



MAPrc

*We mend minds*



# MENDING MINDS

**A MENTAL HEALTH  
COMMUNITY PRESENTATION**

**Proudly brought to you by the  
Monash Alfred Psychiatry  
Research Centre (MAPrc)**



**TheAlfred**



**MONASH** University  
Medicine, Nursing and Health Sciences

# 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 Folia**  
Senior Research Fellow, MAPrc
- **Dr Stuart Lee**  
Senior Research Fellow, MAPrc
- **Professor Paul Fitzgerald**  
MBBS, MPM, PhD, FRANZCP  
Deputy Director, MAPrc





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# SCHIZOPHRENIA – THE SCIENCE, THE ART & THE HUMANITY

Prof Jayashri Kulkarni  
Monash Alfred Psychiatry Research Centre

(03) 9076 6924 - [maprcpa@alfred.org.au](mailto:maprcpa@alfred.org.au) - [www.maprc.org.au](http://www.maprc.org.au)



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# HISTORY

- Schizophrenia has a long dark history
- Fear and stigma were commonly attached to this disorder.
- First called 'démence précoce' by Benédicte 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



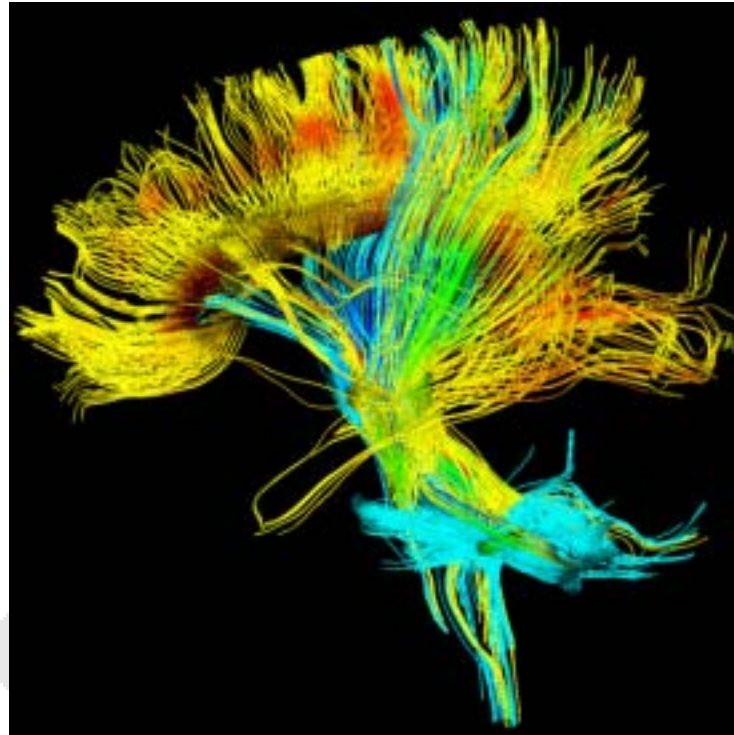
# MEG



# EvestG



# DTI



# TREATMENT OPTIONS



- A biopsychosocial approach is imperative.
- Biological treatments – antipsychotic medications, brain stimulation.
- Psychological treatments – CBT, DBT, cognitive remediation, other psycho therapies.
- 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



# ESTROGEN & SCHIZOPHRENIA

- **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

(Angermeyer and Kuhn 1988; Jablensky, Sartorius et al. 1992; Loffler, Hafner et al. 1994)

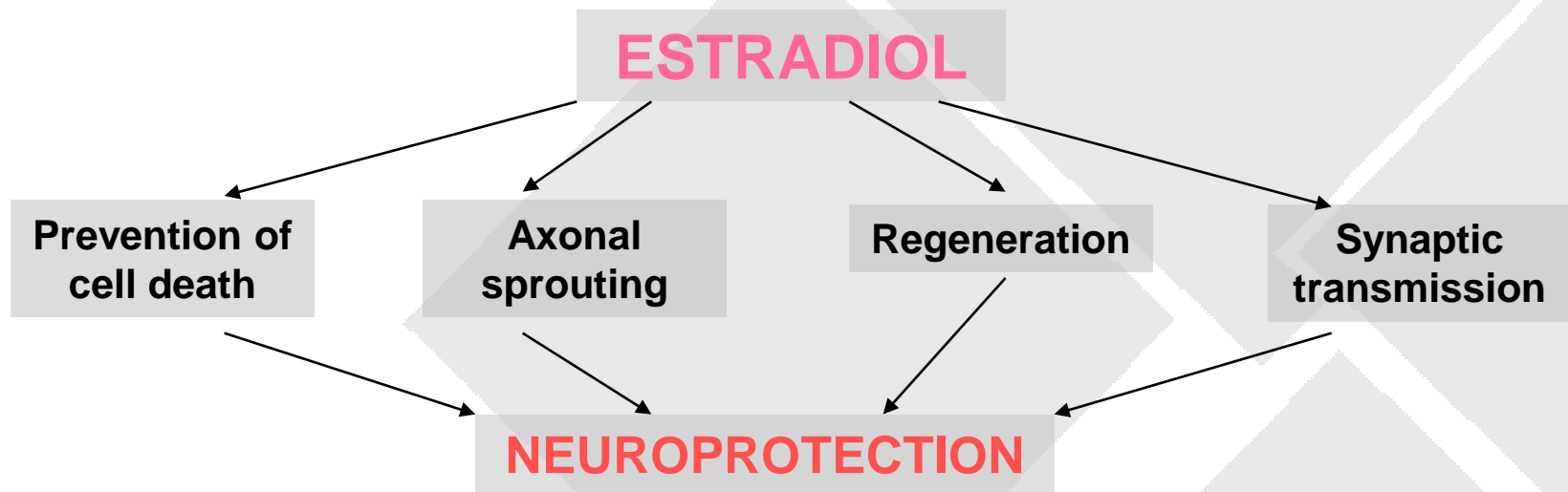
- “estrogen protection hypothesis”

(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)



