



# Behavioral Health is Essential To Health



Prevention Works



Treatment is Effective



People Recover



# Treatment of Behavioral Health Disorders in Adolescents: Depression, Bipolar Disorder, Schizophrenia

ELINORE F. MCCANCE-KATZ, MD, PHD  
CHIEF MEDICAL OFFICER  
SUBSTANCE ABUSE AND MENTAL HEALTH SERVICES ADMINISTRATION  
CMHACY MAY 8, 2014



# Behavioral Health Disorders in Adolescents

- ▶ Common in adolescents
  - ▶ Major Depression
  - ▶ Bipolar Disorder
  - ▶ Attention Deficit Hyperactivity Disorder
  - ▶ Schizophrenia
  - ▶ Substance Use Disorders
    - ▶ Alcohol
    - ▶ Marijuana
    - ▶ Prescription Drugs (Opioids)

# Major Depression

- ▶ Rate of major depression in adolescents estimated to be 5%
- ▶ Low mood, irritability
- ▶ Difficulty with peer relationships
- ▶ Suicidality
- ▶ Treatment for Adolescents with Depression Study (TADS)
- ▶ (n=439, 12-17 yrs)
  - ▶ Examined:
    - ▶ Antidepressant (fluoxetine)
    - ▶ Cognitive Behavioral therapy (alone)
    - ▶ Combined therapy
    - ▶ Placebo (alone) with clinical management

# Treatments

- ▶ Fluoxetine: antidepressant medication, serotonin reuptake inhibitor; helps to normalize serotonin transmission
- ▶ CBT is a therapy that teaches a person how to better cope with the challenges of depression and life in general.
- ▶ education about depression, the possible causes and how to manage it.
- ▶ Setting realistic and positive personal goals
- ▶ encouraging participation in pleasant activities
- ▶ learning to solve social problems
- ▶ Discourage negative thinking
- ▶ Learning how to negotiate and compromise when conflicts arise
- ▶ Foster assertiveness

# TADS Results

- ▶ 12 weeks:
  - ▶ Best results: combined Fluoxetine and Cognitive Behavioral Therapy
  - ▶ 71 percent of participants receiving the combination treatment were much or very much improved.
  - ▶ fluoxetine alone, 61 percent improved
  - ▶ CBT alone, 44 percent improved
  - ▶ placebo, 35 percent improved
- ▶ By 36 weeks, the response rate to combination treatment still remained the highest (86 percent), while response rates to fluoxetine and CBT essentially caught up, at 81 percent each, although CBT had the slowest response rate.

# Suicidal Thinking

- ▶ Suicidal thinking decreased substantially in all active treatment groups.
- ▶ Those taking fluoxetine alone had higher rates of new suicidal thinking or behavior (15 percent) than those in combination treatment (8 percent) and those in CBT alone (6 percent)
- ▶ Most common in the early stages of treatment
- ▶ There were no suicides in the TADS study.

# What Do These Results Mean?

- ▶ Combination treatment is the safest and most effective treatment overall for adolescents with depression.
- ▶ Fluoxetine alone or in combination with CBT accelerates recovery from major depression compared to CBT alone.
- ▶ Response rate of CBT alone “catches up” to the response rate of fluoxetine alone several weeks later and to the combination therapy several months later.
- ▶ Adding CBT also appears to lessen the risk of suicidal thinking and behavior in patients given fluoxetine, and helps them develop new skills to contend with negative emotions.

Essau C, Dobson K. Epidemiology of depressive disorders. In: Essau C, Petermann F, eds. *Depressive Disorders in Children and Adolescents: Epidemiology, Course and Treatment*. Northvale, NJ: Jason Aronson Inc; 1999:69-103.

