

A person wearing a dark hoodie is seen from behind, sitting on a windowsill and looking out a large window. The window is divided into several panes by dark frames. Outside the window, a bright, overexposed landscape with trees is visible. The overall mood is contemplative and somewhat somber.

Recognition and Treatment of Depression in Youth

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IHS/CAO Best Practices Conference
Monday, May 22, 2017

Outline

- Prevalence
- Etiology
- Pathophysiology
- Differences between depression in adults and children
- Screening
- Interview tips
- Treatment



Prevalence

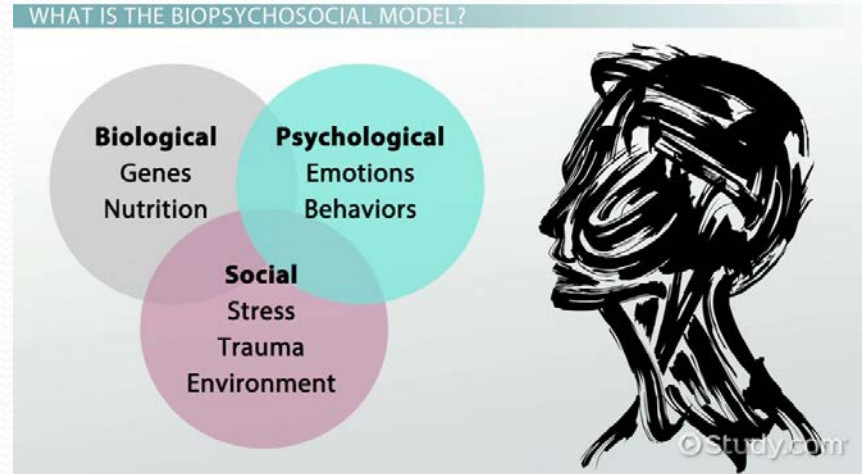
- Large difference in prevalence depending whether self report vs structured clinical diagnosis
- Apples to apples comparison , National Surveys on Drug Use and Health, which is self report, shows increase in 12 month prevalence of adolescent depression (12-17 yo) from 8.7% in 2003 to 11.3% in 2014 (Mojtabi, Olfson, Han, 2016)
- Prevalence in more rigorously defined samples are about 5% in adolescents, and less in younger populations
- Recent prevalence rates for depression in AI/AN youth are lacking. Higher suicide rates in AI/AN young adults compared with gen pop (22 vs 12 per 100,000, CDC 2012-13) suggest higher rates of depression in AI/AN adolescents

Etiology

Etiology of adolescent depression follows classic nature/nurture and biopsychosocial paradigm

Biopsychosocial model

- In general, the larger the genetic risk, the smaller amount of other factors need to be present for expression of depressive illness
- Conversely, with enough stress, only moderate (but, some) genetic risk need exist



Heritability Risk Factors



- In general, the earlier onset the depression, the larger the genetic contribution
- Odds ratio of depression with one parent with depression is 3.0
- The more severe the parental depression, the higher the odds ratio
(www.depressiongenetics.stanford.edu)

Genetic vulnerability mechanisms

- Short allele in 5-HTTLPR (serotonin receptor promoter region) leading to decreased serotonergic activity → less ability to self soothe
- Some “risk” variants of CRHR1 (corticotropin-releasing hormone receptor) genes have been identified, leading to decreased CRH and, therefore increased cortisol levels in response to stress, as compared with individuals with “non-risk” (Heim C, Binder E, 2011)
- “Risk” variants of gene encoding BDNF (brain derived neural factor) cannot stimulate the development of new neurons as rapidly
- Infants born with risk variant of BDNF gene have smaller hippocampi (aan het Rot M, Mathew SJ, Charney DS, 2009)



Epigenetic mechanisms

- Epigenetic modification (sometimes referred to as G x E) refers to change in the function of genes, without changing structure (e.g. turns genes on and off) in the presence of different environmental elements (e.g. childhood maltreatment)
- Children with the 5-HTTLPR and CRHR1 vulnerabilities, exposed to stress, have changes in brain function which then cause failure to develop normal resilience mechanisms
- The timing of stress (in general first 3y>4-10y>11+y) is very important in long term risk of depression, which is consistent with what we know about age and neuroplasticity

