A Revolutionary Approach to Treating Psychosis: Identifying Youth "At Risk"

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The At Risk Phase of Psychotic Disorders

- What is the at risk phase?
- How can we identify young people who may be in this phase?
- What evidence do we have in regard to treatment in this phase?
- What are the current treatment recommendations in this phase?
The Genetics of Mental Disorders

- Psychotic disorders are complex and appear to involve multiple susceptibility genes interacting with multiple environmental factors throughout the development of the person. The nature of these interactions is very complex and poorly understood at this time.

- In order to avoid the deterministic viewpoint of mental illness, it is crucial to emphasize the importance of the environment and lifestyle choices and that there is hope for recovery.

- Taking illicit drugs is a preventable risk factor, as is excess stress.
What Is Psychosis?
Any Severe Mental Disorder in Which Contact With Reality Is Lost or Distorted
Schizophrenia Is the Most Common Psychosis

- Described by Kraepelin 100 years ago
- Prevalence 1% worldwide
- Median age of onset 19
- Onset by age 25 -- 85%
- Monozygotic twin concordance 50%
### Schizophrenia

<table>
<thead>
<tr>
<th>Positive Symptoms</th>
<th>Negative Symptoms</th>
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<tbody>
<tr>
<td>Hallucinations</td>
<td>Lack of interest</td>
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<tr>
<td>Delusions</td>
<td>Lack of motivation</td>
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<tr>
<td>Thought Disorder</td>
<td>Lack of pleasure</td>
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<tr>
<td>Bizarre Behavior</td>
<td>Social withdrawal</td>
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<tr>
<td></td>
<td>Blunted affect</td>
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<td></td>
<td>Lethargy</td>
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<td>Apathy</td>
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Phases of Schizophrenia

PREMORBID

Functioning

Early identification and intervention

Decrease in functioning, Beginning of mild but not yet psychotic symptoms.

AT RISK

Onset of illness

Duration of Untreated Psychosis

*First treatment

ACTIVE

Course of Illness
Many illnesses have at risk phases
Diabetes example
Historically a retrospective concept
  - Retrospective prediction 100% accurate
  - Risk of prospective application is nonspecificity or false positive predictions
Summary of Relevant Research

1) Early Identification and early intervention appear to lead to better prognosis. Australian EPPIC Program

2) It is possible to reduce the duration of untreated Psychosis. Norwegian TIPS Project

3) It appears to help to identify people “at risk” for serious mental illness. British Early Intervention Study

4) It is possible to identify people in a pre-psychotic state. PACE, TOPS, and PRIME Data
TIPS LATE-BREAKING FINDINGS

Baseline ED vs UD Differences

- Less suicidality with ED
- Less involuntary hospitalization with ED
- Holds true even 10 years out
Case for Early Intervention

- Despite recent advances in treatment and rehabilitation, most patients follow a chronic course with poor social and occupational functioning
- At onset, already present are:
  - Measurable cognitive impairment
  - Measurable gray matter volume loss
  - Damaging social development losses
  - Diminished capacity to actively engage in treatment
How Can We Identify Young People Who May Be At Risk?

- Genetic High Risk
  - No relatives: 1 – 3%
  - Sibling: 10%
  - One Parent: 13%
  - Two Parents: 45%
  - Monozygotic twin: 50%

- Clinical High Risk (ultra high risk)
  - Sub-threshold psychotic experiences or genetic risk and functional decline

- Semi-structured
- Diagnoses prodromal states
- Diagnoses presence of psychosis
- Translated & validated into 14 different languages
SIPS Validity Criteria

RENAMED STRUCTURED INTERVIEW FOR PSYCHOSIS – RISK SYNDROMES

VALID ON PERSONS 10 – 45

MUST HAVE MINIMUM IQ OF 70

MUST HAVE NEVER MET CRITERIA FOR ANY PSYCHOTIC DISORDER
Differential Diagnosis

• Schizotypal Personality Disorder
• Obsessive Compulsive Disorder
• Depression
• Bipolar Disorder
• Post Traumatic Stress Disorder
• Substance Use
• Psychotic Disorder
### SUMMARY
Structured Interview for Prodromal Syndromes (SIPS)  
**Predictive Validity**

<table>
<thead>
<tr>
<th>Months</th>
<th>Positive Predictive Value (conversion to schizophrenic psychosis)</th>
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<tbody>
<tr>
<td>6</td>
<td>43%</td>
</tr>
<tr>
<td>12</td>
<td>50%</td>
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<tr>
<td>18</td>
<td>62%</td>
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<tr>
<td>24</td>
<td>69%</td>
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</table>
The prodromal patient: Both symptomatic and at risk.