# Approved Antidepressants for Children

- ▶ escitalopram
- ▶ fluoxetine,
- ▶ fluvoxamine
- ▶ sertraline
- ▶ clomipramine (OCD)

<http://www.nimh.nih.gov/health/trials/practical/tads/index.shtml>

# Side Effects of SSRIs

- ▶ Nausea
- ▶ Insomnia
- ▶ Dizziness
- ▶ Weight gain or loss
- ▶ Tremors
- ▶ Sweating
- ▶ Anxiety and restlessness/agitation
- ▶ Decreased sex drive
- ▶ Drowsiness or fatigue
- ▶ Dry mouth
- ▶ Diarrhea or constipation
- ▶ Headaches
- ▶ Suicidal thinking

# Bipolar Disorder

- ▶ manic-depressive illness
- ▶ brain disorder that causes unusual shifts in mood, energy, and activity levels.
- ▶ Can be difficult to carry out day-to-day tasks, such as going to school or socializing with friends.
- ▶ Mood swings can be severe: euphoria/agitation/psychosis/severe depression, suicidality.
- ▶ Onset: >50% prior to age 25; often first episode in late teens; some presentations in early childhood
- ▶ Genetic contribution: children with bipolar parent six times more likely to develop BPD; but most children of parents with BPD do not develop disorder

# Symptoms of mania/depression in youth:

Symptoms of mania include:

- **Mood Changes** Being in an overly silly or joyful mood that is unusual for your child. It is different from times when he or she is just being silly and having fun.
- Having an extremely short temper and unusual irritability.

**Behavioral Changes** Sleeping little but not feeling tired

- Talking a lot and having racing thoughts
- Having trouble concentrating or paying attention, jumping from one thing to the next in an unusual way
- Talking and thinking about sex more often than usual
- Behaving in risky ways more often, seeking pleasure a lot, and doing more activities than usual.

Symptoms of depression include:

- **Mood Changes** Being in a sad mood that lasts a long time
- Losing interest in activities once enjoyed

• Feeling worthless or guilty.

**Behavioral Changes** Complaining about pain more often, such as headaches, stomach aches, and muscle pains

- Eating a lot more or less than usual and gaining or losing a lot of weight
- Sleeping or oversleeping when these were not problems before
- Losing energy
- Recurring thoughts of death or suicide.

# Mania

- ▶ Severe symptoms; last most of the day every day for at least one week
- ▶ Hypomania: more energy/higher activity than normal; not manic.
- ▶ generally lasts for at least 4 days in a row.

# Differences in Childhood/Adolescent v. Adult BPD

- ▶ BPD with onset in childhood or adolescence more severe than adult onset
- ▶ more frequent mood switches, more mixed episodes
- ▶ greater risk for attempting suicide than those whose symptoms start in adulthood
- ▶ BPD must be distinguished from ADHD, severe irritability with attention deficits which are diagnosed as severe mood dysregulation (SMD) and may develop into depression/anxiety in adulthood
- ▶ Proper diagnosis important to appropriate treatment
- ▶ Activity level, energy, sleep pattern, family history, substance use

# Medications

- ▶ Lithium: first line to treat bipolar disorder. Lithium is approved for the treatment and prevention of manic symptoms in children ages 12 and older; may act as an antidepressant and help prevent suicidal behavior.
- ▶ Side effects
- ▶ Restlessness
- ▶ Frequent urination
- ▶ Dry mouth
- ▶ Bloating or indigestion
- ▶ Acne
- ▶ Joint or muscle pain
- ▶ Brittle nails or hair
- ▶ Blood tests for lithium levels, kidney and thyroid functions periodically

# Lithium Toxicity

- ▶ Diarrhea
- ▶ Drowsiness
- ▶ Muscle weakness
- ▶ Lack of coordination
- ▶ Vomiting
- ▶ Risk of lithium toxicity goes up when a child becomes dehydrated
- ▶ Make sure child has enough to drink when he or she has a fever or sweats a lot during very active play or work.
- ▶ Lithium toxicity is a medical emergency and needs immediate care if these symptoms occur.

