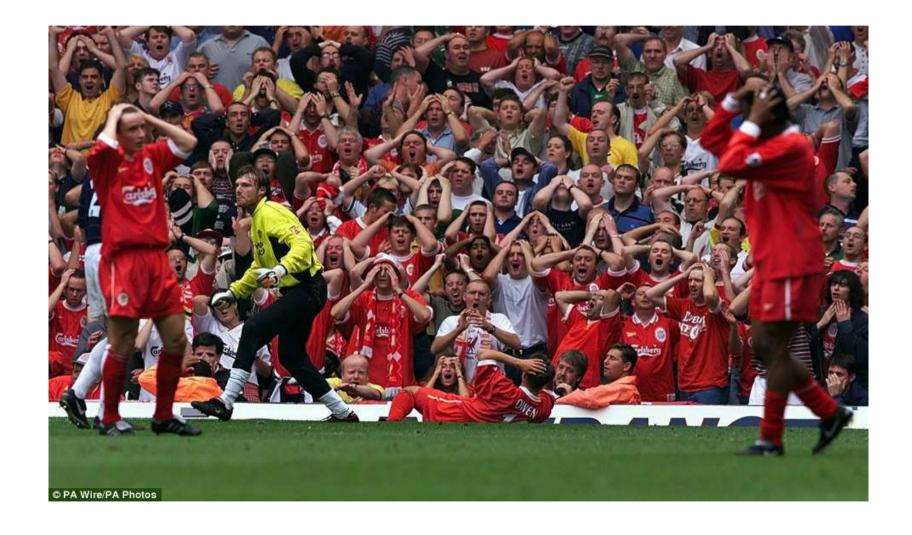
Social cognition in early psychosis: a potential target for early intervention?

Dr Andrew Thompson
Consultant Psychiatrist Sussex Early
Intervention in Psychosis Service and Honorary
Senior Fellow, Orygen Research Centre,
Melbourne



Outline of presentation

- What is social cognition?
- Social cognition in psychosis
- Why is social cognition important in psychosis?
- Social cognition in "at risk" for psychosis groups
- Treatment approaches for social cognition deficits in psychosis

Outline of presentation

What is social cognition?

What is social cognition?

- Definition: domain of cognition that involves the perception, interpretation and processing of social information (Ostrum, 1984)
- Distinct from "non-social cognition"
 - stimuli typically personally relevant and changes over time
 - bi-directionality of the stimulus
 - evaluation of bias as well as deficit

4 particular important domains

Emotion recognition/processing

Theory of Mind (ToM)

