Early Psychosis:
New Approaches to treatment for early stages of psychotic illness

Prevention and Recovery Center for Early Psychosis (PARC)
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IN ARMS

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Overview

• What is psychosis?
• The Burden of Psychosis
• Early Psychosis: a distinct population
• Early Intervention services
  – International evidence base
  – US experience
  – PARC
What is psychosis?

“Mental disorder in which the thoughts, affective [emotional] response, ability to recognize reality, and ability to communicate and relate to others are sufficiently impaired to interfere grossly with the capacity to deal with reality; the classic characteristics of psychosis are impaired reality testing, hallucinations, delusions, and illusions.”

Kaplan and Sadock
What is psychosis?

• More simply:
  – Impaired reality testing

• Psychosis is a symptom, not a diagnosis!
What are psychotic illnesses?

- Schizophrenia
- Schizophreniform disorder
- Brief Psychotic disorder
- Schizoaffective disorder
- Delusional Disorder
- Substance-Induced Psychotic Disorder
- Mood disorder with psychotic features
- Psychotic disorder due to another medical condition
- Unspecified psychotic disorder
- Schizotypal personality disorder
Schizophrenia

• Psychotic or “positive” symptoms
  • Hallucinations (disturbed perceptions)
  • Delusions (disturbed thought content)
  • Disorganization (disturbed thought formation)

• “Negative” symptoms
  • Restricted or inappropriate affect, avolition, alogia

• Cognitive impairment
  • Attention, information processing, verbal memory, insight
Schizophrenia: Diagnosis

A. Two or more of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated). At least one of these must be 1, 2, or 3.
   1. Delusions
   2. Hallucinations
   3. Disorganized Speech
   4. Grossly disorganized behavior
   5. Negative symptoms

B. Level of functioning is markedly below level achieved prior to onset of illness

C. Continuous signs of illness persist for at least 6 months
Schizophrenia ≠ “multiple personality disorder”
What challenges do we face when diagnosing schizophrenia?
Diagnosing Psychotic Disorders

- Psychotic disorders are diagnosed *clinically*
- Brain imaging may show:
  - Larger ventricles
  - Whole brain volume loss
  - None are sensitive and specific enough markers of disease on which we could base a diagnosis
The Burden of Psychosis

- Early mortality
- Medical comorbidities
- Suicide
- Substance use
- Unemployment
- Incarceration
- Homelessness
The Burden of Psychosis

• Individuals with schizophrenia have up to a 20% reduction in life expectancy compared to the general population

• US general population: 76 years
• Individuals with schizophrenia: 61 years

• Lifetime risk for suicide is 5%
The Burden of Psychosis

• Information gathered from CATIE participants showed unemployment rate at 73%

• 16% of individuals in jails and prisons nationwide have severe mental illnesses

• 11% of individuals with schizophrenia are homeless worldwide; between 1/3 and 1/2 of homeless individuals have severe mental illnesses

• Financial burden of schizophrenia
  – Overall cost to U.S. is $62.7 billion annually
Early Psychosis:
A unique population

What do we know about the burden associated with early psychosis?
First Episode Psychosis (FEP)

A unique population

• Age
  – Most often 15-25
• Developmental stage
  – “Who am I and what can I be?” (identity vs. role confusion)
  – “Can I love?” (intimacy vs. isolation)
• Access to resources and relationships
• Less predictable prognosis
• More difficult diagnosis
First Episode Psychosis

• Duration of untreated psychosis (DUP)
  – Period from onset of initial symptoms of a psychotic illness to the initiation of effective treatment

  – Often greater than 12 months

  – This period exists for many reasons
    • Lack of awareness of illness/treatments
    • Stigma associated with treatment
    • Lack of insight into illness
    • Difficulties resulting from early comorbidities/sequelae (substance abuse, incarceration, social isolation)
    • Overwhelmed mental health systems
First Episode Psychosis

• The longer symptoms are untreated or inadequately treated:
  – Increased likelihood of relapse
  – Worsened symptoms
  – Longer periods to remission once treated

• Symptoms are difficult to bear
  – E.g., hearing voices 24-7, cognitive disarray, persecutory delusions
Common course of Schizophrenia

Stages of Illness

- Premorbid
- Prodromal
- Onset/Deterioration
- Residual/Stable

Gestation/Birth 10 20 30 40 50 Years

Healthy

Worsening Severity of Signs and Symptoms

Lieberman 2006
Treatment Options for FEP

How can we address the unique needs of this population?

Can we change the course of illness for psychotic disorders?
Current System

Mental Health Clinic

Help seeking

Stigma
Lack of Knowledge
Distrust
Poor Insight
Insidious Onset

Referral from GP
Lack of Access
Unaffordability and Inefficiency of health care

Dropout from Care or long-term dependence on mental health system

Police

ER/IP

Compton M, Broussard B: Current Psych Reviews 2011, 7, 1-11
Vision

Help seeking → Special EIS
Early Intervention Services

• International evidence base
  – Canada
  – Australia
  – Scandanavia
  – UK
Early Intervention

• The primary principles of early intervention services:
  – Rapid service engagement to reduce duration of untreated psychosis
  – Low dose pharmacologic treatment
  – Assertive case management
  – Patient psychoeducation
  – Family psychoeducation
  – Vocational and education support
Early Intervention

Results in:

• Decreased inpatient admissions and ER visits
• Fewer relapses
• Lower levels of positive and negative symptoms and improved functioning long term
• Improved quality of life
• Increased occupational activity
• Reduced health care costs
  – 66% cost reduction compared to usual treatment
  – $7,500 per person per year cost savings
Bringing Early Intervention Services to the US
RA1SE
A Research Project of the NIMH
Connection Program
RAISE participants demonstrated improvements in:

- Occupational functioning
- Social functioning
- Participation in education or competitive work
- Level of symptoms
- Rates of remission
Coordinated Specialty Care (CSC) Guiding Principles

- Recovery
- Shared Decision Making
- Limiting Disability
Coordinated Specialty Care (CSC)

Small, multi-disciplinary team:

• Team leader
• Outreach and Recruitment
• Primary Clinician
• Supported education and employment specialist
• RN
• Psychiatrist
• Total of 3.5 FTE
Coordinated Specialty Care (CSC)

- Case management
- Supported education and employment
- Psychotherapy
- Family education and support
- Pharmacotherapy
- Primary Care coordination
- Illness self-management and recovery
- Skills training and substance use treatment
- Housing and Income
- Trauma-informed care
- Safety planning and suicide prevention
The Prevention and Recovery Center for Early Psychosis (PARC)

• Clinical Care
  – PARC Prime
  – PARC Coordinated Specialty Care Program (CSC)

• Education
  – IU/Midtown Collaboration

• Research
PARC Eligibility criteria

• 16-30 years old

• Within 3 years of onset of psychotic symptoms

• Excluding affective, organic, and substance-induced psychosis
The CSC experience

• 3 treatment teams
• 111 individuals enrolled
• Improvement seen across all expected clinical domains
• Ongoing outreach and education
6 Outcome Domains

- Adaptive Functioning
- Use of Acute Services
- Work and School Status
- Suicide Prevention
- Substance Use
- Weight and Metabolic Parameters
Case Presentation

1:1 Therapy

Nursing Support
- PCP referral
- Monitoring Health

Case Management
- Housing
- Community Support Linkage

Family Support Services

“James”

Medication Management

Activities of Daily Living (ADL)

Nursing Support

Case Management

Family Support Services

“James”
James MIRECC GAF Baseline – 16 months

MIRECC GAF Rating

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<th>Time of Assessment</th>
<th>GAF Score</th>
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- Symptom: Blue
- Occupational: Red
- Social: Green
James CGI Ratings
Baseline – 16 Months

Clinical Global Impression Rating

Time (months)

Baseline

CGI-S

CGI-I
Year 2 and Beyond

• Continued emphasis on meeting fidelity measures
• Growth of family program
• Increased outreach and education efforts
• Identify creative ways to keep clients engaged in services
• Assess clients subjective view of recovery (RAS)
• Hub and spoke expansion
• Telemedicine model of care
Importance of Research

• **Question:**
  – Why is Schizophrenia research essential?

• **Answer:**
  – The best therapies we have today are not good enough!
Shortcomings of Existing Antipsychotic Drug Treatments

• Inadequate efficacy
  – Positive symptoms (psychosis) fail to respond in 30 to 50%
  – Negative symptoms (social isolation, lack of emotion) and Cognitive impairment (slowed thinking, disorganization) fail to respond for all
  – Relapses common, Underlying problem not treated

• Concerning side effects are common
  – Weight gain, diabetes, EPS, increased prolactin, QTc prolongation, etc

• Bottom Line: Outcomes are not improving and we need a new class of better treatments!
MRI Scans Showing Tissue Loss in Schizophrenia

Healthy Subject  Schizophrenia Patient
Brain Abnormalities in Schizophrenia

• Increased ventricle size
• Increased gliosis – change in glial cells due to damage
• Reduced cortical volume
• Post mortem and genetic evidence supporting **White Matter (WM)/myelin abnormalities** in schizophrenia
• Widespread reduced WM integrity assessed by Diffusion Tensor Imaging (DTI) in first-episode and chronic schizophrenia; **frontal/temporal most affected**
• Global reduction in WM integrity related to **cortical thinning**
Antipsychotic Therapies: 
*Lack of Innovation*

ECT, etc.

- Chlorpromazine
- Fluphenazine
- Thioridazine
- Haloperidol
- Clozapine
- Olanzapine
- Quetiapine
- Risperidone
- Aripiprazole
- Paliperidone
- Asenapine
- Iloperidone
- Lurasidone

Research at PARC and IUPDP

1. **N-acetylcystiene (NAC)** to prevent cortical loss in 1st episode psychosis (SMRI)

2. **Fingolimod (Gilenya)** to decrease inflammation and enhance cortical connectivity (SMRI)

3. **Valacyclovir (Valtrex)** for cognitive impairment in HSV1 (+) early phase schizophrenia (SMRI)

4. **Estrogen receptor-**<em>Beta</em> **agonist** for cognitive impairment/ negative symptoms in schizophrenia (NIH)

5. **Integrated Metacognitive Therapy** (IMT) for insight into person’s illness

6. **rTMS** for cognitive impairment and negative symptoms using a therapeutic magnet
Questions?


Resources


Resources


16. Davis et al., 2003; Kubicki et al., 2007; Lee et al., 2013; Kyriakopoulos, 2009; Sasamoto et al., 2013