20 YEARS OF CCRN RESEARCH

1995 - 2015

A review of the past twenty years of the Centre for Clinical Research in Neuropsychiatry (CCRN) and a vision for the future.

Citation:

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CONTENTS

FOREWORD

Prof Assen Jablensky

Director Centre for Clinical Research in Neuropsychiatry

The Western Australian Centre for Clinical Research in Neuropsychiatry (CCRN) was established in 1995, as a research facility of the University of Western Australia (UWA) Department of Psychiatry and Behavioural Science – currently School of Psychiatry and Clinical Neurosciences. Its formal inauguration by the Minister for Health of Western Australia took place in 1996. At the time, CCRN was one of the youngest psychiatric research institutions in Australia. Today, we celebrate its 20-year rich record of growth and achievement, and look forward to its new horizon. By the end of 1995 we initiated work on research undertakings that marked the beginnings of what became a coherent, long-term program of studies with a sustained focus on severe mental disorders such as schizophrenia and related spectrum of conditions, targeting their biological and psychosocial underpinnings, and exploring their population health implications.

Why schizophrenia? This is a complex disorder which affects approximately 1% of the world's population and accounts for 2.3% of the global burden of disease and disability. In Australia, at any point in time 5 persons per 1000 population aged 15-54 are in treatment for schizophrenia, and some 2000-2500 new cases are diagnosed each year. The discovery of more effective treatments and prevention strategies depends critically on progress in understanding its aetiology and neurophysiology. Our working model of the disorder is that schizophrenia is a composite group of several partially overlapping subtypes with different underlying pathophysiology and causal pathways. In pursuing our search for "keys" to unlock the complexity of schizophrenia, we adopted in our Western Australian Family Study of Schizophrenia (WAFSS) a strategy of multi-domain assessment of individuals and families, using neurocognitive tests, evaluating the personality structure of patients compared to healthy control volunteers, analysing the brain electrical activity in response to various stimuli and, of course, assessing each individual's history and

symptoms. This approach, when combined with molecular genetic studies of patients, families and controls resulted in an impressive number of publications in major, peer-reviewed journals, including quite a few CCRN "firsts" in the exploration of the deep structure of the disorder, as well as in prestigious invitations to membership in large international research consortia.

But schizophrenia was not the only topic of CCRN research. Our early research in autism provided the basis for establishing a Western Australian register of pervasive developmental disorders and its linkage to the Maternal and Child Health Research Database (MCHRDB). In 1997-98 CCRN was entrusted with the design and coordination of the first national multicentre epidemiological survey of psychotic disorders. We collaborated with the UWA Department of Public Health in linking the WA Mental Health Information System with the WA hospital morbidity and mortality registers – resulting in a comprehensive report on the alarmingly poor physical health status of psychiatric patients and their suboptimal medical care. Another major departure was the study of reproductive pathology in women with schizophrenia and affective disorders, and the developmental outcomes of their children. This was the beginning of a long-term research, currently in progress at the affiliated Neuropsychiatric Epidemiology Research Unit (NERU).

On a concluding note, the CCRN has consolidated its research strategy and made considerable advances in areas such as molecular genetics, neuropsychology, neurophysiology, diagnostic assessment procedures and record linkage epidemiology. Our main challenge and tasks ahead relate to the effective translation of research into clinical and psychosocial interventions that would reduce suffering and disablement for people with severe mental disorders and their families. This will require a close alliance with consumer organisations, as well as an active public health engagement for CCRN.

On this occasion I wish to express my deep gratitude to the many people, acknowledged in this report, who contributed to our collective efforts and, especially, to the volunteers – patients, family members and healthy control persons, who donated time and effort in taking part in our research.

"Twenty years CCRN – A lot has changed since then, but CCRN always was and is at the forefront of developments. Interdisciplinary and translational from the outset, it was led by a visionary leader, Prof Jablensky. CCRN embraced basic research without losing sight of the ultimate goal to treat and alleviate the suffering of individuals with mental disorders. When I joined CCRN in 1995, it was still in its infancy. Toddlers grow fast and within a short time our research endeavors began to blossom. Experts in molecular biology, epidemiology, genetics, pharmacology, cognitive and clinical psychology all came together to scheme new projects pushing the boundaries of what can be done. It was really an amazing time. Despite the heavy emphasis on basic science, at the center was always the patient. In addition to all the methodology I learned and projects I collaborated on, one of the most important lessons at CCRN for me was how crucial it is to develop partnerships between patient communities and academic researchers. It was with a heavy heart that I left CCRN after six wonderful years. CCRN had become my scientific home. I often think of the wonderful colleagues and stimulating discussions, the thrill or disappointment, when we assessed our results, and all the crazy and not so crazy ideas we had. CCRN was a major influence on my thinking and development as a researcher and I have no doubt that it will impact the development of mental health research in decades to come."

Prof Joachim Hallmayer MD PhD

Associate Professor of Psychiatry,

Stanford School of Medicine, California, US

CCRN MISSION STATEMENT

- To create and sustain in Western Australia an academic centre of excellence for multidisciplinary research in psychiatry and the neurosciences.

- Provide an enabling environment for individual researchers and groups.

- Provide a facility for postgraduate research.

- Contribute to the upgrading of skills of mental health services staff.

- Build a nexus between research and the delivery of mental health services.

- Communicate knowledge for public education and information.

> "The great challenge for science in the 21st century is not to be found in quantum mechanics, nor in molecular biology, but in understanding what it is that develops in the brain of a human embryo, that gives rise to consciousness."
>
> Francis Crick
> 'The Astonishing Hypothesis'
> 1994

CCRN CORE STAFF

Assen Jablensky MD DMed Sc FRCPsych (UK) FRANZCP

Winthrop Professor of Psychiatry, UWA

Director, CCRN

Assen provides the overall direction, planning and supervision of CCRN research. Having completed his medical degree and training as a psychiatrist in Bulgaria and the UK, Jablensky moved to Australia in 1993 to develop a research centre which would be at the forefront of schizophrenia research. The main focus of his research is on psychiatric epidemiology, genetics, psychiatric classification and psychotic disorders. At WHO Geneva, Jablensky was Principal Investigator of the WHO Ten-Country Study on Schizophrenia and lead author of its report, which remains among the most widely quoted papers in the psychiatric literature. At present, Jablensky is Director of the CCRN, and Consultant Psychiatrist at the Royal Perth Hospital.

Vera Morgan BA GradDipEd MSocSc PhD

Winthrop Professor

Deputy Director CCRN

Vera is a psychiatric epidemiologist with a special interest in studying psychotic disorders using record-linkage and survey methods. Her cross-disciplinary approach to the study of psychosis melds epidemiological, psychiatric, sociological and criminological perspectives on aetiology, course and outcome to help unravel its complex nature. Her current program of research focuses on environmental and genetic contributions to the risk of schizophrenia, as well as physical health comorbidity, including metabolic syndrome and cardiovascular disease, in people with psychotic illness.

Johanna Badcock PhD MA (Clinical), BA (Oxon.)

Research Professor, Specialist Clinical Psychologist

Jo leads the cognitive neuropsychology research programme for CCRN. She is a psychological scientist with particular expertise in clinical and experimental psychology. Her primary research focuses on the mechanisms underpinning the major symptoms of psychosis, using behavioural, neuropsychological and psychophysical methods. However, her research collaborations and graduate supervision cover a broader range of interests including visual functioning in autism spectrum disorder, attitudes to mental illness, and schizotypal personality traits in the general community.

Clea Louw BSc MB ChB FRANZCP

Consultant Psychiatrist

Clea is a consultant psychiatrist who provides the CCRN with expert opinion of the clinician's perspective as well as diagnostic reviews for the WAFSS. She currently works at the Marion Centre in Wembley and as a private psychiatrist in Wanneroo. Clea has a particular interest in the psychosocial management of complex psychiatric disease, with a major focus on schizophrenia.

Nina McCarthy PhD

Research Fellow

Nina is a statistical geneticist and is involved in the genomics research arm of the WAFSS. She works on the whole genome sequencing program, and together with Phil Melton and other members of the team, is responsible for the analysis of these data. She has previously worked on the genetics of cardiovascular disease, and as a new member of the team, is enjoying learning about the field of schizophrenia research.

Phillip Melton PhD MA BA

Statistical Geneticist

Phil is Head of statistical genetics in the Centre for Genetic Origins of Health and Disease. His primary research interest is in the development and application of multivariate methods using supercomputers to identify genomic, cultural, and environmental variables that contribute to complex disease susceptibility. He is primarily interested in the utilization of large family based cohorts to identify rare variants associated with complex diseases, including schizophrenia. He works together with Nina McCarthy on the statistical analyses for the whole genome sequencing program in WAFSS.

Bharti Morar PhD

Research Associate

Bharti is a molecular geneticist and contributes to/develops research projects to identify genes involved in schizophrenia susceptibility. She manages the CCRN Genetics Laboratory and is responsible for the processing and storage of WAFSS biospecimens and related cell culture and genetic studies.

Melanie Clark BPsych (Hons)

Research Associate

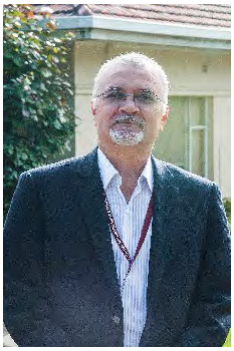
Melanie is the coordinator of WAFSS recruitment and assessment for the CCRN. Commencing in 2010, Melanie conducted cognitive and diagnostic testing and maintained the WAFSS database. Melanie became involved in data analysis and publication preparation throughout 2014 and has recently commenced her PhD on language in schizophrenia with the WAFSS project.