Attributional style/bias

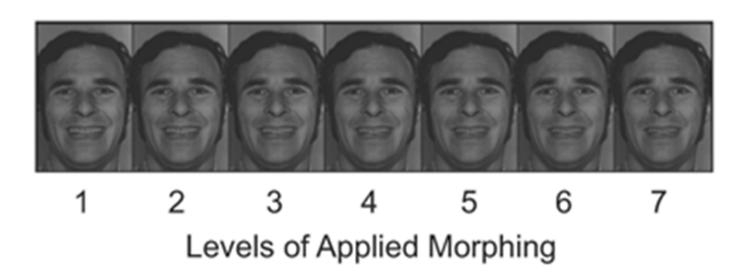
Social perception/knowledge

Emotion recognition – facial affect recognition

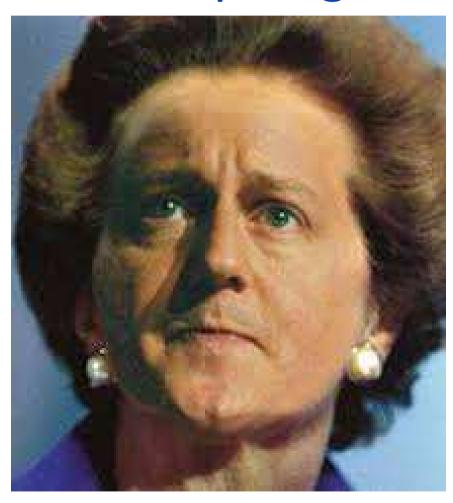


Facial affect recognition -morphing

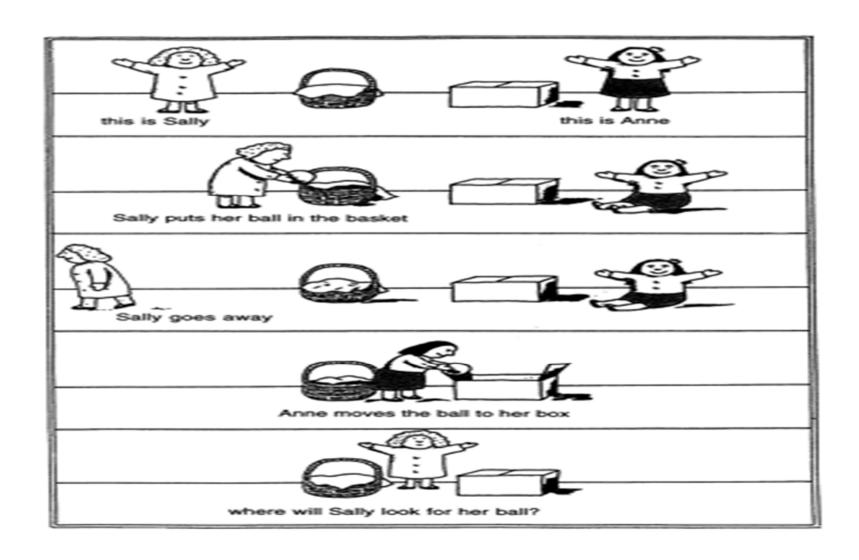




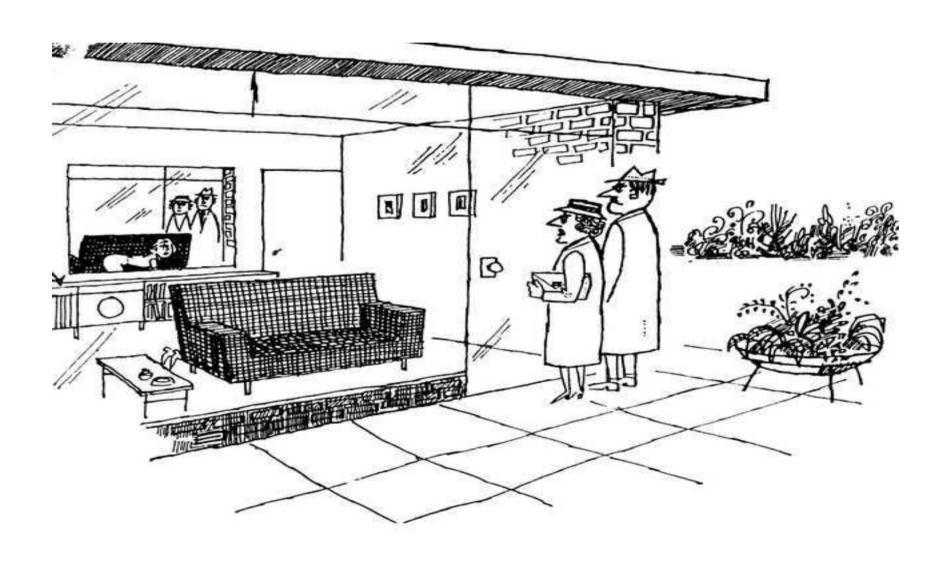
Emotion recognition –alternative facial morphing tasks



Theory of Mind – Sally Anne Task



Theory of Mind – visual jokes



Theory of Mind - Hinting task

- Lucy is broke but she wants to go out in the evening. She knows that David has just been paid. She says to him: "I'm flat broke! Things are so expensive these days."
- QUESTION: What does Lucy really mean when she says this?
- Answer: Lucy means "Will you lend me some money David?" OR "Will you take me out tonight and pay?"
- ADD: Lucy goes on to say: "Oh well, I suppose I'll have to miss my night out."
- QUESTION: What does Lucy want David to do?
- Answer: She wants David to lend her money or offer to take her out and pay.

Emotional states in inanimate objects





Attributional style questionnaires

1. Imagine your class reacts negatively to an important talk you have to give as part of your coursework

Think carefully about the reason for the class reacting negatively to your talk, then answer the questions below

Strongly				Strongly
Agree	Agree	Undecided	Disagree	Disagree

- 1. It is not my fault that people reacted negatively*
- 2. The reason people reacted negatively to my talk will cause failures in all areas of my life
- 3. The reason people reacted negatively to this talk means that others will react negatively to talks I give in the future

Social perception/knowledge

 Role playing social situations that involve interpretation of social rules/context e.g. white lies, misunderstandings, body language

 Navigating familiar social situations e.g. going to the cinema – templates or social scripts What is social cognition?

Social cognition in psychosis

Social cognition deficits in all 4 domains in schizophrenia

- 1) Emotion perception/recognition specific emotion recognition deficits (both for facial affective expression and prosody-voices), esp for negative emotions (Edwards et al, 2002; Kohler and Brennan, 2004)
- 2) **ToM** appears to be impaired in schizophrenia. Includes a number of different tasks that may target different levels of complexity (1st and 2nd order ToM) and attribution of emotion to inanimate objects (Sprong et al, 2007; Brune, 2005)
- 3) Social information processing bias -including causal attribution biases (e.g. Locus of Control (LOC)) (Bentall et al, 1997; Bentall & Kinderman, 1996)
- 4) **Social knowledge/perception** decoding non-verbal social cues (Monti & Fingeret, 1987); recognition of familiar social situations (Corrigan et al, 1992); interpersonal problem solving (Bellack et al, 1994)

Domain	k	ES (g)	CI	\boldsymbol{P}
Theory of mind Social perception Social knowledge Externalizing bias Personalizing bias Emotion perception Emotion processing	50	0.96	±13	<0.001
	13	1.04	±25	<0.001
	7	0.54	±17	<0.001
	5	-0.02	±38	0.918
	5	-0.17	±55	0.532
	62	0.89	±17	<0.001
	12	0.88	±30	<0.001

Social cognition deficits also in First Episode Psychosis (FEP) and are relatively stable over time

- Deficits appear to be present in FEP (Edwards et al, 2001; Pinkham et al, 2007: Addington et al, 2008; Bertrand, 2007)
- Deficits appear relatively stable through phase of illness - some suggestion that deficits are slightly worse in acute illness than in remission (Addington and Addington, 1998; Pinkham et al, 2007; Kee et al, 2003)

Deficits are distinct from neurocognitive deficits and negative symptoms

- Related but distinct from neurocognition and negative symptoms (Sergi et al, 2007; Allen et al, 2007)
- Social cognition and neurocognition contribute unique variance to the prediction of social functioning (Allen et al 2007; Pinkham and Penn 2006)
- Neural activation circuitry for all three are relatively independent (Pinkham et al, 2003)

What is social cognition?

