Depression, affect and psychosis

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Outline

• First Episode Psychosis
• Recovery
• Co-morbidity: Depression, Anxiety
• Treatment options
Early Psychosis stages

Age of functional maturation
Age of brain maturation
Young, fertile, risk-taking,
‘Critical Period’ Hypothesis
Kraepelinian Dichotomy

First episode psychosis: diagnostic uncertainty
Heterogeneity of outcomes
Early-stage heterogeneity:

None
Schizophrenia
Bipolar Disorder
Schizoaffective Disorder
Major Depressive Disorder

FEP

Time
ARMS

Depression 40%
Depression related to functioning *irrespective of transition*
Anxiety Disorder 51%

Longer term outcomes of CHR

CHR: Transition to Psychosis 16-20%
CHR: Non Transition: Remission from CHR state 50%
   High prevalence of Axis 1 disorder: 73%
First Episode Psychosis

Longitudinal cohort study in FEP Upthegrove et al *Acta Psychiatr Scan* 2010
First Episode Psychosis:

39% PTSD

36% Social Anxiety
Importance of Depression in and after FEP

Increased risk of suicidal behaviour (up to 7 years after FEP)

Poor functional recovery
Conceptualization of Depression in Schizophrenia

• Depression which is a psychological reaction to the diagnosis and its implications for social status and position
• Depression as “smoking gun evidence” of historical childhood adversity.
• Depression which is intrinsic to psychosis

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Depression and Schizophrenia: Cause, Consequence, or Trans-diagnostic Issue?

Rachel Upthegrove*1,2, Steven Marwaha3,4, and Max Birchwood3
Psychological Reaction
Depression in psychosis: The role of subordination and shame

![Graph showing depression scores for different conditions: Control, Shame, Loss, Insight. The graph compares depression scores between Depression and No Depression groups.]

Upthegrove et al. Psychiatry Research (2013) 217(3) 177-184
I started to realise, if most of the things that I was scared about, and you know, a lot of my thoughts, were they to do with psychosis? . . . It's come to the stage where I don't one hundred percent trust myself.

When I'm having a bad day, I can't even look in the mirror . . . because I feel so ugly and so, I am not the same as I used to be before the psychosis, I used to fix myself up, I used to do all these things, I used to be outgoing,
Historical Childhood Adversity
Childhood Adversity

- Risk factor for adult disorder
- Influence cognitive schema
- Prone to post psychotic PTSD
- Cognitive schema governing self and social information

Birchwood 2003 BJPsych 182: 5 373-375; Upthegrove et al BJPsych 2105 206(3), 191-197
Intrinsic to Early Psychosis
Recent onset Psychosis: ROP
Recent onset Depression: ROD
Clinical High Risk: CHR
Healthy Controls

3 months treatment onset
Discovery and Replication samples
Heterogeneity and classification of recent onset psychosis and depression

Diagnostic heterogeneity particularly in the early stages.

Aim: to identify prototypes of depression and psychosis and investigate the weight of heterogeneity

154 ROP 146 ROD

Prototype PURE ROD vs. PURE ROP
SVM: transdiagnostic clinical & neurocog & GMV

Models then applied to patients with comorbidity: ROP+D and ROD+P measure the position within the affective-psychotic continuum.

Independent replication in n256

a) **Pure models:**
Classification Balanced Accuracy **79.3%**

**Comorbidity:**
ROP+D more frequently classified as ROD
ROP+D patient classification did not differ from ROD

b) Feature Weights and Cross-Validations: derived from 1000 random permutations of the outcome labels.

c) Significant regions in neuroimaging classification PURE model

Shift of comorbid psychosis patients towards the depression prototype, observed at the clinical and biological levels, suggests that psychosis with affective comorbidity aligns more strongly to depressive rather than psychotic disease processes.
Treatment Options:
Treatment of Depression in Schizophrenia:

Antidepressants for treatment of a depressive episode in schizophrenia

Risk difference

-0.19 p<0.001

NNT=5

Standardised Mean Difference

-0.24 p<0.01

Majority of studies SSRI
Antidepressant not associated with higher risk for mortality

Significantly associated with a decreased risk of completed suicide

Tiihonen et al., Arch Gen Psych 2012
Antidepressants: Depression in Schizophrenia and Early Psychosis

• Antidepressants are likely to be effective in treating a depressive episode in people with schizophrenia.

• Evidence also suggests that combination AD+AP does not cause significant increase in adverse events.

• Individual therapeutic trial

• Antidepressant medication should be discontinued if no benefit is found after adequate trial.
ADEPP: Prevention of depression after First Episode Psychosis

2019-2024

Double blind, multicentre RCT, \( n=508 \)

50mg Sertraline or Matched placebo over 6 months

Primary Outcome: **Prevention** of depression

Secondary Outcome: Anxiety, Positive symptoms, Relapse, Suicidal Behavior, Quality of Life, Functioning

Blood sampling month 1: concordance and biobank
CBT: Cognitive behavioural therapy for psychosis (CBTp) has primarily focused on effectiveness for positive symptoms or transition from high risk status

- No CBTp studies have depression as a primary outcome or target of therapy.
- Secondary analysis: evidence weak
Summary: Depression and Affect in Psychosis

• Depression and Anxiety common in and after FEP
• Poor Recovery and suicide risk related to depression
• Depression is pervasive in FEP: not a distinguishable sub-group
• Antidepressant likely to be effective in treating depression
• Prevention of depression in FEP may improve outcomes: ADEPP
Thankyou
QUESTIONS?

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