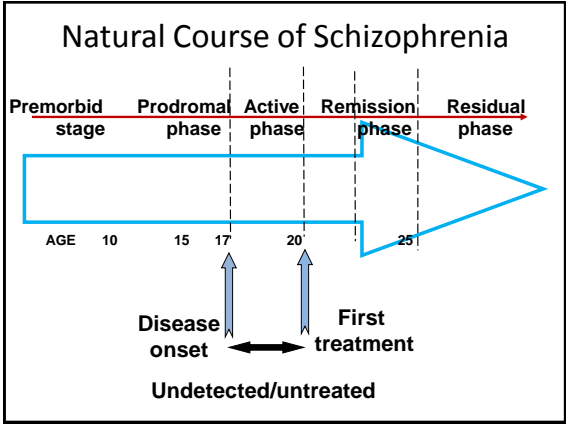


**UNC School of Social Work and Wake AHEC
Clinical Lecture Series**

**Early Identification and Treatment of
Psychosis:
Potential Promise and Pitfalls**

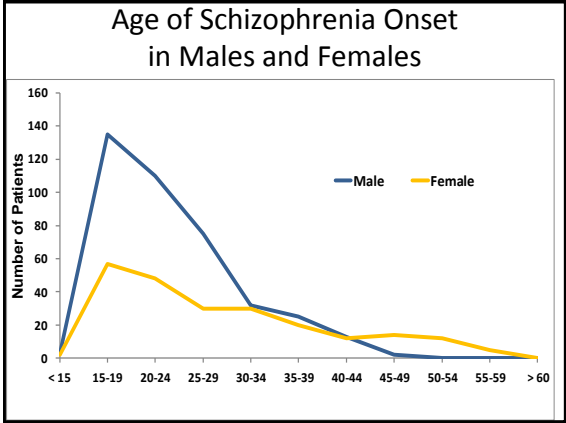
October 14, 2013

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University of North Carolina at Chapel Hill



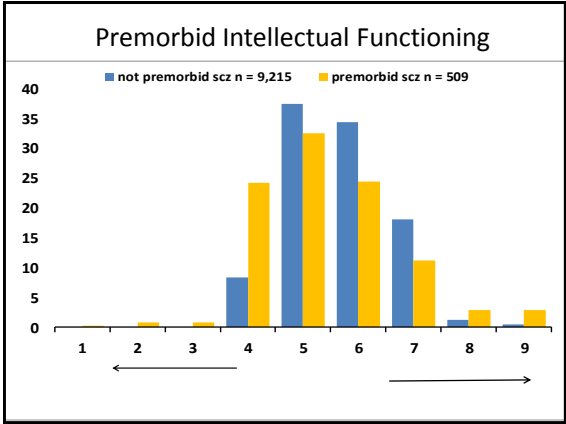
Vulnerability and Course

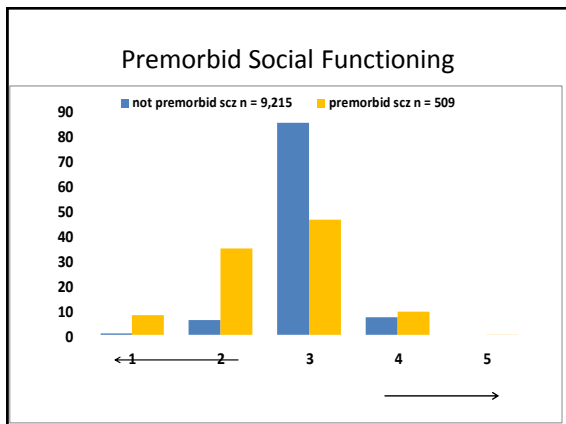
- Ratio of men to women with schizophrenia: 1.4
- Sex differences in:
 - Age of onset
 - Premorbid function
 - Severity of negative symptoms
 - Structural brain abnormalities
 - Substance use



Premorbid Characteristics: Predicting Risk of Schizophrenia

- Intellectual abnormalities
- Impairments in cognitive function
- Socially awkward
- Impulsive
- Minor physical anomalies





- ### Factors Associated with Outcomes: Premorbid Stage
- Sex (male)
 - Poor premorbid function
 - Delayed developmental milestones
 - Poor academic performance
 - Few friends
 - "Odd"

- ### Pre-morbid functioning in Schizophrenia
- Patients often have a history of:
 - Poor scholastic achievements
 - Few friends
 - Psychiatric symptoms
 - **BUT:**
 - More patients have a history of average pre-morbid functioning, hence can we predict/delay/prevent schizophrenia based on pre-morbid functioning?

