negative mental states and cognition, measured by the DASS (Lovibond & Lovibond, 1995) and electroencephalography respectively. Note that the change in EEG activity (active phase minus baseline phase) is reported as 'EEG reactivity'. The active phase refers to the Stroop task and the baseline phase refers to the blank screen (with no Stroop task) - refer to Chapter 2, Section 2.4.5, and Section 2.6 for further explanation of the EEG phases.

Significant associations between negative mental states and EEG variables are displayed in Table 7.1. Values marked with an asterisk indicate findings that remained significant following post-hoc corrections. Findings that remained significant are discussed below.

A topographic EEG map showing the various EEG locations (e.g. FP2, P3, C4, etc.) as mentioned below can be found in Chapter 2, Section 2.4.5, Figure 2.5.

Correlation analysis showed that general psychological wellbeing was not associated with any changes in EEG activity. However, depression was negatively correlated with theta reactivity at locations FP2 (frontal-polar 2) (r=-0.44, p=0.015) and P3 (parietal 3) (r=-0.42, p=0.020) in addition to delta reactivity at locations FP2 (frontal-polar 2) (r=-0.45, p=0.013), CP4 (central-parietal 4) (r=-0.42, p=0.021) in the allied health group.

Positive correlations were also found between stress and delta reactivity at EEG locations C4 (central 4) (r=0.29, p=0.026) (Figure 7.1), P3 (parietal 3) (r=0.29, p=0.027), and P4 (Parietal 4) (r=0.29, p=0.027) for the nursing cohort. Thus, as stress levels increased, delta reactivity at these locations also increased. The allied health group alternatively showed negative correlations between stress and alpha reactivity at location CP4 (central-parietal 4) (r=-0.42, p=0.022) (Figure 7.1), theta reactivity at locations FP2 (frontal-polar 2) (r=-0.42, p=0.022) and P3 (parietal 3) (r=-0.42, p=0.022),

and delta reactivity at locations FP2 (fronto-polar 2) (r=-0.45, p=0.014) and CP4 (central-parietal 4) (r=-0.42, p=0.021). Finally, the doctor cohort showed a negative relationship between stress and theta reactivity at location Fz (frontal midline) (r=-0.50, p=0.034). Thus, as stress levels increased, alpha, theta, and delta activity decreased in the allied health and doctor cohorts.

Higher levels of anxiety were positively correlated with mean parietal delta reactivity (r=0.30, p=0.020), delta reactivity at EEG location O2 (occipital 2) (r=0.28, p=0.032) (Figure 7.1) in the nursing cohort. Conversely, negative correlations between anxiety and beta reactivity at location FT7 (fronto-temporal 7) (r=-0.51, p=0.032) and TP7 (temporo-parietal) (r=-0.56, p=0.017), and gamma reactivity at location FCz (fronto-central midline) (r=-0.51, p=0.032) were seen in the doctor cohort. Thus, as anxiety levels increased, beta was shown to both increase and decrease whilst gamma reactivity decreased only.

Finally, negative correlations were found between depression and gamma reactivity in location FCz (fronto-central midline) (r=-0.57, p=0.013) but was positivity correlated to delta reactivity at location F8 (frontal 8) (r=0.53, p=0.024) in the doctor cohort. Thus, as depression levels increased, there were both increases and decreases in delta reactivity and decreases in theta, and gamma reactivity.

Multiple regression analysis

As there were multiple EEG variables associated with stress following post-hoc correction in the nursing group (informed by the correlation analysis - Table 7.1), a multiple regression analysis was performed to determine predictive capability. The multiple regression for stress was non-significant and did not retain any of the 3 EEG variables (Delta C4, Delta P3, and Delta P4).

Multiple EEG variables were also associated with depression and stress in the allied health group (informed by the correlation analysis - Table 7.1) and thus a multiple regression analysis was again performed to determine predictive capability. The multiple regressions for depression and stress in the allied health group were also non-significant and did not retain any of the 4 EEG variables for depression (Theta FP2,

Theta P3, Delta FP2, Delta CP3) or 5 EEG variables for stress (Alpha CP4, Theta FP2, Theta P3, Delta FP2, Delta CP4).

Finally, multiple EEG variables were associated with anxiety in the doctor group (informed by the correlation analysis - Table 7.1) and thus a multiple regression analysis was performed to determine the strongest predictor. However, the regression analysis was non-significant and did not retain any of the 3 EEG variables for anxiety (Beta FT7, Beta TP7, Gamma FCZ).

Table 7.1: Associations between negative mental states and EEG variables

Cohort	Mental State	EEG Measure	r	p
Nurses (n=81)	GHQ			NS
	Stress	Mean Central Theta	-0.27	.040
		Theta C4	-0.28	.029
		Delta T7	0.26	.047
		Delta C3	0.28	.035
		Delta C4	0.29	.026*
		Delta CP3	0.27	.038
		Delta TP8	0.27	.039
		Delta P3	0.29	.027*
		Delta P4	0.29	.027*
	Anxiety	Mean Parietal Delta	0.30	.020*
		Theta O2	-0.27	.042
		Delta FT7	0.27	.038
		Delta Oz	0.28	.034
		Delta O2	0.28	.032*
	Depression			NS
Allied Health (n=31)	GHQ			NS
	Stress	Mean Central Delta	-0.40	.028
		Alpha CP4	-0.42	.022*
		Theta FP2	-0.42	.022*
		Theta CP4	-0.37	.044
		Theta P3	-0.42	.022*
		Delta FP2	-0.45	.014*
		Delta CP4	-0.42	.021*
		Delta P3	-0.37	.043
	Anxiety			NS
	Depression	Mean Central Delta	-0.41	.026
		Alpha CP4	-0.42	.022
		Theta FP2	-0.44	.015*
		Theta P3	-0.42	.020*
		Delta FP2	-0.45	.013*
		Delta CP4	-0.42	.021*
		Delta P3	-0.38	.037
Doctors (n=20)	GHQ			NS
	Stress	Theta FZ	-0.50	.034*
	Anxiety	Beta FT7	0.51	.032*
		Beta TP7	0.56	.017*
		Gamma FCZ	-0.51	.032*
	Depression	Gamma FCZ	-0.57	.013*
		Beta F8	0.53	.024*

Note: P-values marked in red with an asterisk indicate p-values that remained significant following post-hoc corrections. No rows were included for the NHC group as no significant correlations were found for that cohort. EEG variables are in $\mu V/s^2$.