# Mood Stabilizers

- ▶ **Anticonvulsant medications**, originally developed to treat seizures, are also sometimes used as mood stabilizers.
- ▶ not approved by the FDA for treating bipolar disorder in children
- ▶ may be prescribed "off label"
- ▶ may be helpful for difficult-to-treat bipolar episodes
- ▶ valproic acid (Depakote) and lamotrigine (Lamictal)

# Mood Stabilizers

- ▶ Side Effects
- ▶ Drowsiness
- ▶ Dizziness
- ▶ Headache
- ▶ Diarrhea
- ▶ Constipation
- ▶ Heartburn
- ▶ Mood swings
- ▶ Stuffy or runny nose, or other cold-like symptoms
- ▶ Thoughts of suicide
- ▶ Increased testosterone in adolescent girls (valproate)
- ▶ Polycystic ovaries: obesity, excess body hair, an irregular menstrual cycle (valproate)

# Atypical antipsychotics

## ▶ Several approved by the FDA to treat youth with bipolar disorder:

- ▶ risperidone (Risperdal) 10 y
- ▶ aripiprazole (Abilify) 10-17 y
- ▶ quetiapine (Seroquel) 10-17 y  
(extended release can be used in children)
- ▶ olanzapine (Zyprexa) 13-17 y

## ▶ Side Effects

- ▶ Drowsiness
- ▶ Dizziness when changing positions
- ▶ Blurred vision
- ▶ Rapid heartbeat
- ▶ Sensitivity to the sun
- ▶ Skin rashes
- ▶ Menstrual problems for girls
- ▶ Weight gain
- ▶ Metabolic syndrome: weight gain, hyperlipidemia, diabetes (monitor cholesterol, glucose, weight)

# Antidepressants Approved for Use in Youth

- ▶ fluoxetine (Prozac)
  - ▶ clomipramine
  - ▶ fluvoxamine (Luvox)
  - ▶ sertraline (Zoloft)
  - ▶ Escitalopram (Lexapro)
- Tricyclic antidepressants: imipramine

## Side Effects

- ▶ Headache
- ▶ Nausea
- ▶ Sleep problems, such as sleeplessness or drowsiness
- ▶ Agitation (feeling jittery)
- ▶ Sexual problems
- ▶ Suicidal thinking
- ▶ Can be associated with rapid cycling
- ▶ Antidepressants with mood stabilizer may be no better than mood stabilizer alone

# Psychotherapies are part of treatment of Bipolar Disorder

- ▶ **Cognitive behavioral therapy:** helps change harmful or negative thought patterns and behaviors.
- ▶ **Family-focused therapy:** includes a child's family members. It helps enhance family coping strategies, such as recognizing new episodes early and helping their child; improves communication and problem-solving.
- ▶ **Interpersonal and social rhythm therapy:** helps children and teens with bipolar disorder improve their relationships with others and manage their daily routines. Regular daily routines and sleep schedules may help protect against manic episodes.
- ▶ **Psychoeducation:** teaches young people with bipolar disorder about the illness and its treatment. helps people recognize signs of an impending relapse, allowing them time to seek treatment early, before a full-blown episode occurs. may be helpful for family members and caregivers.

<http://www.nimh.nih.gov/health/publications/bipolar-disorder-in-children-and-adolescents/index.shtml>

# Schizophrenia

- ▶ Brain disorder: chronic, can be severe and disabling
- ▶ Symptoms:
  - ▶ Hallucinations, delusions which are disturbing to the person and produce agitation
  - ▶ Thought disorder: speech may not make sense or very little speech
  - ▶ Negative symptoms: flat affect, poverty of speech, little pleasure in life activities, lack of ability to begin/sustain activities
  - ▶ Cognitive Symptoms: difficulty understanding/assessing information to make decisions, attention and concentration problems, problems with working memory (ability to use information immediately after learning it; remembering things in immediate past that are needed to undertake activities/work/school)
  - ▶ Social withdrawal
  - ▶ Difficulty with relationships, school performance, employment
  - ▶ Most will cope with some level of symptoms for their lifetimes, but there is a wide variation in severity and with treatment/support can live rewarding and meaningful lives in their communities

