



Emotional Dysregulation and Mania

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Disclosures

My spouse/partner and I have the following relevant financial relationships with commercial interests to disclose:

Dr. Janet Wozniak receives research support from the Baszucki Brain Research Fund, PCORI and Demarest Lloyd, Jr. Foundation. In the past, Dr. Wozniak has received research support, consultation fees or speaker's fees from Eli Lilly, Janssen, Johnson and Johnson, McNeil, Merck/Schering-Plough, the National Institute of Mental Health (NIMH) of the National Institutes of Health (NIH), Pfizer, and Shire. She is the author of the book, *"Is Your Child Bipolar"* published May 2008, Bantam Books.

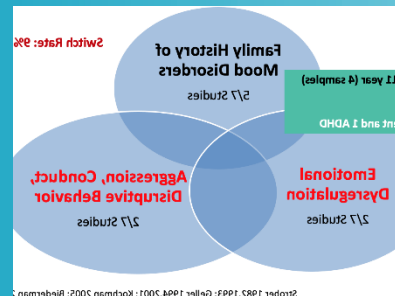
Her spouse receives royalties from UpToDate; consultation fees from Emalex, Noctrix, Disc Medicine, Avadel, HALEO, OrbiMed, and CVS; and research support from Merck, NeuroMetrix, American Regent, NIH, NIMH, the RLS Foundation, and the Baszucki Brain Research Fund. In the past, he has received honoraria, royalties, research support, consultation fees or speaker's fees from: Otsuka, Cambridge University Press, Advance Medical, Arbor Pharmaceuticals, Axon Labs, Boehringer-Ingelheim, Cantor Colburn, Covance, Cephalon, Eli Lilly, FlexPharma, GlaxoSmithKline, Impax, Jazz Pharmaceuticals, King, Luitpold, Novartis, Neurogen, Novadel Pharma, Pfizer, Sanofi-Aventis, Sepracor, Sunovion, Takeda, UCB (Schwarz) Pharma, Wyeth, Xenoport, Zeo.



Overview:

Emotional dysregulation can be considered as a separate entity from mood disorders

Emotional dysregulation is conceptualized as deficits in cortical self regulation of emotions



Children with Emotional Dysregulation often switch:
Emotional dysregulation is a predictor of bipolar disorder

The CBCL can operationalize levels of emotional dysregulation:
Deficient Emotional Self-Regulation versus Severe Emotional Dysregulation

Emotional Dysregulation

- does not necessarily lead to extreme moods
- subsides relatively rapidly
- is conceptualized as deficits in cortical self regulation of emotions
- an inability to effectively modulate emotional responses

Please print **CHILD BEHAVIOR CHECKLIST FOR AGES 6-18**

Please print. Be sure to answer all items.

Below is a list of items that describe children and youths. For each item that describes your child now or within the past 6 months, please circle the 2 if the item is very true or often true of your child. Circle the 1 if the item is somewhat or sometimes true of your child. If the item is not true of your child, circle the 0. Please answer all items as well as you can, even if some do not seem to apply to your child.

0 = Not True (as far as you know) 1 = Somewhat or Sometimes True 2 = Very True or Often True

0 1 2	1. Acts too young for his/her age	0 1 2	120. Statements about the child's behavior
0 1 2	2. Drinks alcohol without parents' approval (describe)	0 1 2	1. Acts too young for his/her age
0 1 2	3. Argues a lot	0 1 2	2. Drinks alcohol without parents' approval (describe)
0 1 2	4. Falls to finish things he/she starts	0 1 2	3. Argues a lot
0 1 2	5. There is very little he/she enjoys	0 1 2	4. Falls to finish things he/she starts
0 1 2	6. Bowel movements outside toilet	0 1 2	5. There is very little he/she enjoys
0 1 2	7. Blagging, teasing	0 1 2	6. Bowel movements outside toilet
0 1 2	8. Can't concentrate, can't pay attention for long	0 1 2	7. Blagging, teasing
0 1 2	9. Can't get his/her mind off certain thoughts, ideas, or feelings (describe)	0 1 2	8. Can't concentrate, can't pay attention for long
0 1 2	10. Can't sit still, restless, or hyperactive	0 1 2	9. Can't get his/her mind off certain thoughts, ideas, or feelings (describe)
0 1 2	11. Cries a lot, especially if denied something	0 1 2	10. Can't sit still, restless, or hyperactive
0 1 2	12. Exaggerates or makes up stories	0 1 2	11. Cries a lot, especially if denied something
0 1 2	13. Lying or cheating	0 1 2	12. Exaggerates or makes up stories
0 1 2	14. Telling lies	0 1 2	13. Lying or cheating
0 1 2	15. Truancy	0 1 2	14. Telling lies
0 1 2	16. Using force	0 1 2	15. Truancy
0 1 2	17. Vandalism	0 1 2	16. Using force
0 1 2	18. Verbal abuse	0 1 2	17. Vandalism
0 1 2	19. Violence	0 1 2	18. Verbal abuse
0 1 2	20. Withdrawn	0 1 2	19. Violence
0 1 2	21. Worrying	0 1 2	20. Withdrawn
0 1 2	22. Yelling or screaming	0 1 2	21. Worrying
0 1 2	23. Zoning out	0 1 2	22. Yelling or screaming
0 1 2	24. Other	0 1 2	23. Zoning out
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0 1 2	218		

Emotional dysregulation can be distinguished from mood disorders



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PSYCHIATRY ACADEMY

Mood Disorders

- requires a distinct protracted episode
- predominant depressed, manic or mixed mood
- leads to functional difficulties

Emotional Dysregulation

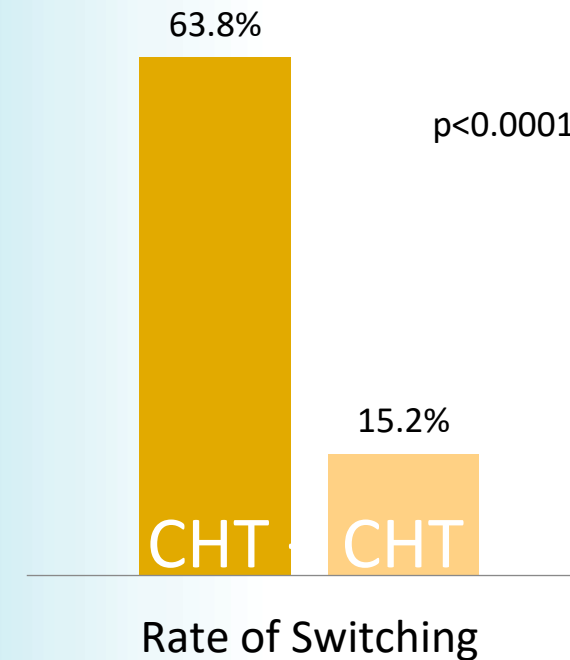
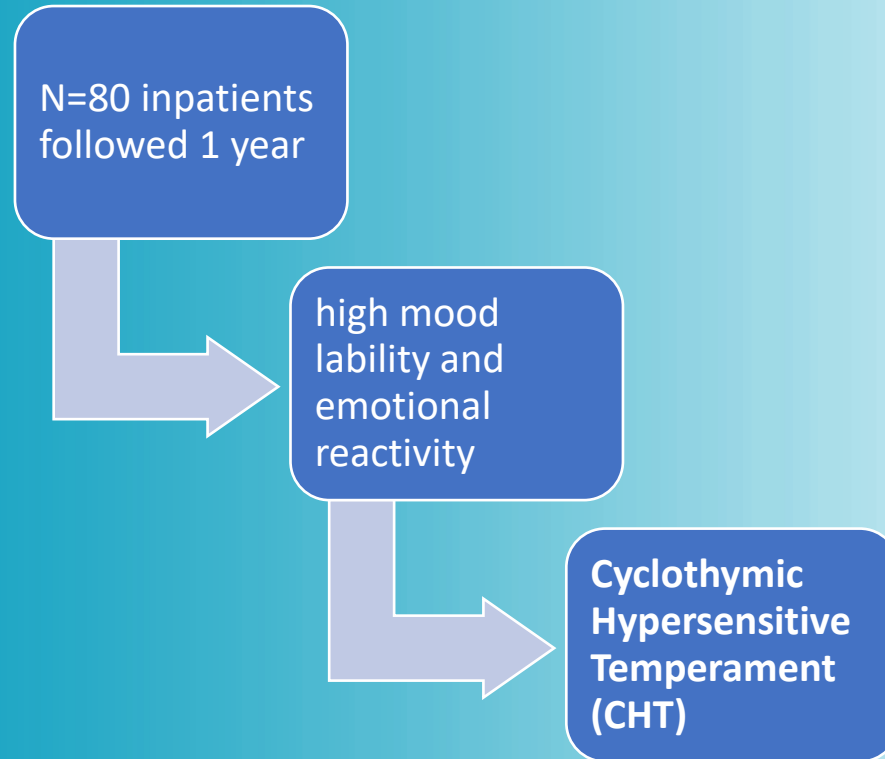
- does not necessarily lead to extreme moods
- subsides relatively rapidly
- is conceptualized as deficits in cortical self regulation of emotions
- an inability to effectively modulate emotional responses to stressors