Social cognition in psychosis

Why is social cognition important in psychosis?

Neurobiological overlap with area affected in psychosis and plausible theories of psychotic symptom formation

- Overlap between neural areas involved in social cognition and those implicated in aetiology and maintenance of schizophrenia – fronto- temporo limbic circuits (Penn et al, 2008)
- Number of plausible theories explaining evolution of psychotic symptoms with regard to social cognition deficits
 - □ failure to metarepresent (ToM) (Frith & Corcoran, 1996)
 - externalising/personalising attributional style
 (Bentall et al, 1994)

Social Cognition strongly related to Social Functioning in Psychosis

- Poor performance on ToM tasks associated with social behavioural abnormalities (Brune, 2005)
- Emotion perception linked to social competence, independent living, community involvement and interpersonal relationships (Mueser et al, 1996; Poole et al, 2000)
- Social perception has been strongly linked to social behaviour (Appelo et al, 1992; Penn et al, 2002) and vocation-related social skills (Vauth et al, 2004)
- Social cognition is a better predictor of social functioning than neurocognition (Brune, 2005; Penn et al, 1996; Vauth et al, 2004)

What is social cognition?

Social cognition in psychosis

Why is social cognition important in psychosis?

Social cognition in "at risk" for psychosis groups

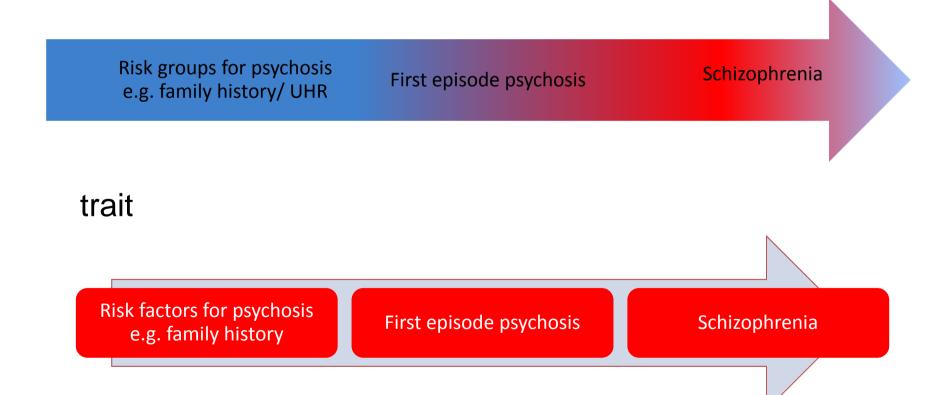
Social cognition in "at risk" for psychosis groups

• State or trait factor?

 Risk factor for developing a psychotic disorder?

Are social cognition deficits state or trait phenomena?

state



Social Cognition deficits in groups at "high risk" for psychosis

 Healthy relatives of people with schizophrenia - some social perceptual deficits (Toomey et al, 1999; Janssen et al, 2003; Mazza et al 2008)

 Schizotypal personality - Poor ToM and affect recognition (Pickup, 2006; Williams et al, 2008)

"Ultra High Risk" (UHR) as an "at risk" for psychosis group?



First Impact Factor released in June 2010 and now listed in MEDLINE!



Early Intervention in Psychiatry 2011; 5: 192-202

doi:10.1111/j.1751-7893.2011.00275.x

Review Article

Social cognition deficits and the 'ultra high risk' for psychosis population: a review of literature

Andrew D. Thompson, 1 Cali Bartholomeusz2 and Alison R. Yung1

Ultra High Risk criteria

- To meet UHR (CAARMS) criteria the young person must either:
 - 1) present with subthreshold psychotic symptoms, or
 - 2) present with definite psychotic symptoms of low frequency
 - 3) have had a brief psychotic episode of less than 1 week where symptoms spontaneously remit
 - 4) have a first degree relative with a diagnosed psychotic disorder, or
 - 5) have a diagnosis of schizotypal personality disorder
- PLUS Have experienced a significant drop in functioning or sustained low functioning over the past year

Some deficits found in UHR group – but not in all studies

- Facial affect recognition deficits (Addington et al, 2008; Amminger et al, 2010) but not found in another study (Pinkham et al, 2007)
- External attributional bias (Ang et al, 2010) but not Locus of Control (LOC) (Paruch et al, 2006)
- ToM deficits (Chung et al, 2008) but another study failed to find such a difference (Couture et al, 2008)
- Social perception deficits (Couture et al, 2008)

Areas of uncertainty in the literature

- Studies with relatively small numbers, not controlling for IQ and often concentrating on single domains of social cognition
- Some inconsistent results from different research groups especially with respect to ToM
- Only one study compared the differential performance in controls/UHR/FEP
- None linked deficits to social functioning/symptoms