CCRN AFFILIATES

Dr Milan Dragović

Psychologist, Statistical Analyst

Clinical Research Centre, North Metropolitan Health Service



Prof Eric Moses

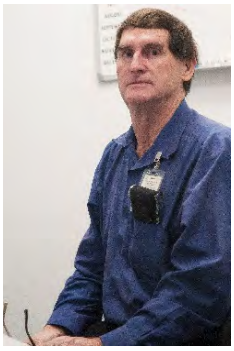
Director

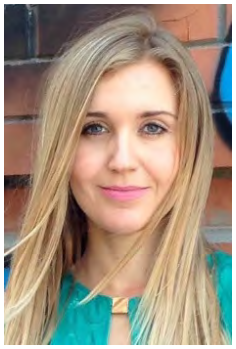
UWA Centre for Genetic Origins of Health and Disease

Dr Greg Price

Electrophysiologist

North Metropolitan Health Service





Dr Daria Smirnova

Go8 Research Fellow, CCRN

Assistant Professor, Samara State Medical University, Russia

Dr Flavie Waters

Associate Professor

Clinical Research Centre, North Metropolitan Health Service

Mr David Vile

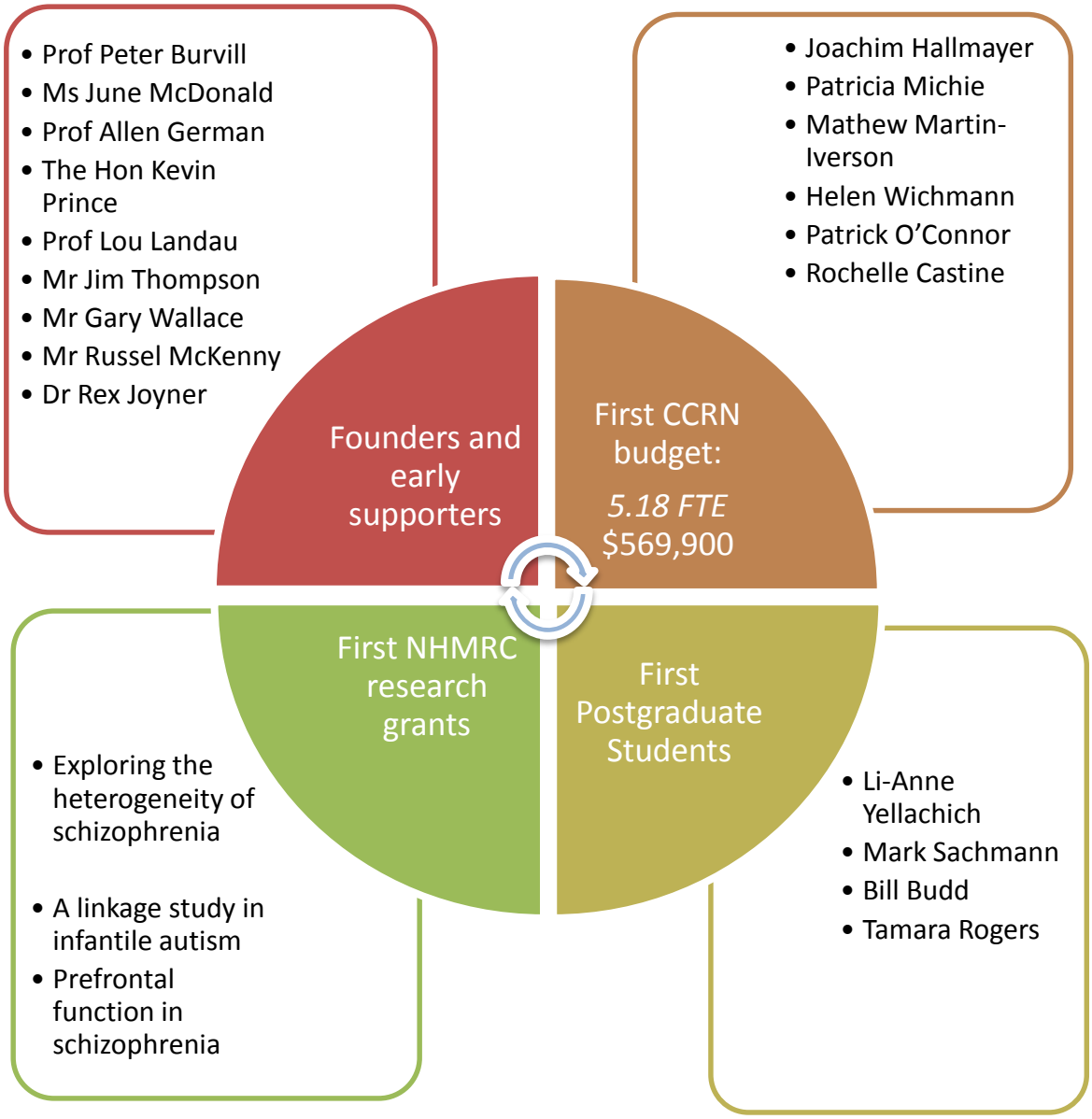
Psychologist, Specialist in Organisational Development

Newmont

"CCRN provided a very stimulating research environment for the period of my tenure from 1995 to 2001. Established under the leadership of Professor Assen Jablensky, a multidisciplinary team was assembled with expertise in genetics, cognition, electrophysiology and animal models for a multipronged attack on understanding the pathophysiology of schizophrenia. It was an honour to be selected to be part of this core team and to establish a line of research that continues to this day. The building was refurbished shortly after I arrived and decorated with art produced by inpatients and outpatients attending the Creative Arts Unit at Graylands Hospital. That artwork is still vivid in my mind - but it was the sheer exhilaration of participating in ground breaking research and the realisation that we were making progress in understanding the disorder, that is most memorable."

Prof Patricia T. Michie BA PhD
Emeritus Professor of Psychology,
University of Newcastle, Australia

CCRN BEGINNINGS



CCRN TIMELINE

1993: Proposal and draft terms of reference for an "Academic Research Unit" … "jointly managed by the Department of Psychiatry at The University of Western Australia (UWA) and Graylands Hospital"

1994: Research Committee established

1995: Designation *"Centre for Clinical Research in Neuropsychiatry"* formally adopted; first business plan submitted; infrastructure grant and budget approved by the Health Department of Western Australia

1995: First CCRN byline published

1996: 25th October: Official inauguration by the Minister for Health Hon. Kevin Prince: *"While its infrastructure is mainly funded by the Health Department of WA, it is substantially funded through research grants"*

1996: CCRN designated as a World Health Organisation (WHO) Collaborating Centre for Research and Training in Mental Health

1997: CCRN accredited by the UWA Senate (*Resolution 191 of 28/07/1997*)

Gascoyne House, Graylands Hospital - Mount Claremont

1997: First Heterogeneity Project (now WAFSS) participants recruited

2003: Re-accreditation by UWA for the period 2003-2008

2008: The epidemiological arm of CCRN became the Neuropsychiatric Epidemiology Research Unit (NERU)

2009: Re-accreditation by UWA for the period 2009-2014

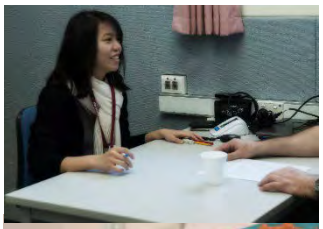
2012: The Clinical Application Unit separates from CCRN, to become the Clinical Research Centre / North Metropolitan Health Service

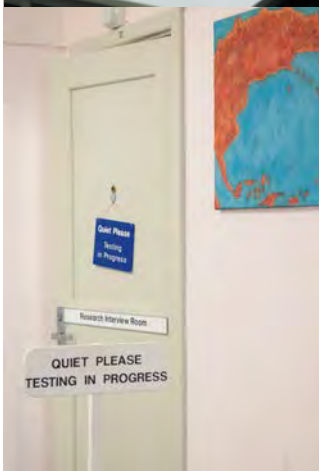
2013: Funding by the North Metropolitan Health Services for CCRN staff positions discontinued

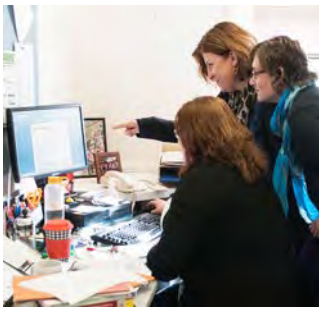
2014: Re-accreditation by UWA for the period 2014-2018

2015: CCRN staff complete relocation to the Medical Research Foundation (MRF) building

2015: Total number of publications (papers in peer reviewed-journals, books and book chapters) reaches 682



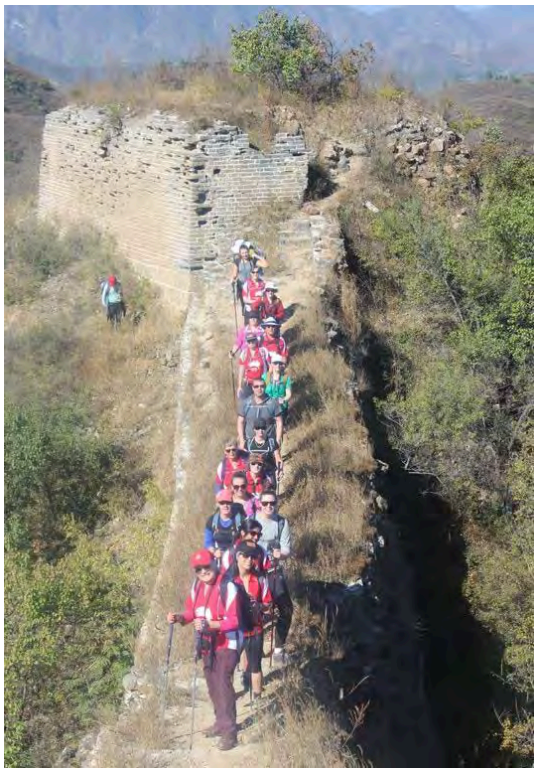




CCRN GRANTS 1995 – 2015

YEARS	NHMRC & ARC	NATIONAL & STATE GOVERNMENT	OTHER - FOUNDATIONS	OTHER – INTERNATIONAL GOVERNMENTS (US & NORWAY)
1995-1996	943,297	573,000	469,022	
1997-1998	410,366	351,854	209,314	
1999-2000	2,017,663	248,465	404,323	
2001-2002	1,142,000	524,504	228,007	
2003-2004	1,884,500		356,712	600,540
2005-2006	5,184,672	303,222		
2007-2008	3,722,700	800,903	10,000	
2009-2010	929,691	5,614,407	40,000	
2001-2012	3,414,354	8,015,883		
2013-2014	1,750,141	136,633	69,633	
TOTAL	$21,399,384	$16,568,851	$1,787,011	$600,540
GRAND TOTAL	$40,355,786			

- CCRN staff are currently applying for over eight million dollars in grant funding for the 2016-2020 period to support two new projects over multiple Australian sites as well as further WAFSS genomics studies.



