MENDING MINDS

A MENTAL HEALTH COMMUNITY PRESENTATION

Proudly brought to you by the Monash Alfred Psychiatry Research Centre (MAPrc)
Introducing the Monash Alfred Psychiatry research centre (MAPrc)

MAPrc is a clinical research centre based at the Alfred Hospital

- MAPrc is part of two organisations
  - Department of Psychiatry, Alfred Health
  - Central Clinical School, Monash University

MAPrc researchers new treatment approaches for mental illnesses, with a focus on

- Schizophrenia
- Depression
- Bipolar Disorder
- Autism & Aspergers

MAPrc research is categorised into four key areas:

- Women’s Mental Health
- Psychopharmacology
- Psychiatric Neurotechnology
- Psychiatric Service Research
Introducing tonight's speakers...

- **Professor Jayashri Kulkarni**
  MBBS, MPM, FRANZCP, PhD
  Director, MAPrc

- **Dr Neil Thomas**
  BSc (Hons), DClinPsych, CPsychol, MAPS, AFBPsS
  Senior Clinical Psychologist, Alfred Health

- **Ms Sacha Filia**
  Senior Research Fellow, MAPrc

- **Dr Stuart Lee**
  Senior Research Fellow, MAPrc

- **Professor Paul Fitzgerald**
  MBBS, MPM, PhD, FRANZCP
  Deputy Director, MAPrc
SCHIZOPHRENIA
– THE SCIENCE, THE ART & THE HUMANITY

Prof Jayashri Kulkarni
Monash Alfred Psychiatry Research Centre

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HISTORY

- Schizophrenia has a long dark history
- Fear and stigma were commonly attached to this disorder.
- First called ‘demence precoce’ by Benidict Morel (1809-1873).
- The focus was on symptom classification and control, plus isolation of the patient.
KEY SYMPTOMS OF SCHIZOPHRENIA

• Positive Symptoms – Hallucinations (commonly ‘voices’), delusions and thought disorder, bizarre behaviour.

• Negative symptoms – Difficulties with motivation, lack of thought content, little speech.

• Cognitive symptoms – difficulties performing higher intellectual functions.
CAUSES OF SCHIZOPHRENIA

Multifactorial:
• Alteration in neurochemistry
• Alteration in brain circuitry
• Possible genetic involvement
• Social factors such as trauma, abuse, street drugs
• Psychological vulnerability.
DIAGNOSIS

- No one test yet, but a number of potential markers of illness are being developed.
- Measures of brain function and images are rapidly advancing.
MRI
TREATMENT OPTIONS

• A biopsychosocial approach is imperative.
• Biological treatments – antipsychotic medications, brain stimulation.
• Psychological treatments – CBT, DBT, cognitive remediation, other psychotherapies.
• Social – Community inclusion, education, vocation.
• Street drug rehabilitation if needed.
ANTIPSYCHOTIC MEDICATION

The main neurochemical systems that are impacted by antipsychotic medications include:

– Dopamine
– Serotonin
– Muscarinic
– Glutamergic
– Cannabinoid
ANTIPSYCHOTIC MEDICATION

• There are currently around 40 different antipsychotics on the market worldwide.
• There is still a high medical need for improvement.
• Many pharmaceutical companies are developing novel strategies for the treatment of schizophrenia.
• Adjunctive treatment strategies are also very important.
• Side effects, dose and type of antipsychotic needs to be tailored to the individual.
EXAMPLES OF NEW ANTIPSYCHOTICS

• Recent antipsychotics include – risperidone, olanzapine, amisulpride, quetiapine, aripiprazole, sertindole, asenapine.

• These antipsychotics mainly work through the dopamine and serotonin systems.

• Other neurochemical systems are being investigated – we are conducting a study to evaluate the effectiveness of a glycine reuptake inhibitor medication in people with persistent negative or positive symptoms of Schizophrenia (Roche Searchlyte study).