# ANIMAL STUDIES

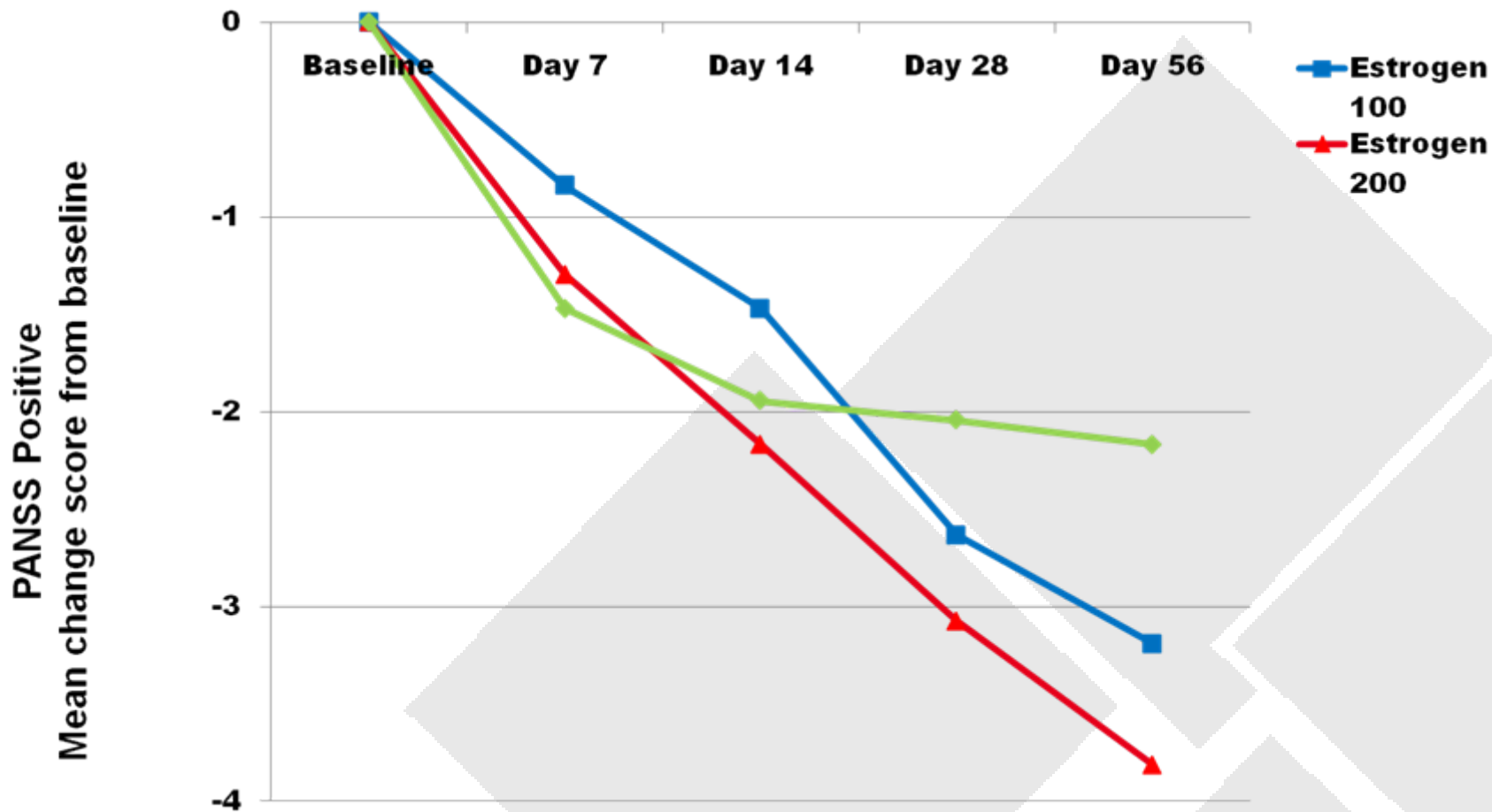
Before Estrogen



After Estrogen



# PANSS POSITIVE



**Group x PANSS Positive:**  
 **$F(6,333) = 2.18, p = 0.045$  (sig.)**



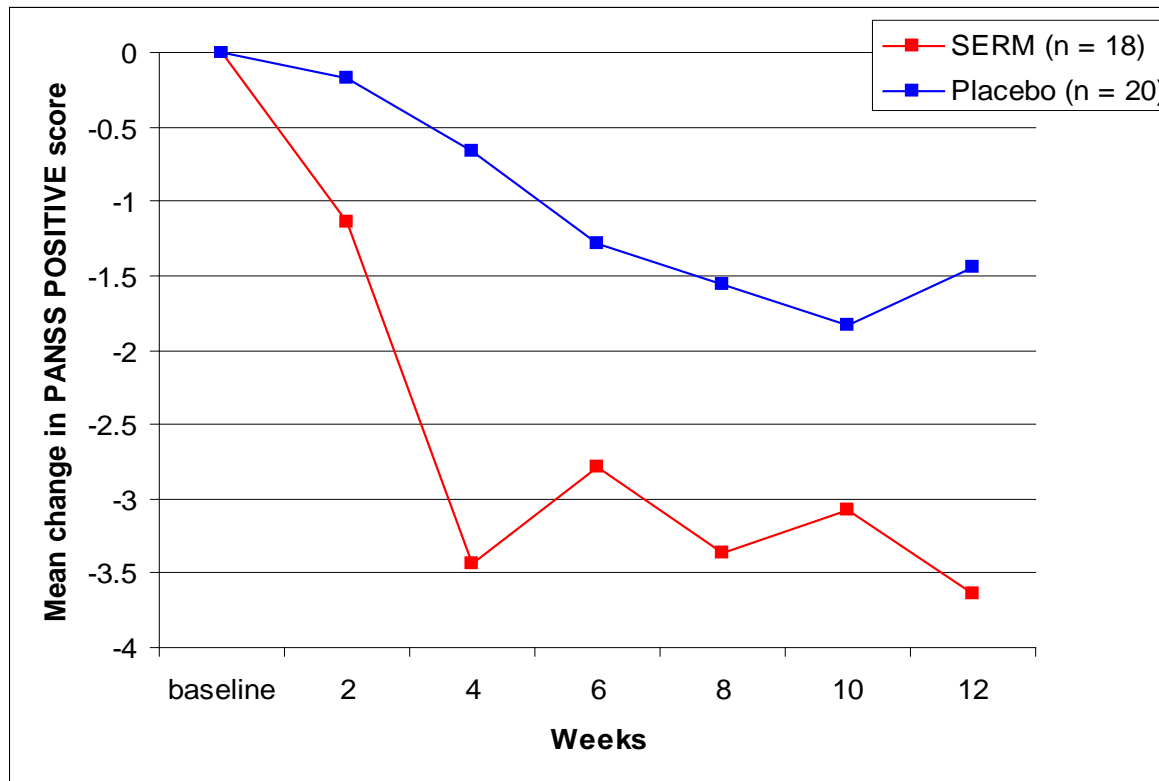
# SERMS

## 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).



# PANSS POSITIVE



- Significant Group by Time interaction ( $p = .042$ ).
- Raloxifene group significantly decreased in positive PANSS scores over time.



# SERMS IN MEN

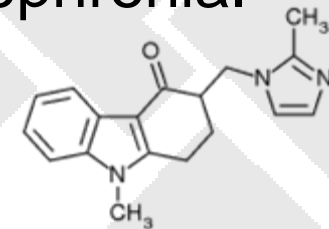
We are offering SERM treatment for men with schizophrenia.



# ONDANSETRON



Ondansetron, a serotonin 5HT<sub>3</sub> 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



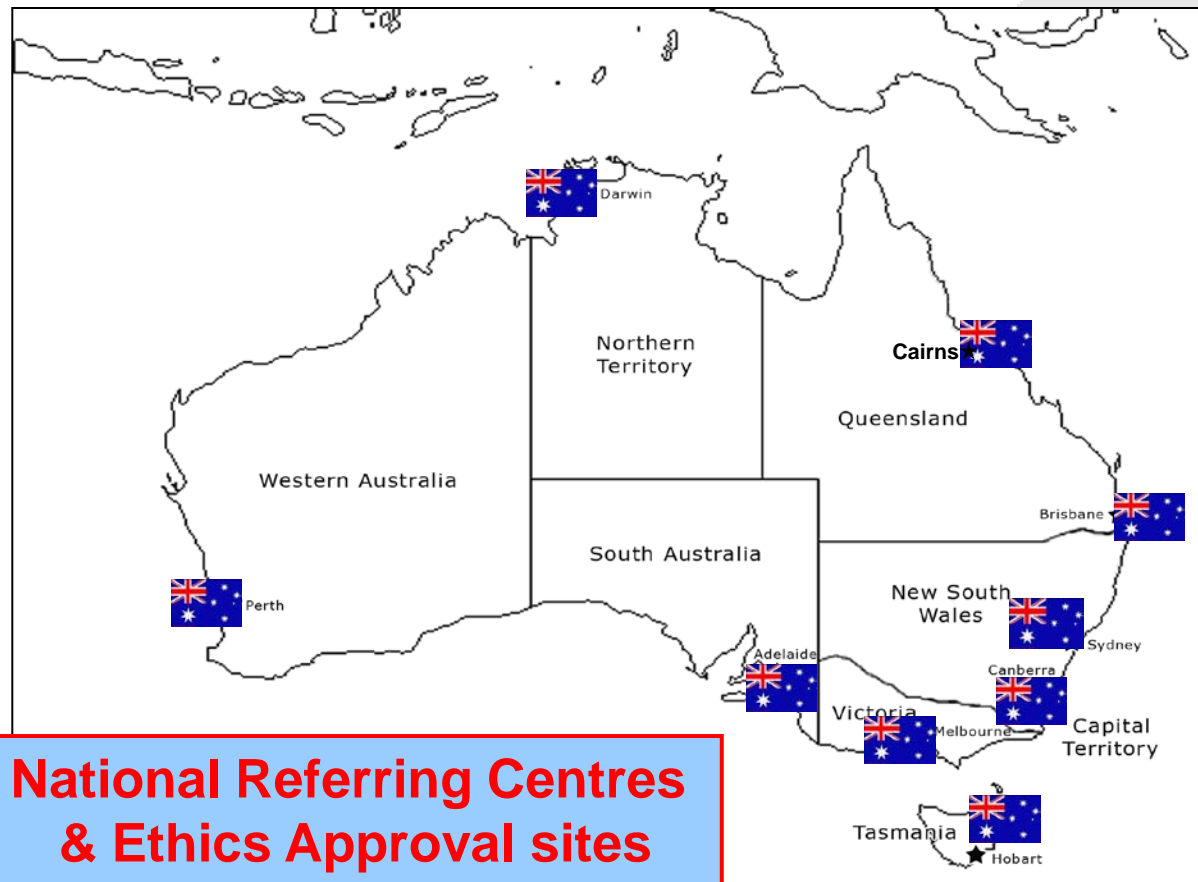
- **Pregnancy**
- **Safety and privacy in inpatient settings.**
- **Menopause.**



# THE NATIONAL REGISTER OF ANTIPSYCHOTIC MEDICATION IN PREGNANCY (*NRAMP*)



# THE NATIONAL REGISTER OF ANTIPSYCHOTIC MEDICATION IN PREGNANCY (NRAMP)



# THE NATIONAL REGISTER OF ANTIPSYCHOTIC MEDICATION IN PREGNANCY (*NRAMP*)



## NRAMP Contacts

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# SAFETY AND PRIVACY

Women's Only Area.