# Schizophrenia: Causes

- ▶ Genetic Factors: runs in families: 1% of general population affected, but 10% of family members with a first degree relative who has schizophrenia; no single gene responsible; may be a combination of genes; people with schizophrenia have higher rates of rare mutations in genes that control brain development
- ▶ Environment: maternal exposure to viruses or malnutrition before birth, problems during birth, psychosocial factors not well defined as yet
- ▶ Brain chemistry and structure: neurotransmitter function (DA/Glu); enlarged ventricles, fetal brain development is altered with abnormal distribution of some neurons possibly leading to faulty connections with other cells.
- ▶ May not see symptoms until puberty when brain undergoes major changes; but psychosis may develop in adolescence/early adulthood and this is when diagnosis is made

# Early Intervention

Can we predict psychosis?

North American Prodrome Longitudinal Study

(individuals identified to be at high risk for psychosis; age: 13-23 y)

## **5 Predictors identified:**

1. Genetic risk with recent deterioration in function
2. High levels of unusual thought content
3. High levels of paranoia/suspiciousness
4. Social impairment
5. \*Substance abuse\* may produce psychosis-promoting changes in brain

35% conversion rate in 2.5 years of follow up

Cannon TD, et al.: Am J Psychiatry 65: 28, 2008

# Early Intervention

- ▶ Nelson B et al. JAMA Psychiatry 70(8): 793-802, 2013
- ▶ Up to 15 years of follow up of a cohort identified as at high risk for psychosis: those with attenuated (subthreshold) psychotic symptoms, those with brief psychosis that spontaneously resolved; genetic vulnerability with low function
- ▶ Highest risk within 2 years of study entry
- ▶ But risk up to 10 years overall
- ▶ Risk of psychosis 34.9% within 10 years of identification
- ▶ Recommended following those at high risk and offering interventions:
  - ▶ Supportive psychotherapy
  - ▶ Omega fatty acids
  - ▶ Cognitive behavioral therapy
  - ▶ No antipsychotics

# Early Intervention

- ▶ May be able to delay or prevent onset of psychotic illness
- ▶ Psychosocial interventions: address low motivation, school failure, social withdrawal and isolation
- ▶ Antipsychotic medication: because of risk of adverse side effects; usually reserved until frank psychosis occurs

# First Episode Psychosis: Modifiable Factors

- ▶ At initiation of treatment of the psychosis; duration of psychosis was found to be correlated with severity of negative symptoms, but not positive symptoms or general psychopathology
- ▶ Short duration of psychosis: study definition varied (4 wks-1 year) vs. long duration > 1 year
- ▶ Shorter duration of untreated psychosis correlates with:
  - ▶ Greater response to antipsychotic treatment
  - ▶ Better resolution of positive (hallucinations) and negative (social withdrawal) symptoms
  - ▶ Improved functional outcomes

Perkins et al. Am J Psychiatry 162: 1785-1804, 2005

# Schizophrenia: Treatment

- ▶ Treatments are aimed at symptom reduction/resolution; no medication can cure; psychosocial treatments can be helpful
- ▶ **Medications: Antipsychotics**
- ▶ First generation (first produced in 1950s); 'typical' antipsychotics
- ▶ Chlorpromazine (Thorazine)
- ▶ Haloperidol (Haldol)
- ▶ Perphenazine (Etrafon, Trilafon)
- ▶ Fluphenazine (Prolixin)

# Second generation antipsychotics

- ▶ Less tremor/rigidity so offered advantages over first generation drugs
- ▶ Risperidone (Risperdal)
- ▶ Olanzapine (Zyprexa)
- ▶ Quetiapine (Seroquel)
- ▶ Ziprasidone (Geodon)
- ▶ Aripiprazole (Abilify)
- ▶ Paliperidone (Invega)