• AMG 747 is a selective small molecule central glycine transporter type-1 (GlyT-1) inhibitor.
ADJUNCTIVE TREATMENT APPROACHES

- Estrogen
- SERM
- Ondansetron
- Other
Sex differences in schizophrenia
- Later onset for women
- Increased vulnerability at periods of hormonal change
  - post-natal & menopause
  - Exacerbation of psychosis during low estrogen phases of menstrual cycle


“estrogen protection hypothesis”
(Seeman, 1996; Seeman and Lang 1990; Riecher-Rossler et al., 1994)
ESTROGENS & THE CNS

• Within CNS, estrogen acts as a neuroprotective agent
  – Genomic (delayed)
    • mediated by the activation of estrogen receptors and gene transcription
  – Non-genomic (rapid)

Figure reproduced from Garcia-Segura et al. (2001) *Progress in Neurobiology*, 63, 29 - 60
ANIMAL STUDIES

Before Estrogen

After Estrogen
Group x PANSS Positive:
\[ F(6, 333) = 2.18, \ p = 0.045 \text{ (sig.)} \]
Selective Estrogen Receptor Modulator

• raloxifene hydrochloride
  – Retain positive estrogenic effects
    • Bone, Brain
      – Able to cross BBB (Sumner et al. 2007; Huang et al., 2007)
      – Estrogen agonist: serotonergic, cholinergic transmission? (Littleton-Kearney et al., 2002)
  – Avoiding adverse estrogenic effects
    • anti-estrogenic actions in breast tissue & uterus (Delmas et al., 1997)
• Significant Group by Time interaction ($p = .042$).
• Raloxifene group significantly decreased in positive PANSS scores over time.
SERMS IN MEN

We are offering SERM treatment for men with schizophrenia.
Ondansetron, a serotonin 5HT3 receptor antagonist has shown promising results in the treatment of schizophrenia symptoms in a number of small scale studies. In particular, ondansetron has shown benefits in reducing the persistent cognitive and negative symptoms experienced by many people with schizophrenia.
SPECIAL ISSUES FOR WOMEN WITH SCHIZOPHRENIA

- Pregnancy
- Safety and privacy in inpatient settings.
- Menopause.
THE NATIONAL REGISTER OF ANTIPSYCHOTIC MEDICATION IN PREGNANCY (NRAMP)
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SAFETY AND PRIVACY
Women’s Only Area.
Science and technology will lead us on to a better level of knowledge and understanding about schizophrenia, but compassion, empathy, caring and special individualised treatment approaches are necessary to get the best from the scientific advances.
Insert Neil Thomas presentation
Advances in Psychological Interventions for Schizophrenia
• CBT
• Cognitive Remediation
• Peer delivered interventions
• Online
No mental health without physical health

Tiihonen et al., 2011 The Lancet
Life expectancy in schizophrenia ↓ by 20+ years

Colton & Manderscheid 2006; Weiss et al 2006
- Mean life span male with schizophrenia = 57 years vs 78.5 years for Australian male
- Mean life span female with schizophrenia = 65 years vs 83.3 years for Australian female

Main reason for shorter lifespan and higher death rates among people with schizophrenia is due to medical conditions not suicide
Many reasons….

- Impact of medications
- Impact of symptoms
- High rates of smoking
- Poor diet
- Physical inactivity
- Lack of knowledge
- Lack of resources
- Poverty
- Stigma/discrimination
- Substance use

Physical health problems in people with mental illness are less likely to be identified, assessed or treated
CVD in mental illness

- Cardiovascular disease (CVD) is the leading cause of death in patients of mental health services in Australia. AIHW 2010

- 50-75% people with schizophrenia will develop CVD. Hennekans et al 2005

- Rates of death from CVD in schizophrenia are 2x higher than in the general population. Brown et al., 2000; Osby et al., 2000
Elevated CVD risk factors in mental illness

These CVD risk factors are significantly elevated in people experiencing psychosis compared to those without mental illness.
How is MAPrc addressing this problem?