# MENOPAUSE





**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



# Poor physical health in people with mental illness

- 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

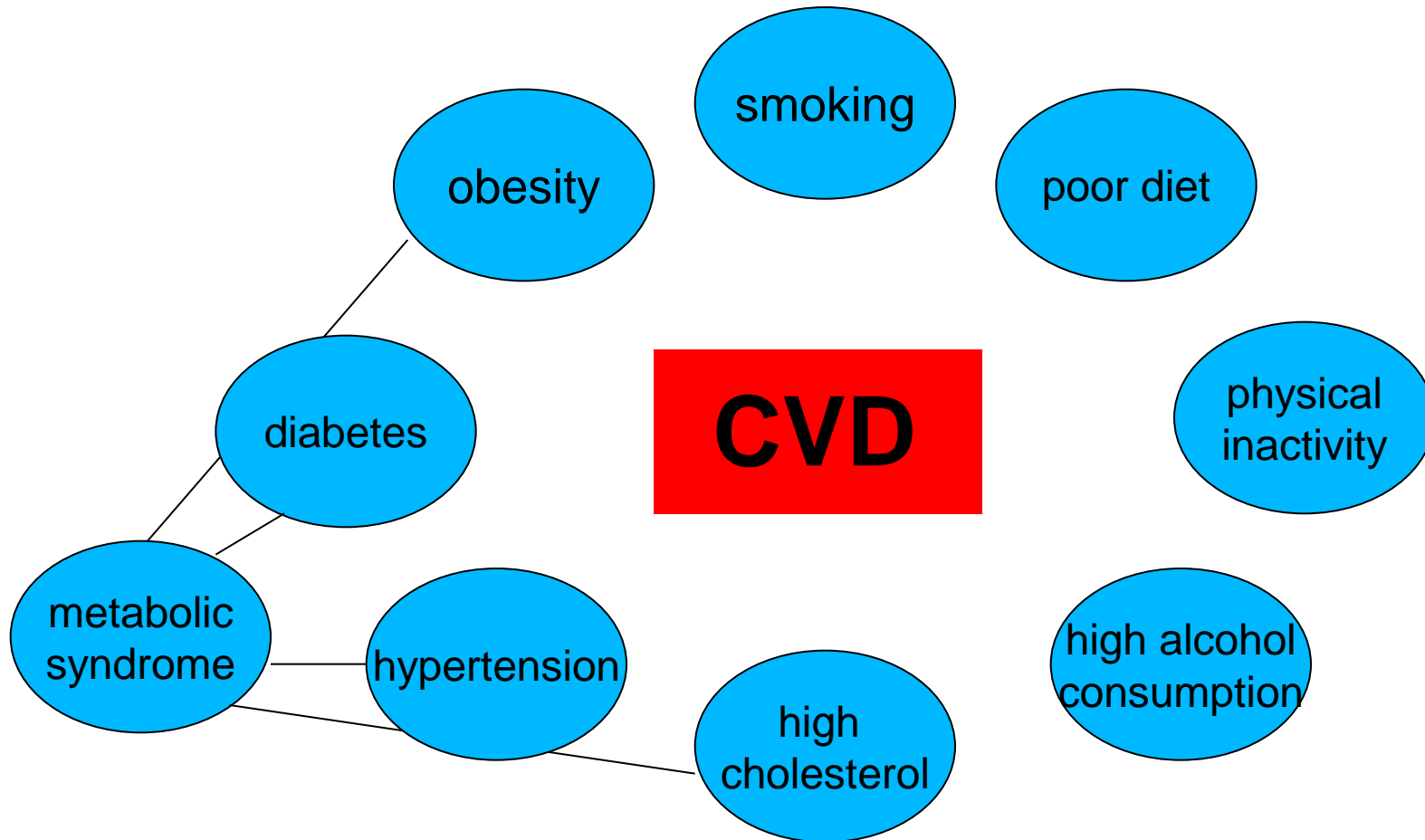


# CVD in mental illness

- 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





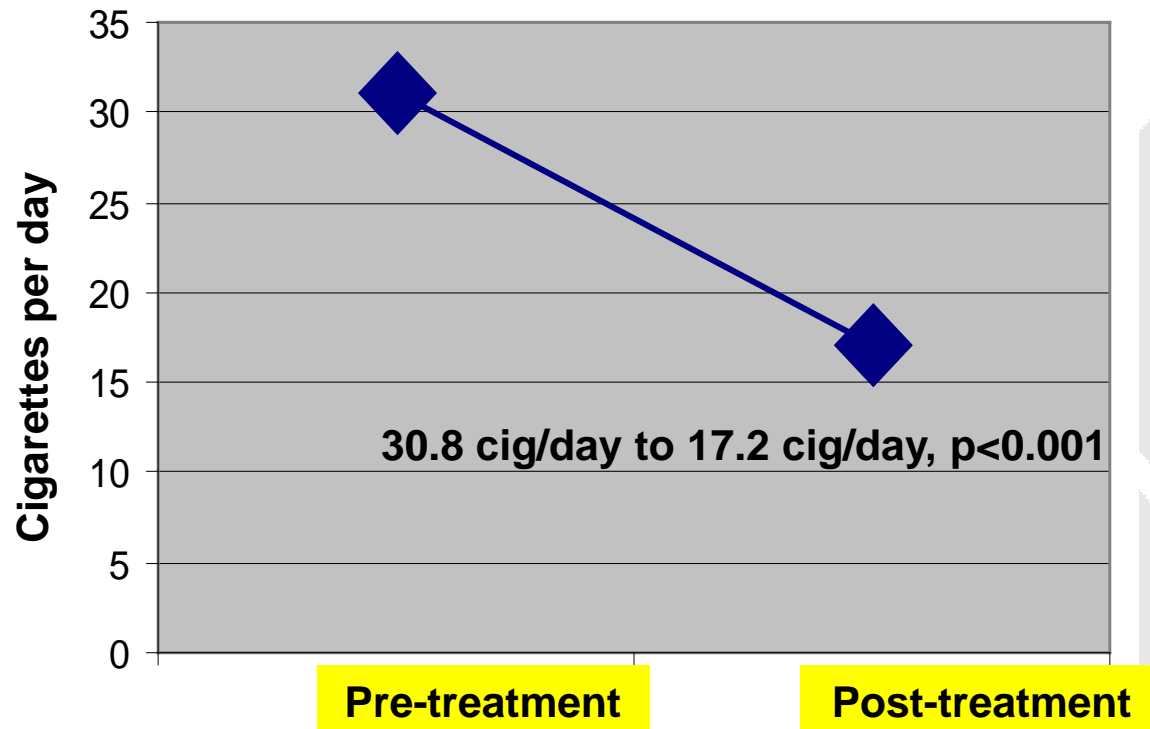
# Healthy Lifestyles Research at MAPrc



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  $\geq$  50%



# 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)



# Champix + Healthy Lifestyles 2009-2010



- 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

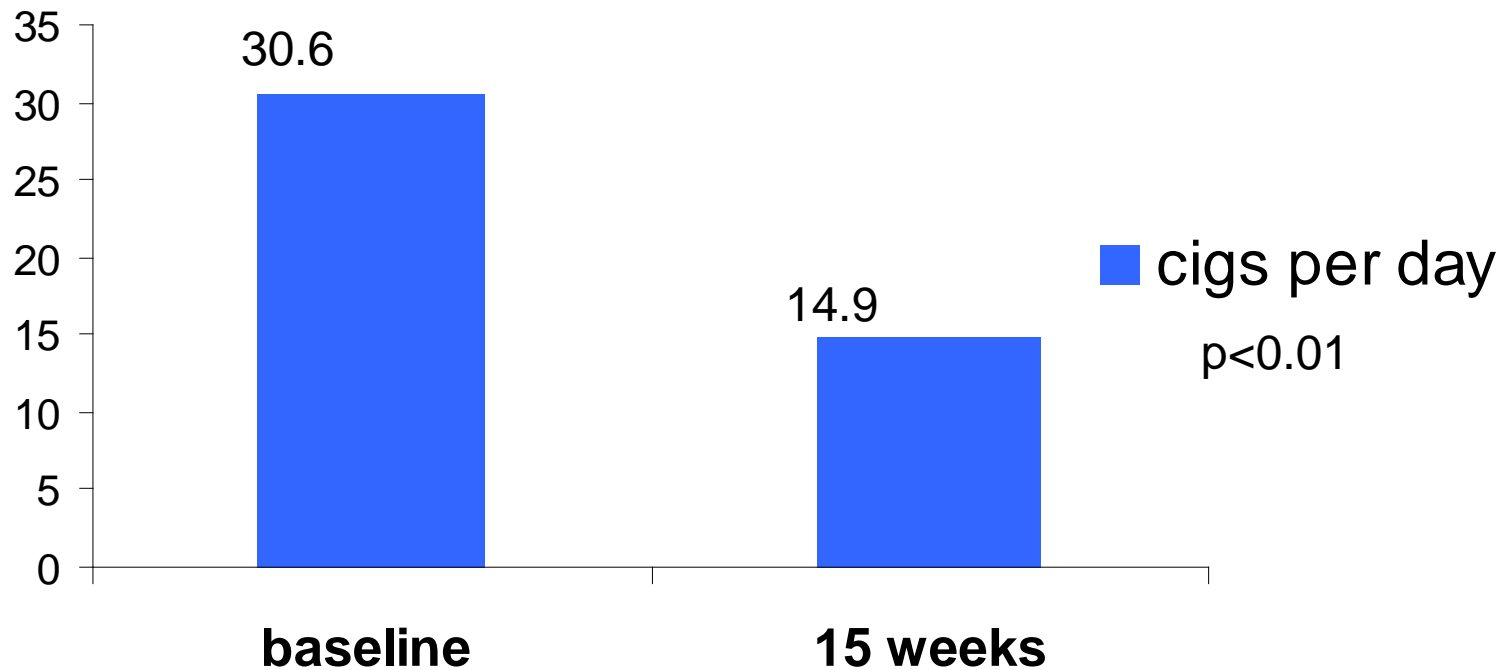


- mean age = 41.7 years (19-69)
- diagnosis: schizophrenia = 58.5%
- asthma = 26.4%
- diabetes = 11%
- CVD event = 9%
- mean number of cigs per day = 28.2 (range: 15-65)
- spend 28.2% of income on cigarettes
- majority considered “Obese” according to BMI= 48.2%
- Low levels of physical activity
- Eat 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  $\geq 50\%$  = 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







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# Research to help services better care for people with schizophrenia

**Dr. Stuart Lee**

**Mental Health Service Evaluation Senior Research Officer**



**TheAlfred**



**MONASH University**  
Medicine, Nursing and Health Sciences



# Post-seclusion Counselling





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MONASH University  
Medicine, Nursing and Health Sciences

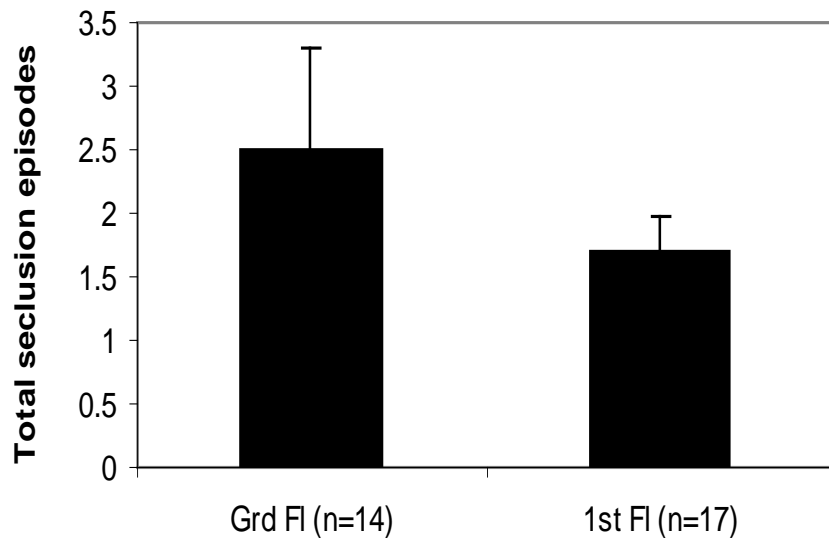
# How post-seclusion counselling helps

- 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.