# Side Effects of Antipsychotics

- ▶ Sedation
- ▶ Dizziness
- ▶ Rapid heartbeat
- ▶ Sun sensitivity
- ▶ Blurred vision
- ▶ Menstrual irregularities
- ▶ **“Typical” Antipsychotics**
  - ▶ Tremor
  - ▶ Stiffness
  - ▶ Akithesia/restlessness
- ▶ **“Atypical” Antipsychotics: metabolic syndrome**
  - ▶ Increased weight, lipids (cholesterol) (risk of cardiovascular disease), diabetes requires ongoing monitoring
- ▶ **Long term:** Tardive dyskinesia: abnormal, uncontrollable movements in face, mouth, tongue, trunk
  - ▶ Often responds to dose reduction or cessation of medication

# Comparison of first/second generation antipsychotics in first episode psychosis

- ▶ Olanzapine vs. haloperidol
- ▶ Both effective in reducing psychotic symptoms; positive and negative symptoms
- ▶ Olanzapine: significantly less parkinsonism and akathisia, but significantly more weight gain
- ▶ 12 week study period showed higher rates of completion in those randomized to olanzapine than haloperidol

Lieberman et al. Am J Psychiatry 160:1396-1404, 2003

# Clozaril: Treatment Resistant Schizophrenia

- ▶ Treatment of choice for schizophrenia symptoms that do not resolve with other antipsychotics
- ▶ Major concern:
- ▶ Agranulocytosis (production of white blood cells ceases)
- ▶ Requires blood count before every prescription is filled

# Schizophrenia: Course of Acute Psychotic Episode Treatment

- ▶ Symptoms such as feeling agitated, hallucinations usually resolve within days of treatment
- ▶ Delusions usually resolve within a few weeks.
- ▶ After about six weeks with continued treatment many people will see substantial improvement.
- ▶ **Relapse can occur:**
- ▶ When medication is stopped or when taken intermittently (most common reason for relapse (relative risk: 4)
- ▶ Some people stop taking the medication because they feel better or they may feel they don't need it anymore which is a risk factor for relapse
- ▶ Antipsychotics should not be abruptly stopped; taper should occur

# Psychosocial Treatments

- ▶ Can be important to recovery following stabilization on medication
- ▶ Psychosocial treatments can help with the everyday challenges of the illness, such as difficulty with communication, self-care, work, and forming and keeping relationships.
- ▶ Learning and using coping mechanisms to address these problems allow people with schizophrenia to socialize and attend school and work.
- ▶ More likely to adhere to medication, less likely to relapse

# Types of Psychosocial Treatment

- ▶ **Illness management skills:** Education about illness so that individual can make their own treatment decisions; learn about warning signs and how to respond, learn how to prevent relapse
- ▶ **Rehabilitation:** programs can include job counseling and training, money management counseling, help in learning to use public transportation, and opportunities to practice communication skills; increases social interactions
- ▶ **Family Education:** family members can help their loved one by learning coping strategies and problem solving skills
- ▶ **Cognitive-behavioral therapy:** patients learn how to test the reality of their thoughts and perceptions, how to "not listen" to their voices, and how to manage their symptoms overall
- ▶ **Self-help groups:** for individuals and their families provide support, source of advocacy for those struggling with the disease and can work to help public understand the discrimination that many with serious mental illness face

# Schizophrenia and Substance Abuse

- ▶ Most common co-occurring disorder is substance abuse
- ▶ Integrated programs needed
- ▶ Standard substance abuse treatment programs will not focus on needs of this population
- ▶ Tobacco is most frequently used substance (75-90% smoke and smoking related illness is responsible for substantial shortening of life in this population)
- ▶ NRT may be better approach as nicotine seems to assist with some of the cognitive issues in schizophrenia
- ▶ Issues of drug interactions (products of cigarette smoke may induce metabolism of antipsychotic medications; emphasizes the need to monitor carefully with smoking cessation for changes needed in medication dosages)