Emotional dysregulation can be highly impairing



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Children with CHT:

- wider range of aggressive behaviors
- higher rate of suicidality
- **switched (64% vs 15%)**

Kochman 2005

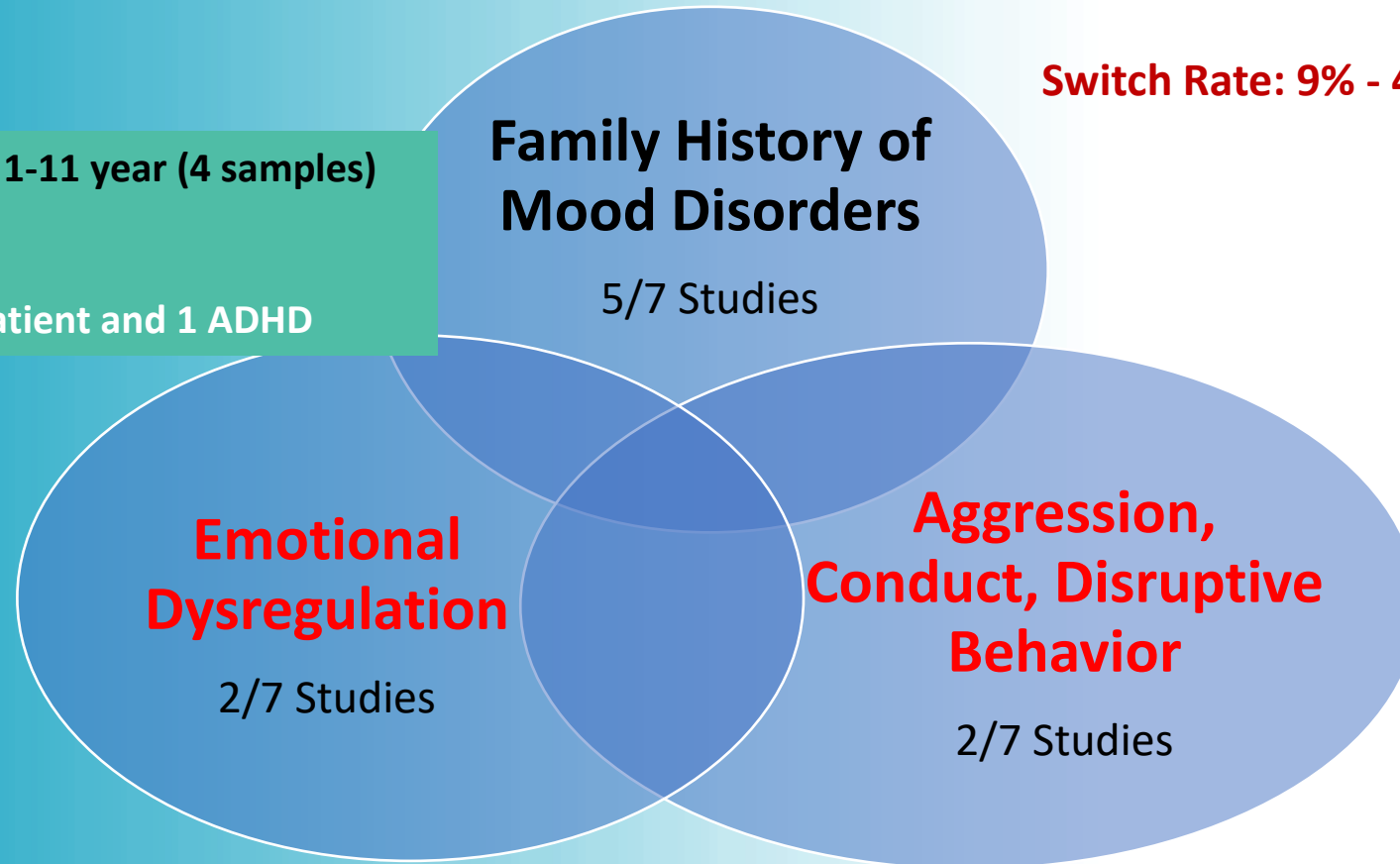
Features of pediatric depression can predict switch to bipolar disorder



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7 follow up studies 1-11 year (4 samples)
N= 985 subjects
ages 6-18 years
2 inpatient, 1 outpatient and 1 ADHD



Switch Rate: 9% - 43%

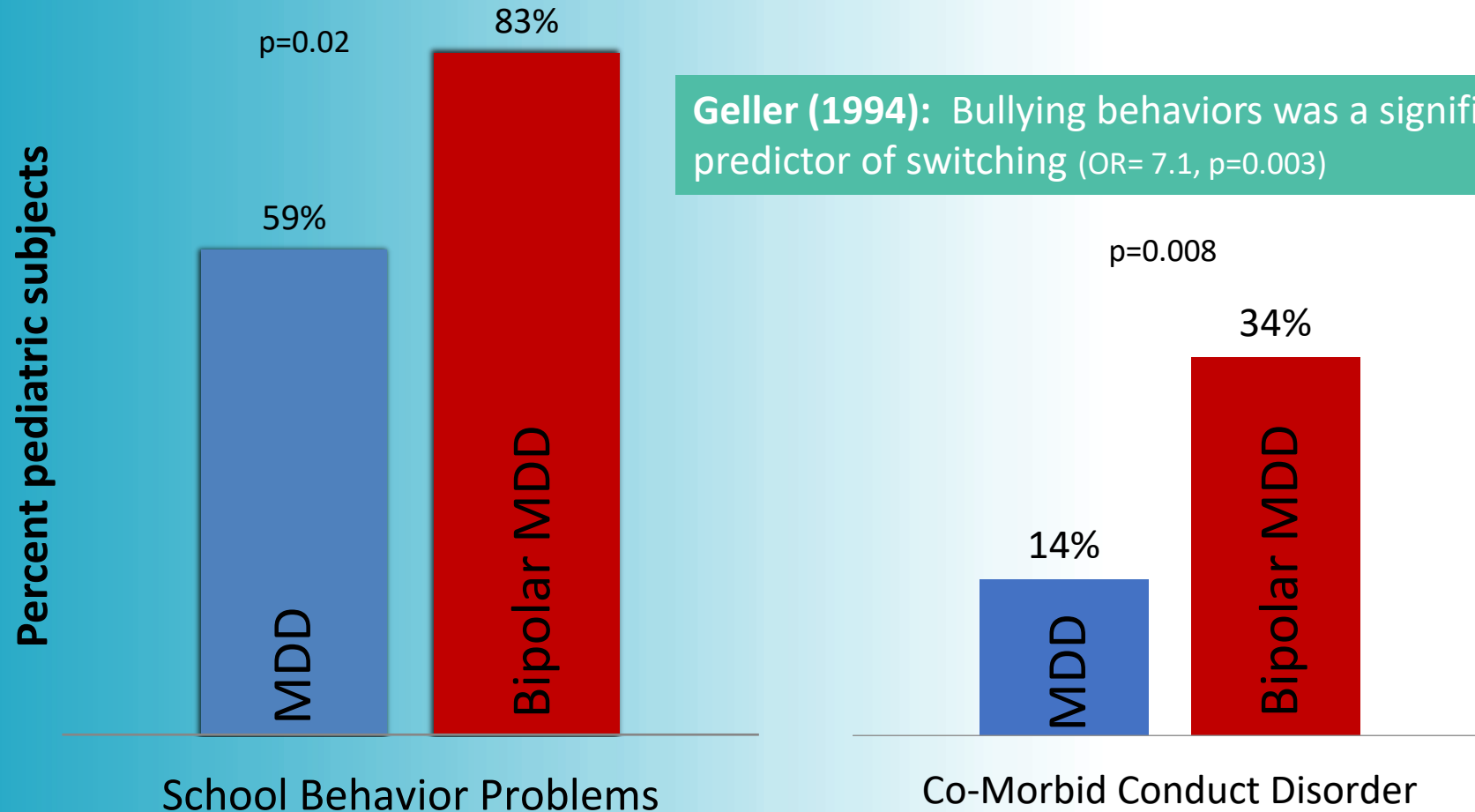
Strober 1982, 1993; Geller 1994, 2001; Kochman 2005; Biederman 2009, 2013