- Research
- Publications
- Consultancy
- Advocacy
- Presentations/teaching
Healthy Lifestyles Research at MAPrc

Helping people towards quitting smoking and a healthier lifestyle
The Healthy Lifestyles Pilot Project 2006-2008

- Funded by Commonwealth Dept Health & Ageing
- n=43 overweight smokers with psychosis
- NRT + 9 sessions MI/CBT
- Abstinence = 19% at 15 weeks
- Half reduced the amount they smoked ≥ 50%

30.8 cig/day to 17.2 cig/day, p<0.001

Cigarettes per day

Pre-treatment
Post-treatment

35
30
25
20
15
10
5
0
The Healthy Lifestyles Pilot Project 2006-2008

- Overall significant ↓
  - Coronary heart disease risk
  - Weight
  - Waist circumference
- Overall significant ↑
  - Physical activity (moderate)
  - Quality of life related to weight
- Improvement in diet
- No significant change in symptoms (e.g. psychosis or depression)
Aim: to establish the efficacy and safety of Champix as an adjunct to a healthy lifestyles intervention for smoking cessation among people with severe mental illness

14 smokers with severe mental illness participated for 6 months

Most common side-effects: sleep disturbance and nausea
1 participant discontinued due to psychiatric reasons

Smoking abstinence rates:
3 months = 36%
6 months = 42%

No significant change from baseline on scales assessing symptoms of psychosis, depression or mania
The Healthy Lifestyles Project
2009 - ongoing

- Large, long-term study n=236
- 3 sites: Newcastle – Professor Amanda Baker
  Melbourne – Professor Jayashri Kulkarni
  Sydney – Professor Robyn Richmond
- Participants = psychosis + smoking 15 cigs/day
- Funded by 2 NHMRC grants
- AIM: evaluate effectiveness of a healthy lifestyles intervention targeting smoking and other CVD risk factors in people with severe mental illness
Baseline results n=236

- Mean age = 41.7 years (19-69)
- Diagnosis: schizophrenia = 58.5%
- Asthma = 26.4%
- Diabetes = 11%
- CVD event = 9%
- Mean number of cigs per day = 28.2 (range: 15-65)
- Spend 28.2% of income on cigarettes
- Majority considered “Obese” according to BMI = 48.2%
- Low levels of physical activity
- Eat few serves of fruit/vegetables per day
- Frequent take-away foods and food high in sugar/fat
Interim results baseline to 15 weeks
n=60

- mean number of sessions = 8 (total = 17)
- ↓ by ≥ 50% = 56.1% sample
- ↑ daily physical activity & improvements in diet
The price of good mental health must not be a lifetime of physical illness

Tiihonen et al., 2011 The Lancet
Research to help services better care for people with schizophrenia

Dr. Stuart Lee
Mental Health Service Evaluation Senior Research Officer
Post-seclusion Counselling
How post-seclusion counselling helps

• Intended to:
  – enhance patients’ understanding of the event
  – diminish the potential negative consequences (emotional or physical) of seclusion for patients
  – prevent future seclusion episodes
  – repair and or improve therapeutic rapport

• BUT – too date literature research addressing effectiveness, timing etc.
Indicators of Outcome - Seclusion

<table>
<thead>
<tr>
<th></th>
<th>Grd Fl (n=14)</th>
<th>1st Fl (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total seclusion episodes</td>
<td>2.5 ± 0.5</td>
<td>2 ± 0.5</td>
</tr>
</tbody>
</table>

No significant group differences ($p = .36$)

<table>
<thead>
<tr>
<th></th>
<th>Grd Fl (n=14)</th>
<th>1st Fl (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total seclusion hours</td>
<td>40 ± 10</td>
<td>10 ± 1</td>
</tr>
</tbody>
</table>

Significant group differences ($p = .012$)
Indicators of Outcome - Trauma

One participant excluded due IES-R response NOT VALID

NO significant differences between floors across any trauma measures

AT GROUP LEVEL
14 (47%) greater than 33 (IES-R Total) suggesting probably Post Traumatic Stress Disorder
Clozapine Transitioning Project
RESEARCH QUESTION: What are perceived barriers and facilitators for determining whether a consumer takes a particular path?