- ### Meet Michael and Ryan
- | | |
|--|--|
| <h4 style="text-align: center;">Michael</h4> <ul style="list-style-type: none"> ▪ "Normal" childhood development ▪ Good student until second semester junior year in high school, where he struggles academically ▪ Shy, with few friends ▪ Talented musically | <h4 style="text-align: center;">Ryan</h4> <ul style="list-style-type: none"> ▪ Normal childhood development ▪ Elite high school athlete, "A" student ▪ Popular, social ▪ Heads off to college, a highly recruited division 1 athlete |
|--|--|

- ### "Prodromal" Characteristics
- Attenuated Psychosis
 - Ideas of reference / suspiciousness /unusual thought content
 - Perceptual abnormalities
 - Disorganized speech
 - Derealization
 - Brief, Intermittent Psychosis

- ### "Prodromal" Char. (cont.)
- Negative Symptoms
 - Emotional / affective blunting
 - Diminished drive / motivation
 - Social withdrawal
 - Affective
 - Depression/anxiety/hostility
 - Mood lability
 - Sub-threshold obsessive compulsive symptoms

Initial “Prodromal” Symptoms

- Cognitive
 - Poor attention/distractibility
 - Impairment initiation or train of thought; intrusive thoughts
 - Difficulty in understanding written or spoken language

Initial “Prodromal” Symptoms

- Behavioral Disturbances
 - Decline in school function
 - Social withdrawal
 - Impaired hygiene
 - Sleep disturbance
 - Suicidal ideation / attempts
 - Aggressive behaviors

Attenuated Psychosis Syndrome

- Characteristic symptoms: at least one of the following in attenuated form with intact reality testing, but of sufficient severity and/or frequency so as to be beyond normal variation:
 - (i) delusions (unusual thought content)
 - (ii) hallucinations (perceptual abnormalities)
 - (iii) disorganization (disorganized communication)
 - Present in past month
 - Occur at least 1 per week
 - Begun or worsened in past year
 - Distressing or significantly impact function
 - Not caused by another disorder (e.g., PTSD)
 - Never met criteria for a psychotic disorder

Unusual Thought Content

- Examples
 - Ideas of reference
 - Sense “something odd is going on”
 - Overvalued beliefs
 - Magical thinking
 - Connections between unrelated event
 - Déjà vu
 - Coincidences
 - Suspiciousness/paranoia
 - Distorted illogical ideas
- “prodromal”=sense of doubt , may be dismissed
- psychotic = sure is true, cannot be dismissed

Thought Content

Attenuated Delusion

A 15-year-old high school student sits in the back of the class because if she sits in the front, she has an uncomfortable feeling that other students are watching her. She knows this is “silly”, but feels better in the back.

Delusion

A 15-year-old high school student believes that other people are talking about her and making fun of her where ever she goes. She is sure this is happening, and she is isolating herself at home because she is uncomfortable in public.

Perceptual Disturbances

- Examples
 - Illusions
 - Heightened or dulled perceptions
 - Distortions
 - Transient hallucinations
- “prodromal”= understood as “mind playing tricks”
- psychotic = certain is a real experience

Perceptual Disturbances

Attenuated Hallucination

~2-3 x/week a 22.y.o. cashier sees shadows, movements, & sometimes formed figures (like an animal) out of corner of eye, but when he turns to look nothing there. He hears beeping sounds that can last for minutes, and once he heard a momentary (second or two), faint, unintelligible voice. He is not sure, but thinks it is his mind playing tricks on him.

Hallucination

On a daily basis a 22-year-old cashier sees fully formed figures that he calls "shadows." The shadows remain for minutes to hours. He hears the "shadows" speak to each other about him, and sometimes criticize him or tell him to do something silly. He believes these shadows are real and he is frightened of them.

Disorganized thoughts/speech

– Examples

- Odd speech, vague, metaphorical, overelaborate
- Circumstantial, tangential, not goal directed
- Redirected through structured questioning

– "prodromal" = can be redirected

– psychotic = not responsive to structuring, disorganized when minimal pressure

Disorganization

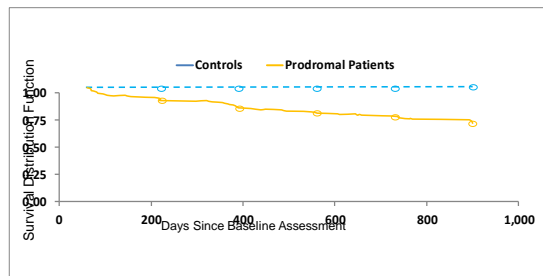
Attenuated Disorganized Speech

A formerly high achieving high school junior reports his friends have great difficulty following him when he explains things to them. This is very frustrating to him. During the interview he had difficulty getting to the point and at times his statements did not answer the question asked. Through direct and structured questioning he was able to answer the questions correctly. He did not have this problem a year ago, and it is getting worse these last few months.