Aggression, conduct and behavioral problems are associated with Bipolar Depression



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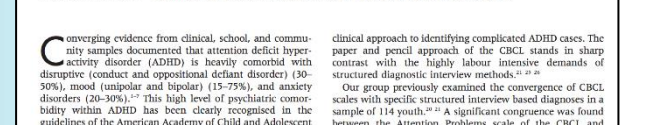
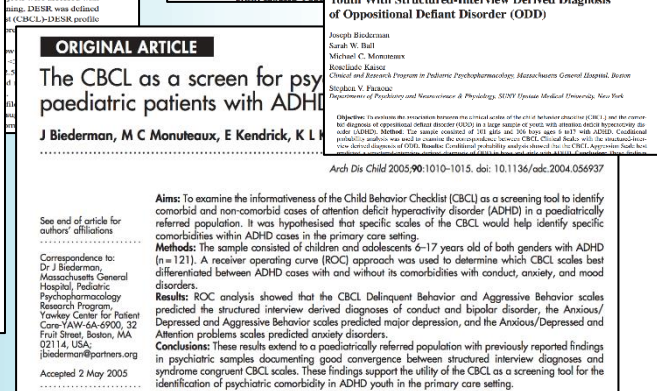
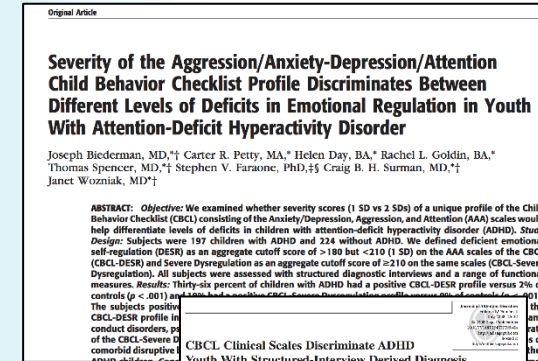
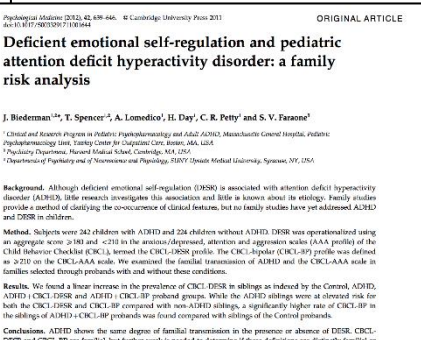
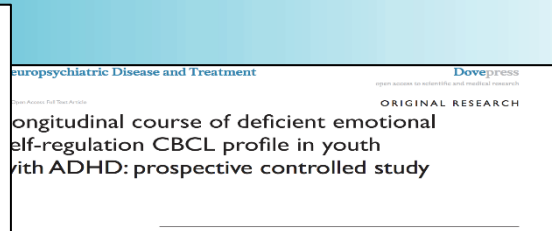
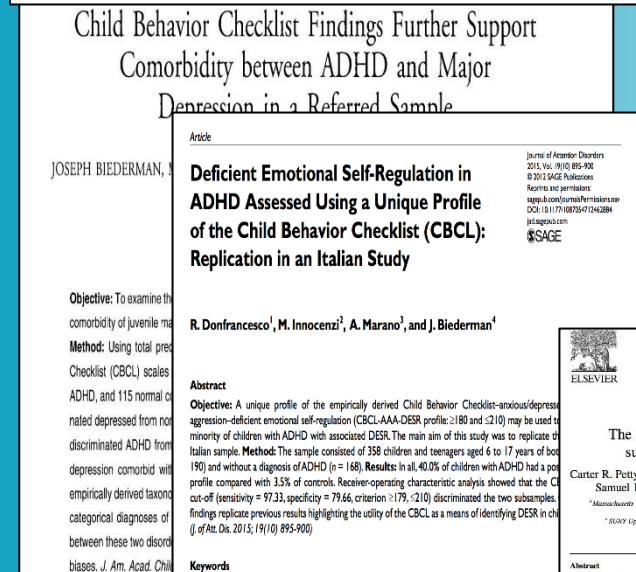
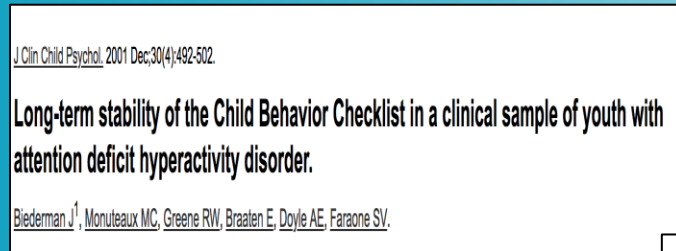


Biederman 2009, 2013

The MGH Research Group has published extensively on the utility of the CBCL in the assessment of ADHD youth



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The CBCL can identify levels of emotional dysregulation in ADHD youth



The MGH Research Group has published extensively on the utility of the CBCL in *identifying Bipolar Disorder in youth*

FOCUS ON CHILDHOOD AND ADOLESCENT MENTAL HEALTH

The Child Behavior Checklist-Pediatric Bipolar Disorder Profile Predicts a Subsequent Diagnosis of Bipolar Disorder and Associated Impairments in ADHD Youth Growing Up: A Longitudinal Analysis

CBCL Clinical Scales Discriminate Prepubertal Children with Structured Interview-Derived Diagnosis of Mania from Those with ADHD

JOSEPH BIEDERMAN, M.D., JANET WOZNIAK, M.D., KATHLEEN KIELY, B.A., ITZHAK ABLOV, B.A., STEPHEN FARAONE, Ph.D., ERIC MICK, B.A., ELIZABETH MUNDY, B.A., and ILANA KRAS, M.D.

ABSTRACT

Objective: To evaluate the discriminative utility of the CBCL Clinical Scales in identifying children with structured interview-derived diagnoses of bipolar disorder. **Method:** We evaluated the convergent validity of CBCL scales with the diagnostic interview in 21 children with mania, 10 children with children with bipolar disorder, and 77 unipolar children with ADHD. **Results:** CBCL Clinical Scales discriminated children with mania from children with bipolar disorder and children with ADHD. **Conclusions:** CBCL Clinical Scales discriminate children with mania from children with bipolar disorder and children with ADHD.

Bipolar disorder is one of the most severe psychiatric conditions in childhood with high morbidity. (Craig Antsh, 1987), much less is known about child-onset bipolar disorder.

Faraone SV, Althoff RR, Hadziak JJ, Monuteaux M, Biederman J. The CBCL predicts DSM bipolar disorder in children: a receiver operating characteristic curve analysis. *Bipolar Disord* 2005; 7: 518-524. © Blackwell Munksgaard, 2005

Background: No clear consensus has been reached yet on how best to characterize children who suffer from pediatric bipolar disorder (PBD). The CBCL-PBD profile on the Child Behavior Checklist

Stephen V Faraone^{a,b}, James Althoff^a, James Michael Monuteaux^{a,b}, Biederman^{a,b,c}

^aMedical Genetics Research Department of Psychiatry, SUNY Upstate Medical U

NEW RESEARCH

Suggestive Linkage of the Child Behavior Checklist Juvenile Bipolar Disorder Phenotype to 1p21, 6p21, and 8q21

Alysa E. Doyle, Ph.D., Joseph Biederman, M.D., Manuel A.R. Ferreira, Ph.D., Patricia Wong, B.A., Jordan W. Smoller, M.D., Sc.D., Stephen V. Faraone, Ph.D.