Aims of the study

 To investigate whether individuals at ultrahigh risk (UHR) of developing psychosis and FEP patients are equally impaired in a number of measures of social cognition

 Compare performance on social cognition measures to levels of social functioning/psychopathology and neurocognition

Methodology -subjects

- The 2 patient groups recruited from Orygen Youth Health, Melbourne
 - FEP clinic (EPPIC) patients experience at least one week of daily psychotic symptoms and have had less than 6 months previous treatment
 - UHR clinic (PACE) fulfilling UHR criteria assessed by the Comprehensive Assessment of At Risk Mental States (CAARMS) (Yung et al, 2005)
- Non psychiatric control participants

Methodology – measures

Social cognition:

- ToM Hinting task (Corcoran et al, 1995); Visual jokes task (Corcoran et al, 1997);
 "Emotional triangles" task (Boraston et al, 2007)
- Emotion recognition DANVA (Nowicki and Duke, 1994)
- Social knowledge/social perception MSCEIT (Mayer et al, 2003); Social Comprehension and Schema Task (Corrigan et al, 1995)
- Attributional style NSIE (Nowicki & Duke, 1974)

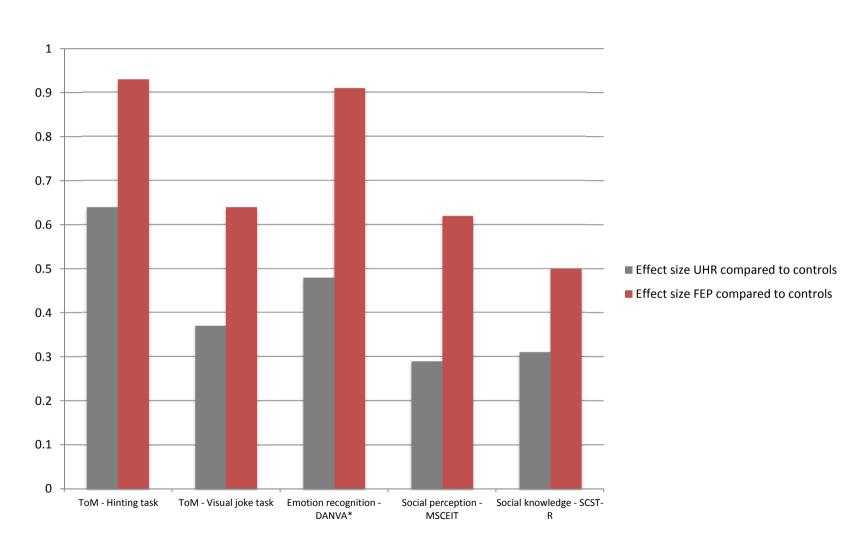
Social functioning:

- SOFAS; Role and social functioning scales (Cornblatt et al, 2007)
- Psychopathology:
 - BPRS; SANS; DASS
- Neuropsychology:
 - WASI/NART; Letter Number Span (verbal working memory); WMS-III Spatial Span (visual working memory); Trails A and B

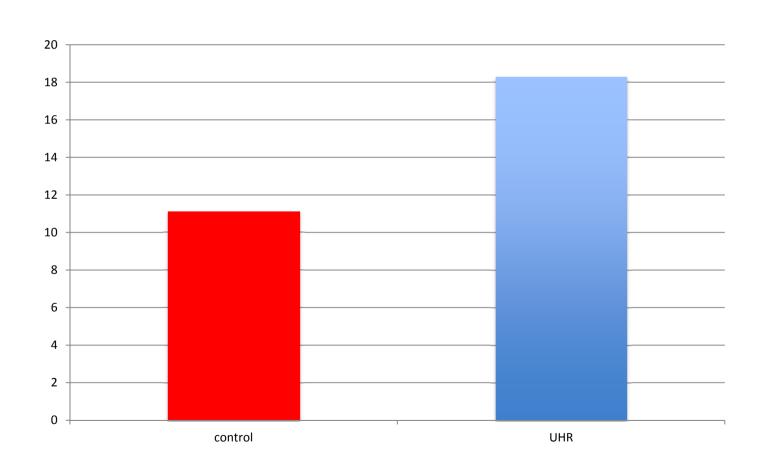
Baseline demographics, IQ, psychopathology and social functioning in the 3 groups

	Controls (n=30)	UHR (n=30)	FEP (n=40)	P value
Age (yrs)	20.0	19.4	20.6	0.23
Females (%)	17 (60.7)	12 (48.0)	14 (36.8)	0.16
Years of education	13.3	12.2	12.7	0.12
IQ (WASI)	103.4	105.7	106.7	0.62
Social Functioning: SOFAS	84.1	64.5	54.5	<0.001
Role functioning Social functioning	8.3 8.8	6.7 6.5	5.7 6.5	<0.001 <0.001
Psychopathology: General symptoms				
(BPRS)	N/A	42.6	46.1	0.31
Negative symptoms (SANS)	N/A	21.3	27.1	0.26

Effect sizes for deficits on social cognition tasks



Externalising bias in UHR group compared to controls



Relationship to symptoms and functioning?