Key: GHQ = General Health Questionnaire, EEG = electroencephalography

Figure 7.1: Correlation graphs for mental health and EEG variables

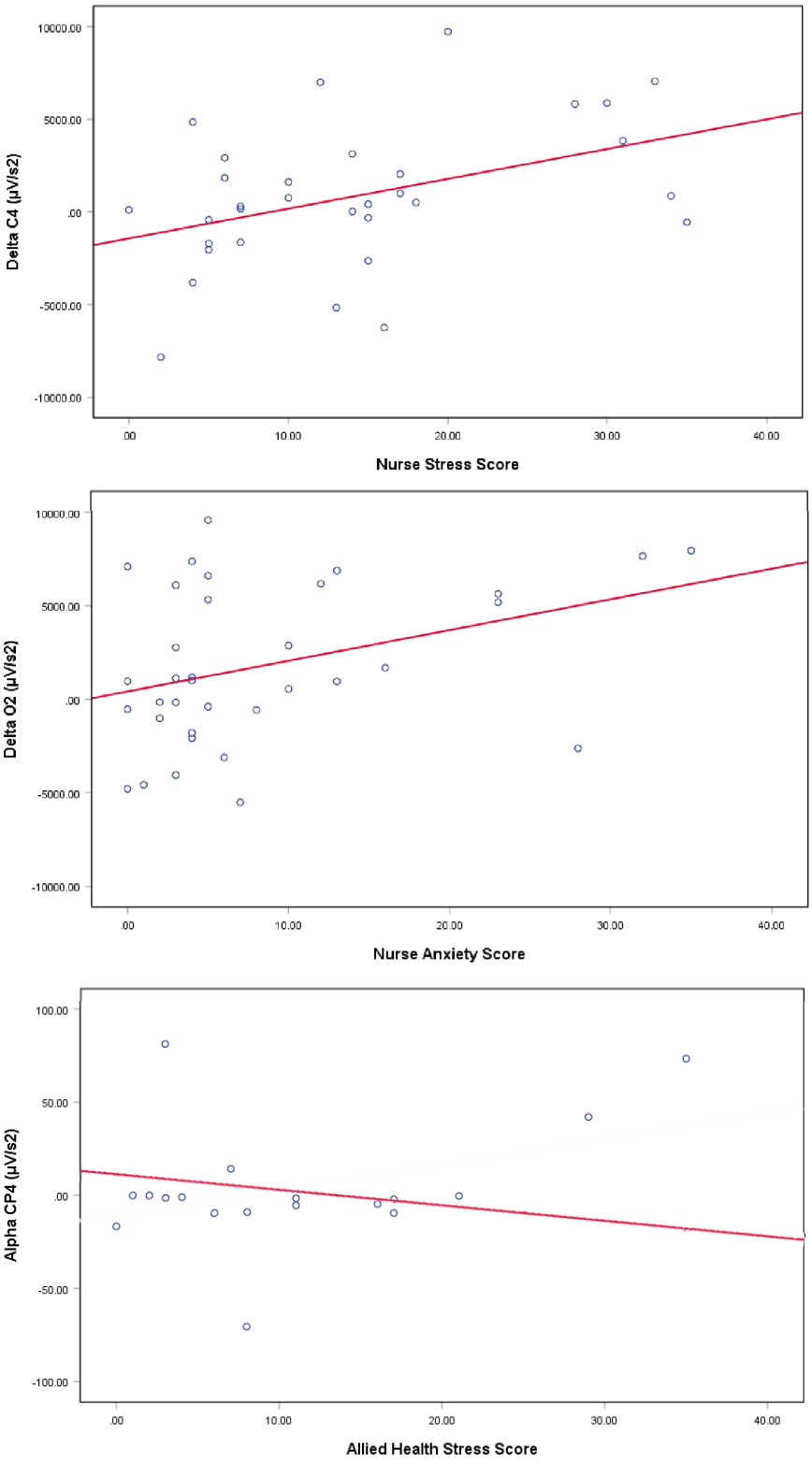


Figure 7.1 displays correlation graphs showing the relationship between:
a) Stress and delta C4 reactivity in nurses (r=0.29, p=0.026)
b) Anxiety and delta O2 reactivity in nurses (r=0.28, p=0.032)
c) Stress and alpha CP4 reactivity in allied health professionals (r=-0.42, p=0.022)

7.2 Discussion

Oscillatory brain activity is indicative of neuronal network functioning in various brain regions (Babiloni et al., 2011a). Electroencephalography (EEG) directly measures ongoing cerebral brain activity and hence represents a promising approach for the investigation of [changes in] cognitive activity. EEG recordings have commonly been used to differentiate healthy individuals from those with various types and severities of cognitive impairment (Jelic et al., 2000; Cui et al., 2014). The present study analysed EEG reactivity (active EEG (during cognitive task) minus baseline EEG (during quiet sitting)) as an index of cognitive function, to understand any physiological changes in cognition and its links to negative mental states. The results of the present analysis indicated that negative mental states were linked to changes in brain activity. This was observed in all five electroencephalographic frequency bands (delta, theta, alpha, beta, gamma). Changes in activity were also found within the frontal, central, temporal, and parietal brain regions, with various electrode site activities in these regions being implicated.

As noted in Chapter 1, Section 1.3.3, fast-wave, high-frequency brain waves (alpha, beta, and gamma rhythms) predominantly underlie higher-order/active cognitive abilities (Koenig et al., 2005). Consequently, changes in activity in these brain waves may be indicative of possible cognitive dysfunction.

The present study noted that depression and stress in the allied health group were associated with decreased alpha reactivity at central-parietal (CP4) regions of the brain; a finding that is supported in available literature (Kan & Lee, 2015; Lee, 2015; Li et al., 2016). Decreases in EEG-alpha activity are also frequently reflective of cognitive impairment/decline (Van der Hiele et al., 2007; Luckhaus et al., 2008; Jackson & Snyder, 2008; Babiloni et al., 2011b; Babiloni et al., 2006a & 2016; Ishii et al., 2017; Smailovic et al., 2018). The synchronisation mechanisms underlying the generation of the EEG-alpha rhythms may be affected in individuals at risk of/with cognitive impairment due to the early neurodegeneration in brain regions involved in alpha-generation, such as the thalamus and neocortex (Cantero et al., 2009), or due to impaired cholinergic system activity, which results in synaptic dysfunction (Babiloni et al., 2011b; Smailovic et al., 2018). It can be noted that while changes in EEG-alpha rhythms associated with

cognitive impairment are most commonly displayed in individuals with Alzheimer's/dementia, it has also been shown in subjective measures of cognition within healthy individuals and in preclinical groups (Tanaka, Ishii, & Watanabe, 2015; López-Sanz et al., 2016) suggesting that disturbances in alpha activity may present as a strong maker for early cognitive decline in addition to late-stage dementia.

The current analysis found that as depression and anxiety levels increased, beta reactivity also increased in frontal (F8), central/midline (C4), fronto-temporal (FT7), and temporal-parietal (TP7) regions of the brain. All changes in beta reactivity were also limited to the doctor cohort which suggests a differing cognitive effect profile to the other healthcare and non-healthcare groups. This increase in beta activity may be due to the doctor group showing higher levels of psychological distress (as noted in Chapter 4, Section 4.1, Table 4.1) (Pizzagalli et al., 2002) or more prominent neuroplastic adaptations (Güntekin et al., 2013; Reid & Evans, 2013), discussed further below. Such findings (of increases in beta activity in depression and anxiety) have also been supported by previous EEG literature assessing depression and anxiety, which have frequently shown frontal brain region hyperactivity (Pizzagalli et al., 2002). Current evidence from Knott *et al.* (2001), and Olbrich & Arns (2013) reported increased beta activity in individuals with depression whilst Leuchter *et al.* (2012) also noted increased beta activity specifically in frontal regions of the brain when assessing individuals with depression. Likewise, subjects with anxiety have also shown increases in beta activity over frontal brain regions (Grillon & Buchsbaum, 1987; Seo & Lee, 2010). However, while depression and anxiety have previously been linked to increases in beta activity (supporting the current findings), cognitive impairment is most commonly associated with decreases in beta activity (Koenig et al., 2005, Gola et al., 2013).

Cognitive activities such as response preparation and cognitive control are largely coupled with the successful modulation of beta activity. However, pathological and uncontrolled increases in beta activity such as those associated with depression and anxiety, are commonly accompanied by a deterioration in cognitive flexibility and control (Engel & Fries, 2010; Leuchter et al., 2012). The literature has also noted that increased beta activity may be interpreted as a physiological adaptation where the brain attempts to use more neural resources to overcome potential impairments or declines in activity (Güntekin et al., 2013; Reid & Evans, 2013; Li et al., 2016).

Neuroplasticity allows the brain to modify its structural and functional organisation to cope with demands (Kolb & Whishaw, 1998), therefore promoting the maintenance of brain activity for intellectual capabilities. Thus, while psychological distress, depression, and/or anxiety may cause neurological/neuroanatomical changes to the brain that result in functional deficits - human brain plasticity attempts to override these deficits in order to preserve higher cognitive functions (Dantas et al., 2011; Li et al., 2016). Accordingly, the results of the present study suggest the activation of focal brain rhythms (beta) associated with depression and anxiety, may still reflect cognitive dysfunction.