Objective: Several studies have documented a profile of elevated scores on the Attention Problems, Aggressive Behavior and Anxious/Depressed scales of the Child Behavior Checklist (CBCL) in youth with bipolar disorder. The sum of these scales, referred to as the CBCL Juvenile Bipolar Disorder (JBD) phenotype, has modest diagnostic utility, and high scores are associated with severity of psychopathology and poor outcome. Recently, a genomewide linkage scan of this measure in ADHD sibling pairs revealed a region of suggestive linkage on chromosome 2q21. The current study aimed to further identify quantitative trait loci that influence the CBCL-JBD phenotype by using a dense and thus, arguably, more powerful set of single-nucleotide polymorphism markers in a different ADHD sibling pair sample. **Method:** Subjects were 765 individuals from 154 families with CBCL data and ADHD. Linkage analyses were completed using a multipoint maximum likelihood approach implemented using the statistical program SOLAR. The CBCL-JBD phenotype was estimated at .71. Although not surpassed empirically derived criteria for significant linkage ($p = .000$), LOD = 2.76), $p = .00054$ (LOD = 2.60), and 8q21.13 (LOD = 2.60) surpassed the threshold for suggestive linkage ($p = .002$). These results

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research report

Personal and familial correlates of bipolar (BP)-I disorder in children with a diagnosis of BP-I disorder with a positive child behavior checklist (CBCL)-severe dysregulation profile: A controlled study

Joseph Biederman^{a,b,c}, MaryKate Martelon^a, Stephen V. Faraone^a, K. Yvonne Woodworth^a, Thomas J. Spencer^{a,b}, Janet R. Wozniak^{a,b}

^aClinical and Research Programs in Pediatric Psychopharmacology and Adult ADHD, Massachusetts General Hospital, Boston, MA 02114, United States
^bDepartment of Psychiatry, Harvard Medical School, Boston, MA 02115, United States
^cDepartment of Psychiatry and Neuroscience and Physiology, SUNY Upstate Medical University, Syracuse, NY 13210, United States

J Affect Disord. 2014 August ; 165: 81–86. doi:10.1016/j.jad.2014.04.021.

Further Evidence that Severe Scores in the Aggression/Anxiety-Depression/Attention Subscales of Child Behavior Checklist (Severe Dysregulation Profile) Can Screen for Bipolar Disorder Symptomatology: A Conditional Probability Analysis

Mai Uchida^{a,b}, Stephen V Faraone^c, MaryKate Martelon^a, Tara Kenworthy^a, K Yvonne Woodworth^a, Thomas Spencer^{a,b}, Janet Wozniak^{a,b}, and Joseph Biederman^{a,b,*}

^aClinical and Research Programs in Pediatric Psychopharmacology and ADHD, Massachusetts General Hospital, Boston, MA, USA

^bDepartment of Psychiatry, Harvard Medical School, Boston, MA, USA

^cDepartments of Psychiatry and of Neuroscience and Physiology, SUNY Upstate Medical University, Syracuse, NY, USA

Abstract

Background—Previous work shows that children with high scores (2 SD, combined score ≥ 16) on the Aggression, Anxiety-Depression, and Attention (A-A-A) subscales of the Child Behavior Checklist (CBCL) are more likely than other children to meet criteria for

Article

A Familial Risk Analysis of Emotional Dysregulation: A Controlled Study

Joseph Biederman^{1,2}, James Chan¹, Stephen V. Faraone^{1,4}, K. Yvonne Woodworth¹, Thomas J. Spencer^{1,2}, and Janet R. Wozniak^{1,2}

Abstract

Objective: Children with deficits in emotional regulation operationalized by scores on the Child Behavior Checklist (CBCL) Attention Problems, Aggressive Behavior, and Anxious-Depressed subscales are more likely than others to manifest adverse outcomes. However, the transmission of this profile has not been well studied. The main aim of this study was to investigate the familiarity of this profile. **Method:** Participants were youth probands with bipolar (BP-I) disorder (N = 140), ADHD (N = 83), and controls (N = 117) and their siblings. Based on the CBCL emotional dysregulation profile, we classified children with severe emotional dysregulation (aggregate cut-off score ≥ 20) and emotional dysregulation

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Genome-Wide Association Study of the Child Behavior Checklist Dysregulation Profile

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Objective: A potentially useful tool for understanding the distribution and determinants of emotional dysregulation in children is a Child Behavior Checklist profile, comprising the Attention Problems, Anxious/Depressed, and Aggressive Behavior clinical subscales (CBCL-DP). The CBCL-DP indexes a heritable trait that increases susceptibility for later psychopathology, including severe mood problems and aggressive behavior. We have conducted a genome-wide association study of the CBCL-DP in children with attention-deficit/hyperactivity disorder (ADHD). **Method:** Families were ascertained at Massachusetts General Hospital and University of California, Los Angeles. Genotyping was conducted with the Illumina Human1M or Human1M-Duo BeadChip platforms. Genome-wide association analyses were conducted with the MQFAM multivariate extension of PLINK. **Results:** CBCL data were available for 341 ADHD offspring from 339 ADHD affected trio families from the

Certain CBCL scores- AAA profile- are associated with a diagnosis of pediatric bipolar disorder

Results: The CBCL-PBD score demonstrated an area under the curve (AUC) of 0.97 for probands and 0.82 for siblings for current diagnosis of

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The Child Behavior Checklist (CBCL) is a parent completed rating scale that is easy to administer and score

Please print **CHILD BEHAVIOR CHECKLIST FOR AGES 6-18** For office use only ID #

PARENTS' INITIAL TYPE OF WORK even if not working now, _____

Please print. Be sure to answer all items.

Below is a list of items that describe children and youths. For each item that describes your child, please circle the **2** if the item is **very true or often true** of your child. Circle the **1** if the item is **true** of your child. If the item is **not true** of your child, circle the **0**. Please answer all items as well as you seem to apply to your child.

0 = Not True (as far as you know) 1 = Somewhat or Sometimes True

0 1 2	1. Acts too young for his/her age	0 1 2	32. Feels he/she
0 1 2	2. Drinks alcohol without parents' approval (describe): _____	0 1 2	33. Feels or con her
0 1 2	3. Argues a lot	0 1 2	34. Feels others
0 1 2	4. Fails to finish things he/she starts	0 1 2	35. Feels worth
0 1 2	5. There is very little he/she enjoys	0 1 2	36. Gets hurt a
0 1 2	6. Bowel movements outside toilet	0 1 2	37. Gets in man
0 1 2	7. Bragging, boasting	0 1 2	38. Gets teased a lot
0 1 2	8. Can't concentrate, can't pay attention for long	0 1 2	39. Hangs around with others who get in trouble
0 1 2	9. Can't get his/her mind off certain thoughts; obsessions (describe): _____	0 1 2	40. Hears sound or voices that aren't there (describe): _____
0 1 2	10. Can't sit still, restless, or hyperactive	0 1 2	41. Impulsive or acts without thinking

_____ rather be alone than with others n't
or cheating ow
fingernails
ous, highstrung, or tense
ous movements or twitching
ibe): _____
mares e
ked by other kids
ipated, doesn't move bowels

0 1 2 20. Destroys his/her own things

120 statements about the child's behavior

1. Acts too young for his/her age
2. Drinks alcohol without parents approval
3. Argues a lot
4. Fails to finish things he/she starts
5.