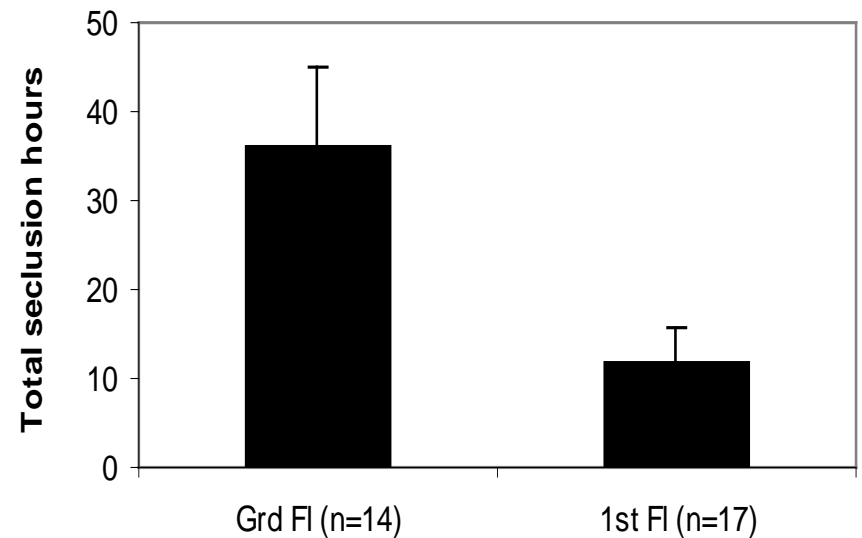
# Indicators of Outcome - Seclusion

## Seclusion Episodes



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

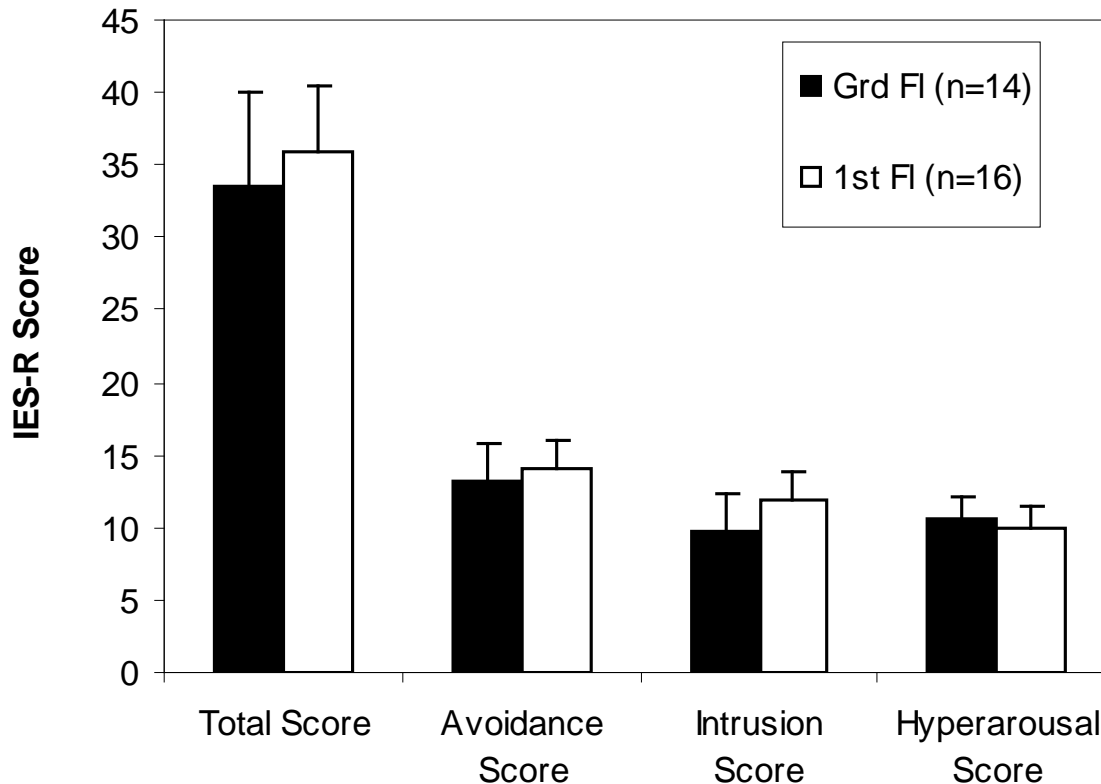
## Seclusion Episodes



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 Overview

## 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

Continue treatment in the Public Mental Health System

Be transitioned from the Public Mental Health System to GP shared care

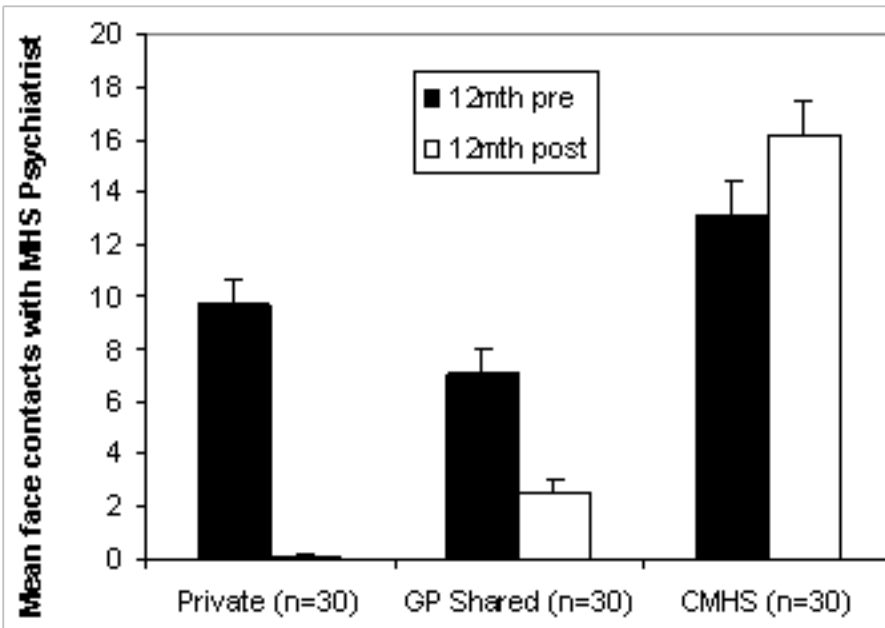
Be transitioned from the Public Mental Health System to the Private Psychiatry setting

## PART 2

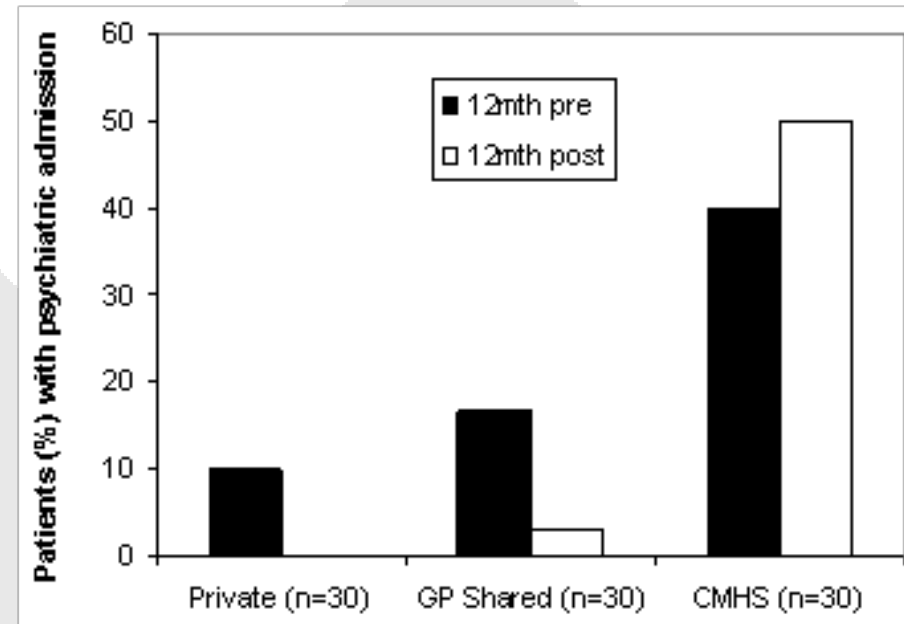
## RESEARCH QUESTION:

Do consumers in these groups differ and what are their outcomes?

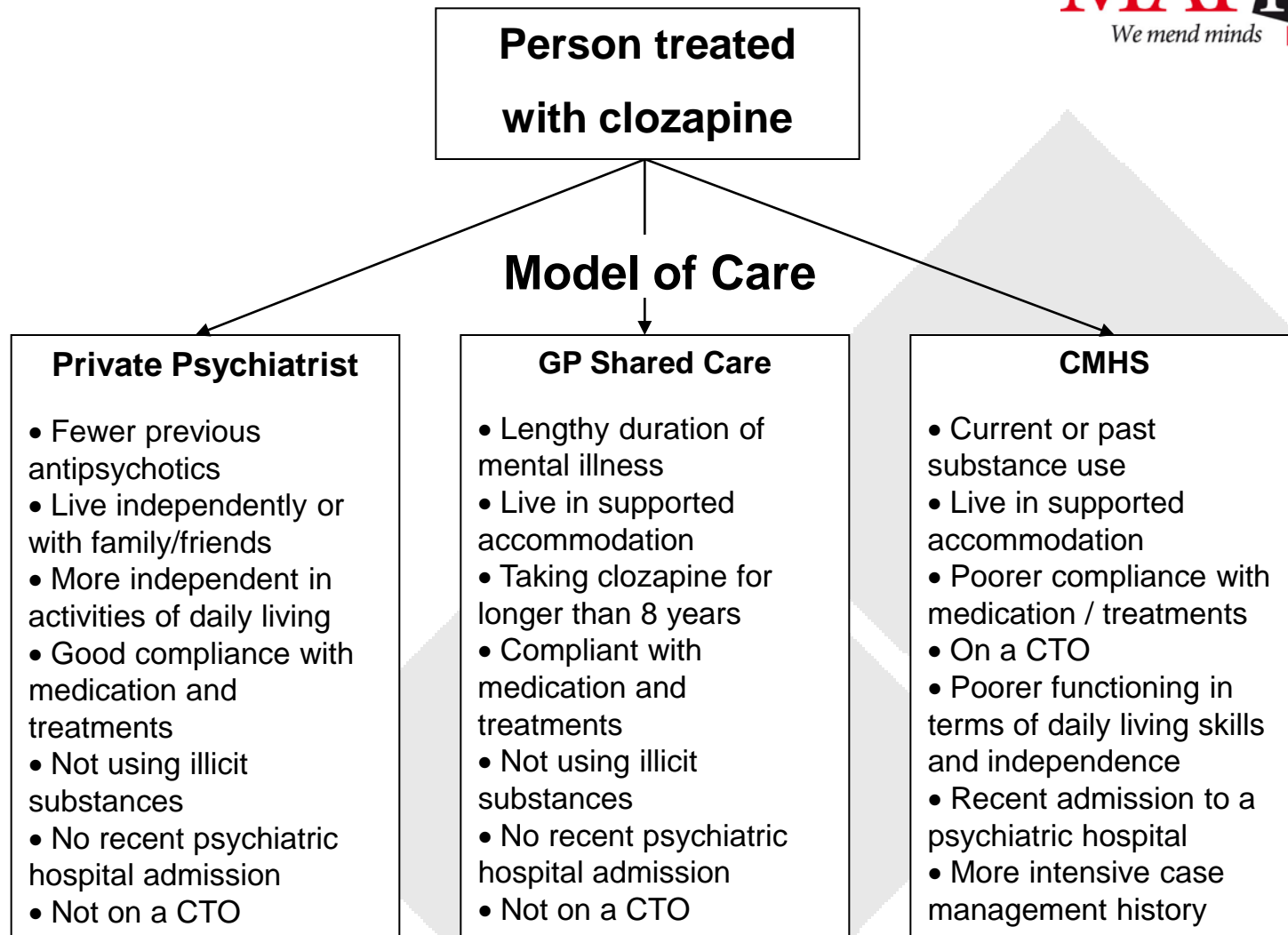
# Service Use Before and After Transitioning