Human gamma-band fluctuations continue to receive considerable attention due to their correlations with cognitive processes (Herrmann et al., 2010). Consensus in current literature states that mental stimulation is reflected by an increase in gamma activity (as gamma activity reflects higher cortical functioning), while cortical dysfunction and impairment is associated with a decrease in gamma activity (Bhattacharya et al., 2001). The current analysis found that as depression and anxiety levels increased, gamma reactivity decreased in fronto-central (FCz) regions of the brain. All changes in gamma reactivity were limited to the doctor cohort. The fact that only the doctor cohort showed reductions in gamma activity could again be due to the fact that they tended to show higher levels of psychological distress which may, as discussed below, cause less than optimal neuronal functioning and which in turn may cause the decrease in gamma activity. Similar findings have been seen in our previously published research in nurses (Maharaj, Lees, & Lal, 2018) however, no other research currently exists implicating a change in gamma activity associated with poor mental health measures in doctors. In line with the current findings, Lee *et al.* (2014) similarly noted decreases in gamma activity in depressive and anxiety disorders and further observed changes in activity primarily at fronto-central sites. Additionally, Ferrarelli *et al.* (2008) and Spironelli & Angrilli (2015) noted that decreases in gamma activity were associated with functional deficits in frontal regions of the brain. The reduction in gamma reactivity over frontal brain regions seen in the current study may thus reflect a reduction in local neural communication which conveys less optimal cortical functioning (Spironelli & Angrilli, 2015; Pachou et al., 2008; Bhattacharya et al., 2001). This reduction in functioning may further be associated with neural changes in the

brain (such as structural changes) attributable to negative mental states (Palazidou, 2012).

Cognitive impairment may also be characterised by increased low-frequency activity (delta and theta rhythms) in addition to decreased high-frequency activity (alpha, beta, and gamma rhythms) (Huang et al., 2000; Babiloni et al., 2011b; Koenig et al., 2005).

The present findings demonstrated that within healthcare workers (Nurses, Doctors, and Allied health professionals), higher rates of stress, anxiety, and/or depression were associated with decreases in theta activity in central (Mean central, C4, CP4), frontal (FP2, Fz), parietal (P3), and occipital (O2) brain regions. The current findings contradict available literature, which suggests that poor mental health is associated with increases in theta activity (Moradi et al., 2011; Kamaradova et al., 2018; Newson & Thiagarajan, 2019) as theta oscillations can provide temporal synchronisation within the pre-frontal and frontal brain regions, the amygdala, and the hippocampus. These brain structures are all implicated in the modulation of emotion and play an important role in mental health disorders (Lesting et al., 2011; Jacinto, Cerqueira, & Sousa, 2016). Increased theta activity is also commonly reflective of cognitive impairment (Jelic et al., 1996; Huang et al., 2000; Van der Hiele et al., 2007; Li et al., 2016; Ishii et al., 2017), possibly due to a compensatory mechanism which aims to preserve cognitive function, similar to that seen with beta activity (Li et al., 2016). The current finding of decreased theta activity is, as mentioned, not in line with current literature and therefore, may represent novel neurophysiological evidence of disrupted theta functioning associated with depression, anxiety, and/or stress in healthcare professionals. The regions implicated in the present findings (frontal, central (midline), and parietal) in addition to medial-temporal regions were similar between the groups and are not only important for emotion and cognition but have also been demonstrated to generate theta oscillations (Kahana, Seelig, & Madsen 2001; Cummins et al., 2008). Hence the decreases in theta activity may reflect potential changes in underlying brain regions that generate theta activity and/or altered theta transmission between several brain regions and may in turn still affect optimal cognitive performance (Kahana, Seelig, & Madsen, 2001; Cummins et al., 2008).

Finally, the present analysis revealed that nurses with higher levels of anxiety and stress showed an increase in delta activity in parietal (mean parietal, P3, P4), frontal (FT7), Temporal/temporo-parietal (T7, TP8), central (C3, C4, CP3), and occipital regions (Oz, O2). In contrast, allied health professionals with higher levels of depression and stress showed decreases in delta activity in the same locations in addition to mean central activity. The contrasting findings between nurses and allied health professionals indicates differing cognitive effect profiles suggesting that while nurses may show a slowing in neuronal activity, possibly due to their poorer overall mental health scores (Kamaradova et al., 2018; Newson & Thiagarajan, 2019), allied health professionals do not show this slowing as indicated by the decrease in delta activity that was seen in their cohort. However, decreases in delta activity have been supported in previous literature, though the finding is less common compared to increases in delta activity (Fingelkurts & Fingelkurts, 2015; Li et al., 2016 & 2017; Huang et al., 2019; Zhang et al., 2019). Li *et al.* (2016) further noted impairments in functional connectivity of low-frequency delta activity between the frontal and parietal/temporal/occipital regions during an attention task (Li et al., 2016) which may reflect functional deficits during cognitive processes, further supporting the sites implicated in the current findings. As decreased delta activity may reflect functional deterioration and/or deficit, this less than optimal cortical functioning may also result in a reduction in cognitive performance.

Increased delta activity has also previously been linked to poor psychological wellbeing (Moon et al., 2018; Kamaradova et al., 2018; Newson & Thiagarajan, 2019) and similar changes in EEG-delta power have also frequently been reported in cognitive impairment and Alzheimer's (Babiloni et al., 2016a; Babiloni et al., 2016b; Lizio et al., 2016). Increased delta activity results in overall EEG slowing possibly reflecting dysfunctional synaptic transmission previously linked to changes in cholinergic transmission in the brain which can indirectly cause increases in slow-frequency EEG activity (Ishii et al., 2017; Smailovic et al., 2018). Delta activity has been seen to increase following damage to the Nucleus Basalis which is the main site of production for acetylcholine (Buzsaki et al., 1988). Furthermore, alterations in delta activity have been reported in diseases/disorders that affect white matter (Huang et al., 2000), of which stress and more-so anxiety has been seen to cause neurostructural changes in

white matter even in younger healthy individuals with trait anxiety (Adluru et al., 2017; Johnson et al., 2017; Lu et al., 2018; Coloigner et al., 2019; Heij et al., 2019). These neurostructural changes may disrupt synaptic connections between subcortical and cortical areas (Huang et al., 2000) further resulting in an overall slowing of activity. Slowing in EEG activity has particularly been shown to occur within frontal, parietal/temporo-parietal and occipital brain regions (Fernandez et al. 2013; Babiloni et al., 2016a; Babiloni et al., 2016b; Ishii et al., 2017) further supporting the current findings.

The present study utilised a 32-lead EEG for the current analysis (chosen to provide a full head montage that ensures full, uniform scalp coverage where no brain region is overlooked). Though multiple electrode sites were employed, future studies may benefit from utilising a 64-lead EEG which would provide a more comprehensive overview of brain activity and while further discriminating individual electrode sites that may be implicated in psychological wellbeing and cognitive performance (Ledwidge, Foust, & Ramsey, 2018; Zheng et al., 2018). Although the temporal resolution is commonly praised, its spatial resolution is lacking. The use of additional imaging techniques with better spatial resolution (such as functional magnetic resonance imaging (fMRI)) (Lystad & Pollard, 2009; Camprodon & Stern, 2013) would complement and validate the current findings.

The findings seen in the present analysis suggest that stress, anxiety, and depression are associated with changes in both high frequency (alpha, beta, and gamma) and low frequency (delta and theta) brain activity. Changes seen in each of the EEG frequency ranges may moreover be reflective of cognitive impairment potentially caused by disrupted neuronal signalling, synaptic dysfunction, structural brain changes, and/or impaired overall cortical activity (Bhattacharya et al., 2001; Kahana, Seelig, & Madsen, 2001; Cummins et al., 2008; Spironelli & Angrilli, 2015); however, in some instances (such as beta modulation), neuroplasticity may attempt to override any potential shortfalls in performance (Güntekin et al., 2013; Reid & Evans, 2013; Li et al., 2016). These findings have larger implications for mental health and its link to cognitive functioning, as there has also been evidence to suggest that such changes in brain

activity are shown to precede severe cognitive decline and overt dementias (Smailovic et al., 2018). However, whether the varied mechanisms behind the changes in high and low-frequency brain activity in healthcare workers present prospective electrophysiological markers for cognitive impairment is a topic that warrants future investigation.