The Schizophrenia Research Institute (SRI) partially funded the Perth site for the Australia Schizophrenia Research Bank project from 2006-2010. In October 2013 Melanie Clark and Tammy Hall took part in a five day, 80km trek of the Great Wall of China to raise funds for the SRI. Tammy and Melanie, with two friends Meg and Ashinka, created a team called 'The Stumbling Dumplings' and raised $12,560 for the institute. In total, the nine SRI trekkers raised $55,000. These funds supported PhD students throughout 2014 across Australia.

The group of trekkers from all over Australia tackled restored and severely damaged areas of the wall, including the area bordering Mongolia. It was a life changing experience but most importantly for Melanie and Tammy, it was a chance to talk to people in the general community about schizophrenia and the benefits of the research taking place at CCRN.

Melanie said, "The third day was our hardest day, 35km along the undulating border of China and Mongolia. Each day we trekked 'for' someone to remain inspired when the two kilometer ascents seemed too much. One day it was for our families, another for everyone living with schizophrenia. That day, the Stumbling Dumplings did it for each other and it was laughs all the way."

Photos courtesy of Inspired Adventures.

Prof Tom McNeil is a long standing active collaborator with the CCRN and The Neuropsychiatric Epidemiology Research Unit (NERU).

Prof McNeil led the Swedish High-Risk Study, conducted over some thirty years, following the children of mothers with a mental disorder.

The study involved measuring a wide range of factors from pre-birth to young adulthood.

The results indicate significant differences in motor activity, eye contact, and response to stimuli, in children with a genetic risk of schizophrenia.

Although weaker than the genetic influence, family stress is another factor, and seems to be most influential in the 6-11 year age range.

Prof Tom McNeil PhD
Department of Psychiatric Epidemiology,
University Hospital, Lund, Sweden

INTERNATIONAL LINKS & COLLABORATIONS

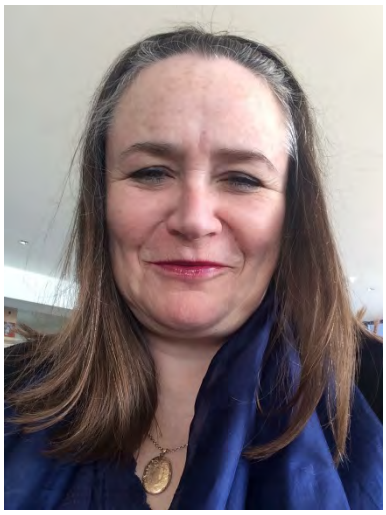
- CCRN is firmly embedded in international and national collaborative networks of research into severe mental disorders.

- We have collaborations and ongoing links with institutions in:

Indonesia	Mongolia	Norway
Russia	Sweden	UK
USA	Vietnam	

- CCRN has hosted 6 national and international research conferences.

- Many CCRN researchers have been invited keynote speakers or presenters at a number of national and international conferences.



"I am a person with lived experience of schizophrenia and have been the Consumer Representative for the CCRN Steering Committee for the past few years. Originally, I volunteered to participate in the WAFSS as I felt this was a way of contributing to future knowledge and treatments. I was then asked to join the Steering Committee.

I feel the work that is being done at CCRN is so valuable and gives hope to those of us who live with mental disorders such as schizophrenia. I believe science is hope. I am inspired by the people of CCRN, such as Professor Assen Jablensky, whose competence, dedication and compassion make me feel that there are people who really do care about what happens to someone like me. This is so important and I think we need to promote and support our scientists and their colleagues who do such a wonderful job.

Professor Jablensky and his team are prepared to listen and talk with people who experience mental illness, valuing their needs and opinions. As a result of my association with CCRN, I have helped found a not-for-profit organisation, Meeting for Minds. The aim is to involve people suffering from schizophrenia and other severe psychotic and mood disorders, with research into better treatments for their improved lives.

Congratulations to CCRN on twenty years of brilliant work and may the next twenty be even more productive and successful."

Ms Susie Hincks

Co-Founder and Director Meeting for Minds

CURRENT PARTNERSHIPS & COLLABORATIONS

- **LOCAL (UWA)**

  Centre for Genetic Origin of Health and Disease

  Harry Perkins Research Institute

  Meeting for Minds (Philanthropic, NGO)

  UWA School of Psychology

- **NATIONAL**

  Australian Schizophrenia Research Bank (ASRB)

  Cooperative Research Centre – Mental Health

  Survey of High Impact Psychosis (SHIP) Study

- **INTERNATIONAL**

  International Schizotypy Consortium

  Pedigree-Based Endophenotype Consortium

  Psychiatric Genomics Consortium (PGC2)

  Wellcome Trust Consortium

  World Health Organisation

"Our vision is to improve health by supporting bright minds in science, the humanities and social sciences, and public engagement"

Wellcome Trust

2015

WHAT IS SCHIZOPHRENIA?

"One of the most extreme states that human beings can in habit"

Spence S, (2005)

"A fundamental disturbance of personality…, involving its most basic functions which give the normal person a feeling of individuality, uniqueness and self-direction"

ICD-10 Glossary of Mental Disorders (1992)

Emil Kraepelin first described *dementia praecox*, now schizophrenia, as a cognitive disorder:

- "Lowered mental efficiency"
- "Unsteadiness of attention"
- "Inability to sift, arrange and correct ideas"
- "Inability to accomplish mental grouping of ideas"
- "Weakening of the mainsprings of volition"

The 'core' of dementia praecox were impairments in cognition, particularly executive functioning.

Emil Kraepelin

WHY FOCUS ON SCHIZOPHRENIA?

- Schizophrenia is a major public health problem, in terms of its heavy toll on individuals, families, and communities. It is a complex disorder, still harbouring many "unknowns" that await unravelling.
- Our concern, at the start of the CCRN program, was that schizophrenia research was ridden with conceptual fallacies such as a selection of:

  A particular, isolated aspect of the syndrome - a symptom

  A neurophysiological dysfunction

  A neurotransmitter abnormality

  A neuroanatomical feature

  A genetic polymorphism

  The demonstration of a difference at $p < 0.05$ in an inadequately small sample of patients.

- Such research, and the resulting loss of the "big picture", has led to numerous "breakthroughs" which have more often than not proved to be illusory (Hayman, S.E., 2014. *Science* editorial).

- Importantly, the clinical entity of schizophrenia appears to be a loose cluster of heterogeneous symptoms and traits, held together by a "deep structure" that still eludes our understanding.

- What makes schizophrenia refractory to the available methods of dealing with heterogeneity is the confounding effect of a phenotype based solely on conspicuous symptoms and behaviours.

EPIDEMIOLOGY OF SCHIZOPHRENIA

- No population has to date been shown to be free of schizophrenia.
- It is one of the 10 leading causes of the global burden of disease and disability (~2.6% of the total).
- Lifetime risk: 0.8 - 1.0%.
- Point prevalence in Australia, 2012: 3.1 per 1000 adults (Survey of High Impact Psychosis, Morgan V et al. 2012, ANZJP 46, 735-752).
- Incidence rates vary modestly across populations (in contrast to other multifactorial diseases, such as diabetes) and over time: WHO data (Jablensky A et al., 1992).
- Unusual populations: genetic isolates, second generation migrants have a higher incidence.
- Contribution of the social and physical environment is likely, but no single factor of major effect size has yet been established.

WHO Ten-Country Study of Schizophrenia; Incidence rates per 10 000, age 15-54

Country	**Incidence Rate**	**Country**	**Incidence Rate**
Aarhus, Denmark	1.1	Cali, Colombia	1.0
Chandigarh (urban), India	2.2	Chandigarh (rural), India	3.5
Dublin, Ireland	2.2	Honolulu, USA	1.6
Ibadan, Nigeria	1.1	Moscow, Russia	2.2
Nagasaki, Japan	1.6	Nottingham, UK	1.9
Prague, Czech Republic	0.9	Rochester, USA	1.5

Jablensky A et al. (1992) *Psychol Med* Suppl 20, 1-97.

THE RIDDLE OF HETEROGENEITY

- Clinical, neurobiological, psychosocial, and genetic characteristics of schizophrenia are varied and heterogeneous.

- No symptom is pathognomonic, though variable subsets of symptoms can be sufficient for the diagnosis.

- Patients may be allocated to the DSM-IV category without having a single symptom in common.

- No uniform neuroanatomical “signature”, present in all cases of the disorder, has been detected.

- No unifying framework for the pathophysiological brain abnormalities has yet emerged.

- No causal genes have yet been unequivocally shown to exist.

- Treatment is essentially symptomatic.

- Feasibility of primary prevention has not yet been demonstrated.

> “Phenotype variability and extensive genetic heterogeneity have been confounding the search for the causes of schizophrenia…The inconsistent results of genetic linkage and association studies using the diagnostic category as the sole schizophrenia phenotype suggest that the current broad concept of schizophrenia does not demarcate a homogeneous disease entity.”
>
> Assen Jablensky
>
> 2006

THE CHALLENGE: BRAIN HYPERCOMPLEXITY

- The adult human brain: 10^{11} neurons; 10^{15} synapses.
- 5,000 – 10,000 different types of neurons.
- Genetic variants affect differentially the expression of different cell types.
- Two phenotypically similar pyramidal cell types may differ by ~100 expressed genes.
- Each neuron communicates with ~10,000 brain cells (~1 quadrillion synapses).
- The post-synaptic density (PSD) proteome: 1100 proteins.
- 76% of PSD proteins interact with each other, resulting in a higher level network: the PSD interactome: $\mathbf{11}^{\mathbf{24}}$ possible interactions.

