Mind & Brain Research Concentration:

This concentrations research area includes chronic stress, depression and obesity, ADHD, bipolar, schizophrenia, anxiety, dementia and many other disorders. There are three arms of research:
- Clinical Research
- Laboratory Research
- Bio-statistic Research

Mind & Brain: Clinical Research

The clinical mental health research group works with human volunteers to determine the effectiveness of treatment regimes, medications and interventions on various disorders.

**Project 1: Chronic fatigue syndrome: Leptin, interleukin 6 and clinical symptoms**
*Supervisors: Professor Julio Licinio, Dr Michael Musker*
*Student: Honours*

Chronic fatigue syndrome (CFS) is characterised by a constellation of symptoms in previously healthy and active individuals. Because of these symptoms, quality of life of persons with CFS can be extremely compromised. While the search for a clear-cut cause remains elusive, we believe that we can make a major contribution to patient’s quality of life by elucidating the biological basis of their clinical symptoms. If the proximal biology underlying the disabling symptoms of CFS is elucidated, we will be able to target treatments aimed at symptomatic improvement. This project will involve assisting the research team in setting up human research study, interviewing participants, sampling and storage processes for blood, collecting data from human participants in a mental health context, data collation and analysis.

Mind & Brain: Laboratory Research

The laboratory research group addresses the mechanisms of mind & brain disorders utilising molecular techniques and models in a laboratory environment.

**Project 2: The role of stress in cancer initiation and progression**
*Supervisors: Professor Julio Licinio, Dr Martin Lewis, Mr Rhys Fogarty*
*Student: Honours*

There is growing evidence that chronic psychosocial stress contributes to cancer initiation and progression, however the molecular mechanisms underlying this phenomenon are poorly understood. Chronic exposure of cells to hormones released during stress may activate pro-malignant pathways that increase the cell’s susceptibility to carcinogens and enhance malignant characteristics.

The aim of this work is to use an in vitro model of chronic stress involving long-term exposure of cancer and normal cell lines to stress hormones. The cells will then be analysed for functional changes relevant to cancer such rates of apoptosis and proliferation, capacity for migration and invasiveness.

The molecular pathways that contribute to malignancy can be analysed by examining changes in gene expression at the mRNA and protein level.
**Project 3: Stress, Depression and Obesity**  
*Supervisors: Professor Ma Li Wong, Dr Martin Lewis*  
*Student type: this project can be modified for either Honours or PhD level.*

Evidence suggests major depressive disorder (MDD) and obesity often go hand in hand. Our laboratory has developed an animal model for the progression from stress to depression to obesity. This project investigates the associations between various antidepressant treatments and obesity following stress-induced depression-like behaviour. Different pharmacological treatments are believed to vary in their modulation of weight gain. Rodents are assessed for depression-like behaviours using a range of tests and video tracking. Biological measurements such as glucose and insulin tolerance can be assessed, followed by protein and gene expression studies from tissues collected at the end of the study. The aim of this project is to understand the mechanisms in which stress followed by antidepressant treatment may lead to obesity.

**Project 4: Can Reducing Inflammation Ameliorate Progression of Alzheimer’s Disease**  
*Supervisors: Professor Ma Li Wong, Dr Martin Lewis*  
*Student type: this project can be modified for either Honours or PhD level.*

The genetic modification of these mice include five familial AD (5xFAD) transgenic mutations in Amyloid Beta (A4) Precursor Protein (K670N/M671L + I716V + V717I), and the Presenilin 1 (M146L + L286V) gene, plus targeted replacement of the mouse apolipoprotein (ApoE) gene with human APOE4, or a targeted mutation causing knockout of the mouse ApoE gene. Assessment of the progression or inhibition of the onset of AD will be by behavioural phenotyping for learning, memory extinction & recognition, and anxiety. Brain tissue will be used to measure Aβ40: Aβ42, and inflammatory proteins. Microarray analysis of RNA expression changes in the brain will be performed, followed by qRT-PCR validation of significant findings. The aim of this study will be to determine if anti-inflammation measure slows the progression of AD and the associated changes in gene and protein expression.