Chapter 8 – Associations between cortisol to negative mental states and cognitive performance in nurses

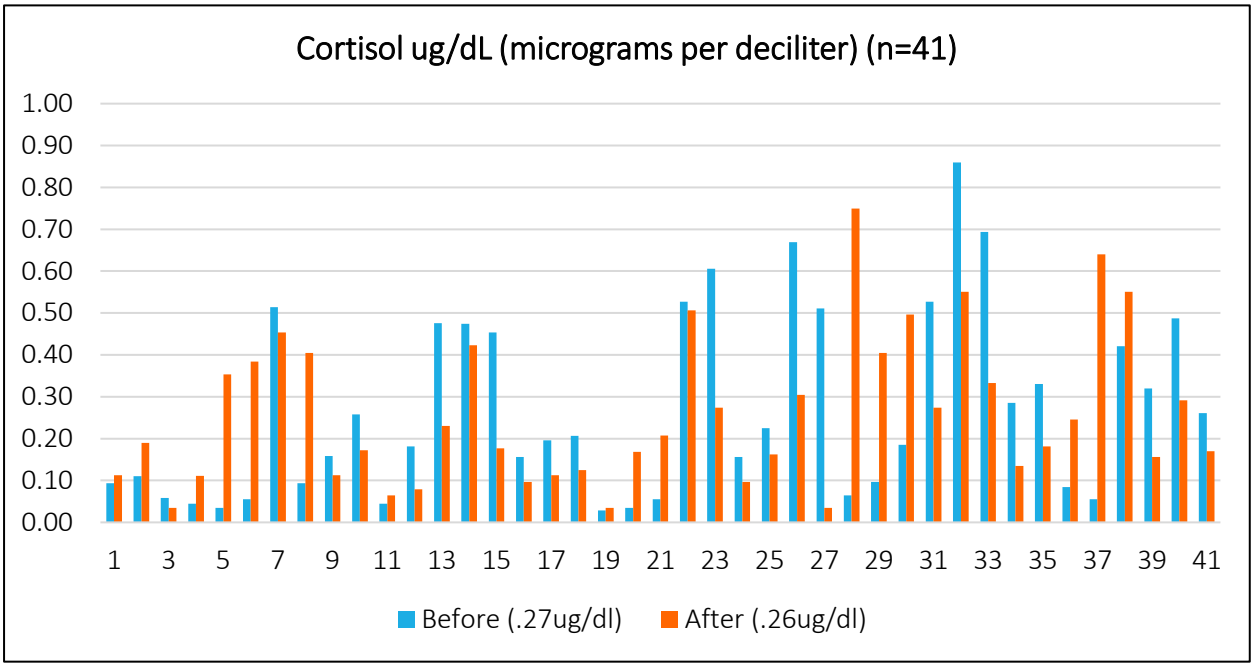
8.1 Results

The current chapter explored the relationship between cortisol and negative mental states, and cortisol and cognitive performance. Data from 41 nurses (all female) are presented in the current analysis. As cortisol levels vary throughout the day (Abudu, 2009), to ensure consistency and enable meaningful comparisons, all salivary samples were obtained between the times of 9am-11am. Cortisol samples were restricted to a specific timeframe and specific healthcare group to allow for meaningful comparisons between the samples.

Cortisol levels averaged .27ug/dl before testing and .26ug/dl after testing. No significant differences were found between the samples taken before and after testing. No associations were found between cortisol and the DASS, GHQ, or cognitive performance measures (MMSE and Cognistat).

Figure 8.1 displays pre-testing and post-testing cortisol measurements for each participant. As can be seen in Figure 8.1, there were large variations between individual participants, with approximately 37% of participants demonstrating large variations (of .2 or more) in their pre-testing and post-testing readings [participants 5, 6, 8, 13, 15, 23, 26-33, 37].

Figure 8.1: Individual cortisol measures before and after testing



Note: cortisol levels seen before testing are indicated in blue whilst cortisol levels seen after testing are indicated in orange.

Key: ug/dL = micrograms per deciliter

8.2 Discussion

Present study data found no significant differences between before testing and after testing cortisol readings, suggesting that the measures were relatively stable. There was also no link between cortisol and the DASS, GHQ, and cognitive performance measures converse to previous literature in the area (Rubinow et al., 1984; Lupien et al., 2002; Bhagwagar, Hafizi, & Cowen, 2005; Buchanan & Tranel, 2008; Hinkelmann et al., 2009; Moica et al., 2016; Qin et al., 2016). A few participants did individually show variations in their before and after cortisol measures, possibly due to any stress encountered before or during participation in the research protocol (as the Stroop task may induce stress (Henderson et al., 2012; Scarpina & Tagini, 2017)). As previously mentioned (Chapter 2, Section 2.4.3) - cortisol levels tend to peak approximately 20-30 minutes following exposure to a stressor (Kirschbaum & Hellhammer, 1989; Gerber et al., 2020) and thus, variations that occurred between pre-testing and post-testing measures may have been due to study participation.

However, cortisol levels are generally expected to be between .01-3 ug/dL (Salimetrics, 2019) and thus, all samples - regardless of variation - remained within the expected range for salivary cortisol readings between 9-11am. Although as previously mentioned, the Stroop task may induce stress in participants (Henderson et al., 2012; Scarpina & Tagini, 2017), the decreases in before and after cortisol levels seen in many of the participants suggests that individuals may not have found the task stressful/stressful enough or that they employed positive coping mechanisms in order to cope with any stress that they felt. Physiologically, cortisol is also known to decrease steadily throughout the day due to the body's natural circadian variations (Burke et al., 2005; Abudu, 2009) which may also account for the slight decrease observed in any of the mean before and after values.

The DASS scores for the nurse cohort (as seen in Chapter 4, Section 4.1) were either within the normal range or were in the mild category of distress and thus may not have been severe enough to warrant significant chronic cortisol hypersecretion (Vedhara et al., 2003). While ongoing stress (including that associated with anxiety and depression) is commonly associated with HPA overactivity, resulting in elevated levels of cortisol (Mackin & Young, 2004), if the stress continues chronically, it may also wear out the stress response system causing under-activity, resulting in low cortisol levels (Dienes et al., 2013; Maripuu et al., 2014; Kunugi, Hori, & Ogawa, 2015). It is also possible that not all individuals are cortisol hyper-responders and thus not all individuals will show excessive cortisol secretion, even in the instance of chronic stress, anxiety, or depression (Knorr et al., 2010) – possibly accounting for the negative findings.

The current chapter does present with limitations such as small sample size and limited sampling. As previously mentioned, cortisol samples were restricted to a specific timeframe and specific healthcare group. However, the time frame in which salivary samples were obtained (9-11am) restricted the number of participants that could participate in cortisol analysis (as the time at which volunteers participated depended on their availability and only those who selected a time between 9-11am participated in the hormone analysis). The collection of multiple samples over a long time period would also require a longitudinal study design to be achieved and could also lead to a high attrition rate and thus, 2 samples were determined to be sufficient for the current

analysis. However, it has been suggested that repeated sampling over a 24-hour period would be more robust as cortisol reference ranges for various times throughout the day are available for comparison (Chan & Debono, 2010). Additionally, the attrition rate for doctors and allied health participants was considerably high and so samples were limited to nursing professionals only – though this did allow for less potential confounders during any comparative analysis.