> "We analysed a phenotypically well-characterised sample of 450 schizophrenia patients and 605 controls for rare non-synonymous single nucleotide polymorphisms in the *GRM1* gene…which encodes the metabotropic glutamate receptor 1 (mGluR1)…Our in-vitro experimental follow-up of the case-specific mutants showed that 4/6 led to significantly reduced inositol phosphate production, indicating impaired function of the major mGluR1 signalling pathway…Our findings suggest a possible mGluR1 contribution to diverse psychiatric conditions."
>
> Mohammed Ayoub et al.
>
> 2012

NEW DIRECTIONS FOR SCHIZOPHRENIA RESEARCH

- Multiple past attempts at rearranging the clinical symptoms into different principal components or clusters have achieved little – simply because symptoms, although diagnostically important, are surface features, remote from the principal site of action of the psychobiological causes.

- As an alternative approach, we adopted the concept of endophenotypes, i.e. traits associated with brain function or structure, which are stable, objectively measurable, heritable and, being relatively independent of the clinical disorder, are statistically correlated with its transmission within families.

- When planning our research program, we selected several promising leads in this direction, including the P50 event-related brain potential (sensory gating), the oculomotor control of eye movements, and some of the neurocognitive tasks of sustained attention and information encoding in short-term and longer-term retention in memory.

Event related potentials at CCRN - Graylands

Dr Daria Smirnova is a UWA Visiting Research Fellow on a prestigious Go8 Fellowship and currently acts as an Assistant Professor of the Department of Psychiatry, Samara State Medical University, Russia.

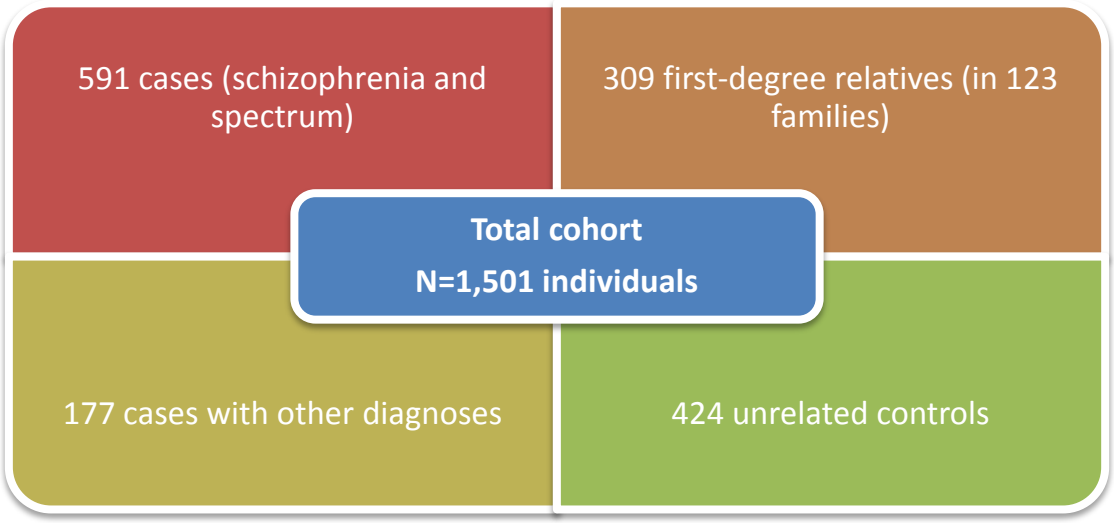
“My research interest is focused on the role of language in development of mental disorders, in particular schizophrenia, and further elaboration of language remediation issues within the treatment of different psychiatric conditions. The current study ‘Language and communication dysfunction in schizophrenia in the Western Australia Family Study of Schizophrenia’ is supervised by Professors Assen Jablensky and Jo Badcock.

Emphasizing the key role of thought, language and communication disorder in pathogenesis of schizophrenia and its negative domain symptoms, which are still resistant to pharmacological treatment, the study results could provide an additional evidence base for future detailed development of cognitive and, in particular, language interventions in therapy of schizophrenia.”

Dr Daria Smirnova MD PhD
Assistant Professor of Psychiatry,
Samara State Medical University, Russia

THE WA FAMILY STUDY OF SCHIZOPHRENIA (WAFSS)

THE FLAGSHIP OF CCRN RESEARCH



The WAFSS cohort has been assessed using various cognitive, diagnostic, neurological, biological, and personality measurements.

- Evaluation of symptoms and history → diagnosis (ICD-10 & DSM-IV) with the Diagnostic Interview for Psychosis (DIP).
- Neurological examination with a modified Neurological Evaluation Scale.
- Personality trait inventories -Temperament and Character Inventory (TCI) and Schizotypal Personality Questionnaire (SPQ).
- Neurocognitive assessment battery (12 tests).
- Event-related brain potentials (ERP): P50, N1, MMN, and P300.
- Saccadic eye movements.
- Structural brain MRI.
- DNA, RNA, plasma / serum, immortalised cell lines.

"The strength of the WAFSS data collection is that it has characterised a substantial number of participants (including family groups) in considerable breadth and detail…There are two additional factors that lift the value of the study to a much higher level, in my view. Firstly, the sampling frame and the associated ascertainment processes…I have not found another study that has a comparable methodology. The second distinct strength is the use of data management and statistical methods that "recompose" the various data streams into empirically plausible (endophenotypically grounded) complexes that can be modelled and tested…It is interesting to consider the parallels between WAFSS and human development – we have had our youthful adolescence and early adulthood, but perhaps it's time for us to move into mature middle age."

3rd September 2010

Prof Daniel Rock BSc MA PhD

Director, Centre for Clinical Research

North Metropolitan Health Service /

Mental Health, Western Australia

STRENGTH: UNIQUELY RICH PHENOTYPE DATABASE

Task	N. Participants	Task	N. Participants
DIP / OPCRIT interview	507	SANS/SAPS scores	333
Diagnostic review	834	SPQ	1,288
TCI	563	IPDE	444
Premorbid IQ (NART)	1,303	Premorbid IQ (WTAR)	440
Current IQ (SILS)	1,273	Current IQ (WASI)	444
TLC	318	CPT-IP	1,195
CPT-DS	658	Dual task	120
Handedness (EHI)	1,347	Neurological exam	399
RAVLT	1,319	RBANS	442
RBANS (digit-symbol)	441	LNS	446
Inspection time	722	FAS verbal fluency	1,347
Action verbal fluency	157	Hayling task	141
P300	188	Structural MRI	107
Antisaccade task	251	P50	248

DIP – Diagnostic Interview for Psychosis, TCI – Temperament and Character Inventory, NART – National Adult Reading Task, SILS – Shipley Institute of Living Scale, TLC – Thought, Language and Communication Disorder Scale, EHI – Edinburgh Handedness Inventory, RAVLT – Rey Auditory Verbal Learning Task, RBANS – Repeatable Battery for the Assessment of Neurological Status, SANS – Scale for the Assessment of Negative Symptoms, SAPS - Scale for the Assessment of Positive Symptoms, IPDE – International Personality Disorder Examination, WTAR – Wechsler Test of Adult Reading, WASI – Wechsler Abbreviated Scale of Intelligence, LNS – Letter Number Sequencing, FAS – Verbal Fluency

STRENGTH: BIOLOGICAL SAMPLES

- DNA samples from the entire cohort (N = 1442) available in storage at the Perkins Institute.

- DNA genotypes from 775 participants (376 cases, 205 family members, 194 controls - genotyped at the Sanger Institute / Cambridge for the WTCCC2 Consortium.

- The exome of 336 individuals from 64 WAFSS families was *genotyped* using the Illumina HumanCoreExome Beadchip (250,000 common SNPs + 250,000 rare exonic variants).

- Whole-genome sequencing of 376 intensively phenotyped members of 88 WA families is now completed and the data are being processed and analysed.

> "The results indicated suggestive linkage for the familial neurocognitive phenotype to a 14 cM area on chromosome 6, including the entire HLA region…The findings suggest …that use of composite neurocognitive and personality trait measurements as correlated phenotypes supplementing clinical diagnosis …augments considerably the power of genetic analysis."
>
> Joachim Hallmayer et al. 2003

STRENGTH: ALLIANCES - GENOMICS RESEARCH

- Partnership with the UWA Centre for Genetic Origins of Health and Disease.
- Collaborations

  PGC2 Psychiatric Genomics Consortium

  Endophenotype Consortium

  Cooperative Research Centre / Mental Health

- Network of international research collaborations.

"Promoter polymorphisms in two overlapping *6p25* genes implicate mitochondrial proteins in cognitive deficit in schizophrenia…Our findings suggest that subtle chronic LYRM4 downregulation could be one of the mechanisms behind impaired oxidative phosphorylation and oxidative stress in schizophrenia, increasingly recognised as contributors to disease and impaired cognitive performance in affected subjects."

"Neurocognitive dysfunction is a core feature of schizophrenia with particularly prominent deficits in verbal episodic memory…In this study we explore the role of polymorphisms in seven genes…Double carrier status of the *GRM3* and *PRKCA* minor alleles was associated with lower memory test scores and with increased risk of schizophrenia…Our study supports the utility of parsing the broad phenotype of schizophrenia into component cognitive endophenotypes that enable the capture of potentially important genetic associations."

Assen Jablensky et al.

2011

CCRN staff held an important role at the 2009 *International Congress on Schizophrenia Research* in San Diego, USA when Dr Barbara Fish was awarded the ICOSR Service Award at a symposium held in her honour.

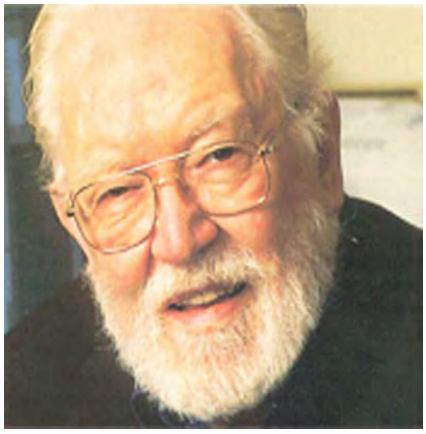
In 1952, Dr Fish began the prospective study of high-risk children of mothers with schizophrenia and in 1957, she published her first paper ('The detection of schizophrenia in infancy') describing abnormal neuromotor development in these high-risk infants. Her work on 'pandysmaturation' lay the ground for the formulation of the neurodevelopmental hypothesis of schizophrenia in the late 1980s, a hypothesis which continues to exert a powerful influence on our understanding of the origins of schizophrenia.