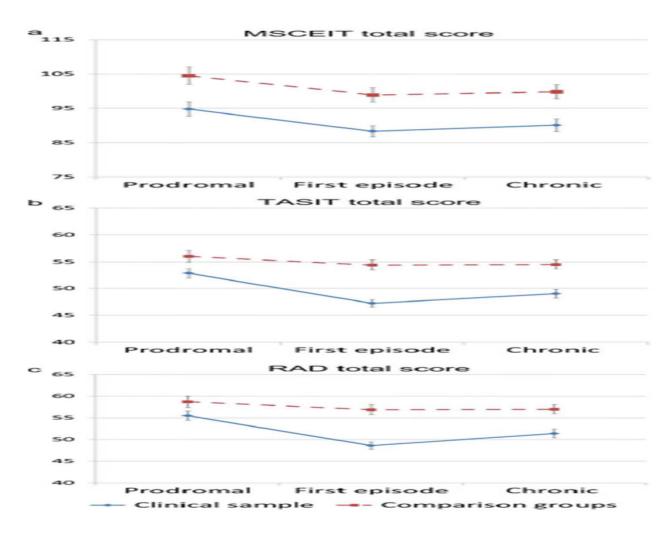
 SC associated with some negative symptoms rated on the PANNS but not positive symptoms

- SC measures correlated to measures of functioning in all groups
 - stronger relationship in controls and FEP than in UHR
 - stronger relationship to social functioning than role functioning

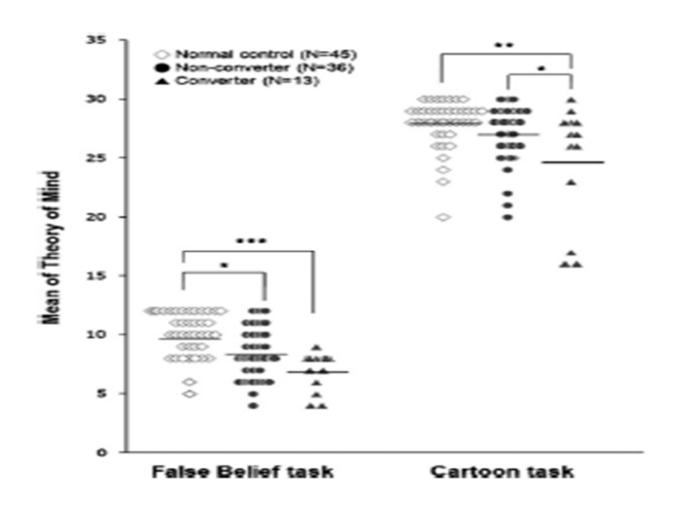
Summary of the study results

- FEP performed significantly worse than controls on all tasks
- UHR intermediate performance to FEP controls but only significantly worse on ToM tasks
- Differences remains when controlling for IQ/age/gender and multiple testing in the analysis
- Externalising bias found in UHR group compared to controls and this was correlated with paranoid symptoms and negative symptoms
- SC performance correlated with some negative symptoms and measures of social functioning

Data from other similar studies



What about as a risk factor for transition to psychosis?



Worse ToM in those who develop psychosis in our study

	Non- psychiatric controls (n=30)	UHR – no psychotic disorder at follow-up	UHR – Psychotic disorder at follow-up (n=5)	First episode psychosis (n=40)	Group effect	
		(n=25)	(II-3)		F	P value
Theory of Mind						
Hinting task score, mean (SD)	18.0 (1.15)	16.6 (2.93)*	16.2 (4.27)	15.7 (3.26)**	4.02	0.01
Overall visual jokes total score, mean (SD)	19.6 (5.25)	17.7 (5.06)	17.4 (5.59)	16.8 (3.26)*	2.24	0.09
Mentalising jokes subscore, mean (SD)	10.1 (2.07)	9.9 (3.24)	9.8 (3.70)	9.0 (2.38)	1.22	0.31
Physical jokes subscore, mean (SD)	9.3 (1.78)	7.8 (2.31)**	7.6 (2.30)	7.8 (1.79)**	4.12	0.008
Combined ToM score, mean (SD)	37.6 (5.45)	34.3 (6.56)*	33.6 (7.30)	32.5 (5.35)**	4.50	0.005

- What is social cognition?
- Social cognition in psychosis
- Why is social cognition important in psychosis?
- Social cognition in "at risk" for psychosis groups
- Treatment approaches for social cognition deficits in psychosis

Treatment of social cognitive deficits in psychosis - current psychosocial approaches

•	eurocognitive enhancement progracial component	ms with additiona
	Cognitive Enhancement Therapy (CET and Flesher 1999b)	(Hogarty and Flesher 1999a; Hogarty
•	aining targeting specific cognitive in E.g. facial affect Training of Affect Rece al, 2005)	•
•	aining programs with a specific focugnition	us on social
	SCET (Social Cognition Enhancement 7 SCIT (Social Cognition Interaction Tra	.