Although the present study did not yield evidence to suggest that cortisol is associated with mental health and cognitive measures, other studies have suggested that cortisol may still be associated with and present an objective measure of stress, anxiety, or depression (Vedhara et al., 2003; Bhagwagar & Cowen, 2005; Hinkelmann et al., 2009; Moica et al., 2016; Qin et al., 2016), and may still alter cognitive functioning (Rubinow et al., 1984; Lupien et al., 2002; Hinkelmann et al., 2009). Given previous literature suggests that elevated cortisol levels can be associated with poor mental health and declines in cognition, these negative findings may still warrant further investigation.

Chapter 9 – Limitations & Future Directions

9.1 Limitations

The present study investigated the associations between negative mental states and cognitive performance in healthcare and non-healthcare professionals using psychological, cognitive, and physiological measures. However, it is important to note that psychological, cognitive, and electroencephalographic measures are highly dynamic and variable (Başar, 1988). Therefore, the cross-sectional nature of the present study only allowed for short-term variations in wellbeing, cognitive performance, and brain activity to be assessed - giving only a preliminary insight into the cognitive disposition that working professionals face and may not always provide information on the potential long-term effects. Subsequent research implementing longitudinal study designs could potentially track ongoing changes in stress, anxiety, and depression symptomology and cognitive performance for a better understanding of the effects of negative mental states over time. The current study also had smaller sample sizes for some of the test groups which limited the statistical analysis that could be conducted. Subsequent research utilising larger sample sizes may be beneficial to increase statistical power and allow for the better controlling of confounding variables (in addition to controlling for extra confounders such as smoking and alcohol intake). Stricter post-hoc corrections would also be beneficial in a non-exploratory research setting in order to decrease the possibility of chance findings.

The present study also used the Depression Anxiety Stress Scale to measure symptom severity of stress, anxiety, and depression. However, assessments for mental health were obtained only once with measures such as the DASS which is only a state measure (Lovibond & Lovibond 1995). Therefore, multiple assessments over a period of time would also help to confirm and establish the stability or variability of symptoms. Though the DASS is a reliable and validated tool (Lovibond & Lovibond 1995), the use of questionnaires remains subjective. Hence, an objective biochemical measure such as cortisol was also measured in the present study via a non-invasive saliva sample.

As stress, anxiety, and depression involve HPA-axis dysregulation which can result in cortisol hypo/hypersecretion, changes in cortisol levels may be seen in individuals affected by these mental states (Burke et al., 2005; Bremmer et al., 2007). However, the analysis of the salivary samples collected in the present doctoral investigation were conducted using commercially available immunoassay kits which vary in their precision and may also cross-react with other steroid hormones (Burt et al., 2013). Current literature has suggested that Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS) may offer greater sensitivity and specificity for determining cortisol concentrations from saliva when compared to traditional immunoassay methods (Bae et al., 2016). Therefore, LC-MS/MS may in the future, allow for a more thorough determination of cortisol levels, though a standardised methodology for quantifying salivary cortisol via LC-MS/MS would first need to be established. Additionally, with regards to cortisol sampling, repeated sampling over a 24-hour period would also be beneficial to compare daytime waking and night-time cortisol concentrations to available reference to determine whether individuals show different cortisol concentrations over a 24-hour time period (Chan & Debono, 2010).

A 32-channel EEG set up was used and allowed for a thorough full head montage. Looking forward, the use of additional electrode positions may provide a more comprehensive overview of the electrophysiological activity and help identify further individual electrode sites that may be implicated in psychological wellbeing and cognitive performance (Ledwidge, Foust, & Ramsey, 2018; Zheng et al., 2018). Quantitative electroencephalography (qEEG) could also be utilised in such research. qEEG is an extension of EEG analysis that is able to highlight specific waveform components and transform EEG data into a format that is able to clarify and build on relevant information whilst associating numerical results with EEG data for comparison (Nuwer, 1997; Kanda et al., 2009; Billeci et al., 2013). qEEG also allows for visual EEG interpretation as processed data is converted into coloured maps commonly referred to as ‘brain maps’ (Figure 9.1) (Nuwer, 1997; Rodrak & Wongsawat, 2013; qEEG-support, 2019). Topographical brain mapping using EEG would allow for a rapid, and non-invasive visual observation of brain regions activated during cognitive performance, which can then be compared between health professionals with high

stress/anxiety/depression symptomology to those with low or no negative mental state symptoms.

Alternative imaging techniques such as position emission tomography (PET), magnetic resonance imaging (MRI), and functional magnetic resonance imaging (fMRI) may also be added to such a study to validate findings whilst also providing further insight into the involvement of deeper brain structures such as the amygdala and hippocampus (Schreckenberger et al., 2006; Lystad & Pollard, 2009; Camprodon & Stern, 2013). The use of imaging modalities such as MRI would allow for structural information that is able to confirm whether specific brain regions (that were previously identified using EEG) differ or are abnormal in those with negative mental state symptomology. fMRI could additionally provide the ability to confirm specific brain structures and cortical areas that may be involved in psychological wellbeing and cognitive processes (Dunlop & Mayberg, 2017; Castanheira et al., 2019).

Previous research has addressed work factors in nursing and medicine (such as shift work and hours worked) asserting their relationship with depression, stress, reduced work performance, burnout, and job dissatisfaction (Olds & Clarke, 2010; Toobaee & Tadioni, 2011). However, for the current risk factor analysis, limited information was collected and available for analysis. A more comprehensive assessment of demographic, personal, and work-related factors that may be considered predictors for poor psychological wellbeing may also be beneficial to such a study. Specifically, further information on occupational life, exercise habits, sleep habits, social activity, support networks, and coping strategies may be utilised in a risk factor analysis as these factors may play a role in mental health symptom severity (Welsh, 2009; Tabrizi & Kavari, 2011; Subih et al., 2011; Cheung & Yip, 2015; Khodadadi et al., 2016; Leggett, Burgard, & Zivin, 2016; Milojevich & Lukowski, 2016; Freeman et al., 2017).

The current study also used the Mini Mental State Examination (Folstein et al., 1975) and the Cognistat (Mueller et al., 2007) to assess cognitive performance. Together the measures provide a thorough investigation of cognitive performance and are commonly utilised, reliable, and well-established tools (Schwamm et al., 1987; Tombaugh & McIntyre, 1992). However, they may still not represent a total measure of cognition. Both tools possess strong psychometric properties (Cronbach's alpha:

Cognistat 0.90 (Gupta & Kumar, 2009), MMSE 0.69 (Lannin & Scarcia, 2004)), and assess multiple cognitive domains but do not provide information on more intricate cognitive skills such as long-term memory, motor control, and reaction time. Additional cognitive assessments (e.g. the Cambridge Neuropsychological Test Automated Battery (Robbins et al., 1994)) may be added to provide a more comprehensive assessment of cognitive performance.