The symposium chaired by Prof Vera Morgan, reflected on Dr Fish's pioneering contribution, with a concluding presentation by Prof Jablensky on 'The future for high risk research'. The audience was reminded of a much earlier symposium on high risk research, organized in Moscow in the early 1980s by Prof Jablensky (then working with WHO) where Dr Fish was a keynote speaker.

L-R: Prof Assen Jablensky, Dr Barbara Fish, and Prof Vera Morgan

STATISTICAL MODELLING OF A MULTIVARIATE PHENOTYPE

- When determining how to analyse multiple variables from multiple domains of functioning, we settled on the Grade of Membership model (GoM*),* developed by Prof Max Woodbury at Duke University, N.C. which simultaneously computes variables and linked individuals.



Prof Max Woodbury

- GoM partitions the data matrix into latent classes ('pure types') by iteratively computing multiple regression relationships among all variables and estimating the maximum likelihood fit to alternative models of varying numbers of pure types. GoM pure types are fuzzy sets, allowing their members to be simultaneously represented on more than one pure type by grade of membership coefficients.

- GoM mirrors the inherent 'fuzziness' of psychiatric classification, where boundaries between syndromes are poorly demarcated or do not exist at all.

- This table highlights that the Cognitive Deficit (CD) group have lower cognitive abilities while the Cognitively Spared (CS) group have higher personality difficulties.

GoM Latent Structure Analysis: Pure Types Probability (Percentages)

Variables	**Deficit Type % (CD)**	**Non-deficit Type % (CS)**
NART IQ 70-95	**100.0**	35.0
Current IQ < 91	**100.0**	0.0
CPT-DS dL < 4.3	**100.0**	0.0
CPT-IP dL < 3.6	**100.0**	42.9
RAVLT Immed words < 20	**100.0**	0.0
VF words total < 25	77.5	0.0
Inspection time > 1 SD (pos)	83.5	24.7
Soft neurol signs > 3	**100.0**	0.0
SPQ total score > 23	0.0	**100.0**
TCI Harm Avoidance > 19	16.3	**100.0**
TCI Self-Transcendence > 19	0.0	**100.0**
Familial aggregation significant	**p = 0.000**	**p=0.045**

NART – National Adult Reading Test, CPT-DS – Continuous Performance Task – Degraded Stimulus, CPT-IP – Continuous Performance Task – Identical Pairs, RAVLT – Rey Auditory Verbal Learning Task, VF – Verbal Fluency, SPQ – Schizotypal Personality Questionnaire, TCI – Temperament and Character Inventory

WAFSS FINDINGS

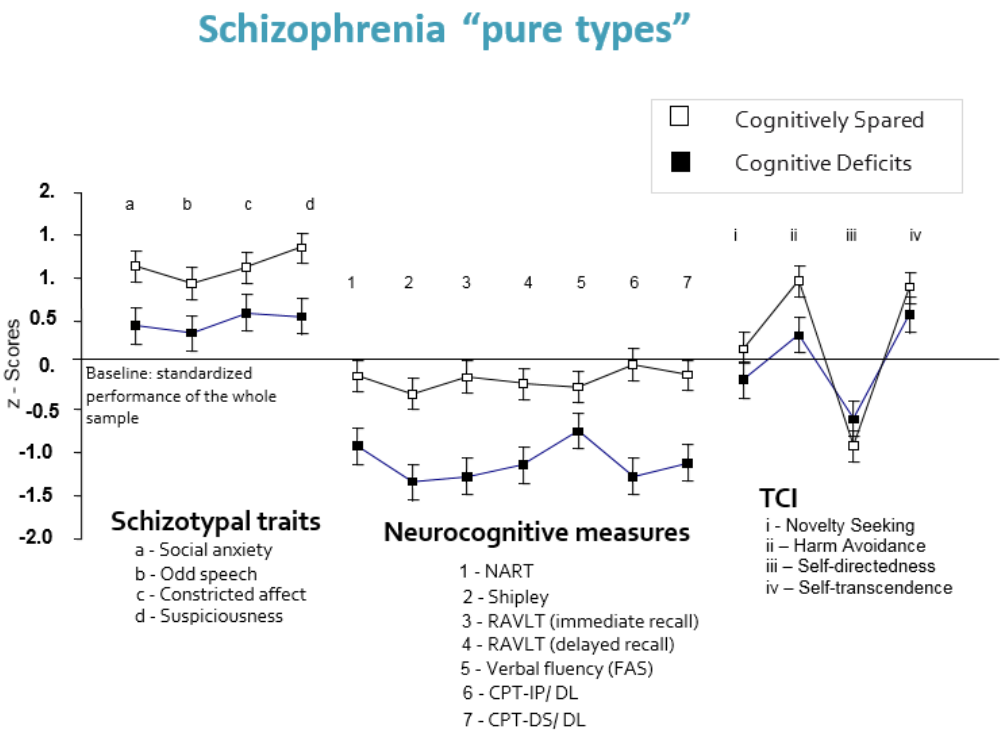
Patients with schizophrenia fall into two prototype groups

- Schizophrenia with pervasive cognitive deficit, CD (memory, attention, speed of information processing) and early signs of developmental abnormalities.

- Schizophrenia with relatively spared cognition, CS, but with prominent psychotic symptoms.

- The two groups are likely to be genetically distinct (whole-genome scan).

- Can CD and CS be reliably distinguished at the level of clinical symptoms, or by length of illness?



Cognitive Deficit (CD) endophenotype: marker of a neurodevelopmental subtype of schizophrenia?

- CD is a homogeneous endophenotype characterised by pervasive deficit across all major cognitive domains.

- Most prominent dysfunctions involve verbal memory, sustained attention, working memory and general intelligence.

- CD cases are also characterised by early developmental delays; poor scholastic performance and social skills; and clustering of 'soft' neurological signs.

- CD captures genetically influenced variation, as demonstrated in:

  Verbrugghe P et al. (2012) Impact of the *Reelin* signaling cascade on cognition in schizophrenia. *Am J Med Genet B Neuropsychiatric Genetics*, 159B, 392-404

  Jablensky A et al. (2012) Promoter polymorphisms in two overlapping 6p25 genes implicate mitochondrial proteins in cognitive deficit in schizophrenia. *Molecular Psychiatry* 17, 1328-1339

> "A novel phenotyping strategy in schizophrenia, targeting different neurocognitive domains, neurobehavioral features, and selected personality traits, has allowed us to identify a homogeneous familial subtype of the disease, characterised by pervasive neurocognitive deficit."
>
> Joachim Hallmayer et al. 2005

Cognitively Spared (CS) endophenotype: a heterogeneous cluster?

- CS is phenotypically heterogeneous, with a common feature of relatively preserved cognition.

- CS cases are characterised by florid, multi-domain psychopathology with complex delusions including the so-called first-rank symptoms.

- CS patients show a high level of performance on a signal/noise discrimination task (CPT-*ds*), suggestive of expression of a gene product that boosts cognitive performance.

- We found a significant association of the CS subset of cases with polymorphisms within the *Neuregulin 3* (NRG3) gene:

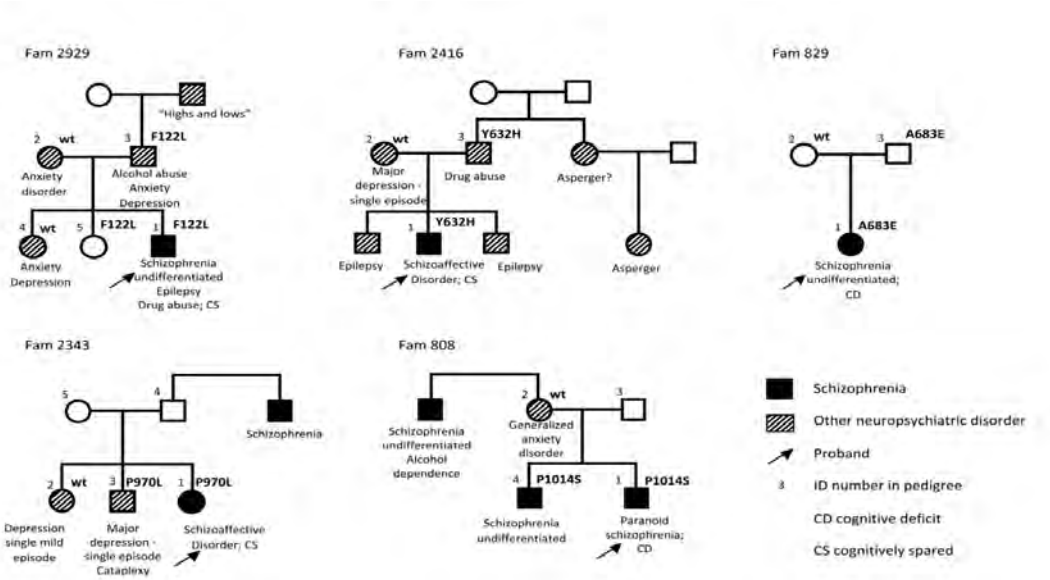
  Morar B et al. (2011) Neuregulin 3 (*NRG3*) as a susceptibility gene in a schizophrenia subtype with florid delusions and relatively spared cognition. *Molecular Psychiatry* 16, 860-866.