Alfred Psychiatrist contact



Alfred Inpatient Psychiatry Admission



# 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

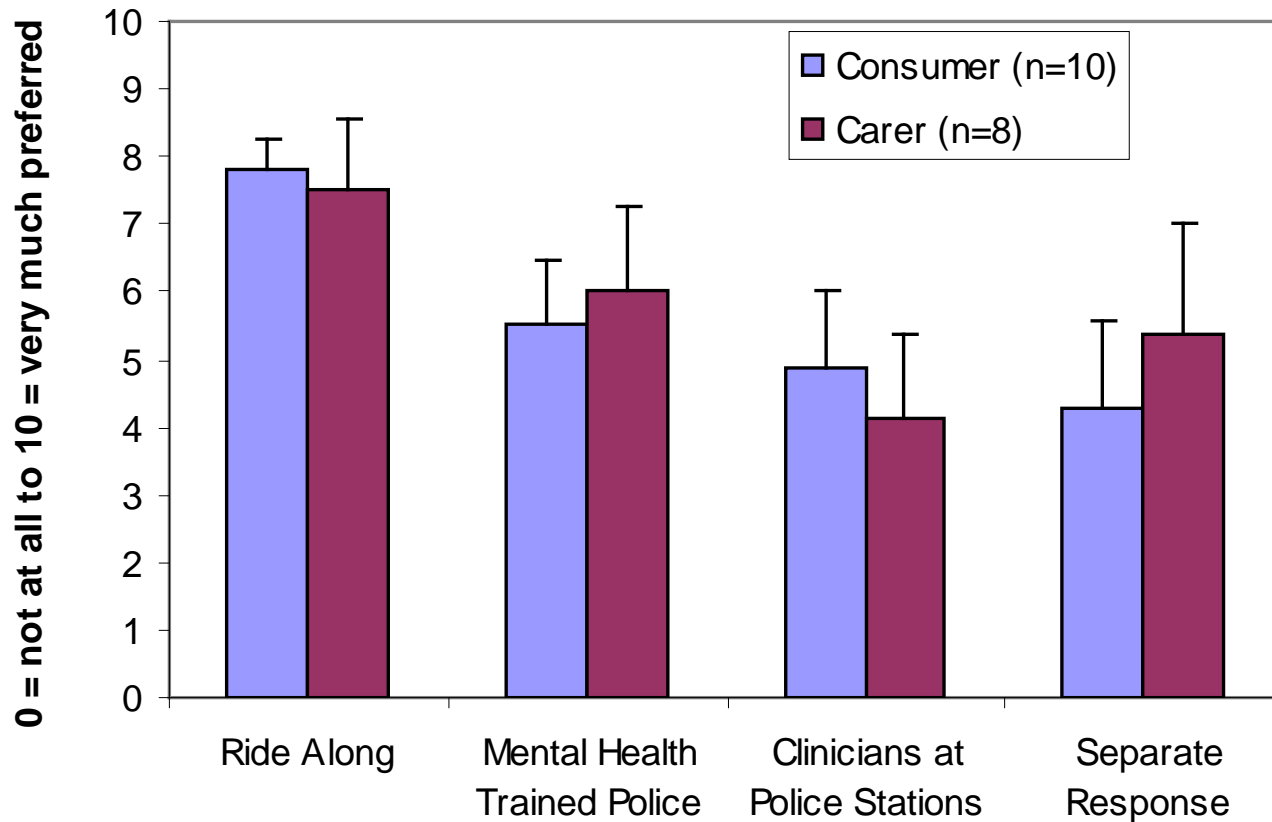
#### • Positives:

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



# Picking up the pace for mental health in Stonnington

HEALTH | 1 NOV 11 @ 07:00AM | BY NICOLE CRIDLAND

[Tweet](#)



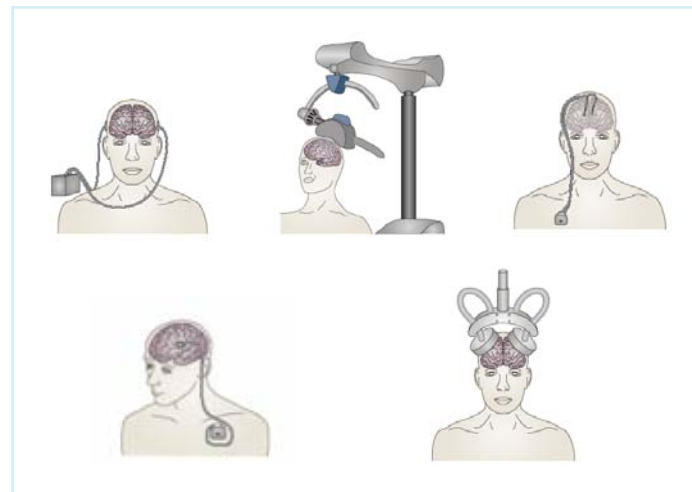
Sgt Doug Bowles with Alfred emergency psychiatric consultations team manager Kathryn Henderson. Picture: Steven Crabtree

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.