Figure 9.1: qEEG brain mapping

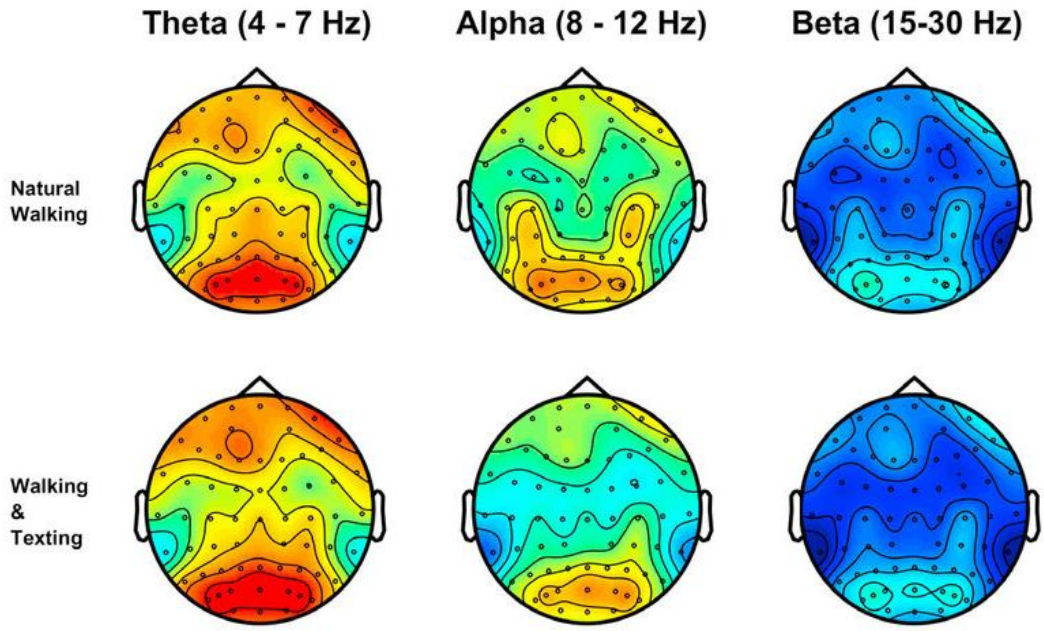


Figure 9.1 displays an example set of brain maps. qEEG allows EEG data to be mapped onto an image of the head. The colours represent varying ranges of activity at a given brain region. The specific image above displays qEEG brain mapping during a single task (walking) and a dual task (walking and texting). *Image adapted from Pizzamiglio et al., 2017.*

9.2 Future Directions

Results from the present doctoral investigation showed high prevalence rates for negative mental states in healthcare providers which ranged from 26-60% for depression, 26-44% for anxiety, and 29-60% for stress. Doctors and nurses also showed poorer domain-specific cognitive performance (specifically in the repetition, memory,

judgement domains). Negative mental states were further associated with domain-specific cognitive declines in doctors (repetition, memory, and attention) and nurses (memory), and global cognitive decline in allied health professionals. Stress, anxiety, and depression were also associated with mixed findings in both low-frequency brain activities (decreased theta, increased delta) and high-frequency brain activities (decreased alpha, increased beta, decreased gamma), potentially reflective of cognitive dysfunction and poor neuronal activity.

The findings reported in the present study have started to fill gaps in the literature as identified previously in Chapter 1. Few studies had previously assessed the prevalence of mental health symptoms in Australian healthcare professional groups, nor had they assessed how stress, anxiety, and depression may affect cognitive performance in these groups.

The results from the present study aim to spur further research into the prevalence of stress, anxiety, and depression in health professionals, and the effects of negative mental states on cognitive performance and subsequently, clinical performance in health professionals. Understanding how poor mental health can affect cognitive performance remains paramount as changes in cognition can have a direct impact on the quality of patient care provided by health professionals. Future prospects based on the results of the current study include; repeating the present study with a longitudinal study design to assess psychological symptom stability or variability, a larger sample size to ensure representation of the groups being assessed and to increase sample power, and using additional cognitive measures to provide a more comprehensive profile of cognitive performance.

Current technological advances have also seen the rise in portable EEG systems (Figure 9.2) which would allow for both portable and wireless EEG assessments via wearable headbands (Cogionics, 2019; Emotiv, 2019; iMotions, 2019) allowing for less intrusive wear in everyday circumstances whilst continuously assessing fluctuations in neuronal activity. An ongoing EEG assessment whilst on the job could also help account for immediate effects of both acute and chronic stress as well as fatigue. If EEG parameter(s) are associated with declines in cognition, this could also lead to the non-invasive monitoring of cognitive performance in the workplace using portable

monitors, which may help reduce complications due to errors associated with cognitive decline. It should be noted that many portable EEG systems utilise dry electrodes which can allow for extra comfort and ease of use but may result in limitations in terms of signal quality (such as high impedance values and artefacts which reduce the accuracy of recordings) (Lopez-Gordo, Sanchez-Morilo & Pelayo Valle, 2014; Di Flumeri et al., 2019). However, research using portable EEG devices can still generate investigations into associations between EEG and cognitive performance to allow for a greater understanding about the involvement of different cortical regions of the brain during possible cognitive decline, and what specific EEG rhythms may underlie various cognitive processes – aiding in the early detection and management of cognitive decline/impairment. As mentioned previously, a large number of individuals affected by mild cognitive impairment may also progress further into more severe impairment and at later stages progress further into dementia (Knopman & Petersen, 2015); which emphasises the importance of identifying and combating declines in cognitive ability as early as possible. If clinically active health professionals are showing higher rates of psychological distress and are in turn more at risk of cognitive impairment, they may also be at a higher risk of later progressing further into dementia. This can also be considered for other high stress professions.

Improving the quality and safety of healthcare services remains a continuing challenge in such a competitive and round-the-clock healthcare industry (Chiang & Chang, 2012), as the industry fights to reduce costs, and decrease waiting times without compromising patient care (Rivers & Glover, 2008). Future research can have wide-ranging implications for both individual health and policy in the workplace as a larger emphasis should be given to mental health and its effects on cognitive performance and decline within healthcare professions. This may lead to the development of interventions and support strategies and programs aimed at reducing the prevalence and adverse outcomes associated with stress, anxiety, or depression on cognitive ability; potentially leading to improved patient care and a reduction in adverse events/errors, in turn, increasing the economic benefit with a reduction in hospital costs associated with medical errors and adverse events, whilst also improving safety, and patient care, as well as improving the overall health and wellbeing of medical professionals.

Figure 9.2: Examples of portable, wireless EEG devices

iMotions

Emotiv

Figure 9.2 displays two portable, wireless EEG devices. The iMotions B-Alert X10 (top) and Emotiv EPOC+ (bottom) (Emotiv, 2019; iMotions 2019). Both devices are currently available on the market. *Images adapted from Emotiv, 2019; iMotions 2019.*

Chapter 10 – Conclusion

Mental health (e.g. stress, anxiety, and depression) in medical and health practise remains a topical issue, in part because these services involve taking care of other peoples' lives, meaning that mistakes and errors could be both costly and sometimes irreversible. It is often expected that health professionals must be or need to be in a perfect state of mind devoid of worry and anxiety as such issues may result in less than optimal levels; and performing at anything less than optimal is of genuine concern (Familoni, 2008; Kakunje, 2011). However, this expectation is flawed, as apart from being affected by the same variables that impose stress on the general population, healthcare providers are especially prone to stress because of the peculiarities and demands of their jobs and the high expectations placed on them by society (Familoni, 2008; Kakunje, 2011). While negative mental states are seen to heavily affect these individuals, prevalence rates in Australian professionals are lacking. Additionally, negative mental states have also been shown to impact on neural health (Sapolsky, 1996; Bishop, 2009) and various cognitive functions (Ashcraft, 2002; Schwabe & Wolf, 2010; Maharaj, Lees, & Lal, 2018). There hence remains a strong need for more research into mental health and cognitive performance within health professional groups.

The first aim of the present research was “to assess the prevalence of negative mental states (i.e. stress, anxiety, and depression) in healthcare professionals”. Prevalence rates for negative mental states in healthcare providers ranged from 26-60% for depression, 26-44% for anxiety, and 29-60% for stress (as discussed in Chapter 4). Examining the results from each representative sample group suggested that healthcare professionals may be at a higher risk of developing negative mental states (particularly doctors and nurses) and that screening and support measures may be needed to support those working in health-related professions. Together, the results allow the first hypothesis “Negative Mental States such as stress, anxiety, and depression will be prevalent in all healthcare professionals” to be accepted, as rates for stress, anxiety, and depression were all prevalent in the nursing, allied health, and doctor sample groups and were comparable to, if not higher, than Australian

population norms (Australian Bureau of Statistics (ABS), 2019) and prevalence rates from other health professional groups from around the world (Caplan, 1994; Opie et al., 2011; Al-Makhaita et al., 2014; Khan Anwar, & Sayed, 2015; Gheshlagh et al., 2017; Kibria, 2018; Almhdawi et al., 2018).