Stress-related factors

- Harlow's monkeys showed extreme, lifelong emotional and social dysfunction with early maternal separation



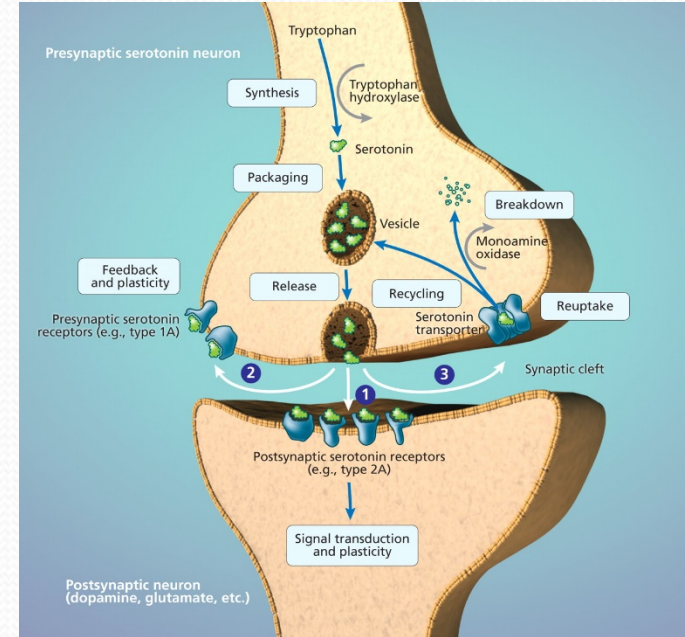
Stress Related Risk Factors (cont'd)

- Maternal depression (emotional separation) has been shown to alter newborn EEG activity
- Adverse childhood events, particularly maltreatment have been associated with early and more severe expression of depressive illness (OR 4.0)



Neurobiological Pathophysiology

- Monoamine hypothesis which was thought to be cause of depression during 1960-90's has been found to be only part of the story
- Now considered a downstream effect rather than cause

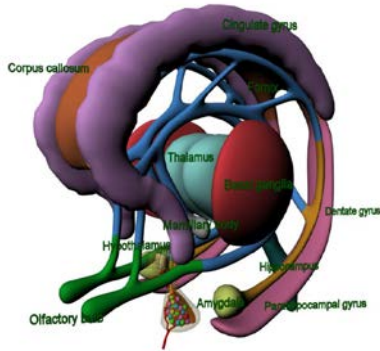


aan het Rot M, Mathew SJ, Charney DS, 2009

Pathophysiology (cont'd)

- Research conducted in the late 90's to present have shown greater role of oxidative stress and inflammation in both grey and white matter structures
- Biomarkers of inflammation including C-reactive protein and cytokines are elevated in individuals with major depression
- Chronic stress causes chronically elevated cortisol, which leads to chronically elevated glutamate which leads to cascade that causes cell damage and death

Abnormalities in Structure of Brain Loci

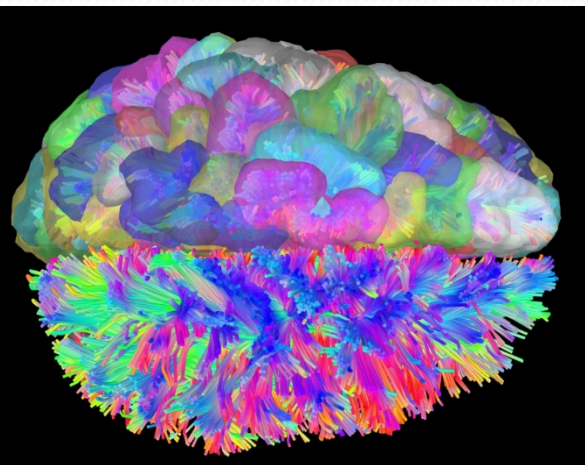


Limbic system abnormalities have long been known to be associated with depression

- More recent research has shown roles of specific loci:
 - Smaller hippocampi in early childhood dep ----> Linked to decreased working memory, which limits behavioral adaptation
 - Ventromedial prefrontal cortex is smaller in depressed children (Marrus et. al, 2015)

Neural Network Abnormalities

Functional MRI of depression have shown disrupted network connectivity:



- Amygdala - Dorsomedial PFC ----> Increased activity in this network enhances negative self-assessment
- Amygdala - Dorsolateral PFC ----> Decreased activity in this network leads to decreased problem solving and helplessness

Dixon et. al. , doi:10.1037/bul0000096 (prepublication)

Presentation of Depression in Youth

Though the phenomenology and presentation of vary according to developmental stage and age, DSM5 uses the same diagnostic criteria for depression in youth as for adults

Coinciding with the termination of puberty at 14-15 years old, depression in this age group looks very much like adult depression



Factors in Differential Presentation

- Greater difficulty with younger children in “mentalization” and description of their internal states
- Difficulty with adult concept of time and comparisons (greater/lesser)

Preschool Onset of Depression

- Irritability is the most frequent presenting affective state at this age, and externalization of affect is common
- Many times this comes in the form of disruptive behavior/ “acting out”
- On the differential with other externalizing conditions such as ADHD, Oppositional Defiant Disorder, Reactive Attachment Disorder, Separation Anxiety and PTSD
- If urinary continence has been recently attained, new-onset depression will sometimes be accompanied by enuresis



Early School Aged (5-10) Presentation

- Will more commonly look “sad”
- Will feel isolated
- Will usually withdraw from others, but sometimes at the same time will be more clingy with caregiver
- Usually deterioration in academic performance
- Sometimes will result in school refusal
- Sometimes will affect appetite and sleep

Depression in Adolescents



- Presents frequently like depression in adults after about 14 years old with respect to neuro-vegetative symptoms
- Negative ruminations frequently include themes of rejection from peers, worthlessness and low self esteem frequent

Depression Screening in Older Adolescents

- Because depression physically similar in adolescents, PHQ-9 is valid in this age group
- For some adolescents, can be valid down to 12



Depression Screening in Preteen and Younger Adolescents



- PHQ-A adapted from PHQ-9
- Validated for ages 11 through 17
- Same questions from DSM5 but in easier language

Depression Screening in School Age Youth

- United States Preventive Services Task Force does not recommend routine screening under 11 due to insufficient evidence
- However, if depression is suspected in a school age child, diagnostic rating scales should be considered

Diagnostic Aids for Depression in School Age

- Self report:
 - Children's Depression Inventory (CDI)
 - Mood and Feelings Questionnaire (MFQ)
 - Columbia Depression Scale (CDS)



Mood and Feelings Questionnaire (MFQ)

Child Self-Report

MOOD AND FEELINGS QUESTIONNAIRE: Long Version

This form is about how you might have been feeling or acting **recently**.

For each question, please check (✓) how you have been feeling or acting ***in the past two weeks***.

If a sentence was not true about you, check NOT TRUE.

If a sentence was only sometimes true, check SOMETIMES.

If a sentence was true about you most of the time, check TRUE.

Score the MFQ as follows:

NOT TRUE = 0

SOMETIMES = 1

TRUE = 2

To code, please use a checkmark (✓) for each statement.	NOT TRUE	SOME TIMES	TRUE
1. I felt miserable or unhappy.			
2. I didn't enjoy anything at all.			
3. I was less hungry than usual.			
4. I ate more than usual.			
5. I felt so tired I just sat around and did nothing.			
6. I was moving and walking more slowly than usual.			
7. I was very restless.			
8. I felt I was no good anymore.			
9. I blamed myself for things that weren't my fault.			
10. It was hard for me to make up my mind.			
11. I felt grumpy and cross with my parents.			
12. I felt like talking less than usual.			
13. I was talking more slowly than usual.			
14. I cried a lot.			

Columbia Depression Scale

Columbia Depression Scale (Ages 11 and over)

Present State (last 4 weeks)

TO BE COMPLETED BY PARENT OF MALE CHILD

If the answer to the question is "No," circle the 0; if it is "Yes," circle the 1.
Please answer the following questions about your son (male child) as honestly as possible.