# Long Term Outcomes of Treatment

- ▶ Antipsychotic medication? For how long? How best to use it?
- ▶ Current guidelines: stabilization and one year of antipsychotic treatment, taper and close monitoring with re-institution if symptoms recur
- ▶ Wunderink et al. JAMA Psychiatry, July 3, 2013:
- ▶ 2 year study of First Episode Psychosis outcomes (n= 128)
- ▶ After 6 months of remission; random assignment to dose reduction and discontinuation (DR) vs. medication maintenance treatment (MT) for 18 mos. Then treatment as clinically determined based on symptoms/course of illness
- ▶ After 7 year follow up the DR group experienced twice the recovery of the MT group (40% vs. 18%).
- ▶ Better DR recovery rates were related to higher functional remission rates (self care, housekeeping, family/partner/peer relationships, social integration, vocational function), but not to symptomatic remission rates
- ▶ Symptomatic remission (DR 69% MT 66%); functional remission (DR 46% MT 20%); 28% neither symptomatic or functional remission
- ▶ Relapse initially higher in the DR group, but at 3 years the differences resolved and rates were similar
- ▶ No relapses occurred in 35% (DR 38.5% MT 31.4%)
- ▶ Antipsychotic dose last two years of follow up: DR 2.2 (2.27) mg v. MT 3.6 (4.01) p=0.03; some were able to successfully stop medications without relapse
- ▶ Less antipsychotic load may be associated with enhanced function by removing medication effects on alertness, curiosity, drive, executive function

# What does it all mean?

- ▶ Schizophrenia/psychotic disorders are chronic diseases
- ▶ It is possible to identify those at high risk and to provide interventions before psychosis either delaying or preventing onset of full blown psychosis that may enhance the lives of those affected
- ▶ Medications effective for remitting symptoms are available and have different side effect profiles; monitoring will be required for safe and effective use
- ▶ How long to treat is an open question at this point with recent studies calling into question the one year course/follow up
- ▶ Shorter treatment periods may be possible with greater function over the long term
- ▶ Questions now should be: what medication, for how long, in what dose (as low as possible), and what psychosocial interventions will be needed to get well, stay well and lead productive lives?

# Citations

- ▶ [http://www.nimh.nih.gov/health/topics/schizophrenia/index.shtml?utm\\_source=publish2&utm\\_medium=referral&utm\\_campaign=www.kpbs.org](http://www.nimh.nih.gov/health/topics/schizophrenia/index.shtml?utm_source=publish2&utm_medium=referral&utm_campaign=www.kpbs.org)
- ▶ Cannon TD, et al.: Am J Psychiatry 65: 28, 2008 Antidepressant Medications: Use in Pediatric Patients
- ▶ Centers for Medicare and Medicaid Services: Antidepressant Medications: Use in Pediatric Patients Fact Sheet: August 2013
- ▶ Perkins et al. Am J Psychiatry 162: 1785-1804, 2005
- ▶ Lieberman et al. Am J Psychiatry 160:1396-1404, 2003
- ▶ Carillo, AJ, et al.: Role of the smoking-induced cytochrome P450 (CYP)1A2 and polymorphic CYP2D6 in steady-state concentration of olanzapine. J Clin Psychopharmacol 23:119-127, 2003.
- ▶ Sharif ZA: Pharmacokinetics, metabolism, and drug-drug interactions of atypical antipsychotics in special populations. Primary care companion J Clin Psychiatry Suppl 6: 22-25, 2003
- ▶ <http://www.nimh.nih.gov/health/publications/bipolar-disorder-in-children-and-teens-easy-to-read/index.shtml>.
- ▶ <http://www.nimh.nih.gov/health/publications/bipolar-disorder-in-children-and-adolescents/index.shtml>
- ▶ <http://www.nimh.nih.gov/health/trials/practical/tads/index.shtml>
- ▶ <http://www.drugabuse.gov/publications/principles-adolescent-substance-use-disorder-treatment-research-based-guide>
- ▶ Nelson B et al. JAMA Psychiatry 70(8): 793-802, 2013
- ▶ Wunderink et al. JAMA Psychiatry, July 3, 2013