Parents score choosing from Likert scale responses

- 0=not true
- 1=somewhat or sometimes true
- 2=Very true or often true

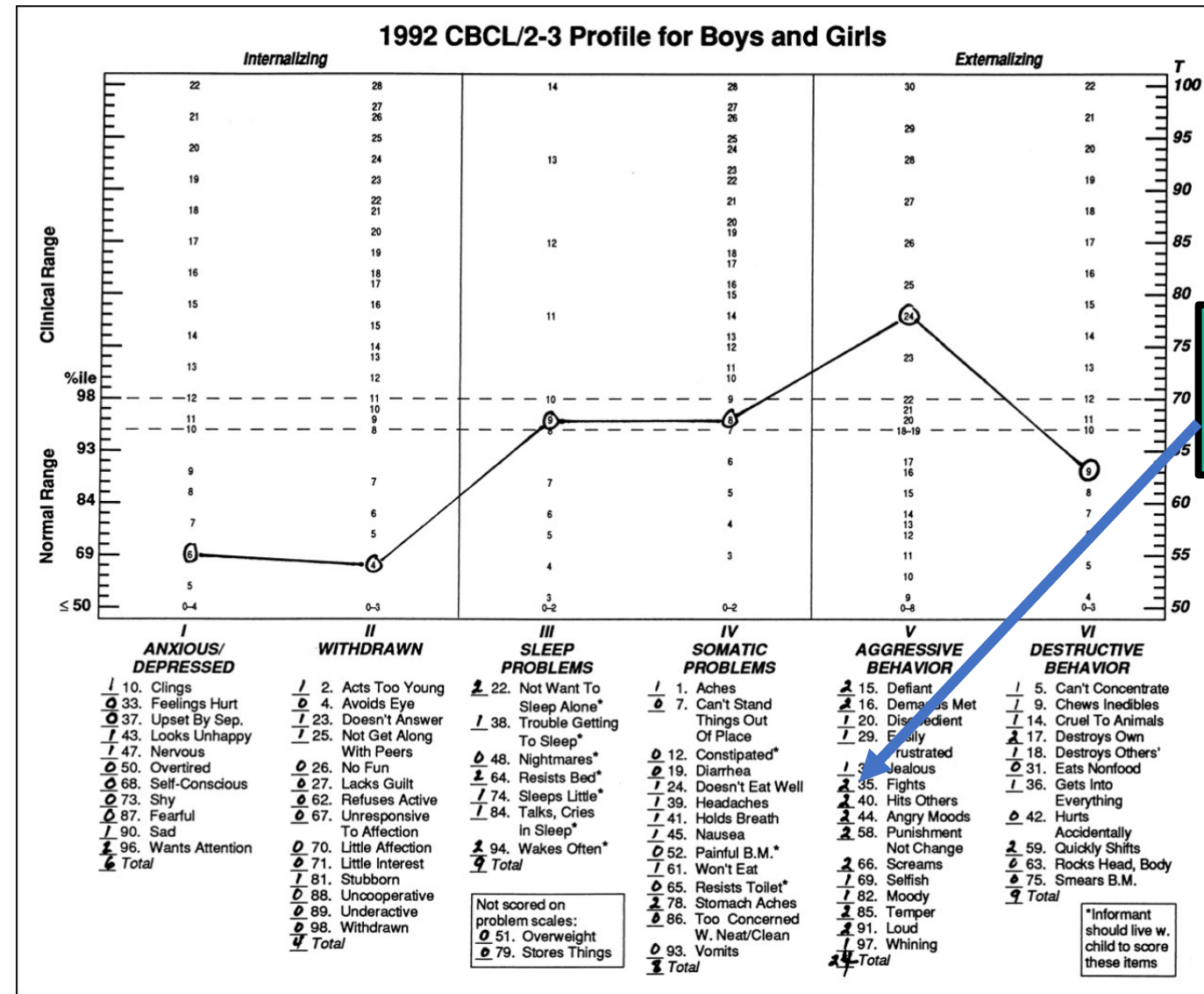
The 120 statements are grouped into 8 subscales or syndrome scales

How to score a CBCL



MASSACHUSETTS
GENERAL HOSPITAL

PSYCHIATRY ACADEMY



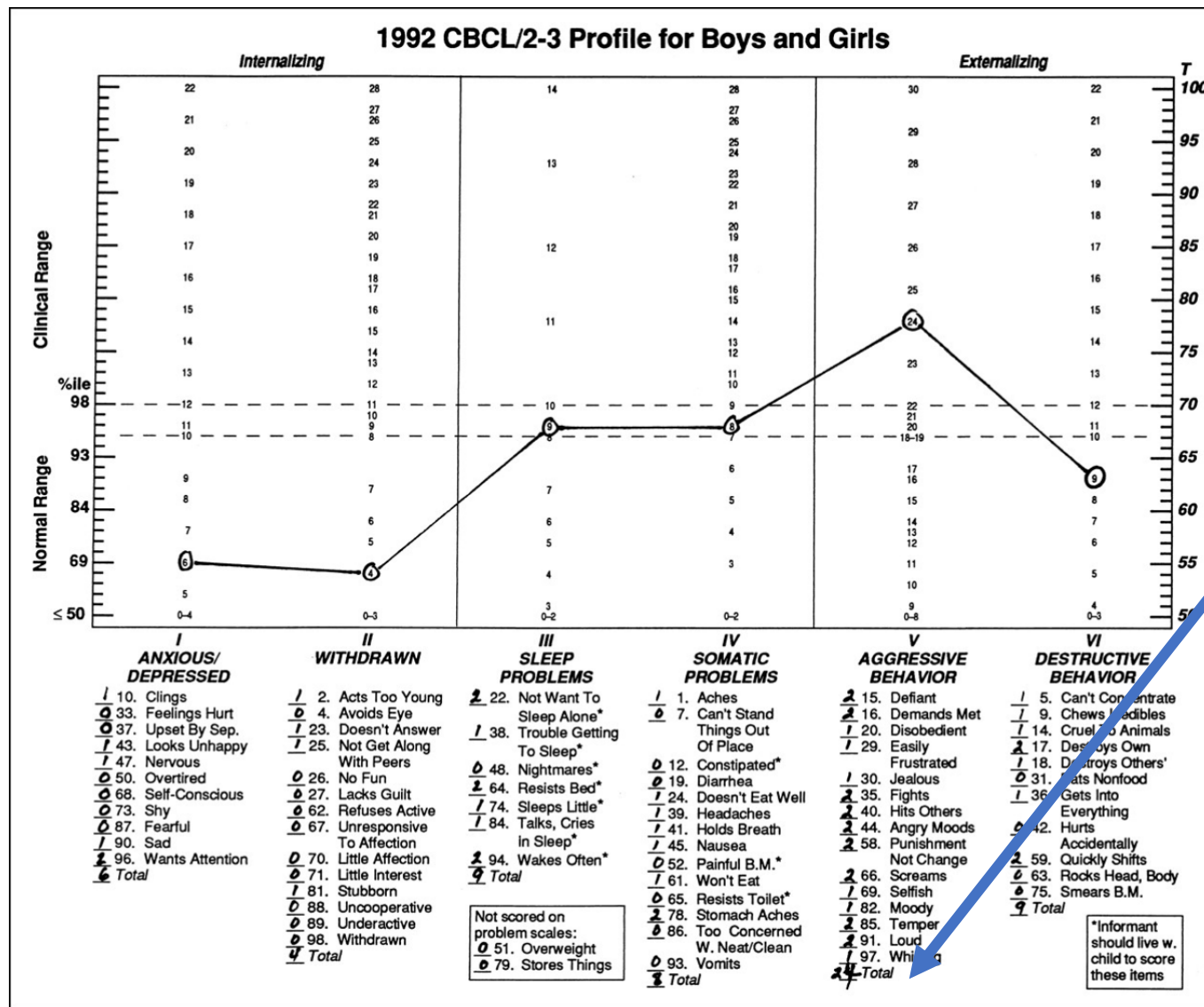
1. Enter all the scores (0, 1, 2) for each of the 120 questions under the different subscale groups