**PART 1**

- Clients taking Clozapine managed in the Public Mental Health System
- Be transitioned from the Public Mental Health System to GP shared care
- Continue treatment in the Public Mental Health System

**PART 2**

- Be transitioned from the Public Mental Health System to the Private Psychiatry setting

RESEARCH QUESTION: Do consumers in these groups differ and what are their outcomes?
Service Use Before and After Transitioning

Alfred Psychiatrist contact

Alfred Inpatient Psychiatry Admission
Person treated with clozapine

Model of Care

Private Psychiatrist
- Fewer previous antipsychotics
- Live independently or with family/friends
- More independent in activities of daily living
- Good compliance with medication and treatments
- Not using illicit substances
- No recent psychiatric hospital admission
- Not on a CTO

GP Shared Care
- Lengthy duration of mental illness
- Live in supported accommodation
- Taking clozapine for longer than 8 years
- Compliant with medication and treatments
- Not using illicit substances
- No recent psychiatric hospital admission
- Not on a CTO

CMHS
- Current or past substance use
- Live in supported accommodation
- Poorer compliance with medication / treatments
- On a CTO
- Poorer functioning in terms of daily living skills and independence
- Recent admission to a psychiatric hospital
- More intensive case management history
Carer and consumer perspectives on service responses to mental health crises
# Themes relating to experience with responding services

## Consumers (N = 11)

**Response speed important**
- Police respond quickly but can be delays when involving mental health service

**Communication with consumers**
- Valued – both to be told what is happening but also to be listened to
- Varied particularly with police encounters

**Humane treatment**
- Police and mental health staff usually respectful and try normalise – calms situation

**Disjointed responses / lack of onsite collaboration**
- Police-mental health staff arriving separately and not effectively communicating

**Personnel’s threatening presentation**
- Power imbalance police to consumers and CATT to consumers can be intimidating

## Carers (N = 10)

**CATT**
- **Positives:** Skilled at de-escalation, trustworthy, can get into hospital, deal with consumer and carers
- **Negatives:** Can be difficult gaining access, long response times

**POLICE**
- **Positives:** Effective in dangerous situations, took risks helping consumer, rapid response, mindful of other family members, explained actions
- **Negatives:** Can over-act at times, presence can exacerbate the situation, lack of mental illness training, excessive force at times
Preferred way for police and mental health services to collaborate

0 = not at all to 10 = very much preferred

- Ride Along
- Mental Health Trained Police
- Clinicians at Police Stations
- Separate Response

Consumer (n=10)
Carer (n=8)
Picking up the pace for mental health in Stonnington

POLICE and health workers have joined forces as part of a pilot program to respond to mental health-related call-outs.

An Operation PACER (Police, Ambulance and Crisis assessment team Early Response) unit will begin in Stonnington and Port Phillip on November 14, responding to calls to police where mental health is a concern.

Sgt Doug Bowles said as part of the $150,000 six-month trial, police officers would travel with a member of The Alfred hospital’s psychiatric team, who would assist in “de-escalating” potentially volatile situations.