In the last four weeks ...	No	Yes
1. Has he often seemed sad or depressed?	0	1
2. Has it seemed like nothing was fun for him and he just wasn't interested in anything?	0	1
3. Has he often been grouchy or irritable and often in a bad mood, when even little things would make him mad?	0	1
4. Has he lost weight, more than just a few pounds?	0	1
5. Has it seemed like he lost his appetite or ate a lot less than usual?	0	1
6. Has he gained a lot of weight, more than just a few pounds?	0	1
7. Has it seemed like he felt much hungrier than usual or ate a lot more than usual?	0	1
8. Has he had trouble sleeping – that is, trouble falling asleep, staying asleep, or waking up too early?	0	1
9. Has he slept more during the day than he usually does?	0	1
10. Has he seemed to do things like walking or talking much more slowly than usual?	0	1

CHILD & ADOLESCENT PSYCHIATRY

11. Has he often seemed restless ... like he just had to keep walking around?	0	1
12. Has he seemed to have less energy than he usually does?	0	1
13. Has doing even little things seemed to make him feel really tired?	0	1
14. Has he often blamed himself for bad things that happened?	0	1
15. Has he said he couldn't do anything well or that he wasn't as good looking or as smart as other people?	0	1
16. Has it seemed like he couldn't think as clearly or as fast as usual?	0	1
17. Has he often seemed to have trouble keeping his mind on his [schoolwork/work] or other things?	0	1
18. Has it often seemed hard for him to make up his mind or to make decisions?	0	1
19. Has he said he often thought about death or about people who had died or about being dead himself?	0	1
20. Has he talked seriously about killing himself?	0	1
21. Has he EVER, in his WHOLE LIFE, tried to kill himself or made a suicide attempt?	0	1
22. Has he tried to kill himself in the last four weeks?	0	1

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For additional free copies of this instrument, contact: Columbia DISC Development Group, 1051 Riverside Drive, New York, NY, 10032.

Interview tips

- Ask about relationships (specifically, ask if it seems like other people, like friends or family don't them, this is almost always present in school age youth)
- Ask about grades
- Ask about bullying
- Ask both parent and child about changes in the family

Interview tips (cont'd)

- Though suicide attempts rare under the age of 10, still best to ask about thoughts of self harm regardless of the age
- In adolescents (and pre-adolescents), ask about drug use

Treatment General Principles

- Management is usually age and severity dependent
- Psychotherapy is indicated for all cases of childhood depression
- In general, suspected depression in youth under 11 years should be referred to specialty mental health services
- Youth who are acutely suicidal should be referred for emergency evaluation (ED is usual entry point)

Referring Youth 11 Years and Younger

- Most licensed mental health clinicians (including LCSWs, MFTs, LPCC, psychologists and some psychiatrists) are qualified to diagnose depression in youth
- Some mental health clinicians (any credential) are qualified to provide therapy
- Those clinicians who identify as child therapists are generally best suited to provide therapy to children

Referrals for Youth 12 and Over

- Psychotherapy referral principles similar to younger age group, but usually more options, because more clinicians comfortable with this age group
- In general, the younger the patient the more specialized the assessment and treatment
- Many adult psychiatrists (especially in public sector) are willing to treat adolescents when no child psychiatry available

Management of adolescent depression in primary care

- GLAD-PC – Guidelines for Adolescent Depression in Primary Care
- This resource available at www.gladpc.org
- 151 page “toolkit” which provides comprehensive guidance on assessment, referral and treatment of depressed teens

Guidelines for Adolescent Depression in Primary Care



Adolescent Depression Therapy Management

- With mild depression, sometimes basic problem solving with primary care provider, child and sometimes parent is adequate for successful outcome
- PST-PC, Problem Solving Therapies for Primary Care is an evidence based treatment that can sometimes be used for mild adolescent depression

PST-PC

- On the SAMHSA NREPP
- 6 to 10, 30 minute sessions
- Can get certified by UW

The screenshot shows a web browser displaying a BMJ article. The browser's address bar shows the URL: <http://www.bmj.com/content/320/7226/26.long>. The page features a blue header with the BMJ logo and navigation links: Research, Education, News & Views, Campaigns, and Search. Below the header, there's a section for 'General Practice' with the article title: 'Randomised controlled trial of problem solving treatment, antidepressant medication, and combined treatment for major depression in primary care'. The article is dated 2000 and has a DOI of 10.1136/bmj.320.7226.26. The authors listed are Laurence M Mynors-Wallis, Dennis H Gath, Ann Day, Frances Baker, and research general practitioner. The article is accepted for publication on 11 August 1999. The abstract states: 'Objectives: To determine whether problem solving treatment combined with antidepressant medication is more effective than either treatment alone in the management of major depression in primary care. To assess the effectiveness of problem solving treatment when given by practice nurses compared with general practitioners when both have been trained in the technique.' On the right side, there's a sidebar with 'Article tools' including PDF, Respond to this article, Print, Alerts & updates, Citation tools, Request permissions, Author citation, Add article to BMJ Portfolio, and Email to a friend. Below that, there's a 'Topics' section with links to 'Mood disorders (including depression)' and 'General practice / family medicine'.