How to score a CBCL



MASSACHUSETTS
GENERAL HOSPITAL

PSYCHIATRY ACADEMY



1. Enter all the scores (0, 1, 2) for each of the 120 questions under the different subscale groups

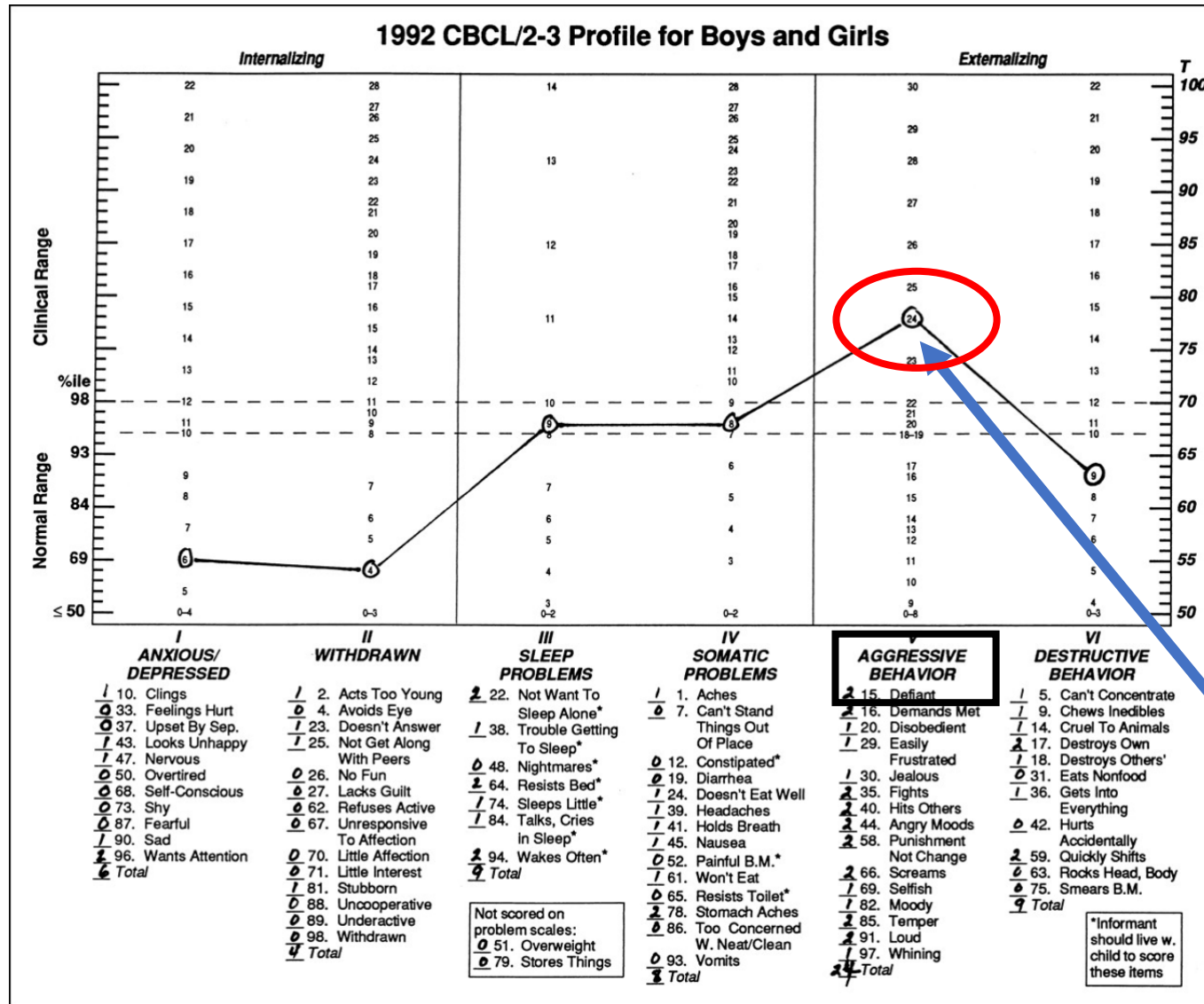
2. Total the score for each subscale

How to score a CBCL



MASSACHUSETTS
GENERAL HOSPITAL

PSYCHIATRY ACADEMY



1. Enter all the scores (0, 1, 2) for each of the 120 questions under the different subscale groups

2. Total the score for each subscale

3. Plot the total score on the scale above

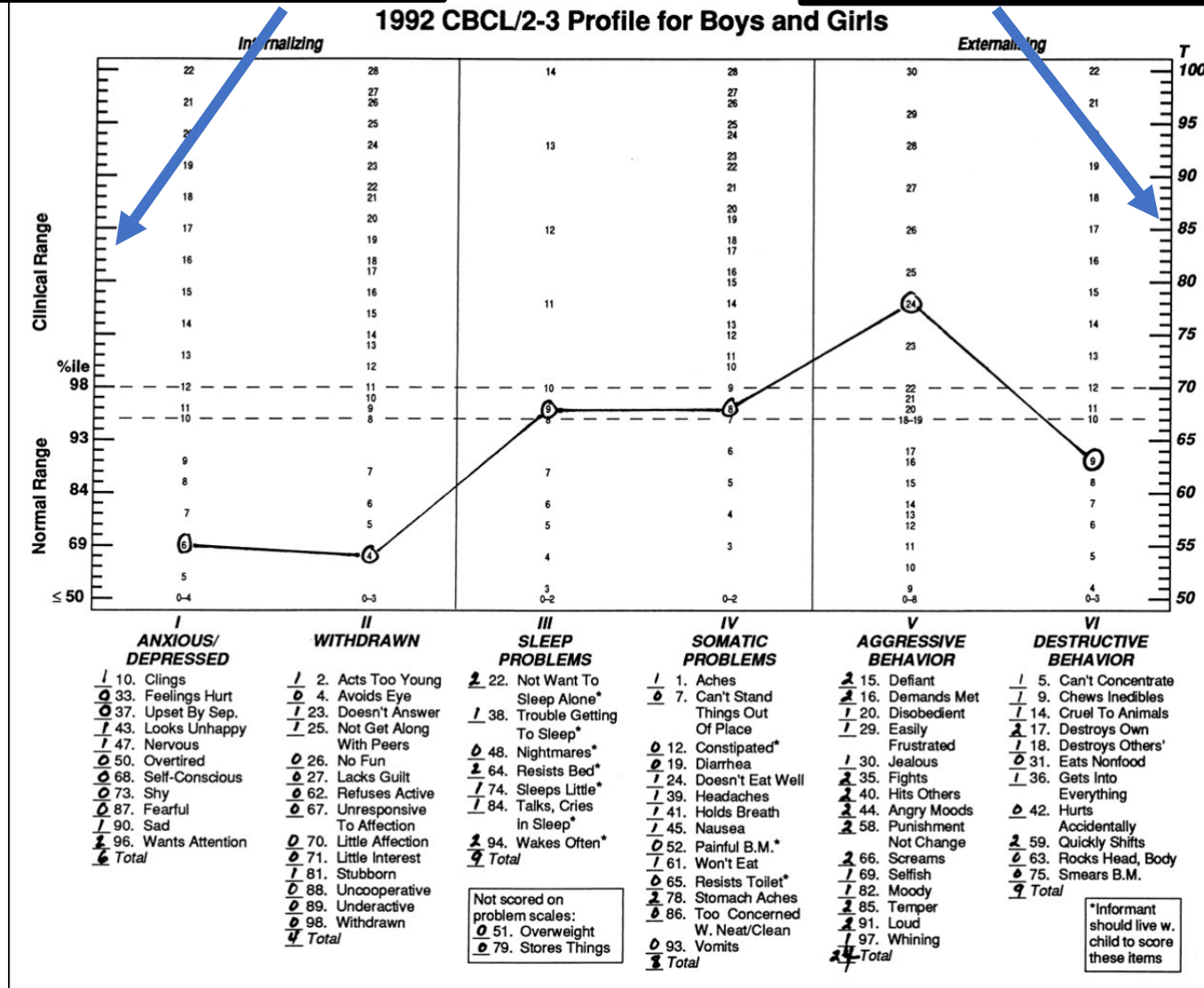
Percentile is on the left

T-Score is on the right



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PSYCHIATRY ACADEMY