The second aim of the present research was "To investigate links between negative mental states and cognitive performance (MMSE, Cognistat, EEG) in healthcare professionals". The results of Chapters 5 and 6 found that doctors and nurses showed poor performance in domain-specific cognitive performance measures (repetition, memory, judgement) while negative mental states were also related to impairments in global and domain-specific cognitive performance in the healthcare groups but not the non-healthcare group. Stress was related to decreases in repetition, memory, and attention in doctors, while anxiety was related to decreased memory in nurses and global cognition in allied health professionals. Finally, depression was related to declines in memory in nurses. Conversely, a single positive correlation between stress and judgement in the doctor cohort was observed. Examining the results together suggests that the relationship between negative mental states and cognitive performance measures may be best reflected by the inverted-U hypothesis (Yerkes & Dodson, 1908; Aerni et al., 2004), the potential effects of cortisol (Buchanan & Tranel, 2008; Oei et al., 2006; Ness & Calabrese, 2016), or alternatively, disruptions in cognitive control abilities (e.g. attentional control, cognitive effort, processing bias, and processing efficiency) (Brand et al., 1992; Eysenck et al., 2007; Hayes & Hirsch, 2007; Weber, 2008; Derakshan & Eysenck, 2009; Sadeh & Bredemeier, 2011). Together, these results allow PART A of hypothesis 2 "Negative mental states will lead to declines in cognitive performance (MMSE, Cognistat) in healthcare professionals" of the present research to be accepted, as stress, anxiety, and depression were associated with declines in global and/or domain-specific cognitive performance variables.

Furthermore, PART B of hypothesis 2 was that "Negative mental states will lead to increases in low-frequency EEG activity and decreases in high-frequency EEG activity - reflective of potential cognitive dysfunction". Available literature has suggested that cognitive decline is commonly characterised by increases in low-frequency activity (delta and theta) in addition to decreases in high-frequency activity (alpha, beta, and

gamma) (Koenig et al., 2005; Huang et al., 2000; Babiloni et al., 2011b). As discussed in Chapter 7, mixed findings in both low-frequency activity (decreased theta, increased delta) and high-frequency activity (decreased alpha, increased beta, decreased gamma) were observed in the present study. Taken together, the changes in EEG activity associated with stress, anxiety, and depression may be due to neurostructural brain changes and/or neurochemical changes (Bhattacharya et al., 2001; Kahana, Seelig, & Madsen, 2001; Cummins et al., 2008; Spironelli & Angrilli, 2015), or in some instances, neuroplasticity (Güntekin et al., 2013; Reid & Evans, 2013; Li et al., 2016). While asymmetry exists between the cerebral hemispheres, changes in EEG activity reported in cognitive decline have been consistently observed in both left and right brain hemispheres (Koenig et al., 2005; Cantero et al., 2009; Babiloni et al., 2011b). Although hemispheric asymmetries are associated with advantages effects (such as the enhancement of an individual's ability to perform different tasks at the same time, increases in neural capacity, and greater uni-hemispheric processing), declines in cognitive ability may result in changes in neuronal communication and ability both uni-hemispherically and inter-hemispherically (Ocklenburg & Güntürkün, 2012); therefore changes in EEG frequencies may not necessarily occur differently between hemispheres, or at the least, may be similar between the hemispheres. These results, therefore, partially confirm PART B of hypothesis 2 that "Negative mental states will lead to increases in low-frequency EEG activity and decreases in high-frequency EEG activity - reflective of potential cognitive dysfunction". However, further validation of the relationship between electroencephalography and cognitive performance would be worthwhile in determining potential EEG markers for mental health and cognitive decline.

The third aim of the present research was "To compare the effects of negative mental states on cognitive performance between different healthcare populations". As seen in Chapter 5, nurses showed impairments in the repetition and judgment domain while the doctor cohort showed impaired memory, but the allied health group performed above the threshold for impairment in all the tasks. The differing scores in performance suggest unique cognitive effect profiles between groups. Furthermore, in Chapter 6, the three healthcare groups showed different relationships between negative mental states and cognitive performance measures. Based on these findings, the third

hypothesis of the present research “Each healthcare population will have a different cognitive impact profile associated with negative mental states” was accepted. It can be suggested that the level of stress, anxiety, and/or depression experienced within the professions may be a modulating factor; with more severe mental health symptomology being associated to more impairments in performance.

The final aim of the present study was “To assess the relationship between cortisol and negative mental states, and cortisol and cognitive performance”. As noted in Chapter 8, no associations were found between cortisol and: DASS, GHQ, or cognitive performance measures. This may be due to mild levels of distress, anxiety, or depression not warranting chronic cortisol hypersecretion (Vedhara et al., 2003) or a lack of cortisol hyper-responders as not all individuals show excess cortisol secretion. Therefore, we reject hypothesis 4 “That cortisol will be associated with both negative mental states and cognitive performance”. However, cortisol’s association to poor mental health and cognition is still well established in available literature, and further research into the area is therefore still warranted.

In conclusion, the findings of the present research demonstrate the prevalence of mental health symptoms in healthcare professions, and the multifaceted nature of the relationships between negative mental states and cognitive performance, where it is possible to observe both improvements and impairments in performance. Unique variations in electroencephalographic variables were also observed when correlated back to stress, anxiety, and depression; possibly allow for a better understanding of what occurs in cortical regions of the brain. Additionally, changes seen in EEG activity may also allow for the understanding behind what specific brain rhythms may underlie negative mental states and how they may link to/affect various cognitive processes. In addition, the present research also determined unique cognitive impact profiles associated with negative mental states as healthcare and non-healthcare professional groups each showed different variations in cognitive performance. Understanding and further exploring these profiles may enable the development and implementation of targeted and potentially industry-specific management, monitoring, and/or intervention strategies aimed at preserving the health and performance of medical and

health professionals alike. This may ensure the quality of patient care and reduce potential adverse medical events and errors that could be associated with poor performance due to mental health issues.

The prevalence and effects that stress, anxiety, and depression have on healthcare staff should not be ignored. These professionals ensure that the health and wellbeing of society are met on a daily and sometimes even hourly, or every minute basis. Their wellbeing is crucial to ours, and though we cannot avoid mental distress in such demanding professions such as medicine and health, we can aim to reduce this distress and take better care of the professionals who care for us.

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Appendices

Recruitment Poster:

WANTED

Volunteers for Cognitive Research

Cognitive Function Associations to Mental States in Healthcare Professionals: A Comparative Study

Healthcare professionals (Doctors, Nurses, Midwives, Allied Health, Pharmacists, Dentists etc.), aged between 18 and 69 are called to participate in cognitive and physiological research, conducted in the Neuroscience Research Unit, at the University of Technology, Sydney.

The experimental protocol is simple, non-invasive and will take approximately 1 - *2 hours* of your time.

All results obtained will remain entirely confidential and secure.

For more information contact:

Name: Shamona Maharaj
Ph:
Email: @student.uts.edu.au

NOTE:
This study has been approved by the University of Technology, Sydney Human Research Ethics Committee (HREC 2014000110). If you have any complaints or reservations about any aspect of your participation in this research which you cannot resolve with the researcher, you may contact the Ethics Committee through the Research Ethics Officer (ph: 02 9514 9615, Research.Ethics@uts.edu.au) and quote the UTS HREC reference number. Any complaint you make will be treated in confidence and investigated fully and you will be informed of the outcome.