"It has been a great honour and privilege for me to be involved in the genetic research conducted at CCRN. From its early days, the Centre set out to explore the theoretically and clinically important concepts of Kraepelin and Bleuler, of an inherent heterogeneity of schizophrenia. The Western Australian Family Study of Schizophrenia applied the tools of psychology, electrophysiology and neuroimaging to outline different disease subtypes hidden under the common schizophrenia "umbrella", as well as those of molecular genetics to understand the biological basis of the differences. At a time, when global psychiatric genetics was aiming at quantity - the collection of thousands of schizophrenia cases and healthy controls, CCRN was a conceptual dissenter, focusing on quality – the meticulous characterisation of patients, their unaffected relatives and control subjects. Inevitably and in the not too distant future, the heterogeneity concept will head the priority list of the international mega-studies of schizophrenia. The CCRN database and its collection of biological samples will be an invaluable resource for solving the puzzle."

Prof Luba Kalaydjieva PhD
Centre for Medical Research,
Harry Perkins Institute of Medical Research,
University of Western Australia

PLEIOTROPY

Family segregation analysis raises questions about phenotype delineation. Currently we are reviewing the pleiotropy in WAFSS families and the big challenge is determining which diagnoses should be accepted as being partially related to schizophrenia and which individuals should be regarded as unaffected.



Ayoub MA et al., 2012, *PLoS ONE*

pleiotropy
/plʌɪˈɒtrəpi/

noun GENETICS

the production by a single gene of two or more apparently unrelated effects.

CCRN FIRSTS

- The first genetic linkage finding pointing to the Major Histocompatibility Complex (HLA) on chromosome 6 (*Molecular Psychiatry*, *2003*).

- The first functional MRI examinations of schizophrenia patients in Australia.

- The first national survey of psychoses (Low-prevalence disorders, LPD) 1997-1998.

- A Psychosis Screener - developed for LPD survey and further modified for the Survey of High Impact Psychosis (SHIP) 2010.

- The first comprehensive study of physical morbidity and mortality of psychiatric patients (the "Duty to Care" report and publications 2001-2004).

- The first application of *Grade of Membership* methodology to a large psychiatric sample demonstrating phenotypic heterogeneity in schizophrenia.

- The design and use of the Diagnostic Interview for Psychosis (DIP)

The DIP is a semi-structured clinical interview providing rule-based scores for symptom profiles of psychosis, depression, mania, and substance use disorders. In addition to the main diagnosis, the OPCRIT computerised scoring algorithm notifies the user of any "confounding" or "comorbid factors" present, e.g. substance abuse / dependence; organic brain disease prior to onset of psychosis.

The DIP has been translated into 9 languages:

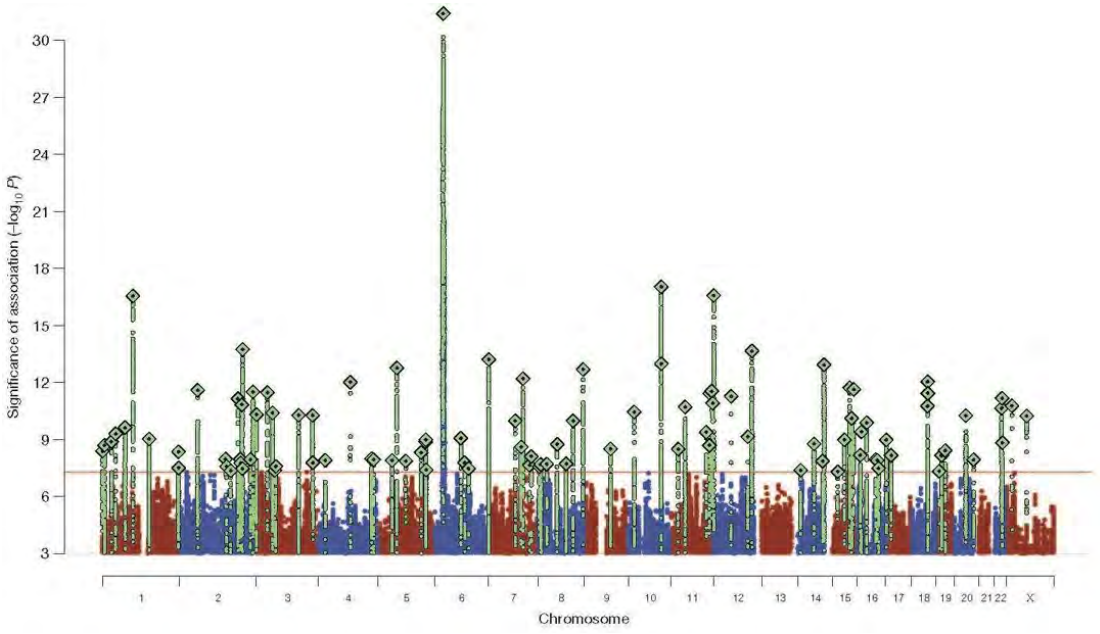
Bulgarian	French	Greek
Italian	Mongolian	Norwegian
Russian	Spanish	Vietnamese

- Genetic studies of 8 candidate genes demonstrating associations with the CD composite endophenotype.

- Link between the immune system on 6p and schizophrenia: first reported in linkage analysis of 61 WAFSS families by Hallmayer et al. (2003).

- One of the first world-wide whole-genome sequencing study of families with schizophrenia.

- Genome-wide association study *Nature*, 24 July 2014: 36,989 cases; 113,075 controls. 108 loci meet genome-wide significance (83 of which have not been previously reported. The Psychiatric Genomics Consortium (PGC) comprises >80 institutions in 25 countries. CCRN / WAFSS is one of them. It is "the largest biological experiment in the history of psychiatry".



Manhattan Plot highlighting the impact of 6p in schizophrenia

Schizophrenia Working Group of the Psychiatric Genomics Consortium, *Nature*, *511*, 2014

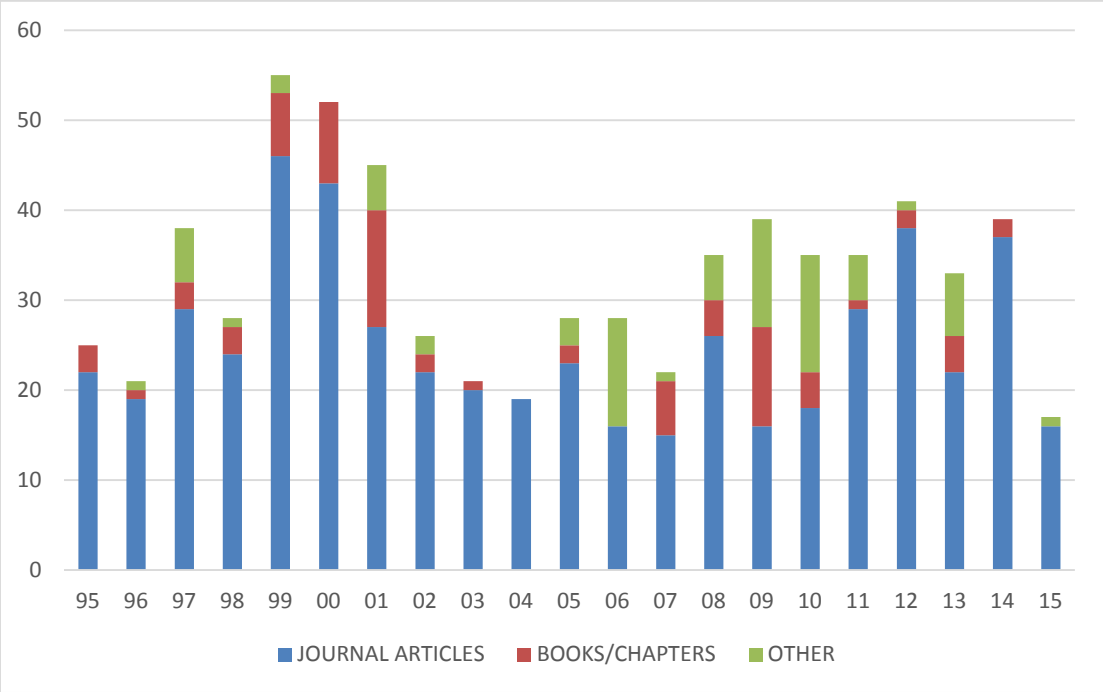
Prof Martin-Iverson began working with CCRN as an Associate Professor in 1997. He was Chief Investigator of the 'Eyeblink reflex modulation: specificity of deficits to schizophrenia and to prepulse inhibition' project. Over the next 15 years Prof Martin-Iverson's neurochemistry and psychopharmacology projects at his laboratory at Graylands Hospital evolved to include animal studies of dexamphetamine, and cannabis studies within people with severe mental illness and healthy community controls.

Of great importance to the CCRN and the wider research community is Prof Martin-Iverson's capacity for teaching. Many students have successfully completed both honours and PhD projects which have had considerable impact in their respective fields under the supervision of Prof Martin-Iverson. Prof Martin-Iverson and his team continue to strive for a better understanding of the neurobiology of schizophrenia and associated disorders with the aim to improve future treatments.

Prof Mathew Martin-Iverson BSc PhD
Professor of Medicine and Pharmacology,
University of Western Australia

CCRN PUBLICATION RECORD

CCRN staff and students have a strong history of publishing meaningful results in high impact journals. Throughout the course of the centre's history, as the number of staff and students has fluctuated based on grant success and collaborations, the aim to publish regularly has always been achieved. The numbers presented below are based on archival records from CCRN annual reports and are as accurate as possible.



Total journal articles 1995 - 2014 = **527**

Total books and chapters 1995 – 2014 = **78**

Total other publications (including reports and published abstracts) = **77**

Combined Total = 682

CURRENT WAFSS PROJECTS

- The Western Australian Family Study of Schizophrenia (WAFSS) remains as the 'flagship' of CCRN research.
- Genome-wide association studies of schizophrenia (PGC2 Consortium).
- Schizophrenia exome: genome-wide linkage and family-based association.
- Schizophrenia under the genomic lens: whole-genome sequencing of Western Australian families with schizophrenia.
- Schizotypy and risk of schizophrenia.
- NIMH Pedigree-based consortium on endophenotypes in schizophrenia.
- Thought and language disorders in schizophrenia.

"Speed of information processing is unimpaired in high schizotypes from the general community. One possibility is that intact processing speed in at-risk groups confers protection to psychosis onset…Assessing the trajectory of processing speed throughout development may provide a useful clinical screening tool to distinguish those at heightened risk of developing psychosis."