1. Enter all the scores (0, 1, 2) for each of the 120 questions under the different subscale groups

2. Total the score for each subscale

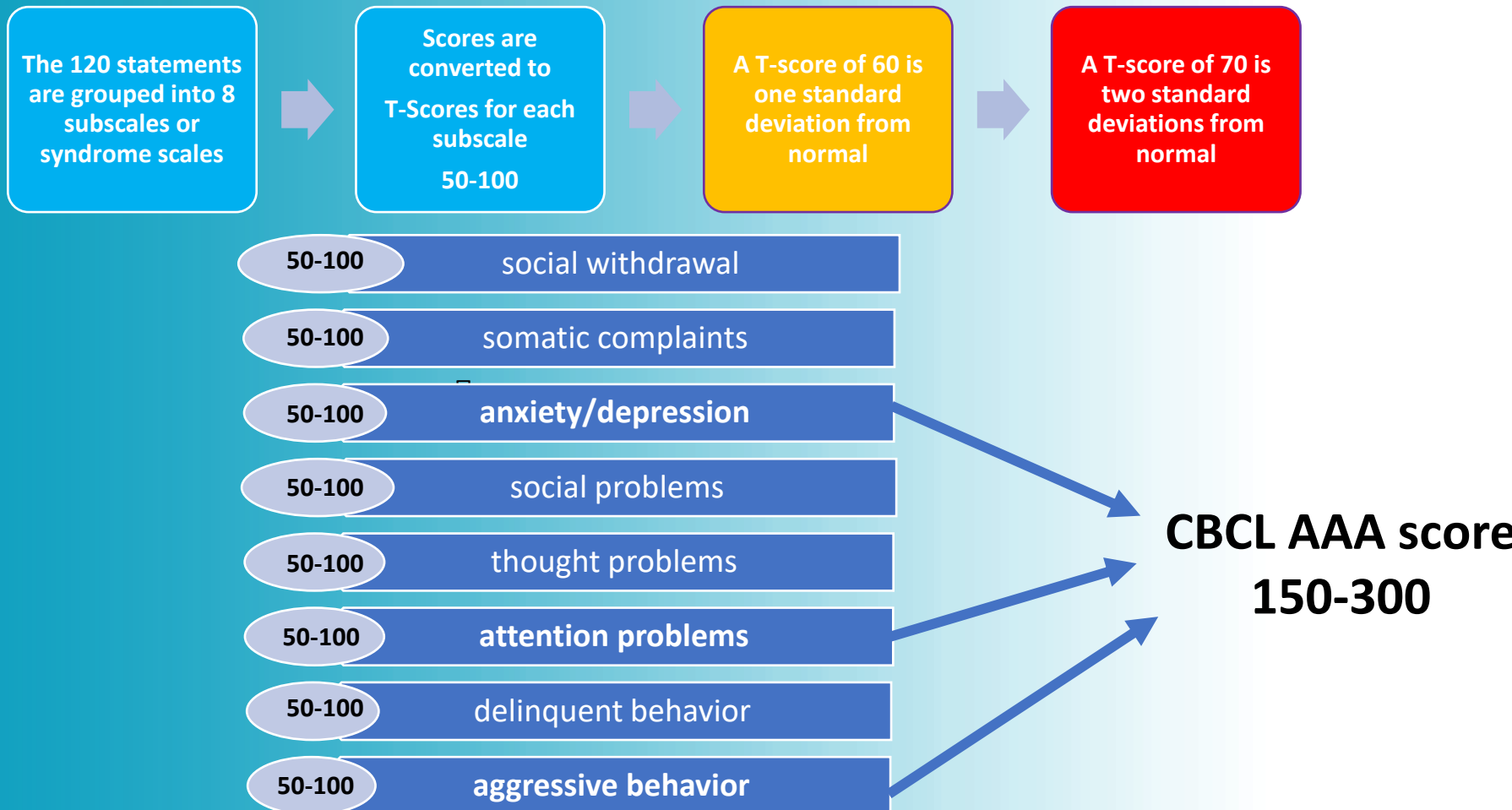
3. Plot the total score on the scale above

The Child Behavior Checklist has 8 clinical subscales



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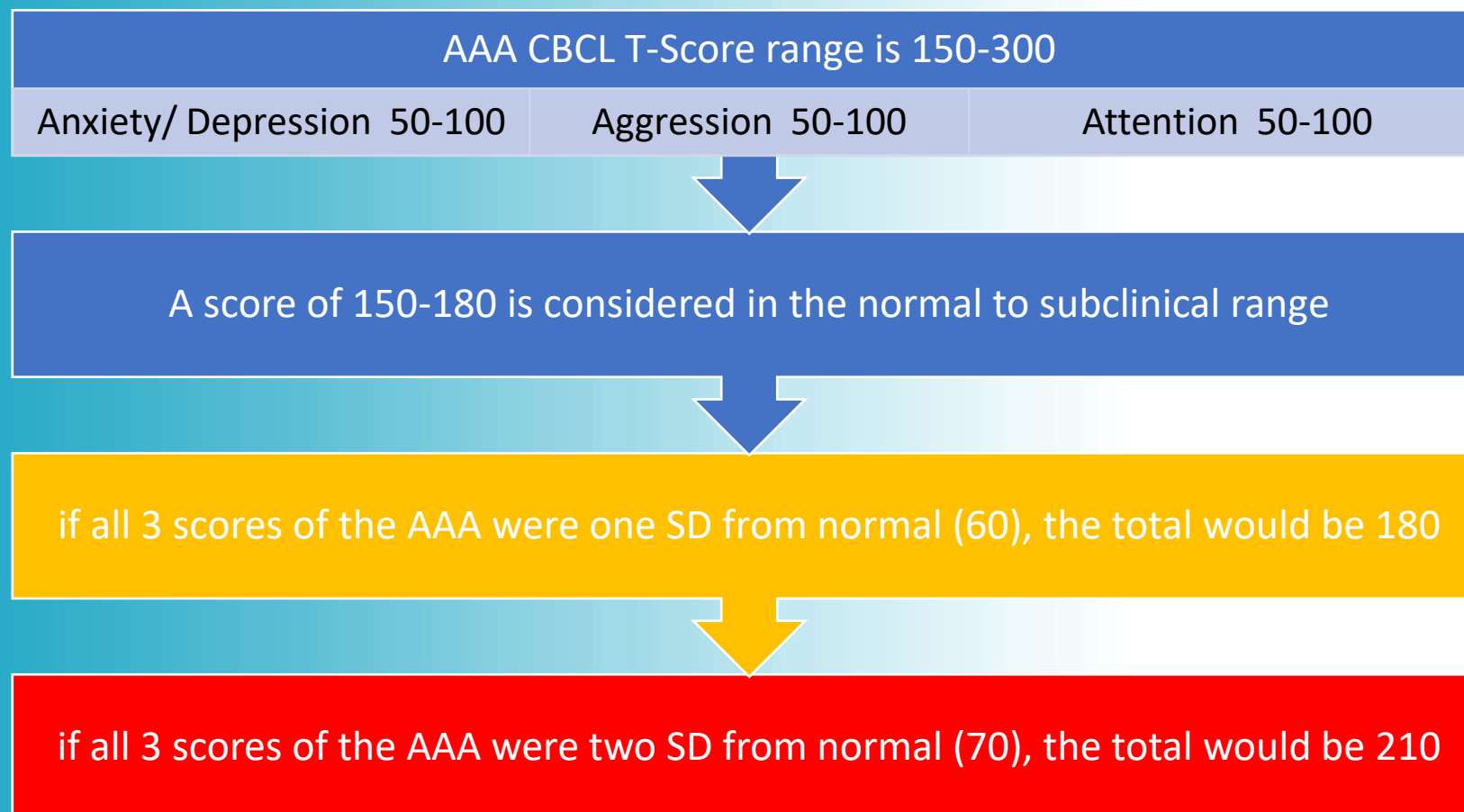


We operationalized profiles of Emotional Dysregulation based on the composite T-Scores of 3 CBCL subscales



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Emotional Dysregulation (ED) can vary in severity, with DESR being a less severely impairing form and SED, a more severely impairing form