Psychotic Intensity Disorganized Speech

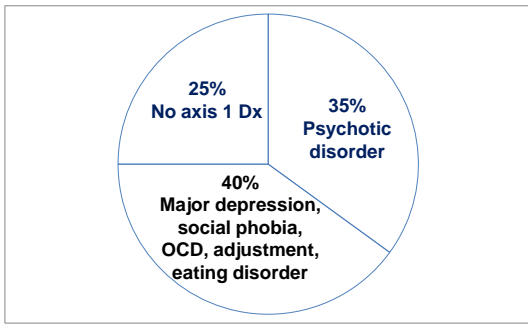
A formerly high achieving high school junior is unable to attend school due to disorganization. He can engage in goal directed speech only when the conversation is highly structured. His speech often doesn't make sense due to loose associations.

Validity of the Attenuated Psychosis Syndrome Criteria



Risk Estimates in Persons Meeting APS Criteria:
 20–25% in 1 year
 30–35% in 2 years

Diagnosis at 1 Year Follow-Up for Patients with Attenuated Psychosis Syndrome



Symptoms Most Predictive of Psychosis

- Unusual thought content / suspiciousness / distorted ideas
- Reduced ideational richness
- Trouble with focus and attention

Reduced Ideational Richness

–Examples

- Unable to make sense of familiar phrases
- Difficulty getting “gist of conversation”
- Decreased fluidity, spontaneity, flexibility of thinking
- Difficulty with abstract thinking
- Poverty content

Trouble with Focus/Attention

–Examples

- Failure in focused alertness/poor concentration
- Distractible
- Difficulty shifting focus
- Loses track of conversations

Case 1

Max is a 21 y.o. art student at a local college, living in an apartment with a friend from HS. He is close to his parents, who live about ½ hour away. His girlfriend attends the same college, and they spend a lot of time together. Both enjoy smoking marijuana several times a week, but do not think they have a problem with it. Max is a gifted artist and has a 3.0 GPA.

At 16, Max saw his best friend die in a skiing accident, which was extremely traumatic. Periodically during the past five years he has had nightmares. Max never went to therapy afterwards, but through the years has talked about the accident with family and friends.

Lately, Max has been feeling anxious and overwhelmed by his course load. Last night he told his girlfriend that he has been hearing his name called periodically for the past several months, but when he checks, no one has been calling him. He's also finding it uncomfortable to be in crowds and worries that people are looking at him when out in public. He wonders if this is due to fatigue or smoking pot.

Max is bothered by these experiences, and his girlfriend is encouraging him to see someone at the school counseling service. He agrees to see a counselor, who then wonders...

Is Max developing a psychotic disorder?

Case 1 - Max

- What symptoms are you concerned about?
- What diagnoses are you considering?

- What recommendations do you have?

Case 1

... **has been hearing his name called periodically for the past several months, but when he checks, no one has been calling him. He's also finding it uncomfortable to be in crowds and worries that people are looking at him when out in public.** He wonders if this is due to fatigue or smoking pot. Max is **beginning to feel bothered by these experiences.**

MAX SHOULD BE considered at increased risk for development of psychosis.

Case 2

Jon is a 17 year-old high school student who lives with his parents and younger brother. He has always been a good student, getting good grades, completing his work, and involved in the chess club 2 afternoons a week.

Jon's chess club teacher, who also happens to be his English teacher, has noticed several changes in him recently. He has stopped going to chess club, and his English grades have been dropping, mostly because of incomplete homework. His teacher also said that Jon has had trouble focusing-- his mind seems to be 'off in space'. Then, Jon passed in a writing assignment that was dark and morose, and contained overly detailed images of death, which worried the teacher significantly.

The teacher took his concerns to the school social worker, who agreed to follow up with Jon & his family. She spoke with his mom who shared that Jon's father had just been diagnosed with cancer. The family has been experiencing a lot of stress due to the uncertainty of Dad's prognosis. This situation has been very difficult for Jon.

After speaking with the mom, the SW determined that Jon's problems started about the same time his father was diagnosed. Of note, there is a family history of Bipolar I Disorder, but not in the immediate family.

is Jon developing a psychotic disorder?

Case 2 - Jon

- What do you think is going on?
- Does family hx of Bipolar disorder place him at increased risk of psychotic disorder?
- What treatment would you recommend?

Case 2

After speaking with the mom, **the social worker determined that Jon's problems started about the same time his father was diagnosed.** There is a family history of Bipolar I Disorder, but not in the immediate family.

Jon's symptoms are most likely related to family stressors.

Case 3

Katie is a 20 y.o. college junior who lives with friends off campus. Since freshman year, she has 3.4 GPA and is active in community theater. Lately, she's forgetting assignments and missing practices. For past 3 years, she volunteered weekly at the food bank with 2 close friends. Recently, she has excuses not to go.