UNIVERSITY OF TECHNOLOGY SYDNEY

UNIVERSITY OF TECHNOLOGY, SYDNEY
CONSENT FORM

I _____ agree to participate in the research project ***'Cognitive function associations to mental states in healthcare professionals: A comparative study'*** (Approval no: UTS HREC REF NO. 2014000110) being conducted by Shamona Maharaj at the Neuroscience Research Unit, University of Technology, Sydney (UTS). Funding for this research has been provided by the School of Medical and Molecular Biosciences (UTS).

I understand that the purpose of this study is to explore any associations of human physiology to brain function as this has implications for the future development of algorithms and/or management programs.

I also understand that participation in this research will involve minimal risk and/or inconvenience to me. Further, I am aware that participation in this study will include measurements of blood pressure and brain activity as well as the completion of questionnaires on lifestyle, brain (cognitive) function, behaviour, and shiftwork. Finally, I understand that I may be invited to participate in non-invasive salivary cortisol testing.

I also understand the study will involve screening for blood pressure and there is the possibility that I may be found to have high blood pressure. If my blood pressure is greater than 140/90 mmHg, I will be advised to consult a doctor. If my blood pressure is greater than 160/100 mmHg prior to commencing the study I will not be included in the study. If my blood pressure is greater than 160/100 mmHg at any time during the study, the study will be stopped. In both latter cases, I will be offered to be escorted to a doctor and/or advised to consult a doctor.

I am aware that I can contact Shamona Maharaj on [redacted] or the supervisor Associate Professor Sara Lal ((02) 9514-1592 or Sara.Lal@uts.edu.au) if I have any concerns regarding the research. Further, I am aware that I am able to withdraw my participation from this research project at any time, without consequences, and without providing a reason.

I agree that Shamona Maharaj has sufficiently answered my questions.

I agree that the data gathered in this project may be published in a form that does not identify me in any way. All salivary samples will be used for the purpose of this study only and will be disposed after use.

_____ ____/____/____
Signature (participant)

_____ ____/____/____
Signature (researcher or delegate)

NOTE:
This study has been approved by the University of Technology, Sydney Human Research Ethics Committee. If you have any complaints or reservations about any aspect of your participation in this research which you cannot resolve with the researcher, you may contact the Ethics Committee through the Research Ethics Officer (ph: 02 9514 9772; Research.Ethics@uts.edu.au) and quote the UTS HREC reference number. Any complaint you make will be treated in confidence and investigated fully and you will be informed of the outcome.

Summary record of research study

To be completed immediately after each lab study

Date: _____

Name of researcher: _____

Name of participant: _____

1. Provide a brief summary of the study (tick one of the following):

- □ The study went smoothly
- □ There were some issues
- □ There were major issues

2. Researchers general account and summary of the study - detail in a few lines or more:

_____

_____

_____

3. Was there any 'out of the ordinary' event or issue in this lab study? Yes / No

If Yes, provide more details:

_____

_____

_____

4. Was there an emergency situation in the lab? Yes / No

If Yes, provide more details:

_____

_____

_____

Note:
If you answered Yes to Question 3, you must notify a senior researcher and/or responsible academic or deputy responsible academic immediately.
If you answered Yes to Question 4, (you SHOULD have followed the emergency protocol and you MUST report the incident using HIRO (Hazard and Incident reporting online) system via the UTS Safety and Wellbeing website: http://www.safetyandwellbeing.uts.edu.au/accidents/index.html
You must then notify a senior researcher and/or responsible academic or deputy responsible academic asap.

Nurse appraisal questionnaire

Directions: Please answer the following questions as accurately as possible. For some questions, you are required to tick the box that corresponds to your response.

Q1. What type of nurse are you?

□ **AIN**
□ **EN**
□ **RN**
□ **Midwife**
□ **Other (If other, please specify)** _____

Q2. Are you presently employed as a nurse? □ **YES** □ **NO**

Q3. How long have you been working in the field? _____

Q4. Do you work in more than one facility? □ **YES** □ **NO**

Q5. What type of facility do you work in? You may choose more than one answer.

□ **Aged Care facility**
□ **Home Care**
□ **Hospital (Public)**
□ **Hospital (Private)**
□ **Other (If other, please specify)** _____

Q6. Do you work shift work? □ **YES** □ **NO**
If yes, do you work long shifts, short shifts or both? _____

Q7. How many hours do you work per shift? _____

Q8. Do you work night shift, day shift, or rotational shifts? _____

Q9. Are you a casual/part time/permanent employee? _____

Q10. How often do you get a break at work? _____

Q11. Do you find your break time sufficient? □ **YES** □ **NO**

Q12. Do you find your work stressful? □ **YES** □ **NO**

Q13. What strategies do you employ to manage fatigue and sleepiness at work?

_____

Q14. Do you get along with your colleagues? □ **YES** □ **NO**

Q15. Do you often get upset or angry while at work? □ **YES** □ **NO**

Q16. Are you satisfied with your current job? □ **YES** □ **NO**

Allied health questionnaire

Directions: Please answer the following questions as accurately as possible. For some questions, you are required to tick the box that corresponds to your response.

Q1. What role in allied health do you have?

□ **Physiotherapist** □ **Optometrist/Orthoptist**
□ **Occupational Therapist** □ **Podiatrist**
□ **Imaging (please specify) _____** □ **Psychologist**
□ **Pharmacist** □ **Pathologist**
□ **Other (If other, please specify) _____**

Q2. Are you presently employed in allied health? □ **YES** □ **NO**

Q3. How long have you been working in the field? _____

Q4. Do you work in more than one facility? □ **YES** □ **NO**

Q5. What type of facility do you work in? You may choose more than one answer.

□ **Private Practice**
□ **General Practice**
□ **Hospital (Public)**
□ **Hospital (Private)**
□ **Other (If other, please specify) _____**

Q6. Do you work shift work? □ **YES** □ **NO**
If yes, do you work long shifts, short shifts or both? _____

Q7. How many hours do you work per shift? _____

Q8. Do you work night shift, day shift, or rotational shifts? _____

Q9. Are you a casual/part time/permanent employee? _____

Q10. How often do you get a break at work? _____

Q11. Do you find your break time sufficient? □ **YES** □ **NO**

Q12. Do you find your work stressful? □ **YES** □ **NO**

Q13. What strategies do you employ to manage fatigue and sleepiness at work?

_____

Q14. Do you get along with your colleagues? □ **YES** □ **NO**

Q15. Do you often get upset or angry while at work? □ **YES** □ **NO**

Q16. Are you satisfied with your current job? □ **YES** □ **NO**

Doctor appraisal questionnaire

Directions: Please answer the following questions as accurately as possible. For some questions, you are required to tick the box that corresponds to your response.

Q1. What type of doctor are you?

□ **Intern/Resident**
□ **Registrar**
□ **Specialist (please specify) _____**
□ **General Practitioner**
□ **Other (If other, please specify) _____**

Q2. Are you presently employed as a doctor? □ **YES** □ **NO**

Q3. How long have you been working in the field? _____

Q4. Do you work in more than one facility? □ **YES** □ **NO**

Q5. What type of facility do you work in? You may choose more than one answer.

□ **Private Practice**
□ **General Practice**
□ **Hospital (Public)**
□ **Hospital (Private)**
□ **Other (If other, please specify) _____**

Q6. Do you work shift work? □ **YES** □ **NO**
If yes, do you work long shifts, short shifts or both? _____

Q7. How many hours do you work per shift? _____

Q8. Do you work night shift, day shift, or rotational shifts? _____

Q9. Are you a casual/part time/permanent employee? _____

Q10. How often do you get a break at work? _____

Q11. Do you find your break time sufficient? □ **YES** □ **NO**

Q12. Do you find your work stressful? □ **YES** □ **NO**

Q13. What strategies do you employ to manage fatigue and sleepiness at work?

_____

Q14. Do you get along with your colleagues? □ **YES** □ **NO**

Q15. Do you often get upset or angry while at work? □ **YES** □ **NO**

Q16. Are you satisfied with your current job? □ **YES** □ **NO**