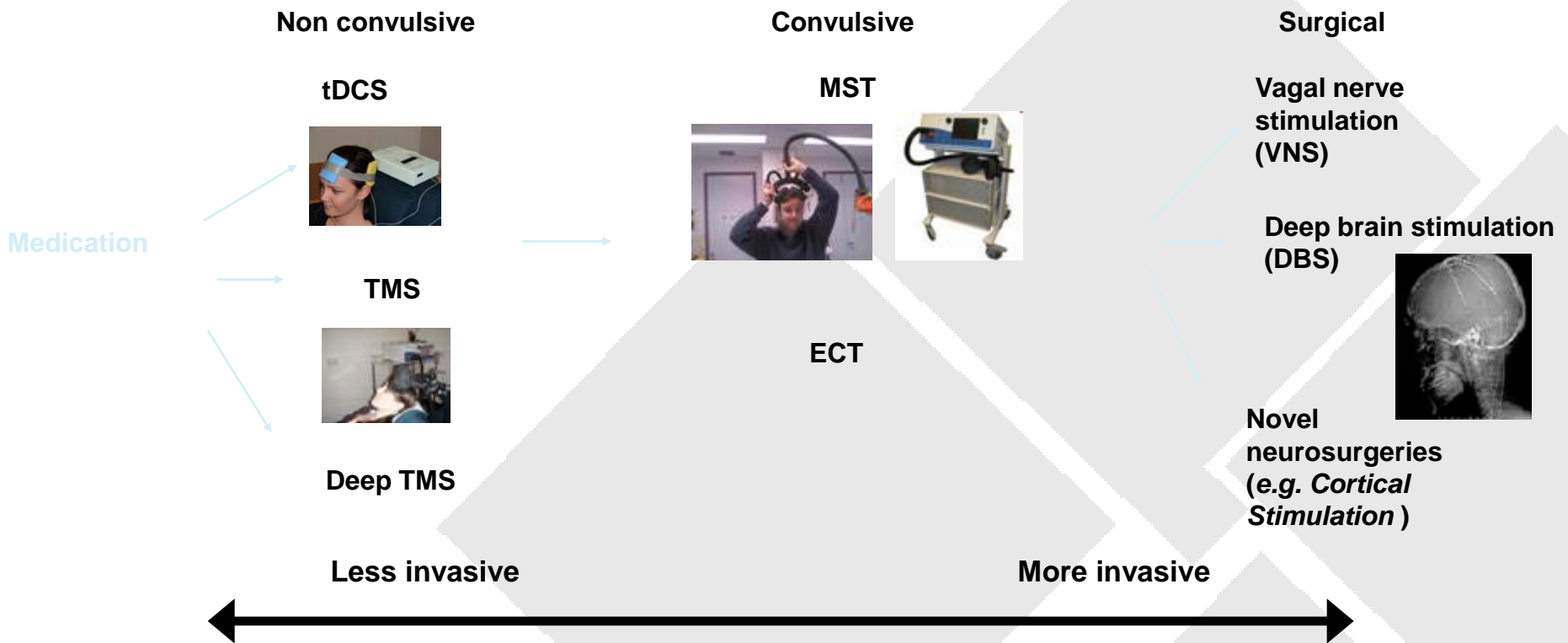
# New Treatments for Schizophrenia

**Professor Paul Fitzgerald**  
Deputy Director, MAPrc





# Developing biological treatments in psychiatry

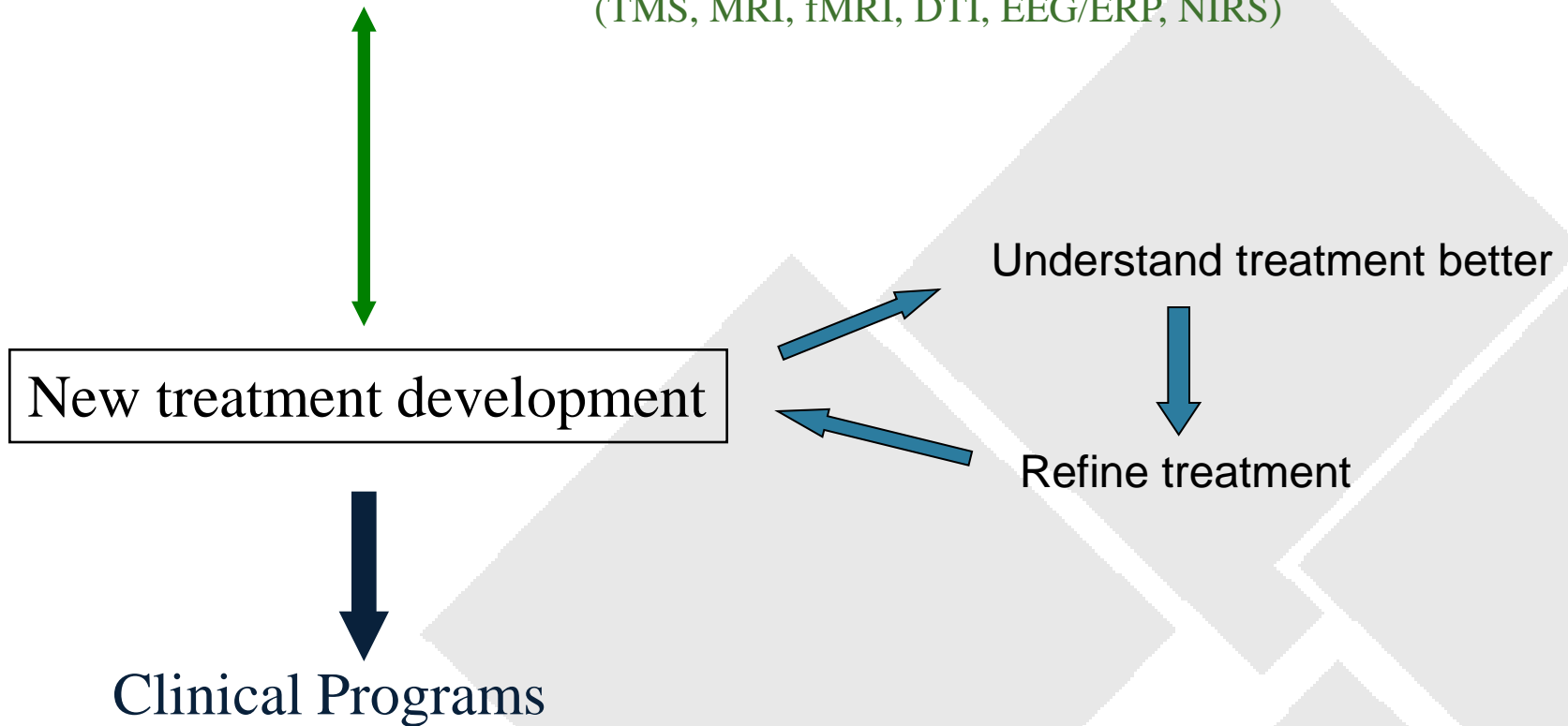


# Treatment Development

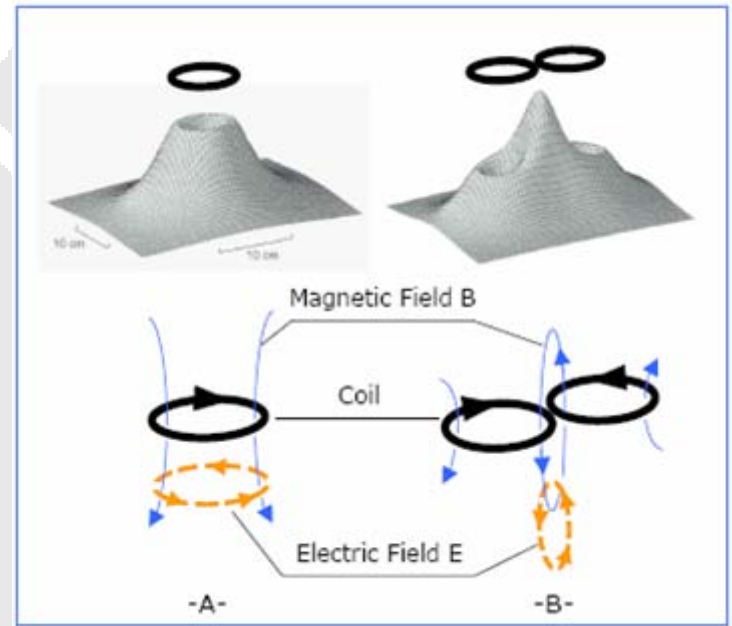


Use modern Neuroscience to help understand the disease better

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



# Transcranial Magnetic Stimulation



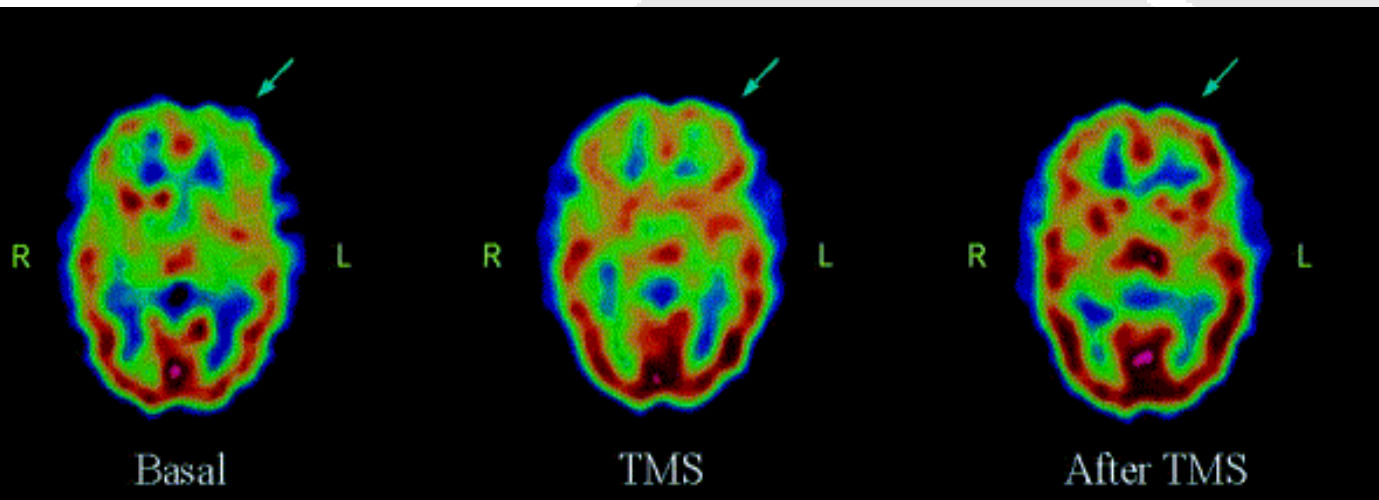
# Transcranial Direct Current Stimulation (tDCS)



- Low amplitude direct current
- Well tolerated
- Increase in brain activity under anode
- Decrease in brain activity under the cathode

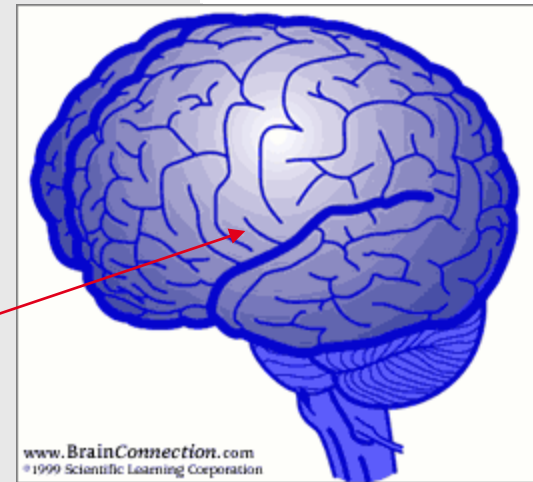
# rTMS as a Therapeutic Tool in Depression

- 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



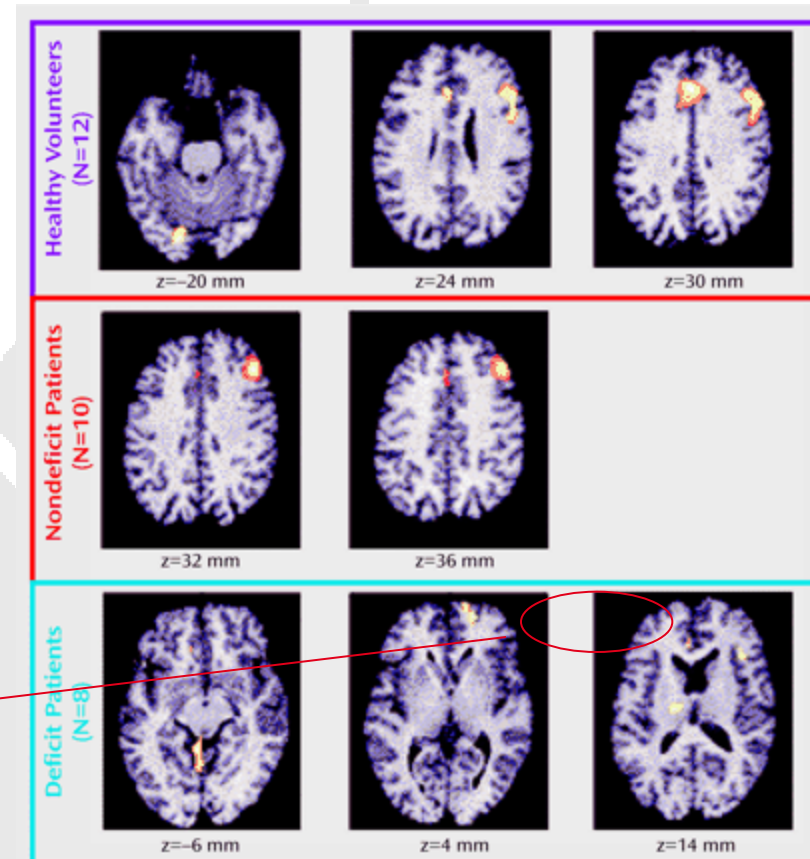
# Potential rTMS Applications in Schizophrenia

- Prefrontal cortex
  - General / non specific
  - Negative symptoms
  - Cognition
  - Depression
- Temporo-parietal cortex
  - Auditory Hallucinations



# Negative Symptoms

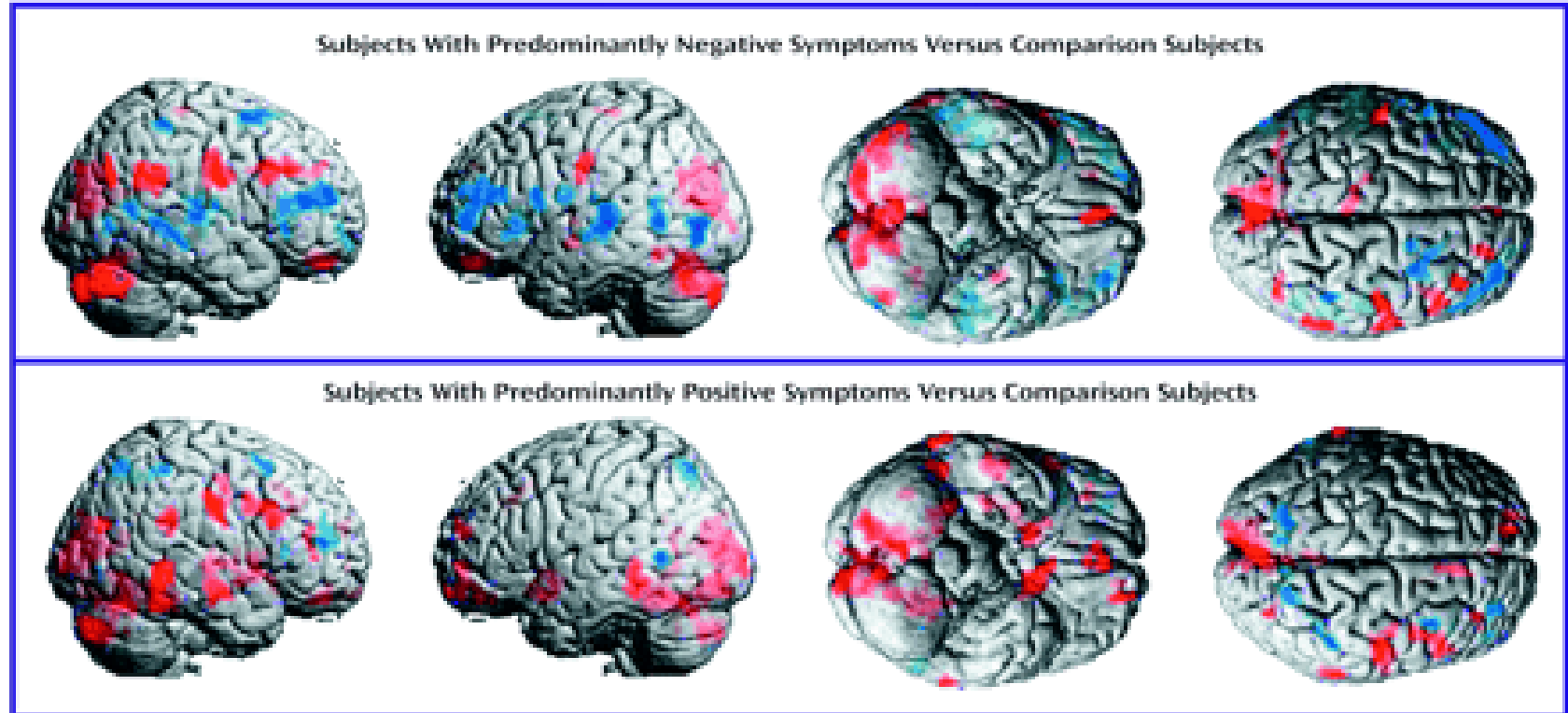
- Lack of drive, energy, motivation, capacity to experience pleasure
- Far less responsive to treatment
- Relate to reduced activity in frontal brain regions