**Project 5: Stress Induced Hippocampal Atrophy**  
*Supervisors: Professor Ma Li Wong, Dr Martin Lewis*  
*Student type: this project can be modified for either Honours or PhD level.*

Major depressive disorder (MDD) affects a large and growing number of people in Australia and around the world. Depression doubles the risk of coronary heart disease, increases the risk of diabetes by 60%, and is associated with obesity. Diet, exercise and stress interactions effect the development and progression MDD. Brain imaging studies show major depressive disorder (MDD) to be associated with a significant reduction in hippocampal volume. The hippocampus is part of the limbic system and a significant region of neurogenesis in the brain. This structure plays vital roles in memory, learning, emotion and neuroendocrine regulation. Psychological stress causes a neuroendocrine cascade response involving catecholamine release from the adrenal medulla, insulin secretion inhibition, corticotrophin-releasing factor (CRF) released from the hypothalamus, adrenocorticotropic hormone (ACTH) release from the anterior pituitary, causing glucocorticoid release from the adrenal cortex. Cortisol, a glucocorticoid, when increased negatively regulated ACTH and CRF. Persistent or chronic psychological stress upsets the homeostatic balance of the hypothalamic-pituitary-adrenal (HPA) axis. Excess circulating cortisol increases mineral corticoid and glucocorticoid
receptors, which then undermines its negative regulation of ACTH and CRF. The hippocampus is an important glucocorticoid target site with a high density of corticosteroid receptors. As the hippocampus exerts a negative regulation of most aspects of the HPA activity, its damage can result in disruption of the HPA axis activity during the stress response. Increases in baseline levels of plasma cortisol are associated with major depression.

This study will examine the efficacy of treatments in the development and progression of stress-induced hippocampal-atrophy. Treatments will include various antidepressants and exercise in groups of animals on a high-fat diet following chronic mild stress. Controls will include non-stressed and normal diet fed animals. Animal behavioural assessments and biochemical plasma data will be collected from the groups throughout the studies. Anatomical, molecular and cellular data will be collected at the completion of the studies from the various tissues. In brief, techniques for this study may include animal handling, behaviour testing, ELISA assays, dissection, qRT-PCR, magnetic resonance imaging (MRI), statistical analysis, and presentation of results. The aim of this study will be to measure the different outcomes between treatments and elucidate the mechanisms involved in hippocampal atrophy.

**Mind & Brain: Biostatistics Research**

New DNA sequencing technologies offer unprecedented opportunities to study human diseases. Genetic analysis, by identifying risk variants and thereby increasing our understanding of how major depressive disorder arises, could lead to improved prevention and the development of new and more effective treatments. Given that around 18,000 genes are expressed in the brain, it is not surprising that some genes may be true risk variants with depression disorder. We are investigating this with bioinformatics methods. We compare the DNA sequences from a large number of people with disorders of the mind or brain people to detect the variants between them and healthy individuals. This work involves big data processing using high-performance supercomputers. We are trying to comprehend the genes are involved in depression, since it is very doubtful that any one gene causes this disorder in any large number of people. A combination of several genetic changes may predispose people to become depressed.

**Project 6: Subtype classification study of major depression based on genetic data**

*Supervisors: Professor Julio Licinio, Dr Chenglong Yu*

*Student type: this project can be modified for either Honours or PhD level.*

Bioinformatics is the application of mathematics, statistics and computational methods to the analysis of -omics data. Our research is focused on developing new bioinformatics methods and applying new and existing methods to analyze and make sense of complex major depression datasets. Much of our efforts are focused on next generation sequencing (whole genome/exome) data. Depression has been clinically classified in multiple ways based on various features that include course, periodicity, qualitative and quantitative types of symptoms, clinical features, age or phase of life, and cause. Those categories are based on historical observations and have never been validated by genetic data. Genetic analysis, by identifying risk variants and thereby increasing our understanding of how major depressive disorder arises, can lead to improved prevention and the development of new and more effective treatments. In this project we are constructing a series of computational subtyping predictive models based on depressed patients’ genetic sequence information. The outcome of this project can also indicate the minimum gene profiles required to define a depression gene array, for the purpose of translation to clinical practice.
Mind & Brain Theme Student Opportunities

**Wellbeing and Resilience Research Concentration:**
This concentration combines measurement and intervention to produce data and new knowledge about the science of positive psychology in the prevention of mental illness at the population level.

**The Wellbeing and Resilience Centre**
The Wellbeing and Resilience Centre in the SAHMRI has a bold vision to build South Australia as the State of Wellbeing, using a public health approach to building mental health. South Australia will lead a society-wide implementation of wellbeing initiatives, promoted and managed by the SAHMRI Wellbeing and Resilience Centre. The state has the distributed networks, high quality of life, and close-knit communities to make the State of Wellbeing a reality. Located within the SAHMRI Mind and Brain theme, the Wellbeing and Resilience Centre is building upon existing research to create new knowledge and practical, easily implemented wellbeing and resilience tools and programs that can be adopted across the community.