At 7, Katie dx w/ ADHD—she's taken Ritalin periodically since then with good results. In the past couple of months, Katie has seemed preoccupied, distractible, and more withdrawn.

Case 3

She shared "dark thoughts" (e.g., fleeting suicidal thoughts & unfounded fears of being watched) with mother, now seeking advice from therapist. She's aware of "connections" between her reading in history class and own life, e.g., during prohibition the US gov put toxins in industrial alcohol; and sometimes worries her alcohol might be adulterated, although she readily admits this is highly unlikely. Such "coincidences" several times/week. Also several episodes of seeing shadows in room in evening, then turning and realizing no one was there.

IS KATIE AT RISK FOR PSYCHOSIS?

Case 3: Katie

- Is Katie psychotic?
- What is her risk for psychosis?
- What symptoms are most concerning?
- What interventions would you recommend?

Prodromal Stage: Michael and Ryan

- | | |
|--|---|
| <p>Michael</p> <ul style="list-style-type: none"> ▪ Struggled Jr & Sr year of HS ▪ Smokes pot senior year ▪ End of HS/start of college: <ul style="list-style-type: none"> ▪ Withdrawl from friends ▪ Thinks other "make fun" of him ▪ Hard to pay attention in class, every thing a distraction ▪ Frequent noticed connections between unrelated events ▪ Begins to think he had "some sort of special mission" ▪ Depressed, suicidal thoughts | <p>Ryan</p> <ul style="list-style-type: none"> ▪ Hard adjustment freshman year ▪ During first semester freshman year: <ul style="list-style-type: none"> ▪ Thought team mates were "saying bad things" about him ▪ Thought team mates might be conspiring against him, attributed to "Jealousy" |
|--|---|

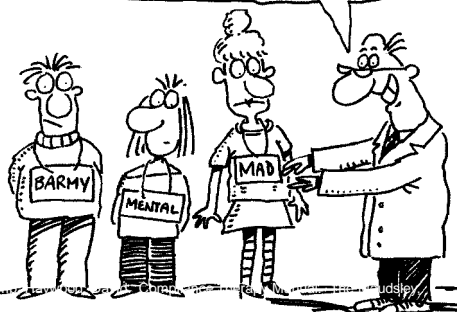
RECOGNITION AND TREATMENT OF PSYCHOSIS RISK:

DOES THE HARM OUTWEIGH THE GOOD?

Potential Risks/Risk Mitigation

- Stigma
 - Is a "risk syndrome" stigmatizing?
 - Imply disease rather than a potential for disease ?
 - Imply possibility of prevention of disease?
 - Does "help-seeking" impact stigma risk?

There you go. After a few weeks you'll hardly notice them.



Potential Risks/Risk Mitigation

- Stigma
 - Does a "risk syndrome" decrease stigma?
 - Imply disease rather than a potential for disease ?
 - Imply possibility of prevention of disease?
 - Does "help-seeking" impact stigma risk?
- Treatment:
 - Inappropriate antipsychotic use may increase
 - Evidenced based interventions of a defined syndrome—could this impact on inappropriate antipsychotic use?

Evidence Base: Treatment of Psychosis Risk Syndrome

Treatment Implications

- Attenuated psychotic symptoms indicate a vulnerability to mental illness
- Eventual diagnosis varied
 - ~ 35% develop a psychotic disorders
 - ~ 40% develop a non-psychotic mood disorder
 - ~ 25% recover
- Conservative treatment indicated

Cannabinoids in Humans

- Endocannabinoid system regulates:
 - Release of multiple neurotransmitters, including dopamine, glutamate, GABA, and serotonin
 - synaptic plasticity
 - neurodevelopment (*in utero* through adolescence)
- Anandamide (AEA): the bodies main (endogenous) cannabinoid receptor agonist

Cannabinoids in Humans

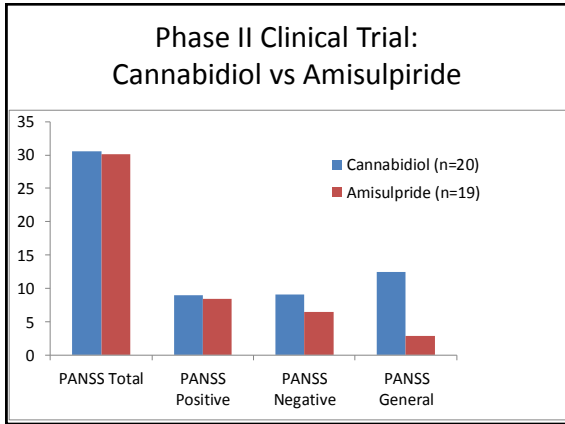
- Marijuana contains
 - **Delta(9)Tetrahydrocannabinol (THC):**
 - CB1 agonist, stimulates cannabinoid system
 - Evidence suggests worsens psychosis
 - **Delta (8) Tetrahydrocannabinol (cannabidiol):**
 - blocks anandamide, down-regulates cannabinoid system
 - May have antipsychotic effects