Johanna Badcock et al.

2015

WHOLE GENOME SEQUENCING OF WAFSS FAMILIES

- Individual single nucleotide polymorphisms (SNPs) or their combinations account for only a fraction of heritability and raise the risk of disease by a modest amount (up to 20% - 30%) which is not very useful for predicting whether an individual will develop the illness.

- It is likely that the 'missing heritability' lies in rare variants, i.e. mutations carried by less than 2% of the population and having a greater effect size. Such rare variants can be captured by Next-generation DNA sequencing of the whole human genome (WGS).

- A promising research pathway is to look for rare variants in families with schizophrenia. Family-based cohorts, in which rare variants segregating in pedigrees are enriched due to Mendelian transmission, have substantially greater power that unrelated cases to detect genetic effects, given an equivalent number of sampled individuals.

- Aiming to compare rare variants with higher effect sizes than common polymorphisms.

GENOMICS RESEARCH 2015-2016

Ascertainment of multiplex families substantially increases power to detect associations because the probability of capturing multiple copies of rare functional variants increases as the number of affected individuals in a family increases.

WA family-based study of rare genetic variation associated with schizophrenia:

- **Stage 1** (Completed): Selection of 88 multiplex families (316 members) meeting inclusion criteria of comprehensive phenotyping of each family member and availability of DNA.

- **Stage 2** (Completed): exome genotyping of the 88 families using the Illumina HumanCore Exome BeadChip (>250,000 functional exonic variants derived from 12,000 individual exome sequences and a range of conditions, including schizophrenia, autism, diabetes, cardiovascular disorder, and cancer).

- **Stage 3** (In progress): Analysis of exome data.

- **Stage 4** (Completed): Full genome sequencing (Macrogen Ltd).

- **Stage 5** (Starting 2015): Analysis of genomic sequencing, reports & publications.

Financial support: NHMRC project grant; CRC-MH contract; UWA support in kind.

Prof Dieter Wildenauer was the Deputy Director of CCRN until his retirement in 2014.

In 1996 Prof Wildenauer began a collaborative project with the University of Indonesia, the University of Bonn and the University of Western Australia, which examined families in a linkage study.

The study recruited 1,117 people with schizophrenia and their immediate family members. The study also examined a control sample of 1,148 health community participants.

Genome wide significance for linkage was obtained on chromosome 3, and weaker signals for regions on chromosomes 1, 5, and 10.

As well as extending the genetics of schizophrenia literature, Prof Wildenauer's project developed a close, long-term collaboration with local psychiatrists and nurses in five major hospitals in Jakarta, Indonesia.

Prof Dieter Wildenauer PhD
Professorial Fellow,
Deputy Director CCRN,
University of Western Australia

TRANSLATIONAL RESEARCH: "BENCH ↔ BEDSIDE"

Translational research should always be a main goal of CCRN research and areas to consider include:

- Importance of early diagnosis and treatment
- Standardisation of clinical tools (e.g. training clinicians in the use of DIP)
- Evaluation of cognition: brief cognitive screen for use by clinicians
- Cognitive deficit is a key factor for impairment in daily activities
- Cognitive remedial therapy: coaching patients for more efficient use of cognitive strategies
- Rehabilitation: Liaising with industry and NGO to provide supported employment for patients – one of the best strategies for prevention of the "social breakdown syndrome" (Gruenberg E et al., 1972)

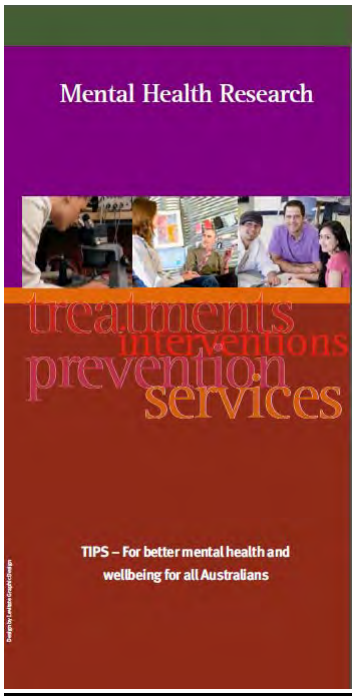
> The intrinsic deficits caused by the psychotic disorder became amplified by environmental factors, resulting in "a socially determined reaction pattern" that involves:
>
> - Loss of social support and peer network
> - Loss of meaningful goals and role fulfillment
> - Disuse of acquired skills and knowledge
> - Downgrading one's attitude and expectation
>
> Ernest Gruenberg et al. 1972

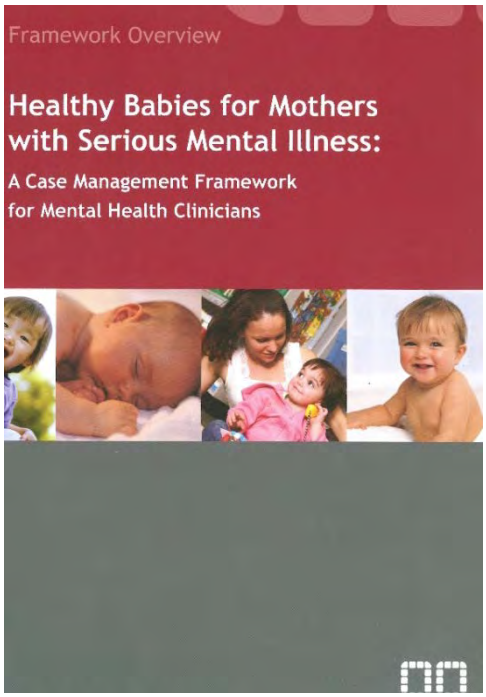
- Future pharmacological tools (personalised treatments)
  - Targeting specific molecular bottlenecks
  - Cognitive enhancers
  - Stimulating neuronal neogenesis → increasing synaptic reserve

Consumers, carers and families should also be equal partners in research. CCRN strives to facilitate this process and has done so through the development of brochures including:

- A brochure for consumers titled 'Mental Health Research: TIPS' explaining Treatments, Interventions, Prevention, and Services

- A brochure for the prevention of obstetric complications which was adopted for routine use in the community mental health services





"Next year I will celebrate my 80th birthday and I have shared half of those years with one of my sons who lives with a severe mental illness.

The first signs of the deeply troubled symptoms of what was to come for the youngest member of our family was evident to us from the time of his fourth birthday. In spite of our efforts to find him the best care, it was not until he attempted suicide at the age of fourteen that any help was offered. After a very turbulent adolescence and early adulthood including a number of hospital admissions and failed treatments and after he had been diagnosed with " Paranoid Schizophrenia", in his mid-twenties he was prescribed an anti-psychotic medication which proved capable of relieving his terribly disabling paranoid symptoms , albeit with some very worrying side effects. As one eminent psychiatrist has said to me "At best, we still only have the best-worst treatments for severe psychotic and mood disorders."

My lived experience of mental illness like that of many other family members, including those involved in CCRN's WAFSS is marked by the myriad observations, at close hand, of day by day presentations of what works and what does not in terms of available treatments and other supports that offer hope of progress to a better and more rewarding life for our loved ones.

Meeting for Minds strives to improve mental health in the community by building strong partnerships and harnessing the creative thinking of researchers, clinicians, people with lived experience of mental illness, and their families and carers.

My observations cover my perspectives as a parent , Health Minister, Chair of the Mental Health Council of Australia and now, Director of the Not for Profit Organisation, Meeting for Minds. As a result I have been and remain a strong advocate for recognition to be given to the lived experience of consumers and carers as an especially valuable body of knowledge to be taken seriously into account at all levels. This particularly includes research into severe mental disorders such as schizophrenia and new and better treatments.

The respectful involvement of patients and families in research conducted by CCRN over 20 years and particularly in the WAFSS has been one of the most heartening and inspiring aspects of the way research is undertaken at this Centre under the eminent leadership of Professor Assen Jablensky."

Hon Keith Wilson AM

Director Meeting for Minds

LOOKING FORWARD: THE NEXT DECADE

- Laboratory facilities, policies and procedures have already been established in our new 'home' at MRF and selective recruitment & assessment of informative families will resume.

- Our collaborative network within WA, Australia and overseas is growing, ensuring CCRN continues to making a difference in understanding and treating severe mental illnesses.

- The quality and integrity of our research, supervision and mentoring will remain the hallmark of what we do at the CCRN.

- As a striving Academic Centre of Excellence our mission to conduct 'research with impact' will be sustained and nurtured, and citations to our work will continue to increase.

- The rich phenotype and genotype database accumulated over the past 20 years will provide the testbed for new hypotheses and conceptual models of schizophrenia, providing answers to the 'big questions' and practical "know-how" to prevent or reduce impairments and disabilities in our patients.

> "The prevalence of the metabolic syndrome was high, affecting 60.8% of participants…Our findings highlight the need for comprehensive, integrative models of recovery to maximise the potential for good health and quality of life for people with psychotic illness".
>
> Vera Morgan et al.
>
> 2014

As CCRN begins this new and exciting phase in its identity, our 5-year research plan will strategically focus on:

- Expanding the talents and skills of our research team, at every stage of their career.

- Research that builds on our unique scientific strengths in genetics, epidemiology and cognitive psychology, e.g. CCRN researchers have submitted two new 5-year NH&MRC project grant applications for funding in 2016, and continue to seek funding from a range of sources.

- Consumer and clinician priorities, e.g. on earning, learning and yearning to belong.

- Developing the next generation of clinician-researchers, e.g. we currently supervise 6 postgraduate students, and have 1 new PhD student about to commence.

- Embracing new approaches and technologies in the recruitment and testing of study participants, ranging from biobanks and crowdsourcing to iPads and Apps.

CONCLUDING COMMENT

- Over the last 20 years CCRN research has been highly successful and, in many ways, pioneering in schizophrenia research, nationally and internationally.

- We have a strong core of multidisciplinary researchers and consumer-advisors and a uniquely rich database.

- Aware of the challenges, we look forward to building on this record of excellence, capitalizing on the opportunities arising from our new location and alliances, and extending our contribution as WA's leading centre for advanced multidisciplinary research into severe mental disorders.