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General Practice

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BMJ 2000 ; 320 doi: <https://doi.org/10.1136/bmj.320.7226.26> (Published 01 January 2000)
Cite this as: BMJ 2000;320:26

Article Related content Metrics Responses

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Accepted 11 August 1999

Abstract

Objectives: To determine whether problem solving treatment combined with antidepressant medication is more effective than either treatment alone in the management of major depression in primary care. To assess the effectiveness of problem solving treatment when given by practice nurses compared with general practitioners when both have been trained in the technique.

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Moderate to Severe Depression in Adolescents

- Psychotherapy should usually be included
- Medication management should be strongly considered



Evidence-based psychotherapy for adolescent depression

Strong evidence for efficacy of:

- Cognitive-behavioral therapy
- Interpersonal therapy
- Most good therapists include elements of CBT, even if not formally performed

Medication therapy

- High placebo response in children and adolescent has made it difficult to demonstrate medication efficacy
- As a result, relatively few FDA-approved antidepressant medications for youth



FDA-approved Antidepressant- Fluoxetine

- Fluoxetine (Prozac) FDA-approved in 2003 for depression in youth 8 and over
- Has the largest research base in children
- Comes in a liquid
- Has 4-5 day half life, so if adolescents who frequently forget meds, can be helpful (even a once per week formulation)

Other FDA-approved SSRIs

- Escitalopram (Lexapro)- Approved for depression for youth over 12 years
- Though not proven in the literature, escitalopram tends to be less activating than fluoxetine
- Sertraline – approved for OCD, age 6 and over
- Fluvoxamine - approved for OCD age 8 and over
- Despite lack of FDA-approval for depression, last two safe and probably effective for depression

Other Medications, FDA-approved for Other Conditions, Sometimes Used for Childhood Depression

- Imipramine - FDA approved for childhood enuresis ages 6 and over, most freq used prior to SSRIs for childhood depression
- Clomipramine - FDA approved for OCD ages 10 and over
- Duloxetine - FDA approved for GAD, 7 and up

Non FDA-approved Antidepressants Also Sometimes Used in Children

- Bupropion sometimes helpful for youth with co-occurring ADHD. Though not FDA approved for ADHD, some research support
- Mirtazapine has research support for depression and anxiety in adolescents. More clinical trials being done
- Contra-indicated – Recent studies have indicated paroxetine neither effective, nor safe in youth

Other therapies

Combined therapy shown to be more effective than either psychotherapy or medication therapy alone

Family therapy can be good adjunct in case of family dysfunction

Sprenger D and Josephson A, 1998

FDA Black Box Warning

- In 2004, the FDA placed a “black box” warning on all anti-depressant use
- This was after a meta-analysis of 372 DBPCT's of antidepressant therapy which showed increased suicidal thinking (4% vs 2%) on medication vs placebo
- No completed suicides in data set

Re-visit of Black Box

- Re-analysis of black box data has called into question validity of conclusion, based on fact of retrospective data and suicidal ideation as secondary outcome
- Further, epidemiologic studies since have shown an increase in suicide rates correlated with the decrease in antidepressant use

Guidelines for use

- Further analysis of black box data showed most first 7-14 days post initiation of medication most significant
- Therefore, recommended to follow-up in one week
- Suggest using FDA-approved meds unless good reason not to (e.g. parent responded differentially to sertraline, Lexapro induced mania in sibling, etc)
- Education of patient and family regarding signs of increased risk (especially agitation)



Summary

Depression in youth can cause life long disability if untreated

Early identification can decrease the risk of relapse and/or severity of subsequent episodes

Due to early vulnerability, intervention with at-risk mothers may be necessary to reverse the increasing prevalence of depression in youth

With integrated treatment models (physical health and behavioral health) childhood treatment can be effectively treated in even in settings with relative few resources



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