Cannabis Use and Schizophrenia Risk

- In the US, by age 18:
 - Up to half of adolescence have tried marijuana
 - 15% report daily use for at least a month
- IV THC produces transient positive and negative symptoms in healthy persons
- Persons who experience cannabis-induced psychosis have a 50% risk of schizophrenia
- Maybe a gene-environment interaction?
 - One study finds 11-fold increase in schizophrenia risk in cannabis users with a low activity metabolic enzyme (COMT) for dopamine

Cannabis Use and Schizophrenia Risk

- Unclear if increase in cannabis use in adolescents is associated with an increase incidence of schizophrenia
- In a small study 4/6 schizophrenia patients who reported cannabis improved symptoms actually experienced improvement with administration of dronabinol (synthetic THC)
- First episode patients who use cannabis have less severe negative symptoms and better functional outcomes

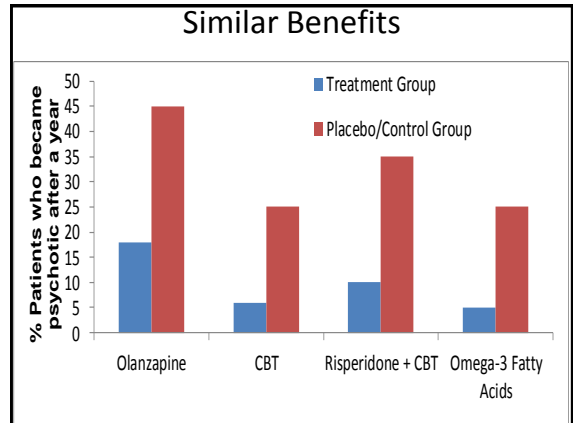


Summary

- Marijuana contains THC and cannabidiol with opposite effects on the CB1 receptor activity
 - Cannabidiol promising as antipsychotic
- Cannabis in an environmental risk factor for the development of schizophrenia
 - Very heavy marijuana use in adolescence increases risk of schizophrenia by 6-fold
 - The “type” of schizophrenia related to cannabis may have less severe negative symptoms and better functional outcome

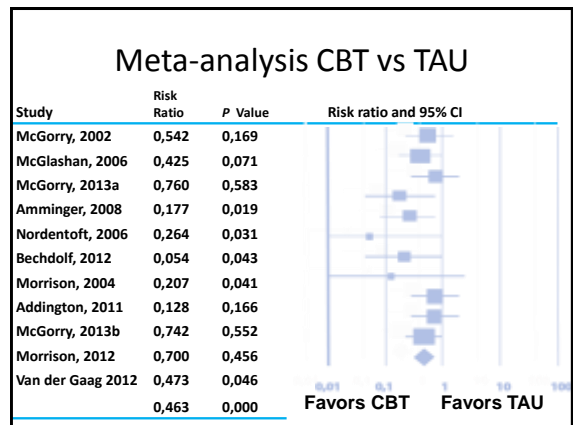
“Prodromal” Stage Interventions Studies with Randomized Clinical Trials