"…It seems to me there is much to reflect on, when one acknowledges the impressive accomplishments in the 20 years of CCRN existence. It is an occasion to plan for the future and take pride in the tremendous potential for CCRN to prosper as an internationally acclaimed academic institution. One has just to glance at the calibre and scope of existing CCRN major projects as an indication of the exciting times lying ahead…I still feel part of the CCRN team, even though more than two years have passed since my departure…In many respects my experience of working with all of you at CCRN has shaped my thinking and influenced my academic directions here in Athens. Mostly, it has reinforced my belief that in order to achieve much in our field, one needs to forge a united team such as yours, dedicated to the pursuit of knowledge."

Prof Nikos Stefanis MD FRANZCP

Professor of Psychiatry,

University of Athens, Greece

APPENDIX A
CCRN STAFF & ASSOCIATES 1995-2015

Lindsey Allet
Nigel Armstrong
Johanna Badcock
Borghild Bo
Juliette Box
Bill Budd
David Castle
Peter Clissa
Matthew Cooper
Nicholas Covich
Sophie Davison
John Dean
Sean Doyle
Travis Endersby
Christina Feldman
Jane Fitch
Dylan Galloghly
Caroline Graham
Joachim Hallmayer
Maggie Hegarty
Sarah Howell
Assen Jablensky
Brendan Jansen
Rochelle Jones
Roland Kaiser
Rick Kellner
Lyn Kløve
Joseph Lee
George Lipton
Marina Lovasz
Osvaldo Almedia
Mohammed Ayoub
Lorraine Bahri
Avijit Bose
Adam Brett
Brigitte Burg
David Chandler
Johan Combrink
Gayle Corbould
Sarah Davenport
Lisa Dawson
Kellie Dedman
Paul Dragicević
Stella Fabrikant
Steve Fenner
Kate Fitzpatrick
Coleman Garrett
Jenny Griffith
Carole Harrison
Wayne Hill
Augie Hwee
Aleksander Janca
Binu Jayawardena
Julie Johnston
Megan Kalucy
Aaron Kent
Mary Kuriyan
Faranak Lillo
Andrée Loney
Danielle Lowe
Dora Angelicheva
Dimitar Azmanov
Alan Bland
Carol Bower
Cath Brett
Rochelle Castine
Melanie Clark
Margaret Cook
George Covich
Philip Davis
Maria D'Ercole
Patsy Di Prinzio
Milan Dragović
Deb Faulkner
Isabel Fernandez
Rinske Frima
Stephanie Gee
Tammy Hall
Yvonne Hauck
Hilary Hodgson
Hamish Innes-Brown
Emilia Janca
Juliette Jones
Linda Johnson
Luba Kalaydjieva
Patrick Kingsep
David Lawrence
Jason Lim
Clea Louw
Trudi Mackenzie

Tegan McNab
Alana Maley
Stephen Marshall
Neilson Martin
Mathew Martin-Iverson
Ralph Martins
Philippa Martyr
Mark McAndrews
Russell McKenney
Bridget McManus
Patricia Michie
Sara Miller
Nick Mondinos
Stephen Moore
Lucia Monte
Bharti Morar
Bronwyn Morgan
Vera Morgan
Daniel Morkell
Elaine Murphy
David Neumann
Patrick O'Connor
Himka Osmancevic
Naima Ouchkire
Sacha Pauly
Rebecca Pedruzzi
Kirsten Peters
Tegan Phillips
Krishna Pillai
John Pinnington
Gregory Price
Maśa Radević
Christina Read
Kate Reid-Milligan
Sean Ricciardo
Geoff Riley
Daniel Rock
Jeff Rogers
Boyd Salmon
Megan Schmitt
Sibylle Schwab
Tony Shackleton
Sonal Shah
Eamon Shanley
Nicky Simmons
Craig Sinclair
Hilary Sitas
Helen Slattery
David Smith
Helen Stain
Renee Stienstra
Johana Stefan
Nikos Stefanis
Chris Stoddart
Raj Tanna
Keira Thomson
Juanita Todd
Maggie Travia
Phebe Verbrugghe
David Vile
Vaike Vohma
Gary Wallace
Matt Walsh
Fahmida Ward
Ellie Warenius
Anna Waterreus
Flavie Waters
Helen Wichmann
Dieter Wildenauer
Rachael Williams
Stephen Wiltshire
Debra Wood
Brigitte Wynne
Peter Wynn Owen
Pip Wynn Owen
LiAnne Yellachich
Steve Zubrick

APPENDIX B
POSTGRADUATE / PHD STUDENTS
1995-2015

PhD students

Matthew Albrecht
Renita Almeida
Avdesh Avdesh
Bill Budd
Sonya Bouwer
Graham Byatt
Saruchi Chhabra
Vivian Chiu
Serena Cribb
Milan Dragović
Deb Faulkner
Dylan Galloghly
Emma Glasson
Leigh Goggin
Kyran Graham
Carole Harrison
Anthony Henderson
Dana Hince
Michelle Hodge
Rebekah Honey
Sean Hood
Seiji Humphries
Karina Kedzior
Ayse Kilicoglu
Ute Kruse
David Lawrence
Shahrzad Mazhari
Alix Mellor
Hayley Mighall
Zak Millar
Rolinda Miocevich
Vera Morgan
Kumurdini Nair-Miranda
Kirsten Panton
Georgie Paulik
Nicole Petterson
Daniel Rock
Tamara Rogers
Mark Sachmann
Boyd Salmon
Emma Savery
Kirsty Scholes
Craig Sinclair
Yathunanthan Sivarajah
Helen Stain
Chris Stoddard
Juanita Todd
Tina Tse
Giulietta Valuri
Anna Waterreus
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Mark Woodman
Dana Wong
Nathanael Yates
Li-Anne Yellacich

Masters students

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Kristina Durrance
Linda Johnson
Ayse Kilicoglu
Evelyn Klove
Katrin Hanken
Sarah Hescham
Nahal Mavadatt
Devon Spaapen

Honours students

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Alexander Barty	Michael Bone	Jarrad Bothe
Alysia Buckley	Saruchi Chhabra	Carol Cheney
Kate Chitty	Aindreas Dorai-Rag	Jeremy Downie
Shayna Driscoll	Brendan Gardner	Kyran Graham
Madeleine Hofmeester	Rebekah Honey	Esha Jamnadass
Nicole Kettlewell	Rahul Khubchandani	Jessica Langley
Tracey Lim	Berenika Luczak	Simone Mahfouda
John McAnearney	Angela McLelland	Zak Millar
Kate Reid-Milligan	Johnathon Noonan	Syerna Ong
Amal Osman	Russell Piper	Peter Smedley
Jeremy Tannenbaum	David Tindiglia	Vikram Rajput
Morgan Wang	Rachael Williams	

APPENDIX C
PSYCHIATRY REGISTRARS 1995-2015

Psychiatry Registrars

Adam Brett	Johan Combrink	Stella Fabrikant
Brendan Jansen	Megan Kalucy	Bridget McManus
Brian Power	Nicole Simmonds	Helen Slattery
Raj Tanna	Debra Wood	Peter Wynn Owen

APPENDIX D
VISITING OVERSEAS SCIENTISTS
1996 – 2015

Belgium

Prof Michael Maes
Dr Bart Nuttin

Brazil

Prof Claudio Soares

Canada

Prof Rick Beninger
Prof James Kennedy

Dubai

Dr Manjusha Sudhadevi

Finland

Prof Risto Näätänen

Germany

Prof Michael Koch
Prof Wolfgang Maier
Prof Friedrich Poustka

Geneva - WHO

Dr John Orley
Prof Norman Sartorius

India

Prof Partha Majunda
Dr Rangaswami Thara

Indonesia

Dr Herlina Handoko
Dr Irmansyah

Italy

Dr Alberto Rossi

Japan

Prof Toshikara Suzuki

Lithuania

Prof Vaidas Kucinskas

Mongolia

Dr Oyunchimeng Norovsambuu
Dr Guljanat Yerlan

Netherlands

Prof Michael Maes

New Zealand

Prof Michael Corballis
Dr David Menkes

Norway

Ms Christine Nyquist
Prof Vidje Nielsen
Dr Ingunn Skre

Russia

Dr Daria Smirnova

Singapore

Prof Markus Wenk

Sri Lanka

Dr Ranil de Silva

Sweden

Prof Christer Allgunlander
Prof Thomas McNeil
Prof Christina Hultman

Switzerland

Prof Mitchell Weiss

United Kingdom

Prof Kathryn Abel
Prof Dorothy Bishop
Dr Sube Banerjee
Dr Nick Bass
Prof Allan Butterfield
Prof John Cooper
Prof Sam Cohen
Prof John Crawford
Dr Paul Fletcher
Dr Vania Gabrovska
Prof Steven Hirsch
Prof David Horrobin
Prof Peter Jones
Prof Robert Kendell
Prof Julian Leff
Prof Anthony Mann
Prof Phillip McGuire
Dr Peter McKenna
Dr Dave Mercer
Prof Robin Murray
Prof David Nutt
Prof Michael Owen
Dr Edith Pomarol-Clotet
Dr Martin Prince
Prof Sergio Della Salla
Prof Ley Sander

Prof Graham Thornicroft	Prof Andrew Whitehouse	Dr Katherine Wulff

United States

Dr Peter Bandettini	Prof Allan Butterfield	Prof Tyrone Cannon
Prof Brendan Carroll	Dr Cameron Carter	Prof Robert Cloninger
Prof Elizabeth Corder	Prof Nelwon Cowan	Prof Hasker Davis
Dr Edwin Fuller Toorey	Prof Marshal Folstein	Prof Susan Folstein
Prof Sam Gandy	Prof Pablo Gejman	Prof Irving Gottesman
Prof Judith Jaeger	Dr Brian Kirkpatrick	Prof Sarnoff Mednick
Dr Aina Puce	Prof Neil Risch	Dr Robert Savoy
Prof Stephen Stahl	Prof Zebulon Taintor	Prof Richard Warner

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From everyone at CCRN,

THANK YOU!

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