Do social cognition psychosocial interventions work?

	k	N	ES	95% CI
		Proximal mea	asures of socia	al cognition
Emotion perception				
Facial affect recognition	15	488	0.71	0.52, 0.90
Facial sffect discrimination	3	89	1.01	0.56, 1.47
Social Perception	8	261	0.13	-0.12, 0.38
Theory of Mind	7	186	0.46	0.15, 0.78
Attributional style				
Aggression bias	4	119	0.25	-0.12, 0.62
Hostility bias	4	119	0.15	-0.24, 0.53
Blame bias	4	119	0.07	-0.3, 0.45
		Measures of generalization		
Symptoms				
Negative symptoms	10	306	0.15	-0.08, 0.38
Positive symptoms	8	258	0.26	-0.01, 0.52
Total symptoms	7	166	0.68	0.33, 1.02
Psychosocial functioning	6	187	0.78	0.45, 1.11

Kurtz and Richardson,

Potential neuroprotective effect of social cognitive interventions?

ORIGINAL ARTICLE

Neuroprotective Effects of Cognitive Enhancement Therapy Against Gray Matter Loss in Early Schizophrenia

Results From a 2-Year Randomized Controlled Trial

Shaun M. Eack, PhD; Gerard E. Hogarty, MSW†; Raymond Y. Cho, MD; Konasale M. R. Prasad, MD; Deborah P. Greenwald, PhD; Susan S. Hogarty, MSN; Matcheri S. Keshavan, MD

Arch Gen Psychiatry. 2010;67(7):674-682

Correlation between improvement in social cognition and brain volume

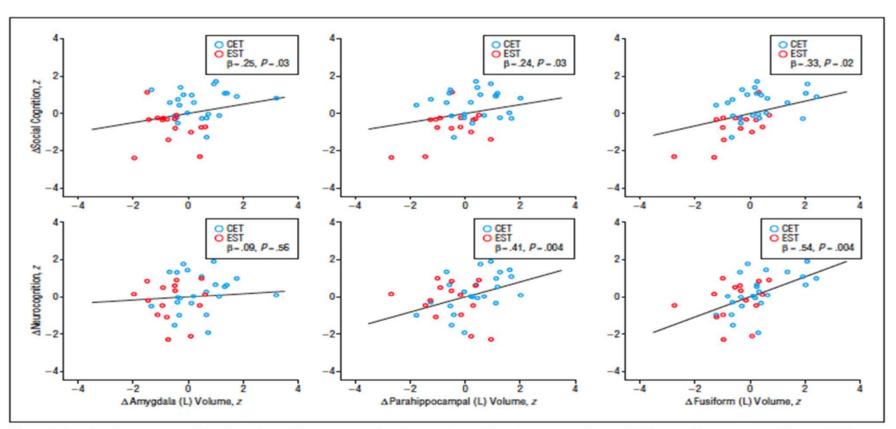


Figure 3. Relations between neurobiologic and cognitive change during 2 years of cognitive enhancement therapy (CET) or enriched supported therapy (EST).

Social Cognition and Interaction Training

- Three distinct phases:
 - 1) Emotion training which involves focusing on defining emotions, emotion mimicry and understanding paranoia
 - 2) Figuring out situations which involves focusing on distinguishing facts from guesses, jumping to conclusions, understanding bad events and attributional style
 - 3) Integration which involves sessions dedicated to checking out guesses in real life by using patients' own examples of past social interactions as well as role play.

SCIT example attributional style characters

Character	Typical Thoughts, Feelings/Emotions, & Actions
Blaming Bill	Thoughts: Blaming Bill always finds somebody else to blame when bad things happen. He blames the weatherman for bad weather. When he stubs his toe on a table, he yells at the person who owns the table. He blames people even when he shouldn't.
	Feelings: When bad things happen, Bill usually feels angry.
	Actions: Blaming Bill has a very angry facial expression. He glares and points his finger at people. He says things like, "This is all your fault!"
My-fault Mary	Thoughts: My-fault Mary always blames herself when bad things happen. If somebody cheats her out of money, she gets upset at herself for trusting them. If somebody acts mean towards her, she thinks she deserves it.
	Feelings: When bad things happen, Mary usually feels sad and upset with herself.
	Actions: Mary has a sad expression on her face, looks down, shakes her head, and holds her hand to her head. She says things like, "I'm so stupid" and "I always mess-up everything."
Easy Eddie	Thoughts: Easy Eddie assumes that bad things happen because of bad luck and accidents. He thinks bad things are nobody's fault, and so he never acts upset. When people are mean to him, he assumes that they are only acting that way because they've had a bad day. Easy Eddie never blames other people even when he should.
	Feelings: When bad things happen, Eddie tries to push away bad feelings. He tries to feel relaxed and easy.

well. I guess it's just bad luck."

Actions: Easy Eddie shrugs his shoulders, raises his palms, cocks his head to one side, and raises his eyebrows. He says thinks like, "Oh

Positive effects of SCIT in social cognition and social functioning in schizophrenia

- Improved performance on social cognition measures emotion perception, social perception, ToM, and attributional style (Combs et al 2007)
- Social functioning improved significantly with SCIT training in comparison to the control group, and independent of change in psychopathology
- Now using SCIT as part of normal clinical practice in parts of New York State (Roberts et al 2010)

Facelook is designed to help you connect and share with the people in your life and in social situations.

This group program is for EPPIC clients and aims to:

- help people better understand and recognise different emotions
- improve skills for interpreting social cues
- learn new ways to evaluate the likely cause of people's actions or events

What will be involved:

You will be asked to attend facelook once a week for 10 consecutive weeks.