“We have the highest incidence of mental health-related incidents across the state,” Sgt Bowles said.
New Treatments for Schizophrenia

Professor Paul Fitzgerald
Deputy Director, MAPrc
Developing biological treatments in psychiatry

Deep brain stimulation (DBS)
Medication

Novel neurosurgeries (e.g. Cortical Stimulation)

Less invasive

tDCS
TMS
Deep TMS

Convulsive

MST
ECT

More invasive

Surgical

Vagal nerve stimulation (VNS)
Deep brain stimulation (DBS)
Novel neurosurgeries (e.g. Cortical Stimulation)
Treatment Development

Use modern Neuroscience to help understand the disease better

(TMS, MRI, fMRI, DTI, EEG/ERP, NIRS)

New treatment development

Clinical Programs

Understand treatment better

Refine treatment
Transcranial Magnetic Stimulation
Transcranial Direct Current Stimulation (tDCS)

- Low amplitude direct current
- Well tolerated
- Increase in brain activity under anode
- Decrease in brain activity under the cathode
rTMS as a Therapeutic Tool in Depression

• Changes in brain activity with TMS
  – increase with rapid TMS
  – reduction with slow TMS

• Now an established treatment for depression
  – Approved in USA and Europe
  – >400 clinical services in US, >200 clinical services in Germany
  – First publically funded clinical service in Australia at Alfred, January 2012
Potential rTMS Applications in Schizophrenia

- Prefrontal cortex
  - General / non specific
  - Negative symptoms
  - Cognition
  - Depression

- Temporo-parietal cortex
  - Auditory Hallucinations
Negative Symptoms

- Lack of drive, energy, motivation, capacity to experience pleasure
- Far less responsive to treatment
- Relate to reduced activity in frontal brain regions
PFC rTMS and Negative Symptoms

- 8 trials to date
- Mixed results

(Potkin et al., 2002)
rTMS and Auditory Hallucinations

- Left T-P cortical focus
- 1 Hz – reduce local ‘over active’ cortical activity

Hoffman et al 2003
rTMS and Hallucinations

- Efficacy supported by multiple trials to date
- Meta-analysis
  - 10 studies included 212 patients
    - Active effect size = 0.51 (p=0.001)
  (9 studies with continual stimulation sessions in separate analysis - Effect size = 0.88 (p<0.001))

Traunalis et al 2008
rTMS and Auditory Hallucinations: Hoffman et al
Repeat Treatment of AH

Change in PANSS AH

Change in HCS

Baseline Trial End Start Repeat Treatment 1 End Repeat Treatment 1 Start Repeat Treatment 2 End Repeat Treatment 2

Patient 1

Patient 2

Fitzgerald 2006
Transcranial Direct Current Stimulation

- Initially investigated in the 1960s as a possible treatment for schizophrenia
- Investigated for its therapeutic potential in a number of neurological and neuropsychiatric disorders.
- Including depression
tDCS in Schizophrenia

Decreased activity in negative and cognitive symptoms

Increased activity in Auditory Hallucinations and possibly other psychotic symptoms

Anodal tDCS

Cathodal tDCS
PFC underactivity in negative symptoms

Temporoparietal (auditory association cortex) hyperactivity associated with auditory hallucinations, thought disorder, possible passivity symptoms
Current tDCS Studies

1. Clinical Trial
   - 3 weeks of daily treatment sessions
   - 20 minutes per day

2. Studies of the effect of tDCS on Working memory (K Hoy)
tDCS in Schizophrenia

- DLPFC – anodal, TP Junction – cathodal
- 3 weeks duration, daily treatment 5 X per week
- Outcomes
  - Negative
  - Positive (AH)
  - Cognitive
The brain stimulation and neurosciences team

Funding sources
NHMRC
Australia Research Council
NARSAD
Stanley Medical Research Institute
Beyond Blue
Victorian Neurotrauma Initiative
Alfred Foundation
Monash University

Studies Currently Recruiting Call: 9076 6595
• rTMS in depression
  – Treatment resistant depression (2 failed med. trials)
  – Depression following mild – moderate closed head injury
  – Bipolar depression
• tDCS in schizophrenia
  – Patients with either significant negative symptoms or persistent auditory hallucinations
THANK YOU FOR COMING & HAVE A GREAT NIGHT!

www.maprc.org.au