- Antipsychotic medication
- Cognitive behavioral therapy
- Omega-3 fatty acids



Meta-analysis Prevention Interventions

Comparison	Total events (events/total)	No. (%) of participants in analysis	Risk ratio (95% CI, random-effects, I ²)	Heterogeneity (I ² , P, I ²)	Quality of evidence (GRADE)
CBT + risperidone vs placebo	0/8	4 (20)	0.02 (0.00 to 0.31)	17, 0.0 (P=0.31)	Low ^b
CBT + risperidone vs placebo	0/12	6 (50)	0.04 (0.00 to 0.86)	0, 0.0 (P=0.98)	Moderate ^c
CBT + risperidone vs placebo	0/4	4 (100)	0.03 (0.00 to 0.86)	0, 0.0 (P=0.98)	Low ^b
CBT and risperidone vs placebo	0/8	4 (50)	0.02 (0.00 to 0.86)	0, 0.0 (P=0.98)	Very low ^d
CBT and risperidone vs placebo	0/12	6 (50)	0.02 (0.00 to 0.86)	0, 0.0 (P=0.98)	Very low ^d
CBT and risperidone vs placebo	0/4	4 (100)	0.02 (0.00 to 0.86)	0, 0.0 (P=0.98)	Very low ^d
CBT and risperidone vs placebo	0/8	4 (50)	0.02 (0.00 to 0.86)	0, 0.0 (P=0.98)	Very low ^d
CBT and risperidone vs placebo	0/12	6 (50)	0.02 (0.00 to 0.86)	0, 0.0 (P=0.98)	Very low ^d
CBT and risperidone vs placebo	0/4	4 (100)	0.02 (0.00 to 0.86)	0, 0.0 (P=0.98)	Very low ^d
CBT and risperidone vs placebo	0/8	4 (50)	0.02 (0.00 to 0.86)	0, 0.0 (P=0.98)	Very low ^d
CBT and risperidone vs placebo	0/12	6 (50)	0.02 (0.00 to 0.86)	0, 0.0 (P=0.98)	Very low ^d
CBT and risperidone vs placebo	0/4	4 (100)	0.02 (0.00 to 0.86)	0, 0.0 (P=0.98)	Very low ^d
Omega-3 fatty acids vs placebo	0/8	4 (50)	0.10 (0.00 to 0.70)	0, 0.0 (P=0.98)	Low ^b
Omega-3 fatty acids vs placebo	0/12	6 (50)	0.10 (0.00 to 0.70)	0, 0.0 (P=0.98)	Low ^b
Omega-3 fatty acids vs placebo	0/4	4 (100)	0.10 (0.00 to 0.70)	0, 0.0 (P=0.98)	Low ^b



Different Risks

- Antipsychotics
 - Weight gain/metabolic effects
 - Sedation
 - Unknown risks for 65% of patients who were not really prodromal for psychosis
- CBT
 - Time intensive
- Omega 3 fatty acids
 - Fishy burp

Interventions in the “at risk” patient: A stepped-care approach

- Mild symptoms/impairments
 - Identify and address vulnerability factors
 - Cannabis use
 - Co-morbid disorders (e.g., major depression)
 - Identify and address functional impairments
 - Discuss option of fish oil supplementation
 - Provide psychoeducation: range of outcome, warning signs of psychosis
 - Monitor symptoms over time
- Moderate/severe
 - Individual and Family Psychotherapy, address stress, stress resiliency

The First Episode of Psychosis

- Defined by psychotic intensity of positive symptoms
 - Delusions
 - Hallucinations

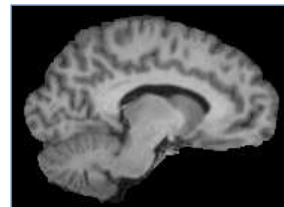
Emergence of Psychosis: Michael & Ryan Michael

- Delusion that he could cure cancer
- Messages from God and spirits
- Professors “praised” his “work”
- Very anxious, still with suicidal thoughts
- Roommate concerned, took him to student health, started on antidepressant
- Thanksgiving Break, isolated self from family
- At school, went to library, took off clothes, was video taped & put on Facebook
- Campus police took to ER, diagnosed as psychotic and admitted to hospital, began antipsychotic

Emergence of Psychosis: Michael & Ryan Ryan

- 2nd semester concerns re: team worsens, isolates
- Won’t eat on campus (thinks food is poisoned)
- Hears whispers outside door (thinks “jokes”)
- Symptoms wax & wane over 4 years
- By junior year, religious bent: “spiritual warfare”
- Joins fundamentalist group, quits team
- School performance low but passes
- Parents seek therapist, who recognizes psychosis, but diagnoses depression
- Became delusional about cat and tried to strangle cat, fights with father, police called, taken to ER, hospitalized, psychosis diagnosed

First Episode Schizophrenia: Change in Brain Volume Over 6 Months Midsagittal



FE Schizophrenia: Change in Brain Volume Over 6 Months

axial slice 1 axial slice 2

Time from Onset of Psychosis to Onset of Treatment

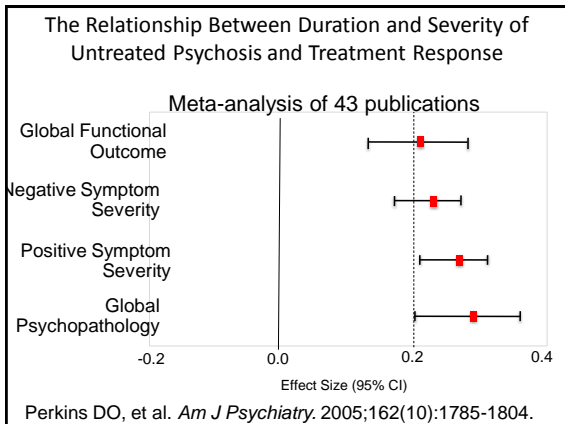
- Treatment delays are common
 - On average a year or more elapses from onset of psychosis to onset of treatment
 - Why the delay?
 - Early stage of psychosis clinically different
 - Patient’s look more “more normal”
 - Less severe negative symptoms
 - Substance use, school failure, behavioral problems may obscure underlying psychosis
 - Symptoms recognized but misinterpreted
 - Stigma