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DESR Deficient Emotional Self Regulation

composite T-score AAA between 1 and 2 SD from normal

greater than 180

less than 210



SED Severe Emotional Dysregulation

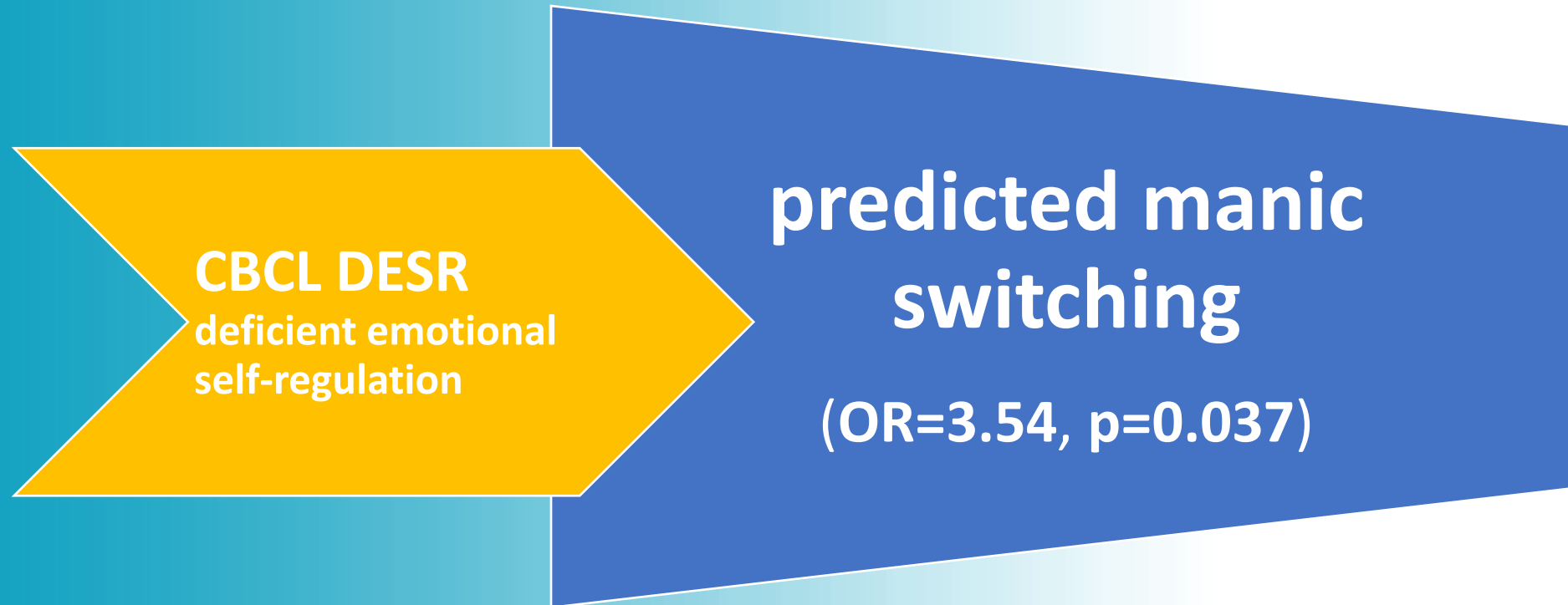
composite T-score AAA greater than 2 SDs from normal

greater than 210

**In ADHD youth followed prospectively
into adulthood a AAA CBCL score > 180
was associated with switching**



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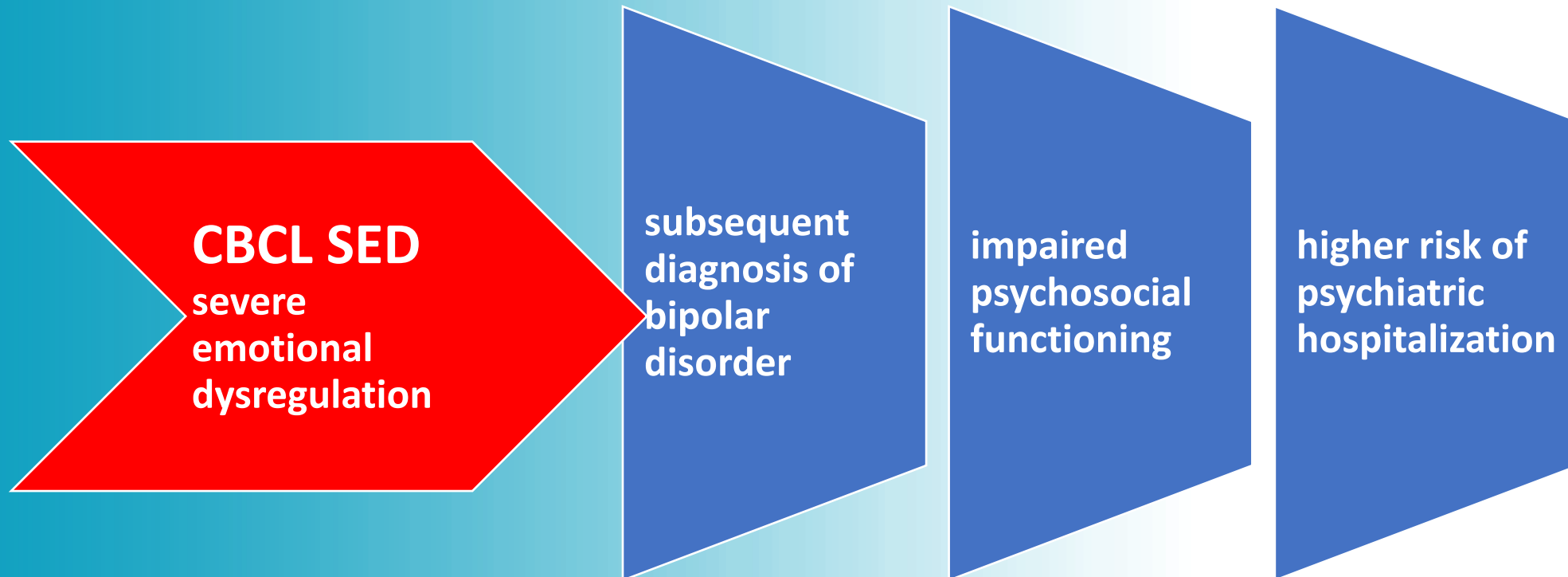
Biederman 2013

**In ADHD youth followed prospectively
into adulthood a AAA CBCL Score > 210
was associated with bipolar disorder**



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PSYCHIATRY ACADEMY

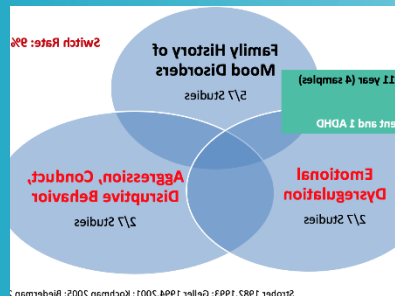


Faroane 2005, Bipolar Disorders
Uchida 2014, Journal of Affective Disorders

Overview:

Emotional dysregulation can be considered as a separate entity from mood disorders

Emotional dysregulation is conceptualized as deficits in cortical self regulation of emotions



Children with Emotional Dysregulation often switch: a predictor of bipolar disorder

CBCL can operationalize levels of emotional dysregulation:
Deficient Emotional Self-Regulation versus Severe Emotional Dysregulation

Emotional Dysregulation

- does not necessarily lead to extreme moods
- subsides relatively rapidly
- is conceptualized as deficits in cortical self regulation of emotions
- an inability to effectively modulate emotional responses

Please print **CHILD BEHAVIOR CHECKLIST FOR AGES 6-18**

Please print. Be sure to answer all items.

Below is a list of items that describe children and youths. For each item that describes your child now or within the past 6 months, please circle the 2 if the item is very true or often true of your child. Circle the 1 if the item is somewhat or sometimes true of your child. If the item is not true of your child, circle the 0. Please answer all items as well as you can, even if some do not seem to apply to your child.

0 = Not True (as far as you know) 1 = Somewhat or Sometimes True 2 = Very True or Often True

0 1 2	1. Acts too young for his/her age	0 1 2	40. Hears and sees voices that aren't there (hallucinations)
0 1 2	2. Drinks alcohol without parents' approval (describe)	0 1 2	41. Impulsive or acts without thinking
0 1 2	3. Argues a lot	0 1 2	42. Would rather be alone than with others
0 1 2	4. Falls to finish things he/she starts	0 1 2	43. Lying or cheating
0 1 2	5. There is very little he/she enjoys	0 1 2	
0 1 2	6. Bowel movements outside toilet	0 1 2	
0 1 2	7. Begging, howling	0 1 2	
0 1 2	8. Can't concentrate, can't pay attention for long	0 1 2	
0 1 2	9. Can't get his/her mind off certain thoughts, ideas, or fears (obsessions) (describe)	0 1 2	
0 1 2	10. Can't eat, sleep, or breathe	0 1 2	
0 1 2	11. Cries to be held or comforted	0 1 2	
0 1 2	12. Experiences of mind	0 1 2	

Parents score choosing from Likert scale responses