- When: Tuesdays from 11am-1.30pm, beginning 6th October 2009
- Where: Residence 21, Orygen Youth Health, Parkville

This group program is part of a research project so you will be asked to attend a research interview before the program starts and again after the 10 weeks.

What are the benefits:

- You will be paid \$50 for attending each of the research interviews (i.e \$100).
- A catered lunch will be provided at each group session/Cab vouchers will be provided if you cannot make it to Orygen on your own.
- You will hopefully gain skills that will help with maintaining friendships/ relationships, meeting new people and getting a job.

What emotions are these people showing?

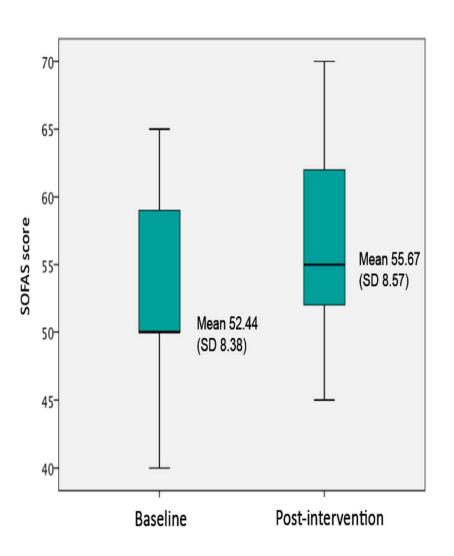


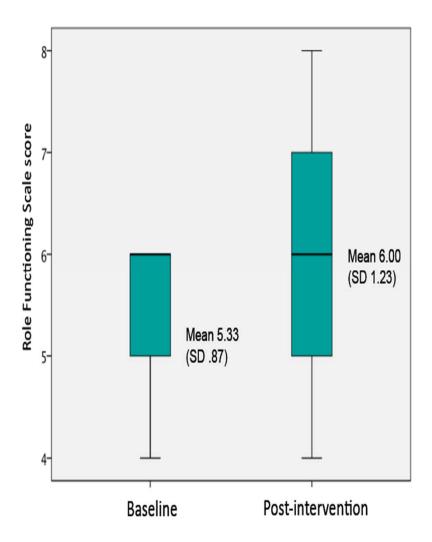
This group program is a joint initiative of Melbourne Neuropsychiatry Research Centre and Orygen Youth Health Research Centre, The University of Melbourne

Pilot SCIT in FEP group at EPPIC

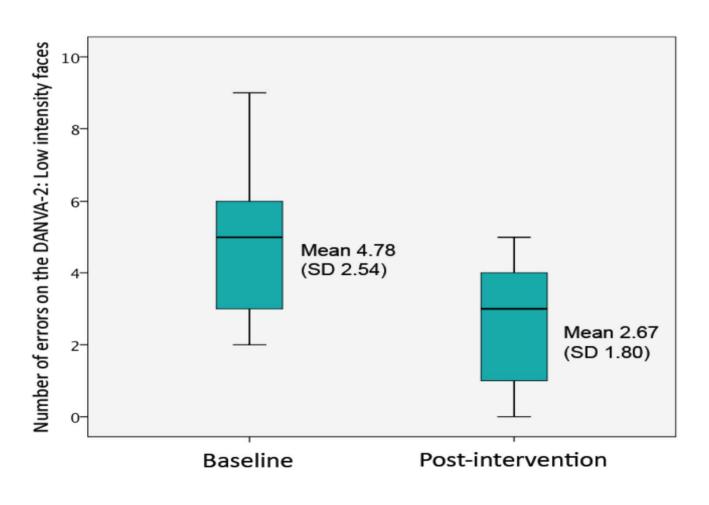
- Two SCIT groups 12 patients (5 males, 7 females; Mean age= 21.6)
- 10 week program –Each session 2 hours long with lunch in between
- Generally good feedback from participants and only one drop out (due to worsening of psychosis) – average attendance 69% (range 55-90%)
- feasible intervention in this group

Improvements in social and role functioning





Improvements in some social cognition tasks



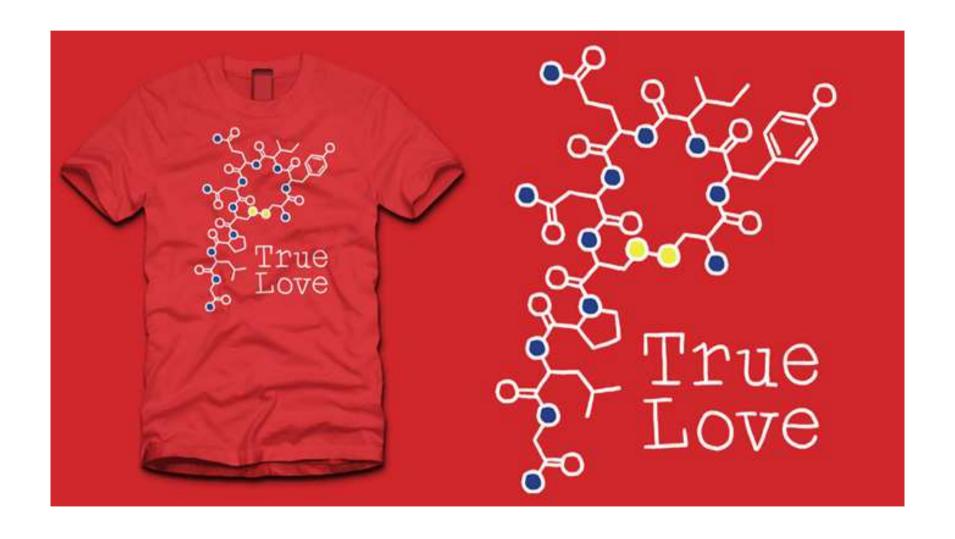
Future work

UHR

 Iongitudinal studies e.g. to investigate role of social cognition in development of psychosis and poor functional outcome