Duration of Untreated Psychosis & Outcomes

- Duration of untreated psychosis (DUP)
 - May impact:
 - Treatment response
 - Risk of relapse
 - Long-term outcomes (clinical and functional)
 - Symptom severity at first treatment
 - May be modifiable prognostic factor

The Longer the Treatment Delay, the Worse the Prognosis

- Greater the chance of aggression and violence prior to first treatment contact
- Social and role function derailment
- Longer time to recovery
- Less likely to recover from first episode
- Chronic symptoms more severe and worse social and role function
- Greater risk of brain tissue loss



Public Education Programs Are Effective in Reducing DUP

Clinician’s need to recognize the early stages of schizophrenia

- In Norway an intense education campaign about the signs and symptoms of psychosis reduced DUP to less than a month. Patients presented with less severe symptoms and recovery rates improved.

Duration of Untreated Psychosis and Treatment
Response: Michael and Ryan

Michael

- DUP: 2 months
- Remission of psychosis after 4 wks antipsychotic
- Residual symptoms included
 - Subjective sense that emotions were dull,
 - Mentally “not as sharp”
 - Easily stressed by small events
 - Depression, discouragement, thoughts life not worth living

Duration of Untreated Psychosis and Treatment
Response: Michael and Ryan

Ryan

- DUP: 45 months
- Marginal response to antipsychotics
 - Hallucinations and delusions improved
 - Residual symptoms included:
 - When “out and about” thinks other talking about him
 - Spirits talk to him infrequently, when stressed
 - Significant negative symptoms
 - Significant cognitive impairments

Variable Outcomes in Schizophrenia

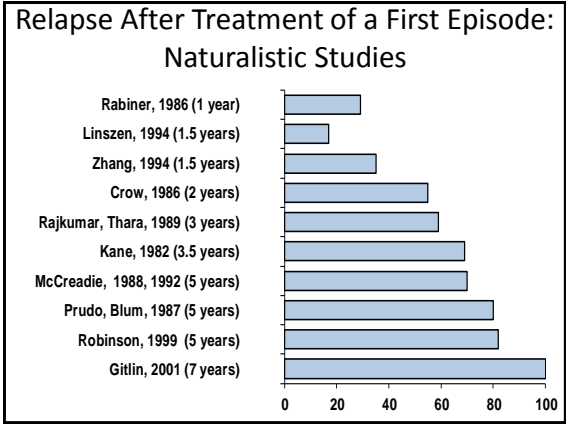
- Most patients experience positive symptom remission after a first episode
- Without maintenance antipsychotic medication, most relapse
- Relapse is associated with symptomatic, functional, and brain progression

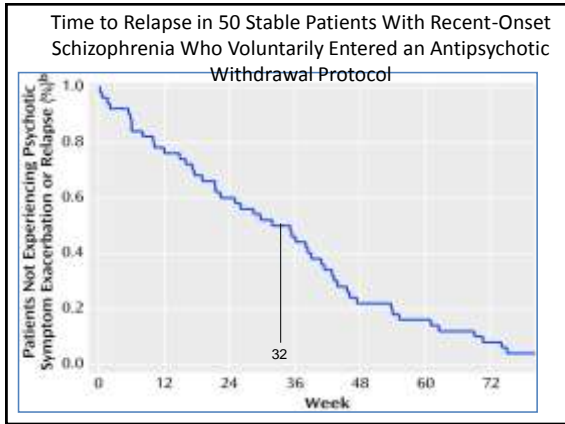
Early Psychosis Treatment Principles

- Low dose antipsychotics (minimize secondary negative symptoms)
- Address stress reactivity:
 - Psychotherapy
 - Complementary treatments (exercise, mindfulness, yoga, L-theanine, NAC, anti-inflammatory medications)
- Relapse management
- Relapse prevention
- Include family, address family concerns

Relapse: Systematic Review and Meta-Analysis

- Clinical definitions of relapse vary widely
 - Worsening of symptoms or rehospitalization within year after discharge
- Among first episode patients:
 - ~ 96% will attain remission within 12 months of treatment
 - ~ 80% will relapse within 5 years
- Relapse associated with:
 - ↑ risk of chronicity psychotic symptoms
 - ↑ cost of treatment (4x that of stable patient)
 - Possible ↓ in medication efficacy
- Incidence ~ 5x greater with nonadherence