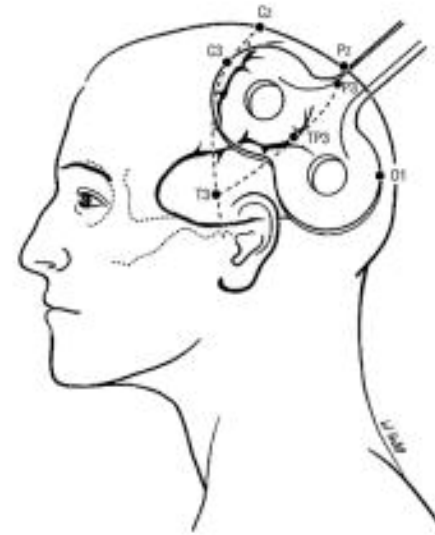
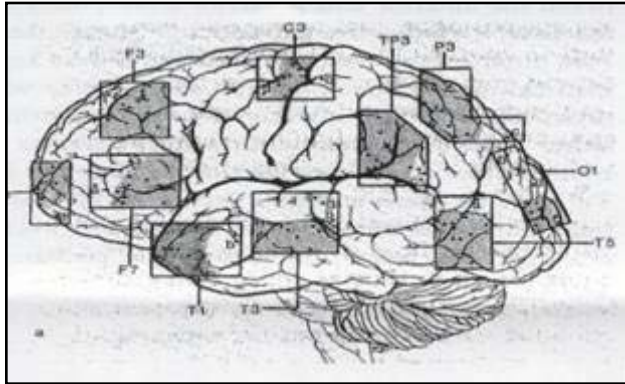
# PFC rTMS and Negative Symptoms

- 8 trials to date
- Mixed results





# rTMS and Auditory Hallucinations



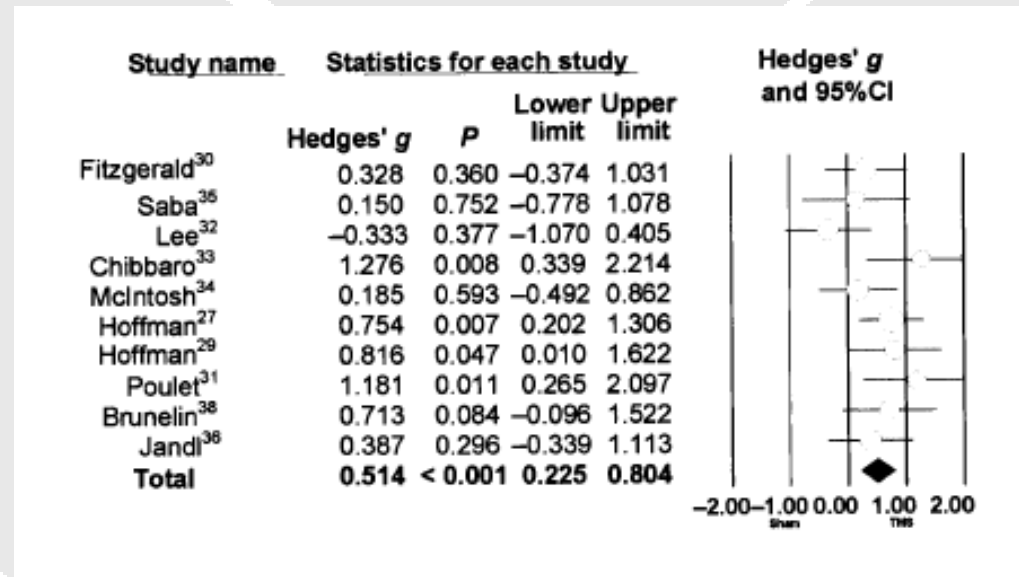
- Left T-P cortical focus
- 1 Hz – reduce local ‘over active’ cortical activity

Hoffman et al 2003

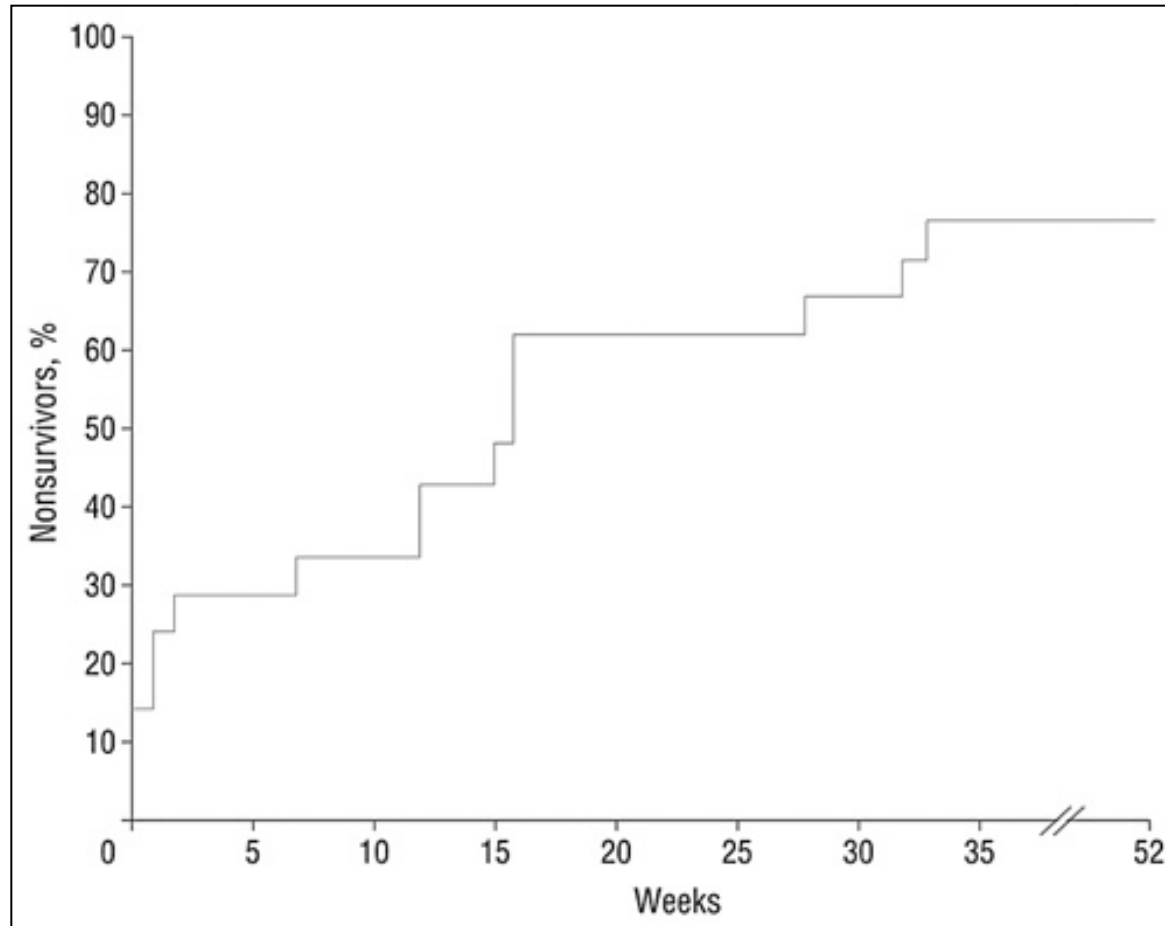


# rTMS and Hallucinations

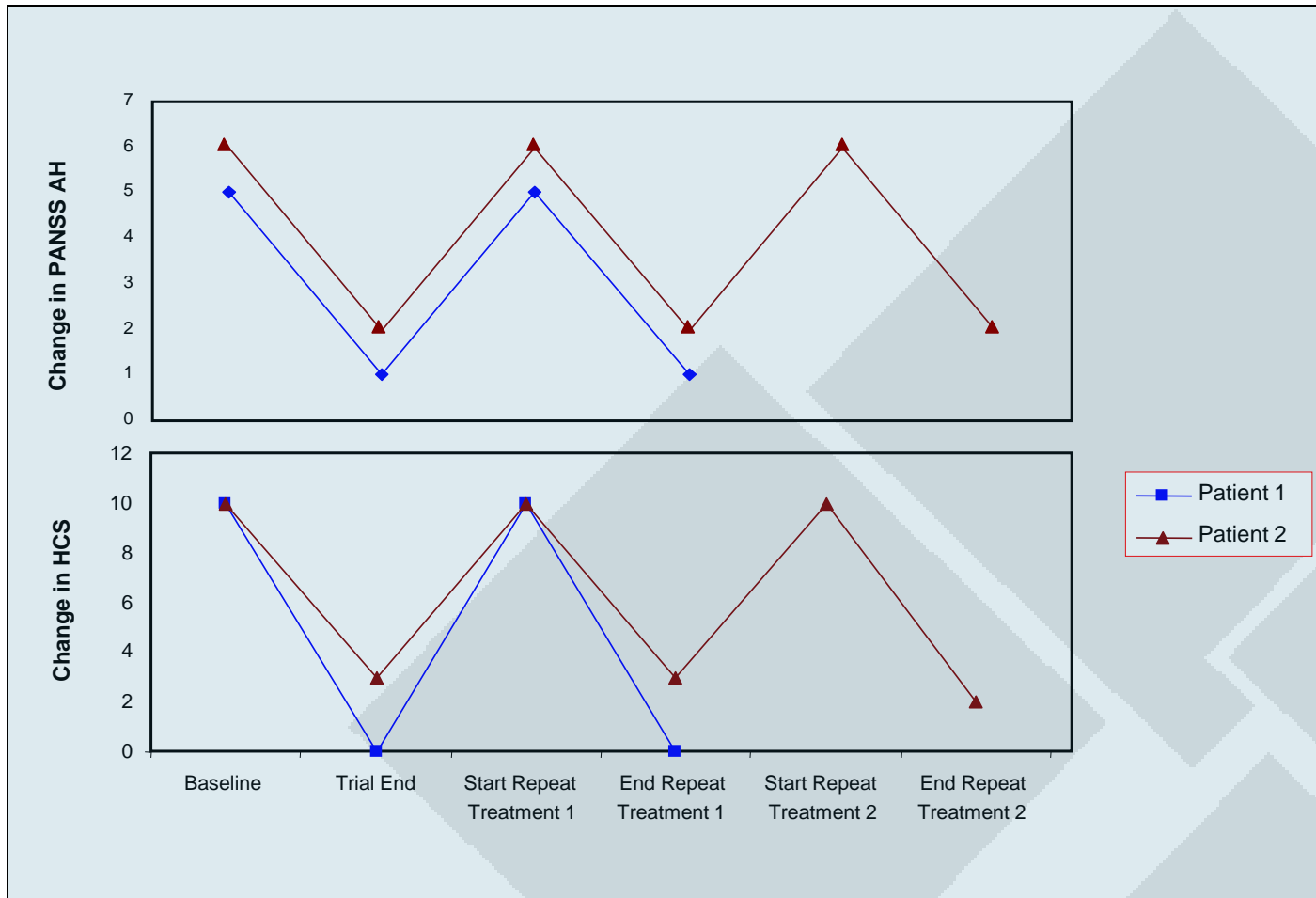
- Efficacy supported by multiple trials to date
  - Meta-analysis
    - 10 studies included 212 patients
      - Active effect size = 0.51 (p=0.001)
- (9 studies with continual stimulation sessions in separate analysis - Effect size = 0.88 (p<0.001))