The Centre combines measurement and intervention to produce data and new knowledge about the science of positive psychology in the prevention of mental illness at the population level. Many South Australian schools and workplaces have already begun to implement interventions proven to reduce mental and physical illness and improve health and wellbeing, with many companies, organisations, aged care facilities, manufacturing and government departments soon to follow. Using an evidence-based approach, we intend to establish Wellbeing and Resilience as a reliable, effective measure of positive mental health in the community and social progress.

- We lead, measure, build, embed and evaluate wellbeing initiatives in citizens across the life course: young people, families, community, elders, and the workplace
- We instigate life course measurement and intervention projects and research, using positive psychology frameworks.
- Conduct and publish research in wellbeing science
- Attract global leaders in wellbeing science to South Australia
- Conduct public lectures and events

Our projects will appeal to students in psychology, social sciences, health sciences, as well as mental health practitioners and those with a general interest in wellbeing and positive psychology.

**PERMA+**
Professor Seligman, founder of positive psychology and former head of the American Psychological association, proposed that South Australia systematically measure and build wellbeing in across the whole society to reduce the number of people experiencing catastrophic mental illness and to improve the resilience of the population in a rapidly changing world.

Wellbeing is not a one-dimensional idea but a multifaceted construct composed of several different elements. The SAHMRI Wellbeing and Resilience Centre incorporates Dr Martin Seligman's PERMA dashboard (Positive Emotion, Engagement, Relationships, Meaning and Accomplishment) PLUS, Physical Activity, Nutrition, Sleep and Optimism, to measure and build wellbeing. The PLUS constructs have been added in response to consultations with global experts in wellbeing measurement, who have indicated that this will provide a more comprehensive evaluation of individual and societal wellbeing.
Our proposition is that PERMA+ can become as memorable in the community as ‘SLIP, SLOP, SLAP’ (a very successful, iconic skin cancer prevention strategy in Australia.) PERMA+ carries within its framework concepts for individual action to build wellbeing. The use of PERMA+ Positive Emotion, Engagement, Relationships, Meaning and Accomplishment PLUS Optimism, Resilience, Physical Activity, Nutrition and Sleep, as a public health message for all citizens, will become the clarion call for a mentally healthy society in Australia.

**Project 7: Ageing and Wellbeing Project: a data analysis**
*Supervisors: Professor Julio Licinio, Janet O’Hehir*
*Student type: Honours*

The participation of the City of Port Adelaide Enfield in the Local Government Wellbeing and Ageing prototype has provided the opportunity for a small group of local residents to participate in a project to measure and build wellbeing. The first phase of this project involved the completion of the PERMA+ survey by residents. Overall, the PERMA+ levels amongst PAE residents are lower than their peers in other similar Councils such as Charles Sturt and Salisbury. While the limited size of the survey sample precludes any detailed analysis or conclusions, the trend is of some concern and warrants further investigation.

As a result, the City of Port Adelaide Enfield has decided to undertake more detailed research into the levels of wellbeing and resilience amongst older residents and to put in place targeted interventions to build wellbeing and resilience. In order to further research the relatively low levels of wellbeing identified in the initial survey, the PERMA+ survey will be used with a sample of at least 400 older residents in order to develop a statistically valid picture of actual levels of wellbeing and resilience across the Council.

A secondary data analysis of the data collected by the City of Port Adelaide Enfield could be undertaken as an Honours project. There would also be the possibility of following up participants to collect qualitative data to enhance the results.

**Project 8: Automotive Workforce in Transition project: A secondary data analysis.**
*Supervisors: Professor Julio Licinio, Tania Marin*
*Student type: Honours*

The flow on effect of the closure of the G.M. Holden plant in 2017 is predicted to be widespread. Several companies involved in the manufacture of automotive component parts have signalled their intention to close, while others are expected to significantly downsize and/or change their operating models. The impact that this will have on workers and their families will be significant. In partnership with two Tier-1 automotive manufacturing companies in the northern suburbs of Adelaide, the Wellbeing and Resilience Centre (WRC) at the South Australian Health and Medical Research Institute (SAHMRI) is undertaking a project to support these companies through the transition to closure, by measuring and building the wellbeing and resilience of workers.

There have been two baseline measurements undertaken so far and both companies are in the process of providing their employees with wellbeing and resilience skills training. We suggest amalgamating both datasets to increase the power for analysis and undertaking a secondary statistical analysis to establish a baseline before training.

A secondary data analysis of these data could be undertaken as an Honours project. There would also be the possibility of following up participants to collect qualitative data to enhance the results.