FEP

- Longitudinal studies of relationship between SC neurocognition and outcome
- Randomised trial of SCIT in FEP combined with vocational intervention – whether this enhances the effect of a vocational intervention (IPS)



Oxytocin can improve social cognition in psychosis and possibly symptoms too?

Intranasal oxytocin reduces psychotic symptoms and improves Theory of Mind and social perception in schizophrenia

Cort A. Pedersen a*, Clare M. Gibson b, Shane W. Rau a, Kayvon Salimi a, Kelly L. Smedley a, Robin L. Casey a, Jane Leserman a, L. Fredrik Jarskog a, David L. Penn b

Department of Psychiatry CB# 7160, The University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, United States
Department of Psychology CB# 3270, The University of North Carolina at Chapel Hill, Chapel Hill, NC 27539, United States

ARTICLE INFO

Article history: Received 9 April 2011 Received in revised form 18 July 2011 Accepted 20 July 2011 Available on line 15 August 2011

Keywords: Schizophrenia Oxytocin Psychosis Social cognition Theory of Mind Social negention

ABSTRACT

Oxytocin has numerous prosocial and antipsychotic-like effects in animals. Prosocial effects of acute intranasal oxytocin administration have also been reported in human subjects. We conducted a randomized, placebo-controlled trial testing the effects of twice daily intranasal oxytocin treatment for 14 days on psychotic symptoms and social cognition in patients with schizophrenia. PANSS scores declined significantly and several social cognition measures improved significantly or nearly significantly in oxytocin (N = 11) but not placebo (N = 9) recipients. Our results suggest that, in addition to reducing classic psychotic symptoms, oxytocin may diminish certain social cognition deficits that are not improved by current antipsychotic medications.

© 2011 Elsevier B.V. All rights reserved.

Adjunctive Intranasal Oxytocin Reduces Symptoms in Schizophrenia Patients

David Feifel, Kai Macdonald, Angel Nguyen, Patrice Cobb, Heather Warlan, Barbara Galangue, Arpi Minassian, Olga Becker, Jason Cooper, William Perry, Mischelle Lefebvre, James Gonzales, and Allison Hadley

Background: Both human and animal studies suggest oxytocin may have antipsychotic properties. Therefore, we conducted a clinical trial to directly test this notion.

Methods: Nineteen schizophrenia patients with residual symptoms despite being on a stable dose of at least one antipsychotic were enrolled in a randomized, double-blind, crossover study. They received 3 weeks of daily intranasal oxytocin (titrated to 40 IU twice a day) and placebo adjunctive to their antipsychotics. Order of intranasal treatment was randomly assigned and there was a 1-week washout between treatments.

Results: Analysis of the 15 subjects who completed all the study visits revealed that oxytocin significantly reduced scores on the Positive and Negative Symptom Scale (p < .001) and Clinical Global Impression-Improvement Scale (p < .001) compared with placebo at the 3-week end point. No benefit was seen at the early time points. Oxytocin was well tolerated and produced no adverse effects based upon patient reports or laboratory analysis.

Conclusions: The results support the hypothesis that oxytocin has antipsychotic properties and is well tolerated. Higher doses and longer duration of treatment may produce larger benefits and should be evaluated in future studies.

Conclusions

- Social cognition deficits are seen in patients with schizophrenia and FEP
- These deficits are linked to poor social and occupational functioning
- Certain deficits are also seen in those "at risk" for psychosis and may represent trait or risk factors
- Preliminary data from suggests Theory of Mind may be particularly important in those at clinical high risk for psychosis

Conclusions

- Current psychosocial approaches to ameliorating social cognition deficits (such as SCIT) in schizophrenia and FEP are promising and may improve both social cognition and social/occupational functioning
- Such approaches are feasible in FEP populations and may be particularly important in FEP where potential gains in functioning may be the greatest
- Combining these approaches with biological treatments such as Oxytocin is a promising area of research

Acknowledgements and thanks

- SCARMS Research team:
 - Alicia Papas
 - Cali Bartholomeusz
 - Stephen Wood
 - Shona Francey
 - Paul Amminger
 - Barnaby Nelson
 - Hok Pan Yuen
 - Alison Yung
 - Funding sources:
 - o Neurosciences Research Grant, Pfizer
 - Royal Melbourne Hospital Home Lottery Grant
 - o NHMRC Early Career Fellowship

SCIPPY research team:

- Eoin Killackey
- Cali Bartholomeusz
- Stephen Wood
- Kelly Allot
- Tina Profitt
- Hok Pan Yuen
- Kathy Martin
- Virginia Lui
- Lori Schell
- Gina Woodhead

All individuals who participated in the studies