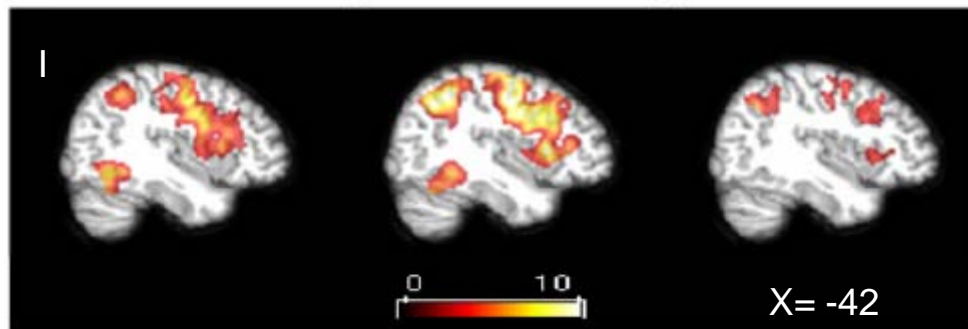
# rTMS and Auditory Hallucinations: Hoffman et al



# Repeat Treatment of AH



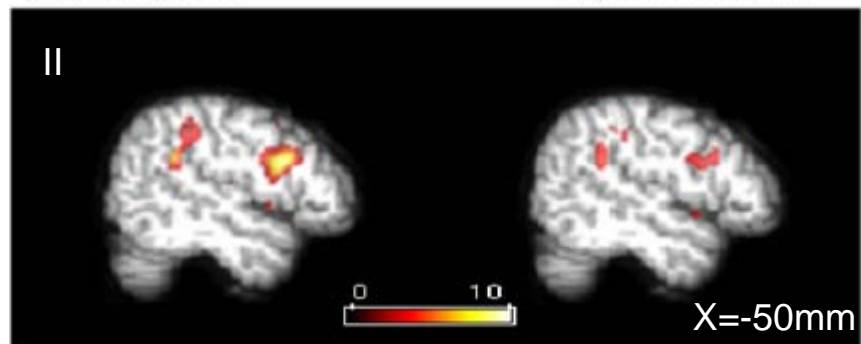
(a) Pre-treatment (b) Post-treatment (c) Post > Pre-treatment



Controls > Patients

(a) Pre-treatment

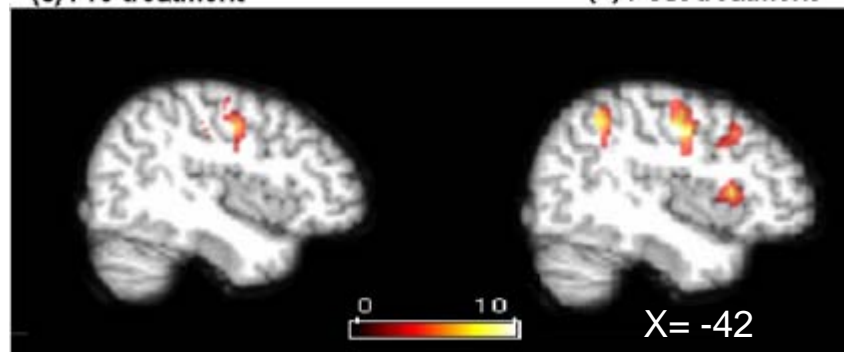
(b) Post-treatment



Patients > Controls

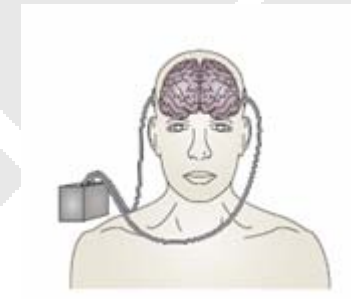
(c) Pre-treatment

(d) Post-treatment



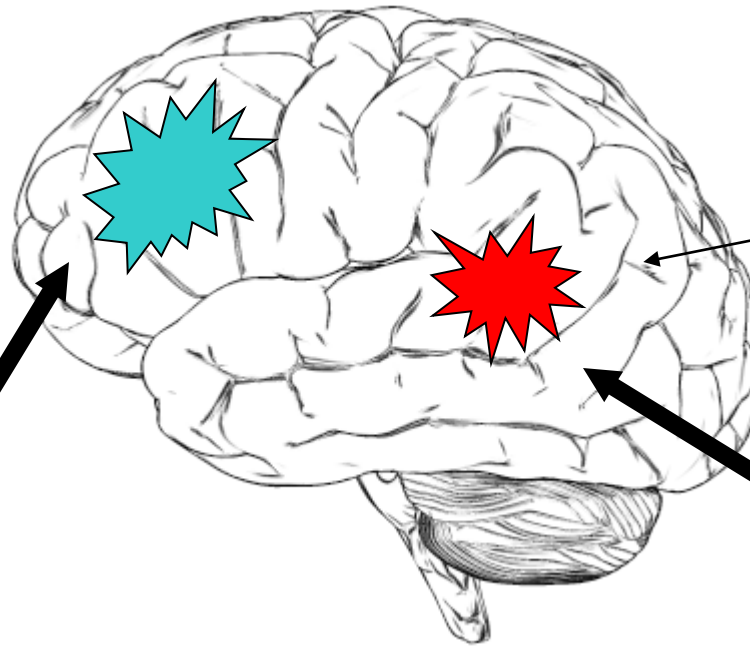
# Transcranial Direct Current Stimulation

- > 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

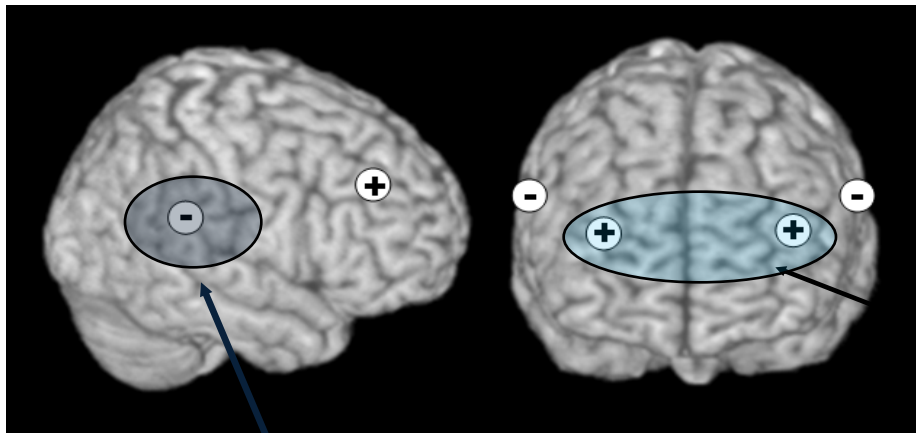


Increased activity in Auditory Hallucinations and possibly other psychotic symptoms



Anodal tDCS

Cathodal tDCS



PFC underactivity in  
negative symptoms

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

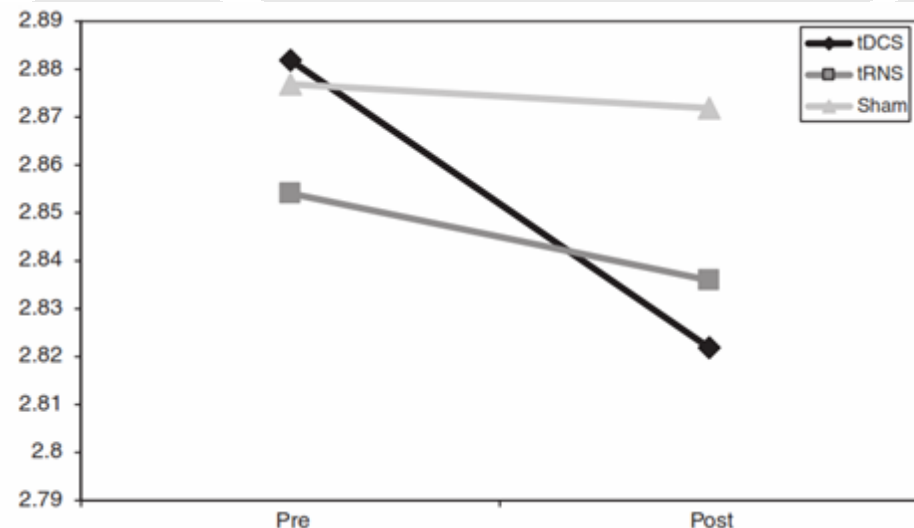


# Current tDCS Studies

## 1. Clinical Trial

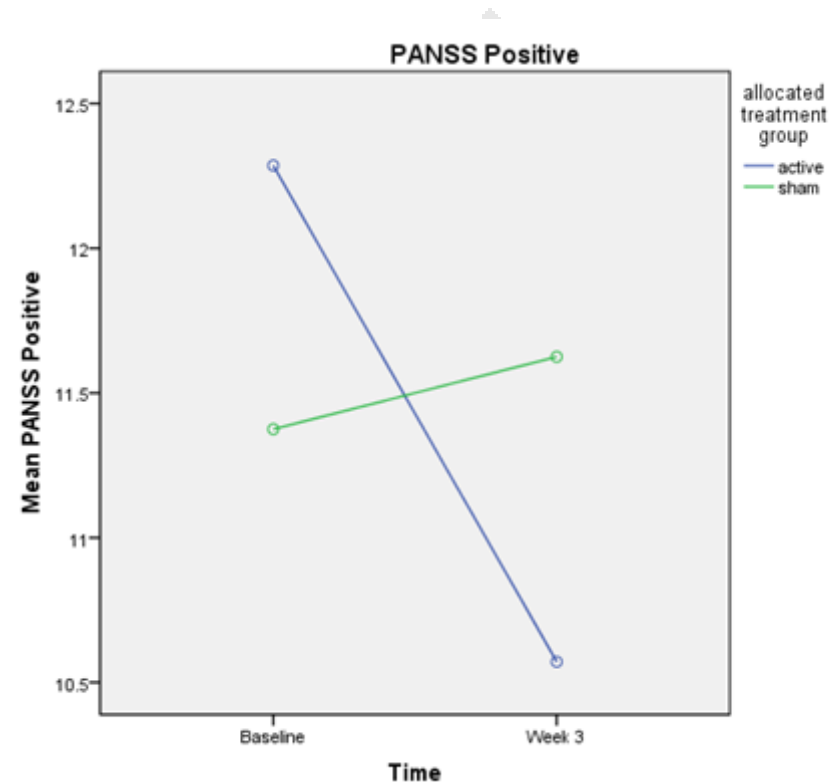
- 3 weeks of daily treatment sessions
- 20 minutes per day

## 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](http://www.maprc.org.au)