Woods SW, Miller TJ, McGlashan TH

*CNS Spectrums* 2001;6(3)223-232

- Diagnosable
- Symptomatic
- Cognitively impaired
- Functionally impaired
- Treatment seeking
- At risk
Prodromal Research Findings

- Supports continuing research
- Positive benefit to risk ratio
- Currently, clinical strategies should include frequent, careful follow-along evaluations with psychoeducation and support over the course of the prodrome to its “resolution” either in remission or in the development of a treatable syndrome

(APA Treatment Guidelines for Schizophrenia, 2004)

* Further data needed to reach medication treatment guideline status.
Improve the Prediction of the Course

- Some go on to develop psychosis
- Some stay the same – not better, not worse
- Some improve – remit on their own
- Watch and learn – what makes the difference
- Watch and intervene – is there something we can do to make the difference
WATCH AND LEARN

NATURALISTIC FOLLOW – ALONG STUDY
FOLLOW ALONG STUDY

- Baseline Assessment of Symptoms
- MRI
- ERP
- Neuro Cognitive Assessment
- Psychoeducation
- Regularly Scheduled Follow-Up Visits
- Community Treatment as Usual
- Rescue Arm if Needed
DISCOVER NEW TREATMENTS

- Does the treatment help symptoms?
- How long do we need to provide the treatment?
- Will improvement remain if the treatment is stopped?
- Does the benefit received from the treatment outweigh the risks (i.e., side effects of the medication)?
WATCH AND INTERVENE

TREATMENT STUDIES

- Zyprexa vs. placebo
- Omega 3
- Glycine
- Abilify
- Glycine vs. placebo
- Ziprasidone vs. placebo
- D-serine vs. placebo
- CBT – Group or Individual
- Cognitive Remediation
COGNITIVE REMEDIATION

Progressive sequence of cognitive exercises
Similar to a computer game
Restores cognitive and work capacity in patients
Improves work performance
Improves quality of life
BENEFITS of Early Intervention

Presenting symptoms may be treated

* p < 0.10, ** p < 0.05
Current Treatment Guidelines

- It is essential to have a specialized assessment carried out to determine whether the person actually meets criteria for the ultra high risk phase.
- Monitor closely for progression to full psychosis (monthly assessments).
- Treat co-existing conditions (anxiety, depression) as appropriate.
- Provide psychosocial support, including the family.
- Recognize that youth meeting ultra high risk criteria are help seeking and in need of care whether or not they develop a full psychotic disorder.
Behaviors of Concern

- Withdrawal/Isolation
- Ongoing Social Difficulties
- Poor Hygiene
- Bizarre Behavior/Appearance
- Falling Asleep in Class Repeatedly
- Sadness/Tearfulness
- Excessive Anxiety
- Absenteeism/Staying in Room

- Poor Concentration/Spacing Out
- Hypervigilance
- Decrease in Work Performance/Activity Level
- Becoming Neglectful and Unfeeling
- Emotional Outbursts/Emotional Flatness
Behaviors of Concern

- Identify recent changes
- Identify more than one behavior of concern
- Identify distress level associated with behavior of concern
- Identify interference with functioning associated with behavior of concern
## Early Warning Signs of Psychosis:

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<th>Sign</th>
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<tr>
<td>Increased difficulty at school or work</td>
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<tr>
<td>Withdrawal from friends or family</td>
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<td>Difficulty concentrating or thinking clearly</td>
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<tr>
<td>Suspiciousness or mistrust of others</td>
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<tr>
<td>Changes in the way things look or sound</td>
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<tr>
<td>Odd thinking or behavior</td>
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<tr>
<td>Emotional outbursts or lack of emotion</td>
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<td>Poor personal hygiene</td>
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Is someone you know at risk?
Some Typical Queries and Responses

- Have you felt that you are not in control of your own ideas or thoughts?
- Do you ever feel that your mind is playing tricks on you? Déjà vu, minding reading?
- Your ears? More sensitive to sounds? Ringing in your ears? Name being called? Cell phone ringing?
- Your eyes? More sensitive to light? Flashes, flames, vague figures or shadows out of the corner of your eyes?
- Do you seem to be having trouble getting your point across? Following multi-step directions?
Changes in the Way Things Look or Sound

- Wind rushing by ears
- Noisy pipes
- Hall to the Cafetería
Odd Thinking

- School class watching him
- Traffic lights have meaning
- Friends might be only pretending
- Teachers might be against