Predictors of Relapse Following Hospital Discharge

- Study to examine relapse in the year after hospital discharge (N = 200)
- At 1 year 57% had experience ≥ 1 relapse
- Relapse more common among patients who were:
 - Non-responsive to treatment at discharge
 - Not in remission at discharge
 - Not receiving atypical antipsychotics
- Predictors of relapse: lack of insight, ↑ Rx side effects, poor attitude about treatment, ↑ HAM-D score, poor discharge planning

Importance of Relapse Prevention

- Each relapse associated with (short-term)
 - Increased distress and dysfunction
 - Vocational and social disruption
 - Increased risk of suicide and violence
 - Increased costs of care
- With each relapse (long-term)
 - Subsequent recovery is less complete
 - Remission takes longer to achieve
 - Illness becomes more resistant to treatment
 - Regaining prior function level more difficult

Guided Discontinuation vs Maintenance Treatment in Remitted First-Episode Psychosis: Relapse Rates and Functional Outcome

- DESIGN
 - 131 remitted first episode patients age 18–45 with < 3 months of antipsychotic (schizophrenia or related psychotic disorders)
 - Randomized to maintenance treatment (n = 63) or guided discontinuation (n = 68)
 - Followed for 18 months
- PRIMARY OBJECTIVES
 - Relapse: clinical deterioration for at least 1 week having consequences (med change, admission, more frequent visits) and PANSS positive item > 5

Relapse: Michael and Ryan

Michael

- Good insight into illness
- Returned to university
 - Intermittently adherent
 - 2 brief relapses
 - long-acting injectable antipsychotic
- Residual symptoms addressed
 - Negative symptoms and stress reactivity responded to L-Theanine
 - Cognition gradually improved

Relapse: Michael and Ryan

Ryan

- Poor insight
- Refused any antipsychotic
- Re-hospitalized after relapse
- Re-started on clozapine
- Began clozapine
 - Hallucinations and delusions much less severe
 - Residual symptoms included:
 - When “out and about” thinks other talking about him
 - Spirits talk to him infrequently, when stressed
 - Significant negative symptoms
 - Significant cognitive impairments


Progressive Loss of Gray and White Matter Occurs in Most Patients with Recurrent Episodes



First Treatment

Progressive Loss of Gray and White Matter Occurs in Most Patients with Recurrent Episodes (cont'd)

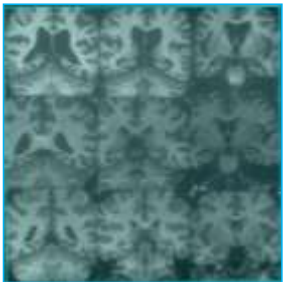
~ 1 Year Later



First Treatment

Progressive Loss of Gray and White Matter Occurs in Most Patients with Recurrent Episodes (cont'd)

~ 3 Years Later



~ 1 Year Later

First Treatment

Why Does the Brain Shrink?

- We don't find: Loss of large neurons
- What we find:
 - Regional loss of connections between neurons
 - Damage to insulation (myelin) of connections between neurons
 - Regional loss of small neurons (interneurons) and supporting cells (glia)
- Hypothesize these are potentially reversible:
 - Connections between neurons remodeled all the time
 - Myelin regrowth
 - New small neurons and supporting cells are regenerated

Recovery Factors

- Biology
- Timing
 - Intervene as early as possible
 - Manage then prevent relapses
- Treatment
 - Address residual symptoms
 - Engage families in recovery process

Factors Associated with Outcomes: Recovery/Residual

- Environment
 - Rural better than urban
 - Family and friends make a big difference

**Factors Associated with Outcomes:
Recovery/Residual**

Quality of treatment / Remediation interventions

- Social consequences of psychosis
 - Stigma; Family relationships; Friendships
- Psychological consequence psychosis
 - Self-stigma; Demoralization
- Biological consequences of psychosis/treatment
 - Higher dose antipsychotic may impair functional recovery
 - Prevent relapse; Control psychosis; Address residual symptoms

Recovery/Residual Stage

Michael

- Good insight into illness
 - Fully adherent to treatment
 - Well-developed illness management strategy
- Complete recovery
 - No symptoms
 - Full functional recovery
 - Lives independently

Ryan

- Partial insight
 - Family helps with adherence
- Partial recovery
 - No psychosis
 - Residual negative and cognitive symptoms
 - Attends community college part time
 - Lives with parents, active productive family member

Staged Intervention: Key Principles

- Attenuated Psychosis Syndrome
 - Accurate identification of syndrome
 - Evidence base supports psychotherapeutic treatment
 - Antipsychotics NOT indicated
- Early Active Phase: Psychosis
 - Intervene early (minimize time of untreated psychosis)
 - Adherence and relapse management key
- Recovery/Residual
 - Engage patient in recovery process
 - Patient needs good illness management strategies
 - Identify and address residual symptoms
 - Low-dose antipsychotic minimizes iatrogenic symptoms